Original Investigation

Association of Inpatient vs Outpatient Onset of ST-Elevation Myocardial Infarction With Treatment and Clinical Outcomes

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IMPORTANCE Reperfusion times for ST-elevation myocardial infarction (STEMI) occurring in outpatients have improved significantly, but quality improvement efforts have largely ignored STEMI occurring in hospitalized patients (inpatient-onset STEMI).

OBJECTIVE To define the incidence and variables associated with treatment and outcomes of patients who develop STEMI during hospitalization for conditions other than acute coronary syndromes (ACS).

DESIGN, SETTING, AND PARTICIPANTS Retrospective observational analysis of STEMIs occurring between 2008 and 2011 as identified in the California State Inpatient Database.

EXPOSURES STEMIs were classified as inpatient onset or outpatient onset based on present-on-admission codes. Patients who had a STEMI after being hospitalized for ACS were excluded from the analysis.

MAIN OUTCOMES AND MEASURES Regression models were used to evaluate associations among location of onset of STEMI, resource utilization, and outcomes. Adjustments were made for patient age, sex, comorbidities, and hospital characteristics. The analysis allowed for the location of inpatient STEMI to have a multiplicative rather than an additive effect for resource utilization since these measures were highly skewed.

RESULTS A total of 62 021 STEMIs were identified in 303 hospitals, of which 3068 (4.9%) occurred in patients hospitalized for non-ACS indications. Patients with inpatient-onset STEMI were older (mean, 71.5 [SD, 13.5] years vs 64.9 [SD, 14.1] years; $P < .001$) and more frequently female (47.4% vs 32%; $P < .001$) than those with outpatient-onset STEMI. Patients with inpatient-onset STEMI had higher in-hospital mortality (33.6% vs 9.2%; adjusted odds ratio (AOR), 3.05; 95% CI, 2.76-3.38; $P < .001$), were less likely to be discharged home (33.7% vs 69.4%; AOR, 0.38; 95% CI, 0.34-0.42; $P < .001$), and were less likely to undergo cardiac catheterization (33.8% vs 77.8%; AOR, 0.19; 95% CI, 0.16-0.21; $P < .001$) or percutaneous coronary intervention (21.6% vs 65%; AOR, 0.23; 95% CI, 0.21-0.26; $P < .001$). Length of stay and inpatient charges were higher for inpatient-onset STEMI (mean length of stay, 13.4 days [95% CI, 12.8-14.0 days] vs 4.7 days [95% CI, 4.6-4.8 days]; adjusted multiplicative effect, 2.51; 95% CI, 2.35-2.69; $P < .001$; mean inpatient charges, $245 000 [95% CI, $235 300-$254 800] vs $129 000 [95% CI, $127 900-$130 100]; adjusted multiplicative effect, 2.09; 95% CI, 1.93-2.28; $P < .001$).

CONCLUSIONS AND RELEVANCE Patients who had a STEMI while hospitalized for a non-ACS condition, compared with those with onset of STEMI as an outpatient, were less likely to undergo invasive testing or intervention and had a higher in-hospital mortality rate.

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Early reperfusion with percutaneous coronary intervention (PCI) or thrombolytic therapy remains the primary goal in the initial treatment of eligible patients presenting to a hospital with ST-elevation myocardial infarction (STEMI). Over the last decade, recognition that this strategy is of critical importance has prompted the development of a number of regional and national initiatives to facilitate and improve systems of care for STEMI. These initiatives, including the Reperfusion of Acute Myocardial Infarction in North Carolina Emergency Departments initiative,[1] the American College of Cardiology (ACC) D2B Alliance,[2] and the American Heart Association (AHA) Mission: Lifeline initiative,[3] have enhanced recognition, reduced time to treatment, improved systems of care, and facilitated access of patients to PCI-capable facilities. Consequently, national median door-to-balloon times improved by more than 30 minutes between 2005 and 2010.[4]

ACS *acute coronary syndrome*

CA-SID *California State Inpatient Database*

ICD-9-CM International Classification of Diseases, Ninth Revision, Clinical Modification

PCI *percutaneous coronary intervention*

STEMI *ST-elevation myocardial infarction*

These initiatives have focused exclusively on patients who develop STEMI outside of a hospital setting (outpatient-onset STEMI), and little is known about the incidence and outcomes of STEMI in patients hospitalized for non-acute coronary syndrome (ACS) conditions (inpatient-onset STEMI). Large national databases set up for quality improvement such as the National Cardiovascular Data Registry's ACTION Registry-Get With The Guidelines exclude patients who develop STEMI while already hospitalized.[5]

A recent single-center study found that patients who develop inpatient-onset STEMI were older and more often female, had more comorbidities, were less likely to receive reperfusion therapy, had longer electrocardiogram-to-first-device activation times, and were less likely to survive than patients with an outpatient STEMI.[6] In the current study, we aimed to define the incidence and outcomes of inpatient-onset STEMI in a large multicenter cohort. In addition, we sought to understand the variables that are associated with the development of inpatient-onset STEMI, which may be potential targets for strategies to improve processes and systems of care for this population.

