Prevalence and Determinants of Atrial Fibrillation-Associated In-Hospital Ischemic Stroke in Patients With Acute Myocardial Infarction Undergoing Percutaneous Coronary Intervention

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Atrial fibrillation (AF) is an established risk factor ischemic stroke (IS) and is commonly encountered in patient hospitalized with acute myocardial infarction (AMI). Uncommonly, IS can occur as a complication resulting from percutaneous coronary intervention (PCI). There is limited real world data regarding AF-associated in-hospital IS (IH-IS) in patients admitted with AMI undergoing PCI. We queried the National Inpatient Sample database from January 2010 to December 2014 to identify patients admitted with AMI who underwent PCI. In this cohort, we determined the prevalence of AF associated IH-IS and compared risk factors for IH-IS between patients with AF and without AF using multivariable logistic regression models. IH-IS was present in 0.46% (n = 5,938) of the patients with AMI undergoing PCI (n = 1,282,829). Prevalence of IH-IS in patients with AF was higher compared with patients without AF (1.05% vs 0.4%; adjusted odds ratio: 1.634, 95% confidence interval: 1.527 to 1.748, p <0.001). Regardless of AF status, prevalence and risk of IH-IS was higher in females and increased with advancing age. There was significant overlap among risk-factors associated with increased risk of IH-IS in AF and non-AF cohorts, except for obesity in AF patients (adjusted odds ratio: 1.268, 95% confidence interval: 1.023 to 1.572, p = 0.03) in contrast to renal disease, malignancy, and peripheral vascular disease in non-AF patients. In conclusion, IH-IS is a rare complication affecting patients undergoing PCI for AMI and is more likely to occur in AF patients, females, and older adults, with heterogeneity among risk factors in patients with and without AF. **(Am J Cardiol 2021;144:1−7)**

Atrial fibrillation (AF) is a well-established risk factor for ischemic stroke (IS) and the most prevalent arrhythmia in the elderly population, particularly in the western world.[1] Older age further augments the risk of IS, and AF often coexists with other cardiovascular diseases such as coronary artery disease and heart failure in the elderly population. With a progressive rise in life expectancy burden of both, AF related strokes and acute myocardial infarction (AMI) is anticipated to increase in the future.[2,3] Moreover, new-onset AF can frequently complicate AMI and previous studies have reported an increased risk of IS among patients with AF during hospitalization for AMI.[4] IS is an uncommon but serious complication that can occur after AMI.[5] Rarely, IS can occur as a complication resulting from percutaneous coronary intervention (PCI) and its incidence has gradually risen over the past decade.[6] Despite the close relations between AF, AMI, and IS, there is sparse real-world data regarding AF-associated IS in patients hospitalized with AMI undergoing PCI. In this study, we aimed to describe the prevalence and determinants of AF-associated in-hospital IS (IH-IS) in patients admitted with AMI undergoing PCI in the United States.

Methods

We performed a 5-year population-based retrospective cross-sectional analysis using nationally representative data from the January 2010 to December 2014 National Inpatient Sample (NIS) database which is the largest publicly available all-payer inpatient care database from the United States. It is developed as a part of the Healthcare Cost and Utilization Project (HCUP) and is sponsored by the Agency for Healthcare Research and Quality available at https://www.hcup-us.ahrq.gov/overview.jsp. The NIS includes data from all nonfederal, short-term, general, and other specialty hospitals in the United States (excluding rehabilitation and long-term acute care hospitals) in the form of deidentified patient information containing demographics, discharge diagnoses, co-morbidities, procedures, outcomes, and hospitalization costs. All the states that participate in HCUP provide data to the NIS, covering >95% of the US population. The database was designed to include data from

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a 20% sample of discharges from all participating hospitals. This design of the NIS reduces the margin of error for estimates and delivers more stable and precise estimations. The study was exempt from an Institutional Review Board approval because HCUP-NIS is a publicly available database containing only deidentified patient information.

We used the International Classification of Diseases-Ninth Edition-Clinical Modification (ICD-9-CM) diagnosis codes 410.01, 410.11, 410.21, 410.31, 410.41, 410.51, 410.61, 410.71, 410.81, 410.91 to identify all patients who were 18 years of age or older and hospitalized with a primary discharge diagnosis of AMI. This approach is consistent with previous studies using the NIS database to accurately identify patients with acute MI.[7–9] We identified the patients who underwent PCI using the ICD-9 procedure codes: 96.06, 96.07, 0.66, and 17.55. In this cohort, we identified patients who developed acute IS (ICD-9-CM code: 433.x, 434.x, 436) during the hospitalization. These codes have been validated in previous studies and accurately identify patients with IS.[10] The study population was divided into 2 groups on the basis of presence of AF (Figure 1). We excluded patients who underwent CABG during the hospitalization. In addition, we excluded patients with incomplete data for gender, length of stay, and in-hospital mortality. Also, in order to reduce the possibility of data duplication, the patients with an indicator for transfer to another acute−care facility were excluded.

