Quality and Outcomes

Regional Variation Across the United States in Management and Outcomes of ST-Elevation Myocardial Infarction: Analysis of the 2003 to 2010 Nationwide Inpatient Sample Database

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ABSTRACT

Background: Regional differences in the treatment and outcomes of patients with ST-elevation myocardial infarction (STEMI) within the United States remain poorly understood.

Hypothesis: Treatment choice and outcomes in patients with STEMI differ between regions within the United States.

Methods: We used the 2003 to 2010 Nationwide Inpatient Sample databases to identify all patients age ≥40 years hospitalized with STEMI. Patients were divided into 4 groups according to region: Northeast, Midwest, South, and West. Multivariable logistic regression was used to identify differences in treatment choice and outcomes (in-hospital mortality, acute stroke, and cardiogenic shock) among the 4 regions.

Results: Of 1 990 486 patients age ≥40 years with STEMI, 350 073 (17.6%) were hospitalized in the Northeast, 483 323 (24.3%) in the Midwest, 784 869 (39.4%) in the South, and 372 222 (18.7%) in the West. Compared with the Northeast, patients in the Midwest, South, and West were less likely to receive medical therapy alone and more likely to receive percutaneous coronary intervention and coronary artery bypass grafting. Risk-adjusted in-hospital mortality was higher in the Midwest (odds ratio [OR]: 1.07, 95% confidence interval [CI]: 1.05-1.09, P <0.001), South (OR: 1.03, 95% CI: 1.01-1.05, P = 0.001), and West (OR: 1.06, 95% CI: 1.04-1.08, P <0.001), as compared with the Northeast. When adjusted further for regional variation in treatment selection, risk-adjusted in-hospital mortality was even higher in the Midwest, West, and South.

Conclusions: Despite higher reperfusion and revascularization rates, STEMI patients in the Midwest, West, and South have paradoxically higher risk-adjusted in-hospital mortality as compared with patients in the Northeast.

Introduction

There is a large variation in the clinical treatment and outcomes among patients with acute myocardial infarction (AMI) across different countries, as well as different regions within countries.[1–4] Clinical practice, and hence the outcome, is likely to be influenced by several factors, including differences in the prevalence of underlying cardiovascular risk factors and the incidence of coronary artery disease (CAD) in the local population, the availability of resources, the current perceptions within the medical community of available treatments, and the prevailing treatment guidelines.[5–7] Prior studies have demonstrated substantial variation in the treatment of AMI within hospital referral regions, states, and census regions in the United States, as well as variation in outcomes, with lower mortality in the Northeast.[3,5,7–9] However, most of these studies have examined AMI patients hospitalized prior to 2001, which is before some of the important advances in the management of AMI.[5,8,9] Further, some of these studies

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have used data from randomized controlled trials, and therefore may not accurately reflect the differences in treatment and outcomes in AMI patients in the real world.[5] Others have used population-based administrative databases but have examined differences in specific patient populations such as Medicare beneficiaries, veterans, or Hispanics, and therefore lack important considerations such as influence of regional variations in insurance status and racial/ethnic composition of local population on differences in management and outcomes.[7–12] Lastly, most of these studies have included all patients with AMI (ie, those with ST-elevation myocardial infarction [STEMI] as well as non-STEMI). Hence, regional differences in the treatment and outcomes of patients with STEMI across the United States remain poorly understood.

The main objectives of this study were to examine differences in baseline characteristics, treatment strategies, and outcomes (in-hospital mortality, acute stroke, and cardiogenic shock) among patients with STEMI across the 4 census regions (Northeast, Midwest, West, and South) within the United States using the Nationwide Inpatient Sample (NIS) database, and to determine whether differences in outcomes can be explained by differences in baseline characteristics and treatment choices.

Methods

Data Source

Data were obtained from the NIS databases for years 2003 to 2010. The NIS, sponsored by the Agency for Healthcare Research and Quality (AHRQ) as a part of the Healthcare Cost and Utilization Project (HCUP), is the largest publicly available all-payer inpatient care database in the United States. The NIS contains discharge-level data from approximately 8 million hospital stays from about 1000 hospitals designed to approximate a 20% stratified sample of all community hospitals in the United States. A discharge weight is provided for each patient discharge record and was used to obtain national estimates of all STEMI hospitalizations from 2003 to 2010.

Study Population

We used the International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) diagnosis codes 410.0x, 410.1x, 410.2x, 410.3x, 410.4x, 410.5x, 410.6x, and 410.8x to identify all patients age ≥40 years with the principal diagnosis of STEMI (N = 1 990 486). We chose the principal diagnosis because it is considered the primary reason for hospital admission. We excluded patients age <40 years, as this might minimize the inclusion of those patients with nonatherosclerotic causes of STEMI (eg, cocaine abuse, coronary vasculitis). In administrative databases, the diagnosis of AMI using ICD-9-CM codes has been shown to have a specificity of 99.5% with a sensitivity of 72.4%, a negative predictive value of 96.1%, and a positive predictive value of 95.9%.[13,14] Based on the hospital location, patients with STEMI were then divided into the following 4 groups: Northeast, Midwest, South, and West, corresponding to the census regions as defined by the US Census Bureau.[15]

Outcome Measures

We used ICD-9-CM and HCUP Clinical Classification Software (CCS) codes to identify whether patients received thrombolysis (V45.88, 99.10), percutaneous coronary intervention (PCI; 00.66, 36.01, 36.02, 36.05, 36.06, and 36.07), or coronary artery bypass grafting (CABG; CCS procedure code 44). Those without any of these codes were considered to have received medical therapy alone. For patients with ≥1 procedure code, we considered the least invasive therapy as the intended treatment. For example, patients who had thrombolysis and PCI were assigned to the thrombolysis group. Similarly, patients who underwent PCI and CABG were assigned to the PCI group. This approach has been used in previous studies using the NIS database.[16]

The primary outcome measure of interest was all-cause in-hospital mortality, defined as death during the hospitalization encounter in the NIS database. Acute stroke (CCS code 109) and cardiogenic shock (ICD-9-CM 785.51) were used as secondary outcomes.

