Impact of Patient and Target-Vessel Characteristics on Arterial and Venous Bypass Graft Patency
Insight From a Randomized Trial

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Background—The purpose of this investigation was to determine optimal patient and target-vessel characteristics to maximize arterial and venous graft patency on the basis of data from a large clinical trial.

Methods and Results—Angiographic data on 440 radial artery grafts and 440 saphenous vein grafts were analyzed with methodology to account for within-patient clustering. Multivariable models that incorporated patient demographic, operative, anatomic, and postdischarge medical management were constructed to determine predictors of graft occlusion. Radial artery use was strongly protective against graft occlusion at 1 year after adjustment for all covariates, with a larger protective effect seen in women (P=0.05 for a subgroup-by-treatment interaction). Among all grafts, diabetes and small target-vessel diameter were associated with an increased risk of graft occlusion, and grafting to a target vessel with more severe proximal stenosis was associated with a decreased risk of graft occlusion. With regard to gender, radial artery graft occlusion at 1 year occurred in similar proportions of men (8.6%) and women (5.3%, P=0.6), whereas, for saphenous vein grafts the comparable occlusion rates were 12.0% and 23.3% respectively (P=0.02). A history of peripheral vascular disease was associated with an elevated risk of radial artery occlusion but was not associated with early vein graft occlusion (P=0.02 for a subgroup-by-treatment interaction).

Conclusions—Patients benefit from radial artery—coronary artery bypass conduits as opposed to saphenous vein conduits, and this effect is especially strong in women. Small target-vessel size adversely affected graft patency, and grafting to a target vessel with more severe proximal stenosis improved graft patency. (Circulation. 2007;115:684-691.)

Key Words: angiography ▪ arteries ▪ arteriosclerosis ▪ grafting, coronary artery bypass ▪ coronary disease ▪ grafting ▪ surgery

The ultimate goal of coronary artery bypass grafting is to achieve complete revascularization with conduits that will remain patent for the duration of the patient’s lifetime. Use of the left internal thoracic artery yields better long-term patency rates than do saphenous vein grafts, and authors have speculated about whether multiple arterial grafts can incrementally improve outcomes.1,2 The radial artery has recently emerged as an alternative coronary bypass conduit, although its long-term patency outcomes have not been well characterized.3 We initiated the Multi-Centre Radial Artery Patency Study, a randomized clinical trial, in 1996 to determine the relative patency of radial arteries to saphenous vein grafts.4 The primary results revealed that fewer radial artery grafts were totally occluded at 1 year as compared with saphenous veins.3 The purpose of this investigation was to determine the impact of patient and target-vessel characteristics on coronary bypass graft patency to develop recommendations for optimal conduit selection in multivessel bypass grafting.

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Methods

Study Population
Details of the study protocol have been previously published.4 Patients <80 years of age who were scheduled to undergo nonemergent primary isolated coronary bypass surgery and had graftable triple-vessel disease with an estimated left ventricular ejection fraction >35% were eligible for the study. The left internal thoracic artery was used to bypass the anterior circulation. Preoperative angiograms were assessed visually by the operating surgeon before randomization. The target coronary vessels for the study grafts were the left circumflex and the right coronary arteries, which, by protocol, had proximal lesions with at least 70% diameter narrowing,
were \( \geq 1.5 \) mm in diameter, and were deemed to be of acceptable quality according to visual assessment. The percent stenosis of proximal target-vessel stenosis was coded in a continuous manner, and the size of the target vessel and size of the distal myocardial bed filled by the target vessel were coded in an ordinal fashion as small, medium, or large. Patients with a dominant circumflex coronary artery were eligible if they had sequential high-grade lesions in the circumflex and suitable obtuse marginal and posterior descending branches. Patients were assessed preoperatively with a modified Allen’s test to ensure adequate collateral circulation in the hand.

