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Myocardial Infarction

Evolution in Cardiovascular Care for Elderly Patients With Non–ST-Segment Elevation Acute Coronary Syndromes

Results From the CRUSADE National Quality Improvement Initiative

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OBJECTIVES This study evaluated the impact of age on care and outcomes for non–ST-segment elevation acute coronary syndromes (NSTE ACS).

BACKGROUND Recent clinical trials have expanded treatment options for NSTE ACS, now reflected in guidelines. Elderly patients are at highest risk, yet have previously been shown to receive less care than younger patients.

METHODS In 56,963 patients with NSTE ACS at 443 U.S. hospitals participating in the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines (CRUSADE) National Quality Improvement Initiative from January 2001 to June 2003, we compared use of guidelines-recommended care across four age groups: <65, 65 to 74, 75 to 84, and ≥85 years. A multivariate model tested for age-related differences in treatments and outcomes after adjusting for patient, provider, and hospital factors.

RESULTS Of the study population, 35% were ≥75 years old, and 11% were ≥85 years old. Use of acute anti-platelet and anti-thrombin therapy within the first 24 h decreased with age. Elderly patients were also less likely to undergo early catheterization or revascularization. Whereas use of many discharge medications was similar in young and old patients, clopidogrel and lipid-lowering therapy remained less commonly prescribed in elderly patients. In-hospital mortality and complication rates increased with advancing age, but those receiving more recommended therapies had lower mortality even after adjustment than those who did not.

CONCLUSIONS Age impacts use of guidelines-recommended care for newer agents and early in-hospital care. Further improvements in outcomes for elderly patients by optimizing the safe and early use of therapies are likely. (J Am Coll Cardiol 2005;46:1479–87) © 2005 by the American College of Cardiology Foundation

The optimal management of patients with acute coronary syndromes (ACS) continues to evolve rapidly with the development of new therapeutics and strategies of care. The American College of Cardiology/American Heart Association (ACC/AHA) recently updated their treatment guidelines for non–ST-segment elevation (NSTE) ACS to reflect these advancements (1,2). The guidelines emphasize the need to provide intensive and early medical and interventional therapy, particularly for those at highest risk for short-term events (3).

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Prior work has shown that elderly patients with NSTE ACS are at greater risk of mortality and morbidity than younger patients, and that medication and catheter-based therapies have the greatest benefit on outcomes among patients at highest risk (4,5). Studies from the 1990s documented widespread underuse of cardiac medications in elderly populations with ST-segment elevation myocardial infarction (6–13), and many have emphasized the need for evidence-based cardiac care in all patients, particularly elderly patients (14,15). Recent efforts to increase physician awareness of age disparities and the arrival of new guidelines-

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Abbreviations and Acronyms

ACC/AHA	= American College of Cardiology/ American Heart Association
BP	= blood pressure
CHF	= congestive heart failure
CRUSADE	= Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/ American Heart Association Guidelines
NSTE ACS	= non–ST-segment elevation acute coronary syndromes

recommended therapies for NSTE ACS may have altered current practice patterns for elderly ACS patients.

This analysis compares contemporary in-hospital treatment patterns and outcomes of elderly patients with NSTE ACS with their younger counterparts. We used the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the ACC/AHA Guidelines (CRUSADE) National Quality Improvement Initiative database to address this question across 443 hospitals in 46 states (16). Using this large database, we provide specific insight into the early and discharge use of medications, reported contraindications, use of an invasive strategy, and the relationship between guidelines-recommended care and mortality in young and old patients.

METHODS

Population. The CRUSADE initiative is an ongoing database of patients with high-risk NSTE ACS admitted to U.S. hospitals. The current analysis includes 56,963 patients who were treated at 443 hospitals between January 1, 2001, and June 30, 2003. Inclusion criteria for participation in the database were ischemic symptoms lasting ≥10 min combined with positive cardiac markers or ischemic ST-segment electrocardiograph changes (ST-segment depression or transient ST-segment elevation). Patients were ineligible for the CRUSADE initiative if they transferred into a participating hospital >24 h after the last episode of ischemic symptoms. Patients were ineligible for this analysis if they transferred out of a participating hospital resulting in incomplete data on acute care, in-hospital outcomes, and discharge therapies (n = 8,385), or had missing age information (n = 76), leaving a final population of 56,963 patients.

