An early invasive approach in patients with non–ST-segment–elevation acute coronary syndrome (NSTEACS) has been shown to reduce death and myocardial infarction (MI) compared with a more conservative strategy and is thus recommended by the American Heart Association, the American College of Cardiology, and the European Society of Cardiology. Early revascularization is also recommended for patients with diabetes mellitus (DM) presenting with NSTEACS.

DM is found in 25% of patients with ACS undergoing angiography, and given the increasing prevalence of obesity, the number of diabetic patients undergoing both coronary artery bypass graft surgery (CABG) and percutaneous coronary intervention (PCI) is increasing. The optimal revascularization strategy in diabetic patients with ACS remains unclear. In the Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial, CABG resulted in greater freedom from the composite end point of death, stroke, or MI compared with PCI with first-generation drug-eluting stents (DES) at a median follow-up of 3.8 years, with fewer deaths and MIs, although with a greater rate of stroke. Although there were ACS patients with unstable angina in FREEDOM and...
WHAT IS KNOWN

• In general, an early invasive approach in patients with non-ST-segment-elevation acute coronary syndrome has been shown to reduce death and myocardial infarction compared with a more conservative strategy.

• However, the preferred revascularization strategy for diabetic patients with non-ST-segment-elevation acute coronary syndrome and multivessel coronary artery disease is uncertain.

WHAT THE STUDY ADDS

• This study demonstrates comparable 1-year survival and myocardial infarction rates with percutaneous coronary intervention and coronary artery bypass grafting in diabetic patients presenting with non-ST-segment-elevation acute coronary syndrome, multivessel disease, and left anterior descending involvement requiring revascularization.

• Distinctions between revascularization modalities should be weighted to varying degrees by individual patients and physicians in a heart-team-based decision-making approach.

84% of patients had triple vessel disease, NSTEACS patients undergoing emergent or urgent angiography were excluded. The optimal revascularization strategy for patients with diabetes mellitus, multivessel disease, and NSTEACS after early angiography is not certain.

The international, prospective, randomized Acute Catheterization and Early Intervention Triage Strategy (ACUITY) trial enrolled 13819 patients with moderate and high-risk NSTEACS undergoing an early invasive strategy.¹² We recently reported the outcomes from this study in patients with multivessel disease.¹³ The purpose of the present study is to compare the outcome of PCI versus CABG in patients with DM and multivessel disease, specifically in high-risk patients with involvement of the left anterior descending (LAD) coronary artery.

Methods

Study Design

ACUITY was a prospective, open-label, randomized, multicenter trial which compared 3 different antithrombotic regimens in patients presenting with moderate and high-risk ACS undergoing an early invasive management strategy at 450 academic and community-based institutions in 17 countries. Clinical follow-up was complete through 1 year. The study design and protocol as well as its principal results have been described previously.¹² In brief, 13819 patients presenting with NSTEACS were randomized to receive unfractionated heparin or enoxaparin plus a glycoprotein IIb/IIIa inhibitor, bivalirudin plus a glycoprotein IIb/IIIa inhibitor, or bivalirudin alone. Angiography was required in all patients within 72 hours of randomization with subsequent triage to PCI, CABG, or medical management according to investigator discretion.

Enrolled patients were aged ≥18 years with symptoms of ACS lasting ≥10 minutes within the preceding 24 hours and with ≥1 of the following criteria: new ST-segment depression or transient elevation ≥1 mm; elevated troponin I, troponin T, or creatine kinase-MB; known coronary artery disease; or the presence of all 4 other thrombolysis in myocardial infarction risk criteria.¹²,¹³ Major exclusion criteria were acute ST-segment-elevation MI or shock; bleeding diathesis or major bleeding within 2 weeks; thrombocytopenia; creatinine clearance ≤30 mL/min; or recent administration of abciximab, warfarin, fondaparinux, fibrinolytic agents, bivalirudin, or >1 dose of low-molecular-weight heparin.

