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In-Hospital acute ischemic stroke following ST-elevation myocardial infarction

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ABSTRACT

Background: In-hospital ischemic stroke following acute ST-elevation myocardial infarction (STEMI) has not been evaluated on a national scale in the United States.
Methods: We used 2003 to 2014 Nationwide Inpatient Sample data to identify adults with a principal diagnosis of STEMI. Patients were divided into two groups defined by presence or absence of ischemic stroke. Clinical characteristics and in-hospital outcomes were studied using relevant statistics. Multiple linear and logistic regression models identified factors associated with ischemic stroke, national trend of in-hospital stroke incidence and in-hospital mortality.
Results: Of 1,842,529 STEMI patients hospitalized from 2003 to 2014, 22,268 (1.2%) developed acute in-hospital ischemic stroke. Those with acute strokes were older (age $\geq$ 65 years: 70% vs 46%), more likely female (51% vs 33%), and had higher rates of atrial fibrillation (28.9% vs 12.2%) and heart failure (40.5% vs 21.1%). Age and gender adjusted incidence of in-hospital ischemic stroke following STEMI remained stable; 1.4% in 2003 and 1.5% in 2014 (P trend = 0.50). However, age and gender adjusted in-hospital mortality declined in STEMI patients with and without in-hospital ischemic stroke [AOR 0.97 (0.95–0.99) P trend = 0.03, and AOR 0.98 (0.98–0.99) P trend < 0.001, respectively]. Patients with ischemic strokes had higher in-hospital mortality (25.7% Vs 7.2%, p < 0.001), [AOR 2.11, 95% CI (1.92–2.32)].
Conclusion: In the United States, the incidence of acute in-hospital stroke remained stable from 2003 to 2014 following STEMI with significant decrease of in-hospital mortality trends. Despite slight improvement in mortality trends, in-hospital mortality rates remained elevated calling for interventions to optimize health care delivery.

1. Introduction

Ischemic stroke following acute myocardial infarction is a devastating event that carries high mortality and morbidity [1–5]. Studies have investigated factors or predictors of ischemic stroke in order to set strategies to alleviate modifiable factors and therefore reduce stroke incidence and mortality [6–11]. Changes in reperfusion strategies and techniques over the years such as using radial access, smaller catheters, fewer exchange wires, and avoiding thrombectomy were associated with lower periprocedural stroke [12,13]. In addition, advances in antiplatelet and guideline directed therapies for acute myocardial infarction, stroke and heart failure has led to substantial improvement in myocardial function and cerebral perfusion with expected lower incidence of stroke [14–16]. On the other hand, increased complexity of lesions, and a higher proportion of the elderly population with increased comorbidities (atrial fibrillation, heart failure, renal failure, hypercoagulable states, etc.) have certainly contributed to an increase of ischemic strokes. Therefore, the combination of these factors could partially explain the static state of ischemic stroke incidence following myocardial infarction. Evaluating real life experience of a national database can provide a useful base to compare and monitor for improvements over time. We sought to study national trends and factors associated with acute ischemic stroke and in-hospital mortality following admission for STEMI.

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2. Methods

Data were obtained from the 2003–2014 Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample (NIS). A brief description of the data base was previously published and can be accessed in detail on the HCUP website [17–19]. We used International Classification of Diseases, Ninth Edition Clinical Modification (ICD-9-CM) codes of ST-elevation myocardial infarction (410.01, 410.11,410.21,410.31, 410.41, 410.51, 410.61, and 410.81) to identify adults ≥ 18 years of age with a principal diagnosis of STEMI. These codes have been utilized to identify patients with STEMI [17,20,21]. The code 410.91 was not included as it may reflect NSTEMI [20].

The validity of ICD-9 codes for the diagnosis of acute myocardial infarction and acute stroke were evaluated by multiple studies [22–27]. The reported sensitivity and specificity of ICD-9 codes to identify stroke varied between different studies, but in general they carried very good sensitivity of ≥ 82% and specificity of ≥ 95% [22–24]. Similarly, ICD-9 codes carried high sensitivity and specificity to identify acute myocardial infarction [25–27]. We adhered to the standard methods of using administrative database as outlined by Khera et al. [28] We avoided the use of non-specific codes such as 432, 435, 437, and 438 as outlined in a systematic review by McCormick et al. [22] In addition, we accounted for survey design complexity, sampling weights, primary sampling units and strata as recommended by HCUP [19]. The Agency for Health Care and Quality has released the HCUP-NIS years 2015–2017. However, due to the changes in coding from ICD to 9 to ICD-10 in October 2015. We chose to restrict analyses to years 2003 to 2014 to limit coding utilization to one coding system (ICD-9), which has been extensively validated and therefore decrease the chance of misclassification.

In order to ensure that STEMI was the primary reason for admission, STEMI ICD-9-CM codes with fifth digit subclassification of 0 (episode of care unspecified) or 2 (subsequent episode of care) were excluded. We also excluded patients who were transferred from another hospital to avoid duplication of records. The final study sample included 1,842,529 STEMI patients. Thereafter, we identified patients with ischemic stroke using appropriate ICD-9 codes (Supplement etable1) and divided the sample into two groups: STEMI patients with in-hospital ischemic stroke and STEMI patients without in-hospital ischemic stroke (Supplement eFigure1).

Inpatient outcomes of interest included: **(A)** Factors associated with the ischemic stroke following STEMI, ***(B)*** In-hospital complications following STEMI (hemorrhagic stroke, acute renal failure, gastrointestinal bleed, cardiogenic shock, in-hospital arrest, and mortality), ***(C)*** length of hospital stay (days), **(D)** total hospital charges (US $) adjusted for inflation using the 2019 consumer price index, **(E)** factors associated with increased mortality in STEMI patients who developed ischemic stroke.

