Acute Ischemic Heart Disease

The influence of risk status on guideline adherence for patients with non–ST-segment elevation acute coronary syndromes

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Background Practice guidelines for patients with non–ST-segment elevation (NSTE) acute coronary syndromes (ACS) recommend targeting evidence-based therapies for the highest-risk patients. We characterized guideline adherence for NSTE ACS by risk status.

Methods We analyzed inhospital treatments and outcomes for 77760 patients with NSTE ACS (ischemic ST-segment changes and/or positive cardiac markers) included in the CRUSADE initiative from January 2001 to September 2003 at 457 US hospitals. Compliance with the American College of Cardiology/American Heart Association Class I guideline recommendations for NSTE ACS was evaluated in subgroups of eligible patients without listed contraindications at increased risk for mortality and among risk categories designated by an adapted version of the PURSUIT risk model designed to predict inhospital mortality.

Results Inhospital mortality was increased in patients with diabetes mellitus (5.8% vs 4.3%), renal insufficiency (10.0% vs 3.9%), signs of congestive heart failure on presentation (10.6% vs 3.1%), and age ≥75 years (8.6% vs 2.7%), compared with patients without these features. Use of guideline-recommended acute medications, invasive cardiac procedures, and discharge medications and interventions was significantly lower in patients with these high-risk features. Patients designated as high-risk for inhospital mortality were less likely to be treated with guideline-recommended therapies compared with low-risk and moderate-risk patients.

Conclusions Patients with NSTE ACS with the highest risk of mortality are less likely to receive guideline-recommended therapies and interventions. These findings highlight the need to clarify guideline recommendations for high-risk patients and to develop novel quality improvement approaches that target undertreated subgroups of patients with NSTE ACS. (Am Heart J 2006;151:1205-13.)

Treatments for patients with acute coronary syndromes (ACS) have evolved with the incorporation of results from large-scale clinical trials into clinical practice guidelines that provide a framework for the management of patients with acute ischemic heart disease.[1,2] Temporal studies over the last decade have demonstrated that most patients with ACS have non–ST-segment elevation (NSTE) ACS (including unstable angina and NSTE myocardial infarction).[3] Because improved guideline adherence is associated with reduced mortality in patients with NSTE ACS, widespread use of guideline-recommended therapies may substantially impact clinical outcomes in this expanding population.[4,5]

The American College of Cardiology (ACC)/American Heart Association (AHA) guidelines for the management of NSTE ACS recommend targeting evidence-based therapies for the highest-risk patients who would be expected to have the greatest relative benefit from aggressive treatment.[1] However, the guidelines

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Table I. Inhospital outcomes and acute treatment patterns for high-risk subgroups

		Age		Diabetes mellitus	
	Overall	<75 y	≥75 y	No	Yes
	(n = 77760)	(n = 50658)	(n = 26986)	(n = 52360)	(n = 25400)
Outcomes					
Death	4.8	2.7	8.6	4.3	5.8
Reinfarction	3.2	2.8	4.0	3.0	3.5
Death or reinfarction	7.4	5.1	11.5	6.8	8.5
Congestive heart failure	9.1	6.4	14.2	7.7	12.2
Red blood cell transfusion	14.7	12.8	18.2	12.8	18.5
Medications (%)*					
Aspirin	91.5	92.5	89.5	92.0	90.4
β-Blockers	78.8	79.7	76.9	78.7†	78.9†
Heparin	83.1	85.2	78.9	83.9	81.4
Unfractionated heparin	48.9	53.1	43.6	50.8	48.0
LMWH	39.4	38.8	40.6	39.4†	39.4†
GpIIb-IIIa inhibitor	54.2	56.6	45.0	55.7	50.1
Procedures (%)					
Catheterization	61.9	71.1	44.6	63.6	58.2
Cath < 48 h	42.5	50.8	27.0	45.5	36.3
PCI	36.6	43.8	23.6	39.2	31.4
PCI < 48 h	26.3	32.8	14.5	45.5	36.3
CABG	11.4	13.6	7.5	11.2	11.8

LMWH, Low-molecular-weight heparin; *Cath*, cardiac catheterization; *CABG*, coronary artery bypass grafting.
*Medications administered within 24 hours of presentation for eligible patients without listed contraindications except for GpIIb-IIIa inhibitors which are listed only for patients who underwent cardiac catheterization < 48 hours.
†$P > .05$; all other comparisons between subgroups significant with $P < .05$.

