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ORIGINAL RESEARCH

Temporal Trends, Predictors, and Outcomes of Acute Ischemic Stroke in Acute Myocardial Infarction in the United States

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BACKGROUND: There are limited contemporary data prevalence and outcomes of acute ischemic stroke (AIS) complicating acute myocardial infarction (AMI).

METHODS AND RESULTS: Adult (>18 years) AMI admissions using the National Inpatient Sample database (2000–2017) were evaluated for in-hospital AIS. Outcomes of interest included in-hospital mortality, hospitalization costs, length of stay, discharge disposition, and use of tracheostomy and percutaneous endoscopic gastrostomy. The discharge destination was used to classify survivors into good and poor outcomes. Of a total 11 622 528 AMI admissions, 183 896 (1.6%) had concomitant AIS. As compared with 2000, in 2017, AIS rates increased slightly among ST-segment–elevation AMI (adjusted odds ratio, 1.10 [95% CI, 1.04–1.15]) and decreased in non–ST-segment–elevation AMI (adjusted odds ratio, 0.47 [95% CI, 0.46–0.49]) admissions (*P*<0.001). Compared with those without, the AIS cohort was on average older, female, of non-White race, with greater comorbidities, and higher rates of arrhythmias. The AMI-AIS admissions received less frequent coronary angiography (46.9% versus 63.8%) and percutaneous coronary intervention (22.7% versus 41.8%) (*P*<0.001). The AIS cohort had higher in-hospital mortality (16.4% versus 6.0%; adjusted odds ratio, 1.75 [95% CI, 1.72–1.78]; *P*<0.001), longer hospital length of stay, higher hospitalization costs, greater use of tracheostomy and percutaneous endoscopic gastrostomy, and less frequent discharges to home (all *P*<0.001). Among AMI-AIS survivors (N=153 318), 57.3% had a poor functional outcome at discharge with relatively stable temporal trends.

CONCLUSIONS: AIS is associated with significantly higher in-hospital mortality and poor functional outcomes in AMI admissions.

Key Words: acute ischemic stroke ■ acute myocardial infarction ■ cerebrovascular circulation ■ complications ■ outcomes research

Cardiovascular disease remains the leading cause of morbidity and mortality in the developed world.[1] Acute ischemic stroke (AIS) is the third leading cause of death globally and the leading cause for disability.[1] Cardiovascular and cerebrovascular diseases share common pathophysiological mechanisms and risk factors of diabetes mellitus, hypertension, smoking, and age.[1,2] Patients with a history of AIS have been shown to have a higher risk of future acute myocardial infarction (AMI) in several studies.[3,4] Procedures such as percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), which are commonly performed for the management of AMI, are associated with an increased risk of stroke.[5]

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CLINICAL PERSPECTIVE

What Is New?

- Acute ischemic stroke (AIS) was seen in 1.6% in >11 million acute myocardial infarction (AMI) admissions in the United States during an 18-year period.
- AIS rates increased in ST-segment–elevation AMI admissions, whereas there was a decrease in rates in non–ST-segment–elevation AMI admissions.
- The AIS cohort had higher in-hospital mortality, longer hospital length of stay, higher hospitalization costs, and less frequent discharges to home.

What Are the Clinical Implications?

- Although AIS occurs in a small proportion of AMI admissions, it is associated with significantly higher mortality and greater resource utilization.
- Further research on mitigating the incidence and severity of AIS in AMI is needed.

Nonstandard Abbreviations and Acronyms

AIS	acute ischemic stroke
HCUP	Healthcare Cost and Utilization Project
NIS	National/Nationwide Inpatient Sample

Studies have shown high long-term risk of AIS and associated mortality in patients with AMI.[6,7] However, the data describing the prevalence and in-hospital outcomes related to AIS in patients with AMI are limited.[2] Prior studies in this field are limited by their small sample sizes and differential reporting of clinical outcomes.[8–10] More aggressive treatment of vascular risk factors including hypertension, diabetes mellitus, aggressive lipid-lowering therapies, and anti-thrombotic treatment and reperfusion with PCI has been shown to improve post-AMI strokes incidence. Early detection and anticoagulation management of MI complications such as atrial fibrillation and left ventricular thrombus complicating heart failure have also shown favorable effects on stroke incidence.[11] To fill this gap, we sought to conduct a retrospective study utilizing a nationally representative database in the United States spanning between 2000 and 2017. We hypothesized that during this 18-year period, there would be a decrease in the prevalence and outcomes of in-hospital acute ischemic stroke (AIS) complicating acute myocardial infarction (AMI). Furthermore, we sought to elucidate the predictors and clinical outcomes of in-hospital AIS in AMI admissions.

METHODS

Study Population, Variables, and Outcomes

The National (Nationwide) Inpatient Sample (NIS) is the largest all-payer database of hospital inpatient stays in the United States. NIS contains discharge data from a 20% stratified sample of community hospitals and is a part of the Healthcare Quality and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality.[11] Information regarding each discharge includes patient demographics, primary payer, hospital characteristics, principal diagnosis, up to 24 secondary diagnoses, and procedural diagnoses. The HCUP-NIS does not capture individual patients but captures all information for a given admission. Institutional Review Board approval was not sought because of the publicly available nature of this de-identified database. These data are available to other authors via the HCUP-NIS database with the Agency for Healthcare Research and Quality.