**Randomization and Surgical Technique**

All surgeries were performed by cardiopulmonary bypass and cardioplegic arrest. Patients were randomly assigned to 1 of 2 graft strategies: (1) The radial artery was used to graft the circumflex territory, and a saphenous vein graft was used for the right coronary system; or, (2) the radial artery was directed to the right coronary territory, and a saphenous vein graft was used for the circumflex system. The details of the randomization protocol have previously been published. The nondominant arm was used exclusively to harvest radial arteries. The technique used to harvest radial arteries has previously been published. The free radial artery pedicle was dilated in situ by a slow intraluminal injection of 4 to 5 mL of a dilute solution of verapamil and papaverine (5 mg verapamil and 65 mg papaverine buffered in 16 mL of lactated Ringer’s solution). Two saphenous vein grafts and 2 radial artery grafts were used as sequential grafts. Two saphenous vein grafts and 2 radial artery grafts were used as Y-grafts.

**Postoperative Medical Management**

Patients were given aspirin 325 mg daily within 6 hours postoperatively and continued indefinitely. By protocol, patients received intravenous nitroglycerin 1 to 10 \( \mu \)g/kg per minute during the first 24 hours postoperatively in the intensive care unit. Vasoconstrictor agents were used only in settings of significant peripheral vasodilatation by protocol. Oral nifedipine was initiated on the first postoperative day and continued for 6 months postoperatively for prophylaxis against radial artery spasm.

**Follow-Up Angiography**

Patients were scheduled to undergo follow-up angiography 8 to 12 months after surgery. Nitroglycerin was injected into each graft before filming. Postoperative angiograms were adjudicated in an independent blinded fashion by 2 cardiologists, with a third review in the case of disagreement. Patency of only the 2 randomized grafts (study radial artery and study saphenous vein) was adjudicated. Grafts were determined to be occluded if no contrast dye injected into the graft opacified the distal coronary artery (ie, TIMI 0).

**Statistical Methods**

The primary end point of graft occlusion was calculated using the McNemar test for paired proportional data. Bivariate comparisons were performed with \( \chi^2 \) test for dichotomous data, and the continuous variables were compared with the Student \( t \) test where appropriate. Multivariate predictors of radial artery and saphenous vein occlusion were determined. Because the trial design was clustered (ie, the patient received both the study radial and control vein graft randomized to 2 different territories), the occlusion rates of these 2 grafts were not independent of each other. In these secondary analyses, within-patient clustering of graft occlusions was accounted for by using generalized estimating equations, a robust multivariable model.

Model predictors were specified a priori on the presumption that these were clinically relevant. These included graft type (radial artery or saphenous vein); age in years (continuous); myocardial infarction within 30 days before operation (yes or no); gender (male or female); preoperative smoking status (yes [any history of smoking] or no); preoperative diagnosis of diabetes (yes [any known diagnosis of diabetes before operation] or no); preoperative history of hypertension (yes or no); preoperative history of hyperlipidemia (yes or no); preoperative history of any peripheral or cerebral vascular disease (which includes stroke, transient ischemic attack, carotid endarterectomy, claudication, peripheral arterial angioplasty, bypass or endarterectomy surgery, and aneurysm repair) (yes or no); left ventricular dysfunction with estimated global left ventricular ejection fraction <35% (yes or no); proximal stenosis of target native coronary vessel graded by percent stenosis (continuous); size of target native coronary vessel graded on a visual scale in which vessel size was rated small, medium, or large (baseline) by the operating surgeon’s visual assessment of the angiogram (categorical) before operation; number of bypass grafts (continuous); graft to the right coronary artery (yes or no); use of perioperative vasopressors (yes or no); aspirin prescribed at discharge (yes or no); calcium channel blocker therapy prescribed at discharge (yes or no); and lipid-lowering agent prescribed at discharge (yes or no). Our dataset also contained a qualitative assessment of the size of the distal myocardial bed size of the target vessel. Because there was high correlation between the distal myocardial bed size of the target vessel and size of distal vessel (Pearson \( R=0.8, P<0.0001 \)), distal myocardial bed size was subsumed stratified by graft type.

By use of the generalized estimating equations model, overall predictors of graft occlusion in the study patients were determined. Tests of all 2-way statistical interactions between individual risk factors and graft type on graft occlusion revealed a significant differential effect of 2 risk factors on radial artery and saphenous vein graft occlusion \((P<0.05\) for interaction terms). These significant interaction terms were included in the final model.