Table II. Acute treatment patterns after excluding patients with renal insufficiency

	Age		Diabetes mellitus		Signs of CHF on presentation	
	<75 y	≥75 y	No	Yes	No	Yes
	(n = 44206)	(n = 21107)	(n = 46307)	(n = 19105)	(n = 51992)	(n = 12295)
Medications (%)*						
Aspirin	93.0	89.8	92.4	91.1	92.9	88.6
β-Blockers	79.8	77.0	78.8†	79.2†	79.9	74.7
Heparin	86.1	78.9	84.7	82.8	85.1	79.9
GpIIb-IIIa inhibitor	57.3	45.2	56.2	51.0	56.2	45.5
Procedures (%)						
Catheterization < 48 h	53.8	29.8	56.2	51.0	50.5	27.8

*Medications administered within 24 hours of presentation for eligible patients without listed contraindications except for GpIIb-IIIa inhibitors which are listed only for patients who underwent cardiac catheterization < 48 hours.
†$P > .05$; all other comparisons between subgroups significant with $P < .05$.

document specifically acknowledges that diverse clinical situations confound treatment decisions, especially for patients with high-risk features, so clinical judgments regarding patient care must be individualized based upon presenting circumstances and concomitant comorbid conditions.[1] Furthermore, interactions among specialties are becoming increasingly important for guideline implementation because some of the guideline-recommended therapies are tied to the use of invasive cardiac procedures that are only performed by cardiologists. Therefore, we evaluated guideline adherence in the CRUSADE quality improvement initiative to characterize contemporary treatment patterns in high-risk subgroups of patients with NSTE ACS and delineate clinical characteristics and provider features that influence care delivery.

Signs of CHF on presentation		Renal insufficiency	
No	Yes	No	Yes
(n = 59190)	(n = 17183)	(n = 65412)	(n = 10380)
3.1	10.6	3.9	10.0
2.9	3.9	3.0	4.3
5.6	13.3	6.4	13.0
4.5	25.0	7.8	17.2
12.9	21.0	13.0	25.2
92.5	88.1	92.0	88.5
79.9	74.9	78.9	78.0
84.4	78.6	84.1	76.8
51.5	44.6	50.5	46.4
39.4†	39.3†	39.9	35.9
55.6	45.1	54.9	43.5
67.1	44.4	65.2	42.0
48.1	23.9	46.1	21.4
41.7	19.8	39.6	19.4
48.0	23.9	46.0	21.4
12.1	8.9	12.2	6.5

Methods

Patient inclusion criteria

Patients included in the CRUSADE database from January 2001 through September 2003 from 457 US hospitals were evaluated for this analysis. Patients in the CRUSADE initiative presented with acute ischemic symptoms (lasting for at least 10 minutes), were at rest within 24 hours before hospital arrival, and had at least one of the following diagnostic features recommended in the ACC/AHA guidelines to distinguish patients with an increased risk of adverse outcomes: ST-segment depression ≥0.5 mm, transient ST-segment elevation 0.5 to 1.0 mm (lasting for <10 minutes), and/or positive cardiac markers (elevated troponin I or T and/or creatine kinase–MB > upper limit of normal for the local laboratory assay used at each institution).[1,2]

Data collection

Data were collected during the initial hospitalization in an anonymous fashion without obtaining informed consent. The institutional review board of each institution approved participation in CRUSADE. Data collection did not continue after hospital transfer.

Participating institutions were instructed to collect data on consecutive eligible patients, but methods were not available to verify whether consecutive patients were included. Data collectors underwent standardized training before entering patient data including clinical characteristics, use of acute (within 24 hours of presentation) and discharge medications, use and timing of invasive cardiac procedures, and laboratory results. Data collectors were instructed to record major contraindications to guideline-recommended therapies that were delineated in medical records, as detailed in Appendix A. Data were not queried after submission, and clinical outcomes were not centrally adjudicated.

Data validation

In September 2002, CRUSADE formally assessed the reliability of data abstraction. Sites and records were randomly selected. Study coordinators from one fourth of CRUSADE hospitals were contacted and asked to send copies of medical records without patient identifiers. The records were audited by trained site management personnel who were knowledgeable about CRUSADE variable definitions and who had had prior monitoring experience. In addition to selected clinical characteristics, audited variables included all medical therapies, procedures, and inhospital clinical events. The overall accuracy of audited records was 94.8%, exceeding the typical reliability threshold of 90%.