Patients' clinical characteristics and comorbidities were compared between the two groups and included: age, gender, race, hypertension, diabetes, history of coronary artery disease, acute and chronic heart failure, left ventricular thrombus, atrial fibrillation, carotid artery disease, aortic disease, peripheral arterial disease, chronic renal failure, acute and chronic deep venous thrombosis/pulmonary embolism (DVT/PE), STEMI location (anterior/anterolateral, inferior/inferolateral/inferoposterior, lateral/posterior/unspecified), left ventricular aneurysm, left heart valvular disease (aortic stenosis, aortic regurgitation, mitral stenosis, and mitral regurgitation), hypocoagulable state (coagulation factors deficiency, thrombocytopenia), drug abuse, alcohol use, smoking, dyslipidemia, obesity, previous myocardial infarction, previous percutaneous coronary intervention (PCI), and previous coronary artery bypass grafting (CABG), thrombolytic use, admission PCI, admission CABG. Relevant co-morbidities that were not readily available in the Nationwide Inpatient Sample were obtained using the appropriate ICD-9-CM codes (Supplemental eTable 1).

Statistical analyses were performed using Stata 12.0, accounting for survey design complexity, sampling weights, primary sampling units and strata. Subsequently, population estimates of proportions, means and regression coefficients were obtained. Standard errors were estimated using Taylor series linearization. First, patient demographics and co-morbidities were compared between STEMI patient with and without ischemic stroke using Pearson χ^2 test for categorical variables and linear regression (1-way ANOVA) for continuous variables. Second, means and proportions of outcomes of interest were similarly compared. Third, multiple logistic regression models were conducted to examine factors associated with acute ischemic stroke following STEMI. These models were adjusted for age, gender, race, atrial fibrillation, history of coronary artery disease, acute and chronic heart failure with reduced ejection fraction, acute and chronic heart failure with preserved ejection fraction, left ventricular thrombus, left ventricular aneurysm, left ventricular valvular disease, STEMI location, acute and chronic DVT/PE, PCIs, the use of thrombolytics, use of mechanical support devices [Intra-Aortic Balloon Pump (IABP), Impella, Tandem Heart, Extracorporeal Membrane Oxygenation (ECMO)], hypocoagulopathy, alcohol use, hypertension, diabetes, dyslipidemia, obesity, prior myocardial infarction, prior PCIs, prior CABG, and chronic renal failure. Fourth, factors associated with in-hospital mortality were explored using univariate and multivariate logistic regression (supplement eTables 2,3,4). Fifth, we evaluated differences in the distribution of factors that were associated with increased in-hospital mortality in STEMI patients with ischemic stroke in 2013 and 2014, using Pearson χ^2 test for categorical variables and linear regression (1-way ANOVA) for continuous variables (supplement eTable 5). Sixth, we studied factors associated with hemorrhagic stroke using multivariate regression analyses (eTable6). Seventh, we performed case-control 1:1 matching of the following variable (age, gender, race, DM, CKD, DVT/PE, LV thrombus, history of CVA, heart failure, atrial fibrillation, PCI, CABG, and mechanical support) , then performed conditional multivariate regression analyses for factors associated with in hospital mortality (eTable 7,8,9).

Categorical variables were expressed as n (%) and continuous variables as mean ± SEM. The OR/β coefficients and 95% confidence interval were used to report results of regression models. All P values were 2-sided and Type I error was set at 0.05.

3. Results

The study included 1,842,529 STEMI patients admitted to U.S hospitals from 2003 to 2014. Acute in-hospital ischemic stroke developed in 22,268 patients (1.2%). Age and gender adjusted incidence of in-hospital ischemic stroke following STEMI remained stable over the study period; 1.4% in 2003 and 1.5% in 2014 (P trend = 0.50). However, age and gender adjusted in-hospital mortality declined in STEMI patients with and without in-hospital ischemic stroke [AOR 0.97 (0.95–0.99) P trend = 0.03, and AOR 0.98 (0.98–0.99) Ptrend < 0.001, respectively] (Fig. 1).

Patients who developed stroke following STEMI were older (mean age 71.5 years Vs 63.9 years P < 0.001), more likely to be female (51% Vs 33% P < 0.001), and less likely to be white (58.5% Vs 62.7%, P < 0.001).In univariate analyses, patients who developed stroke during their hospitalization were more likely to have atrial fibrillation, chronic or acute heart failure, chronic renal failure, prior history of cerebrovascular accident (CVA), diabetes mellitus,