Baseline patient characteristics included demographics, clinically relevant characteristics (type of MI, cardiogenic shock, congestive heart failure, use of intra-aortic balloon pump, use of mechanical ventilation, previous stroke, carotid artery stenosis, previous PCI, previous CABG, peripheral vascular disease, renal disease, hypertension, diabetes, hyperlipidemia, smoking, use of long-term anticoagulation), and Charlson co-morbidity index score modified for stroke studies.[11,12] Supplementary Table 1 lists the ICD-9-CM and Clinical Classification Software codes used to identify co-morbidities and procedures.

The main outcomes investigated in this cohort of AMI patients undergoing PCI were threefold: (1) compare the prevalence and in-hospital outcomes of in-hospital IS between AF and non-AF patients; (2) determine the association of AF and IH-IS; and (3) analyze and compare risk factors for IH-IS in patients with AF and without AF.

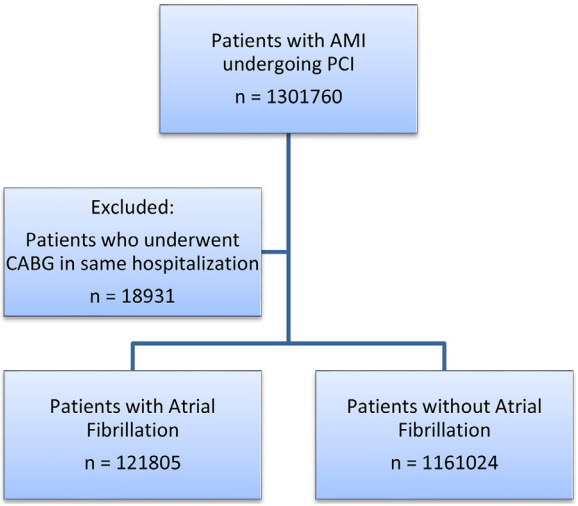

Figure 1. Flow chart of selection of study population.

We compared the baseline patient characteristics between patients with acute MI undergoing PCI according to the presence or absence of AF using the Pearson chi-square test/Fisher's exact test for categorical variables, and Student *t* test/Mann-Whitney *U* test for continuous variables with normal and skewed distribution respectively. National estimates were calculated by applying discharge weights to the discharge data. Prevalence rates were calculated in the overall cohort and further stratified by AF, age, and gender. Confidence intervals (95% CI) were estimated using the Clopper Pearson exact method.

Predictors of in-hospital IS were assessed using univariate logistic regression analysis and those with p values of <0.10 were then further assessed in multivariate logistic regression analysis models. Variables analyzed for association by univariate logistic regression were age, gender, race, and clinically relevant and Charlson co-morbidities. We excluded cerebrovascular disease and hemiplegia /paraplegia, which are items of the original Quan et al version of the Charlson Index because these conditions were reflected in the condition being evaluated.[11,12]

SPSS Statistics 25.0 (IBM Corp., Armonk, New York) and R statistical software (R Core Team 2020) were used to perform the statistical analysis. All p values were 2-sided with a significance threshold of <0.05. Categorical variables were expressed as percentages and continuous variables as mean ± SD for normally distributed data or median with interquartile range for skewed data. Odds ratio and 95% CIs were used to report the results of logistic regression.

Results

A total of 1,282,829 patients aged ≥18 years hospitalized with AMI underwent percutaneous intervention over a 5-year period from 2010 to 2014. AF was present in 121,805 (9.5%) of the patients in the study cohort. Overall, in-hospital IS was present in 5,938 (0.46%) of the patients undergoing PCI for AMI. Prevalence of in-hospital IS in patients with AF was higher compared with patients without AF (1.05% vs 0.4%; p <0.001). Patients with AF were more likely to be older, female and have more underlying co-morbidities (Table 1). Overall, prevalence of stroke was higher in females compared with males (AF: 0.82% vs 1.49%, p <0.001; Non-AF: 0.33% vs 0.57%, p <0.001) and increased with age in both AF and non-AF patients (Figures 2 and 3, Supplementary Table 2). There were no IH-IS in females <45 years of age in the AF group.

Overall, 1,703 (28.7%) patients who developed IS died during the hospitalization before discharge. Compared with non-AF patients who developed IS, patients with AF had higher in-hospital mortality, prolonged hospitalization stay and increased costs (Table 2).