The overall degree of missing data was quite low for a registry, averaging approximately 5% across all collected data elements. Notably, variables such as age and sex are missing in <0.5% of all cases. Various routine procedures have been established to maintain and monitor the data quality of the CRUSADE database. At data entry and during quarterly quality control procedures, values that exceed expected ranges are flagged and excluded from analyses. In addition, every quarter, sites receive a report summarizing any data quality problems observed in their submitted data. Issues are specified on a per-record level. Sites are encouraged to make corrections, thus iteratively improving the overall quality of the database.

Statistical analysis

The use of acute medications (within 24 hours of presentation) given class I recommendations in the ACC/AHA guidelines was evaluated for all patients without contraindications.[1,2] Because the 2002 update to the ACC/AHA guidelines denotes a class I recommendation for platelet glycoprotein IIb/IIIa (GpIIb-IIIa) inhibitors for patients in whom catheterization or percutaneous coronary intervention (PCI) is planned, the use of GpIIb-IIIa inhibitors was evaluated only in patients who underwent catheterization within 48 hours of hospital presentation.[2] Other class I acute guideline recommendations evaluated included aspirin, β-blockers, and heparin (unfractionated or low molecular weight).[1,2] Inhospital outcomes were evaluated only for patients who were not transferred out to another institution because data collection did not continue after transfer because of privacy regulations.

Discharge treatment patterns for class I recommendations (aspirin; clopidogrel for at least 1 month in patients in whom a noninterventional approach or PCI is planned; lipid-lowering agents for low-density lipoprotein cholesterol levels >125 mg/dL; angiotensin-converting enzyme [ACE] inhibitors for congestive heart failure [CHF], ejection fraction <40% diabetes mellitus, or hypertension; β-blockers; smoking cessation counseling; dietary counseling; and cardiac rehabilitation referral) were evaluated for patients without contraindications, those who survived the initial hospitalization, and those who were not transferred to another institution.[1,2] Use of discharge clopidogrel was also analyzed separately among patients who underwent PCI and among those who did not.

Table III. Discharge treatment patterns for high-risk subgroups

Discharge treatments	Overall (n = 77760)	Age <75 y (n = 50658)	Age ≥75 y (n = 26986)	Diabetes mellitus No (n = 52360)	Diabetes mellitus Yes (n = 25400)
Medications (%)*					
Aspirin	89.7	90.9	87.3	90.3	88.5
Clopidogrel	53.5	57.3	46.1	54.8	50.9
PCI patients	89.9	90.2	88.8	90.2†	89.2†
Non-PCI patients	30.3	29.5	31.4	29.5	31.7
β-Blockers	83.4	83.8	82.8	83.1	84.2
ACE inhibitor‡	60.6	61.0†	60.0†	58.8	63.5
Lipid-lowering agent§	79.7	82.0	73.8	79.5†	79.9†
Interventions (%)					
Smoking counseling‖	65.4	67.4	47.4	67.3	59.3
Dietary counseling	71.6	75.1	64.7	70.9	73.0
Cardiac rehabilitation¶	41.2	46.0	32.3	42.3	38.9

*For eligible patients without listed contraindications, medications administered at time of hospital discharge.
†$P > .05$; all other comparisons between subgroups significant with $P < .05$.
‡Only for patients with ejection fraction <40%, history of congestive heart failure, hypertension, or diabetes mellitus.
§Only for patients with documented hyperlipidemia or measured low-density lipoprotein cholesterol >125 mg/dL.
‖Only for current smokers.
¶Only for patients with documented NSTE myocardial infarction (positive cardiac markers).

Clinical outcomes and treatment patterns were compared among selected high-risk subgroup populations in CRUSADE using the χ^2 test for categorical variables or Wilcoxon rank sum test for continuous variables. The subgroups chosen for this analysis were identified by clinical characteristics that were not used as inclusion criteria for CRUSADE or NSTE ACS clinical trials but are important predictors of mortality in patients with NSTE ACS (age, diabetes mellitus, signs of CHF on presentation, and renal insufficiency).[6-10] Of the overall population, the degree of missing data for these primary comparison groups was low (missing data for age in 0.15% of patients, diabetes mellitus in 0%, signs of CHF in 1.78%, and renal insufficiency in 2.53%). Treatment patterns were also compared separately after excluding patients with renal insufficiency (serum creatinine >2.0 mg/dL, estimated creatinine clearance <30 mL/min, or need for dialysis) to further evaluate the treatment patterns within each of these subgroups without the confounding effects from potential safety concerns related to drug clearance and bleedings risks associated with renal insufficiency.

