Coronary Heart Disease

Predictors of Outcomes in Medically Treated Patients With Acute Coronary Syndromes After Angiographic Triage
An Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) Substudy

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Background—Outcomes of patients presenting with acute coronary syndromes are improved with an early invasive approach; however, approximately one third of these patients are treated medically after angiographic screening. We sought to assess the predictors of adverse cardiac events in patients with acute coronary syndrome assigned to medical management.

Methods and Results—This substudy of the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial included 4491 acute coronary syndrome patients treated medically after angiographic triage. Rates of bleeding and composite ischemia (death, myocardial infarction, revascularization) were compared among the 3 antithrombotic treatment arms. Composite ischemia occurred in 399 patients (9.5%) at 1 year. Treatment with bivalirudin glycoprotein IIb/IIIa inhibitors significantly reduced major bleeding at 30 days (2.5% bivalirudin monotherapy; \( P=0.005 \), 2.0% bivalirudin plus glycoprotein IIb/IIIa inhibitors; \( P=0.0002 \) versus 4.4% heparin with glycoprotein IIb/IIIa inhibitors). Composite ischemic events at 1 year were not significantly different in the 3 groups (bivalirudin monotherapy, 9.6%; bivalirudin plus glycoprotein IIb/IIIa inhibitors, 9.7%; heparin plus glycoprotein IIb/IIIa inhibitors, 9.1%). Independent predictors of composite ischemia were mostly angiographic factors at 30 days, including jeopardy score and coronary ectasia, and at 1 year, including previous percutaneous coronary intervention, jeopardy score, coronary ectasia, and increasing number of diseased vessels.

Conclusions—Among the ACUITY acute coronary syndrome patients treated medically after angiographic triage, bivalirudin therapy significantly reduced bleeding complications compared with heparin without any negative impact on ischemic outcomes at 1 year. The most powerful predictors of ischemic outcomes were angiographic rather than traditional clinical parameters, supporting the early use of angiographic screening in the moderate- and high-risk but medically treated acute coronary syndrome population.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00093158.

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Key Words: acute coronary syndromes \( \square \) antithrombotic agents \( \square \) medical management \( \square \) risk factors

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Table 1. Baseline Characteristics of Medical Management Patients by Randomized Treatment Group