Because differential effects of risk factors on arterial and venous grafts are biologically plausible, we created 2 regression models to determine individual risk factors for saphenous vein graft occlusion and radial artery occlusion (ie, logistic regression). For these models, there is no within-patient clustering because each patient contributed data on 1 graft to each model. Because there were relatively few clinical events (ie, occluded grafts), we validated the logistic models by computer-intensive methods. Specifically, bootstrap estimates of odds ratios (ORs) and 95% confidence intervals (CIs) for each predictor were calculated from median values of 10 000 iterations of each logistic regression model.

Predictive models for graft patency (ie, 1 minus the proportion of occluded grafts) were developed to compare the predicted graft patency for specific risk factors stratified by graft type. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

**Results**

**Patient Characteristics**

Of 561 randomized patients, 440 eligible patients underwent coronary angiography at 12 months. As previously reported, there were no demographic differences between patients who were randomized and those who underwent study angiography. Complete graft occlusion occurred in 13.6% (95% CI, 12.0% to 15.2%) of saphenous vein grafts and 8.2% (95% CI, 6.9% to 9.5%) of radial artery grafts (60 of 440 versus 36 of 440, \( P=0.009 \) by McNemar’s test). The within-patient correlation for occlusion between graft types was 2.5% (95% CI, –7% to 12%).

Medical therapy at discharge included aspirin in 92.3%, other antithrombotic medications in 8.7%, lipid-lowering drugs in 66.7%, \( \beta \)-blockers in 70.6%, and calcium channel blockers in 95.2% of patients.

**Predictors of Graft Patency**

Univariate analyses revealed significant differences in demographic profile between patients with occluded grafts and those with patent grafts (Table 1). Saphenous vein graft occlusion was more likely to occur in female patients, diabetic patients, patients with target vessels that were deemed small by preoperative visual assessment, and patients...
who were not discharged on daily aspirin. Radial artery graft occlusion was more likely to occur in patients with peripheral vascular disease and among patients with target-vessel proximal stenosis ≥90%. Hypertension and hyperlipidemia also tended to be more common among patients with occluded radial artery grafts.

On the basis of a multivariate model for all grafts, significant overall predictors of graft occlusion included diabetes and small target coronary artery vessel (Table 2). Grafting to a target vessel with more severe proximal stenosis was associated with a decreased risk of graft occlusion. Graft type was also a significant predictor, where radial arteries were significantly less likely to be occluded than were saphenous veins (relative risk 0.59; 95% CI, 0.37 to 0.92 versus saphenous veins). Tests of statistical interactions between individual patient risk factors of interest and graft occlusion revealed a significant differential effect of