Among the 1,282,829 patients with AMI undergoing PCI included in the multivariate logistic regression analysis, AF was independently associated with increased risk of IS (adjusted odds ratio: 1.634, 95% CI: 1.527 to 1.748, p <0.001). Age, female gender, STEMI, congestive heart failure,

Table 1
Baseline characteristics of patients with acute myocardial infarction undergoing percutaneous coronary intervention stratified by presence or absence of atrial fibrillation

Characteristics	Atrial fibrillation		p Value
	Yes (N = 121,805)	No (N = 1,161,024)	
Age, Mean (SD), (years)	71.3 (11.4%)	61.5 (12.5%)	
Women	41,028 (33.7%)	352,302 (30.3%)	<0.001
Race			<0.001
White	93,012 (76.4%)	805,094 (69.3%)	
Black	6,156 (5.1%)	100,612 (8.7%)	
Hispanic	5,968 (4.9%)	81,553 (7%)	
Asian or Pacific Islander	2,187 (1.8%)	23,388 (2%)	
Native American	535 (0.4%)	6,619 (0.6%)	
Other	2,979 (2.4%)	3,8746 (3.3%)	
Primary insurance			<0.001
Medicare	84,070 (69%)	473,436 (40.8%)	
Medicaid	5,092 (4.2%)	92,256 (7.9%)	
Private insurance	24,861 (20.4%)	432,258 (37.2%)	
Self-pay	4,529 (3.7%)	108,395 (9.3%)	
No charge	337 (0.3%)	107,08 (0.9%)	
Other	2,749 (2.3%)	41,339 (3.6%)	
Weekend admission	31,950 (26.2%)	307,868 (26.5%)	
Median household income, percentile			<0.001
0-25th	31,565 (25.9%)	329,152 (28.4%)	
26th-50th	33,048 (27.1%)	306,879 (26.6%)	
51st-75th	29,561 (24.3%)	277,385 (23.9%)	
76th-100th	25,102 (20.6%)	219,985 (18.9%)	
Type of acute myocardial infarction			
ST-elevation myocardial infarction	52,310 (42.9%)	557,333 (48%)	<0.001
Non-ST-elevation myocardial infarction	69,495 (57.1%)	603,690 (52%)	<0.001
Procedural characteristics			
Stent type			
Bare metal stent	39,598 (32.5%)	282,132 (24.3%)	<0.001
Drug eluting stent	73,440 (60.3%)	829,191 (71.4%)	<0.001
Intra-aortic balloon pump	8,962 (7.4%)	45,091 (3.9%)	<0.001
Mechanical ventilation	10,828 (8.9%)	44,729 (3.9%)	<0.001
Co-morbidities			
Cardiogenic shock	12,812 (10.5%)	51,353 (4.4%)	<0.001
Congestive heart failure	46,692 (38.3%)	190,553 (16.4%)	<0.001
Prior percutaneous coronary intervention	21,541 (17.7%)	175,264 (15.1%)	<0.001
Prior coronary artery bypass graft	8,962 (7.4%)	52,353 (4.5%)	<0.001
Smoker	44,244 (36.3%)	570,070 (49.1%)	<0.001
Hyperlipidemia	80,836 (66.4%)	806,893 (69.5%)	<0.001
Hypertension	67,853 (55.7%)	693,680 (59.7%)	<0.001
Diabetes mellitus			
Uncomplicated	38,522 (31.6%)	332,827 (28.7%)	<0.001
Complicated	6,152 (5.1%)	40,643 (3.5%)	<0.001
Obesity (BMI ≥30)	9,073 (7.4%)	90,974 (7.8%)	
Carotid artery disease	2,657 (2.2%)	14,049 (1.2%)	<0.001
Prior stroke	11,895 (9.8%)	58,460 (5%)	<0.001
Long-term anticoagulation use	17,470 (14.3%)	16,505 (1.4%)	<0.001
Peripheral vascular disease	15,757 (12.9%)	90,802 (7.8%)	<0.001
Renal disease	26,169 (21.5%)	123,854 (10.7%)	<0.001
Chronic pulmonary disease	31,118 (25.5%)	187,276 (16.1%)	<0.001
Dementia	1,180 (1%)	4,409 (0.4%)	<0.001
Rheumatologic disease	2,952 (2.4%)	22,838 (2%)	<0.001
Peptic ulcer disease	1,090 (0.9%)	6,887 (0.6%)	<0.001
Nonmetastatic malignancy, including leukemia and lymphoma	3,478 (2.9%)	19,717 (1.7%)	<0.001
Metastatic solid tumor	736 (0.6%)	4,259 (0.4%)	<0.001
Mild Liver disease	3,885 (3.2%)	22,782 (2%)	<0.001
Moderate - Severe liver disease	224 (0.2%)	1,446 (0.1%)	<0.001
Human immunodeficiency virus/Acquired immunodeficiency syndrome	69 (0.1%)	1,898 (0.2%)	<0.001
Charlson comorbidity index score, Median (Q1, Q3)	2 (1,4)	2 (1,3)	
Charlson comorbidity index = 1-2	62,796 (51.6%)	846,689 (72.9%)	<0.001
Charlson comorbidity index = 3-4	38,032 (31.2%)	225,755 (19.4%)	<0.001
Charlson comorbidity index ≥ 5	20,977 (17.2%)	88,580 (7.6%)	<0.001