Methods

Data Source

We examined admissions to nonfederal hospitals in the state of California using 2008-2011 discharge data from the State Inpatient Database (CA-SID), which were obtained from the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality.[7] The CA-SID is an all-payer administrative database including 100% of the state's inpatient discharge records. For the purpose of this study, all records were used except those from stand-alone psychiatric hospitals, stand-alone physical and substance use rehabilitation facilities, and individuals younger than 18 years. Each CA-SID record includes (1) basic demographic information, including age, sex, race, and primary payer; (2) up to 30 *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnosis codes; (3) up to 21 *ICD-9-CM* procedure codes; and (4) outcome information, such as discharge disposition, length of stay, and inpatient charges. The CA-SID contains an indicator of whether each discharge diagnosis code was present on admission, which enabled the classification of each STEMI as inpatient-onset or outpatient-onset. The CA-SID (covering approximately 12% of the US population) was used rather than a national sample because the Nationwide Inpatient Sample does not contain present-on-admission information, which would have made it unsuitable for this analysis.

The University of North Carolina at Chapel Hill Institutional Review Board exempted this study from review.

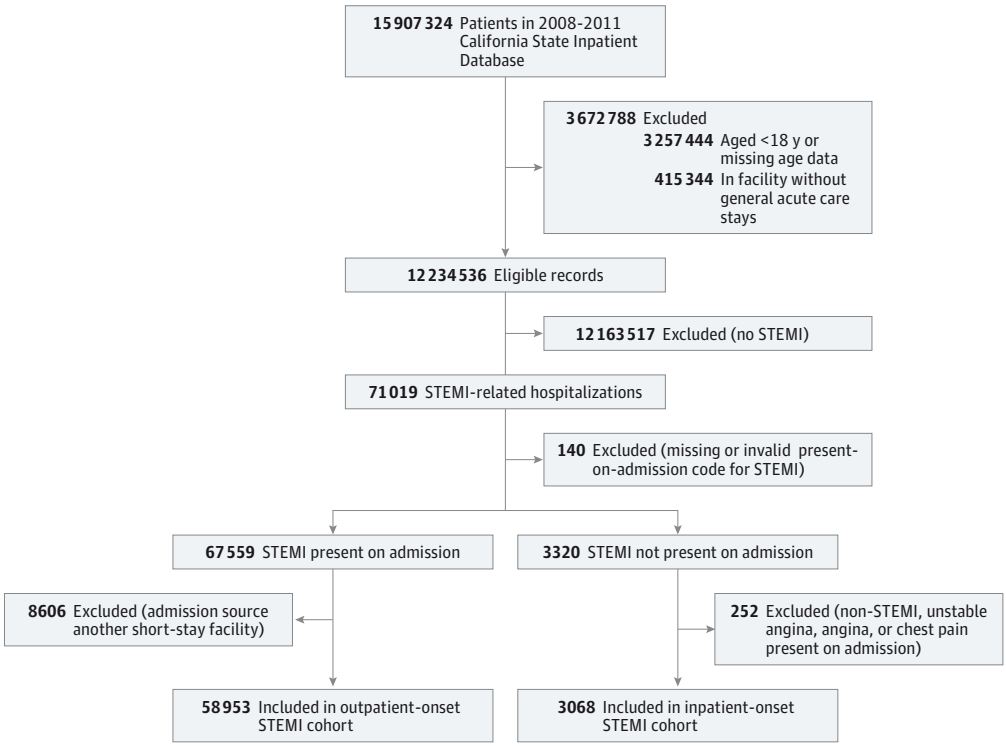
Identification of STEMI-Related Hospital Stays

STEMI-related hospitalizations were identified using *ICD-9-CM* diagnosis codes 410.X1, excluding 410.71 (non-ST-elevation MI) and 410.91 (acute MI, not otherwise specified) in any position. The validity of using this approach for defining MI in administrative data has been previously documented.[8] Admissions were classified as outpatient-onset or inpatient-onset STEMI based on present-on-admission codes (**Figure**). To improve identification of unambiguously inpatient-onset STEMI, we excluded patients with diagnosis codes present on admission that were consistent with non-ST-elevation MI or unstable angina (codes 410.71, 411.1, 411.81, 411.89) as well as angina pectoris or chest pain (codes 413.x, 768.50, 768.51, 786.59). For patients with STEMI recorded as present on admission, we excluded those who were admitted via transfer from another short-stay hospital because we could not discern whether the STEMI was incident at the previous facility (inpatient-onset STEMI) or prior to admission to the previous facility (outpatient-onset STEMI).

Identification of Cohort at Risk of Non–Cardiac Procedure–Related Inpatient-Onset STEMI

To evaluate the association between surgical procedures and risk of inpatient-onset STEMI, we constructed a supplementary cohort, starting with all adult patients hospitalized in acute care hospitals. Patients listed as having ACS, angina, or chest pain present on admission were excluded. For the remaining patients, we examined *ICD-9-CM* procedure codes to identify receipt of surgical procedures listed in current ACC/AHA guidelines on perioperative cardiovascular care.[9] Using these guidelines, *ICD-9-CM* procedure codes were assigned into 3 risk categories (low, intermediate, and vascular/high risk) as well as cardiac surgeries (which were limited to the first 2 days following admission in an effort to identify cardiac surgeries likely preceding STEMI) by 2 investigators (H.B. and L.Z.) with review of

Figure. Identification of STEMI-Related Hospitalizations



STEMI indicates ST-elevation myocardial infarction.

assignments by a third (P.K.); a complete listing of grouped codes is provided in the eTable in the Supplement. Admissions during which patients received multiple surgical procedures that fell into different categories were classified based on the highest-risk surgical procedure. For patients who had a surgical procedure performed and experienced a STEMI during the same hospitalization, the assumption was made that the STEMI occurred subsequent to the surgical procedure. It was thought unlikely that a surgical procedure would have been performed during the same hospitalization following a STEMI.