<table>
<thead>
<tr>
<th>Overall (n=4491)</th>
<th>Heparin (UFH or LMWH) Plus GPI (n=1493)</th>
<th>Bivalirudin Plus GPI (n=1496)</th>
<th>P*</th>
<th>Bivalirudin Monotherapy (n=1502)</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR), y</td>
<td>62 (53–71)</td>
<td>62 (53–71)</td>
<td>61 (53–72)</td>
<td>0.83</td>
<td>62 (53–71)</td>
</tr>
<tr>
<td>Sex (male), n (%)</td>
<td>2780 (61.9)</td>
<td>950 (63.6)</td>
<td>926 (61.9)</td>
<td>0.33</td>
<td>904 (60.2)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>1191/4438 (26.8)</td>
<td>412/1475 (27.9)</td>
<td>373/1477 (25.3)</td>
<td>0.10</td>
<td>406/1486 (27.3)</td>
</tr>
<tr>
<td>Insulin-treated diabetes mellitus, n (%)</td>
<td>385/4438 (8.7)</td>
<td>126/1475 (8.5)</td>
<td>121/1477 (8.2)</td>
<td>0.73</td>
<td>138/1486 (9.3)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3109/4458 (69.7)</td>
<td>1024/1482 (69.1)</td>
<td>1049/1484 (70.7)</td>
<td>0.34</td>
<td>1036/1492 (69.4)</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>2679/4404 (60.8)</td>
<td>877/1462 (60.0)</td>
<td>890/1467 (60.7)</td>
<td>0.71</td>
<td>912/1475 (61.8)</td>
</tr>
<tr>
<td>Current smoking, n (%)</td>
<td>1154/4401 (26.2)</td>
<td>380/1463 (26.0)</td>
<td>392/1466 (26.7)</td>
<td>0.64</td>
<td>382/1472 (26.0)</td>
</tr>
<tr>
<td>Previous MI, n (%)</td>
<td>1534/4354 (35.2)</td>
<td>515/1463 (35.6)</td>
<td>495/1453 (34.1)</td>
<td>0.39</td>
<td>524/1454 (36.0)</td>
</tr>
<tr>
<td>Previous PCI, n (%)</td>
<td>1994/4430 (45.0)</td>
<td>665/1475 (45.1)</td>
<td>643/1476 (43.6)</td>
<td>0.41</td>
<td>686/1479 (46.4)</td>
</tr>
<tr>
<td>Previous CABG, n (%)</td>
<td>1032/4464 (23.1)</td>
<td>365/1484 (24.8)</td>
<td>325/1489 (21.8)</td>
<td>0.07</td>
<td>342/1491 (22.9)</td>
</tr>
<tr>
<td>Weight, median (IQR), kg</td>
<td>82 (71–95)</td>
<td>82.0 (71–94)</td>
<td>82.0 (71–95)</td>
<td>1.00</td>
<td>84 (71–97)</td>
</tr>
<tr>
<td>Renal insufficiency, n (%)‡</td>
<td>846/4150 (20.4)</td>
<td>273/1380 (19.8)</td>
<td>290/1371 (21.2)</td>
<td>0.37</td>
<td>283/1399 (20.2)</td>
</tr>
<tr>
<td>ST-segment–deviation or CK-MB or troponin elevation, n (%)</td>
<td>2503/4153 (60.3)</td>
<td>835/1371 (60.9)</td>
<td>833/1379 (60.4)</td>
<td>0.79</td>
<td>835/1403 (59.5)</td>
</tr>
<tr>
<td>CK-MB/troponin elevation, n (%)</td>
<td>1767/4009 (44.1)</td>
<td>579/1330 (43.5)</td>
<td>592/1331 (44.5)</td>
<td>0.62</td>
<td>596/1348 (44.2)</td>
</tr>
<tr>
<td>TIMI risk score, n (%)</td>
<td>1275/4480 (28.5)</td>
<td>422/1490 (28.3)</td>
<td>423/1492 (28.4)</td>
<td>0.99</td>
<td>430/1498 (28.7)</td>
</tr>
<tr>
<td>0–2</td>
<td>665/3923 (17.0)</td>
<td>226/1307 (17.3)</td>
<td>226/1307 (17.3)</td>
<td>1.00</td>
<td>213/1309 (16.3)</td>
</tr>
<tr>
<td>3–4</td>
<td>2228/3923 (56.8)</td>
<td>744/1307 (56.9)</td>
<td>749/1307 (57.3)</td>
<td>0.84</td>
<td>735/1309 (56.1)</td>
</tr>
<tr>
<td>5–7</td>
<td>1030/3923 (26.3)</td>
<td>337/1307 (25.8)</td>
<td>332/1307 (25.4)</td>
<td>0.82</td>
<td>361/1309 (27.6)</td>
</tr>
</tbody>
</table>

UFH indicates unfractionated heparin; LMWH, low-molecular-weight heparin; and IQR, interquartile range.

*Comparison between bivalirudin plus GPI and heparin (UFH or LMWH) plus GPI.
†Comparison between bivalirudin monotherapy and heparin (UFH or LMWH) plus GPI.
‡Renal insufficiency was defined as calculated creatinine clearance <60 mL/min with the Cockcroft-Gault equation.

30 days and 1 year, with significantly fewer 30-day bleeding complications compared with heparin plus glycoprotein IIb/IIIa inhibitors (GPIs). To date, studies have demonstrated that in NSTE ACS, bivalirudin is effective in patients in a number of clinical scenarios, including patients with diabetes mellitus, those treated with percutaneous coronary intervention (PCI), and those being switched from heparin to bivalirudin.9–11

In this post hoc study, we sought to determine whether the results observed in the overall ACUITY trial would apply to the subgroup of patients treated medically (ie, those who did not undergo coronary revascularization within the first 30 days). We also evaluated the association between composite ischemic events and demographic, clinical, and angiographic characteristics in this subgroup.