Data collection. Hospitals participating in the CRUSADE initiative collect detailed process of care and in-hospital outcomes data through retrospective chart review. Data are collected anonymously during the initial hospitalization, and because no patient identifiers are collected, individual informed consent is not required. The institutional review board of each institution approves participation in the CRUSADE initiative. Data collected include the use of acute medications (within 24 h of presentation), use and timing of invasive cardiac procedures, laboratory results, physician and hospital characteristics, and discharge therapies and interventions.

Data definitions. Charts were abstracted using specified definitions from the CRUSADE initiative data collection forms. Hypertension was defined as systolic blood pressure (BP) >140 mm Hg, diastolic BP >90 mm Hg on repeated measurements, or hypertension chronically treated with anti-hypertensive medications. Renal insufficiency was defined by serum creatine >2.0 mg/dl, creatinine clearance <30 ml/min, or need for renal dialysis. Signs of congestive heart failure (CHF) were indicated by exertional dyspnea, orthopnea, shortness of breath, labored breathing, fatigue either at rest or with exertion, rales in more than one-third of the lung fields, elevated jugular venous pressure, S_3 gallop, or pulmonary congestion on X-ray believed to represent cardiac dysfunction. Hyperlipidemia was defined as total cholesterol >200 mg/dl or treatment with a lipid-lowering agent. Recurrent infarction was defined by clinical signs and symptoms of a new infarction distinct from the presenting ischemic event and meeting predefined cardiac marker and electrocardiogram criteria. Cardiogenic shock was defined by systolic BP <90 mm Hg for >1 h, not responsive to fluid resuscitation alone, and thought to be secondary to cardiac dysfunction. Transfusions were defined as any non-autologous transfusion(s) of either whole blood or packed red blood cells. The attending physician who primarily cared for the patient during the hospitalization was determined by the most frequent and consistent notations in the medical record; specialties included cardiologist, internist, family practitioner, and other.

Contraindications. The CRUSADE initiative collects information regarding contraindications to all guidelines-recommended medications that were clinically documented in the patient's medical record. Specific clinical contraindications for given agents were as follows: aspirin (intolerance, allergy, active bleeding/history of bleeding, ulcer or serious gastrointestinal or genitourinary bleeding, dyspepsia, platelet count <100,000/mm^3, anemia, use of warfarin); beta-blockers (allergy/hypersensitivity, bradycardia, heart block greater than first degree, cardiogenic shock, hypotension, chronic obstructive pulmonary disease/asthma/bronchospasm); glycoprotein IIb/IIIa inhibitors (active/recent bleeding, allergy/intolerance/hypersensitivity, platelet count <100,000/mm^3, severe hypertension, recent major surgery, recent stoke/any previous hemorrhagic stroke, serum creatine >4.0 mg/dl, severe comorbid illness); heparin (active/recent bleeding, platelet count <100,000/mm^3, ulcer or serious gastrointestinal or genitourinary bleeding, history of known heparin induced thrombocytopenia, severe comorbid illness); lipid-lowering agents (allergy/hypersensitivity, hepatic or renal dysfunction, abnormal liver function test results, primary biliary cirrhosis); angiotensin-converting enzyme inhibitors (allergy/intolerance, hypersensitivity, history of angioedema, impaired renal function, hypotension, hyperkalemia, pregnancy, liver disease). Importantly, beyond this pre-specified list, we allowed clinicians to document contraindications that precluded them from treating a patient. This conservative approach ensured that medication use was assessed only among patients with true eligibility for each therapy.

Outcomes. Acute and discharge use of ACC/AHA guidelines-recommended therapies was then determined for those patients in our population who had indications but no reported contraindications for each therapy (Appendix) (1,2). We considered only those therapies receiving a class IA (evidence and/or general agreement that a given procedure or treatment is useful and effective from data derived from multiple randomized clinical trials that involved large numbers of patients) or class IB (data derived from a limited number of randomized trials that involved small numbers of patients or from careful analyses of non-randomized studies or observational registries) designation. All decisions regarding the use of medications or procedures were made by the treating physicians. We examined early use of medications, defined as those administered within 24 h of admission, and at discharge. Early medications included aspirin, clopidogrel, beta-blockers, heparin, low-molecular-weight heparin, and platelet glycoprotein IIb/IIIa inhibitors (1). Early invasive strategy, defined as cardiac catheterization within 48 h of admission, was also determined. Discharge medications included aspirin, clopidogrel, beta-blockers, angiotensin-converting enzyme inhibitors (with an ejection fraction <40%, or the presence of diabetes mellitus or hypertension), and lipid-lowering agents (with hyperlipidemia or low-density lipoprotein >100 mg/dl) per ACC/AHA guidelines recommendations (1). In-hospital clinical outcomes of interest included in-hospital mortality, myocardial infarction, CHF, recurrent stroke, revascularization, and bleeding requiring transfusion.