Patient and Hospital Characteristics

Baseline patient characteristics used included demographics (age, sex, race, primary payer status, weekday vs weekend admission, median household income for patient's ZIP code), 29 Elixhauser comorbidities as defined by AHRQ, other clinically relevant comorbidities (smoking, dyslipidemia, known CAD, family history of CAD, prior AMI, carotid artery disease, and dementia), STEMI location (anterior, inferior, and other), and in-hospital procedures (left-heart catheterization, Swan-Ganz catheterization, intra-aortic balloon pump placement, and blood transfusion).[17,18] A list of ICD-9-CM and CCS codes used to identify comorbidities and in-hospital procedures is provided in Supplementary Table 1. Hospital characteristics such as bed size (small, medium, and large), location (rural or urban), and teaching status were also included as described in the NIS database.[19]

Statistical Analysis

We initially compared baseline patient and hospital characteristics across the 4 regions using the Pearson χ^2 test for categorical variables and 1-way analysis of variance for continuous variables to identify significant univariate associations. In addition, we used standardized differences, calculated as the difference in means or proportions divided by a pooled estimate of the SD, to compare baseline characteristics across the 4 regions, using Northeast as the reference. Absolute standardized difference (ASD) >10 was considered significant.[20] We then used multivariate logistic regression to compare treatment choices (medical therapy alone, thrombolysis, PCI, or CABG) across the 4 regions after adjusting for demographics, hospital characteristics, all comorbidities, and STEMI location. Similarly, for each outcome, a multivariable logistic regression model was estimated to compare the associations with geographic region, using Northeast as the reference region. The model adjusted for demographics, hospital characteristics, all comorbidities, and STEMI location. In addition, treatment choice (medical therapy alone [reference], thrombolysis,

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PCI, or CABG) was added to the regression model to explore whether differences in outcomes can be explained by differences in treatment choice.

We also conducted subgroup analysis after stratifying patients into 4 groups according to the treatment received, comparing outcomes across the 4 regions in each subgroup using logistic regression models, to determine if outcomes were different for the different treatment modalities used. The regression models adjusted for confounding variables as mentioned above.

Statistical analysis was performed using SPSS Statistics version 20.0 (IBM Corp., Armonk, NY). We used a 2-sided P value of <0.05 to assess for statistical significance for all analyses. Categorical variables are expressed as percentage and continuous variables as mean ± SD. Odds ratio (OR) and 95% confidence interval (CI) are used to report the results of logistic regression models.

Results

Patient and Hospital Characteristics

We identified 1 990 486 patients age ≥40 years with STEMI in the 2003 to 2010 NIS databases. Of these, 350 073 (17.6%) patients were hospitalized in the Northeast, 483 323 (24.3%) in the Midwest, 784 869 (39.4%) in the South, and 372 222 (18.7%) in the West (Table 1). Mean age for the overall cohort was 66.1 years. Patients in the South were significantly younger than those in the Northeast (mean age, 65.2 vs 67.1 years, $P < 0.001$). Male predominance was seen in all 4 regions. Compared with the Northeast, the Midwest had a higher proportion of Whites (88.8% vs 84%), the South had a higher proportion of Blacks (10.5% vs 5.7%), and the West had a higher proportion of Hispanics (14.2% vs 5%) and Asians/Pacific Islanders (7% vs 1.3%). The proportion of uninsured patients was lowest in the Northeast and highest in the South (5.1% vs 9.6%). In the Northeast, 18.4% of patients had median household income in the 0 to 25th percentile as compared with 39.4% in the South, whereas 33.4% patients had median household income in the 76th to 100th percentile as compared with 13.5% in the South. Patients in the overall cohort were admitted to large (67%), urban (87%) hospitals. Northeast had the highest proportion of teaching hospitals (63.5%, vs 52.6% in the Midwest, 37.5% in the South, and 32.9% in the West, $P < 0.001$). The prevalence of most comorbidities did not differ much across the 4 regions, with the exception of smoking and deficiency anemia (Table 1). Smoking was more prevalent in the Midwest and South, whereas deficiency anemia was more prevalent in the West, as compared with the Northeast.

In-hospital Procedures

There were some notable differences in in-hospital procedures among the 4 regions (Table 2). Left-heart catheterization rates were significantly higher in the Midwest (70.7%) and South (68.8%), as compared with the Northeast (62.2%, $P < 0.001$, ASD >10). Swan-Ganz catheterization and intra-aortic balloon pump use did not differ much across the 4 regions. The Midwest had significantly lower blood transfusion rates than the Northeast (5.2% vs 7.8%, ASD 10.5).

Treatment Choice

Unadjusted analysis showed that STEMI patients in the Northeast were more likely to not undergo any reperfusion/revascularization therapy and receive medical therapy alone (40.5%, vs 34.0% in the Midwest, 35.9% in the South, and 36.8% in the West, $P < 0.001$), whereas those in the West were more likely to receive thrombolysis (5.6%, vs 4.2% in the Northeast, 2.6% in the Midwest, and 3.3% in the South, $P < 0.001$; Table 3). Use of PCI was more prevalent in the Midwest (57.1%, vs 49% in the Northeast, 53.3% in the South, and 50.9% in the West, $P < 0.001$) and that of CABG was more prevalent in the South (7.5%, vs 6.3% in the Northeast, 6.4% in the Midwest, and 6.6% in the South, $P < 0.001$).