Methods

Study Population and Design

The design and results of the ACUITY trial have previously been published.12–14 In summary, patients >18 years of age were eligible if they presented within 24 hours of symptom onset and had either new ST-segment depression or transient elevation of at least 1 mm; elevated troponin I, troponin T, or creatine kinase-MB (CK-MB) levels; known coronary artery disease (CAD); or 4 of the other variables of the Thrombolysis in Myocardial Infarction (TIMI) risk score for unstable angina. Eligible patients were randomly assigned to treatment with 1 of 3 antithrombotic regimens starting immediately after randomization: heparin (unfractionated or enoxaparin, given at site discretion) plus GPI, bivalirudin plus GPI, or bivalirudin monotherapy. Patients assigned to heparin plus GPI or bivalirudin plus GPI were randomly assigned again in a 2-by-2 factorial design to either upstream or deferred initiation. The use of GPI was permitted before angiography in patients with severe breakthrough ischemia who were randomly assigned to deferred GPI use or bivalirudin monotherapy. Antithrombins and GPI were discontinued according to the protocol at the completion of angiography or PCI but could be continued if they were clinically indicated for up to 72 hours after the procedure. The choice of PCI coronary artery bypass grafting, or medical management was left to the discretion of the investigator. The study was approved by the institutional review board or ethics committee at each participating center, and all patients signed written informed consent.

Angiographic Analysis

Quantitative coronary angiography was performed in 6921 prespecified consecutive US patients enrolled in ACUITY, 2340 of whom were in the medically treated arm. Angiographic analysis was performed at the Cardiovascular Research Foundation (New York, NY) as previously described.15 A comprehensive assessment, performed to define and quantify the extent and burden of CAD, included the number of diseased vessels, the extent of disease burden defined as the total length in millimeters of all lesions with a >30% diameter stenosis in all 3 vessels and major side branches, Duke jeopardy score,16 baseline TIMI flow,17 and myocardial blush grade.18

Clinical Definitions and End Points

TIMI risk score was calculated and divided into 3 risk categories: low risk, 0 to 2 factors; intermediate risk, 3 to 4 factors; and high risk, 5 to 7 factors.19 The end points of this analysis were composite ischemia (defined as death from any cause, myocardial infarction [MI], or unplanned revascularization for ischemia at 30 days and 1 year) and major bleeding at 30 days. The definitions of primary end points have previously been detailed.14 An unplanned revascularization was performed if severe anginal symptoms were present despite optimal antianginal medication. In patients without NSTE MI at admission, an MI was defined as any elevation of troponin or
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Table 2. Baseline Angiographic Characteristics of Medical Management Patients by Randomized Treatment Group

<table>
<thead>
<tr>
<th>Overall (n = 1493)</th>
<th>Heparin (UFH or LMWH) Plus GPI (n = 1493)</th>
<th>Bivalirudin Plus GPI (n = 1496)</th>
<th>P*</th>
<th>Bivalirudin Monotherapy (n = 1502)</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients analyzed by core laboratory, n (%)</td>
<td>2340 (52.1)</td>
<td>792 (53.0)</td>
<td>753 (50.3)</td>
<td>N/A</td>
<td>795 (52.9)</td>
</tr>
<tr>
<td>Lesions per patient, n</td>
<td>3.0±3.0</td>
<td>3.2±3.1</td>
<td>2.9±3.0</td>
<td>0.12</td>
<td>3.0±3.0</td>
</tr>
<tr>
<td>Extent of disease per patient, median (IQR), mm</td>
<td>23.2 (12.0–41.0)</td>
<td>23.4 (12.0–43.9)</td>
<td>24.0 (12.0–40.0)</td>
<td>0.61</td>
<td>22.9 (12.0–41.0)</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

*Comparison between bivalirudin plus GPI and heparin (UFH or LMWH) plus GPI.
†Comparison between bivalirudin monotherapy and heparin (UFH or LMWH) plus GPI.