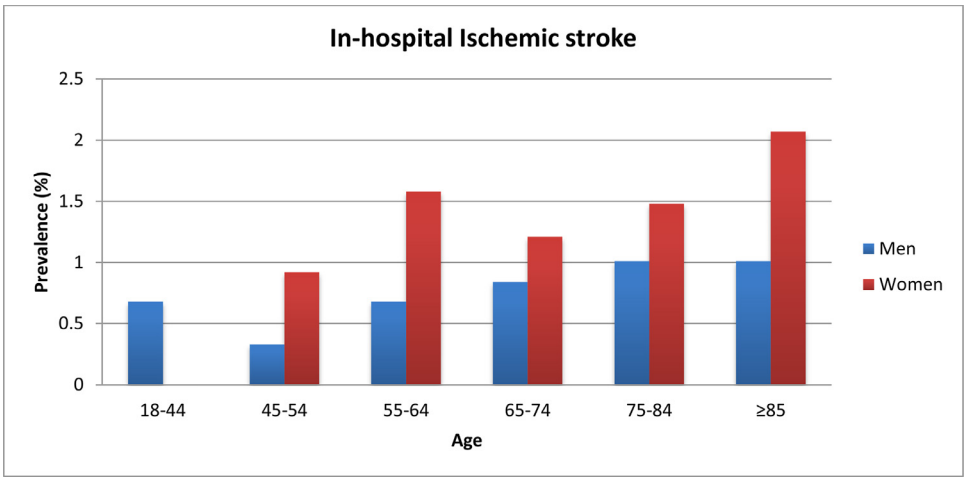

Figure 2. Prevalence of in-hospital ischemic stroke associated with acute MI undergoing PCI in patients with atrial fibrillation stratified by age and gender. MI = myocardial infarction; PCI = percutaneous coronary intervention.

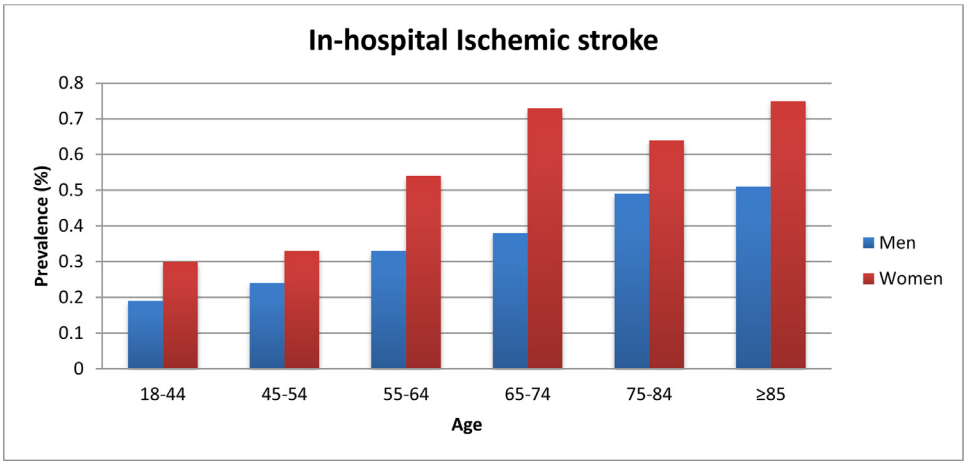

Figure 3. Prevalence of in-hospital ischemic stroke associated with acute MI undergoing PCI in patients without atrial fibrillation stratified by age and gender. MI = myocardial infarction; PCI = percutaneous coronary intervention.

cardiogenic shock, previous stroke, carotid artery stenosis, peripheral vascular disease, use of Intra-aortic balloon pump (IABP), mechanical ventilation, diabetes, metastatic cancer, kidney, and liver disease were also among other significant predictors of stroke (Table 3, Supplementary Table 3).

Regardless of the presence or absence of AF, there was significant overlap among risk-factors associated with increased risk of stroke: age, female gender, STEMI, congestive heart failure, previous stroke, carotid artery stenosis, use of IABP, mechanical ventilation, diabetes, and liver disease were associated with higher risk of stroke in both cohorts, albeit with different strengths of association. In the AF cohort, obesity was associated with increased risk of stroke but not in non-AF cohort. In the non-AF cohort, peripheral vascular disease, renal disease, metastatic cancer, and dementia were associated with increased stroke risk but this was not observed in the AF cohort (Table 4).