After adjusting for demographics, hospital characteristics, all comorbidities, and STEMI location, compared with patients in the Northeast, those in the Midwest, South, and West were 40%, 37%, and 30% less likely to receive medical therapy alone (ie, no reperfusion/revascularization), respectively (Table 3). On the other hand, compared with the Northeast, STEMI patients in the West were 23% more likely to receive thrombolysis. Use of PCI was significantly higher in the Midwest (odds ratio [OR]: 1.70, 95% confidence interval [CI]: 1.68-1.72, $P < 0.001$), South (OR: 1.47, 95% CI: 1.46-1.49, $P < 0.001$) and West (OR: 1.25, 95% CI: 1.24-1.27, $P < 0.001$), as compared with the Northeast. Similarly, patients in the Midwest, South, and West were more likely to undergo CABG (for Midwest, OR: 1.04, 95% CI: 1.01-1.06, $P < 0.001$; for South, OR: 1.29, 95% CI: 1.27-1.32, $P < 0.001$; and for West, OR: 1.12, 95% CI: 1.09-1.14, $P < 0.001$).

Primary Outcome (In-hospital Mortality)

In-hospital mortality was 9.5% in the overall study cohort. Unadjusted analysis showed that compared with the Northeast (9.8%), in-hospital mortality was slightly lower in the Midwest (9.3%), South (9.4%), and West (9.6%). However, after adjusting for demographics, hospital characteristics, comorbidities, and STEMI location, compared with the Northeast, in-hospital mortality was higher in the Midwest (OR: 1.07, 95% CI: 1.05-1.09, $P < 0.001$), South (OR: 1.03, 95% CI: 1.01-1.05, $P = 0.001$), and West (OR: 1.06, 95% CI: 1.04-1.08, $P < 0.001$) (Table 4). Further, when adjusted for regional variation in treatment selection, in-hospital mortality was even higher in the Midwest (OR: 1.15, 95% CI: 1.13-1.17, $P < 0.001$), South (OR: 1.10, 95% CI: 1.08-1.11, $P < 0.001$), and West (OR: 1.12, 95% CI: 1.09-1.14, $P < 0.001$).

To determine if there is regional variation in in-hospital mortality according to the different treatment modalities used, we stratified the study cohort into subgroups depending on the treatment received. Compared with the Northeast, adjusted in-hospital mortality was higher in the Midwest, South, and West among patients receiving medical therapy alone, PCI, or CABG (Table 5).

Secondary Outcomes

We used acute stroke and cardiogenic shock as the secondary outcomes of interest. The incidence of acute stroke and cardiogenic shock in the overall cohort was 1.7% and 7.9%, respectively. In univariate analysis, patients in the West had higher rates of acute stroke and cardiogenic shock

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Table 1. Baseline Demographics, Hospital Characteristics, and Comorbidities in Patients With STEMI According to Region

							Absolute Standardized Difference		
Variable	Total	Northeast	Midwest	South	West	*P* Value	MW vs NE	S vs NE	W vs NE
No. of cases (weighted)	1 990 486	350 073	483 323	784 869	372 222	—	—	—	—
Age, y	66.1 ± 13.9	67.1 ± 14.0	66.6 ± 14.3	65.2 ± 13.6	66.6 ± 13.6	<0.001	3.2	13.3	3.4
Female sex, %	36.3	37.8	37.7	35.9	33.7	<0.001	0.2	4.0	8.5
Race, %						<0.001			
White	79.8	84	88.8	78.2	71.1		14.2	14.8	31.3
Black	7.3	5.7	5.9	10.5	3.8		0.8	17.7	8.9
Hispanic	7	5	1	7	14.2		23.9	8.4	31.7
Asian or Pacific Islander	2.1	1.3	0.5	0.9	7		9.3	4.5	28.5
Other	3.7	4	3.9	3.5	4		0.6	3.0	0.3
Primary expected payer, %						<0.001			
Medicare	50.4	52.2	52	50	47.4		0.4	4.3	9.6
Medicaid	5.2	6.2	4.4	4.6	6.5		7.9	6.8	1.2
Private insurance	34.2	34.9	35.5	32.0	36.4		1.1	6.2	3.1
Uninsured	7.1	5.1	5.8	9.6	5.5		2.9	17.2	1.9
Other	3.2	1.6	2.4	3.8	4.3		5.3	13.4	15.5
Weekend admission, %	26.6	25.7	27.4	26.4	26.6	<0.001	3.8	1.7	2.0
Median household income, %						<0.001			
0–25th percentile	27.4	18.4	21.2	39.4	18.9		7.1	47.7	1.3
26th–50th percentile	27.9	23.0	34.2	27.6	24.6		25.1	10.7	3.8
51st–75th percentile	24.1	25.2	27.6	19.5	28.0		5.4	13.9	6.3
76th–100th percentile	20.7	33.4	17.0	13.5	28.5		38.6	48.2	10.6
Hospital characteristics, %									
Bed size						<0.001			
Small	10.2	12.7	12.6	8.4	8.8		0.3	14.2	12.5
Medium	22.8	22.8	21.4	22.6	25.0		3.4	0.5	5.2
Large	67	64.5	66	69	66.1		3.2	9.7	3.5
Urban location	87	90.7	84.0	84.7	92.3	<0.001	20.3	18.4	5.5
Teaching hospital	44.9	63.5	52.6	37.5	32.9	<0.001	22.3	53.9	64.5
Comorbidities, %									
Smoker	33.1	29.1	34.3	34.4	32.7	<0.001	11.2	11.3	7.7
Dyslipidemia	46	45.5	48.5	44.3	47.1	<0.001	6.1	2.3	3.3
CAD	72.9	71.5	74.1	73.1	71.8	<0.001	5.9	3.6	0.6
Family history of CAD	6.8	6.5	6.7	7.1	6.7	<0.001	0.7	2.3	0.5
Prior MI	7.0	7.2	7.1	6.4	8.1	<0.001	0.3	3.1	3.3