Using the HCUP-NIS data from January 1, 2000 through December 31, 2017, a cohort of adult admissions (>18 years) with AMI in the primary diagnosis field (*International Classification of Diseases, Ninth Revision, Clinical Modification* [*ICD-9-CM*] 410.x and *ICD-10-CM* I21.x-22.x) were identified.[12–14] A concomitant diagnosis of AIS was identified using *ICD-9-CM* 433.x1, 434.x1, 436, and *ICD-10-CM* I63.x. These codes have been previously validated in multiple studies and show a high sensitivity and specificity for the identification of AIS.[2,15–17] The Deyo's modification of the Charlson Comorbidity Index was used to identify the burden of comorbid diseases.[18] Demographic characteristics, hospital characteristics, acute organ failure, mechanical circulatory support, cardiac procedures, fibrinolytic use, tracheostomy, percutaneous endoscopic gastrostomy, and other noncardiac organ support use were identified for all admissions using previously used methodologies from our group and others (Table S1).[13,19–24] Predictors of AIS were identified using baseline and in-hospital characteristics.

In AIS, discharge destination was previously reported to be strongly correlated with measure of disability in these patients.[25] Prior studies classified clinical functional outcomes based on discharge destination as good (none to minimal disability) defined as discharge to self-care with or without home health services, and poor (moderate to severe disability) defined as discharge to extended care facility including short-term hospital/rehabilitation facility, intermediate care, or long-term care facilities.[26]

The primary outcome of interest was the in-hospital mortality of AMI admissions with and without concomitant AIS. The secondary outcomes included hospitalization costs, hospital length of stay, discharge disposition, tracheostomy use, percutaneous endoscopic gastrostomy placement, and vascular complications in those with and without AIS. In those with AIS, temporal trends of poor outcomes stratified by type of AMI were evaluated. Multiple subgroup analyses were performed to confirm the results of the primary analysis stratifying the population by age (≤/>75 years), sex (male/female), race (White/non-White), type of AMI (ST-segment elevation [STEMI] versus non-ST-segment elevation [NSTEMI]), receipt of PCI and CABG.

Statistical Analysis

In accordance with HCUP-NIS recommendations, survey procedures using discharge weights provided with the HCUP-NIS database were used to generate national estimates.[27] Samples from 2000 to 2011 were reweighted using the trend weights provided by the HCUP-NIS to adjust for the 2012 HCUP-NIS redesign.[27] Chi-square and *t* tests were used to compare categorical and continuous variables, respectively. Multivariable logistic regression was used to analyze trends over time (referent year 2000) accounting for clustering for hospital characteristics. Univariable analysis for trends and outcomes was performed and was represented as odds ratio (OR) with 95% CI. Multivariable logistic regression analysis incorporating age, sex, race, primary payer status, socio-economic stratum, hospital characteristics, comorbidities, acute organ failure, AMI type, cardiac procedures, and noncardiac procedures was performed for assessing temporal trends of prevalence and in-hospital mortality. Predictors of AIS were assessed using a multivariable logistic regression analysis with relevant baseline and in-hospital variables. Temporal trends in the proportion of poor outcomes in AMI-AIS admissions and in-hospital mortality were plotted and adjusted ORs were calculated using multivariable logistic regression analysis incorporating age, sex, race, primary payer status, hospital characteristics, comorbidities, acute organ failure, AMI type, cardiac procedures, and noncardiac procedures. For the multivariable modeling, regression analysis with purposeful selection of statistically (liberal threshold of $P<0.20$ in univariate analysis) and clinically relevant variables was conducted. Two-tailed $P<0.05$ was considered statistically significant.

The inherent restrictions of the HCUP-NIS database related to research design, data interpretation, and data analysis were reviewed and addressed.[27] Pertinent considerations include not assessing individual hospital-level volumes (because of changes to sampling design detailed above), treating each entry as an "admission" as opposed to individual patients, restricting the study details to inpatient factors since the HCUP-NIS does not include outpatient data, and limiting administrative codes to those previously validated and used for similar studies. All statistical analyses were performed using SPSS v25.0 (IBM Corp, Armonk, NY).

RESULTS

Prevalence and Temporal Trends of AIS

In the period from January 1, 2000 to December 31, 2017, there were 11 622 528 admissions for AMI, of which 183 896 (1.6%) had concomitant AIS. In the AIS cohort, STEMI and NSTEMI were noted in 33.4% and 66.6%, respectively. During this 18-year period, STEMI admissions had a relatively stable trend of concomitant AIS, with a slight increase in the middle period over the 18 years, while NSTEMI admissions had a higher prevalence of AIS and showed an increase during 2005–2010 followed by a subsequent decline (Figure 1A). Adjusted temporal trends showed a slight increase in STEMI admissions (adjusted OR, 1.00 in 2000 versus adjusted OR, 1.10 in 2017), whereas there was a decrease in AIS complicating NSTEMI admissions (adjusted OR, 1.00 in 2000 versus adjusted OR, 0.47 in 2017) in recent years (Figure 1B).

Differences in Admissions With and Without AIS

Compared with AMI admissions without AIS, those who had AIS were on average older, female, of non-White race, Medicare insured, had greater comorbidities, and higher rates of atrial and ventricular arrhythmias (Table 1). AMI admissions complicated by AIS had higher rates of concomitant acute organ failure, cardiac arrest, cardiogenic shock, and use of mechanical circulatory support and invasive mechanical ventilation use (Table 2). Compared with admissions without AIS, the AMI-AIS admissions received less frequent coronary angiography (46.9% versus 63.8%) and PCI (22.7% versus 41.8%) but had higher rates of CABG (13.1% versus 9.2%) (all $P<0.001$). In a multivariable logistic regression analysis, female sex, non-White race, lower socio-economic status, higher comorbidity, STEMI presentation, atrial fibrillation/flutter, coronary thrombectomy, CABG, use of mechanical circulatory support, and invasive mechanical ventilation were identified as individual predictors of AIS after AMI (Table S2).