CK-MB greater than the upper limit of normal (or CK greater than the upper limit of normal in the absence of MB determination). In patients with NSTE MI at presentation in whom the elevated troponin or CK-MB (or CK) level was documented to be decreasing or had returned to normal, diagnosis of a second infarction required a new elevation of troponin or CK-MB greater than the upper limit of normal (or CK greater than the upper limit of normal in the absence of MB determination) if the troponin or CK-MB (or CK) level had returned to less than the upper limit of normal, or an increase by >50% above the previous nadir level if the troponin or CK-MB (or CK) level had not returned to less than the upper limit of normal. In patients with NSTE MI at presentation in whom the peak troponin or CK-MB (or CK) had not yet been reached, diagnosis of a second infarction required recurrent chest pain ≥30 minutes or new ECG changes consistent with MI and elevation of the next troponin or CK-MB (or CK) level measured ≥8 to 12 hours after the event by at least 50% above the previous level. All end points were adjudicated by a clinical events committee that was blinded to treatment assignment.

Statistical Analyses

All of the analyses were based on intention to treat. Categorical values were compared by χ² or Fisher exact test. P values for continuous variables were calculated with the nonparametric Kruskal-Wallis test. One-year follow-up analysis was performed with time-to-event methodology, and the cumulative composite events in relation to TIMI risk score and the number of diseased vessels were determined according to the Kaplan-Meier method with the use of log-rank tests for statistical assessment. The P values are given for informational purposes, and no multiplicity adjustment was performed. Stepwise logistic regression analysis was performed to evaluate the clinical and angiographic factors associated with 30-day and 1-year composite ischemic events, death/MI, and death in the prespecified quantitative coronary angiography cohort. The specific variables entered into the models were treatment group, bivalirudin plus GPI versus heparin plus GPI, bivalirudin monotherapy versus heparin plus GPI, age, sex, diabetes mellitus, insulin-treated diabetes mellitus, hypertension, hyperlipidemia, current smoking, previous MI, previous PCI, previous coronary artery bypass grafting, renal insufficiency, ECG deviation or biomarker elevation, extent of disease (10-mm increments), number of diseased vessels, jeopardy score, TIMI flow grade 0/1, blush grade 0/1, eccentricity, ulceration, aneurysm, ectasia, moderate/severe calcification, thrombus, collaterals, and worst percent diameter stenosis. The P values, odds ratios, and corresponding 2-sided 95% confidence intervals for predictors are presented. All of the statistical analyses were performed by SAS version 8.2 (SAS Institute, Inc, Cary, NC).

Results

Baseline Characteristics by Randomized Treatment Group

Of the 13,819 patients enrolled in ACUITY, 4,491 (32.5%) were triaged to medical treatment after coronary angiography, 7,789 (56.4%) were treated with PCI, and 1,539 (11.1%) received coronary artery bypass grafting. We found that 15.7% of patients had low TIMI risk score, 54.6% had intermediate TIMI risk score, and 29.7% had high TIMI risk score. Baseline characteristics among medically treated pa-
Patients were similar regardless of antithrombin treatment arm (Table 1). The prevalence of male sex tended to be lower and weight tended to be slightly higher in the bivalirudin monotherapy arm compared with the heparin plus GPI arm. There was no significant difference in baseline angiographic findings and medications taken after hospital discharge through 30 days by randomized treatment group (Tables 2 and 3). Angiography was performed during the initial hospitalization in 97% of medically treated patients at a median of 4.8 hours after antithrombotic study drug initiation. GPI was used in 0.5% of patients assigned to the bivalirudin monotherapy arm (Table 3).

### Clinical Outcomes

At the 30-day follow-up, 139 patients (3.1%) in the medically treated population had developed composite ischemia, with 66 deaths (1.5%), 42 MIs (1.0%), and 53 unplanned revascularizations (1.2%; Table 4). At 1 year, 399 of the medically treated patients (9.5%) had sustained composite ischemia, including 175 deaths (4.3%), 115 MIs (2.7%), and 177 unplanned revascularizations (4.4%).