Aspirin was administered daily during the hospitalization (300–325 mg orally or 250–500 mg IV) and ≥75 mg daily indefinitely in all patients after hospital discharge. A loading dose of ≥300 mg of clopidogrel was administered either before or within 2 hours after PCI in all cases. A 5-day clopidogrel wash-out period was recommended before surgery for patients who received clopidogrel and in whom CABG was subsequently planned. Clopidogrel (75 mg daily) was recommended for 1 year in all patients undergoing PCI and at operator discretion after CABG. All patients were anticoagulated during CABG with unfractionated heparin, with dosing per standard institutional practice. The study was approved by institutional review boards or ethics committee at each center, and all patients provided written informed consent.

End Points and Definitions

Prespecified major adverse cardiovascular events were assessed at 1 month and 1 year after the procedure, consisting of all-cause death, MI, or unplanned revascularization for recurrent ischemia and were adjudicated by a blinded clinical events committee. The specific definitions of the components of major adverse cardiovascular event have been previously published.¹² Major bleeding was defined as intracranial or intracerebral bleeding; access site hemorrhage requiring intervention; ≥2 cm diameter hematoma; reduction in hemoglobin of ≥4 g/dL without or ≥3 g/dL with an overt bleeding source; operation for bleeding; or blood product transfusion. Acute kidney injury was defined as a relative ≥25% increase or absolute 0.5 mg/dL increase in serum creatinine postprocedure compared with baseline.

Present Analysis

In the present study we compared the 1-month and 1-year outcomes of patients with multivessel coronary artery disease involving the LAD who underwent PCI or CABG as their initial management strategy. An angiographic core laboratory (Cardiovascular Research Foundation, New York, NY) performed quantitative coronary angiography on all lesions in the coronary tree from 6921 patients in a prespecified formal angiographic substudy.¹⁴ A diseased epicardial vessel was defined as a major vessel (LAD, left circumflex, or right coronary artery, including its branches) containing ≥1 lesions with a diameter stenosis by quantitative coronary angiography of ≥30% (roughly equivalent to a diameter stenosis of ≥50% by visual estimation). Multivessel disease was defined as ≥2 diseased epicardial coronary arteries.

Statistical Analysis

Categorical variables were compared by χ² or Fisher exact test. Continuous variables were compared by the nonparametric Wilcoxon rank-sum test. Time-to-event data are displayed using Kaplan–Meier methodology and were compared with the log-rank test. Cox proportional hazards regression analysis was used to identify whether treatment with PCI versus CABG was an independent predictor of 1-month and 1-year outcome events. CABG versus PCI triage was forced into the model along with clinically relevant variables (candidate variable entry/stay criteria were 0.10/0.10). To further adjust for the baseline differences between the groups, we performed a propensity score analysis using a logistic regression model that included the following patient characteristics: age, sex, weight, insulin treatment, hypertension, hyperlipidemia, previous MI, previous PCI, previous CABG, renal insufficiency; elevated cardiac biomarkers, ST-segment deviation ≥1 mm, thrombolysis in myocardial infarction risk score, left main disease, number of diseased vessels, and left ventricular ejection fraction.
Patients from the PCI group were then matched with patients from the CABG group according to their propensity score (probability of receiving PCI) resulting in 163 pairs of propensity-matched patients (326 patients total) in whom early and late outcomes were determined. The C-statistic for the propensity model which was used to calculate the propensity score matching for the 2 groups was 0.86. All analyses were performed with SAS v9.2 (SAS Institute, Cary, NC).

Results

Patients and Baseline Characteristics

Among 13819 moderate and high-risk ACS patients enrolled in the ACUITY trial, 5627 had multivessel disease with LAD involvement, with 4412 and 1215 treated with PCI and CABG, respectively. Among these patients, 1772 were diabetic, 1349 (76.1%) and 423 (23.9%) of whom were treated with PCI and CABG, respectively, comprising the current study population.

Baseline clinical and angiographic characteristics are shown in Table 1. Patients undergoing PCI were more often women, more likely to have hypertension, obesity, hyperlipidemia, previous MI, previous PCI, previous CABG, renal insufficiency, cardiac biomarker elevation, and high thrombolysis in myocardial infarction risk score. In contrast, patients undergoing CABG were more likely to have ST-segment deviation ≥1 mm, left main disease, or triple vessel disease.