Analysis. In-hospital care patterns and outcomes were compared between groups of relatively older and younger patients with NSTE ACS. We clustered patients into four age groups: <65, 65 to 74, 75 to 84, and ≥85 years old; in our analysis, young patients refers to those <65 years of age. We compared patients' baseline demographics, clinical characteristics, care patterns, and in-hospital outcomes, as well as the features of the admitting hospital. Continuous variables were reported as means with standard deviations, and categorical variables were reported as percentages. Significance was determined using chi-square tests and Kruskal-Wallis tests for categorical and continuous variables, respectively.

For medications, interventions, and in-hospital clinical outcomes, we used generalized estimating equations to adjust for patient comorbidity and provider characteristics. Generalized estimating equations provided a variant of the multiple logistic regression model, through which we were able to adjust for the clustering that results from patients admitted to the same hospital being more similar to each other than to those admitted to other hospitals (17). The model also incorporated a broad range of patient and hospital characteristics that included insurance type (Medicare/Medicaid, self/none, or health maintenance organization/private), age, female gender, body mass index, white race, family history of coronary artery disease, hypertension, diabetes, current/recent smoker, hyperlipidemia, prior myocardial infarction, prior percutaneous coronary intervention, prior coronary artery bypass grafting surgery, prior CHF, prior stroke, renal insufficiency, ST-segment depression, transient ST-segment elevation, signs of CHF at presentation, heart rate, systolic blood pressure, total number of hospital beds, teaching versus academic institution, and cardiologist care. From the multivariable analyses, the effect of age was then determined after adjustment for confounding factors between comparison groups.

Finally, we explored in-hospital mortality for older and younger patients after adjusting for baseline characteristics and the number of recommended ACS treatments they received in which we modeled the number of recommended treatments as an ordinal variable. Five treatments were considered: 1) early aspirin, 2) early beta-blockers, 3) early heparin (any), 4) early glycoprotein IIb/IIIa inhibition and catheterization within 48 h, and 5) catheterization within 48 h. All analyses were performed with SAS software version 8.2 (SAS institute Inc., Cary, North Carolina).

RESULTS

Demographics and clinical characteristics of the 56,963 NSTE ACS patients are shown by four age groups (Table 1). The majority of our population was age 65 years or older (58%), with 11.2% being ≥85 years old, and the oldest patient being 103 years old. The vast majority of patients had positive cardiac markers (>85%), and many had ST-segment depression at presentation as well (~40%). Elderly patients were more likely to have positive markers and CHF at presentation than younger patients (91.6% positive markers and 41.4% CHF in the ≥85 age group). With advancing age, elderly patients had a declining prevalence of cardiac risk factors (diabetes, hyperlipidemia, smoking), but an increasing history of known cardiac disease (prior CHF, myocardial infarction, or coronary artery bypass grafting). In addition, elderly patients had more comorbidity (renal insufficiency, stroke, and hypertension). Thus, among an already high-risk population, older age predicted a greater burden of comorbidity and disease severity at presentation. In addition, older patients were more likely to be treated at smaller, non-academic hospitals, and less likely to be treated by specialists.

With advancing age, medication contraindications were reported more often for early and discharge therapies. Among medications, contraindication rates varied from 2.6% for contraindications to lipid-lowering agents to 13.4% for glycoprotein IIb/IIIa inhibitors. Reported con-

Table 1. Baseline Demographics and Clinical Characteristics*

	<65 Yrs (n = 23,694)	65–74 Yrs (n = 13,033)	75–84 Yrs (n = 13,835)	≥85 Yrs (n = 6,401)
Patient factors (%)				
Age (yrs, mean ± SD)	53.1 ± 7.9	69.6 ± 2.9	79.3 ± 2.8	88.8 ± 3.3
Male	69.1	60.5	51.6	38.0
White	74.6	81.2	85.3	87.3
Diabetes mellitus	29.6	38.8	35.5	24.7
Renal insufficiency	8.7	14.3	18.7	21.5
Hypertension	61.8	73.3	75.3	72.8
Hypercholesterolemia	48.5	53.0	45.0	28.2
Smoking	46.4	21.6	10.2	4.0
Prior MI	26.7	33.4	34.6	35.2
Prior stroke	5.9	11.4	16.5	17.7
Prior CHF	9.8	18.8	26.4	36.2
Prior CABG	15.5	26.2	25.9	14.5
Prior PCI	22.1	24.9	22.2	11.9
CHF at presentation	12.5	22.4	31.1	41.4
ECG changes at presentation				
ST-segment depression	38.0	42.1	41.7	39.5
Transient ST-segment elevation	12.8	9.7	7.6	6.9
Positive cardiac markers	86.7	87.3	88.9	91.6
Provider factors (%)				
Cardiology in-patient care	67.0	60.8	51.5	38.2
Hospital factors (%)				
Academic†	32.6	28.4	27.3	24.3
Catheterization laboratory	97.8	96.6	95.2	91.2
Bed size (mean ± SD)	422 ± 197.5	413 ± 200.9	408 ± 203.1	393 ± 206.4