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patent Vein Grafts (n=380)</th>
<th>Occluded Vein Grafts (n=60)</th>
<th>P</th>
<th>Patent Radial Grafts (n=404)</th>
<th>Occluded Radial Grafts (n=36)</th>
<th>P</th>
</tr>
</thead>
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<td>Age</td>
<td>60.6±8.4</td>
<td>61.8±8.0</td>
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<td>60.7±8.5</td>
<td>61.3±7.5</td>
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<td>Age &gt;70</td>
<td>60 (15.8)</td>
<td>8 (13.3)</td>
<td>0.62</td>
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<td>5 (13.9)</td>
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<td>26 (43.4)</td>
<td>0.61</td>
<td>185 (45.8)</td>
<td>19 (52.8)</td>
<td>0.49</td>
</tr>
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<td>Male gender</td>
<td>337 (88.7)</td>
<td>46 (76.7)</td>
<td>0.02*</td>
<td>350 (86.6)</td>
<td>33 (91.7)</td>
<td>0.60*</td>
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<td>Female gender</td>
<td>43 (11.3)</td>
<td>14 (23.3)</td>
<td></td>
<td>54 (13.4)</td>
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<td>276 (72.6)</td>
<td>41 (68.3)</td>
<td>0.49</td>
<td>288 (71.3)</td>
<td>29 (80.6)</td>
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<td>Diabetes</td>
<td>93 (24.5)</td>
<td>22 (36.7)</td>
<td>0.05</td>
<td>104 (25.7)</td>
<td>11 (30.6)</td>
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<td>Hypertension</td>
<td>171 (45.0)</td>
<td>32 (53.3)</td>
<td>0.23</td>
<td>181 (44.8)</td>
<td>22 (61.1)</td>
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<td>Elevated lipids</td>
<td>257 (67.6)</td>
<td>46 (76.7)</td>
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<td>273 (67.6)</td>
<td>30 (83.3)</td>
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<td>LV function†</td>
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<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>185 (48.7)</td>
<td>28 (46.7)</td>
<td>197 (48.7)</td>
<td>16 (44.4)</td>
<td>6 (16.7)</td>
<td>0.84</td>
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<tr>
<td>2</td>
<td>188 (49.5)</td>
<td>32 (53.3)</td>
<td>201 (49.7)</td>
<td>19 (52.7)</td>
<td>9 (25.0)</td>
<td>0.03†</td>
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<td>3</td>
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<td>5 (1.2)</td>
<td>1 (2.8)</td>
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<td>4</td>
<td>1 (0.3)</td>
<td>0 (0)</td>
<td>0.72</td>
<td>1 (0.25)</td>
<td>0 (0)</td>
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<td>Proximal stenosis of target vessel</td>
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<tr>
<td>70% to 79.9%</td>
<td>79 (20.8)</td>
<td>10 (16.7)</td>
<td>76 (18.8)</td>
<td>13 (36.1)</td>
<td>14 (38.9)</td>
<td>0.08</td>
</tr>
<tr>
<td>80% to 89.9%</td>
<td>50 (13.2)</td>
<td>15 (25.0)</td>
<td>73 (18.1)</td>
<td>7 (19.4)</td>
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<tr>
<td>90% to 99.9%</td>
<td>132 (34.7)</td>
<td>15 (25.0)</td>
<td>126 (31.2)</td>
<td>9 (25.0)</td>
<td>16 (44.4)</td>
<td>0.04‡</td>
</tr>
<tr>
<td>100%</td>
<td>119 (31.3)</td>
<td>20 (33.3)</td>
<td>129 (31.9)</td>
<td>7 (19.4)</td>
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<tr>
<td>Target-vessel size</td>
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<tr>
<td>Small</td>
<td>48 (12.6)</td>
<td>16 (26.7)</td>
<td>43 (10.6)</td>
<td>6 (16.7)</td>
<td>14 (38.9)</td>
<td>0.53</td>
</tr>
<tr>
<td>Medium</td>
<td>173 (45.5)</td>
<td>27 (45.0)</td>
<td>0.009</td>
<td>189 (46.8)</td>
<td>15 (41.7)</td>
<td></td>
</tr>
<tr>
<td>Large</td>
<td>159 (41.8)</td>
<td>17 (28.5)</td>
<td>172 (42.6)</td>
<td>15 (41.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of grafts</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>3</td>
<td>142 (37.4)</td>
<td>16 (26.7)</td>
<td>144 (35.6)</td>
<td>14 (38.9)</td>
<td>16 (44.4)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>190 (50.5)</td>
<td>38 (63.3)</td>
<td>212 (52.5)</td>
<td>16 (44.4)</td>
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</tr>
<tr>
<td>≥5</td>
<td>48 (12.6)</td>
<td>6 (10.0)</td>
<td>0.16</td>
<td>48 (11.9)</td>
<td>6 (16.7)</td>
<td>0.57</td>
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<tr>
<td>Graft location</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>RCA territory</td>
<td>189 (49.8)</td>
<td>30 (50)</td>
<td>202 (50)</td>
<td>17 (47.2)</td>
<td>19 (52.8)</td>
<td>0.89</td>
</tr>
<tr>
<td>LCX territory</td>
<td>191 (50.2)</td>
<td>30 (50)</td>
<td>1.0</td>
<td>202 (50)</td>
<td>19 (52.8)</td>
<td></td>
</tr>
<tr>
<td>Perioperative use of vasopressors</td>
<td>15 (4.0)</td>
<td>1 (1.7)</td>
<td>0.38</td>
<td>13 (3.2)</td>
<td>3 (8.3)</td>
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<tr>
<td>ASA at discharge</td>
<td>357 (94.0)</td>
<td>52 (86.7)</td>
<td>0.05</td>
<td>377 (93.3)</td>
<td>32 (88.9)</td>
<td>0.31</td>
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<td>CCB at discharge</td>
<td>361 (95.0)</td>
<td>58 (96.7)</td>
<td>0.57</td>
<td>386 (95.5)</td>
<td>33 (91.7)</td>
<td>0.30</td>
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<tr>
<td>LLA at discharge</td>
<td>265 (69.7)</td>
<td>44 (73.3)</td>
<td>0.64</td>
<td>279 (69.0)</td>
<td>30 (83.3)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