Table 2
In-hospital outcomes of ischemic stroke in patients with acute myocardial infarction undergoing percutaneous coronary intervention

Variable		Ischemic stroke with atrial fibrillation	Ischemic stroke without atrial fibrillation	p Value
In-hospital mortality	Overall	489 (38.%2)	1,214 (26.1%)	<0.001
	Male	214 (32.2%)	636 (23.9%)	<0.001
	Female	275 (44.8%)	578 (28.9%)	<0.001
Length of stay, median (IQR)		7 (5,11)	6(4,10)	<0.001
Total charges, median (IQR)		$ 113,098 ($83814, $169953)	$ 106,151($72662, $162036)	<0.001

IQR = inter-quartile range.

Table 3
Predictors of in-hospital ischemic stroke in patients with acute myocardial infarction undergoing percutaneous coronary intervention

Variable	aOR	95% CI	p Value
Age	1.013	1.010-1.015	<0.001
Women	1.465	1.389-1.545	<0.001
White race	0.772	0.731-0.816	<0.001
Non-white race (Reference)	-	-	-
Atrial fibrillation	1.634	1.527-1.748	<0.001
ST-elevation myocardial infarction	1.245	1.178-1.317	<0.001
Non-ST-elevation myocardial infarction (Reference)	-	-	-
Cardiogenic shock	1.103	1.003-1.213	0.044
Congestive heart failure	1.404	1.324-1.489	<0.001
Intra-aortic balloon pump	1.234	1.123-1.357	<0.001
Use of mechanical Ventilation	4.625	4.283-4.994	<0.001
Prior stroke	1.806	1.666-1.959	<0.001
Carotid artery stenosis	4.485	4.028-4.995	<0.001
Prior percutaneous coronary intervention	0.824	0.762-0.892	<0.001
Peripheral vascular disease	1.254	1.324-1.489	<0.001
Long-term anticoagulation use	0.895	0.776-1.032	0.127
Hypertension	0.990	0.930-1.054	0.752
Diabetes mellitus without complication	1.264	1.195-1.338	<0.001
Diabetes mellitus with complication	1.563	1.400-1.745	<0.001
Hyperlipidemia	0.689	0.653-0.728	<0.001
Smoking	0.822	0.777-0.870	<0.001
Obesity	0.722	0.690-0.864	<0.001
Renal disease	1.092	1.005-1.187	<0.001
Nonmetastatic Malignancy, including leukemia and lymphoma	1.175	0.996-1.385	0.055
Metastatic solid tumor	1.856	1.413-2.438	<0.001
Mild liver disease	1.514	1.362-1.683	<0.001
Moderate to severe liver disease	2.413	1.775-3.280	<0.001
Peptic ulcer disease	1.266	0.995-1.612	0.055
Dementia	1.203	0.936-1.547	0.148

Table 4
Comparison of risk factors for in-hospital ischemic stroke in patients with acute myocardial infarction undergoing percutaneous coronary intervention by presence of atrial fibrillation

Variable	With atrial fibrillation			Without atrial fibrillation		
	aOR	95% CI	p Value	aOR	95% CI	p Value
Age	1.018	1.012-1.024	<0.001	1.011	1.008-1.013	<0.001
Women	1.510	1.345-1.696	<0.001	1.440	1.356-1.529	<0.001
White race	0.821	0.724-0.930	0.002	0.760	0.715-0.817	<0.001
Non-white race (Reference)	-	-	-	-	-	-
ST-elevation myocardial infarction	1.435	1.271-1.621	<0.001	1.203	1.130-1.281	<0.001
Non-ST-elevation myocardial infarction (Reference)	-	-	-	-	-	-
Cardiogenic shock	1.175	0.982-1.407	0.078	1.078	0.964-1.205	0.186
Congestive heart failure	1.389	1.235-1.562	<0.001	1.384	1.293-1.481	<0.001
Intra-aortic balloon pump	1.235	1.028-1.484	0.024	1.217	1.090-1.359	<0.001
Use of mechanical ventilation	3.131	2.692-3.642	<0.001	5.260	4.814-5.747	<0.001
Prior stroke	1.298	1.093-1.541	<0.001	2.007	1.831-2.200	<0.001
Carotid artery stenosis	3.551	2.815-4.479	<0.001	4.768	4.222-5.385	<0.001
Prior percutaneous coronary intervention	0.756	0.633-0.904	0.002	0.840	0.769-0.917	<0.001
Peripheral vascular disease	1.131	0.965-1.325	0.128	1.288	1.179-1.406	<0.001
Long-term anticoagulation use	0.923	0.774-1.101	0.376	0.853	0.667-1.092	0.203
Hypertension	1.116	0.968-1.286	0.130	0.949	0.884-1.018	0.143
Diabetes mellitus without complication	0.940	0.827-1.068	0.342	1.365	1.281-1.455	<0.001
Diabetes mellitus with complication	1.479	1.169-1.871	0.001	1.570	1.385-1.778	<0.001
Hyperlipidemia	0.628	0.559-0.705	<0.001	0.713	0.670-0.759	<0.001
Smoking	0.782	0.686-0.892	<0.001	0.835	0.784-0.889	<0.001
Obesity	1.268	1.023-1.572	0.030	0.666	0.582-0.761	<0.001
Renal disease	1.048	0.884-1.243	0.588	1.105	1.004-1.215	0.040
Nonmetastatic malignancy, including leukemia and lymphoma	1.291	0.954-1.749	0.098	1.145	0.941-1.393	0.177
Metastatic solid tumor	1.549	0.892-2.692	0.120	1.931	1.410-2.646	<0.001
Mild liver disease	1.403	1.128-1.745	0.002	1.561	1.383-1.762	<0.001
Moderate to severe liver disease	-	-	-	3.067	2.247-4.189	<0.001
Peptic ulcer disease	1.565	0.992-2.470	0.054	1.158	0.871-1.541	0.312
Dementia	0.547	0.288-1.039	0.065	1.588	1.209-2.086	0.001

