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Emergency Department Administration of Thienopyridines in NSTEMI: Results from the ACTION Registry®-GWTG™ Registry

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Abstract

Objective—AHA/ACC guidelines recommend that patients with definite unstable angina or non-ST segment elevation myocardial infarction (NSTEMI) receive dual antiplatelet therapy on presentation to the hospital when undergoing early invasive management or “as soon as possible” after admission when being managed conservatively. The guidelines do not specify whether these medications should be administered in the emergency department (ED). Our aim was to determine whether ED administration of a thienopyridine was associated with clinical outcomes among patients with NSTEMI.

Methods—We examined thienopyridine use in 39,454 patients with NSTEMI who received a thienopyridine within 24 hours of presentation in the NCDR's ACTIONRegistry®-GWTG™ from 1/2007–6/2010. Patients who were not seen initially in the ED, were transferred in, or were missing time data were excluded. We analyzed the association between ED administration of thienopyridines and outcomes and patient demographics.

Results—Of the cohort receiving a thienopyridine within 24 hours, 9534 (24.2%) received it in the ED. ED administration of a thienopyridine was not associated with in-hospital major bleeding

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(multivariable adjusted OR 0.99; 95% confidence interval [CI]: 0.91–1.09) or in-hospital mortality (adjusted 1.02, 95% CI 0.86–1.20). Independent predictors most strongly associated with ED thienopyridine administration were elevated troponin, ED length of stay, prior percutaneous coronary intervention, and initial electrocardiogram showing ischemic changes.

Conclusions—There was no association between ED thienopyridine administration and in-hospital major bleeding or mortality. ED length of stay, ECG changes and elevated troponin were associated with ED thienopyridine administration.

Keywords

Thienopyridines; Non-ST segment elevation myocardial infarction; Outcomes

Introduction

Background

Thienopyridines reduce major adverse cardiac events in patients with acute coronary syndromes. Based on the results of multiple clinical trials (1), the updated American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for Non-ST-elevation Myocardial Infarction (NSTEMI)/Unstable Angina recommend that thienopyridines be administered as soon as possible after presentation in patients managed with a conservative strategy and at presentation in patients at high or medium risk for whom an invasive strategy planned.(2, 3) An invasive strategy is generally preferred for patients who have high cardiac risk scores, elevated cardiac biomarkers, and new or presumed new ST-segment depression. (2–3)

Importance

In many hospitals in which patients with NSTEMI undergo diagnostic catheterization within 24 hours of admission, thienopyridines are commonly withheld until it is clear that the patient will not need coronary artery bypass graft (CABG) surgery.(2) This well-documented practice results in differences between local practice and guideline based recommendations.(4, 5)

Goals of This Investigation

Using data from the National Cardiovascular Data Registry Acute Coronary Treatment and Intervention Outcomes Network-Get With The Guidelines Registry (ACTION Registry®-GWTG™), our primary aim was to determine whether ED administration of a thienopyridine was associated with in-hospital mortality and/or in-hospital major bleeding. Secondarily, we wanted to determine presenting factors predictive of ED thienopyridine administration.

Methods

Study Design and Setting

This is a retrospective analysis that utilized data from ACTION Registry®-GWTG™, a nationally representative, quality improvement MI registry that began enrolling patients

January 1, 2007.(6) Patients with a primary diagnosis of acute MI – either STEMI or NSTEMI - presenting within 24 hours of the onset of an ischemic syndrome were eligible to be included in the registry. At each participating site, this registry was either approved by an institutional review board or considered quality assurance data not subject to institutional review board approval.

Selection of Participants

From January 1, 2007 to June 30, 2010, 430 hospitals enrolled a total of 205,718 patients with acute MI (NSTEMI or STEMI). Patients were excluded from this analysis for the following reasons (Supplement Table 1): patients who were transferred in, who had STEMI, whose sex was unknown, who did not receive a thienopyridine or received one >24 hours after presentation, who presented to locations other than the ED, who had missing data regarding time of thienopyridine administration, who were given both clopidogrel and prasugrel, and who had data collected only on the ACTION Registry®-GWTG™ Limited form. The ACTION Registry®-GWTG™ Limited form is a condensed form intended for transferred patients that does not contain data on all the outcomes we included.