ASA indicates aspirin; CCB, calcium channel blocker; LLA, lipid-lowering agent; MI, myocardial infarction; PVD, peripheral vascular disease; LV, left ventricular; RCA, right coronary artery; and LCX, left circumflex coronary artery.

*For comparison of males to females for each graft type.
†LV function was graded with the following scale: 1 = estimated global LV ejection fraction (LVEF) of 50 or more; 2 = LVEF of 35 to 49; 3 = LVEF of 20 to 34; 4 = LVEF of <20.
‡For comparison of proximal stenosis ≥90% vs proximal stenosis ≤90%; P = 0.07 for overall trend.
§For comparison of proximal stenosis ≥90% vs proximal stenosis ≤90%; P = 0.08 for overall trend.
¶P value that tested null hypothesis that patent and occluded groups have the same mean or the same distribution across categories.
female gender (P=0.05 for interaction term) and history of peripheral vascular disease (P=0.02 for interaction term) on radial artery and saphenous vein graft patency. Interactions terms between graft type and severity of proximal target-vessel stenosis (P=0.16 for interaction term) and size of distal target vessel were not statistically significant (P=0.28 for interaction term with small target vessel, P=0.56 for interaction term with medium target vessel).

Two distinct logistic regression models were also created to identify risk factors for saphenous vein and radial artery occlusion separately. Preoperative history of peripheral vascular disease (OR, 5.0; 95% CI, 1.9 to 13.3) was a significant predictor of radial artery occlusion. Grafting to a target coronary artery with more severe proximal stenosis was protective (OR, 0.95; 95% CI, 0.93 to 0.99, for each 1% increase in percent proximal stenosis). Significant risk factors for vein graft occlusion included female gender (OR, 2.3; 95% CI, 1.1 to 5.0) and grafting to a smaller target coronary artery (OR, 3.0; 95% CI, 1.3 to 6.6, for comparison of grafting to a small target vessel versus a reference large target vessel). The effect of proximal stenosis appeared to be more prominent among radial artery grafts (OR, 0.95 versus 1.0 for veins), and the importance of small vessel size appeared to be more prominent in the vein grafts (OR, 2.9 versus 1.7 for arteries). To assess model fit, 10,000 iterations of each regression model were run in a bootstrap modeling procedure to determine median ORs and CIs. The bootstrap analysis yielded results that were similar to the original models.

Impact of Target-Vessel Characteristics

Parameter estimates from the logistic regression models were used to generate predictions of the expected graft patency of radial artery and saphenous veins, stratified by gender, according to severity of proximal target-vessel stenosis (Figure 1) and size of target vessel (Figure 2).