Identification of STEMI-Related Treatments, Comorbid Conditions, and Other Covariates

Using the data provided in CA-SID records, several additional variables were constructed. Using *ICD-9-CM* procedure codes, we identified potentially STEMI-related treatments provided during the stay, including PCI (codes 00.66, 36.01, 36.02, 36.05, 36.06, 36.07, 36.09) and cardiac catheterization (codes 37.22, 37.23, 88.5x). Comorbid conditions were identified by applying Elixhauser comorbidity criteria to all diagnosis codes listed as present on admission.[10] The original formulation of the Elixhauser criteria excludes comorbidities related to the diagnosis-related group assigned to the inpatient stay; because the objective in this analysis was to identify conditions other than STEMI that were present on admission, we removed this exclusion.

Development of a Model of In-Hospital Mortality Risk

We modeled the association between inpatient mortality and patient age, sex, procedural risk category, and comorbid conditions among patients in the California database who did not experience an inpatient-onset STEMI. Using the resultant regression model, we estimated the risk of inpatient death among patients who did experience an inpatient-onset STEMI and divided these patients into quartiles of risk for ease of presentation. We then evaluated the association between mortality and use of PCI in patients in the different quartiles and fit regression models allowing for interactions between interventional treatment strategies and the quartiles of patient risk.

Statistical Analyses

Unadjusted comparisons between patients with inpatient-onset and outpatient-onset STEMI were made using *t* tests for continuous variables and χ^2 tests for categorical variables as appropriate. To evaluate adjusted comparisons among location of STEMI onset and treatment (PCI and cardiac catheterization), outcomes (in-hospital death and discharge to home), and resource use (length of stay and inpatient charges), regression models were constructed using logistic regression for treatment and outcome end points, a negative binomial model for the length-of stay end point, and a generalized linear model with log link and γ distribution for the charges end point. The analysis allowed the location of

STEMI to have an adjusted multiplicative effect. For example, a multiplicative effect of 1.1 would reflect a 10% increase. All models were adjusted for patient age, sex, comorbid conditions present on admission, and hospital characteristics (**Table 1**). Unadjusted associations between the rate of noncardiac surgical risk class and incidence of inpatient-onset STEMI were assessed using χ^2 tests, while adjusted results were reported using logistic regression. To account for potential correlation of patients within hospitals, clustered standard errors were used in adjusted regression models.

All inferential statistics were performed using α=.05. Significance testing was 2-sided. Data set construction was performed in SAS , version 9.3 (SAS Institute Inc) and statistical analyses in Stata/SE, version 12.1 (StataCorp).

Results

Cohort Characteristics

Between 2008 and 2011 in the state of California, there were approximately 12 million adult hospitalizations in acute care hospitals. After excluding patients who developed STEMI after being hospitalized for an ACS or had a STEMI present on transfer from another facility, 62 021 patients were found to have had a STEMI that was either present on admission (outpatient-onset STEMI group) or occurred while they were hospitalized for a non-ACS condition (inpatient-onset STEMI group) in a total of 303 hospitals (Figure). Of these, 58 953 (95.1%) were outpatient-onset STEMIs and 3068 (4.9%) were inpatient-onset STEMIs. The incidence of inpatient-onset STEMI was 2.7 per 10 000 admissions.

Comparison of Inpatient-Onset and Outpatient-Onset STEMI

Patients with inpatient-onset STEMI were older and more often female and had more comorbidities, including congestive heart failure, chronic lung disease, renal failure, and peripheral vascular disease, than patients with outpatient-onset STEMI (Table 1). The prevalence of hypertension was slightly higher and the prevalence of diabetes without complications slightly lower in the inpatient-onset STEMI group. The prevalence of diabetes with complications was more than twice as high in inpatient-onset STEMI compared with outpatient-onset STEMI.

Risks Factors Associated With Inpatient-Onset STEMI

Both procedural and patient-level factors were associated with onset of STEMI in hospitalized patients (**Table 2**). After adjustment, patients who underwent any surgical procedure as part of their hospitalization had a higher risk of inpatient-onset STEMI compared with those who did not (4.1 vs 2.0 per 10 000 admissions; odds ratio [OR], 2.36; 95% CI, 2.17-2.58). The risk of inpatient-onset STEMI was lowest in patients with no procedures and highest in patients undergoing cardiac surgical procedures (**Table 3**). In total, 49.6% of inpatient-onset STEMIs occurred following a surgical procedure. Congestive heart failure, metastatic cancer, coagulopathy, low-risk surgery, valvular disease, and peripheral vascular disease were other variables associated with developing inpatient-onset STEMI. In adjusted models in which hospitals were divided into quartiles based on number of annual discharges, facility size was not associated with occurrence of inpatient-onset STEMI (P = .63).