Results in the Entire Study Cohort

Early (1-month) and intermediate term (1-year) unadjusted clinical outcomes are shown in Table 2. Patients undergoing PCI compared

### Table 1. Baseline and Angiographic Characteristics Before Matching

<table>
<thead>
<tr>
<th></th>
<th>CABG (n=423)</th>
<th>PCI (n=1349)</th>
<th>PValue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>65.0 (57.0, 73.0)</td>
<td>65 (57.0, 71.0)</td>
<td>0.28</td>
</tr>
<tr>
<td>Male</td>
<td>309 (73.0%)</td>
<td>895 (66.3%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>89.0 (78.0, 102.0)</td>
<td>86.0 (77.0, 99.9)</td>
<td>0.01</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>423 (100.0%)</td>
<td>1349 (100.0%)</td>
<td>…</td>
</tr>
<tr>
<td>Insulin-treated</td>
<td>139 (32.9%)</td>
<td>419 (31.1%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Hypertension</td>
<td>336 (79.4%)</td>
<td>1154/1343 (85.9%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>252/408 (61.8%)</td>
<td>966/1329 (72.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Current smoker</td>
<td>99/413 (24.0%)</td>
<td>278/1322 (21.0%)</td>
<td>0.22</td>
</tr>
<tr>
<td>Previous MI</td>
<td>125/415 (30.1%)</td>
<td>525/1303 (40.3%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>109/421 (25.9%)</td>
<td>674/1326 (50.8%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>24 (5.7%)</td>
<td>417/1345 (31.0%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>67/402 (16.7%)</td>
<td>281/1262 (22.3%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Baseline cardiac biomarker elevation</td>
<td>273/396 (68.9%)</td>
<td>738/1260 (58.6%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>ST-segment deviation ≥1 mm</td>
<td>206 (48.7%)</td>
<td>472 (35.0%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Baseline cardiac biomarker elevation or ST-segment deviation ≥1 mm</td>
<td>338/404 (83.7%)</td>
<td>908/1290 (70.4%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TIMI risk score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (0–2)</td>
<td>20/390 (5.1%)</td>
<td>61/1187 (5.1%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Intermediate (3–4)</td>
<td>204/390 (52.3%)</td>
<td>510/1187 (43.0%)</td>
<td>0.001</td>
</tr>
<tr>
<td>High (5–7)</td>
<td>166/390 (42.6%)</td>
<td>616/1187 (51.9%)</td>
<td>0.001</td>
</tr>
<tr>
<td>No. of diseased vessels</td>
<td>3.0 (2.0, 3.0)</td>
<td>2.0 (2.0, 3.0)</td>
<td></td>
</tr>
<tr>
<td>Two-vessel disease</td>
<td>93 (22.0%)</td>
<td>495 (36.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>330 (78.0%)</td>
<td>854 (63.3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diseased vessels</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>423 (100.0%)</td>
<td>1349 (100.0%)</td>
<td>…</td>
</tr>
<tr>
<td>LCX</td>
<td>373 (88.2%)</td>
<td>1074 (79.6%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RCA</td>
<td>380 (89.8%)</td>
<td>1129 (83.7%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>LM</td>
<td>113 (26.7%)</td>
<td>74 (5.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>55.0 (45.0, 60.0)</td>
<td>50.0 (41.0, 60.0)</td>
<td>0.07</td>
</tr>
<tr>
<td>Vessels and lesions treated</td>
<td>…</td>
<td>1 (1, 1) and 1 (1, 2)</td>
<td>…</td>
</tr>
<tr>
<td>Grafts per patient</td>
<td>3 (3, 4)</td>
<td>…</td>
<td></td>
</tr>
<tr>
<td>Admission to revascularization, d</td>
<td>3.6 (1.7, 6.7)</td>
<td>0.8 (0.4, 1.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total hospitalization, d</td>
<td>11.0 (8.0, 17.0)</td>
<td>3.0 (2.0, 5.0)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are expressed as n (%) for categorical variables or median (25th, 75th percentile) for continuous variables. CABG indicates coronary artery bypass grafting; LAD, left anterior descending; LCX, left circumflex; LM, left main; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery; and TIMI, thrombolysis in myocardial infarction.
Ben-Gal et al  Revascularization in Diabetes Mellitus With NSTEACS