Clinical outcomes and treatment patterns were also compared among categories of risk determined by the PURSUIT risk model with χ^2 statistics.[10] The PURSUIT 30-day mortality risk model for NSTE ACS was adapted to predict the risk of inhospital mortality rather than the outcome of 30-day mortality in the original PURSUIT population. We adapted this model to predict inhospital mortality because only inhospital mortality data were captured in the CRUSADE population. The original PURSUIT population was categorized into equal tertiles (termed *low-risk, moderate-risk*, and *high-risk*) based on predicted inhospital mortality rates to develop boundaries for mortality rates that define low-risk, moderate-risk, and high-risk groups in the reference population from the PURSUIT trial. This inhospital mortality model was then applied to the CRUSADE population (n = 74 217 patients with adequate data for risk score analysis), which was categorized into risk groups based upon the predicted inhospital mortality rate calculated for each patient.

Independent factors associated with acute medications (aspirin, heparin, β-blockers) and discharge medications (aspirin, β-blockers, ACE inhibitors, and lipid-lowering agents) among patients without contraindications were analyzed to further characterize how clinical features influence medication use. Factors associated with acute use of GpIIb-IIIa inhibitors and early catheterization within 48 hours have been published in separate manuscripts from the CRUSADE database.[11,12] We did not analyze predictors of discharge clopidogrel given confounding related to the decision to perform PCI that would be expected to significantly influence the use of discharge clopidogrel. Independent factors associated with the use of each medication class were determined using multivariable generalized estimating equation models with adjustment for correlations among clustered responses (within-hospital correlations) and a standard list of variables such as clinical and demographic characteristics.[13] A stepwise approach was used to determine how high-risk clinical features evaluated in this analysis (age, signs of CHF, diabetes mellitus, renal insufficiency), CRUSADE inclusion criteria designated as high-risk features by the ACC/AHA guidelines (positive cardiac markers, ischemic ST-segment changes), and cardiology inpatient care, defined by participating sites as the admitting service that primarily cared for the patient during the hospitalization (the variable most significantly associated with early catheterization and acute GpIIb-IIIa inhibitor use in the CRUSADE population in prior analyses), were associated with the use of each medication class.[1,2,11,12]

$P < .05$ was established as the level of statistical significance for all tests. All analyses were performed using SAS software (versions 8.2, SAS Institute, Cary, NC).

Signs of CHF		Renal insufficiency	
No	Yes	No	Yes
(n = 59190)	(n = 17183)	(n = 65412)	(n = 10380)
90.7	86.2	90.3	86.1
56.8	41.6	55.0	44.4
90.3	87.1	90.2	87.5
30.8	28.9	29.7	32.7
83.9	82.0	83.3†	84.1†
59.0	65.7	60.8†	59.6†
80.9	74.4	80.0	77.7
67.3	56.8	66.7	51.1
72.3	69.2	72.1	68.7
43.6	33.6	42.8	31.8

Results

Patient and hospital characteristics

A total of 77760 patients were included in the CRUSADE database from 457 US hospitals (23% from the northeast, 32% from the midwest, 34% from the south, and 11% from the west). The median number of beds per hospital was 367 (25th, 75th percentiles: 245, 500), and 27% of hospitals were academic institutions. Most hospitals (74%) had capabilities to perform diagnostic catheterization, PCI, and coronary artery bypass grafting, whereas other hospitals had capabilities for catheterization and PCI (7%), just catheterization (13%), or no catheterization (6%). Of the patients included in CRUSADE, 56% were admitted to a cardiology inpatient service, 2.4% were enrolled in a clinical trial, and 13% were transferred out to another institution during the index hospitalization.

Treatment patterns in high-risk subgroups

Patients with age ≥75 years (34.8% of the total population), diabetes mellitus (32.7%), signs of CHF on presentation (22.5%), and renal insufficiency (13.7%) had higher rates of adverse outcomes and transfusion compared with patients without these features (Table I). Acute medications and invasive cardiac procedures (except for β-blockers) were used less commonly in these high-risk patients, compared with their lower-risk counterparts. These findings persisted after excluding patients with renal insufficiency (Table II). Discharge care among high-risk subgroups was more variable than with acute care (Table III). Aspirin, lipid-lowering agents, and secondary preventative interventions were used less frequently in high-risk patients; ACE inhibitors were used more commonly in patients with diabetes mellitus and signs of CHF; and clopidogrel (broken down by PCI and non-PCI patients) and β-blockers were used in similar frequencies among all high-risk subgroups.