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Table 1. *Continued*

Variable	Total	Northeast	Midwest	South	West	*P* Value	Absolute Standardized Difference		
							MW vs NE	S vs NE	W vs NE
Carotid artery disease	0.9	0.9	0.9	0.9	0.8	<0.001	0.8	0.0	0.2
Dementia	4.4	4.6	4.6	4.1	4.4	<0.001	0.2	2.7	0.9
AIDS	0.1	0.2	0.1	0.1	0.1	<0.001	3.4	0.5	0.6
Alcohol abuse	2.6	2.6	2.4	2.6	2.8	<0.001	1.1	0.2	1.0
Deficiency anemia	9.8	8.7	9.9	9.3	11.7	<0.001	4.3	2.2	10.1
RA/collagen vascular diseases	1.8	1.8	2.0	1.6	1.8	<0.001	1.7	0.9	0.1
Chronic blood-loss anemia	1.0	0.8	1.2	0.9	1.0	<0.001	4.0	1.4	1.8
CHF	25.1	26.6	25.0	24.3	25.2	<0.001	3.6	5.2	3.2
Chronic pulmonary disease	16.8	15.6	17.4	17.6	15.7	<0.001	5.0	5.4	0.2
Coagulopathy	3.3	2.9	3.2	3.4	3.4	<0.001	2.0	2.6	3.0
Depression	4.5	4.7	5.2	4.0	4.3	<0.001	2.3	3.8	2.0
DM (uncomplicated)	23.3	23.3	22.7	23.7	23.2	<0.001	1.5	0.8	0.3
DM (complicated)	3.3	3.2	3.2	2.9	4.3	<0.001	0.0	2.0	5.9
Drug abuse	1.4	1.4	1.2	1.4	1.7	<0.001	2.2	0.4	1.9
Hypertension	56.5	57.7	56.2	56.1	56.6	<0.001	3.1	3.1	2.3
Hypothyroidism	6.9	7.1	7.5	6.2	7.6	<0.001	1.5	3.7	2.2
Liver disease	0.8	0.8	0.6	0.8	1.0	<0.001	2.1	0.3	2.1
Lymphoma	0.4	0.5	0.4	0.3	0.4	<0.001	1.6	2.4	1.1
Fluid and electrolyte disorder	15.1	13.1	15.6	15.2	15.7	<0.001	7.4	6.2	7.6
Metastatic cancer	0.8	0.9	0.8	0.7	0.8	<0.001	0.8	2.0	1.4
Other neurological disorders	4.7	4.8	5.0	4.6	4.7	<0.001	0.8	0.7	0.7
Obesity	8.2	6.8	8.8	8.1	9.0	<0.001	7.3	4.9	8.0
Paralysis	1.3	1.3	1.3	1.1	1.6	<0.001	0.1	1.7	2.7
PVD	7.3	7.3	7.7	7.1	7.1	<0.001	1.5	0.8	0.9
Psychoses	1.4	1.5	1.5	1.4	1.4	<0.001	0.1	1.5	0.9
Pulmonary circulation disorders	0.1	<0.1	0.1	0.1	0.1	<0.001	0.7	0.4	0.8
Renal failure (chronic)	8.3	8.1	8.2	8.1	8.9	<0.001	0.3	0.0	2.8
Solid tumor without metastasis	1.2	1.4	1.3	1.1	1.3	<0.001	0.7	2.4	1.1
Peptic ulcer (nonbleeding)	<0.01	0.1	<0.1	<0.1	<0.1	<0.001	1.8	2.1	0.7
Valvular disease	0.2	0.2	0.2	0.2	0.2	<0.001	0.2	0.4	0.1
Weight loss	1.3	0.9	1.5	1.3	1.4	<0.001	5.3	3.7	4.3
STEMI location, %						<0.001			
Anterior	31.8	33.8	30.4	31.3	33.0		7.4	5.2	1.7
Inferior	42.6	43.3	42.6	42.7	41.6		1.4	1.1	3.4
Other	25.6	22.9	27.1	25.9	25.4		9.6	6.9	5.8

Abbreviations: AIDS, acquired immunodeficiency syndrome; CAD, coronary artery disease; CHF, congestive heart failure; DM, diabetes mellitus; MI, myocardial infarction; MW, Midwest; NE, Northeast; PVD, peripheral vascular disease; RA, rheumatoid arthritis; S, South; STEMI, ST-elevation myocardial infarction; W, West.

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Table 2. In-hospital Procedures in Patients With STEMI According to Region

							Absolute Standardized Difference		
Procedure	Total	Northeast	Midwest	South	West	*P* Value	MW vs NE	S vs NE	W vs NE
No. of cases (weighted)	1 990 486	350 073	483 323	784 869	372 222	—	—	—	—
Left-heart catheterization, %	67.6	62.2	70.7	68.8	66.1	<0.001	18.1	13.9	8.2
Swan-Ganz catheterization, %	1.3	1.5	1.4	1.0	1.6	<0.001	0.7	4.3	1.1
IABP placement, %	8.4	9.0	9.2	7.6	8.2	<0.001	0.6	5.1	2.9
Blood transfusion, %	6.2	7.8	5.2	5.5	7.5	<0.001	10.5	9.4	1.3

Abbreviations: IABP, intra-aortic balloon pump; MW, Midwest; NE, Northeast; S, South; STEMI, ST-elevation myocardial infarction; W, West.

