Optimal Medical Therapy for Non–ST-Segment–Elevation Acute Coronary Syndromes
Exploring Why Physicians Do Not Prescribe Evidence-Based Treatment and Why Patients Discontinue Medications After Discharge

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Background—Acute coronary syndrome (ACS) patients in the highest risk categories are least likely to receive evidence-based treatments (EBTs). We sought to determine why physicians do not prescribe EBTs for patients with non–ST-segment–elevation ACSs and the factors determining use of these treatments after 1 year.

Methods and Results—One thousand nine hundred fifty-six non–ST-segment-elevation ACS patients were enrolled in the prospective, multicenter Canadian ACS registry II between October 2002 and December 2003. Each patient’s physician gave reasons why guideline-indicated medication(s) was not prescribed during hospitalization. Medication use and reason(s) for discontinuation after 1 year were obtained by telephone interview of the patients. The commonest reason for not prescribing EBTs was “not high-enough risk” or “no evidence/guidelines to support use.” However, Global Registry of Acute Coronary Events scores of patients not treated for this reason were often similar to or higher than those of patients prescribed such treatment. After 1 year, 77% of patients not on optimal ACS treatment at discharge remained without optimal treatment, and overall antiplatelet, α-blocker, and angiotensin-converting enzyme inhibitor use declined. Approximately one third of patients not taking EBTs had stopped their medication without instruction from their doctor.

Conclusions—Nonprovision of EBTs may be due to subjective underestimation of patient risk and hence, likely treatment benefit. Oversights in care delivery were also apparent. Objective risk stratification, combined with efforts to ensure provision and adherence to EBTs, should be encouraged.

Key Words: acute coronary syndrome ■ medical therapy ■ guideline

C
urrent management of non–ST-segment–elevation acute coronary syndromes (NSTE ACSs) is a combination of pharmacologic treatments and invasive revascularization that aims to prevent recurrent ischemic events while minimizing bleeding complications.1 Antiplatelet drugs (aspirin, thienopyridines, glycoprotein IIb/IIIa antagonists [GPAs]), statins, angiotensin-converting enzyme inhibitors (ACEIs), and β-blockers have each been shown in randomized, clinical trials to reduce recurrent adverse cardiovascular events or mortality after ACSs. Provision of evidence-based medical treatments (EBTs) is associated with improved survival.2–6 Quality-improvement initiatives have thus focused on improving adherence to guideline recommendations for secondary prevention.7–9 Despite this, most observational data suggest that treatment-eligible patients in the highest objective risk score categories are the least likely to receive EBTs.10–14 To minimize this “risk-treatment paradox,” it is first critical to understand the factors that influence clinical decision making in such cases, so that the benefits of EBTs demonstrated in randomized, controlled trials can be translated into “real-world” practice.

Accordingly, we sought to examine the precise reasons why physicians chose not to prescribe guideline-recommended medications in a large registry of NSTE ACS patients. Furthermore, we conducted telephone interviews with patients at 1 year to determine their medication use and...
the reason(s) why EBTs were discontinued or not taken after hospital discharge.

WHAT IS KNOWN

- Provision of EBTs after ACS is associated with improved survival. High-risk patients are the least likely to receive EBTs.

WHAT THE STUDY ADDS

- Physician underestimation of patient risk status and suboptimal adherence to practice guidelines are the most common reasons for omission of EBTs at hospital discharge. At 1 year after ACS hospitalization, approximately one third of patients either independently discontinued or could not recall why they were no longer taking various evidence-based medications that were prescribed at discharge. Patients who underwent PCI during ACS hospitalization were more likely to be taking EBT both at discharge and at 1 year.

Methods

Registry Design

The Canadian ACS registry II was a prospective, multicenter, observational study of the clinical characteristics, management practices, and in-hospital and 1 year outcomes of patients with NSTE ACSs. The design of ACS II has previously been described. All patients provided informed consent, and ethics board approval for the study was obtained at each hospital.