aOR = adjusted odds ratio; CI = confidence interval.

Discussion

Our analysis of the United States National Inpatient Sample database of over a million patients admitted with AMI undergoing PCI showed that in-hospital IS is an uncommon complication. Previous studies have shown varying prevalence of IH-IS based in patients with AMI depending on the study design and characteristics of the cohort analyzed. A study by Hachet et al reported IH-IS in 1.25% of AMI patients regardless of the reperfusion strategy utilized.[5] An analysis of the British Cardiovascular Intervention Study (BCIS) registry reported IH-IS in 0.08% of ACS patients who underwent PCI.[13] A study utilizing the NIS database reported post-PCI IH-IS in 0.86% of AMI patients.[6] However, no previous studies have analyzed the prevalence of IH-IS based on presence or absence of AF in patients hospitalized with AMI who underwent PCI and to the best of our knowledge, our study is the first to report this. Our analysis revealed that IH-IS disproportionately affected patients with AF compared with patients without AF. It is not surprising that AF was independently associated with this complication after controlling for multiple confounding factors and this association has been shown by multiple previous studies.[4,6,14–16]In patients with AMI undergoing PCI, regardless of the presence or absence AF, the elderly patient cohort had higher rates of IH-IS. Similarly, females had higher burden of IH-IS. Previous studies have reported increased rates of IH-IS across all age groups in females compared with males undergoing PCI.[17,18] This trend was also observed in all age groups in our study, except, females less than 45 years of age with AF developed no IH-IS, but females without AF in the same age cohort suffered from IH-IS. This finding underscores the differential impact of age and gender on IH-IS risk in AF compared with non-AF patients who underwent PCI for AMI and needs further investigation. More importantly, once IH-IS occurred as a complication, the proportion of in-hospital deaths in patients with AF was 1.5 times higher compared with non-AF patients. Also, length of hospitalization and costs were higher in the AF group. This is likely due to the fact that patients in the AF group were older and had a higher burden of co-morbidities.

In addition to AF, older age and female gender, our study also showed a number of other independent risk factors such as STEMI, cardiogenic shock, congestive heart failure, previous stroke, carotid artery stenosis, peripheral vascular disease, use of IABP, recipient of mechanical ventilation, diabetes mellitus, metastatic cancer, liver, and renal disease were associated with increased risk of IH-IS similar to results from multiple previous studies.[6,13,19]

In AF patients, the risk of stroke is substantially influenced by the presence of other cardiovascular and noncardiovascular factors. In our study, further subgroup analysis for IH-IS risk factors in AF and non-AF cohorts revealed an overlap of multiple risk factors associated with IH-IS between the two groups. However, interestingly the presence of obesity (BMI $\geq$30 kg/m^2) was associated with an increased risk of IH-IS in the AF cohort, but was protective in non-AF patients. Obesity and AF frequently co-exist, however, the relation of obesity and IS in AF patients is debated. The Danish Diet, Cancer and Health study, showed an increased risk stroke in obese patients with AF.[20] Other studies have shown either a neutral or protective effect of obesity, often referred to as the "obesity paradox," on the occurrence of IS.[21] Further research should focus on obesity and its relation with IS among AF patients with AMI undergoing PCI as it represents a highly prevalent modifiable risk factor. In the non-AF cohort, renal disease and metastatic solid cancer were associated with the increased risk of IH-IS, but not in AF patients. Similarly, peripheral vascular disease was independently associated with IH-IS in non-AF patients, but not in AF patients. However, presence of carotid artery disease was associated with IH-IS in both groups. These findings highlight the heterogeneity in risk factors and underlying mechanisms related to the development of IH-IS between AF and non-AF patients and emphasizes the need for research aimed to address this rare but devastating complication.