Treatment patterns by risk model categories

The modified PURSUIT risk model distinguished low-risk (n = 17838; 24%), moderate-risk (n = 18453; 25%), and high-risk (n = 37926; 51%) categories of patients. The frequencies of adverse outcomes increased in a stepwise fashion across risk groups, and the c-index for predicting inhospital mortality with this model was 0.79 (Figure 1, *A*). Acute medications and invasive procedures were used least commonly in high-risk patients, but the greatest differences among risk groups were demonstrated by the use of GpIIb-IIIa inhibitors, catheterization within 48 hours, and PCI within 48 hours (Figure 1, *B*). The use of discharge β-blockers, ACE inhibitors, and clopidogrel was consistent across risk groups, whereas aspirin and lipid-lowering agents were used less commonly in high-risk patients (Figure 1, *C*).

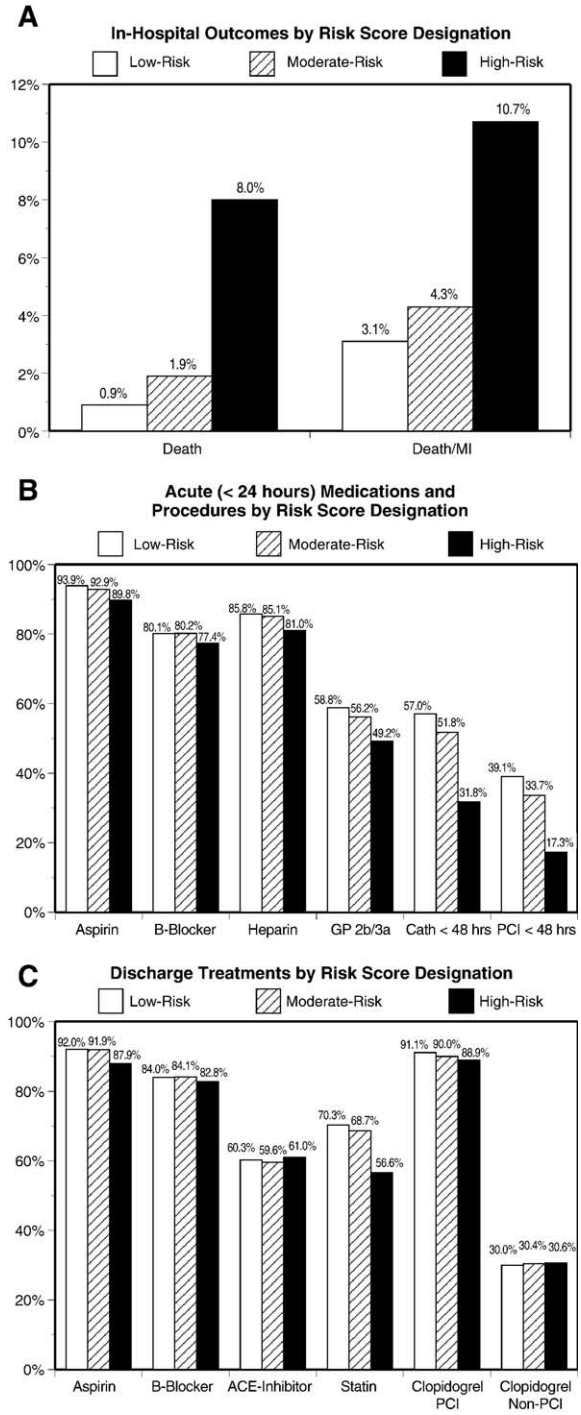
Factors associated with medication use

Cardiology inpatient care, ischemic ST-segment changes, and positive cardiac markers were factors that were significantly associated with increased use of acute medications, whereas signs of CHF, renal insufficiency, and advanced age were factors associated with decreased use (Table IV). Diabetes mellitus was associated only with decreased use of aspirin. Positive cardiac markers and cardiology care were significantly associated with increased use of discharge medications. Signs of CHF were associated with decreased use of discharge aspirin, β-blockers, and lipid-lowering agents but were associated with increased use of ACE inhibitors. Renal insufficiency was associated with decreased use of discharge aspirin and ACE inhibitors, and advanced age was associated with decreased use of discharge lipid-lowering agents (Table V).