with CABG had significantly lower unadjusted 1-month rates of mortality (1.6% versus 4.7%; \( P<0.0003 \)), MI, major bleeding, and acute renal injury, but underwent more repeat revascularization procedures. There was no significant difference between the PCI and CABG groups in the 1-year rate of death (6.3% versus 7.2%, respectively; \( P=0.23 \)), but Q-wave MI occurred more frequently in the CABG group, whereas ischemia-driven repeat revascularization was more frequent in the PCI group.

By multivariable analysis (Table 2), PCI compared with CABG was associated with significantly lower rates of MI and mortality at 1 month, but not at 1 year. CABG was associated with fewer ischemia-driven repeat revascularization procedures at 1 year compared with PCI. There were 2 patients in the PCI group (0.1%) and 4 patients in the CABG group (0.9%) who had a preprocedural myocardial infarction (\( P=0.031 \)). This difference might be attributed to the longer treatment delay for surgery versus for PCI (6.0 versus 1.2 days; \( P<0.0001 \)).

### Results in Propensity-Matched Pairs

The baseline clinical and angiographic characteristics of the 2 propensity-matched groups (163 pairs; n=326 total) were well matched (Table 3). Among PCI-treated patients, stents were implanted in 89.5% of patients, with DES used in 60.7%. Median (Q1–Q3) number of vessels and lesions treated in the PCI group were 1.0 (1.0–2.0) and 2.0 (1.0–3.0), respectively.

Each final adjusted model includes CABG triage, age, and sex along with the following selected variables: *renal insufficiency; †ST-segment deviation ≥1 mm; ‡randomization to bivalirudin; §renal insufficiency, anemia, baseline white blood cell; ||insulin-treated diabetic, current smoker, previous CABG, ST-segment deviation ≥1 mm, and renal insufficiency; ¶insulin-treated diabetic, previous CABG, ST-segment deviation ≥1 mm; #renal insufficiency, current smoker, and previous CABG; and **previous PCI, ST-segment deviation ≥1 mm.