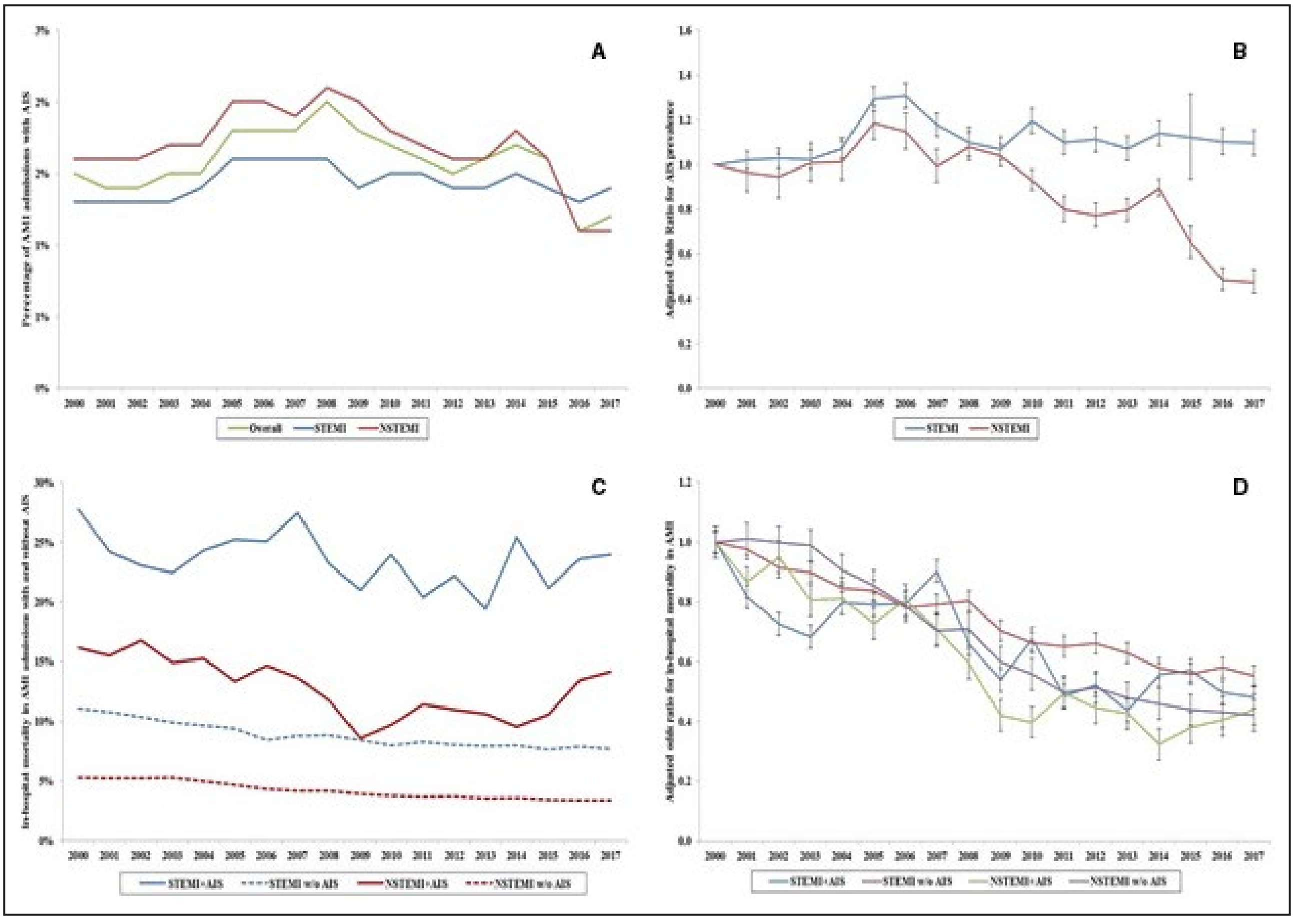

Figure 1. Trends in the prevalence and in-hospital mortality with and without AIS in AMI admissions.
A, Unadjusted temporal trends of the proportion of AMI admissions with AIS overall and stratified by type of AMI (*P*<0.001 for trend over time); (**B**) Adjusted odds ratio* for AIS in STEMI and NSTEMI admissions by year (with 2000 as the referent) (*P*<0.001 for trend over time); (**C**) Unadjusted in-hospital mortality in AMI admissions stratified by type of AMI and the presence of AIS (*P*<0.001 for trend over time); (**D**) Adjusted odds ratio* for in-hospital mortality by year (with 2000 as the referent) in AMI admissions stratified by type of AMI and the presence of AIS (*P*<0.001 for trend over time). *Adjusted for age, sex, race, comorbidity, primary payer, hospital region, hospital location and teaching status, hospital bed size, acute organ failure, cardiogenic shock, atrial fibrillation/flutter, cardiac arrest, coronary angiography, percutaneous coronary intervention, coronary artery bypass grafting, pulmonary artery catheterization, use of fibrinolytic, coronary thrombectomy, vascular complications, mechanical circulatory support, invasive mechanical ventilation, and acute hemodialysis. AIS indicates acute ischemic stroke; AMI, acute myocardial infarction; NSTEMI, non–ST-segment–elevation myocardial infarction; and STEMI, ST-segment–elevation myocardial infarction.