Setting and Participants

In brief, the ACS Registry II collected data from 36 Canadian hospitals between October 1, 2002, and December 31, 2003. Patients were eligible for inclusion if they were ≥18 years old and had been admitted to hospital with a presumptive diagnosis of ACS within 24 hours of symptom onset that was not precipitated by another significant comorbidity, such as severe anemia, trauma, or recent surgery. To exclude patients with ST-segment elevation myocardial infarction, those with ≥0.1 mV of ST-segment elevation in 2 or more contiguous leads or new/presumed new left bundle branch block myocardial infarction, those with an indication for OA therapy. ACEIs have a class Ia indication in patients with NSTE ACS in the presence of either hypertension, diabetes mellitus, chronic kidney disease, or heart failure and have a class IIa indication for all other NSTE ACS patients in the absence of contraindications. Optimal medical therapy (OMT) was therefore defined as the combination of any antplatelet or OA, β-blocker, ACEI, and statin at the time of hospital discharge.

Statistical Analysis

Patients were stratified into 3 groups according to their GRACE risk score on presentation: low risk (GRACE risk score ≤108), intermediate risk (GRACE risk score 109 to 140), and high risk (GRACE risk score ≥141). GRACE scores could not be calculated for 12% of patients because of missing data for any variable. In a sensitivity analysis, we imputed GRACE risk scores for patients with incomplete data. Rates of individual reasons for not taking each EBT were analyzed by direct questioning of patients within hospitals. The Mann-Whitney U test was used to compare continuous variables, and McNemar’s test was used for paired comparisons (discharge and 1-year follow-up). We used SPSS 15.0 (SPSS Inc, Chicago, Ill) for data analysis.

Results

Patient Demographics

One thousand nine hundred fifty-six patients had a final diagnosis of NSTE ACS, and complete data on discharge medication use were available for 1921 patients (50.1% NSTE myocardial infarction, 45.9% unstable angina) who survived to hospital discharge (Figure 1). Baseline demographic and presenting characteristics of the 1921 survivors included in the analysis are presented in Table 1 and have been reported previously. Most (85.5%) patients had a class I indication for ACEIs. When stratified by GRACE risk score, 38.8%, 34.2%, and 27.0% of patients were in the low, intermediate, and high risk groups, respectively. Overall, 65.4% of patients underwent coronary angiography during admission (invasive management), and 31.3% were revascularized by PCI and 10.9% by CABG.
EBT Use Within 24 Hours of Admission

The use of aspirin, clopidogrel, GPAs, and heparins in hospital within the first 24 hours is illustrated in Figure 2A. Low-molecular-weight heparin (LMWH) was used more commonly by noncardiologists (77.5% vs 58.5%, \( P < 0.015 \)) and at nonacademic hospitals (74.4% vs 45.9%, \( P = 0.03 \)). GPAs were used more commonly by cardiologists (13.1% vs 7.8%, \( P < 0.046 \)), at academic hospitals (18.9% vs 7.3%; \( P < 0.001 \)), and at hospitals with an on-site cardiac catheterization facility (18.3% vs 8.4%, \( P < 0.009 \)).

EBT and OMT Use at the Time of Discharge

The provision of EBTs and OMT at the time of discharge and after 1 year is illustrated in Figure 2B. For patients who did not have a class I indication for ACEIs (\( N = 279 \)), 69.5% were discharged taking the indicated medication (antiplatelet/OAs, \( \beta \)-blockers/statin). By comparison, 49.2% of patients with an indication for ACEIs were discharged on the indicated medication (antiplatelet/OAs, ACEIs, \( \beta \)-blockers/statin; \( P < 0.001 \)). There were no differences in the provision of aspirin, clopidogrel, \( \beta \)-blockers, ACEIs, statins, or OMT between patients cared for by cardiologists compared with other specialists or among patients cared for at academic hospitals compared with nonacademic sites. Patients treated at hospitals with on-site catheterization facilities were more likely to be discharged on aspirin (93.6% vs 86.6%, \( P = 0.01 \)) and statins (84.1% vs 77.5%, \( P = 0.041 \)). Provision of OMT at discharge was greater in those who underwent coronary angiography compared with those who were managed conservatively (55.9% vs 45.3%, respectively; \( P < 0.001 \)). There were no differences in the type of in-hospital revascularization associated with significant differences in OMT use (PCI 60.4% vs CABG 38.5%, \( P < 0.001 \)).