Table 3. Regional Variation in Treatment of STEMI

Treatment	Northeast	Midwest	South	West
Medical therapy alone, %	40.5	34.0	35.9	36.8
Unadjusted OR	Ref	0.76 (0.75-0.76)	0.82 (0.82-0.83)	0.86 (0.85-0.87)
Adjusted OR[a]	Ref	0.60 (0.59-0.61)	0.63 (0.63-0.64)	0.70 (0.69-0.71)
Thrombolysis, %	4.2	2.6	3.3	5.6
Unadjusted OR	Ref	0.60 (0.59-0.61)	0.78 (0.77-0.80)	1.35 (1.32-1.38)
Adjusted OR[a]	Ref	0.54 (0.53-0.56)	0.67 (0.65-0.68)	1.23 (1.20-1.26)
PCI, %	49.0	57.1	53.3	50.9
Unadjusted OR	Ref	1.38 (1.37-1.39)	1.18 (1.18-1.19)	1.08 (1.07-1.09)
Adjusted OR[a]	Ref	1.70 (1.68-1.72)	1.47 (1.46-1.49)	1.25 (1.24-1.27)
CABG, %	6.3	6.4	7.5	6.6
Unadjusted OR	Ref	1.02 (1.01-1.04)	1.21 (1.20-1.23)	1.06 (1.04-1.08)
Adjusted OR[a]	Ref	1.04 (1.01-1.06)	1.29 (1.27-1.32)	1.12 (1.09-1.14)

Abbreviations: CABG, coronary artery bypass grafting; OR, odds ratio; PCI, percutaneous coronary intervention; Ref, reference region (OR: 1.00); STEMI, ST-elevation myocardial infarction.
Of 1 990 486 patients with STEMI, 724 546 (36.4%) received medical therapy alone, 74 383 (3.7%) received thrombolysis, 1 055 226 (53%) received PCI, and 136 331 (6.8%) received CABG. Numbers in parenthesis represent 95% confidence interval.
[a]Adjusted for all demographics, hospital characteristics, all comorbidities, and STEMI location.

(Supplementary Table 2). After adjusting for confounding variables, compared with the Northeast, patients in the Midwest, South, and West were more likely to have acute stroke (for Midwest, OR: 1.05, 95% CI: 1.01-1.10; for South, OR: 1.11, 95% CI: 1.07-1.15; for West, OR: 1.14, 95% CI: 1.09-1.19) and cardiogenic shock (for Midwest, OR: 1.24, 95% CI: 1.21-1.27; for South, OR: 1.05, 95% CI: 1.03-1.06; for West, OR: 1.21, 95% CI: 1.19-1.24).

When stratified according to treatment selection, patients receiving medical therapy alone or CABG in the Midwest, South, and West had a significantly higher likelihood of acute stroke than those in the Northeast (Supplementary Table 2). On the other hand, patients receiving thrombolysis in the Midwest, South, and West were 39%, 33%, and 19% less likely to have acute stroke than those in the Northeast, respectively. There was no significant difference in acute stroke among patients undergoing PCI across the 4 regions. Similarly, in the subgroups of patients receiving medical therapy alone or thrombolysis, patients in the Midwest, South, and West had a higher likelihood of cardiogenic shock than those in the Northeast. Lastly, in patients receiving PCI or CABG, cardiogenic shock was higher in the Midwest and West but lower in the South, as compared with the Northeast (Supplementary Table 2).

Length of Stay, Total Hospital Cost, and Discharge Disposition

The average length of stay and total hospital cost for the overall study cohort was 4.8 days and $21 065, respectively. Patients in the Midwest had a shorter unadjusted average length of stay than those in the Northeast (4.6 vs 5.3 days; Supplementary Table 3). Compared with the Northeast, the unadjusted total hospital cost for STEMI was significantly lower in the Midwest and South, and higher in the West (average, $22 399 vs $20 497 in the Midwest, $18 748 in the South, and $25 557 in the West). Even after adjusting for confounding variables, patients in the West accrued the highest total hospital cost regardless of the treatment

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Table 4. Regional Variation in In-hospital Mortality in Patients With STEMI

	Northeast	Midwest	South	West
Percent	9.8	9.3	9.4	9.6
Unadjusted OR	Ref	0.95 (0.93-0.96)	0.95 (0.94-0.97)	0.99 (0.97-1.00)
Adjusted OR (95% CI)				
Age, sex, and race	Ref	1.01 (1.00-1.03)	1.07 (1.05-1.08)	1.01 (0.99-1.03)
All demographics, comorbidities, and STEMI location[a]	Ref	1.03 (1.01-1.05)	1.02 (1.00-1.04)	1.05 (1.03-1.07)
All demographics, comorbidities, STEMI location, and hospital characteristics	Ref	1.07 (1.05-1.09)	1.03 (1.01-1.05)	1.06 (1.04-1.08)
All demographics, comorbidities, STEMI location, hospital characteristics, and treatment choice	Ref	1.15 (1.13-1.17)	1.10 (1.08-1.11)	1.12 (1.09-1.14)

Abbreviations: CI, confidence interval; OR, odds ratio; Ref, reference region (OR: 1.00); STEMI, ST-elevation myocardial infarction.
[a]All demographics include age, sex, race, primary payer status, weekday vs weekend admission, and median household income.