*All p values < 0.0001; data presented as percentages unless otherwise indicated. †Academic hospitals were members of the Council of Teaching Hospitals.

CABG = coronary artery bypass grafting; CHF = congestive heart failure; ECG = electrocardiograph; MI = myocardial infarction; PCI = percutaneous coronary intervention; SD = standard deviation.

traindication rates tended to increase with advancing patient age (Fig. 1).

The percentages and adjusted odds ratios for use among eligible patients of early in-hospital medications by age group are shown in Table 2 and Figure 2A. In-hospital use of aspirin and beta-blockers had small but statistically significant reductions in use past 65 years of age, and heparin had a small but significant reduction in use past 85 years of age. Age had its most notable impact on use of acute clopidogrel and platelet glycoprotein IIb/IIIa inhibitors. Despite 92% of patients age >85 years having positive cardiac markers, only 30% received clopidogrel, whereas 12.8% received platelet glycoprotein IIb/IIIa inhibitors.

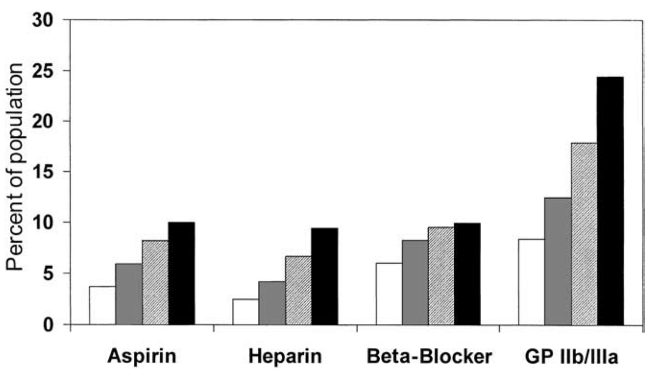

Figure 1. Contraindications to short-term therapies by age and drug type. Includes contraindications defined by clinical criteria or provider discretion that use of the agent was contraindicated in specific patients. **Open bars** = <65 years old; **grey bars** = 65 to 74 years old; **ruled bars** = 75 to 84 years old; **black bars** = ≥85 years old. GP = glycoprotein.

During their hospitalization, elderly patients were less likely to undergo early invasive care or revascularization procedures (Fig. 2B, Table 2). The use of an early invasive strategy, defined as diagnostic coronary angiography within 48 h of admission, tapered with age starting around the age of 70 years (Fig. 2B). Past the age of 75 years, only 40% underwent early invasive care, and past age 85 that number was <20%. We also examined therapies used among invasively managed patients. As seen in Table 3, use of clopidogrel and glycoprotein IIb/IIIa inhibitors was significantly lower among invasively managed elderly patients compared with similarly managed younger patients.

The risk of in-hospital death increased continuously with patient age from 1.9% for age <65 to 11.5% for age ≥85 years (Fig. 2C). After adjustment for patient and hospital factors, the odds ratio of in-hospital death for older age groups compared with age <65 was 1.88 for patients age 65 to 74 years, 2.46 for those ages 75 to 84 years, and 3.00 for those age ≥85 years. (Table 4) Other adverse in-hospital events also increased steadily with age, and included recurrent myocardial infarction, CHF, stroke, and transfusion. Most notable among these was CHF, which increased three-fold between age 65 and 85 years (unadjusted rates: age <65 years, 5.1%, vs. age ≥85 years, 16.7%).