Physician-Reported Reasons for Not Prescribing EBTs

The percentage of patients not prescribed EBTs within 24 hours of admission or at the time of discharge, along with the reason(s) (not mutually exclusive) cited by the most responsible physician for not prescribing each medication, is presented in Table 2. The most common reason for not prescribing clopidogrel, GPAs, statins, and ACEIs was the belief that the patient was “not high-enough risk” or that there were “no evidence/guidelines to support use.” Obstructive airway disease and allergy/intolerance (including heart block or bradycardia) were the commonest reasons for not prescribing \( \beta \)-blockers. Physicians were unable to identify a specific reason for omission for 60% of the patients who were not given aspirin.

Table 3 shows the median GRACE risk scores of patients for whom the “not high-enough risk/no evidence” code was used. Aspirin use was excluded from analysis because only 3 patients had aspirin withheld for this reason. With the exception of ACEIs, GRACE scores for “not high-enough
risk/no evidence” patients either did not differ from (clopidogrel, GPA, any heparin, β-blockers) or were higher than (LMWH, statins) those of treated patients. Analysis with imputed GRACE risk scores for patients with missing data showed similar results. Of the patients not given treatment because of “not high-enough risk/no evidence,” 58.5% (clopidogrel), 60.3% (GPA), 59.1% (heparin), 65.4% (LMWH), 52.9% (β-blockers), 55.9% (ACEIs), and 69.2% (statins) of cases were in the intermediate- or high-risk groups. Physicians from academic hospitals were more likely to use the “not high-enough risk/no evidence” code to explain why β-blockers (21.7% vs 6.3% of patients not given β-blockers; \( P = 0.007 \)) were not provided at discharge. With the exception of clopidogrel (\( P \) for trend = 0.046), there was no association between GRACE risk category and EBT omission without an identifiable reason.

**EBT and OMT Use at 1 Year**

After 1 year, 185 patients (9.5%) were lost to follow-up, and a total of 122 patients (6.2%) had died since study entry. Thus, data were available for 1649 patients (Figure 1). At 1 year, use of aspirin (89.0% vs 86.7%, \( P = 0.027 \)), clopidogrel (59.8% vs 33.2%, \( P < 0.001 \)), β-blockers (84.9% vs 75.0%, \( P < 0.001 \)), and ACEIs (65.3% versus 60.3%, \( P < 0.001 \)) had declined (Figure 2B), whereas the use of OAs (8.1% vs 9.4%; \( P = 0.055 \)) and statins (80.3% vs 82.2%; \( P = 0.07 \)) was unaltered. The overall proportion of patients taking OMT decreased (51.7% vs 46.5%, \( P < 0.001 \)). Use of OMT fell in all groups except in those
revascularized by CABG (38.4% vs 39.5%, \(P=0.91\)). Patients revascularized by PCI remained more likely to be taking OMT at 1 year (PCI 52.6%; CABG 39.5%; angiography but no revascularization 47.8%; conservative treatment 41.4%; \(P=0.001\)).

### Table 2. Proportion of Patients Not Prescribed EBT Within 24 Hours of Admission or at Time of Discharge and Physician-Reported Reasons for Not Prescribing Such Treatment