Discussion

We have shown that patients with NSTE ACS with the highest risk of mortality are treated less commonly with class I guideline recommendations compared with lower-risk patients. These findings highlight a significant opportunity for further clarification of guideline recommendations for high-risk patients who are typically excluded from randomized clinical trials that form the foundation for evidence-based decision making and for developing novel quality improvement approaches that target undertreated subgroups of the NSTE ACS population.[14]

Figure 1



A, Inhospital outcomes by risk category calculated from the adapted PURSUIT risk model for inhospital mortality. *MI*, Myocardial infarction. **B**, Acute treatment patterns by risk category. Glycoprotein IIb/IIIa inhibitor use is listed only for patients who underwent cardiac catheterization <48 hours. *GP*, Glycoprotein; *cath*, catheterization. **C**, Discharge treatment patterns by risk category.

Table IV. Association of high-risk clinical features with acute (<24 hours) medication use*

	Adjusted OR (95% CI)	*P*
Aspirin		
Positive cardiac markers	1.37 (1.26-1.49)	<.0001
Signs of CHF	0.80 (0.75-0.85)	<.0001
Cardiology inpatient care	1.25 (1.17-1.35)	<.0001
Renal insufficiency	0.84 (0.78-0.80)	<.0001
Age (per 10 y)	0.95 (0.93-0.98)	.0002
Diabetes mellitus	0.91 (0.85-0.97)	.0096
β-Blockers		
Positive cardiac markers	1.47 (1.38-1.58)	<.0001
Signs of CHF	0.75 (0.72-0.79)	<.0001
Cardiology inpatient care	1.26 (1.20-1.33)	<.0001
ST depression†	1.15 (1.10-1.20)	<.0001
Transient ST elevation†	1.16 (1.07-1.24)	<.0001
Age (per 10 y)	0.97 (0.96-0.99)	.0003
Heparin (unfractionated heparin or LMWH)		
Positive cardiac markers	2.22 (2.04-2.40)	<.0001
Cardiology inpatient care	1.58 (1.47-1.70)	<.0001
ST depression†	1.33 (1.27-1.40)	<.0001
Transient ST elevation†	1.50 (1.36-1.64)	<.0001
Renal insufficiency	0.79 (0.74-0.83)	<.0001
Age (per 10 y)	0.95 (0.92-0.97)	<.0001
Signs of CHF	0.90 (0.85-0.95)	.0001

OR, Odds ratio.
*High-risk features (age, signs of congestive heart failure, diabetes mellitus, and renal insufficiency) that are not significantly associated with use of each medication class ($P > .05$) are not listed.
†Compared with neither.

Acute care decision making

The ACC/AHA guidelines recommend targeting acute medical therapies and invasive procedures for patients with NSTE ACS with high-risk features including ischemic electrocardiographic changes, positive cardiac markers, age >75 years, signs of CHF, and/or hemodynamic instability.[1,2] Although ischemic electrocardiographic changes and positive cardiac markers have commonly been used as inclusion criteria for NSTE ACS clinical trials that have been incorporated into guideline recommendations for acute care, patients with other high-risk features such as advanced age, CHF, and renal insufficiency were excluded from these clinical trials or underrepresented in trial enrollment.[15-17] Consequently, these high-risk features were associated consistently with lower use of acute medications and procedures in this analysis, while positive cardiac markers and ischemic ST-segment changes were associated with higher use of acute therapies.[11,12]

High-risk clinical characteristics are typically interrelated and clustered together, so clinicians may be influenced by safety concerns relating to antiplatelet and antithrombotic medications and invasive procedures in high-risk populations that were not delineated by clinical trials. Furthermore, the association between cardiology inpatient care and increased use of acute care

Table V. Association of high-risk clinical features with discharge medication use*

	Adjusted OR (95% CI)	*P* Value
Aspirin		
Cardiology inpatient care	1.41 (1.32-1.51)	<.0001
Positive cardiac markers	1.39 (1.27-1.52)	<.0001
Renal insufficiency	0.82 (0.77-0.88)	<.0001
Signs of CHF	0.88 (0.83-0.94)	.0001
ST depression	1.07 (1.01-1.14)	.0055
Transient ST elevation	1.19 (1.07-1.33)	.0055
β-Blockers		
Positive cardiac markers	1.57 (1.44-1.71)	<.0001
Cardiology inpatient care	1.15 (1.09-1.22)	<.0001
ST depression†	1.12 (1.06-1.19)	<.0001
Transient ST elevation†	1.23 (1.12-1.36)	<.0001
Signs of CHF	0.90 (0.85-0.96)	.0006
ACE inhibitors‡		
Signs of CHF	1.35 (1.27-1.43)	<.0001
Positive cardiac markers	1.26 (1.18-1.36)	<.0001
Renal insufficiency	0.83 (0.77-0.88)	<.0001
ST depression†	1.14 (1.06-1.22)	.0065
Transient ST elevation†	1.00 (0.95-1.05)	.0065
Cardiology inpatient care	1.07 (1.02-1.13)	.0033
Lipid-lowering agents§		
Age (per 10 y)	0.86 (0.84-0.89)	<.0001
Signs of CHF	0.86 (0.80-0.92)	<.0001
Cardiology inpatient care	1.17 (1.09-1.26)	<.0001
Positive cardiac markers	1.14 (1.05-1.24)	.0024