The use of five guidelines-recommended therapies

Table 2. Early (≤24 h of Admission) Medications and Early Procedural Care (≤48 h of Admission) by Age Group*

	<65 yrs	65–74 yrs		75–84 yrs		≥85 yrs	
	%	%	Adjusted OR (95% CI)†	%	Adjusted OR (95% CI)†	%	Adjusted OR (95% CI)†
Medications							
Aspirin	93.1	90.6	0.86 (0.80–0.94)	89.6	0.87 (0.80–0.96)	88.5	0.92 (0.81–1.04)
Beta-blockers	79.7	78.1	0.94 (0.89–1.00)	76.1	0.89 (0.84–0.95)	75.8	0.96 (0.88–1.04)
Heparin, any	84.8	83.7	1.07 (1.00–1.14)	80.4	0.99 (0.92–1.06)	72.8	0.77 (0.70–0.85)
Clopidogrel	45.2	40.8	0.93 (0.88–0.98)	35.0	0.83 (0.78–0.88)	29.9	0.82 (0.76–0.87)
GP IIb/IIIa inhibitors	44.6	35.9	0.90 (0.84–0.95)	25.8	0.68 (0.63–0.73)	12.8	0.39 (0.35–0.44)
Procedures							
Cath	83.1	77.8	0.95 (0.88–1.02)	64.0	0.60 (0.55–0.65)	32.2	0.20 (0.17–0.23)
Cath <48 h	62.8	53.5	0.88 (0.83–0.94)	40.4	0.63 (0.59–0.67)	18.0	0.25 (0.22–0.28)
PCI	50.4	42.2	0.89 (0.84–0.95)	33.4	0.74 (0.68–0.80)	18.8	0.43 (0.39–0.49)
PCI <48 h	38.7	29.6	0.88 (0.82–0.94)	21.0	0.68 (0.63–0.73)	10.1	0.37 (0.32–0.42)
CABG	14.5	16.8	1.37 (1.27–1.48)	12.1	1.02 (0.93–1.12)	3.1	0.25 (0.20–0.30)

*All p values < 0.0001; all medication use in patients without contraindications (see Appendix). †In comparison with patients <65 years of age. All percentages represent use among those with no contraindications, thus the number of patients vary slightly from the age group total shown in Table 1. For example, among patients age <65, the number of patients range from 20,731 to 23,694, and among patients age ≥85, the number of patients range from 4,837 to 6,401.

Cath = catheterization; CI = confidence interval; GP = glycoprotein; OR = odds ratio; other abbreviations as in Table 1.

(aspirin, heparin, β-blockers, glycoprotein IIb/IIIa inhibition, and catheterization) was also associated with a lower likelihood of in-hospital mortality (Fig. 3). After adjusting for other factors, in-hospital death was lowered by an increasing use of recommended therapies for both patients age ≥75 years and patients age <75 years alike