<table>
<thead>
<tr>
<th></th>
<th>Within 24 Hours of Admission</th>
<th>At Discharge</th>
<th>GPA</th>
<th>Any Heparin</th>
<th>LMWH</th>
<th>Aspirin</th>
<th>Clopidogrel</th>
<th>(\beta)-Blocker</th>
<th>ACEI</th>
<th>Statin</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Total population not taking drug (n)</td>
<td>88.4 (1729)</td>
<td>9.7 (189)</td>
<td>36.9 (721)</td>
<td>11.1 (213)</td>
<td>41.1 (788)</td>
<td>15.0 (289)</td>
<td>33.8 (650)</td>
<td>20.4 (391)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Reasons for not prescribing treatment (n)</td>
<td></td>
<td></td>
<td></td>
<td>16.4 (35)</td>
<td>...</td>
<td>20.8 (60)</td>
<td>4.2 (27)</td>
<td>5.1 (20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergy/intolerance*</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not high-enough risk or no evidence/guidelines to support use†</td>
<td>82.7 (1430)</td>
<td>34.4 (65)</td>
<td>29.3 (211)</td>
<td>1.4 (3)</td>
<td>41.2 (325)</td>
<td>13.1 (38)</td>
<td>48.3 (314)</td>
<td>53.5 (209)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concurrent oral anticoagulant</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding/coagulopathy</td>
<td>...</td>
<td>7.9 (15)</td>
<td>1.0 (7)</td>
<td>3.3 (7)</td>
<td>2.0 (16)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other safety concerns/surgery/comorbidity‡</td>
<td>6.8 (117)</td>
<td>12.7 (24)</td>
<td>6.5 (47)</td>
<td>...</td>
<td>10.7 (84)</td>
<td>12.1 (35)</td>
<td>...</td>
<td>11.5 (45)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma/COPD</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>8.2 (53) ...</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>4.8 (14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other LLT</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>17.1 (67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No reason provided</td>
<td>11.0 (190)</td>
<td>45.5 (86)</td>
<td>63.2 (456)</td>
<td>62.0 (132)</td>
<td>30.3 (239)</td>
<td>21.5 (62)</td>
<td>9.8 (64)</td>
<td>7.9 (31)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

COPD indicates chronic obstructive pulmonary disease; LLT, lipid-lowering therapy. Other abbreviations are as defined in text.

*Includes bradycardia/heart block for \(\beta\)-blockers.
†Includes normal left ventricular ejection fraction for ACEIs.
‡Includes peripheral artery disease and hypoglycemia for \(\beta\)-blockers.

### Table 3. Comparison of GRACE Risk Scores of Patients Provided With EBT and Those for Whom EBT Was Withheld Because Either They Were Deemed “Not High Risk” or There Was “No Evidence/Guidelines to Support Use”

<table>
<thead>
<tr>
<th></th>
<th>Prescribed</th>
<th>Not Prescribed Because “Not High Risk/No Evidence”</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPA</td>
<td></td>
<td></td>
<td>0.28</td>
</tr>
<tr>
<td>GRACE risk score*</td>
<td>113 (95, 135)</td>
<td>117 (96, 141)</td>
<td>0.51</td>
</tr>
<tr>
<td>Any heparin</td>
<td>1583</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>GRACE risk score*</td>
<td>118 (96, 145)</td>
<td>113 (102, 131)</td>
<td>0.025</td>
</tr>
<tr>
<td>LMWH</td>
<td>1133</td>
<td>179</td>
<td></td>
</tr>
<tr>
<td>GRACE risk score*</td>
<td>115 (94, 140)</td>
<td>118 (102, 145)</td>
<td>0.25</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>1005</td>
<td>280</td>
<td></td>
</tr>
<tr>
<td>GRACE risk score*</td>
<td>115 (95, 138)</td>
<td>117 (95, 144)</td>
<td>0.17</td>
</tr>
<tr>
<td>(\beta)-Blocker</td>
<td>1443</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>GRACE risk score*</td>
<td>117 (97, 143)</td>
<td>110 (88, 132)</td>
<td>0.023</td>
</tr>
<tr>
<td>ACEI</td>
<td>1146</td>
<td>247</td>
<td></td>
</tr>
<tr>
<td>GRACE risk score*</td>
<td>117 (96, 144)</td>
<td>113 (94, 132)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Statin</td>
<td>1347</td>
<td>182</td>
<td></td>
</tr>
<tr>
<td>GRACE risk score*</td>
<td>116 (96, 140)</td>
<td>134 (102, 164)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations are as defined in text. GRACE risk score categories were as follows: low risk, \(\leq108\); intermediate risk, 109–140; high risk, \(>141\).

*Median (25th, 75th percentiles).