At 30 days, there was a trend toward superior net clinical outcome in each of the bivalirudin arms compared with the heparin plus GPI arm (P=0.06 versus bivalirudin plus GPI; Table 4).

### Table 3. Procedures and Medications of Medical Management Patients by Randomized Treatment Group

<table>
<thead>
<tr>
<th>Procedure/Drug Description</th>
<th>Overall (n=4491)</th>
<th>Heparin (UFH or LMWH) Plus GPI (n=1493)</th>
<th>Bivalirudin Plus GPI (n=1496)</th>
<th>Bivalirudin Monotherapy (n=1502)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiography performed, n (%)</td>
<td>4349 (96.8)</td>
<td>1456 (97.5)</td>
<td>1440 (96.3)</td>
<td>1453 (96.7)</td>
</tr>
<tr>
<td>Time from admission to randomization, median (IQR), h</td>
<td>7.4 (2.4–16.4)</td>
<td>7.2 (2.2–16.5)</td>
<td>7.5 (2.4–16.6)</td>
<td>7.3 (2.4–16.1)</td>
</tr>
<tr>
<td>Time from randomization to initiation of antithrombotic study drug, median (IQR), h</td>
<td>0.6 (0.3–1.1)</td>
<td>0.4 (0.1–0.9)</td>
<td>0.7 (0.4–1.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Time from antithrombotic study drug to angiography, median (IQR), h</td>
<td>4.8 (1.3–19.8)</td>
<td>5.1 (1.6–19.2)</td>
<td>4.3 (1.2–19.3)</td>
<td>5.0 (1.1–20.7)</td>
</tr>
<tr>
<td>Use of GPI, n (%)</td>
<td>1402 (31.2)</td>
<td>721/1493 (48.3)</td>
<td>674 (45.1)</td>
<td>7 (0.5)</td>
</tr>
</tbody>
</table>

### Table 4. Clinical Outcomes at 30 Days and at 1 Year in Medical Management Patients

<table>
<thead>
<tr>
<th>Outcome Description</th>
<th>Overall (n=4491), n (%)</th>
<th>Heparin (UFH or LMWH) Plus GPI (n=1493), n (%)</th>
<th>Bivalirudin Plus GPI (n=1496), n (%)</th>
<th>Bivalirudin Monotherapy (n=1502), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net clinical outcome</td>
<td>246 (5.5)</td>
<td>97 (6.6)</td>
<td>73 (4.9)</td>
<td>76 (5.1)</td>
</tr>
<tr>
<td>Composite ischemia</td>
<td>139 (3.1)</td>
<td>42 (2.8)</td>
<td>46 (3.1)</td>
<td>51 (3.5)</td>
</tr>
<tr>
<td>Death/MI</td>
<td>100 (2.3)</td>
<td>34 (2.3)</td>
<td>27 (1.8)</td>
<td>39 (2.6)</td>
</tr>
<tr>
<td>Death</td>
<td>66 (1.5)</td>
<td>19 (1.3)</td>
<td>23 (1.6)</td>
<td>24 (1.6)</td>
</tr>
<tr>
<td>MI</td>
<td>42 (1.0)</td>
<td>19 (1.3)</td>
<td>4 (0.3)</td>
<td>19 (1.3)</td>
</tr>
<tr>
<td>Unplanned revascularization</td>
<td>53 (1.2)</td>
<td>16 (1.1)</td>
<td>21 (1.4)</td>
<td>16 (1.1)</td>
</tr>
<tr>
<td>Major bleeding (non-CABG related)</td>
<td>131 (3.0)</td>
<td>65 (4.4)</td>
<td>29 (2.0)</td>
<td>37 (2.5)</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; other abbreviations as in Table 1.