Table 5. Regional Variation in In-hospital Mortality Stratified According to Treatment Choice

Treatment	Northeast	Midwest	South	West
Medical therapy alone, %	18.3	19.1	18.2	17.7
Unadjusted OR (95% CI)	Ref	1.05 (1.03-1.07)	0.99 (0.97-1.01)	0.96 (0.94-0.98)
Adjusted OR (95% CI)[a]	Ref	1.11 (1.09-1.14)	1.07 (1.04-1.09)	1.06 (1.03-1.08)
Thrombolysis, %	5.1	4.4	5	5.3
Unadjusted OR (95% CI)	Ref	0.85 (0.76-0.95)	0.98 (0.89-1.07)	1.05 (0.95-1.15)
Adjusted OR (95% CI)[a]	Ref	0.97 (0.83-1.14)	0.96 (0.86-1.08)	1.19 (1.06-1.33)
PCI, %	3.6	4.1	4.2	4.7
Unadjusted OR (95% CI)	Ref	1.15 (1.11-1.19)	1.16 (1.13-1.20)	1.33 (1.29-1.37)
Adjusted OR (95% CI)[a]	Ref	1.26 (1.20-1.31)	1.16 (1.12-1.21)	1.20 (1.15-1.25)
CABG, %	5.7	5.7	5.8	5.9
Unadjusted OR (95% CI)	Ref	0.99 (0.92-1.06)	1.02 (0.95-1.09)	1.02 (0.94-1.10)
Adjusted OR (95% CI)[a]	Ref	1.27 (1.14-1.40)	1.25 (1.15-1.36)	1.21 (1.09-1.34)

Abbreviations: CABG, coronary artery bypass grafting; OR, odds ratio; PCI, percutaneous coronary intervention; Ref, reference region (OR: 1.00).
Of 1 990 486 patients with STEMI, 724 546 (36.4%) received medical therapy alone, 74 383 (3.7%) received thrombolysis, 1 055 226 (53%) received PCI, and 136 331 (6.8%) received CABG.
[a]Adjusted for all demographics, hospital characteristics, all comorbidities, and STEMI location.

received (Supplementary Table 4). Patients in the Northeast were less likely to be discharged home and more likely to be discharged/transferred to short-term hospital or skilled nursing facility (Supplementary Table 3).

Discussion

We observed a substantial variation in the management and outcomes of STEMI across different regions within the United States in this large, multi-institutional, nationwide cohort of patients.

Despite higher reperfusion/revascularization rates, STEMI patients in the Midwest, West, and South had paradoxically higher risk-adjusted in-hospital mortality as compared with the Northeast. Even when stratified by treatment strategies, the same pattern for in-hospital outcomes was observed. In addition, in-hospital costs also varied by region, with STEMI patients hospitalized in the West and Northeast accruing significantly greater costs compared with those in the South and Midwest.

Previous studies have shown that treatment of AMI in the Northeast, particularly in New England, is characterized by a higher use of medical therapies and lower use of cardiac procedures than other regions in the United States.[5,8,10–12] The New England survival advantage (lower in-hospital and 30-day mortality) after AMI has also been previously demonstrated.[9] However, most of these studies have examined AMI patients hospitalized prior to 2001. Others have used data from randomized clinical trials as opposed to population-based databases, or have studied only specific patient populations such as fee-for-service Medicare beneficiaries, veterans, or Hispanics, and/or have included all patients with AMI (ie, STEMI as well as non-STEMI). Our current analysis of the NIS database overcomes some of these limitations of previous studies.

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In this contemporary, nationwide cohort of STEMI patients age ≥40 years, irrespective of race, insurance status, or income, the Northeast had a higher use of medical therapy alone and lower use of PCI or CABG than the Midwest, South, or West. However, despite higher revascularization rates in the Midwest, South, and West, adjusted in-hospital mortality was also higher in these regions as compared with the Northeast.

The regional paradox (worse outcomes in regions with higher revascularization rates) observed in our study is difficult to explain. In our study, the prevalence of most comorbidities (except smoking and deficiency anemia) did not differ much across the 4 geographic regions (Table 1). Patient demographics were as one might expect in our study population. Patients in the South were relatively younger. Compared with the Northeast, the Midwest had a higher proportion of Whites, the South had a higher proportion of Blacks, and the West had a higher proportion of Hispanics and Asians/Pacific Islanders. Prior studies have shown small differences in door-to-balloon time but not in-hospital mortality among different races/ethnicities in patients undergoing primary PCI for STEMI.[21] The South had the highest proportion of uninsured patients in our study. Patients in the South also had relatively lower median household income. Previous studies have linked lower socioeconomic status to poorer hospital performance and modestly higher mortality in AMI.[22] In our study, the Northeast had the highest proportion of urban, teaching hospitals. Urban location and teaching status of hospital have been shown to be associated with improved quality of care and lower mortality in patients with AMI.[22–24] Findings from the Global Registry of Acute Coronary Events (GRACE) also revealed higher use of β-blockers, statins, and glycoprotein IIb/IIIa inhibitors in teaching than in nonteaching hospitals.[25]

Primary PCI of the infarct artery is the treatment of choice for STEMI when time-to-treatment delays are short and the patient presents at a PCI-capable hospital.[26] Compared with thrombolysis, primary PCI is associated with improved outcomes including lower mortality.[27] However, the higher rates of PCI in the Midwest, South, and West as compared with the Northeast in our study did not translate into improved outcomes in these regions. On the contrary, in-hospital mortality was higher in these regions than in the Northeast, even in the subgroup of patients undergoing PCI (Table 5). In an analysis of 44 639 fee-for-service Medicare beneficiaries hospitalized with AMI, Ko et al demonstrated that regions with higher intensity of invasive therapy did not differentiate procedure selection based on patients' cardiac catheterization appropriateness or their baseline risk as estimated using the GRACE risk score.[28] Cardiac catheterization was used most frequently in the lowest-risk patients and least frequently in the highest-risk patients. Although the NIS database lacks sufficient information to determine patients' baseline risk or appropriateness for PCI, it is possible that regional variation in patient selection could account for the observed differences in in-hospital mortality, especially within the subgroup of patients undergoing PCI.