Methods and Measurements

Data were extracted to a web-based case record form from existing medical records using a trained data collector. Standardized references have been provided at (http://www.ncdr.com/WebNCDR/NCDRDocuments/ACTION_v2_CodersDataDictionary_2.1.1.pdf). The proportion of patients taking medications was based on ideal candidates, determined by excluding those who had listed contraindications to that specific therapy. Endpoints were reported by sites and were not centrally adjudicated. Audits from this registry report 90% agreement between the NCDR-ACTION variable definitions and the hospital chart.(7)

Outcome measures

The primary outcome measures were in-hospital mortality and major bleeding. Major bleeding was defined as an absolute Hemoglobin (Hgb) drop of ≥ 4 g/dL (initial to nadir), intracranial hemorrhage, documented or suspected retroperitoneal bleed, any red cell blood transfusion with the baseline Hgb ≥ 9 g/dL, or a Hgb <9 g/dL and a suspected bleeding event. Given that a majority of patients undergoing CABG receive blood transfusions related to the surgery, bleeding events were considered only if they occurred prior to CABG. Additional details regarding the ACTION Registry – GWTG in-hospital major bleeding risk model have been described previously.(8)

The predictor variable was the ED administration of a thienopyridine. Patients were categorized as receiving ED administration of a thienopyridine when the time of drug administration of clopidogrel or prasugrel was before the time of transfer from the ED, and within 24 hours of presentation. Patients were categorized as receiving early postED administration of a thienopyridine when the start time of clopidogrel or prasugrel was after time of transfer from the ED but within 24 hours of hospital presentation. Because some patients may have taken thienopyridines prior to arrival and had their first or loading dose adjusted accordingly, all thienopyridine doses were included.

Analysis

Hospital and patient characteristics were compared between patients with ED administration of thienopyridine and those with early post-ED administration. Continuous variables are presented as median (25th, 75th percentiles) and categorical variables are presented as percentages. Additionally, odds ratios and 95% confidence intervals (CIs) are presented for the association of hospital and patient characteristics and ED administration of a thienopyridine. To evaluate the association between quality metrics, acute treatments and thienopyridine use by site, the Spearman rank correlation coefficient and 95% (CIs) were calculated for each variable at the site level.

To investigate the association between in-hospital mortality and major bleeding with ED thienopyridine administration, a logistic generalized estimating equations (GEE) method with exchangeable working correlation matrix was used to account for within-hospital clustering because patients at the same hospital are more likely to have similar treatments relative to patients at other hospitals (i.e., within-center correlation for treatments).(9) This method produces estimates similar to those from ordinary logistic regression, but variances are adjusted for the correlation of outcomes within a hospital. Continuous variables that became non-linear or flat in relationship ED administration of thienopyridines were fit with linear splines or truncated, respectively. For all covariates included in the model, the percent of missing data was less than 2%. Missing variables were imputed to the most frequently occurring group for categorical variables and to the median for continuous variables. Missing weight, initial serum creatinine and initial hemoglobin were imputed to the sex-specific median of the non-missing values. Variables included in the adjusted models were from the validated ACTION in-hospital mortality and major bleeding models. (8, 10) Variables in the ACTION in-hospital mortality model (10) included: age, systolic blood pressure on presentation, heart rate on presentation, height of initial troponin elevation, initial serum creatinine, heart failure (HF only on admission, shock only or HF with shock on admission, vs. None), electrocardiogram (ECG) findings (ST-segment changes vs. No ST-segment changes), and prior peripheral arterial disease (PAD). Variables in the ACTION in-hospital major bleeding model (8) include: age, gender, weight, heart rate on presentation, systolic blood pressure on presentation (SBP≤130 mmHg, SBP 130–160 mmHg and SBP>=160 mmHg), initial Hbg <12 g/dL (vs. ≥12 g/dL), initial serum creatinine, ECG findings (ST-segment changes vs. No ST-segment changes), HF on presentation (HF only, Shock only or HF with Shock, vs. None), diabetes, PAD, and home warfarin. Adjusted associations for outcomes were displayed as odds ratios (OR) (95% confidence intervals [CI]).