Impact of AIS on Clinical Outcomes of AMI Admissions

AMI admissions complicated by AIS had significantly higher unadjusted (16.4% versus 6.0%; OR, 3.06 [95% CI, 3.02–3.10]; *P*<0.001) and adjusted all-cause in-hospital mortality (OR, 1.75 [95% CI, 1.72–1.78]; *P*<0.001) (Table S3). The 18-year unadjusted and adjusted temporal trends of in-hospital mortality in AMI admissions with and without AIS are presented in Figure 1C and 1D. There was a steady decrease in the adjusted in-hospital mortality in AMI admissions with and without AIS during the study period, but the in-hospital mortality for those with concomitant AIS remained significantly higher than those without. The AMI admissions with AIS had longer hospital length of stay and higher hospitalization costs, and less frequent discharges to home (Table 3). These admissions also had higher rates of tracheostomy, percutaneous endoscopic gastrostomy, and vascular complications compared with admissions without AIS (Table 3). To confirm the primary results, multiple subgroup analyses stratifying by AMI type were performed. These analyses demonstrated consistently higher adjusted in-hospital mortality in admissions with AIS compared with those without (Figure 2).

Functional Outcomes Associated With AIS

In order to estimate the functional burden of AIS in AMI admissions, we performed a subgroup analysis of AMI admissions with AIS that survived in-hospital stay (n=153 318). Among these admissions, 57.3% had a

Table 1. Baseline Characteristics AMI Admissions With and Without In-Hospital AIS

Characteristic	AIS (N=183 896)	No AIS (N=11 438 632)	*P* Value
Age, y	73.5±12.6	67.5±14.2	<0.001
Female sex	52.4	39.5	<0.001
Race			<0.001
White	61.4	63.6	
Black	10.5	7.9	
Others*	28.0	28.5	
Primary payer			<0.001
Medicare	73.5	57.5	
Medicaid	5.6	6.2	
Others†	21.0	36.4	
Quartile of median household income for zip code			<0.001
0–25th	26.2	24.4	
26th–50th	26.5	27.2	
51st–75th	24.0	24.5	
75th–100th	23.3	23.9	
Charlson Comorbidity Index			<0.001
0–3	9.0	38.0	
4–6	44.0	44.5	
≥7	47.0	17.5	
Hospital teaching status and location			<0.001
Rural	10.4	11.2	
Urban nonteaching	40.0	39.5	
Urban teaching	49.6	49.3	
Hospital bed-size			<0.001
Small	10.3	11.2	
Medium	24.9	25.5	
Large	64.8	63.3	
Hospital region			0.40
Northeast	19.6	19.6	
Midwest	22.7	22.9	
South	40.2	40.1	
West	17.4	17.4	
AMI type			<0.001
ST-segment–elevation	33.4	37.2	
Non–ST-segment–elevation	66.6	62.8	
Atrial fibrillation/flutter	29.6	17.2	<0.001
Supraventricular tachycardia	1.1	0.9	<0.001
Ventricular tachycardia/fibrillation	9.5	8.0	<0.001

Represented as percentage or mean±SD. AIS indicates acute ischemic stroke; and AMI, acute myocardial infarction.

*Hispanic, Asian or Pacific Islander, Native American, Others.

†Private, self-pay, no charge, others.

poor functional outcome. The cohort with poorer outcomes was on average older, female, of White race, had higher comorbidity, STEMI presentation, concomitant atrial arrhythmias, cardiogenic shock, and cardiac arrest rates (Table S4). The 18-year unadjusted temporal trends of poor functional outcomes showed a slight increase in both STEMI (61.2% in 2000 versus 65.3% in 2017) and NSTEMI (54.3% versus 60.6%) admissions with STEMI admissions consistently having a higher proportion of poor functional outcome compared with NSTEMI (Figure 3A). In adjusted analyses, the proportion of AMI survivors who had a poor functional outcome increased slightly during the study period in both STEMI and NSTEMI admissions, though the trend was relatively stable in the last one third of the study period (Figure 3B).

DISCUSSION

In the largest dedicated study evaluating the prevalence and outcomes of AIS in AMI admissions, we noted that AIS complicated 1.6% of all AMI admissions. Concomitant AIS was associated with higher in-hospital mortality, greater in-hospital resource utilization, and less frequent discharge to home. Through this 18-year study period, AIS rates were relatively stable in STEMI admissions, but have decreased in NSTEMI admissions. Older age, female sex, non-White race, higher number of comorbidities, and greater acuity of illness were predictive of in-hospital AIS. Coronary angiography and PCI were used less frequently in this population, while CABG was used more. Nearly 58% of those with AIS have poor function outcomes at discharge with a relatively stable trend during the study period.

AIS is a rare, but important complication of AMI. The association of AIS and AMI was recognized many decades ago in a Chinese study that showed high risk of AMI within 72 hours of admission for AIS.[28] The acute management of this metachronous presentation—infarction of 1 vascular territory after the other—lacks clear guidelines.[29] AMI is traditionally considered a cause of AIS only if both occur within 1 month of each other.[30,31] Various mechanisms may explain the risk of AIS in patients with AMI. New-onset atrial fibrillation, left ventricular thrombus after anterior MI, and severe generalized atherosclerosis can account for the heightened risk of AIS in AMI. AMI and AIS have very similar pathophysiology, both stemming from shared risk factors.[31] Atherosclerotic burden from older age, obesity, smoking, lack of exercise, high cholesterol levels, diabetes mellitus, and hypertension is associated with both AIS as well as AMI. Simultaneous inflammatory response of vulnerable atherosclerotic plaques in both coronary and carotid vascular territories is eventually the final pathogenic mechanism in causing AMI and AIS.[32] Sympathetic activity in AMI may also promote inflammation and prothrombotic state predisposing to AIS.[33]