Our study has several strengths. First, our study utilizes a national representative sample from the NIS database, which reflects a real-world experience that includes high risk patients encountered in daily practice often not included in clinical trials. Second, the large sample size of our study allows the analysis of a number of risk factors for sustaining IH-IS present in patients who underwent PCI for AMI, and therefore, permitting us to compare and contrast the occurrence of IH-IS in 2 different patient cohorts. Third, this study will assist health care providers, in particular interventional cardiologists, in risk stratifying patients with respect to the development of IH-IS in patients who underwent PCI for AMI based on AF status and other relevant clinical characteristics.

There are also several limitations to our study. The diagnosis of stroke was solely based on validated ICD-9 CM codes used primarily for billing purposes, and therefore, coding errors can potentially limit the findings of our study. The NIS database does not capture the timing of the stroke in relation to cardiovascular interventions. We cannot ascertain if IH-IS in patients hospitalized with AMI undergoing PCI occurred as a consequence of the coronary event or PCI itself. Angiographic data on extent and complexity of the culprit lesion or underlying coronary artery disease, access site (transfemoral vs transradial), whether AF was pre-existing or new onset, severity of heart failure (left ventricular ejection fraction) and more importantly the role of medications used in treatment of AMI, during PCI and the hospitalization at large, are not available in the NIS database. Management of anticoagulation and antiplatelet regimens can be very complicated during an AMI admission and our database gives no specifics on those details. Hence, their impact on the occurrence of IH-IS could not be determined. Lastly, the NIS database allows for analysis of only in-hospital outcomes and therefore IS rates after discharge could not be estimated.

In conclusion, IH-IS is a rare complication affecting patients undergoing PCI for AMI and is more likely to occur in females, older adults, and those with AF. There is also heterogeneity among the risk factors associated with this complication in patients with and without AF and further studies are needed to understand the underlying pathophysiologic mechanisms to develop effective preventive strategies.

Authors' Contributions

Shivaraj Patil: Conceptualization, Methodology, Software, Formal Analysis, Writing - Original draft preparation. **Karthik Gonuguntla**: Data curation, Validation, Writing - Original draft preparation. **Chaitanya Rojulpote:** Data curation, Validation, Writing- Original draft preparation. **Manish Kumar**: Visualization, Validation, Writing - Review & Editing, Supervision. **Srinivas Nadadur:** Visualization, Writing - Review & Editing, Supervision. **Robert J. Nardino**: Visualization, Writing - Review & Editing, Supervision. **Christopher Pickett:** Visualization, Writing - Reviewing and Editing, Supervision.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.12.066.