Treatment, Clinical Outcomes, and Resource Utilization of Inpatient-Onset STEMI

In unadjusted analyses, patients with inpatient-onset STEMI had worse outcomes and greater resource utilization than patients with outpatient-onset STEMI (**Table 4**). After adjustment for age, sex, comorbidities, and hospital characteristics, patients with inpatient-onset STEMI were less likely than patients with outpatient-onset STEMI to undergo cardiac catheterization (33.8% vs 77.8%; OR, 0.19; 95% CI, 0.16-0.21; P < .001) or PCI (21.6% vs 65%; OR, 0.23; 95% CI, 0.21-0.26; P < .001) (**Table 5**). Inpatient-onset STEMI patients consumed greater resources as indicated by longer length of stay (mean, 13.4 days [95% CI, 12.8-14.0 days] vs 4.7 days [95% CI, 4.6-4.8 days]; adjusted multiplicative effect, 2.51; 95% CI, 2.35-2.69; P < .001) and inpatient charges (mean, $245 000 [95% CI, $235 300-$254 800] vs $129 000 [95% CI, $127 900-$130 100]; multiplicative factor, 2.09; 95% CI, 1.93-2.28; P < .001). Adjusted in-hospital mortality was more than 3 times as high for inpatient-onset STEMI (OR, 3.05; 95% CI, 2.76-3.38; P < .001), and patients were much less likely to be discharged home following an inpatient-onset STEMI (OR, 0.38; 95% CI, 0.34-0.42; P < .001).

Association of PCI With Survival

To determine whether use of PCI or mortality in patients treated with PCI varied with risk, inpatient-onset STEMI patients were divided into quartiles of increasing risk of in-hospital mortality using a model developed from patients in the California database who did not experience an inpatient-onset STEMI. The use of invasive procedures (cardiac catheterization and PCI) decreased in higher-risk quartiles (Table 5). However, patients who received PCI had higher survival in all quartiles vs those who did not (Table 5). Specifically, the OR of mortality associated with PCI in quartile 1 (lowest risk) was 0.26 (95% CI, 0.16-0.40), in quartile 2 was 0.37 (95% CI, 0.28-0.52), in quartile 3 was 0.34 (95% CI, 0.23-0.50), and in quartile 4 was 0.57 (95% CI, 0.41-0.79). A test of linear trend for differences across quartile was nonsignificant (P = .10); in pairwise comparisons only the comparison between quartiles 4 and 1 was statistically significant (P = .003).

Discussion

This multicenter study confirms previously published studies[6,11,12] demonstrating increased mortality among patients who develop inpatient-onset STEMI compared with

Table 1. Baseline Characteristics for STEMI-Related Hospitalizations in California, 2008-2011[a]

Characteristics	Overall (n = 62 021)	Outpatient-Onset STEMI (n = 58 953)	Inpatient-Onset STEMI (n = 3068)	*P* Value[b]
Demographic characteristics				
Age, mean (SD), y	65.2 (14.1)	64.9 (14.1)	71.5 (13.5)	<.001
Female[c]	20 316 (32.8)	18 865 (32.0)	1451 (47.4)	<.001
Race/ethnicity[c]				
White	37 701 (63.8)	35 787 (63.7)	1914 (64.9)	<.001
Black	3106 (5.3)	2928 (5.2)	178 (6)	
Hispanic	11 391 (19.3)	10 913 (19.4)	478 (16.2)	
Asian	5069 (8.6)	4756 (8.5)	313 (10.6)	
Native American	38 (0.1)	35 (0.1)	3 (0.1)	
Other	1812 (3.1)	1749 (3.1)	63 (2.1)	
Coronary artery disease risk factors				
Hypertension	40 692 (65.6)	38 588 (65.5)	2104 (68.6)	<.001
Diabetes				
Without chronic complications	15 526 (25)	14 814 (25.1)	712 (23.2)	.02
With chronic complications	3538 (5.7)	3195 (5.4)	343 (11.2)	<.001
Obesity	7582 (12.2)	7279 (12.3)	303 (9.9)	<.001
Current smoker	14 337 (23.1)	14 032 (23.8)	305 (9.9)	<.001
Former smoker	8445 (13.6)	7964 (13.5)	481 (15.7)	<.001
Major comorbid conditions				
Congestive heart failure	13 456 (21.7)	12 546 (21.3)	910 (29.7)	<.001
Valvular disease	5358 (8.6)	4941 (8.4)	417 (13.6)	<.001
Pulmonary circulation disease	1598 (2.6)	1427 (2.4)	171 (5.6)	<.001
Peripheral vascular disease	5056 (8.2)	4490 (7.8)	466 (15.2)	<.001
Paralysis	1313 (2.1)	1134 (1.9)	179 (5.8)	<.001
Other neurological disorders[d]	3261 (5.3)	2948 (5)	313 (10.2)	<.001
Chronic pulmonary disease	9452 (15.2)	8718 (14.8)	734 (23.9)	<.001
Hypothyroidism	4861 (7.8)	4483 (7.6)	378 (12.3)	<.001
Renal failure	7880 (12.7)	7075 (12)	805 (26.2)	<.001
Liver disease	1104 (1.8)	964 (1.6)	140 (4.6)	<.001
AIDS	160 (0.3)	152 (0.3)	8 (0.3)	.98
Lymphoma	296 (0.5)	257 (0.4)	39 (1.3)	<.001
Metastatic cancer	738 (1.2)	552 (0.9)	186 (6.1)	<.001
Solid tumor without metastasis	921 (1.5)	811 (1.4)	110 (3.6)	<.001
Peptic ulcer	30 (0.1)	25 (0.1)	5 (0.2)	.03
Rheumatoid arthritis	1131 (1.8)	1039 (1.8)	92 (3)	<.001
Coagulopathy	1859 (3)	1613 (2.7)	246 (8)	<.001
Weight loss	1464 (2.4)	1171 (2.0)	294 (9.6)	<.001
Fluid and electrolyte disorders	8748 (14.1)	7884 (13.4)	864 (28.2)	<.001
Chronic blood loss anemia	437 (0.7)	359 (0.6)	78 (2.5)	<.001
Deficiency anemia	8144 (13.1)	7296 (12.4)	848 (27.6)	<.001
Depression	2907 (4.7)	2694 (4.6)	213 (6.9)	<.001
Psychosis	1286 (2.1)	1175 (2.0)	111 (3.6)	<.001
Alcohol abuse	2145 (3.5)	2000 (3.4)	145 (4.7)	<.001
Drug abuse	1906 (3.1)	1842 (3.1)	64 (2.1)	<.001
Hospital characteristics				
PCI capability	53 168 (85.7)	50 979 (86.5)	2189 (71.4)	<.001
Diagnostic cardiac catheterization only	3645 (5.9)	3345 (5.7)	300 (9.8)	<.001
No cardiac catheterization capability	5208 (8.4)	4629 (7.9)	579 (18.9)	<.001
Facility size, based on annual discharges[e]				<.001
Quartile 1 (lowest)	419 (0.7)	340 (0.6)	79 (2.6)	
Quartile 2	5638 (9.1)	5253 (8.9)	381 (12.4)	
Quartile 3	16 667 (26.9)	15 821 (26.8)	846 (27.6)	
Quartile 4 (highest)	39 301 (63.4)	3739 (63.7)	1762 (57.4)	