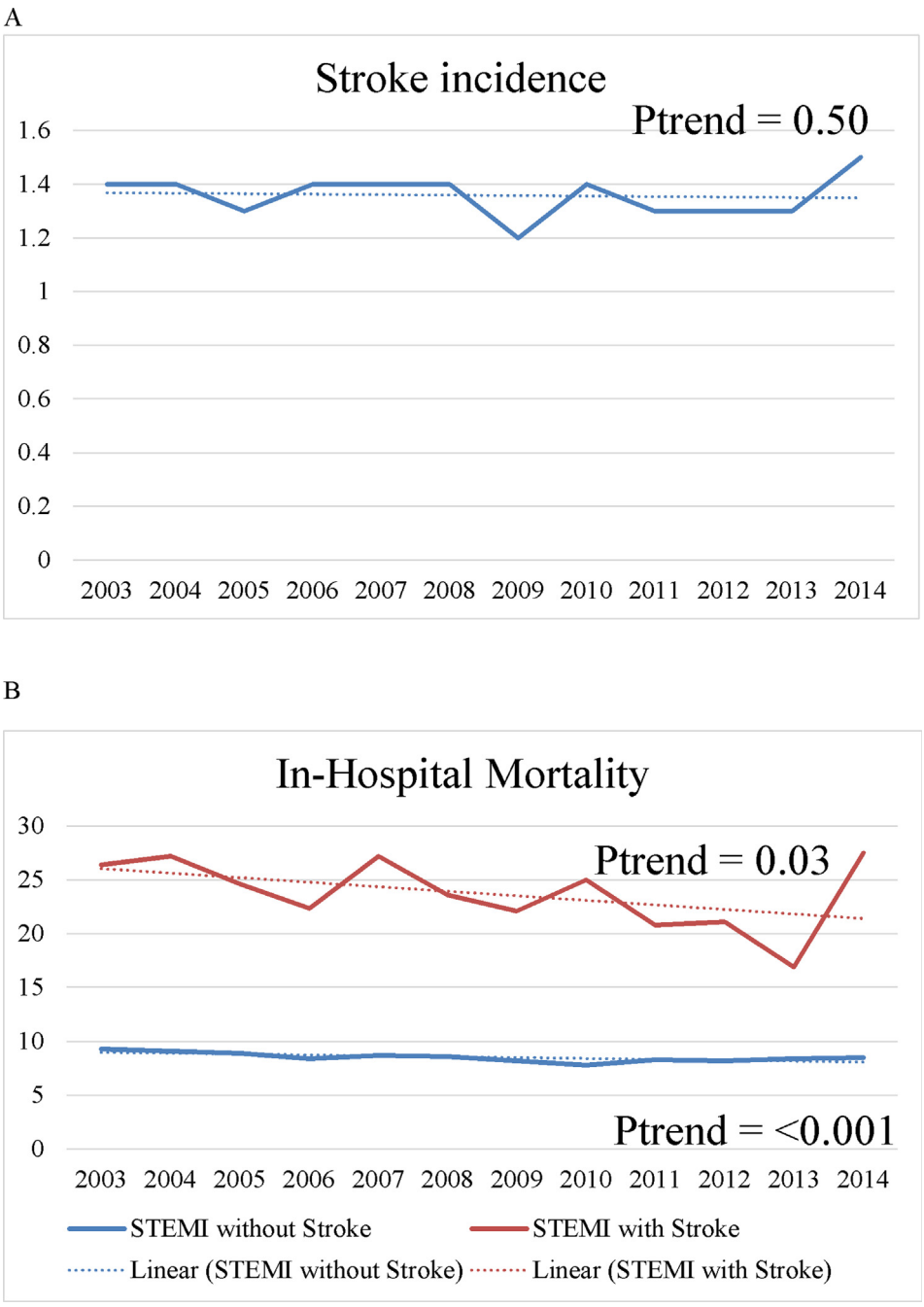

Fig. 1. A. Age and gender adjusted incidence of ischemic stroke following STEMI. B. Age and gender adjusted in-hospital Mortality following admission for STEMI in patients with and without ischemic stroke.

carotid artery and aortic artery disease, history of chronic or acute pulmonary embolism or deep venous thrombosis (PE/DVT), hypercoagulable state, left ventricular thrombus, CABG during hospitalization, and use of mechanical circulatory support. Compared to those with no ischemic stroke, patients with ischemic stroke were less likely to have prior CABG or PCIs, and less likely to have PCI during hospitalization (42.1% in STEMI with stroke Vs 66.7% in STEMI without Stroke) [table1].

Compared to patients without strokes, those with ischemic stroke were more likely to have higher in-hospital mortality (25.7% Vs 7.2%, p < 0.001) in univariate analysis and multivariate analyses [AOR 2.11, 95% CI (1.92–2.32)], and more likely to have higher in-hospital complications that eventually lead to increase mortality (table2 and supplement eTable 4). Patient with ischemic stroke had higher hospital length of stay (11.2 ± SEM 0.21 days vs. 4.5 ± SEM 0.03 days, P < 0.001), and higher hospital charges ($147,216 ± SEM $3,222 vs. $82,373 ± SEM $927, P < 0.001). Other in-hospital complications following STEMI are shown in table 2.

Factors associated with ischemic stroke following STEMI included: age, female gender, minorities (Black, Hispanic and Asian) compared to white patients, history of atrial fibrillation, diabetes mellitus, left ventricular thrombus, left ventricular aneurysms, DVT/PE, hypercoagulable state, carotid and aortic artery disease, acute and chronic heart failure, use of mechanical circulatory support and CABG during hospitalization for STEMI. On the other hand, admission PCIs and prior revascularization whether

Table 1
Demographic and Clinical Characteristics of ST elevation Myocardial Infarction in the NIS Years 2003 to 2014.