### Table 4. Patient-Reported Reasons for Not Taking EBT at 1 Year

Reasons given by patients for not taking EBTs at 1 year are presented in Table 4. Lack of prescription at the time of discharge was the most common reason for not taking
Table 4. Proportion of Patients Not Taking EBT After 1 Year and Patient-Reported Reason(s) for Not Taking EBT*

<table>
<thead>
<tr>
<th>Reason</th>
<th>Aspirin</th>
<th>Clopidogrel</th>
<th>β-Blocker</th>
<th>ACEI</th>
<th>Statin</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Of total population not taking drug (n)</td>
<td>13.3 (208)</td>
<td>66.7 (1037)</td>
<td>25.0 (391)</td>
<td>39.7 (618)</td>
<td>17.8 (280)</td>
</tr>
<tr>
<td>% Reasons for not taking medication (n)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergy/side effects/intolerance/bleeding</td>
<td>15.4 (32)</td>
<td>2.8 (29)</td>
<td>7.2 (28)</td>
<td>10.0 (62)</td>
<td>11.8 (33)</td>
</tr>
<tr>
<td>Not prescribed at discharge</td>
<td>22.6 (47)</td>
<td>42.7 (443)</td>
<td>28.6 (112)</td>
<td>43.5 (269)</td>
<td>42.1 (118)</td>
</tr>
<tr>
<td>Stopped by physician for reasons other than side effects/intolerance</td>
<td>25.0 (52)</td>
<td>19.3 (200)</td>
<td>24.8 (97)</td>
<td>14.9 (92)</td>
<td>11.8 (33)</td>
</tr>
<tr>
<td>No reason provided</td>
<td>43.3 (90)</td>
<td>37.3 (387)</td>
<td>41.2 (161)</td>
<td>35.3 (218)</td>
<td>37.5 (105)</td>
</tr>
</tbody>
</table>

*Not mutually exclusive.

Discussion

To the best of our knowledge, this is the first study to examine in detail the reasons for not using EBTs at hospital discharge and after 1 year from the perspective of both the physician and the patient in a large cohort of unslected NSTE ACS patients. The main findings of this study are as follows: (1) In patients without specific contraindications or proven drug intolerance, the most common reason for not prescribing clopidogrel, GPAs, statins, or ACEIs was the physician’s subjective assessment that the patient was “not high-enough risk” or that there was “no evidence/guideline to support use”; (2) After 1 year, 77% of patients not on OMT at discharge remained without optimal treatment, and overall antiplatelet, β-blocker, and ACEI use declined; and (3) Among patients who were not taking EBT at 1 year, approximately one third had stopped treatment without specific instructions from their physician.

Clinical trials have established the benefit of individual secondary prevention medications in reducing mortality and morbidity after ACSs. Data from registries confirm that their combined use in real-world patients is associated with a similar improvement in outcome. Indeed, better adherence to guideline recommendations is associated with incremental improvements in survival, whereas discontinuation of medication is associated with a worse outcome. Quality improvement initiatives, including the Guidelines Applied in Practice and Get With The Guidelines programs, have thus focused on strategies to improve the proportion of patients receiving OMT at the time of discharge. However, few studies have examined in detail the factors that influence clinical decision making in real-world patients in an attempt to understand why eligible patients are sometimes not given EBTs. Furthermore, little is known directly from patients about why medications are not taken in the longer term. A clear understanding of such factors is likely to help refine the design of quality improvement initiatives and maximize the uptake and adherence to appropriate medications in eligible patients.

Data from registries of real-world ACS patients illustrate a risk-treatment paradox wherein patients in the highest risk categories are the least likely to receive EBT or to undergo invasive management during admission. One aspect of this paradox may result from a subjective underestimation of a patient’s risk and hence, an underestimation of the likely treatment benefit by the responsible physician. We have previously shown this to be the case regarding referral for angiography after ACS, whereas others have demonstrated a “risk-adverse” policy in high-risk patients. In this current study, we found that more than half of the patients who were assessed as “not high-enough risk” or “no evidence/guidelines to support use” of EBT were in fact at intermediate or high risk when assessed by a well-validated objective risk score. This was most clearly evident for statins, where 44% of patients for whom this code was used were in the highest GRACE risk group. Although we were unable to further dissect the decision-making process for individual cases, this may reflect a perceived lack of long-term benefit of statins in patients with the worst prognosis. These data suggest that objective risk score assessment should complement sound clinical judgment in selecting the optimal management strategies for ACS patients.