### Clinical Outcomes in the Entire Study Cohort, Unadjusted, and Adjusted

<table>
<thead>
<tr>
<th>Outcome</th>
<th>CABG (n=423)</th>
<th>PCI (n=1349)</th>
<th>( P ) Value</th>
<th>Adjusted HR (95% CI)</th>
<th>Adjusted ( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-mo outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major adverse cardiovascular events*</td>
<td>69 (16.4%)</td>
<td>149 (11.1%)</td>
<td>0.005</td>
<td>1.52 (1.14–2.04)</td>
<td>0.005</td>
</tr>
<tr>
<td>Death</td>
<td>20 (4.7%)</td>
<td>22 (1.6%)</td>
<td>0.0003</td>
<td>3.05 (1.66–5.61)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Cardiac</td>
<td>19 (4.5%)</td>
<td>21 (1.6%)</td>
<td>0.0004</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Myocardial infarction†</td>
<td>49 (11.7%)</td>
<td>95 (7.1%)</td>
<td>0.003</td>
<td>1.57 (1.11–2.22)</td>
<td>0.01</td>
</tr>
<tr>
<td>Q wave</td>
<td>17 (4.1%)</td>
<td>20 (1.5%)</td>
<td>0.001</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Ischemia-driven revascularization</td>
<td>5 (1.2%)</td>
<td>63 (4.7%)</td>
<td>0.001</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Ischemia-driven TVR</td>
<td>2 (0.5%)</td>
<td>34 (2.6%)</td>
<td>0.01</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Ischemia-driven TLR</td>
<td>1 (0.2%)</td>
<td>30 (2.3%)</td>
<td>0.007</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Stroke</td>
<td>3 (0.7%)</td>
<td>3 (0.2%)</td>
<td>0.15</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Major bleeding‡</td>
<td>227 (54.1%)</td>
<td>132 (9.8%)</td>
<td>&lt;0.0001</td>
<td>6.80 (5.49–8.44)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Blood transfusion§</td>
<td>179 (42.6%)</td>
<td>83 (6.2%)</td>
<td>&lt;0.0001</td>
<td>8.91 (6.77–11.71)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>136/377 (36.1%)</td>
<td>188/1178 (16.0%)</td>
<td>&lt;0.0001</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>1-y outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major adverse cardiovascular events</td>
<td></td>
<td></td>
<td>88 (21.0%)</td>
<td>326 (26.0%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Death¶</td>
<td>30 (7.2%)</td>
<td>74 (6.3%)</td>
<td>0.23</td>
<td>1.41 (0.90–2.22)</td>
<td>0.13</td>
</tr>
<tr>
<td>Cardiac</td>
<td>20 (4.8%)</td>
<td>50 (3.9%)</td>
<td>0.34</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Myocardial infarction#</td>
<td>51 (12.2%)</td>
<td>154 (12.1%)</td>
<td>0.68</td>
<td>1.22 (0.87–1.70)</td>
<td>0.25</td>
</tr>
<tr>
<td>Q wave</td>
<td>17 (4.1%)</td>
<td>31 (2.7%)</td>
<td>0.053</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Ischemia-driven revascularization**</td>
<td>16 (4.0%)</td>
<td>209 (16.8%)</td>
<td>&lt;0.0001</td>
<td>0.25 (0.15–0.41)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ischemia-driven TVR</td>
<td>3 (0.7%)</td>
<td>141 (11.1%)</td>
<td>&lt;0.0001</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Ischemia-driven TLR</td>
<td>2 (0.5%)</td>
<td>122 (9.6%)</td>
<td>&lt;0.0001</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Stroke</td>
<td>4 (0.9%)</td>
<td>3 (0.2%)</td>
<td>0.06</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

Rates are displayed as Kaplan–Meier percentage estimates (number of events). HR is for CABG triage vs PCI triage. Variables with too few events for multivariable adjustment are presented as unadjusted data only. \( P \) values for unadjusted comparisons are derived from the log-rank test. \( P \) values for adjusted comparisons are derived from the Wald \( \chi^2 \) statistic. CABG indicates coronary artery bypass grafting; CI, confidence interval; HR, hazard ratio; PCI, percutaneous coronary intervention; TVR, target lesion revascularization; and TLR, target vessel revascularization.

Each final adjusted model includes CABG triage, age, and sex along with the following selected variables: *renal insufficiency; †ST-segment deviation ≥1 mm; ‡randomization to bivalirudin; §renal insufficiency, anemia, baseline white blood cell; ||insulin-treated diabetic, current smoker, previous CABG, ST-segment deviation ≥1 mm, and renal insufficiency; ¶insulin-treated diabetic, previous CABG, ST-segment deviation ≥1 mm; #renal insufficiency, current smoker, and previous CABG; and **previous PCI, ST-segment deviation ≥1 mm.
differences in mortality or MI between the groups. PCI compared with CABG was associated with less major bleeding and acute renal injury at 1 month, but more frequent revascularization procedures for ischemia. The 1-year rates of mortality and MI were also not significantly different in the propensity-matched groups, although ischemia-driven repeat revascularization was more common after PCI when compared with CABG.

Discussion

Diabetes mellitus is a major procedural risk factor for both PCI and CABG. Patients with DM have a more aggressive form of atherosclerosis and have higher rates of restenosis compared with nondiabetic patients. Smaller vessel size, longer lesion length, greater plaque burden, negative vessel remodeling, and glycation-dependent pathways of smooth muscle cell activation after arterial injury contribute to increased rates of both restenosis and bypass graft occlusion in diabetic patients.\textsuperscript{17-19}

Comparative outcomes in diabetic patients after PCI versus CABG has been a topic of great interest since the introduction of balloon angioplasty in the late 1970s. A comprehensive meta-analysis of trials performed before the DES era suggested improved survival after CABG compared with PCI in diabetic patients.\textsuperscript{20} Much of this finding relied on a subgroup analysis from the Bypass Angioplasty Revascularization Investigation (BARI) trial,\textsuperscript{21} although these data have been supported by other studies, including FREEDOM.\textsuperscript{11,22,23} In contrast, the SYNTAX Score II analysis from the Synergy Between PCI With Taxus and Cardiac Surgery (SYNTAX) trial suggests