Abbreviations: PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

[a] Data are expressed as No. (%) of patients unless otherwise indicated.

[b] *P* values for comparison of outpatient-onset STEMI vs inpatient-onset STEMI by *t* test for continuous variables and χ^2 test for binary/categorical variables.

[c] Values were missing for sex (n=59) and race/ethnicity (n=2904).

[d] Other neurological disorders is a specific term defined by the Healthcare Cost and Utilization Project.

[e] The mean number of annual discharges was 1422 (range, 172-2228) for quartile 1, 4561 (range, 2249-6111) for quartile 2, 9627 (range, 6112-12 680) for quartile 3, and 19 392 (range, 12 762-47 502) for quartile 4.

Table 2. Associations Between Patient Demographic and Clinical Characteristics and Occurrence of STEMI During Hospitalizations for Non–Acute Coronary Syndrome Conditions

Characteristics	Adjusted Odds Ratio (95% CI)[a]	*P* Value
Cardiac surgery[b]	24.44 (19.41-30.78)	<.001
High-risk/vascular surgery[b]	3.48 (2.82-4.30)	<.001
Intermediate-risk surgery[b]	2.15 (1.4-2.38)	<.001
Low-risk surgery[b]	1.56 (1.37-1.79)	<.001
Age, per y	1.03 (1.03-1.04)	<.001
Female	0.76 (0.71-0.82)	<.001
Comorbid conditions[c]		
AIDS	1.41 (0.76-2.61)	.28
Chronic pulmonary disease	1.10 (1.00-1.21)	.04
Coagulopathy	1.58 (1.37-1.82)	<.001
Congestive heart failure	1.71 (1.53-1.91)	<.001
Diabetes		
Without chronic complications	1.19 (1.09-1.30)	<.001
With chronic complications	1.26 (1.09-1.45)	.002
Fluid and electrolyte disorders	1.29 (1.19-1.40)	<.001
Hypertension	1.21 (1.10-1.32)	<.001
Hypothyroidism	0.85 (0.76-0.96)	.008
Liver disease	1.02 (0.84-1.23)	.87
Lymphoma	1.15 (0.84-1.57)	.39
Metastatic cancer	1.74 (1.50-2.02)	<.001
Obesity	1.00 (0.89-1.13)	.97
Paralysis	1.37 (1.18-1.59)	<.001
Peptic ulcer disease	2.05 (0.89-4.76)	.09
Peripheral vascular disease	1.46 (1.31-1.63)	<.001
Pulmonary circulation disease	0.94 (0.78-1.12)	.48
Renal failure	1.15 (1.04-1.26)	.005
Rheumatoid arthritis	1.14 (0.95-1.38)	.17
Solid tumor without metastasis	1.23 (1.02-1.48)	.03
Valvular disease	1.36 (1.21-1.52)	<.001
Weight loss	1.26 (1.09-1.45)	.002

Abbreviation: STEMI, ST-elevation myocardial infarction.

[a] Adjustment was made for the variables listed in the table plus smoking status, facility characteristics, chronic blood loss anemia, deficiency anemia, psychosis, alcohol abuse, drug abuse, and calendar year.

[b] The comparator group is hospitalized patients who did not undergo surgery.

[c] For all variables, the comparator group is patients without STEMI.