*High-risk features (age, signs of congestive heart failure, diabetes mellitus, and renal insufficiency) that are not significantly associated with use of each medication class ($P > .05$) are not listed.
†Compared with neither.
‡Only for patients with ejection fraction <40%, history of congestive heart failure, hypertension, or diabetes mellitus.
§Only for patients with documented hyperlipidemia or measured low-density lipoprotein cholesterol >125 mg/dL.

guideline recommendations suggest that cardiologists may be more comfortable using the whole complement of acute therapies.[11,12,18] However, because patients who undergo early catheterization are more likely to receive all acute guideline-recommended medications, the influence of cardiology care may center upon targeting patients for invasive management and concomitant aggressive medical treatment.[11]

Balancing efficacy and safety with acute therapies

During the acute care period, patients with NSTE ACS with high-risk features are more likely to suffer an adverse outcome and are also more likely to experience bleeding complications and to undergo blood transfusions.[6-10,19,20] Furthermore, recent analyses have demonstrated that high-risk patients with NSTE ACS have improved outcomes with invasive management but also have a higher rate of bleeding complications.[21-23] The ACC/AHA guidelines give class I recommendations for acute heparin and acute GpIIb-IIIa inhibitors combined with early invasive management, but the guidelines do not specify dose adjustments for these medications (such as dose reductions for renal insufficiency and desired ranges for antithrombin monitoring) and do not delineate approaches to mitigate the risks of procedural complications (especially for patients with renal insufficiency or class IV CHF).[1,2] Our findings of increased transfusion rates for high-risk subgroups despite lower use of aspirin, heparin, GpIIb-IIIa inhibitors, and early catheterization may be explained by excessive dosing of adjustable anticoagulant medications when they are administered to these patients but may also relate to intrinsic bleeding risks in high-risk populations. Thus, the appropriateness of the acute management of patients with NSTE ACS is difficult to ascertain, given the challenges in balancing the risks and benefits of medical therapies and invasive management in patients at increased risk for both adverse outcomes and bleeding complications.

Discharge care decision making

Compared with acute care decisions, treatment decisions upon hospital discharge for patients with NSTE ACS may not be as strongly influenced by safety concerns because invasive procedures have been completed by the time of discharge, and bleeding risks associated with long-term oral medications are likely to be less prominent than the bleeding risks associated with intravenous antithrombin and antiplatelet therapies used during the hospitalization. As a result, discharge medications in CRUSADE appear to be appropriately targeted for certain indications, such as increased use of β-blockers for patients with positive cardiac markers and decreased use for patients presenting with signs of CHF, and increased use of ACE inhibitors for patients with signs of CHF and decreased use for patients with renal insufficiency.

The association of cardiology care with increased use of discharge medications may have influenced these discharge treatment patterns. However, patients with signs of CHF were less likely to receive aspirin and lipid-lowering agents, and elderly patients were less likely to receive lipid-lowering agents—findings that have been reported in other recent analyses.[7,24] Furthermore, these high-risk patients were less likely to receive inpatient secondary preventative interventions such as smoking cessation and dietary counseling, which do not impose a financial burden nor safety risk upon patients. Unmeasured factors such as the high cost of long-term medications and uncertainty among clinicians regarding the impact of medications and lifestyle changes in patients with a limited expected lifespan may have influenced discharge management decision making, but persistent undertreatment of high-risk patients also likely explains these findings.