Table 2. In-Hospital Course and Management of AMI Admissions With and Without AIS

Characteristic	AIS (N=183 896)	No AIS (N=11 438 632)	*P* Value
Cardiac arrest	7.9	5.0	<0.001
Cardiogenic shock	8.5	4.7	<0.001
Multiorgan failure	22.2	9.2	<0.001
Coronary angiography	46.9	63.9	<0.001
Percutaneous coronary intervention	22.7	41.8	<0.001
Coronary artery bypass grafting	13.1	9.2	<0.001
Coronary thrombectomy	0.5	0.6	<0.001
Mechanical circulatory support	7.2	4.7	<0.001
Fibrinolytic therapy	2.2	2.2	0.34
Pulmonary artery catheterization	1.8	1.1	<0.001
Invasive mechanical ventilation	17.1	5.8	<0.001
Acute hemodialysis	1.5	0.6	<0.001

Represented as percentage. AIS indicates acute ischemic stroke; and AMI, acute myocardial infarction.

The rate of AIS after AMI in our analysis falls within the range of previous reports. In a meta-analysis published in 2006, the risk of AIS after AMI was 1.45%.[34] In the GRACE (Global Registry of Acute Coronary Events) registry, the incidence of AIS was 0.9% in patients with AMI (1.3%, 0.9%, and 0.5% in patients with STEMI, NSTEMI, and unstable angina, respectively).[35] Despite the risk of periprocedural AIS with PCI for AMI, studies have reported lesser incidence of AIS in patients who undergo early revascularization strategy with this benefit unrelated to improvement in cardiac function.[36] In another study of >2 million Medicare beneficiaries, the risk of 1-year AIS in patients discharged after hospitalization for AMI was shown to have decreased from 1999 to 2010 but 30-day and 1-year mortality remained high.[37] Our study shows that the difference in risk of AIS was different in patients with STEMI and NSTEMI. One possible explanation for this could be that incidence of STEMI has reduced over the past few years and with better antithrombotic and lipid-lowering agents the incidence of stroke in these patients has also been reducing, thus keeping the ratio of strokes to STEMI diagnosis stable.[38] In contrast, with better diagnostic tests such as high-sensitivity troponin and computed tomography coronary artery scan, detection rates of NSTEMI have increased, thus reducing the overall rate of AIS in proportionately higher NSTEMI cases.[39] Previous reports have also confirmed high burden of arrhythmias in patients with AIS, which may further worsen morbidity and mortality in patients with AMI.[22,40]

Another rare cause of AIS in patients with AMI can be post-PCI or CABG. The overall incidence is 0.07% to 0.4% in patients undergoing PCI.[5] This might be related to dislodgement of calcified debris, thrombus material from atherosclerotic plaques in the aortic arch, and proximal carotid and vertebral arteries.[41] Also, catheter and guidewire tips can be an additional nidus for thrombus formation and can potentially cause AIS. Although theoretically there is a higher

Table 3. Clinical Outcomes of AMI Admissions With and Without AIS

Characteristic	AIS (N=183 896)	No AIS (N=11 438 632)	*P* Value
In-hospital mortality	16.4	6.0	<0.001
Length of stay, d	10.2±10.8	5.0±5.7	<0.001
Tracheostomy	4.2	3.9	<0.001
Percutaneous endoscopic gastrostomy	7.0	5.0	<0.001
Vascular complications	1.2	0.8	<0.001
Hospitalization costs (×1000 US dollars)	101.0±154.8	59.2±75.9	<0.001
Discharge disposition			<0.001
Home	28.4	63.0	
Transfer	7.6	12.7	
Skilled nursing facility	49.3	12.9	
Home with home health care	14.2	10.5	
Against medical advice	0.5	0.9	

Represented as percentage or mean±SD. AIS indicates acute ischemic stroke; and AMI, acute myocardial infarction.