Table 3. Covariate-Adjusted Incidence of STEMI Stratified by ACC/AHA Procedural Risk Classification

	Incidence Per 10 000 Admissions, Mean (SD)
No surgery	2.0 (0.1)
Low-risk surgery[a]	3.1 (0.2)
Intermediate-risk surgery[a]	4.2 (0.2)
High-risk/vascular surgery[a]	6.9 (0.7)
Cardiac surgery	47.7 (5.2)

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; STEMI, ST-elevation myocardial infarction.

[a] Compared with hospitalized patients who did not undergo surgery.

outpatient-onset STEMI. To the best of our knowledge, the present study is the largest of its kind and the only multicenter study specifically assessing the incidence and variables associated with outcomes of patients developing STEMI while hospitalized for a non-ACS condition.

In California between 2008 and 2011, patients developing inpatient-onset STEMI had more than 3-fold greater in-hospital mortality than those with outpatient-onset STEMI (33.6% vs 9.2%; $P < .001$). In a recent single-center study of patients developing inpatient-onset STEMI after admission for other non-ACS conditions, mortality was 39.6% for inpatient-onset STEMI vs 4% for outpatient-onset STEMI.[6] In the Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) study, which prospectively registered 5888 patients with STEMI in 54 hospitals in southwest Germany, inpatient-onset STEMI had a 2-fold higher in-hospital mortality compared with outpatient-onset STEMI (27.3% vs 13.9%).[11] Unlike the present study, the MITRA study included patients with inpatient-onset STEMIs who were admitted with either stable or unstable angina. A retrospective study of 7054 veterans hospitalized for acute MI (STEMI and non-STEMI) in 127 Veterans Affairs hospitals between July 2003 and August 2004 found that the 792 (11.2%) inpatient-onset acute MIs were at a much higher risk of in-hospital and 30-day mortality compared with outpatient-onset acute MI.[13] Recently, data from 3795 consecutive patients with STEMI treated at a single center between March 2003 and January 2013 were reported.[12] The 83 patients with inpatient-onset STEMI who were described had a higher 1-year mortality compared with those with outpatient-onset STEMI who presented via emergency medical services (16.9% vs 10.3%).

The difference in mortality in the current study between those with inpatient-onset STEMI and outpatient-onset STEMI is at least partially related to those already hospitalized being older, having more comorbid conditions, and having a concurrent illness or recent surgery. However, significant differences in outcomes remained after adjustment for age, sex, and comorbidities. Although it is impossible to completely adjust for confounders in an observational study, other potential reasons for differences in mortality should be considered. One of these is the lower utilization of cardiac catheterization and primary PCI in inpatient-onset STEMI. Although primary PCI has not been studied in inpatient-onset STEMI, data from outpatient-onset STEMI show that reperfusion in general and primary PCI in particular improves outcomes.[14,15] While the inpatient-onset STEMI population has a higher percentage of patients compared with those with outpatient-onset STEMI, who are not candidates for primary PCI because of excessive risk of bleeding, acute neurological symptoms, family and/or patient wishes, and/or severe comorbidities,[6] there are few data to guide these decisions.

This study demonstrates that mortality associated with inpatient-onset STEMI was progressively higher in patients deemed at higher risk (based on a model developed from patients in the California database who did not experience an inpatient-onset STEMI). Invasive procedures were used

Table 4. Treatments and Outcomes in Patients With STEMI by Location of Onset

	Overall (n = 62 021)	Outpatient-Onset STEMI (n = 58 953)	Inpatient-Onset STEMI (n = 3068)	Unadjusted Odds Ratio (95% CI)[a]	Adjusted Odds Ratio (95% CI)[a]	*P* Value
Inpatient mortality, No. (%)	6476 (10.4)	5446 (9.2)	1030 (33.6)	4.95 (4.52-5.43)	3.05 (2.76-3.38)	<.001
Length of hospital stay, mean (SD), d	5.2 (5.1-5.2)	4.7 (4.7-4.8)	13.4 (12.8-14.0)	2.83 (2.67-3.01)	2.51 (2.35-2.69)	<.001
Hospital charges, mean (SD), $, in thousands	134.5 (133.3-135.6)	129.0 (127.9-130.1)	245.0 (235.3-254.8)	1.90 (1.76-2.05)	2.09 (1.93-2.28)	<.001
Patients discharged home, No. (%)	41 914 (67.6)	40 880 (69.4)	1034 (33.7)	0.22 (0.20-0.25)	0.38 (0.34-0.42)	<.001
Use of cardiac catheterization, No. (%)	46 918 (75.7)	45 881 (77.8)	1037 (33.8)	0.15 (0.13-0.17)	0.19 (0.16-0.21)	<.001
Use of PCI, No. (%)	38 979 (62.9)	38 317 (65.0)	662 (21.6)	0.15 (0.13-0.17)	0.23 (0.21-0.26)	<.001

Abbreviations: PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

[a] Results are presented as odds ratios for death, home, PCI, and cardiac catheterization and as multiplicative effect (eg, 2.0 = doubling) for length of stay and charges outcomes. Adjustment was made for patient age, sex, facility characteristics, and comorbid conditions present on admission. Values were missing for mortality (n=2), length of hospital stay (n=3), and hospital charges (n=5043).