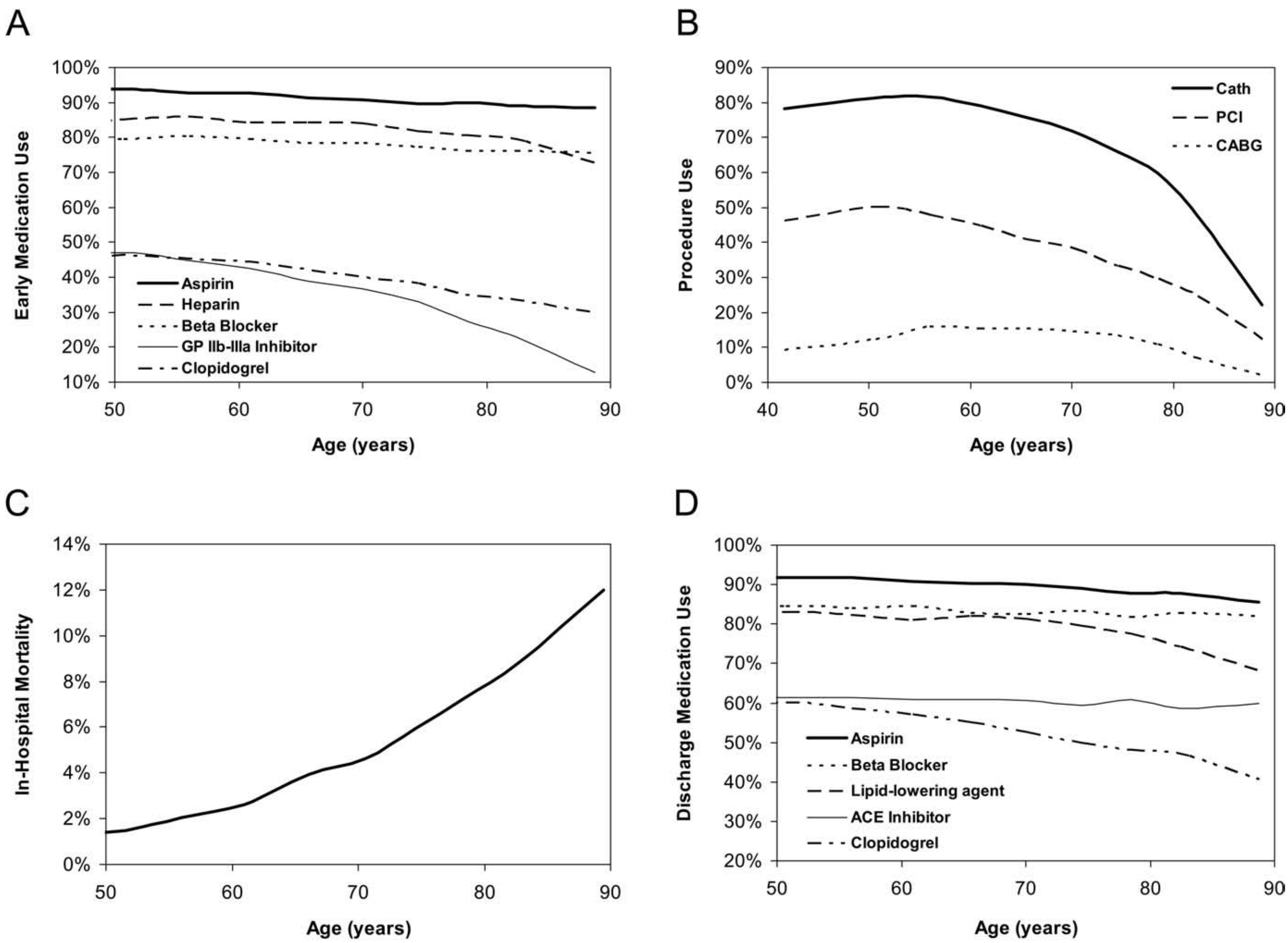

Figure 2. **(A)** Short-term use of medications within the first 24 h of admission by age (among those with no contraindications). **(B)** Use of in-hospital diagnostic and invasive procedures by age. **(C)** In-hospital mortality by age. **(D)** Discharge use of medications by age (among those with no contraindications). ACE = angiotensin-converting enzyme; CABG = coronary artery bypass grafting; Cath = catheterization; GP = glycoprotein; PCI = percutaneous coronary intervention.

Table 3. Early Clopidogrel and Glycoprotein IIb/IIIa Inhibitor Use in Patients Managed With Early Invasive Strategy (Cath ≤48 h From Admission) Versus Conservative Care (Cath >48 h After Admission or No Cath)*

	<65 yrs	65–74 yrs	75–84 yrs	≥85 yrs
Clopidogrel				
Overall	45.2	40.8	35.0	29.9
Early invasive (%)	55.0	51.4	47.8	51.0
Conservative (%)	30.8	30.6	28.1	26.5
GP IIb/IIIa inhibitors				
Overall	44.6	35.9	25.8	12.8
Early invasive (%)	58.8	51.9	45.5	42.8
Conservative (%)	22.1	18.4	13.4	7.0

*In patients without contraindications (see Appendix) and alive at discharge (patient denominator varies slightly from total n for age group).
Abbreviations as in Table 2.

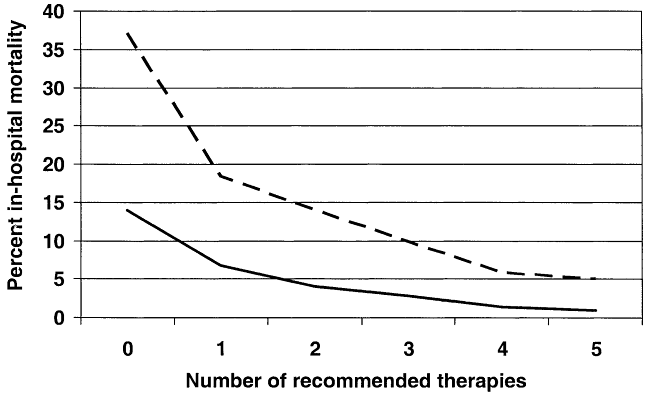

Figure 3. Adjusted in-hospital mortality among older and younger patients undergoing an early invasive strategy by the number of guideline recommendations applied (cardiac catheterization, short-term aspirin, short-term beta-blocker, short-term heparin, and short-term glycoprotein IIb/IIIa inhibitors). **Dashed line** = ≥75 years old; **solid line** = <75 years old.