Table 3. Baseline and Angiographic Characteristics of the Propensity-Matched Groups

<table>
<thead>
<tr>
<th></th>
<th>CABG (n=163)</th>
<th>PCI (n=163)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y\textsuperscript{*}</td>
<td>65.0 (57.0, 71.0)</td>
<td>65.0 (57.0, 72.0)</td>
<td>0.68</td>
</tr>
<tr>
<td>Male</td>
<td>114 (69.9%)</td>
<td>110 (67.5%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Weight, kg\textsuperscript{*}</td>
<td>85.4 (77.0, 100.0)</td>
<td>86.0 (75.0, 99.4)</td>
<td>0.78</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>163 (100.0%)</td>
<td>163 (100.0%)</td>
<td>…</td>
</tr>
<tr>
<td>Insulin-treated</td>
<td>49 (30.1%)</td>
<td>44 (27.0%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Hypertension</td>
<td>134 (82.2%)</td>
<td>132 (81.0%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>97 (59.5%)</td>
<td>100 (61.3%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Current smoker</td>
<td>33/160 (20.6%)</td>
<td>47/161 (29.2%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Previous MI</td>
<td>46 (28.2%)</td>
<td>54 (33.1%)</td>
<td>0.40</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>51 (31.3%)</td>
<td>51 (31.3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>11 (6.7%)</td>
<td>15 (9.2%)</td>
<td>0.54</td>
</tr>
<tr>
<td>Diabetic</td>
<td>163 (100.0%)</td>
<td>163 (100.0%)</td>
<td>…</td>
</tr>
<tr>
<td>Insulin-treated</td>
<td>49 (30.1%)</td>
<td>44 (27.0%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Hypertension</td>
<td>134 (82.2%)</td>
<td>132 (81.0%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>97 (59.5%)</td>
<td>100 (61.3%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Current smoker</td>
<td>33/160 (20.6%)</td>
<td>47/161 (29.2%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Previous MI</td>
<td>46 (28.2%)</td>
<td>54 (33.1%)</td>
<td>0.40</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>51 (31.3%)</td>
<td>51 (31.3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>11 (6.7%)</td>
<td>15 (9.2%)</td>
<td>0.54</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>27 (16.6%)</td>
<td>29 (17.8%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Baseline cardiac biomarker elevation</td>
<td>114 (69.9%)</td>
<td>116 (71.2%)</td>
<td>0.90</td>
</tr>
<tr>
<td>ST-segment deviation ≥1 mm</td>
<td>110/159 (69.2%)</td>
<td>108/158 (68.4%)</td>
<td>0.90</td>
</tr>
<tr>
<td>Baseline cardiac biomarker elevation or ST-segment deviation ≥1 mm</td>
<td>79 (48.5%)</td>
<td>73 (44.8%)</td>
<td>0.58</td>
</tr>
<tr>
<td>TIMI risk score</td>
<td>138 (84.7%)</td>
<td>135 (82.8%)</td>
<td>0.76</td>
</tr>
<tr>
<td>Low (0–2)</td>
<td>10 (6.1%)</td>
<td>10 (6.1%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Intermediate (3–4)</td>
<td>83 (50.9%)</td>
<td>86 (52.8%)</td>
<td>0.82</td>
</tr>
<tr>
<td>High (5–7)</td>
<td>70 (42.9%)</td>
<td>67 (41.1%)</td>
<td>0.82</td>
</tr>
<tr>
<td>No. of diseased vessels\textsuperscript{*}</td>
<td>3.0 (2.0, 3.0)</td>
<td>3.0 (2.0, 3.0)</td>
<td>…</td>
</tr>
<tr>
<td>Two-vessel disease</td>
<td>42 (25.4%)</td>
<td>37 (20.7%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>121 (74.6%)</td>
<td>126 (79.3%)</td>
<td>0.36</td>
</tr>
<tr>
<td>LAD</td>
<td>163 (100.0%)</td>
<td>163 (100.0%)</td>
<td>…</td>
</tr>
<tr>
<td>LCX</td>
<td>141 (86.5%)</td>
<td>140 (85.9%)</td>
<td>1.00</td>
</tr>
<tr>
<td>RCA</td>
<td>143 (87.7%)</td>
<td>149 (91.4%)</td>
<td>0.36</td>
</tr>
<tr>
<td>LM</td>
<td>13 (8.0%)</td>
<td>14 (8.6%)</td>
<td>1.00</td>
</tr>
<tr>
<td>LVEF (%)\textsuperscript{*}</td>
<td>50.0 (40.0, 60.0)</td>
<td>53.0 (42.0, 60.0)</td>
<td>0.79</td>
</tr>
<tr>
<td>Vessel and lesion treated\textsuperscript{*}</td>
<td>…</td>
<td>1 (1, 2) and 2 (1, 3)</td>
<td>…</td>
</tr>
<tr>
<td>Grafts per patient\textsuperscript{*}</td>
<td>3 (3, 4)</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>Admission to revascularization, d\textsuperscript{*}</td>
<td>3.7 (1.8, 7.0)</td>
<td>0.8 (0.4, 1.4)</td>
<td>0.008</td>
</tr>
<tr>
<td>Total hospitalization, d\textsuperscript{*}</td>
<td>11.0 (7.0, 16.0)</td>
<td>3.0 (2.0, 6.0)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CABG indicates coronary artery bypass grafting; LAD, left anterior descending; LCX, left circumflex; LM, left main; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery; and TIMI, thrombolysis in myocardial infarction.