*Comparison between bivalirudin plus GPI and heparin (UFH or LMWH) plus GPI.
†Comparison between bivalirudin monotherapy and heparin (UFH or LMWH) plus GPI.
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patients with high TIMI risk and 3-vessel disease (Figure 3A). The same trends were observed for the hard end points of death/MI (Figure 3B) and death alone (Figure 3C). In particular, among patients with intermediate TIMI risk score, the number of diseased vessels had a significant impact on prognosis, enabling stratification of patients into lower risk or higher risk on the basis of the extent of CAD.

Discussion

This analysis adds important information to our knowledge of patients with NSTE ACS treated medically after screening angiography. First, patients enrolled in the ACUITY trial and treated medically were mostly intermediate- and high-TIMI-risk patients (>80% had TIMI risk ≥3). Second, the rate of composite ischemia in the medically treated patients was 3.1% at 30 days and 9.5% at 1 year. In particular, the 4.3% mortality at 1 year among medically treated patients in ACUITY is considerable. Thus, optimizing pharmacological strategies for these patients is essential if their prognosis is to be improved. Third, among patients undergoing medical management, the use of bivalirudin monotherapy or bivalirudin plus GPI resulted in similar rates of composite ischemia and less major bleeding compared with heparin plus GPI. Fourth, composite ischemia in the short term (first 30 days) was influenced exclusively by angiographic factors, including jeopardy score and coronary ectasia, whereas 1-year composite ischemia was influenced mostly by angiographic factors, including jeopardy score, coronary ectasia, and the number of diseased vessels, as well as previous PCI. Finally, the addition of the number of diseased vessels to the TIMI risk score added significant prognostic value, underscoring the importance of angiographic screening among moderate- and high-risk patients with ACS even when destined for medical therapy as defined by this ACUITY subgroup.

The present analysis demonstrates that patients with NSTE ACS who are managed medically after angiographic triage can be treated safely with bivalirudin monotherapy. These findings are consistent with the overall results of the ACUITY trial.9–13 Although bleeding was not common in patients undergoing medical management compared with patients receiving PCI or coronary artery bypass grafting.
(because of procedure-related bleeding and earlier antithrombin discontinuation among patients with minimal CAD), the finding that bleeding is decreased with bivalirudin even in patients managed medically is clinically relevant because recent data indicate an association between bleeding and mortality. Therefore, bivalirudin monotherapy appears to be a suitable antithrombotic alternative for patients with NSTE ACS who do not undergo early revascularization. Furthermore, patients treated with bivalirudin plus GPI had a better prognosis with regard to MI (0.3% versus 1.3%; \(P=0.002\)) and less major bleeding at 30 days (2.0% versus 4.4%; \(P=0.0002\)) compared with those receiving heparin plus GPI. This supports the safety of bivalirudin in reducing major bleeding even with the addition of a GPI in medically treated patients with NSTE ACS.

The TIMI risk score is an integrated approach derived from clinical baseline variables to identify patients at high risk for death and other major cardiac ischemic events. However, a previous study has demonstrated that the extent of coronary disease measured simply by the number of affected major
epicardial vessels has been correlated with long-term mortality. In this analysis, medically treated patients with a high TIMI risk score represented a high-risk subgroup with a 1-year composite ischemic event rate nearly 3 times that of patients with a low TIMI risk score. Including the extent and severity of CAD added significant prognostic value by increasing ischemic events 2- to 4-fold for patients with low and intermediate to high TIMI risk scores. Similarly, patients with more extensive and severe CAD had increasingly higher rates of composite ischemia at 1 year. Combining the TIMI risk score with the number of diseased vessel(s) more appropriately risk stratified NSTE ACS patients with regard to death, death/MI, and composite ischemia through the follow-up period than either parameter alone. These data reemphasize the need to select adjunctive therapies that conform to the clinical and angiographic severity of disease and underscore the value of angiographic screening even among moderate- and high-risk ACS patients destined for medical therapy.