To identify factors associated with ED administration of thienopyridines, a hierarchical logistic regression model was used to adjust for patient level risk factors as well as hospital level factors. Candidate patient factors included in this model included patient demographics, baseline medical history, home medications, vital signs at presentation, and diagnostic test results (including height of initial troponin elevation). To account for variations in hospital practice patterns, we included hospital region, rural/urban location, teaching status, and size. These candidate variables were selected based on clinical relevance.(11–14) The following interactions were also included: age and risk factors;

gender and baseline troponin ratio and region; and hospital size and hospital teaching status. Although all variables were considered to be clinically relevant, backward selection with a stay criterion of 0.05 significance level was used to identify patient and hospital level factors associated with ED administration of thienopyridines.

All analyses were performed using SAS software (version 9.2, SAS Institute, Cary, North Carolina, USA).

Funding Source and Role of the Sponsors

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Results

Characteristics of Study Subjects

Of the 39,454 NSTEMI patients enrolled in ACTION Registry®-GWTG™ who met inclusion criteria (Supplement Figure 1), 9534 (24.2%) received a thienopyridine in the ED. Clopidogrel was the thienopyridine administered in 98.6% of patients, with the remaining receiving prasugrel. The median time to thienopyridine administration was 2.48 hours (IQR 1.33, 4.27) and 11.33 (IQR 6.67, 16.9) in those who received a thienopyridine in the ED and outside the ED, respectively. (Table I) The median length of ED stay was 4.5 hours (IQR 2.9, 7.2) in those with ED administration and 3.7 hours (IQR 2.5, 5.2) in those with non-ED administration ($p<0.001$).

Main Results

Clinical Outcomes—In univariable analyses, no clinical differences were observed with respect to major bleeding between patients with thienopyridine administered in the ED or outside of the ED. There was a clinically small but statistically significant difference in in-hospital mortality between patients with ED or non-ED administration (2.2% vs 2.4%, OR 0.82, 95% CI 0.69–0.97). After adjusting for variables in the ACTION mortality model, there was no difference in in-hospital mortality (adjusted OR 1.02, 95% CI 0.86–1.20) between groups. Patients with ED administration of thienopyridines did have a higher percentage of blood transfusions (12.0 % vs. 8.8%). However, no difference was noted in major bleeding when adjusting for variables included in the ACTION bleeding model (adjusted OR 0.99, 95% CI 0.91–1.09). For the in-hospital mortality model the c-index is 0.84 and for the in-hospital major bleeding model the c-index is 0.73.

Patient-level Factors Associated with ED Administration of a Thienopyridine—

Distribution of demographics, laboratory values, physical examination parameters and hospital characteristics are presented in Table I. No clinical difference in SBP or heart rate was observed between those patients who did or did not receive a thienopyridine in the ED. In contrast, patients who did not receive a thienopyridine in the ED had a higher prevalence of diabetes and more prior cardiovascular disease.

In the adjusted multivariable analysis (Table II), presenting factors independently associated with receiving a thienopyridine in the ED included longer ED length of stay, ischemic ST changes or T wave changes on the initial ECG, and elevated initial troponin levels, and undergoing no intervention or PCI compared to surgery (Table II). In contrast, patients with home thienopyridine use, elevated serum creatinine, a history of heart failure, and a history of stroke were less likely to receive a thienopyridine in the ED.

Procedure Use—Diagnostic catheterization was performed in 80.7% of those with ED administration and in 79.6% of those with post-ED administration of a thienopyridine with no clinical difference in the time to catheterization between the two groups. (Table III) The majority of patients in both groups underwent revascularization, although patients with ED administration of a thienopyridine were less likely to undergo PCI (49.4% vs. 58.1%,) and more likely to undergo a CABG (9.5% vs. 3.8%,) than those with later administration of a thienopyridine.