Grafting to target vessels with <90% proximal stenosis occurred in 154 of 440 (35.0%) saphenous vein grafts and 169 of 440 (38.4%) radial arteries (P=0.3). Target vessels with <90% stenosis were more common in grafts placed to the left circumflex coronary circulation (188 of 440 [42.7%]) than those placed to the right coronary territory (135 of 440 [30.7%]), P=0.002. Among 169 radial arteries grafted to target vessels with <90% proximal stenosis, 156 (92%) were grafted to target vessels of medium or large caliber. Small target-vessel size was observed in 64 of 440 (14.5%) saphenous vein grafts and 49 of 440 (11.1%) of radial artery grafts. Among vein grafts, 17.5% of women and 14.1% of men had target coronary arteries rated as small (P=0.5). Among radial artery grafts, 8.7% of women and 11.5% of men had small coronary arteries (P=0.4). There was an imbalance in the proportions of vein grafts (17.5%) versus radial artery grafts (8.7%, P=0.2) anastomosed to small targets in women. There was no difference in proportion of small target vessels between the right and circumflex coronary systems. Among 64 saphenous veins grafted to small distal targets, 45 (70.3%) were grafted to target vessels with >90% proximal stenosis. A comparison of predicted radial artery and saphenous vein graft patency for varying rates of target-vessel size and proximal stenosis revealed that radial artery grafting was superior regardless of target-vessel size where the target vessel had at least 80% stenosis. Predicted vein graft patency was slightly higher than predicted radial artery graft patency when the proximal target coronary stenosis was 70% and the target vessel had a large diameter.

Differential Impact of Patient Characteristics

Relative risks for each graft type stratified by gender and peripheral vascular disease were calculated with the generalized estimating equations model and are presented in Figure 4. The risk estimates for radial artery and saphenous vein graft occlusion in female patients with peripheral vascular disease had wide CIs because of the limited number of subjects in these subgroups. The overall regression model found that predicted graft patency for radial arteries in patients with peripheral vascular disease was 76.1%, versus 95.2% for radial arteries in patients without peripheral vascular disease. For saphenous veins, predicted graft patency in patients with peripheral vascular disease was 83.4%, versus 87.2% for saphenous veins in patients without peripheral vascular disease. With regard to gender, radial artery graft occlusion at 1 year occurred in similar proportions of men (8.6%) and women (5.3%, P=0.6), whereas the comparable occlusion rates for saphenous vein grafts were...
12.0% and 23.3%, respectively \( (P = 0.02) \). Predicted radial artery graft patency was 94.0% in men and 97.0% in women. Predicted vein graft patency was 89.0% in men and 73.3% in women. The differential impact of gender on vein and radial graft patency is summarized by Figures 1 and 2.

**Discussion**

This clinical trial was designed to compare the patency of the radial artery and the saphenous vein as a coronary bypass graft at 1 year. To date, this is the largest prospective randomized study with angiographic follow-up comparing patency of any arterial conduit to a saphenous vein when used to bypass non–left anterior descending artery targets. The overall patency was superior for the radial artery, and we have now identified risk factors that may guide selection of patients and target vessels for both saphenous vein and radial artery grafts to improve patency in patients who will undergo coronary bypass with a left internal thoracic artery graft to the anterior circulation.

Overall predictors of bypass graft occlusion to non–left anterior descending artery targets included use of a radial artery graft (protective), grafting to a target vessel with more severe proximal stenosis (protective), size of distal target vessel (small size is detrimental), gender (vein graft patency was poorer in women), diabetes (detrimental), and a history of peripheral vascular disease (detrimental in radial artery grafts). Previous studies have shown that patient and target-vessel risk factors of arterial and vein graft patency may be different as a result of the inherent differences in the vascular biology of these conduits. We explored the relative effect of several risk factors stratified by graft type and determined that 2 variables, female gender and history of peripheral vascular disease, had differential effects on graft patency that depended on the conduit used (saphenous vein or radial artery). Target-vessel characteristics, which included severity of proximal stenosis and target-vessel size, affected saphenous vein graft and radial artery patency. Indeed, the directional effect of smaller target-vessel diameter was to decrease graft patency in both radial artery and vein grafts. The magnitude of this effect appeared to be more prominent for vein grafts. Similarly, less severe proximal stenosis was associated with diminished patency in both types of grafts, with a more prominent effect seen in radial arteries.