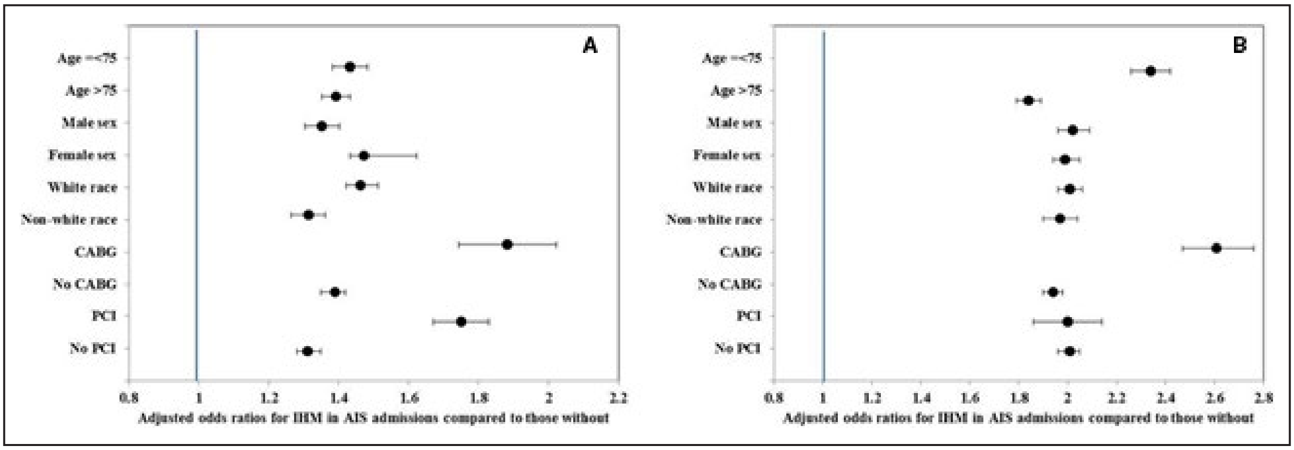

Figure 2. Subgroup analyses for in-hospital mortality in AMI admissions with AIS compared with those without AIS stratified by type of AMI.
Multivariable adjusted odds ratios (95% CIs) for in-hospital mortality in STEMI (**A**) and NSTEMI (**B**) admissions with AIS compared with admissions without AIS; all *P*<0.001. Each subgroup was adjusted for age, sex, race, comorbidity, primary payer, hospital region, hospital location and teaching status, hospital bed size, acute organ failure, cardiogenic shock, atrial fibrillation/flutter, cardiac arrest, coronary angiography, percutaneous coronary intervention, coronary artery bypass grafting, pulmonary artery catheterization, use of fibrinolytic, coronary thrombectomy, vascular complications, mechanical circulatory support, invasive mechanical ventilation, and acute hemodialysis. AIS indicates acute ischemic stroke; AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; IHM, in-hospital mortality; NSTEMI, non–ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention; and STEMI, ST-segment–elevation myocardial infarction.

risk of AIS with a transradial approach because of proximity of the subclavian artery to the common carotid and vertebral artery, recent studies have shown otherwise. This could be from the likelihood of lower catheter contact with the aortic arch in a radial approach. The highest likelihood of stroke postcatheterization is in the first 24 hours.[42] In patients with recent CABG surgery, incident of stroke or transient ischemic attack is close to 1.5% to 3%.[43] Almost half of these strokes occur intraoperatively and almost all strokes within the first 48 hours.[44] The most common causative mechanism is embolism from hemodynamic changes, perioperative atrial fibrillation, aortic manipulations, and dislodgement of debris from the

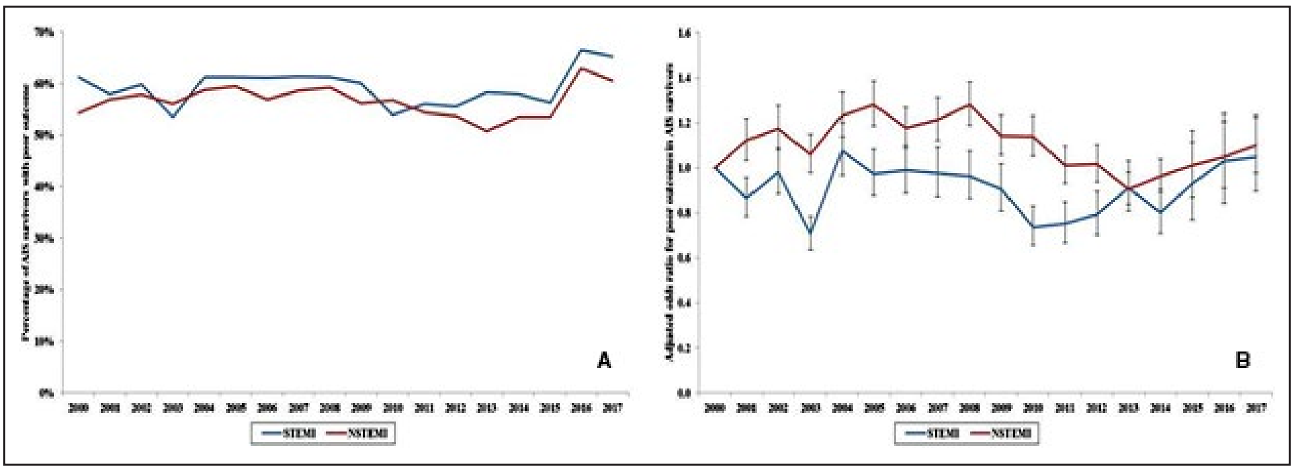

Figure 3. Trends in the prevalence of poor functional outcomes in AIS survivors.
A, Unadjusted temporal trends of the proportion of patients with AMI-AIS with poor functional outcome stratified by type of AMI (*P*<0.001 for trend over time); **(B)** Adjusted odds ratio for poor functional outcome in STEMI and NSTEMI admissions by year (with 2000 as the referent); adjusted for age, sex, race, comorbidity, primary payer, hospital region, hospital location and teaching status, and hospital bed size, acute organ failure, atrial fibrillation/flutter, cardiogenic shock, cardiac arrest, coronary angiography, percutaneous coronary intervention, coronary artery bypass grafting, pulmonary artery catheterization, mechanical circulatory support, invasive mechanical ventilation, and acute hemodialysis (*P*<0.001 for trend over time). AIS indicates acute ischemic stroke; AMI, acute myocardial infarction; NSTEMI, non–ST-segment–elevation myocardial infarction; and STEMI, ST-segment–elevation myocardial infarction.

ascending aorta.[45,46] Perioperative hypotension and arterial dissection can also lead to AIS.