Hospital Level Associations with ED Administration of a Thienopyridine—

Large variations were observed among hospitals in the proportion of NSTEMI patients receiving thienopyridine in the ED, ranging from 0 to 100% of eligible patients (Figure 1). Of the 430 hospitals included in this analysis, only 1.6% administered thienopyridine in the ED to > 90% of the eligible patients with NSTEMI. Over 80% of all the sites administered thienopyridines to <40% of patients in the ED. (Figure 1) Several hospital level characteristics were associated with decreased likelihood of ED thienopyridine use. When compared to EDs in the south, EDs in the west were 41% less likely to administer a thienopyridine. The overall model c-statistic was 0.79. Patients in teaching hospitals and in hospitals in the South and Northeast were more likely to receive a thienopyridine in the ED.

As the hospital level percentage of patients receiving a thienopyridine in the ED increases, the hospital level percentage of patients receiving angiotensin converting enzyme inhibitor and glycoprotein IIb/IIIa inhibitor administration within 24 hours of admission decreases. (Table IV) Hospitals with higher percentages of patients receiving thienopyridines in the ED had a lower proportion of patients undergoing catheterization and PCI. As the hospital level percentage of patients receiving thienopyridines in the ED increased, the number of patients undergoing CABG, the median time to cardiac catheterization, and the median time to PCI also increased, although the time to CABG decreased.

Discussion

In this study, we did not find any association between ED administration of thienopyridines and in-hospital mortality or major bleeding. Despite current guidelines recommending

thienopyridine administration as soon as possible in high risk patients in whom an invasive strategy is planned, the vast majority (>75%) of EDs administer thienopyridines less than one-third of the time. The result is that among individuals who receive a thienopyridine within 24 hours of presentation for NSTEMI, only a quarter of patients with NSTEMI receive it in the ED. Ischemic ECG changes, higher troponin elevations, and longer ED length of stay were associated with ED thienopyridine administration whereas home thienopyridine use, renal dysfunction, and a history of heart failure and stroke were associated with later administration of a thienopyridine. Our findings suggest that patients with objective findings of ACS in the ED and without complicating factors were most likely to receive a thienopyridine in the ED. Thus, patients at highest risk for cardiac ischemia were appropriately identified for ED thienopyridine administration.

Perceived Risks of ED Administration of a Thienopyridine

Data from the CURE Trial demonstrated that patients who received clopidogrel compared to those treated with placebo received a significant clinical benefit, without increasing life threatening bleeding.⁽¹⁾ Despite this benefit, administration of clopidogrel is often delayed. The explanation often given for deferring thienopyridine administration in the ED is the concern regarding increased risk of bleeding if the patient needs CABG.^(15–17) Although only a minority of patients will require emergent CABG, the ability to identify these patients is limited.^(18–20) Concerns about potential CABG-related bleeding may guide local practices at individual institutions. Similar to prior descriptive studies of patients with NSTEMI, we noted that only a small percentage (5.1%) of the patients who received a thienopyridine within 24 hours of presentation underwent CABG.^(21–23) Consistent with our data that patients with more obvious ischemia were more likely to receive a thienopyridine in the ED, we found a 3-fold higher in-hospital CABG rate in patients who received a thienopyridine in the ED. It is notable that we did not observe either a delay in time to CABG or an increase in major bleeding in this group. In our study, ED administration of a thienopyridine did not appear to be associated with a delay to CABG. Our data suggest that ED thienopyridine administration in collaboration with cardiology consultation should be considered for patients who are at high risk for cardiac ischemia based on their ECG and troponin findings.

Potential Benefits of ED Clopidogrel Administration

ED administration of clopidogrel is theoretically important for several reasons. The antiplatelet activity of clopidogrel is not realized for up to 15 hours.⁽²⁴⁾ Thus, administration at time of coronary intervention will not provide adequate anti-platelet inhibition. Upstream administration would therefore result in decreased platelet inhibition at the time of the procedure.