(odds ratio, 0.79; 95% confidence interval, 0.75 to 0.83; and odds ratio, 0.71; 95% confidence interval, 0.67 to 0.75, respectively). A formal test for interaction between treatment and age was significant because of the larger difference in mortality between younger and older patients given fewer therapies compared with those given all five therapies. This indicates a similar or greater impact of treatment on outcomes in elderly patients.

For those who survived to hospital discharge, percentages and adjusted odds ratios for use of discharge medications by age group are shown only among those with no reported contraindications and with specific indications (Table 5 and Fig. 2D). After adjustment, discharge use of aspirin, beta-blockers, and angiotensin-converting enzyme inhibitors was not influenced by patient age. However, lipid-lowering agents and clopidogrel use were significantly lower in elderly patients than in younger patients.

DISCUSSION

The ACC/AHA guidelines for the treatment of NSTE ACS do not alter therapeutic recommendations based on age, apart from encouraging attention to comorbidities, preferences, and appropriate dosing of medications in elderly patients (1,2). In contrast to these guidelines, however, we found that use of many recommended therapies was lower among elderly patients even after controlling for contraindications and comorbidities. Remaining age gaps were particularly notable in three areas: 1) early use of intravenous medications, 2) use of invasive care, and 3) use of lipid-lowering agents and clopidogrel at discharge. We consider reasons and implications for remaining age gaps in guidelines-recommended care.

Early use of medications. Age had a relatively modest impact on the early use of aspirin and beta-blockers. However, the early use of heparin, platelet glycoprotein IIb/IIIa inhibitors, and clopidogrel decreased significantly among those age ≥75 years. The remaining gaps in recommended care may originate from uncertainty regarding the impact of age on expected treatment effects (18,19). However, randomized clinical trials have found that unfractionated heparin and low-molecular-weight heparin are effective in both young and old patients (20–22). Similarly, evidence also shows a benefit of platelet glycoprotein IIb/IIIa inhibitors in young and elderly patients with electrocardiograph changes or positive enzymes regardless of age, particularly if undergoing invasive management (23,24).

Delayed identification of ACS in elderly patients may further explain lower use of early therapies. Elderly patients are much less likely to present with classic chest pain, so diagnosis may wait until cardiac markers are elevated (25). In addition, elderly patients often have ACS coexisting with other acute illnesses, such as CHF or pneumonia, which may be the focus of initial care. However, because recurrent events are most likely to occur early in the hospitalization, this gap in early use of therapies contributes to adverse short-term outcomes such as reinfarction, CHF, and death.

Table 4. In-Hospital Outcomes After Acute Coronary Syndrome by Age*

	<65 yrs	65–74 yrs		75–84 yrs		≥85 yrs	
Outcomes	%	%	Adjusted OR (95% CI)†	%	Adjusted OR (95% CI)†	%	Adjusted OR (95% CI)†
Death	1.9	4.6	1.88 (1.65–2.14)	7.3	2.46 (2.14–2.83)	11.5	3.00 (2.53–3.55)
Repeat MI	2.5	3.5	1.22 (1.08–1.37)	4.0	1.36 (1.18–1.56)	4.1	1.39 (1.18–1.63)
CHF	5.1	9.4	1.29 (1.18–1.40)	13.5	1.56 (1.42–1.71)	16.7	1.62 (1.45–1.80)
Stroke	0.5	1.0	1.94 (1.50–2.51)	1.3	2.41 (1.86–3.13)	1.3	2.29 (1.63–3.22)
Blood transfusion	10.1	17.9	1.64 (1.52–1.76)	19.6	1.65 (1.52–1.79)	15.7	1.14 (1.02–1.27)

*All p values <0.0001. †In comparison with patients <65 years of age.
Abbreviations as in Table 2.