Previous studies of patients with NSTE ACS have not included a systemic angiographic assessment, and they re-
ported that the risk of adverse cardiac events was related to clinical factors, including age, female sex, diabetes mellitus, previous history of CAD, ECG changes on admission, and elevated CK-MB or cardiac troponin levels. When angiographic characteristics are included, as in this study, the angiographic factors were important independent predictors of adverse events, along with such clinical factors as a prior history of PCI, renal insufficiency, and age. The jeopardy score and number of diseased vessels are measures of the extent of coronary atherosclerosis and jeopardized myocardium. As expected, patients in the present population with more severe atherosclerotic burden had a poorer prognosis.

Coronary ectasia, another important angiographic morphological predictor of cardiac ischemic events, has been described as an uncommon manifestation of atherosclerosis and may be an exaggeration of the remodeling process. Its clinical significance is uncertain. It has been hypothesized that altered coronary blood flow caused by ectasia predisposes patients to adverse cardiac events. Histological evaluation of de novo arterial expanded plaques shows coronary atherosclerosis to be associated with inflammation, calcification, and medial thinning, which appear to be a feature of plaque instability. Results from the present study suggest that ectasic lesions may be more likely to be clinically “vulnerable” in this population.

Limitations

This analysis has several limitations. First, the findings of this study apply only to the ACUITY population, which comprised moderate- and high-risk ACS patients undergoing an early invasive strategy, including early angiography. The findings of this study do not apply to the lower-risk ACS patients intended for medical therapy without angiography. Second, the findings of the benefit of bivalirudin among the
medically treated patients in ACUITY should be considered only hypothesis generating because it was not the primary intent of the trial. Nonetheless, the findings in this subgroup are consistent with those observed in the overall trial, and the reduction in bleeding events with bivalirudin is so statistically robust that it is unlikely to be due to chance. Third, medically treated patients in the present study had substantial risk; in other words, nearly 25% of medically treated patients were in the highest TIMI risk group, and 50% had multivessel coronary disease. The ACUITY trial did not determine the reason for selection to medical treatment, and this group likely represents a heterogeneous population ranging from patients with nonobstructive or no CAD to more complex patients with extensive CAD who presumably were unsuitable for revascularization. Finally, the ACUITY trial did not capture the exact timing of study drug discontinuation, although antithrombins were likely discontinued after diagnostic angiography in patients with minimal CAD.32,33

Conclusions
Among patients treated medically for NSTE ACS after angiographic triage in ACUITY, composite ischemia occurred in 9.5% at 1 year, including death in 4.3% of patients. Use of bivalirudin was associated with decreased rates of bleeding at 30 days compared with treatment with heparin plus GPI, without significantly increasing composite ischemic event rates. Angiographic markers of more extensive and severe CAD and coronary ectasia were important independent predictors of outcome within the first year of presentation, adding incremental prognostic value beyond clinical markers. These results emphasize the utility of angiographic screening for risk stratification among moderate- and high-risk ACS patients even when destined for medical therapy alone. Further studies are warranted to assess the optimal management strategies for this subset of patients.

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Disclosures
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References
CLINICAL PERSPECTIVE

The management of patients with moderate- and high-risk acute coronary syndromes has been dramatically improved with the implementation of an early invasive strategy; the use of stents, thienopyridines, and glycoprotein IIb/IIIa inhibitors; and the direct thrombin inhibitor bivalirudin, regardless of the addition of glycoprotein IIb/IIIa inhibitors, was associated with significant reductions in bleeding at 30 days compared with those treated with heparin plus glycoprotein IIb/IIIa inhibitors, without increasing the rate of composite ischemic events. In addition, angiographic markers of more extensive and severe coronary artery disease and coronary ectasia were important independent markers of outcome and provided significant added prognostic value to the clinically based Thrombolysis in Myocardial Infarction risk score. These results emphasize the utility of angiographic screening for risk stratification among moderate- and high-risk acute coronary syndrome patients, including those triaged to medical therapy.

Predictors of Outcomes in Medically Treated Patients With Acute Coronary Syndromes After Angiographic Triage: An Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) Substudy
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