Variables		STEMI without Stroke n = 1,820,261	STEMI with Stroke n = 22,268	*P* Value
Age, mean (SE)		63.9 (0.07)	71.5 (0.2)	<0.001
Age group				<0.001
	18–64 years	986,024 (54%)	6,762 (30%)	
	≥ 65 years	834,236 (46%)	15,506 (70%)	
	Female	609,071 (33%)	11,352 (51%)	<0.001
	Race			<0.001
	White	1,141,610 (62.7%)	13,022 (58.5%)	
	Black	112,354 (6.2%)	2,027 (9.1%)	
	Hispanic	112,382 (6.2%)	1,542 (6.9%)	
	Asian/Pacific Islander	34,350 (1.9%)	490 (2.2%)	
	Native American	6,466 (0.3%)	94 (0.4%)	
	Other/missing	413,099 (22.7%)	5,094 (22.9%)	
Comorbidities				
	Alcohol abuse	53,697 (3.0%)	890 (4.0%)	<0.001
	Smoking	177,611 (9.7%)	1,427 (6.4%)	<0.001
	Drug abuse	37,962 (2.1%)	359 (1.6%)	0.02
	Obesity	189,210 (10.4%)	1,425 (6.4%)	<0.001
	Dyslipidemia	951,573 (52.3%)	7,148 (32.0%)	<0.001
	Hypertension	1,052,259 (58.2%)	12,761 (57.7%)	0.53
	Diabetes mellitus	473,779 (26.0%)	6,932 (31.1%)	<0.001
	History of Coronary artery disease	1,427,790 (78.4%)	13,274 (59.6%)	<0.001
	Chronic Renal Failure	109,739 (6.0%)	2,484 (11.1%)	<0.001
	Acute/chronic DVT/PE	17,577 (1.0%)	859 (3.9%)	<0.001
	LV Thrombus	3,551 (0.2%)	217 (1.0%)	<0.001
	History of CVA	63,116 (3.5%)	1,670 (7.5%)	<0.001
	Atrial Fibrillation	222,935 (12.2%)	6,443 (28.9%)	<0.001
	All Heart failure	383,394 (21.1%)	9,010 (40.5%)	<0.001
	HFpEF	19,445 (1.0%)	440 (2.0%)	<0.001
	HFrEF	380,161 (20.9%)	8,908 (40.0%)	<0.001
	Carotid artery disease	15,009 (0.8%)	1,330 (6.0%)	<0.001
	Aortic disease	9,796 (0.5%)	276 (1.2%)	<0.001
	PAD	127,400 (7.0%)	2,320 (10.5%)	<0.001
	Hypercoagulable state	4,811 (0.3%)	185 (0.8%)	<0.001
	Left Valvular Disease	149,868 (8.2%)	2,748 (12.3%)	<0.001
	LV aneurysm	3,545 (0.2%)	107 (0.5%)	<0.001
	Thrombocytopenia/ Coagulopathy†	60,111 (3.3%)	1,801 (8.1%)	<0.001
	Prior CABG	61,911 (3.4%)	562 (2.5%)	0.001
	Prior PCI	161,795 (8.9%)	905 (4.1%)	<0.001
	Prior MI	134,836 (7.4%)	1,091 (4.9%)	<0.001
	Thrombolytics	68,125 (3.7%)	781 (3.5%)	0.43
	Coronary angiography	1,422,682 (78.2%)	12,998 (58.4%)	<0.001
	Total PCI	1,214,246 (66.7%)	9,379 (42.1%)	<0.001
	Primary PCI	1,185,250 (67.6%)	9,004 (41.9%)	<0.001
	CABG	128,674 (7.1%)	2,756 (12.4%)	<0.001
	Use of MCS Device	166,157 (9.1%)	3,507 (15.7%)	<0.001
	STEMI location			<0.001
	Anterior/Anterolateral	697,263 (38.3%)	9,391 (42.2%)	
	Inferior/Inferolateral/Inferoposterior	946,829 (52.0%)	10,211 (45.9%)	
	Lateral/posterior/unspecified	176,169 (9.7%)	2,666 (12.0%)	

SE: standard error, %: percentage. *: indicates very small number. NIS: nationwide inpatient sample, LV: left ventricular, HFrEF: heart failure with reduced ejection fraction, HFpEF: heart failure with preserved ejection fraction, CABG: coronary artery bypass grafting, PCI: percutaneous coronary intervention, MI: myocardial infarction, DVT/PE: Deep venous Thrombosis/Pulmonary Embolism, MCS: Mechanical Circulatory Support, STEMI: ST-elevation myocardial infarction.
†Thrombocytopenia/ Coagulopathy indicates primary and secondary thrombocytopenia, hypo-coagulable states due to factors deficiency (i.e. Factor IIIV, Factor IX, Factor X, Factor XI, afibrinogenemia), Von Willebrands Disease.

previous CABG or PCI were associated with lower incidences of ischemic stroke (table 3).

We further evaluated factors associated with increased in-hospital mortality in the whole sample and in subgroups of patients with and without in-hospital ischemic strokes. Those factors were: age, female gender, cardiogenic shock, septic shock, cardiac arrest, respiratory failure, acute renal failure, and pulmonary embolism. On the other hand, the use of PCI was associated with reduced in-hospital mortality (eTable 2,3,4).

Due to increased mortality in 2014 in STEMI patients who developed in-hospital ischemic stroke compared to 2013 that had the lowest in-hospital mortality in this subgroup, we compared the distribution of those mortality related factors between those two years. The distribution of modifiable factors that were associated with increased mortality (cardiogenic shock, septic shock, in-hospital cardiac arrest, respiratory failure, acute renal failure, and pulmonary embolism) were higher in 2014 compared to 2013. Use of PCI was slightly lower in 2014 (62.2% Vs 66.5%, P < 0.001) (eTable 5).

As expected, hemorrhagic stroke was associated with thrombolytics use, advanced age, female gender, non-white race, and factors that require treatment with anticoagulation and increase the risk of ischemic stroke such as: atrial fibrillation, LV thrombus and hypercoagulable states. (eTable6). Results of case-control matched sample were similar to overall sample and presented in eTables (7,8,9).

Table 2
In-hospital Outcomes in Patients with ST Elevation Myocardial Infarction in the NIS Years 2003 to 2014.