Limitations

Certain limitations were present with this analysis. First, we evaluated only a fraction of the overall NSTE

Table VI. Suggested methods to improve translation of guideline recommendations into practice

Expand enrollment criteria for clinical trials
Selectively target high-risk patients
Develop standardized contraindications for guideline recommendations
Identify "ideal" candidates for class IA/IB guideline recommendations
Incorporate dosing recommendations for anticoagulant medications into guidelines
Continue to evaluate how guideline adherence influences clinical outcomes
Incorporate quality indicators for acute coronary syndromes care into clinical practice standards

ACS population admitted to US hospitals during the analysis period, so a selection bias related to the unequal geographic distribution of participating hospitals may have influenced these results. Similarly, the low percentage of community hospitals without full-service catheterization and/or revascularization capabilities in CRUSADE limits the applicability of our findings to these hospitals. Second, we could not evaluate clinical outcomes, procedural use, and discharge treatment patterns in the 13% of patients who were transferred out to other institutions because of current privacy regulations that restrict anonymous data collection after hospital transfer. Third, we identified cardiology inpatient care as a significant predictor of increased use of guideline recommendations, but we could not precisely detail the influence of cardiology inpatient care and/or cardiology consultation on care patterns. Fourth, we were unable to account for undocumented contraindications to guideline recommendations that were not detailed in medical records but may have led to appropriate withholding of certain medications. Fifth, we were not able to quantify the impact of absolute differences in treatments on mortality rates because the relationship between guideline adherence and mortality is complicated by multiple possible permutations in the use and timing of several medications and procedures for individual patients. Sixth, hospitals were encouraged to submit data on consecutive patients meeting the inclusion criteria for CRUSADE, but anonymous data collection and privacy regulations prevented verification of consecutive patient inclusion by participating institutions. Thus, we could not compare characteristics of patients included in CRUSADE with those of all patients with NSTE ACS treated by participating institutions during the period of the analysis. Finally, the initial ACC/AHA guideline recommendations for NSTE ACS published in 2000 were revised and released in March, 2002, but our analysis period (January 2001 to March 2003) spanned the 2 iterations of the guideline revisions.[1,2] We did not evaluate temporal changes in treatment patterns for individual class I guideline recommendations, but we recognize that changing indications for guideline recommendations may have influenced treatment patterns demonstrated in this analysis.

Translating guidelines into practice

Contemporary adherence to the ACC/AHA guidelines for treatment of NSTE ACS at US hospitals appears to be strongly influenced by patient risk status because patients with the highest risk of mortality are least likely to receive guideline-recommended therapies and interventions. However, a recent study has demonstrated that comprehensive use of guideline recommendations at hospital discharge leads to the greatest relative reduction in long-term mortality in patients with the highest predicted risk of mortality upon hospital presentation.[25] The translation of practice guideline recommendations into treatment decisions in practice could be improved if significant changes were made in the conduct of clinical trials, the development of practice guidelines, and the surveillance of clinical care provided to patients with NSTE ACS (Table VI). Furthermore, the significant association of cardiology inpatient care with the increased use of all guideline-recommended therapies and interventions suggests that collaboration among cardiologists and noncardiologists will be essential to improve the care of high-risk patients with NSTE ACS.[11,12,18]

Ongoing quality improvement initiatives such as CRUSADE, Get with the Guidelines, and the Guidelines Applied in Practice initiative are focusing upon improving the care of ACS patients, but novel quality improvement approaches that target increased use of evidence-based therapies specifically for the highest-risk patients with NSTE ACS may further enhance these initiatives.

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Appendix A

Contraindications to medication use*

Aspirin or clopidogrel: active or recent bleeding, serious gastrointestinal or genitourinary bleeding, platelet count <100 000/mm^3, anemia, and use of warfarin.

Glycoprotein IIb/IIIa inhibitor: bleeding diathesis, bleeding within 30 days, severe hypertension, recent major surgery, recent stroke, any prior hemorrhagic stroke, platelet count <100 000/mm^3, and serum creatinine >4.0 mg/dL.

Low-molecular-weight or unfractionated heparin: active bleeding, bleeding history, hypersensitivity to pork products, and platelet count <100 000/mm^3.

β-Blockers: bradycardia, >1st-degree atrioventricular block, cardiogenic shock, hypotension, and chronic obstructive pulmonary disease/asthma/bronchospasm.

Angiotensin-converting enzyme inhibitors: history of angioedema, impaired renal function, hypotension, hyperkalemia, pregnancy, and liver disease.

Lipid-lowering agents: hepatic or renal dysfunction, abnormal liver function tests, and primary biliary cirrhosis.

**These contraindications were listed in the instructions for the CRUSADE Data Collection Form. Allergy/hypersensitivity was listed as a contraindication for each medication.*