There are limited data on AIS prevention after AMI, especially in patients presenting without concomitant atrial fibrillation.[47] In a phase III trial, ATLAS ACS-2 (Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects With Acute Coronary Syndromes—Thrombolysis in Myocardial Infarction 51), addition of low-dose rivaroxaban to dual antiplatelet therapy led to significant reduction in death, AMI, and stroke but increased major bleeding.[48,49] In a meta-analysis of 6 trials, adding oral anticoagulants to antiplatelets after AMI was associated with a reduction in the primary end point of cardiovascular death, AMI, and stroke, though the benefit was only seen in patients with STEMI.[50]

Limitations

This study has several limitations, despite the HCUP-NIS database's attempts to mitigate potential errors by using internal and external quality control measures. The administrative codes for AMI and AIS have been previously validated, which reduces the inherent errors in the study. Important factors such as the delay in presentation from time of onset of AMI symptoms, cerebral imaging, and reasons for not receiving aggressive medical care, and timing of multi-organ failure, could not be reliably identified in this database. The timing of AIS relative to AMI and cardiac procedures could not be reliably identified in this database. However, since AMI was the primary diagnosis on all admissions, it represents the reason the patient was most likely admitted to the hospital. The results of our study should be interpreted with caution because even small differences that may not be clinically relevant appear statistically significant because of large sample sizes. It is possible that despite best attempts at controlling for confounders by a multivariate analysis, observed results could be caused by residual confounding. Finally, AIS in our cohort includes periprocedural strokes from PCI or CABG performed for AMI, and our data are only reflective of in-hospital outcomes. Despite these limitations, this study addresses an important knowledge gap highlighting the national temporal trends of AIS in AMI in a contemporary population.

CONCLUSIONS

Although AIS occurs in a small proportion of AMI admissions, it is associated with significantly higher mortality and greater resource utilization during and after the hospitalization. Even among the AMI admissions with AIS that survived in-hospital stay, the early functional outcome of a majority of these patients appears to be poor. Further research to mitigate the occurrence and the severity of AIS in these vulnerable populations is needed to improve healthcare delivery to patients critically ill with cardiovascular and cerebrovascular disease.

ARTICLE INFORMATION

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Supplementary Material

Tables S1–S4

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SUPPLEMENTAL MATERIAL

Table S1. Administrative codes used for identification of diagnoses and procedures.

Comorbidity	International Classification of Diseases 9.0 Clinical Modification Codes
Cardiac arrest	427.5, 427.4, 427.41, 427.42, 99.60, 99.63
Coronary angiography	37.22, 37.23, 88.53-88.56
Percutaneous coronary intervention	00.66, 36.01, 36.02, 36.05, 36.06, 36.07, 88.57
Invasive hemodynamic assessment	89.63, 89.64, 89.66, 89.67, 89.68
Mechanical circulatory support	37.61, 37.68, 39.65
Invasive mechanical ventilation	96.7, 96.70, 96.71, 96.72
Hemodialysis	39.95
Multi-organ failure	570.0, 572.2, 573.3, 573.4
	518.81, 518.82, 518.85, 786.09, 799.1, 96.7, 96.70, 96.71, 96.72
	584, 584.5, 584.6, 584.7, 584.8, 584.9
	286.6-286.9, 287.4, 287.5
	293, 293.0, 293.1, 293.8, 293.81-293.84, 293.89, 293.9, 348.1, 348.3, 348.30, 348.81, 348.39, 780.01, 780.09, 89.14
Tracheostomy	311, 312, 3121, 3129
Percutaneous endoscopic gastrostomy	430, 431, 4311, 4319, 4432, 4438, 4439

Table S2. Predictors of acute ischemic stroke in acute myocardial infarction.

Total cohort (N=11,622,528)		Odds ratio	95% confidence interval		*P*
			Lower Limit	Upper Limit	
Age (years)	**≤75 years**	Reference category			
	>75 years	0.82	0.81	0.83	<0.001
Female sex		1.39	1.37	1.40	<0.001
Race	**White**	Reference category			
	Black	1.33	1.31	1.35	<0.001
	Others	1.08	1.07	1.09	<0.001
Primary payer	**Medicare**	Reference category			
	Medicaid	1.37	1.34	1.40	<0.001
	Private	1.14	1.12	1.15	0.28
	Others	1.30	1.27	1.33	<0.001
Quartile of median household income for zip code	**0-25th**	Reference category			
	26th-50th	0.96	0.94	0.97	<0.001
	51st-75th	0.96	0.95	0.98	<0.001
	75th-100th	0.96	0.94	0.97	<0.001
Hospital teaching status and location	**Rural**	Reference category			
	Urban Non-Teaching	1.21	1.19	1.23	<0.001
	Urban Teaching	1.32	1.30	1.34	<0.001
Hospital bed-size	**Small**	Reference category			
	Medium	1.10	1.08	1.12	<0.001
	Large	1.21	1.19	1.23	<0.001
Hospital region	**Northeast**	Reference category			
	Midwest	1.06	1.04	1.07	<0.001

	South	1.10	1.08	1.11	<0.001
	West	1.03	1.02	1.05	0.001
Charlson Comorbidity Index	**0-3**	Reference category			
	4-6	3.89	3.82	3.96	<0.001
	≥ 7	11.03	10.81	11.25	<0.001
Type of AMI	**STEMI**	Reference category			
	NSTEMI	0.85	0.84	0.86	<0.001
Tertile of admission year	**200-2005**	Reference category			
	2005-2010	1.09	1.08	1.10	<0.001
	2011-2017	0.88	0.87	0.90	<0.001
Cardiogenic shock		0.97	0.95	0.99	<0.001
Atrial fibrillation/flutter		1.34	1.32	1.35	<0.001
Coronary angiography		0.82	0.81	0.83	<0.001
Coronary thrombectomy		1.27	1.18	1.35	<0.001
Percutaneous coronary intervention		0.70	0.69	0.71	<0.001
Coronary artery bypass grafting		1.37	1.35	1.39	<0.001
Pulmonary artery catheterization		0.98	0.95	1.02	0.35
Mechanical circulatory support		1.25	1.23	1.28	<0.001
Invasive mechanical ventilation		2.46	2.43	2.50	<0.001

AIS: acute ischemic stroke; AMI: acute myocardial infarction; NSTEMI: non-ST-segment-elevation myocardial infarction; STEMI: ST-segment-elevation myocardial infarction

Table S3. Multivariable regression for in-hospital mortality in AMI.