For a considerable proportion of patients, we found that the responsible physician was unable to identify a specific reason why treatment had not been prescribed. Although we cannot accurately determine the rationale in such “no reason given” cases, it is plausible (by a process of elimination of available reasons) that these EBTs were simply “missed” in treatment-eligible patients. This conclusion is supported by the lack of association of the frequency of “no reason” codes with GRACE risk score, suggesting that omissions were probably random events. The reduction of such system errors has been a key element in the success of the Guidelines Applied in Practice quality-improvement initiative. One tool used in this program was the introduction of standardized sets of admission and discharge orders to help minimize accidental omission and the requirement for physicians to document why EBTs had not been prescribed. Use of such tools was associated with improvement in guideline medication provision and 1-year mortality. When not prescribed, clear statements on the rationale for omission may be of further help to physicians providing long-term care, so that informed deci-
sions on subsequent EBT use and intended treatment duration may be made.

We found that use of most EBTs had declined after 1 year, despite the fact that the majority of EBTs for ACSs were well tolerated. Side effects or adverse events, including bleeding, were relatively rare, accounting for only ~1 in 10 cases of discontinuation. However, physicians commonly discontinued EBT after discharge in the absence of specific side effects or intolerance. Clopidogrel is currently the only secondary preventative medication for which a prespecified duration of treatment (up to 12 months) is recommended. Discontinuation may have adverse consequences, and strategies to maintain adherence should be encouraged. Approximately one third of patients were unable to provide a specific reason why they were not taking EBT. This subset of patients is distinct from those for whom their responsible physician provided specific discontinuation instructions. It is likely that some of these patients will have decided independently to stop treatment. A variety of reasons may underlie such decisions, including cost (for patients not covered by Canadian healthcare benefits), lack of perceived effectiveness or symptom improvement, poor understanding of the benefits of secondary prevention, misperception of the intended duration of treatment, concerns about drug interactions, and difficulty with taking large numbers of pills. Furthermore, there appears to be an ongoing need to reassess whether all eligible patients are still provided with and taking optimal therapy during follow-up. The use of a discharge “contract” signed by the patient, combined with cardiac rehabilitation and education, may help to improve medication adherence by actively engaging patients in their goals for treatment and lifestyle modification.

Study Limitations and Strengths

This study included a broad spectrum of real-world NSTE ACS patients and obtained data directly from both patients and their treating physicians. However, we relied on each group’s interpretation of the possible reasons for not prescribing or taking EBT. We cannot exclude the possibility that there may have been some overlap between categories, particularly with relation to drug allergy/intolerance (actual versus potential) and relative contraindications (eg, use of β-blockers in patients with mild asthma or chronic nonreactive airway disease). Physicians had to complete the case report form within 4 weeks of patient discharge. Therefore, inaccurate recall might potentially account for “no reason” recorded when EBT was not prescribed in some cases. For 1-year data, we were also dependent on the patient’s recall and understanding of why a medication had been discontinued or not initiated. Although this methodology may have produced some inaccurate reasons for discontinuation, it does provide important and novel insights into the patient’s understanding of their treatment. This will be influenced by the information communicated by the responsible physician, which is a quality marker of ACS treatment itself. Although encouraged, we were unable to independently verify consecutive patient enrollment in the ACS II registry. Unrecognized selection bias may thus have occurred because of the requirement for informed consent and telephone follow-up of patients. Finally, 9.5% of patients were lost to follow-up. Although this figure is lower than reported for other ACS registries, by excluding the perhaps less health-conscious patients who did not maintain contact with their healthcare providers, it is possible that we have underestimated the rates of medication discontinuation or nonadherence.

Conclusions

The risk-treatment paradox in the medical management of NSTE ACSs may in part be due to a subjective underestimation of patient risk and a consequent underestimation of likely treatment benefit. We also found oversights and considerable gaps in the system of care delivery. More widespread use of objective risk-scoring systems, combined with systematic efforts to ensure optimal provision and adherence to secondary prevention therapies in ACS patients, should be encouraged.

Acknowledgments

We thank all of the study investigators, coordinators, and patients who participated in these registries.

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Disclosures

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