Table 5. Use of PCI and Mortality in Patients With Inpatient-Onset STEMI Stratified by Risk of In-Hospital Mortality[a]

	Quartile 1 (n = 766)	Quartile 2 (n = 766)	Quartile 3 (n = 766)	Quartile 4 (n = 765)
Predicted mortality rate, mean (range), %	1.13 (0.19-1.71)	2.38 (1.72-3.17)	4.38 (3.18-6.08)	12.76 (6.09-58.21)
Use of cardiac catheterization, No. (mean %) [95% CI]	358 (46.7) [43.2-50.3]	287 (37.5) [34.0-41.0]	212 (27.7) [24.5-31.0]	179 (23.4) [20.4-26.5]
Use of PCI, No. (mean %) [95% CI]	242 (31.6) [28.3-35.0]	184 (24.0) [21.0-27.2]	127 (16.6) [14.0-19.4]	109 (14.2) [11.8-16.9]
Mortality without PCI, No. (mean %) [95% CI]	138 (26.3) [22.6-30.3]	208 (35.7) [31.8-39.8]	256 (40.1) [36.2-44.0]	294 (44.8) [41.0-48.7]
Mortality with PCI, No. (mean %) [95% CI]	26 (10.7) [7.1-15.3]	39 (21.2) [15.5-27.8]	30 (23.6) [16.5-32.0]	36 (33.0) [24.3-42.7]

Abbreviations: PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

[a] The association between in-hospital mortality and patient age, sex, procedural risk category, and comorbid conditions was modeled among patients in the California database who did not experience an inpatient STEMI. Using the resultant regression model, the risk of in-hospital death was determined among patients with an inpatient STEMI and the patients were divided into 4 quartiles of risk. The sum of the quartiles is 3063 rather than 3068 because 5 observations were missing information on sex, so the patient could not be assigned to a risk quartile. For all quartiles, mortality was higher without PCI than with PCI ($P < .001$).

less frequently in patients with inpatient-onset STEMI in higher risk quartiles but the use of PCI was associated with higher rates of survival in all risk quartiles, suggesting that in appropriately selected patients, PCI may be of benefit even among patients with comorbid conditions that increase their risk of mortality.

The question of how to improve outcomes and define optimum treatment in hospitalized patients who experience a STEMI is an area that merits more attention and concern. Although there have been improvements in treatment times and clinical outcomes in outpatients who have onset of STEMI, few initiatives have focused on optimizing care of hospitalized patients with onset of STEMI after admission. Previous studies[6,11-13] point toward the likelihood that process measures, such as time from onset of symptoms to electrocardiogram and time from symptom onset to device activation, play an important role in outcomes in this population. Extrapolation of data from outpatient-onset STEMI would suggest that any benefit with reperfusion would be dependent on the rapidity of restoring flow.[14,15] Thus, for patients who are candidates for reperfusion, it is likely that delays in initiating treatment have a negative effect on outcomes. A previous study found significant delays in recognition of inpatient-onset STEMI, obtaining an electrocardiogram, interpreting the electrocardiogram, and making the decision to perform emergency coronary angiography.[6] In contrast to these delays observed with recognition and decision making, once the STEMI team was activated, there was no difference in reperfusion times between inpatient-onset and outpatient-onset STEMI. Garberich et al,[12] reporting data from a single-center registry of patients diagnosed as having STEMI after hospital admission, showed that implementation of a standard STEMI protocol for inpatient-onset STEMI was associated with reduced in-hospital mortality (from 15.4% to 5.3%), with a moderate decrease in median reperfusion times (from 85 minutes to 67 minutes). These data demonstrate that systems designed to improve care of inpatient-onset STEMI have the potential for a significant beneficial effect on mortality.

There is no regional or national database that collects information on process measures in inpatient-onset STEMI. Large national databases set up for quality improvement specifically exclude patients who develop STEMI while already hospitalized. Development of a reporting infrastructure, either through existing databases or programs established for this purpose, is needed to enhance understanding of inpatient-onset STEMI.

Multivariable analysis identified several "risk factors" associated with inpatient-onset STEMI. There were the traditional risk factors associated with cardiovascular disease, including age, male sex, diabetes, hypertension, and peripheral vascular disease. There were also several factors that have not previously been associated with acute MI, including paralysis, hypothyroidism, weight loss, and metastatic cancer. These results remained significant after adjustment for age, sex, and comorbidities. Further studies are needed to define what role these conditions play in increasing the risk of acute coronary thrombosis.

We found that the risk of inpatient-onset STEMI increased with the complexity of surgical procedures as defined by the 2007 ACC/AHA perioperative guidelines (unchanged in the 2009 focused update).[9] These results mimic studies designed to identify patients at risk of perioperative MI and provide further evidence of the discriminative power of the categories defined by the guidelines.