Total cohort		Odds ratio	95% confidence interval		*P*
			Lower Limit	Upper Limit	
Acute ischemic stroke		1.75	1.72	1.78	<0.001
Age groups (years)	**19-49**	Reference category			
	50-59	1.41	1.38	1.43	<0.001
	60-69	1.91	1.87	1.95	<0.001
	70-79	2.98	2.91	3.04	<0.001
	≥80	5.14	5.03	5.25	<0.001
Female sex		1.11	1.10	1.12	<0.001
Race	**White**	Reference category			
	Black	0.87	0.86	0.88	<0.001
	Others	1.09	1.09	1.10	<0.001
Primary payer	**Medicare**	Reference category			
	Medicaid	0.95	0.94	0.97	<0.001
	Others	0.77	0.76	0.78	<0.001
Quartile of median household income for zip code	**0-25th**	Reference category			
	26th-50th	1.03	1.02	1.04	<0.001
	51st-75th	1.00	0.99	1.01	0.78
	75th-100th	1.00	0.99	1.01	0.74
Hospital teaching status and location	**Rural**	Reference category			
	Urban Non-Teaching	1.04	1.03	1.05	<0.001
	Urban Teaching	1.11	1.10	1.12	<0.001
Hospital bed-size	**Small**	Reference category			
	Medium	1.08	1.07	1.09	<0.001

	Large	1.21	1.20	1.22	<0.001
Hospital region	**Northeast**	Reference category			
	Midwest	0.98	0.97	0.99	<0.001
	South	1.06	1.05	1.07	<0.001
	West	0.84	0.83	0.85	<0.001
Charlson Comorbidity Index	**0-3**	Reference category			
	4-6	1.57	1.55	1.59	<0.001
	≥ 7	1.72	1.70	1.75	<0.001
Type of AMI	**ST-segment elevation**	Reference category			
	Non-ST-segment elevation	0.40	0.39	0.40	<0.001
Multi-organ failure		2.87	2.85	2.89	<0.001
Cardiogenic shock		2.96	2.93	2.99	<0.001
Atrial fibrillation/flutter		1.06	1.05	1.07	<0.001
Cardiac arrest		10.25	10.16	10.34	<0.001
Coronary angiography		0.37	0.36	0.37	<0.001
Fibrinolytic therapy		0.62	0.60	0.63	<0.001
Percutaneous coronary intervention		0.39	0.38	0.39	<0.001
Coronary artery bypass grafting		0.45	0.45	0.46	<0.001
Pulmonary artery catheterization		1.33	1.30	1.35	<0.001
Mechanical circulatory support		2.04	2.02	2.07	<0.001
Invasive mechanical ventilation		3.20	3.18	3.23	<0.001
Acute hemodialysis		1.89	1.85	1.93	<0.001

AMI: acute myocardial infarction

Table S4. Characteristics of AIS stratified by functional outcome.

Characteristic		Poor Outcome (N=87,993)	Good outcome (N=65,325)	*P*
Age (years)		75.3 ± 11.9	70.3 ± 13.0	<0.001
Female sex		54.7	49.1	<0.001
Race	**White**	62.3	59.9	<0.001
	Black	10.3	11.3	
	Others[a]	27.04	28.8	
Primary payer	**Medicare**	78.8	64.5	<0.001
	Medicaid	4.6	7.3	
	Private	13.2	20.2	
	Others[b]	3.3	8.0	
Charlson Comorbidity Index	**0-3**	6.4	13.6	<0.001
	4-6	40.9	49.7	
	≥ 7	52.7	36.8	
Hospital teaching status and location	**Rural**	11.1	9.0	<0.001
	Urban non-teaching	41.4	38.7	
	Urban teaching	47.4	52.2	
Hospital bed-size	**Small**	11.3	9.2	<0.001
	Medium	25.7	24.2	
	Large	63.0	66.5	
Hospital region	**Northeast**	20.7	17.2	<0.001
	Midwest	23.9	21.8	
	South	38.6	42.6	
	West	16.8	18.4	

AMI type	**STEMI**	31.5	29.1	<0.001
	NSTEMI	68.5	70.9	<0.001
Multi-organ failure		22.3	11.2	<0.001
Atrial fibrillation or flutter		32.1	24.2	<0.001
Cardiogenic shock		8.0	3.9	<0.001
Cardiac arrest		5.8	3.3	<0.001
Fibrinolytics		2.1	2.0	0.07
Coronary angiography		42.4	58.5	<0.001
Percutaneous coronary intervention		19.0	29.5	<0.001
Coronary artery bypass grafting		15.4	10.8	<0.001
Pulmonary artery catheterization		1.8	1.2	<0.001
Mechanical circulatory support		7.3	4.4	<0.001
Invasive mechanical ventilation		16.1	6.3	<0.001
Acute hemodialysis		1.4	0.6	<0.001
Tracheostomy		4.6	4.5	0.25
Percutaneous endoscopic gastrostomy		6.7	7.4	<0.001

AIS: acute ischemic stroke; AMI: acute myocardial infarction