**Role of Target-Vessel Characteristics**

**Target-Vessel Location**

Because the unit of randomization was the target-vessel location within the patient, the study was uniquely designed to determine the role of target-vessel location on arterial and vein graft patency. In our multivariate model, there was no difference in patency of either graft type when used to bypass the right coronary or left circumflex systems. Several angiographic trials have previously documented that although vein graft patency is superior when revascularizing the non–left anterior descending artery, there is no difference in vein graft patency between right coronary and left circumflex targets. Target location appears to have a consistent association with right internal thoracic artery (RITA) graft patency, with poorer patency seen in RITA grafts to the right coronary system. \(^8\) Our study and others suggest that such a relationship does not exist with radial arteries, even when
data are controlled for severity of target-vessel stenosis. Early RITA graft attrition in the right coronary territory may be caused by inadequate length when an in situ RITA graft to the posterior interventricular branch is used, a problem less often encountered when either a free RITA graft or a radial artery is used. Alternatively, when the RITA is used to bypass more proximally on the right coronary artery, progression of downstream disease may eventually compromise graft outflow and lead to early occlusion.

**Target-Vessel Size**

Several factors may lead to diminished patency in conduits grafted to smaller target vessels. Size mismatch, particularly when larger (3.5- to 4-mm) saphenous veins are grafted to small targets, may predispose to impaired nonlaminar flow patterns, which result in stimulus for endothelial dysfunction and early intimal hyperplasia or graft occlusion. Small distal targets may be more technically difficult to graft and may have significant disease at or adjacent to the anastomotic site itself. Larger-caliber target vessels may also have better distal run-off. Subjective visual assessment of the distal bed size was recorded at the time of study enrollment and was correlated strongly with the size of distal target vessel.

**Severity of Proximal Stenosis**

We also found a significant relationship between graft patency and severity of proximal target-vessel stenosis. Despite highly selective entry criteria that mandated the target vessels have >70% stenosis, we observed a significant gradient in radial graft patency with decreasing severity of the proximal target lesion. Although we did not directly measure intraoperative graft flows in the present study, we and others have hypothesized that the likely mechanism of failure in these grafts is flow competition from the native coronary vessel. We have previously reported that diffuse narrowing among patent radial arteries, known as angiographic string sign, is also a consequence of competitive flow. We speculate that progressive auto-regulated adaptive narrowing of the radial conduit in the setting of competitive flow may eventually lead to graft occlusion. Although the signaling mechanism by which flow competition provides a stimulus for graft dysfunction has not been well characterized, low flow and resultant low shear stress in the radial conduit may impair endothelial function. Among various arterial conduits, the radial artery is known to have a greater contractile response to a variety of stimuli. Histological properties, which include increased density of myocytes in the arterial wall, are likely factors that contribute to the contractile response in the setting of flow competition. Flow competition may also occur in the setting of high-volume flow from collateral vessels, even when the target vessel has a high-grade stenosis. Such relationships were not explored in this analysis.

**Patient Characteristics**

**Diabetes**

Diabetes was associated with an elevated risk of graft attrition in this study. These findings are congruent with previous longitudinal angiographic studies by Sabik and colleagues, who examined >10 000 venous and internal thoracic artery arterial bypass grafts. The impact of diabetes on a wide variety of metabolic processes leads to more rapid progression of atherosclerosis. The effect of diabetes on graft patency is, however, not consistent among angiographic studies. Follow-up studies by Shah and colleagues and the Bypass Angioplasty Revascularization Investigator Group.
tigation (BARI) did not find diabetes to be a significant risk factor for saphenous graft attrition in follow-up.16,19 We had no information on glycemic control preoperatively or postoperatively in these patients.