Variables	STEMI without Stroke n = 1,820,261	STEMI with Stroke n = 22,268	*P* Value
Cerebral Hemorrhage	4,957 (0.3%)	2,443 (11.0%)	<0.001
Acute renal failure	148,862 (8.2%)	5,755 (25.8%)	<0.001
Gastrointestinal bleed	82,062 (4.5%)	2,480 (11.1%)	<0.001
Cardiogenic shock	158,536 (8.7%)	4,069 (18.3%)	<0.001
In-Hospital cardiac arrest	43,439 (2.4%)	974 (4.4%)	<0.001
Mortality	131,676 (7.2%)	5,725 (25.7%)	<0.001
Mechanical ventilation	108,985 (6.0%)	4,564 (20.5%)	<0.001
Non-invasive ventilation (BIPAP/CPAP)	14,963 (0.8%)	455 (2.0%)	<0.001
Tracheostomy	9,124 (0.5%)	1,051 (4.7%)	<0.001
Gastrostomy	6,064 (0.3%)	1,417 (6.4%)	<0.001
Palliative Care consult	17,839 (1.0%)	1,165 (5.2%)	<0.001
Length of hospital stay, mean (±SE)	4.5 (0.03)	11.2 (0.21)	<0.001
Total hospital charges, mean (±SE)	$82,371 ($927)	$147,383 ($3,223)	<0.001

SE: standard error, %: percentage. NIS: nationwide inpatient sample, LV: left ventricular.

4. Discussion

In this large national database, the in-hospital incidence of acute ischemic stroke following admission with ST-elevation myocardial infarction remained stable between 2003 and 2014. Factors associated with incidence of stroke included age, female gender, atrial fibrillation, heart failure, diabetes mellitus, chronic renal failure, atherosclerotic cardiovascular disease, left ventricular thrombus, hypercoagulable state, and CABG during admission.

Despite slight improvement in in-hospital mortality trends, it remained substantially elevated and one fourth of patients who developed stroke died during hospitalization. The high mortality rate in this group was mainly driven by higher in hospital complications that eventually lead to death (cardiogenic shock, septic shock, respiratory failure, renal failure, and cardiac arrest). Factors associated with in-hospital mortality included age, female gender, cardiac arrest, septic shock, cardiogenic shock, respiratory failure, acute renal failure, and pulmonary embolism. On the other hand, PCI was associated with reduced in-hospital mortality.

In-hospital incidence of ischemic stroke in our study was 1.4–1.5% which is consistent with literature reports, [4,7,8,29] and it remained stable from 2003 to 2014. Saczynski JS et al. studied stroke incidence following acute myocardial infarction and showed relatively stable incidence between 1986 and 2005 with no statistically significant difference in yearly odds of stroke incidence[10]. Studies evaluating the incidence of stroke following myocardial infarction have reported different results, depending on the study population and design. Post PCI studies reported a slight increase in the incidence of ischemic stroke following myocardial infarction [5,13,30–32]. This is because PCI can slightly increases immediate post-procedure risk due to procedure complexity and possible manipulation of arterial atherosclerosis plaques [33,34]. The incidence of ischemic stroke following complicated PCI ranges between 0.3 and 0.9% [13,30,31,34,35]. This could be alleviated with adherence to strict measures in high risk groups (severely reduced cardiac function, presence of aortic disease, history of CVA, etc.), such as using smaller and more flexible catheters, shorter fluoroscopy times, avoiding routine ventriculography, paying meticulous attention with careful use of catheters that have higher association with scraping debris from aorta such as Judkins left (JL) and multi-purpose [33,34].

On the other hand, studies that included all post myocardial infarction patients showed significant reduction in 30 days and one-year incidence of ischemic stroke in those who received PCI [8,9,11]. This is because cardiac reperfusion therapies will eventually lead to improved cardiac function, reduce incidence of heart failure and left ventricular thrombus and increased adherence to dual antiplatelets and statin therapies [8,11]. The lower rates of PCI in the stroke group in our study could be due multiple factors such as: the presence of more relative or absolute contraindications for PCI in the stroke group (acute and chronic renal failure, gastrointestinal bleed, hemorrhagic stroke), older patients in the stroke group with higher prevalence of comorbidities such as history of CVA which could classify them as not being candidates for aggressive interventions, and the net positive effect of reperfusion on improving cardiac function, reducing infarct size, and decreasing incidence of heart failure and thrombus formation. The development of left ventricular thrombus following STEMI was associated with increased ischemic stroke incidence in our study similar to prior reports [17,36]. Other factors associated with increased ischemic stroke in our study were similar to factors reported in literature such as: advance age, female gender, atrial fibrillation, diabetes, heart failure, chronic renal disease, prior history of stroke, carotid and aortic artery disease, hypercoagulable state, use of mechanical support and CABG during the same hospitalization for STEMI [9,11,37]. The stable incidence of ischemic stroke following STEMI warrant further investigations and implementation of various treatment modalities, in addition to continuous efforts to modify risk factors for stroke.

In the current study, we noticed a significant but modest decrease in age and gender adjusted mortality trends over the study period. This is a finding that could be promising but requires sustained efforts to achieve lower rate of in-hospital mortality. The overall age and gender adjusted in-hospital mortality following ischemic stroke in STEMI patients was 25.7%, which is consistent with literature reports [1,3–5]. The lowest level of in-hospital mortality in STEMI patients following ischemic stroke was 16.9% in 2013 (Fig. 1), which then went up again to 27.6% in 2014 and is

Table 3
Association of Select Factors with Acute in hospital ischemic stroke in patients admitted with ST Elevation Myocardial Infarction in the NIS Years 2003 to 2014.