Our study has several limitations. It is a retrospective observational analysis, and identification of STEMI cases and location of onset were based on administrative data rather than adjudicated end points. The data set does not have information on admitting diagnoses, elective vs urgent admission, or mortality following discharge. It is possible that the numbers presented herein underrepresent the problem, as patients with inpatient-onset STEMI might have died prior to diagnosis. Unobserved case-mix measures likely confound the estimated association between inpatient-onset STEMI and mortality. If the unobserved case-mix severity is greater for inpatient STEMI, then our results may overestimate the potential effect of having an inpatient STEMI on mortality and other outcomes. Furthermore, incomplete coding of comorbid conditions on hospital claims may limit our ability to completely control for severity of disease. The estimated associations remain large, however, even after adjustment for observed covariates, suggesting that some portion of the difference in outcomes may be due to delayed recognition and/or lack of revascularization in inpatient STEMI. The database does not have information on cause-specific mortality, so it is unknown whether mortality was related to STEMI. The most recent data in the CA-SID at the time of this study were from 2011 and it is unknown whether the study findings reflect current outcomes. We chose to focus on PCI as a reperfusion strategy because the limitations of the administrative database prevented us from determining how many STEMI patients were treated with thrombolytic therapy. Thrombolytic therapy is commonly used to treat select outpatient-onset STEMI at facilities that do not have PCI capability. The limitations of the database also prevented us from determining how many patients with inpatient-onset STEMI would not have been candidates for thrombolytic therapy because of elevated bleeding risk.

Conclusions

In this multicenter observational study, approximately 5% (2.7 per 10 000 admissions) of all STEMIs occurred in patients hospitalized for non-ACS conditions. Patients who developed STEMI while hospitalized for a non-ACS condition, compared with those with onset of STEMI as an outpatient, were less likely to undergo invasive testing or intervention and had a higher in-hospital mortality rate.

ARTICLE INFORMATION

Author Contributions: Dr Federspiel had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Kaul, Federspiel, Dai, Steams, Yeung, Stouffer.
Acquisition, analysis, or interpretation of data: Kaul, Federspiel, Smith, Yeung, Beyhaghi, Zhou, Stouffer.
Drafting of the manuscript: Kaul, Federspiel, Beyhaghi, Zhou, Stouffer.
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Statistical analysis: Kaul, Federspiel, Steams.
Obtained funding: Federspiel, Stouffer.
Administrative, technical, or material support: Kaul, Beyhaghi, Zhou.
Study supervision: Kaul, Yeung, Stouffer.

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REFERENCES

1. Jollis JG, Roettig ML, Aluko AO, et al; Reperfusion of Acute Myocardial Infarction in North Carolina Emergency Departments Investigators. Implementation of a statewide system for coronary reperfusion for ST-segment elevation myocardial infarction. *JAMA*. 2007;298(20):2371-2380.

2. Krumholz HM, Bradley EH, Nallamothu BK, et al. A campaign to improve the timeliness of primary percutaneous coronary intervention: Door-to-Balloon: An Alliance for Quality. *JACC Cardiovasc Interv*. 2008;1(1):97-104.

3. Jacobs AK, Antman EM, Faxon DP, Gregory T, Solis P. Development of systems of care for ST-elevation myocardial infarction patients: executive summary. *Circulation*. 2007;116(2):217-230.

4. Krumholz HM, Herrin J, Miller LE, et al. Improvements in door-to-balloon time in the United States, 2005 to 2010. *Circulation*. 2011;124 (9):1038-1045.

5. Peterson ED, Roe MT, Rumsfeld JS, et al. A call to ACTION (Acute Coronary Treatment and Intervention Outcomes Network): a national effort to promote timely clinical feedback and support continuous quality improvement for acute myocardial infarction. *Circ Cardiovasc Qual Outcomes*. 2009;2(5):491-499.

6. Dai X, Bumgarner J, Spangler A, Meredith D, Smith SC, Stouffer GA. Acute ST-elevation

myocardial infarction in patients hospitalized for noncardiac conditions. *J Am Heart Assoc*. 2013;2(2):e000004.

7. *Healthcare Cost and Utilization Project State Inpatient Databases*. Rockville, MD: Agency for Healthcare Research and Quality; 2005-2009.

8. McCormick N, Lacaille D, Bhole V, Avina-Zubieta JA. Validity of myocardial infarction diagnoses in administrative databases: a systematic review. *PLoS One*. 2014;9(3):e92286.

9. Fleisher LA, Beckman JA, Brown KA, et al; American College of Cardiology; American Heart Association Task Force on Practice Guidelines (writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery); American Society of Echocardiography; American Society of Nuclear Cardiology; Heart Rhythm Society; Society of Cardiovascular Anesthesiologists; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology; Society for Vascular Surgery. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. *J Am Coll Cardiol*. 2007;50(17):e159-e241.

10. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care*. 1998;36(1):8-27.

11. Zahn R, Schiele R, Seidl K, et al; Maximal Individual Therapy in Acute Myocardial Infarction Study Group. Acute myocardial infarction occurring in vs out of the hospital: patient characteristics and clinical outcome. *J Am Coll Cardiol*. 2000;35(7):1820-1826.

12. Garberich RF, Traverse JH, Claussen MT, et al. ST-elevation myocardial infarction diagnosed after hospital admission. *Circulation*. 2014;129(11):1225-1232.

13. Maynard C, Lowy E, Rumsfeld J, et al. The prevalence and outcomes of in-hospital acute myocardial infarction in the Department of Veterans Affairs Health System. *Arch Intern Med*. 2006;166(13):1410-1416.

14. De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. *Circulation*. 2004;109(10):1223-1225.

15. McNamara RL, Wang Y, Herrin J, et al; NRMI Investigators. Effect of door-to-balloon time on mortality in patients with ST-segment elevation myocardial infarction. *J Am Coll Cardiol*. 2006;47(11):2180-2186.