**Gender**

The impact of gender on patency outcomes of coronary surgery has been difficult to assess because of the limited number of female patients recruited in clinical trials, which include the present study. Seminal prospective postoperative patency studies by FitzGibbon et al as well as from the Veteran’s Affairs System included only male subjects.20,21 Seven percent of the patients enrolled in the Post–Coronary Artery Bypass Graft (Post-CABG) study22 and 13% of patients enrolled in the Coronary Artery Bypass Graft Occlusion by Aspirin, Dipyridamole, and Acenocoumarol/Phenprocoumon (CABADAS) Study23 were female. Because of the limited sample size of female patients in these and other angiography studies, meaningful subgroup analyses of the role of gender in vein graft patency are often underpowered. In the Post-CABG Study, although female gender was associated with diminished graft occlusion, no information about the age of female patients at the time of operation was provided. In CABADAS, the mean age of female patients was 61 years, versus 58 years for men, and there was a modest but nonsignificant increase in graft occlusion in women (OR, 1.6; \( P = 0.1 \)). Our study also enrolled 13% female patients with a mean age of 64.3 years, versus 60.3 years in men, and only 5% of female patients were <50 years old. In this study, women were more likely to experience early vein graft attrition, and this gender effect was not present in radial arteries. Additionally, we have demonstrated that the effect of female gender on vein graft patency exists independent of target-vessel size and that gender did not influence target-vessel size in the patients selected for this clinical trial. This observation has previously been described in a series of consecutive patients who were prospectively followed up.24 Changes in inflammatory cytokine milieu in postmenopausal women may lead to the observed acceleration in vein graft disease. Use of multiple arterial grafts does appear, in this early patency study, to be a vastly superior approach in postmenopausal women.

**Peripheral Vascular Disease**

Our study protocol excluded patients with a history of severe peripheral vascular disease because of concerns about the safety of follow-up angiography. Previous studies have shown that a history of peripheral vascular disease is associated with an increased risk of radial artery atherosclerosis at the time of harvest.25 With intravascular ultrasound, the overall proportion of in situ radial arteries before harvest with at least 1 discrete narrowing of \( >50\% \) is estimated to be up to 8.6%, and an additional 8.6% have hemodynamically nonsignificant calcification.26 In this trial, patients with a history of peripheral vascular disease were significantly more likely to experience early graft failure. Many radial artery grafts in these patients may have had subclinical atherosclerosis at the time of harvest. We recommend against the use of the radial artery in patients with peripheral vascular disease, as the likelihood of occlusion is greater than that of saphenous vein occlusion. Preoperative ultrasound examination of the radial arteries in patients with peripheral vascular disease could potentially be used to identify subclinical atherosclerosis. There were insufficient data about the concurrent effects of peripheral vascular disease and female gender on graft patency in this study to determine with confidence the ideal conduit in women with peripheral vascular disease.

**Optimization of Revascularization Strategy**

On the basis of predictions from our multivariate models, optimal selection of the target vessel can improve graft patency in saphenous vein and radial artery grafts. Radial arteries grafted to severely stenotic targets (\( >90\% \)) are expected to have a 1-year patency similar to that of an internal mammary artery grafted to the anterior circulation of the heart. In this trial, surgeons were not permitted to deviate from the randomized target vessel, and consequently variation in severity of proximal stenosis and size of distal targets was observed. In most instances where small target-vessel size appeared to negatively influence vein graft patency, that target vessel had a higher-grade proximal stenosis and an arterial conduit could be expected to have excellent patency. Similarly, in most instances where competitive flow compromised radial artery patency, the target-vessel size was medium or large and a vein graft could be expected to have adequate patency, at least in men.

**Study Limitations**

This study was a secondary analysis of a multicenter clinical trial. We did not have baseline or follow-up laboratory documentation of lipid levels, glycemic control, or inflammatory markers. Although the present study is one of the largest coronary surgery clinical trials with angiographic end points, sample size was somewhat limited in certain subgroups. The severity of the target stenosis and size of the target vessel were derived from single-observer visual assessment at the time of patient enrollment and not quantitative angiography. Previous studies have shown that visual assessment tends to overestimate the severity of stenosis in comparison to quantitative angiography.27 We did not have accurate information about the location of the vein graft harvest site (thigh versus calf) or intraoperative luminal diameter of the bypass conduit.

**Conclusions**

Target-vessel characteristics significantly influence both radial artery and saphenous vein graft patency. Optimal patency rates are experienced when radial arteries are grafted to target vessels with severe proximal stenosis and when vein grafts are grafted to larger target vessels. Radial artery use in patients with a known preoperative history of peripheral vascular disease should be avoided, and there is a preferential advantage to multiple arterial grafts in women.

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**Disclosures**

None.
target vessel characteristics and graft patency


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Impact of Patient and Target-Vessel Characteristics on Arterial and Venous Bypass Graft Patency: Insight From a Randomized Trial

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