Variables	Unadjusted OR (95% CI)	*P* Value	Adjusted OR (95% CI)	*P* Value
Age	1.039 (1.037–1.041)	<0.001	1.018 (1.015–1.021)	<0.001
Female	2.07 (1.95–2.19)	<0.001	1.46 (1.37–1.56)	<0.001
LV thrombus	5.02 (3.70–6.83)	<0.001	4.26 (3.05–5.95)	<0.001
Atrial Fibrillation	2.92 (2.73–3.12)	<0.001	1.77 (1.65–1.91)	<0.001
Diabetes	1.28 (1.21–1.37)	<0.001	1.25 (1.17–1.34)	<0.001
Hypertension	0.98 (0.92–1.04)	0.53	1.00 (0.94–1.07)	0.95
History of CVA	2.26 (2.02–2.53)	<0.001	1.50 (1.33–1.69)	<0.001
PAD	1.55 (1.40–1.71)	<0.001	1.08 (0.97–1.21)	0.15
Heart failure	2.55 (2.39–2.71)	<0.001	1.31 (1.21–1.41)	<0.001
Left valvular disease	1.57 (1.43–1.72)	<0.001	0.92 (0.83–1.01)	0.09
LV aneurysm	2.48 (1.63–3.76)	<0.001	1.92 (1.26–2.94)	0.002
Hypercoagulable state†	3.16 (2.28–4.38)	<0.001	3.03 (2.11–4.35)	<0.001
DVT/PE	4.12 (3.52–4.81)	<0.001	2.48 (2.10–2.93)	<0.001
Carotid Artery disease	7.64 (6.73–8.68)	<0.001	6.16 (5.33–7.11)	<0.001
Aortic disease	2.32 (1.79–3.02)	<0.001	1.48 (1.11–1.98)	0.007
Chronic Renal Failure	1.96 (1.78–2.15)	<0.001	1.22 (1.10–1.35)	<0.001
PCI	0.36 (0.34–0.39)	<0.001	0.68 (0.63–0.74)	<0.001
Use of MCS Device	1.86 (1.71–2.03)	<0.001	1.57 (1.43–1.74)	<0.001
CABG	1.85 (1.70–2.03)	<0.001	1.24 (1.11–1.39)	<0.001
Prior PCI	0.43 (0.37–0.50)	<0.001	0.69 (0.59–0.81)	<0.001
Prior CABG	0.74 (0.61–0.88)	0.001	0.77 (0.64–0.93)	0.008
Race				
White	Reference		Reference	
Black	1.58 (1.41–1.77)	<0.001	1.63 (1.45–1.83)	<0.001
Hispanic	1.20 (1.07–1.35)	0.002	1.29 (1.15–1.46)	<0.001
Asian/Pacific Islander	1.25 (1.04–1.51)	0.02	1.24 (1.02–1.50)	0.03
Native American	1.27 (0.85–1.91)	0.24	1.39 (0.90–2.15)	0.14
Other/missing	1.08 (0.99–1.17)	0.06	1.07(0.99–1.16)	0.07

NIS: Nationwide Inpatient Sample, OR: odds ratio, CI: confidence interval, LV left ventricular, PAD: peripheral arterial disease, DVT/PE: Deep Venous Thrombosis/Pulmonary Embolism.
†Hypercoagulable state: (antithrombin III deficiency, Factor V Leiden mutation, Lupus anticoagulant, protein C deficiency, protein S deficiency, prothrombin gene mutation, activated protein C resistance, secondary hypercoagulable state, and homocystinuria).

similar to the high rates seen in prior years. This finding motivated the search for factors that were associated with increased mortality in stroke patients and whether those factors were more prevalent in 2014 compared to 2013. The implications of our study's findings are the identification of in-hospital mortality risk factors for patients with STEMI who subsequently develop stroke. These risk factors included advanced age, female gender, in-hospital shock (cardiogenic and septic), respiratory failure, acute renal failure, pulmonary embolism, and in-hospital cardiac arrest. Lower mortality was noted in patients who had PCI for STEMI. Modifiable in-hospital mortality risk factors included shock, acute renal failure, pulmonary embolism, respiratory failure and cardiac arrest, which were all more prevalent in 2014. Our findings call for more aggressive patient care strategies in order to improve their survival. Interventions should include adequate hydration and precautions to lower rates of contrast induced or shock induced renal failure, aggressive aseptic precautions to minimize the incidence of sepsis and septic shock, appropriate deep venous thrombosis prevention for critically ill patients, and possibly creating multi-disciplinary approach for treating high risk population (elderly, female, respiratory failure and shock patients) by cooperation between interventional cardiology, critical care, heart failure, neurology and nephrology teams to optimize healthcare delivery and reach the best possible outcome. The lower mortality rate in STEMI patients with stroke in 2013 compared to other years could not be fully explained, however its coincidence with the publications of STEMI and stroke guidelines,[14,15] might denote the extensive efforts to achieve better outcome in the same year.

This study should be interpreted with the following limitations. First, the NIS is an administrative database; therefore, the validity of the data highly depends on the accuracy of coding. Second, the database contains only inpatient information; therefore, follow-up after hospital discharge is lacking, which will limit evaluation of long-term outcomes. Third, our study sample included a wide variety of US hospitals with differences in resources and expertise availability, therefore different approaches and variable practices will be expected.

Fourth, rates of PCI performed after STEMI in our study was lower than rates reported by the National Cardiovascular Data Registry.38 However, our database included all comers following STEMI, which included subgroups of patients in whom PCI might be considered inappropriate given advanced dementia, multiple comorbidities and short life expectancy. In addition, there is a subset of patients who needed emergent coronary artery bypass grafts (CABG), as their anatomy was not amenable to PCI. Other barriers to PCI might have included complications of myocardial infarction requiring surgery or cardiogenic shock unresponsive to non-surgical approaches [13,39]. Rates of PCIs in our study increased significantly from 47% in 2003 to 84% in 2014, which was similar to prior national and international reports of all comers [40,41].