Table 5. Discharge Medications by Age Group*

Medications	<65 yrs	65–74 yrs		75–84 yrs		>85 yrs	
	%	%	Adjusted OR (95% CI)†	%	Adjusted OR (95% CI)†	%	Adjusted OR (95% CI)†
Aspirin	91.4	89.7	1.00 (0.92–1.08)	87.9	0.98 (0.89–1.08)	85.6	1.03 (0.90–1.17)
Beta-blockers	83.6	83.0	0.97 (0.90–1.05)	82.4	0.97 (0.89–1.05)	82.2	1.06 (0.97–1.16)
ACE inhibitors‡	61.0	60.7	0.98 (0.92–1.03)	59.5	0.94 (0.88–1.00)	60.2	1.01 (0.93–1.11)
Clopidogrel§	58.3	53.0	0.89 (0.84–0.94)	47.5	0.82 (0.77–0.87)	40.5	0.80 (0.77–0.87)
Lipid-lowering agents‖	82.0	80.5	0.92 (0.86–1.00)	75.6	0.79 (0.73–0.85)	65.2	0.59 (0.53–0.66)

*Discharge medication use only in patients without contraindications (see Appendix) and alive at discharge (patient denominator varies slightly from total n for age group). †In comparison with patients <65 years of age. ‡p values = NS; for congestive heart failure, ejection fraction <40%, diabetes mellitus, or hypertension. §Among patients without interventional procedures. ‖For history of hyperlipidemia or measured LDL >100 mg/dl.
ACE = angiotensin-converting enzyme; other abbreviations as in Table 2.

Physicians may also withhold therapy in elderly patients because of safety concerns arising from comorbidity and potential drug contraindications with age (Fig. 1). Age-related alterations in drug clearance increase bleeding risks (26). However, we found that use was still lower in elderly patients after excluding those with investigator-documented non-eligibility. Safety concerns should be considered in light of the potential harm caused by withholding effective therapies in high-risk elderly patients.

Less invasive care. The use of an invasive management strategy declines most precipitously with age. In the CRUSADE initiative, <50% of patients over the age of 65 years and only 11.2% of patients over the age of 85 years received early invasive care, despite 90% having positive cardiac markers. This conservative management of elderly ACS patients is similar to that found in prior studies (27). Although the debate about the ideal management for ACS continues, evidence from recent studies confirms a benefit of an early invasive approach in both young and old patients (28–31). The Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy (TACTICS) Thrombolysis In Myocardial Infarction (TIMI)-18 trial found an early invasive strategy conferred a 56% relative reduction in death or myocardial infarction at six months in patients with NSTE ACS older than 75 years of age who received early invasive management compared with those treated with a conservative management strategy (32). Similarly, the Trial of Invasive versus Medical therapy in Elderly patients (TIME) study (33,34) and the Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) study emphasized that older patients who underwent aggressive revascularization therapies had greater absolute risk reductions than younger patients (35).

Although patient preferences may also play a role in the conservative care of elderly patients, most elderly patients are willing to consider revascularization if recommended by their physicians (36). Thus, increasing the use of early invasive care and revascularization may be another opportunity for improving outcomes for elderly patients with NSTE ACS.

Discharge medications. The discharge use of aspirin, beta-blockers, and angiotensin-converting enzyme inhibitors did not decline with advancing age, suggesting that age gaps have narrowed over time in the use of these discharge medications (7,11–13). The limited use of lipid-lowering agents in elderly patients was the most notable finding among discharge medications. Although debate continues regarding the benefit of lipid-lowering drugs in the >85 years age group, their benefits in patients of all ages have been confirmed in two large recent studies (37,38). Mounting evidence confirms benefit from lipid-lowering therapy in the short term after ACS, such that even those with limited life expectancy will benefit (39).

The use of clopidogrel at discharge largely parallels the use of an invasive strategy during hospitalization in elderly patients. Most notably, the CURE study found that use of clopidogrel after ACS without invasive procedures was effective in reducing death, myocardial infarction, and stroke in both young and older patients (40–42).

Study limitations. The CRUSADE initiative is an observational study, thus unmeasured biases that influence the use of therapies may not have been captured. Specifically, contraindications were obtained during chart abstraction, not directly from the care team. However, this limitation should apply equally to patients of all ages, thereby minimally affecting observations across age groups. The CRUSADE initiative reports in-hospital outcomes, so conclusions about long-term mortality and quality of life implications for adherence to guidelines recommendations cannot be made from these data.

CONCLUSIONS

Optimizing the care of elderly patients with NSTE ACS is a timely imperative given the aging of the population. Applying evidence to the treatment of elderly patients falls short of recommendations in several areas. Physicians are understandably cautious regarding the application of newer therapies and early invasive care to high-risk elderly patients, and concerns over risks and side effects influence practice (43). Thus, future work on early recognition of ACS, safe application of acute treatments, and the use of secondary preventions in elderly patients should enable providers to further improve their outcomes after NSTE ACS.

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APPENDIX

For the class IA/IB recommended hospital and discharge medications from the ACC/AHA guidelines for the management of patients with unstable angina and non–ST-segment elevation myocardial infarction, please see the online version of this article.