Stroke and cardiogenic shock are important complications in patients with STEMI and are associated with increased mortality.[29,30] To our knowledge, this is the first study demonstrating regional variation in acute stroke and cardiogenic shock in patients with STEMI. Compared with the Northeast, patients in the Midwest, South, and West had higher rates of acute stroke and cardiogenic shock. This might have, at least partially, contributed to the higher in-hospital mortality in these regions. However, the NIS database does not allow differentiation of acute stroke or cardiogenic shock present on admission vs that developing during hospitalization. Therefore, our findings should be interpreted in light of this important limitation.

We also observed a significant variation in the total cost of hospitalization for STEMI across the 4 regions. Wang et al demonstrated a similar regional variation in the hospitalization costs for AMI in patients age 18 to 64 years using the 2006 to 2008 MarketScan Commercial Claims and Encounter inpatient database.[31] They identified CABG and PCI as the biggest drivers of hospital costs for AMI. However, in our study, although PCI and CABG rates were highest in the Midwest and the South, respectively, even after adjusting for demographics, hospital characteristics, and comorbidities, the total hospital cost in these 2 regions was lower than that in the Northeast. Further, the total hospital cost was highest in the West, regardless of the treatment modality used. Our findings suggest that other, yet-unmeasured factors are likely responsible for the regional differences in the cost of care for STEMI.

Our study has certain limitations. First, because NIS is an administrative database, there is the potential for unrecognized miscoding of diagnostic and procedure codes. Second, as this is a retrospective, observational study, there is a possibility of selection bias. However, these 2 limitations are partially compensated by the large size of the NIS database and the ability to obtain nationwide estimates using the discharge weights provided. Third, there is the possibility that residual measured or unmeasured confounding and some prognostically important variables are not available in the NIS database. Fourth, the NIS database does not include information such as door-to-balloon time, laboratory data, medication use, and PCI capability of hospitals, which could influence treatment choice and, hence, outcomes. Lastly, outcomes in the NIS database are limited to in-hospital events and causes of death are not differentiated.

Conclusion

We observed a significant variation in the management and outcomes of STEMI across different regions within the United States. Compared with STEMI patients in the Northeast, those in the Midwest, West, and South were more likely to receive PCI and CABG. Despite higher reperfusion and revascularization rates in the Midwest, South, and West, adjusted in-hospital mortality was paradoxically higher in these regions, as compared with the Northeast. Regional variations in demographics, comorbidities, hospital characteristics, and treatment selection did not completely explain this regional paradox. Other aspects of care such as adherence to treatment guidelines, distribution of health care resources, and availability of PCI-capable hospitals merit further investigation to better understand these regional differences. Recently, Yeh et al showed that from 2000 to

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2008, although wide regional differences in the incidence of AMI and PCI utilization have continued, disparities in short-term mortality have improved.[32] Wider implementation of national quality-improvement initiatives and systems of care, such as the Acute Coronary Treatment and Intervention Outcomes Network (ACTION) Registry–Get With The Guidelines and the American Heart Association's Mission: Lifeline, may be needed to improve quality of care and adherence to treatment guidelines to minimize these regional differences in the management and outcomes of STEMI.[3,33]