However, little data are available regarding safety and outcomes with ED administration of thienopyridines.^(24, 25) Alexander, et al., reported that in patients with NSTEMI not undergoing PCI, those treated with clopidogrel at admission had lower adjusted in hospital mortality than those who did not receive clopidogrel at admission (adjusted odds ratio 0.68, 95% CI 0.61–0.77).⁽²⁶⁾ The CURE trial randomized patients with early acute coronary syndrome to receive either clopidogrel (300mg) or placebo in addition to aspirin within 24

hours of symptom onset but did not report the location of clopidogrel administration.(1) Similarly, the majority of clinical trials evaluating antiplatelet agents do not enroll patients in the ED setting.(1) This prevents definitive conclusions about whether it is critical to add anti-platelet agents in the first few hours after presentation.

In our cohort, the majority of patients underwent an invasive strategy. The net clinical benefit of administering a thienopyridine at the time of presentation, as recommended by current guidelines, has not been previously studied. (2) We did not find a difference in clinical outcomes based on ED administration. Importantly, we did not find that ED administration was associated with an increased risk of major bleeding. The fact that we did not find a significant reduction in cardiac events does not necessarily mean that there is no role for ED administration of thienopyridines. The small difference in time to thienopyridine administration between those who did and did not receive a thienopyridine in the ED likely prevented us from finding an effect. However, it is also possible that pretreatment with thienopyridines has limited benefit in this patient population as noted in a recent meta-analysis.(27)

System Issues

As we evaluated ED administration of an early medication, we also identified some systems issues. We also noted that the ED administration of thienopyridines did not correlate with most other acute quality metrics further suggesting that decisions about the administration of this medication in the ED are guided by local factors.

It was interesting to note that ED length of stay was associated with ED administration of a thienopyridine. However, we have reported in the past that prolonged ED stay was associated with a decreased adherence to guideline recommendations and a higher risk of recurrent myocardial infarction.(28) In this study, our data suggest that as a patient's time in the ED increases, at least this component of guideline recommended care is more likely to be initiated in the ED setting. This may reflect the ED physicians desire to maximize medical management while in the ED setting, or it may represent more engagement of specialists participating selectively in the care of patients who are not transferred to the cardiac care unit in a timely manner. Our study does not allow us to address these possibilities.

Limitations

A significant number of patients included in the NCDR's ACTION Registry®-GWTG™ were excluded from our study as we only analyzed those patients who received a thienopyridine within 24 hours of presentation. While this decision may limit the generalizability of our results, we chose focus on these patients because the guidelines define an acute medication as one that is administered within 24 hours of presentation. As emergency physicians are focused on the administration of acute medications this study aimed to evaluate associations during this time frame. The patient population was largely Caucasian and insured which may also limit the generalizability of our findings. In addition, we were unable to adjust for the dose of thienopyridine administered. The actual dose was recorded in the registry for data collected using data collection form 2.0, but our analysis

uses data collection form 2.0 as well as earlier versions. Similarly, we combined all thienopyridines in our analysis, but the vast majority of patients received clopidogrel. Thus, our results may not apply to prasugrel, which has been associated with increased bleeding risk and is not recommended for administration prior to PCI or CABG.(29) We were unable to determine to what extent hospital protocols affect the decision to give a thienopyridine in the ED. We are also unable to definitively report where the thienopyridines are administered outside of the ED. We were unable to assess the risk for intra-operative bleeding that may have been noted in the patients undergoing CABG. In addition we describe an association between thienopyridine use and number and timing of patients undergoing CABG, but we cannot determine why. Verification bias is possible since all events were adjudicated locally. We only have information on in-hospital events, which would decrease the likelihood of observing a difference in outcomes. Lastly, we recognize the possibility of a chance finding due to the number of statistical tests included in this analysis. Caution has been taken to not overstate any conclusions reached from statistically significant results and rather focus on clinically relevant differences.