Furthermore, the time of ischemic stroke in relation to STEMI cannot be determined from an administrative database, therefore it is not possible to determine in the subset of patients who received thrombolytics, if it was administered as part of treatment for STEMI or stroke. In addition, the database does not provide information about medications, procedural details (access site, number and types of catheters used, amount of contrast , etc) or cardiac catheterization reports (number and complexity of coronary lesions) which all could affect the incidence of stroke [13]. Finally, similar to other observational studies, the presence of residual confounding by measured or unmeasured confounders could not be completely eliminated.

In summary, the incidence of ischemic stroke following STEMI in the United States has remained stable over the study period, with modest decrease of in-hospital mortality. Further efforts are needed to provide superior level of care for those at high risk for

developing stroke, and proactive modulation of risk factors that increase in hospital mortality are of paramount importance to achieve higher survival rates.

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none.

Declaration of Competing Interest

Aiham Albaeni, Ché Matthew Harris, Hesham Nasser, Sirhley Sifontes, S.Mustajab Hasan, Sai Guduru, Khalid Abusaada, Syed Gilani, and Wissam I. Khalife declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2020.100684.

References

[1] A. Brammås, S. Jakobsson, A. Ulvenstam, T. Mooe, Mortality after ischemic stroke in patients with acute myocardial infarction: predictors and trends over time in Sweden, Stroke 44 (11) (2013 Nov) 3050–3055.
[2] B. Ovbiagele, Nationwide trends in in-hospital mortality among patients with stroke, Stroke. 41 (8) (2010 Aug) 1748–1754.
[3] F.A. Spencer, J.M. Gore, J. Yarzebski, et al., Trends (1986 to 1999) in the incidence and outcomes of in-Hospital stroke complicating acute myocardial infarction (the Worcester Heart Attack Study), Am J Cardiol. 92 (4) (2003 Aug 15) 383–388.
[4] J.T. Guptill, R.H. Mehta, P.W. Armstrong, et al., Stroke after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction: timing, characteristics, and clinical outcomes, Circ Cardiovasc Interv. 6 (2) (2013 Apr) 176–183.
[5] C.S. Kwok, E. Kontopantelis, P.K. Myint, et al., Stroke following percutaneous coronary intervention: type-specific incidence, outcomes and determinants seen by the British Cardiovascular Intervention Society 2007–12, Eur Heart. 36 (25) (2015 Jul 1) 1618–1628.
[6] T. Mooe, P. Eriksson, B. Stegmayr, Ischemic stroke after acute myocardial infarction, A population-based study. Stroke 28 (4) (1997 Apr) 762–767.
[7] B.J. Witt, K.V. Ballman, R.D. Brown Jr, R.A. Meverden, S.J. Jacobsen, V.L. Roger, The incidence of stroke after myocardial infarction: a meta-analysis, Am J Med. 119 (4) (2006) 354.e1–354.e9.
[8] O. Hachet, C. Guenancia, K. Stamboul, et al., Frequency and predictors of stroke after acute myocardial infarction: specific aspects of in-hospital and post discharge events, Stroke. 45 (12) (2014) 3514–3520.
[9] U. Kajermo, A. Ulvenstam, A. Modica, T. Jernberg, T. Mooe, Incidence, trends, and predictors of ischemic stroke 30 days after an acute myocardial infarction, Stroke. 45 (2014) 1324–1330.
[10] J.S. Saczynski, F.A. Spencer, J.M. Gore, et al., Twenty-year trends in the incidence of stroke complicating acute myocardial infarction: Worcester Heart Attack Study, Arch Intern Med 168 (19) (2008 Oct 27) 2104–2110.
[11] A. Ulvenstam, U. Kajermo, A. Modica, T. Jemberg, L. Söderström, T. Mooe, Incidence, trends, and predictors of ischemic stroke 1 year after an acute myocardial infarction, Stroke. 45 (11) (2014) 3263–3268.
[12] S. Shoji, S. Kohsaka, H. Kumamaru, et al., Stroke After Percutaneous Coronary Intervention in the Era of Transradial Intervention, Circ Cardiovasc Interv. 11 (12) (2018) e006761.
[13] S.J. Hoffman, H.C. Routledge, R.J. Lennon, et al., procedural factors associated with Percutaneous coronary intervention-related ischemic stroke, JACC Cardiovasc Interv. 5 (2) (2012 Feb) 200–206.
[14] O'Garcia PT, Kushner FG, Ascheim DD, et al. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines .2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2013;127: e362-425.
[15] E.C. Jauch, J.L. Saver, H.P. Adams Jr, et al., Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association, Stroke. 44 (3) (2013 Mar) 870–947.
[16] C.W. Yancy, M. Jessup, B. Bozkurt, et al., 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, J Am Coll Cardiol. 62 (16) (2013) e147–e239.
[17] Albaeni A, Chatila K, Beydoun HA, Beydoun MA, Morsy M, Khalife WI. In-Hospital Left Ventricular Thrombus following ST-Elevation Myocardial Infarction. Int J Cardiol. 2019 Jul 23. pii: S0167-5273(19)31953-9.