\textsuperscript{*}Means continuous variables.
that the presence of DM does not, in and of itself, discriminate between the relative outcomes of PCI versus CABG. Rather, concomitant conditions that are more frequent in diabetics, such as advanced coronary artery disease and renal insufficiency, are responsible for greater survival with CABG when compared with PCI.24

These results notwithstanding, relatively few diabetic patients in prior randomized trials were enrolled with NSTEACS and treated with an early invasive strategy. Although FREEDOM included also patients with unstable angina, ACS patients with NSTEMI were excluded and the procedural complications and prognosis in this cohort may thus differ from those in FREEDOM. The results of the present large-scale, prospective study indicate that in patients with DM with NSTEACS undergoing early angiography in whom multivessel disease with LAD involvement is present, while there may be early differences in outcomes between PCI and CABG, the 1-year results with CABG versus PCI are not substantially different, in terms of most major end points. In the entire cohort, PCI was associated with shorter hospital stay and substantially less periprocedural bleeding, transfusions, acute kidney injury, fewer periprocedural MIs, and reduced mortality. At 1 year, however, there were similar rates of death and MI in the 2 groups, with fewer repeat revascularization procedures after CABG. There were no significant differences in stroke.

In the propensity-matched comparison, PCI and CABG resulted in nonsignificantly different 1-month and 1-year rates of death, MI, and stroke. PCI was associated with lower 1-month rates of major bleeding and acute kidney injury, whereas CABG was associated with greater freedom from recurrent ischemia necessitating repeat revascularization procedures at 1 month and 1 year after the procedure. Our findings of different bleeding and new revascularization rates in PCI versus CABG document a well-known difference between surgery and catheter-based interventions.

As prospective, randomized, controlled trials comparing PCI with DES to CABG in diabetic patients presenting with NSTEACS have not been performed, the findings from the present study may provide some guidance to choose between these alternatives in this high-risk patient group. Although both procedures may be considered as acceptable alternatives, PCI might be preferred in the patient at particularly at high risk for bleeding complications or acute kidney injury. In this regard, it is of note that in the FREEDOM trial of patients with DM and multivessel disease, acute kidney injury requiring dialysis was 88% less common with PCI when compared with CABG (0.1% versus 0.84%; \( P = 0.02 \)), and major bleeding tended to be less common.26 PCI might also be preferred immediately after angiography in NSTEACS patients with ongoing ischemia when rapid reperfusion is essential. Conversely, CABG should be preferred as anatomic disease complexity increases.11,24,25