References

1. Giugliano RP, Llevadot J, Wilcox RG, et al. Geographic variation in patient and hospital characteristics, management, and clinical outcomes in ST-elevation myocardial infarction treated with fibrinolysis: results from InTIME-II. *Eur Heart J.* 2001;22:1702–1715.
2. Gupta M, Chang WC, Van de Werf F, et al. International differences in in-hospital revascularization and outcomes following acute myocardial infarction: a multilevel analysis of patients in ASSENT-2. *Eur Heart J.* 2003;24:1640–1650.
3. Laskey W, Spence N, Zhao X, et al. Regional differences in quality of care and outcomes for the treatment of acute coronary syndromes: an analysis from the Get With The Guidelines coronary artery disease program. *Crit Pathw Cardiol.* 2010;9:1–7.
4. Alter DA, Austin PC, Tu JV. Community factors, hospital characteristics and inter-regional outcome variations following acute myocardial infarction in Canada. *Can J Cardiol.* 2005;21:247–255.
5. Pilote L, Califf RM, Sapp S, et al; GUSTO-1 Investigators. Regional variation across the United States in the management of acute myocardial infarction. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. *N Engl J Med.* 1995;333:565–572.
6. Akkerhuis KM, Deckers JW, Boersma E, et al. Geographic variability in outcomes within an international trial of glycoprotein IIb/IIIa inhibition in patients with acute coronary syndromes: results from PURSUIT. *Eur Heart J.* 2000;21:371–381.
7. Ko DT, Krumholz HM, Wang Y, et al. Regional differences in process of care and outcomes for older acute myocardial infarction patients in the United States and Ontario, *Canada. Circulation.* 2007;115:196–203.
8. O'Connor GT, Quinton HB, Traven ND, et al. Geographic variation in the treatment of acute myocardial infarction: the Cooperative Cardiovascular Project. *JAMA.* 1999;281:627–633.
9. Krumholz HM, Chen J, Rathore SS, et al. Regional variation in the treatment and outcomes of myocardial infarction: investigating New England's advantage. *Am Heart J.* 2003;146:242–249.
10. Krumholz HM, Radford MJ, Wang Y, et al. National use and effectiveness of beta-blockers for the treatment of elderly patients after acute myocardial infarction: National Cooperative Cardiovascular Project. *JAMA.* 1998;280:623–629.
11. Subramanian U, Weinberger M, Eckert GJ, et al. Geographic variation in health care utilization and outcomes in veterans with acute myocardial infarction. *J Gen Intern Med.* 2002;17:604–611.
12. Krim SR, Vivo RP, Krim NR, et al. Regional differences in clinical profile, quality of care, and outcomes among Hispanic patients hospitalized with acute myocardial infarction in the Get With The Guidelines–Coronary Artery Disease (GWTG-CAD) registry. *Am Heart J.* 2011;162:988–995.
13. Quan H, Drosler S, Sundararajan V, et al. Adaptation of AHRQ Patient Safety Indicators for Use in ICD-10 Administrative Data by an International Consortium. 2008.
14. Khera S, Kolte D, Palaniswamy C, et al. ST-elevation myocardial infarction in the elderly—temporal trends in incidence, utilization of percutaneous coronary intervention and outcomes in the United States. *Int J Cardiol.* 2013;168:3683–3690.
15. US Census Bureau. Census Bureau regions and divisions with state FIPS codes. http://www.census.gov/geo/maps-data/maps/pdfs/reference/us_regdiv.pdf. Published 2010. Accessed February 12, 2013.
16. Francis ML, Varghese JJ, Mathew JM, et al. Outcomes in patients with rheumatoid arthritis and myocardial infarction. *Am J Med.* 2010;123:922–928.
17. Elixhauser A, Steiner C, Harris DR, et al. Comorbidity measures for use with administrative data. *Med Care.* 1998;36:8–27.
18. Healthcare Cost and Utilization Project (HCUP). HCUP Comorbidity Software. Rockville, MD: Agency for Healthcare Research and Quality; September 2013. http://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp. Accessed April 25, 2013.
19. Healthcare Cost and Utilization Project (HCUP). HCUP NIS Description of Data Elements. Rockville, MD: Agency for Healthcare Research and Quality; December 2012. http://www.hcup-us.ahrq.gov/db/nation/nis/nisdde.jsp. Accessed February 12, 2013.
20. Austin PC. Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. *Commun Stat Simulation Comput.* 2009;38:1228–1234.
21. Cavender MA, Rassi AN, Fonarow GC, et al. Relationship of race/ethnicity with door-to-balloon time and mortality in patients undergoing primary percutaneous coronary intervention for ST-elevation myocardial infarction: findings from Get With the Guidelines–Coronary Artery Disease. *Clin Cardiol.* 2013; doi: 10.1002/clc.22213.
22. Bradley EH, Herrin J, Curry L, et al. Variation in hospital mortality rates for patients with acute myocardial infarction. *Am J Cardiol.* 2010;106:1108–1112.
23. Allison JJ, Kiefe CI, Weissman NW, et al. Relationship of hospital teaching status with quality of care and mortality for Medicare patients with acute MI. *JAMA.* 2000;284:1256–1262.
24. Baldwin LM, MacLehose RF, Hart LG, et al. Quality of care for acute myocardial infarction in rural and urban US hospitals. *J Rural Health.* 2004;20:99–108.
25. Fox KA, Goodman SG, Klein W, et al. Management of acute coronary syndromes. Variations in practice and outcome: findings from the Global Registry of Acute Coronary Events (GRACE). *Eur Heart J.* 2002;23:1177–1189.
26. O'Gara PT, Kushner FG, Ascheim DD, et al. 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. *J Am Coll Cardiol.* 2013;61:e78–e140.
27. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet.* 2003;361:13–20.
28. Ko DT, Wang Y, Alter DA, et al. Regional variation in cardiac catheterization appropriateness and baseline risk after acute myocardial infarction. *J Am Coll Cardiol.* 2008;51:716–723.
29. Budaj A, Flasinska K, Gore JM, et al. Magnitude of and risk factors for in-hospital and postdischarge stroke in patients with acute coronary syndromes: findings from Global Registry of Acute Coronary Events. *Circulation.* 2005;111:3242–3247.
30. Reynolds HR, Hochman JS. Cardiogenic shock: current concepts and improving outcomes. *Circulation.* 2008;117:686–697.
31. Wang G, Zhang Z, Ayala C, et al. Cost of hospitalizations with a primary diagnosis of acute myocardial infarction among patients aged 18–64 years in the United States. In: Gaze D, ed. Ischemic Heart Disease. Rijeka, Croatia: InTech; 2013. http://www.intechopen.com/books/ischemic-heart-disease/costs-of-hospitalizations-with-a-primary-diagnosis-of-acute-myocardial-infarction-among-patients-age.
32. Yeh RW, Normand SL, Wang Y, et al. Geographic disparities in the incidence and outcomes of hospitalized myocardial infarction: does a rising tide lift all boats? *Circ Cardiovasc Qual Outcomes.* 2012;5:197–204.
33. Xian Y, Pan W, Peterson ED, et al. Are quality improvements associated with the Get With The Guidelines–Coronary Artery Disease (GWTG-CAD) program sustained over time? A longitudinal comparison of GWTG-CAD hospitals versus non–GWTG-CAD hospitals. *Am Heart J.* 2010;159:207–214.

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