[18] U.S. Agency for Healthcare Research and Quality. Overview of the National (Nationwide) Inpatient Sample. Available at: https://www.hcup-us.ahrq.gov/nisoverview.jsp. 2016 Accessed on June 1, 2019.
[19] U.S. Agency for Healthcare Research and Quality. HCUP Methods Series. Nationwide Inpatient Sample Redesign Final Report. Available at: https://www.hcup-us.ahrq.gov/reports/methods/2014-04.pdf. 2014 Accessed on June 1, 2019.
[20] R.W. Yeh, S. Sidney, M. Chandra, M. Sorel, J.V. Selby, A.S. Go, Population Trends in the Incidence and Outcomes of Acute Myocardial Infarction, N Engl J Med 362 (2010) 2155–2165.
[21] S. Khera, D. Kolte, T. Gupta, et al., Temporal trends and sex differences in revascularization and outcomes of ST-Segment elevation myocardial infarction in younger adults in the United States, J Am Coll Cardiol 66 (2015) 1961–1972.
[22] N. McCormick, V. Bhole, D. Lacaille, J.A. Avina-Zubieta, Validity of Diagnostic Codes for Acute Stroke in Administrative Databases: A Systematic Review, PLoS One. 10 (8) (2015) e0135834.
[23] M. Orso, F. Cozzolino, S. Amici, et al., Validity of cerebrovascular ICD-9-CM codes in healthcare administrative databases, The Umbria Data-Value Project. PLoS One. 15 (1) (2020) e0227653.
[24] D.L. Tirschwell, W.T. Longstreth Jr., Validating administrative data in stroke research, Stroke. 33 (10) (2002) 2465–2470.
[25] F. Cozzolino, A. Montedori, I. Abraha, et al., A diagnostic accuracy study validating cardiovascular ICD-9-CM codes in healthcare administrative databases, The Umbria Data-Value Project. PLoS One. 14 (7) (2019) e0218919.
[26] N. McCormick, D. Lacaille, V. Bhole, J.A. Avina-Zubieta, Validity of myocardial infarction diagnoses in administrative databases: a systematic review, PLoS One. 9 (3) (2014) e92286.
[27] Y. Kiyota, S. Schneeweiss, R.J. Glynn, C.C. Cannuscio, J. Avorn, D.H. Solomon, Accuracy of Medicare claims-based diagnosis of acute myocardial infarction: estimating positive predictive value on the basis of review of hospital records, Am Heart J. 148 (1) (2004) 99–104.
[28] R. Khera, S. Angraal, T. Couch, et al., Adherence to Methodological Standards in Research Using the National Inpatient Sample, JAMA. 318 (20) (2017) 2011–2018.
[29] S. Jakobsoon, A. Graipe, D. Huber, F. Björklund, T. Mooe, The risk of ischemic stroke after an acute myocardial infarction in patients with decreased renal function, Cerebrovasc Dis. 37 (6) (2014) 460–469.
[30] M. Alkhouli, F. Alqahtani, A. Tarabishy, G. Sandhu, C.S. Rihal, Incidence, Predictors, and Outcomes of Acute Ischemic Stroke Following Percutaneous Coronary Intervention, JACC Cardiovasc Interv. 15 (2019 Aug 12) 1497–1506.
[31] A. Aggarwal, D. Dai, J.S. Rumsfeld, et al., Incidence and predictors of stroke associated with percutaneous coronary intervention, Am J Cardiol. 104 (3) (2009 Aug 1) 349–353.
[32] V.G. Patel, K.M. Brayton, D.J. Kumbhani, et al., Meta-analysis of stroke after transradial versus transfemoral artery catheterization, Int J Cardiol. 168 (6) (2013 Oct 15) 5234–5238.
[33] E.C. Keeley, C.L. Grines, Scraping of aortic debris by coronary guiding catheters: a prospective evaluation of 1,000 cases, J Am Coll Cardiol. 32 (7) (1998 Dec) 1861–1865.
[34] N. Werner, R. Zahn, U. Zeymer, Stroke in patients undergoing coronary angiography and percutaneous coronary intervention: incidence, predictors, outcome, and therapeutic options, Expert Rev Cardiovasc Ther. 10 (10) (2012 Oct) 1297–1305.
[35] S. Fuchs, E. Stabile, T.D. Kinnaird, et al., Stroke Complicating Percutaneous Coronary Interventions, Circulation. 106 (1) (2002 Jul 2) 86–91.
[36] N. Maniwa, M. Fujino, M. Nakai, et al., Anticoagulation combined with antiplatelet therapy in patients with left ventricular thrombus after first myocardial infarction, Eur Heart J 39 (2018) 201–208.
[37] Yaghi S, Pilot M, Song C, et al. Ischemic Stroke Risk After Acute Coronary Syndrome. J Am Heart Assoc. 2016 Jul 13;5(7). pii: e002590. doi: 10.1161/JAHA.115.002590
[38] Masoudi FA, Ponirakis A, de Lemos JA, et al. Executive Summary: Trends in U.S. Cardiovascular Care: 2016 Report from 4 ACC National Cardiovascular Data Registries. J Am Coll Cardiol. 2017 Mar 21;69(11):1424-1426.
[39] B. Ibanez, S. James, S. Agewall, et al., 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC), Eur Heart J. 39 (2) (2018) 119–177.
[40] Shah RU, Henry TD, Rutten-Ramos S, et al. Increasing percutaneous coronary interventions for ST- segment elevation myocardial infarction in the United States: progress and opportunity. JACC Cardiovasc Interv. 2015 Jan;8(1pt B):139-146.
[41] E. Puymirat, T. Simon, P.G. Steg, et al., Association of changes in clinical characteristics and management with improvement in survival among patients with ST-elevation myocardial infarction, JAMA 308 (2012) 998–1006.