Conclusions and Clinical Implications

We did not find an association between ED administration of thienopyridines and in-hospital mortality or major bleeding. Only 25% of all NSTEMI patients who presented to the ED and received a thienopyridine within 24 hours of presentation received their first dose in the ED. Patients most likely to receive ED administration of thienopyridines are those with high risk features such as ischemic ECG changes or elevated initial cardiac biomarkers and those patients with a longer ED stay. To improve the likelihood that guidelines contain evidence based recommendations relevant to upstream management of patients, studies need to be specifically designed to determine the role of ED medical management and to address outcomes other than mortality, such as recurrent ischemia or re-infarction.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Histogram of percent of hospitals with a fixed percentage of patients receiving thienopyridine in ED

Table I

Clinical Characteristics – Location of Administration

Variable	Overall N=39,454	ED Thienopyridine N=9,534	Non-ED Thienopyridine N=29,920	Odds Ratio for ED Thienopyridine	95% CI for OR (Lower)	95% CI for OR (Upper)
<u>Demographics</u>						
Age (yrs)*	65 (55.77)	63 (54.75)	66 (55.78)	0.99	0.99	0.99
White Race (%)	81.9%	79.3%	82.8 %	0.97	0.90	1.03
Gender (male)	63.1%	64.0%	62.8%	1.10	1.05	1.16
<u>Insurance Status (%)</u>						
HMO/private	58.4%	58.2%	58.5%	1.09	1.04	1.15
Medicare	27.8%	26.3%	28.3%	0.82	0.77	0.87
Military/VAMC	1.1%	1.2%	1.1%	1.21	0.94	1.55
Medicaid	3.8%	4.1%	3.7%	1.02	0.90	1.17
Self/none	8.2%	9.5%	7.8%	1.21	1.11	1.32
Other	0.52%	0.60%	0.49%	1.11	0.79	1.56
<u>Medical History (%)</u>						
Hypertension	75.7%	73.5%	76.4%	0.79	0.75	0.84
Diabetes Mellitus	35.1%	32.0%	36.1%	0.78	0.74	0.82
Peripheral Arterial Disease	12.7%	10.3%	13.5%	0.73	0.67	0.79
Current/recent smoker	31.3%	33.4%	30.6%	1.20	1.13	1.26
Dyslipidemia	64.7%	61.9%	65.6%	0.85	0.81	0.89
Prior MI	32.6%	28.0%	34.1%	0.76	0.72	0.80
Prior PCI	31.9%	26.8%	33.5%	0.75	0.71	0.79
Prior CABG	21.5%	18.1%	22.5%	0.78	0.74	0.83
Prior CHF	16.0%	12.5%	17.0%	0.62	0.58	0.67
Prior stroke	9.4%	7.4%	10.0%	0.67	0.61	0.73
On Dialysis	2.9%	2.1%	3.1%	0.56	0.47	0.66
<u>Home Medications</u>						
Aspirin	50.8%	45.1%	52.6%	0.77	0.73	0.81
Clopidogrel	28.5%	19.5%	31.4%	0.52	0.49	0.55
Prasugrel	0.18%	0.05%	0.22%	0.29	0.09	0.97
<u>Presentation Features</u>						