1. Chugh SS, Havmoeller R, Narayanan K, Singh D, Rienstra M, Benjamin EJ, Gillum RF, Kim Y-H, McAnulty JH, Zheng Z-J, Forouzanfar MH, Naghavi M, Mensah GA, Ezzati M, Murray CJL. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. *Circulation* 2014;129:837–847.
2. Chen LY, Chung MK, Allen LA, Ezekowitz M, Furie KL, McCabe P, Noseworthy PA, Perez MV, Turakhia MP, American Heart Association Council on Clinical Cardiology, Council on Cardiovascular and Stroke Nursing, Council on Quality of Care and Outcomes Research, Stroke Council. Atrial Fibrillation Burden. Moving beyond atrial fibrillation as a binary entity: a scientific statement from the American Heart Association. *Circulation* 2018;137:e623–e644.
3. Börschel CS, Schnabel RB. The imminent epidemic of atrial fibrillation and its concomitant diseases - Myocardial infarction and heart failure - A cause for concern. *Int J Cardiol* 2019;287:162–173.
4. Saczynski JS, McManus D, Zhou Z, Spencer F, Yarzebski J, Lessard D, Gore JM, Goldberg RJ. Trends in atrial fibrillation complicating acute myocardial infarction. *Am J Cardiol* 2009;104:169–174.
5. Hachet O, Guenancia C, Stamboul K, Daubail B, Richard C, Béjot Y, Yameogo V, Gudjoncik A, Cottin Y, Giroud M, Lorgis L. Frequency and predictors of stroke after acute myocardial infarction: specific aspects of in-hospital and postdischarge events. *Stroke* 2014;45:3514–3520.
6. Alkhouli M, Alqahtani F, Tarabishy A, Sandhu G, Rihal CS. Incidence, predictors, and outcomes of acute ischemic stroke following percutaneous coronary intervention. *JACC Cardiovasc Interv* 2019;12:1497–1506.
7. Gupta T, Harikrishnan P, Kolte D, Khera S, Subramanian KS, Mujib M, Masud A, Palaniswamy C, Sule S, Jain D, Ahmed A, Lanier GM, Cooper HA, Frishman WH, Bhatt DL, Fonarow GC, Panza JA, Aronow WS. Trends in management and outcomes of ST-elevation myocardial infarction in patients with end-stage renal disease in the United States. *Am J Cardiol* 2015;115:1033–1041.
8. Khera S, Kolte D, Gupta T, Mujib M, Aronow WS, Agarwal P, Palaniswamy C, Jain D, Ahmed A, Fonarow GC, Frishman WH, Panza JA. Management and outcomes of ST-elevation myocardial infarction in nursing home versus community-dwelling older patients: a propensity matched study. *J Am Med Dir Assoc* 2014;15:593–599.
9. Khera S, Kolte D, Aronow WS, Palaniswamy C, Subramanian KS, Hashim T, Mujib M, Jain D, Paudel R, Ahmed A, Frishman WH, Bhatt DL, Panza JA, Fonarow GC. Non-ST-elevation myocardial infarction in the United States: contemporary trends in incidence, utilization of the early invasive strategy, and in-hospital outcomes. *J Am Heart Assoc* 2014;3.
10. Andrade SE, Harrold LR, Tjia J, Cutrona SL, Saczynski JS, Dodd KS, Goldberg RJ, Gurwitz JH. A systematic review of validated methods for identifying cerebrovascular accident or transient ischemic attack using administrative data. *Pharmacoepidemiol Drug Saf*;21 Suppl 1:100−28.
11. Goldstein LB, Samsa GP, Matchar DB, Horner RD. Charlson Index comorbidity adjustment for ischemic stroke outcome studies. *Stroke* 2004;35:1941–1945.
12. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, Januel J-M, Sundararajan V. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *Am J Epidemiol* 2011;173:676–682.
13. Myint PK, Kwok CS, Roffe C, Kontopantelis E, Zaman A, Berry C, Ludman PF, de Belder MA, Mamas MA, British Cardiovascular Intervention Society and the National Institute for Cardiovascular Outcomes Research. Determinants and outcomes of stroke following percutaneous coronary intervention by indication. *Stroke* 2016;47:1500–1507.
14. Kinjo K, Sato H, Sato H, Ohnishi Y, Hishida E, Nakatani D, Mizuno H, Fukunami M, Koretsune Y, Takeda H, Hori M, Osaka Acute Coronary Insufficiency Study (OACIS) Group. Prognostic significance of atrial fibrillation/atrial flutter in patients with acute myocardial infarction treated with percutaneous coronary intervention. *Am J Cardiol* 2003;92:1150–1154.
15. Mehta RH, Dabbous OH, Granger CB, Kuznetsova P, Kline-Rogers EM, Anderson FA, Fox KAA, Gore JM, Goldberg RJ, Eagle KA, GRACE Investigators. Comparison of outcomes of patients with acute coronary syndromes with and without atrial fibrillation. *Am J Cardiol* 2003;92:1031–1036.
16. Pokorney SD, Rao M, Nilsson KR, Piccini JP. Atrial fibrillation complicating acute coronary syndromes. *J Atr Fibrillation* 2012;5:611.
17. Alkhouli M, Alqahtani F, Elsisy MF, Kawsara A, Alasnag M. Incidence and outcomes of acute ischemic stroke following percutaneous coronary interventions in men versus women. *Am J Cardiol* 2020;125:336–340.
18. Lichtman JH, Wang Y, Jones SB, Leifheit-Limson EC, Shaw LJ, Vaccarino V, Rumsfeld JS, Krumholz HM, Curtis JP. Age and sex differences in inhospital complication rates and mortality after percutaneous coronary intervention procedures: evidence from the NCDR(®). *Am Heart J* 2014;167:376–383.
19. Kwok CS, Kontopantelis E, Myint PK, Zaman A, Berry C, Keavney B, Nolan J, Ludman PF, de Belder MA, Buchan I, Mamas MA, British Cardiovascular Intervention Society, National Institute for Cardiovascular Outcomes Research. Stroke following percutaneous coronary intervention: type-specific incidence, outcomes and determinants seen by the British Cardiovascular Intervention Society 2007-12. *Eur Heart J* 2015;36:1618–1628.
20. Overvad TF, Rasmussen LH, Skjøth F, Overvad K, Lip GYH, Larsen TB. Body mass index and adverse events in patients with incident atrial fibrillation. *Am J Med* 2013;126:640.. e9-17.
21. Proietti M, Guiducci E, Cheli P, Lip GYH. Is there an obesity paradox for outcomes in atrial fibrillation? A systematic review and meta-analysis of non-vitamin K antagonist oral anticoagulant trials. *Stroke* 2017;48:857–866.