### Limitations

As a post hoc analysis of a nonrandomized subgroup, our study has several limitations. Despite the use of multivariable analysis and propensity score matching, we cannot exclude the presence of unmeasured confounders that may add imprecision to the results. The number of stroke events was relatively low, perhaps explaining why differences in stroke favoring PCI were not observed, as has been present in most other trials.26 Similarly, however, sample size considerations may have masked modest differences in death or MI between the groups favoring surgery. Follow-up of our retrospective subgroup analysis was for only 1 year, this might not be long enough to show significant differences in survival. In SYN-TAX it took 2 years to see any benefit of CABG over PCI in diabetic patients, in FREEDOM it took 2 to 3 years. DESs were not used in all patients in the PCI arm, and no second-generation DESs were used, which have both greater safety and efficacy compared with earlier devices.27 Nonetheless, the present study provides the largest carefully collected and adjudicated data set from which evidence may be drawn to guide revascularization decisions in high-risk diabetic patients presenting with NSTEACS in whom an early invasive strategy demonstrates multivessel disease.

In conclusion, the present study demonstrates comparable 1-year survival and MI rates with PCI and CABG in diabetic patients presenting with NSTEACS, multivessel disease, and LAD involvement requiring revascularization. There may
be differences between these procedures, however, in early complications and late durability of revascularization, as well as invasiveness and quality of life; these distinctions will be weighted to varying degrees by individual patients and physicians. Revascularization decisions should also consider associated comorbidities and more nuanced considerations such as frailty, as well as anticipated life expectancy. Thus, as with and anatomic risk, as well as preferences and life goals. Making process, which considers each individual's clinical and anatomic grant support from The Medicines Company, Bristol-Myers, Squibb/Sanofi-Aventis, Lilly/Daiichi Sankyo, Regado Biosciences, and serves as a consultant to the Medicines Company, Bristol-Myers Squibb/Sanofi-Aventis, Lilly/Daiichi Sankyo, Regado Bioskiences, STENTYS, and Advisory board member of Coviend, Janssen Pharmaceuticals, Merck, Sanofi-Aventis, Endothelix, Inc. EQUITY/Shareholder: Endothelix, Inc. Dr Stone reports serving as a past consultant to Bristol Scientific. Johnson & Johnson and the Medicines Company and as a consultant to Valve Medical, Previz Ventures and Core Scientific Creations. Dr Feit is a shareholder at Boston Scientific, Johnson & Johnson and the Medicines Company and serves as a consultant to the Medicines Company, Dr Ohman reports receiving research grants and consultant fees from Daiichi sankyo, Eli Lilly, Gilead Sciences, Obimed, Janssen Pharmaceuticals, Pozen Inc, Sanofi Aventis, The Medicines Company and WebMD. Dr Kirtane reports receiving research grants from Medtronic, Boston Scientific, Abbott Vascular, St. Jude Medical, Abiomed, Eli Lilly, Vascular Dynamics. Dr Mehran reports being a consultant for Abbott Vascular, AstraZeneca, Boston Scientific, Coviend, CSL Behring, Janssen (JNJ), May Medical, and Merck and for receiving institutional grant support from The Medicines Company, Bristol-Myers Squibb/Sanofi-Aventis, Lilly/Daiichi Sankyo, Regado Bioskiences, STENTYS, and Advisory board member of Coviend, Janssen Pharmaceuticals, Merck, Sanofi-Aventis, Endothelix, Inc. EQUITY/ Shareholder: Endothelix, Inc. Dr Stone reports serving as a past consultant to Boston Scientific. The other authors report no conflicts.

References


Surgical Versus Percutaneous Coronary Revascularization for Multivessel Disease in Diabetic Patients With Non–ST-Segment–Elevation Acute Coronary Syndrome: Analysis From the Acute Catheterization and Early Intervention Triage Strategy Trial

Yanai Ben-Gal, Rephael Mohr, Frederick Feit, E. Magnus Ohman, Ajay Kirtane, Ke Xu, Roxana Mehran and Gregg W. Stone

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