Variable	Overall N=39,454	ED Thienopyridine N=9,534	Non-ED Thienopyridine N=29,920	Odds Ratio for ED Thienopyridine	95% CI for OR (Lower)	95% CI for OR (Upper)
Symptom Onset to Hospital Arrival (hrs)*	2.6 (1.3, 6.3)	2.8 (1.3, 7.4)	2.5 (1.2, 5.9)	1.00	1.00	1.01
Systolic Blood pressure (mmHg)*	148 (128, 168)	148 (129, 168)	148 (128, 168)	1.00	1.00	1.00
Heart Rate (beats/min)*	82 (70, 97)	83 (70, 97)	82 (70, 97)	1.00	1.00	1.00
Signs of CHF	18.0%	16.4%	18.5%	0.75	0.70	0.81
ST depression or Transient ST elevation	27.6%	29.5%	27.0%	1.22	1.15	1.29
T-wave inversion	14.4%	15.7%	14.0%	1.14	1.07	1.23
Initial troponin ratio (xULN)*	2.0 (0.5, 9.6)	3.1 (0.8, 14.5)	1.7 (0.4, 8.3)	1.00	1.00	1.00
LOS (days)*	3.0 (2.5)	3 (2.6)	3 (2.5)	1.00	0.99	1.00
ED LOS (hours)*	3.8 (2.6, 5.6)	4.5 (2.9, 7.2)	3.7 (2.5, 5.2)	--	--	--
<u>Acute In-hospital medication (within 24 hours of arrival)</u>						
Aspirin	98.3%	98.6%	98.3%	1.26	1.03	1.56
B-Blocker	92.5%	92.7%	92.4%	1.11	1.00	1.23
ACE inhibitor/ARB	46.5%	45.0%	46.9%	0.87	0.83	0.92
GP IIa/III inhibitor	43.0%	41.6%	43.4%	1.27	1.20	1.34
Heparin (any)	88.6%	91.4%	87.7%	1.50	1.37	1.63
Bivalirudin	19.0%	17.9%	19.4%	0.87	0.81	0.93
Time to thienopyridine administration (hours)*	8.77 (3.87, 15.07)	2.48 (1.33, 4.25)	11.32(6.67, 16.9)	0.64	0.63	0.65
<u>Hospital Characteristics</u>						
<i>Region</i>						
West	14.3%	10.4%	15.5%	0.72	0.55	0.95
Northeast	10.4%	14.1%	9.2%	1.72	1.29	2.28
Midwest	35.3%	33.3%	35.9%	0.70	0.57	0.86
South	40.1%	42.2%	39.4%	1.27	1.04	1.55
Teaching Hospital vs nonteaching	25.1%	33.2%	22.5%	1.35	1.06	1.72
Rural Hospital	8.3%	8.1%	8.3%	1.00	0.72	1.38

Table II

Factors Associated with ED administration of Clopidogrel and Prasugrel within 24 hrs of admission (c-index = 0.79)

Variable	Adjusted OR	95% CI for OR (Lower)	95% CI for OR (Upper)
Length of ED stay (per 5 hr increase)	2.26	2.17	2.36
Baseline troponin (per 1 xULN increase & <5 xULN)	1.15	1.13	1.17
Baseline troponin (per 1 xULN increase & 5–50 xULN)	1.00	1.00	1.01
Clopidogrel (home)	0.60	0.56	0.64
ST depression or Transient ST elevation (vs. None)	1.47	1.38	1.57
T-wave inversion (vs. None)	1.22	1.13	1.32
Baseline serum creatinine (per 1 mg/dL increase)	0.91	0.88	0.94
Age (per 5 year increase)	0.97	0.96	0.98
Prior CHF	0.82	0.75	0.89
Prior Stroke	0.79	0.72	0.88
Baseline Hgb (per 5 g/dL decrease)	0.83	0.76	0.90
HR (per 10 bpm decrease & HR<95 bpm)	1.00	1.00	1.00
HR (per 10 bpm increase & HR>=95 bpm)	0.93	0.91	0.96
Beta Blocker (home)	0.92	0.86	0.97
Midwest (vs. South)	0.75	0.59	0.94
Northeast (vs. South)	1.26	0.93	1.70
West (vs. South)	0.59	0.44	0.79
Female (vs. Male)	0.93	0.87	0.98
Diabetes Mellitus	0.93	0.88	0.99
Prior PCI	1.08	1.01	1.15
No services (vs. Surgery)	1.46	1.00	2.15
Cath lab only (vs. Surgery)	1.47	0.99	2.20
PCI, no surgery (vs. Surgery)	1.56	1.14	2.14

Table III

In Hospital Management and Events

Variable	Overall N=39,454	ED Thienopyridine N=9,534	Non- ED Thienopyridine N=29,920	Odds Ratio for ED Thienopyridine	95% CI for OR (Lower)	95% CI for OR (Upper)
<u>In Hospital Procedures</u>						
Diagnostic cath	79.9%	80.7%	79.6%	1.30	1.22	1.40
Cath within 24 hours	55.7%	53.6%	56.3 %	1.23	1.16	1.30
Arrival to cath (hours)	16.3 (5.2, 28.2)	17.0 (4.6, 30.0)	16.1 (5.4, 27.5)	1.00	1.00	1.00
PCI	56.0%	49.4%	58.1%	0.86	0.82	0.91
PCI within 24 hours	42.1%	34.2%	44.6 %	0.87	0.82	0.91
Arrival to PCI (hours)	14.5 (4.5, 23.7)	15.2 (4.2, 27.3)	14.3 (4.6-22.9)	1.00	1.00	1.00
CABG	5.2%	9.5%	3.8%	2.16	1.95	2.38
Arrival to CABG (hours)	96.5 (52.6, 148.7)	80.5 (43.7, 131.7)	111.9 (64.7, 161.2)	0.99	0.99	1.00
<u>In Hospital Clinical Events</u>						
Death	2.4%	2.2%	2.4%	0.82	0.69	0.97
Post- admission infarction	1.0%	1.0%	1.0%	0.96	0.74	1.25
Cardiogenic Shock	2.2%	2.5%	2.1%	1.14	0.96	1.35
RBC Transfusion	9.5%	12.0%	8.8%	1.15	1.06	1.25
ACTION GWTG Major Bleeding	8.3%	7.9%	8.5%	0.87	0.79	0.96

Table IV

Correlation between ED administration of thienopyridines and quality metrics, acute medications, procedures and time to procedures (at the hospital level)

Variable	Number of Sites	Spearman correlation coefficient (ρ)	Lower Confidence Limit for (ρ)	Upper Confidence Limit for (ρ)	P-value
Overall AMI Performance Measure	424	-0.174	-0.265	-0.080	<.001
Individual Quality Metrics					
% Aspirin at Arrival	422	-0.048	-0.142	0.048	0.3301
% Aspirin At Discharge	421	-0.102	-0.196	-0.007	0.0356
% Beta Blocker at Discharge	422	-0.123	-0.216	-0.028	0.0113
% Evaluation of LV Systolic Function	423	0.032	-0.064	0.127	0.5139
% ACE-I or ARB for LVSD at Discharge	378	-0.151	-0.248	-0.051	0.0031
% Statin at Discharge	417	-0.091	-0.185	0.005	0.0638
% Adult Smoking Cessation Advice	392	-0.027	-0.125	0.073	0.5987
% Cardiac Rehabilitation Referral	417	-0.163	-0.255	-0.068	<.001
Acute Medications					
% Acute Aspirin	429	-0.074	-0.168	0.021	0.1245
% Acute Beta blocker	430	-0.085	-0.178	0.010	0.0782
% Acute ACE inhibitor	428	-0.109	-0.201	-0.014	0.0243
% Acute Angiotensin receptor blocker	427	-0.013	-0.108	0.082	0.7838
% Acute ACE Inhibitor or ARB	428	-0.103	-0.195	-0.008	0.0337
% Acute Aldosterone blocking agent	428	0.036	-0.059	0.130	0.4617
% Acute Statin	429	-0.079	-0.172	0.016	0.1037
% Acute other lipid-lowering agent	428	-0.143	-0.235	-0.049	0.0029
% Acute any lipid-lowering agent	429	-0.102	-0.195	-0.008	0.0342
% GP IIb-IIIa	429	-0.237	-0.324	-0.146	<.001
% Bivalirudin	428	-0.053	-0.147	0.042	0.2719
Procedures					
Diagnostic Cath	429	-0.141	-0.233	-0.047	0.0033
PCI	428	-0.302	-0.386	-0.213	<.001
CABG	428	0.181	0.087	0.271	<.001
Time to Procedures					
Median Arrival to Cath (hrs)	400	0.351	0.262	0.434	<.001

Variable	Number of Sites	Spearman correlation coefficient (ρ)	Lower Confidence Limit for (ρ)	Upper Confidence Limit for (ρ)	P-value
Median Arrival to PCI (hrs)	369	0.309	0.213	0.398	<.001
Median Arrival to CABG (hrs)	261	-0.216	-0.328	-0.096	<.001