Radial Artery Versus Saphenous Vein Patency Randomized Trial
Five-Year Angiographic Follow-Up

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Background—Graft patency is a fundamental predictor of long-term survival after coronary artery bypass surgery. Left and right internal thoracic artery (arterial) graft patency has been shown to be superior to that of saphenous vein grafts. More recently, the radial artery has been used as an aortocoronary graft, but little is known about the midterm and long-term patency of this conduit. We performed a single-center prospective randomized trial comparing the angiographic patency of radial artery and saphenous vein aortocoronary bypass grafts at 5 years after surgery.

Methods and Results—We enrolled 142 patients randomized at a single center to have either the radial artery or saphenous vein grafted to a stenosed branch of the native left circumflex coronary artery. The primary end point was angiographic graft patency 5 years postoperatively. At 5 years, 134 patients were alive and eligible for reangiography (5-year survival, 94.4%). Angiography was performed in 103 patients (77%); 98.3% of radial artery grafts and 86.4% of saphenous vein grafts were patent (P=0.04). Graft narrowing occurred in 10% of patent radial artery grafts and 23% of patent saphenous vein grafts (P=0.01).

Conclusions—Radial artery aortocoronary bypass grafts to a stenosed branch of the circumflex coronary artery have an excellent patency rate at 5 years. This was significantly better than the patency rate for saphenous vein grafts and comparable to reported patency rates for internal thoracic artery grafts. (Circulation. 2008;117:2859-2864.)

Key Words: arteries ■ coronary disease ■ follow-up studies ■ revascularization ■ surgery

The therapeutic options for patients with multivessel coronary artery disease consist of medical therapy only, percutaneous coronary intervention with coronary arterial stents, and coronary artery bypass grafting (CABG). It had been hoped that drug-eluting stents would address some of the limitations of percutaneous coronary intervention with bare metal stents. However, a number of recent publications have questioned both the clinical results and cost-effectiveness of drug-eluting stents in the management of coronary artery disease.1–3 This has resulted in renewed interest in the midterm and long-term results that may be achievable with CABG.1–3 The ultimate goal of this operation is to achieve complete revascularization of the patient with conduits that will remain patent for the duration of the patient’s lifetime.4 The excellent patency rates achieved with the pedicled left internal mammary artery are well described. Over the past decade, there has been considerable interest in whether the left internal mammary radial artery may provide results comparable to the arterial conduit. Observational studies have reported satisfactory early and midterm postoperative radial artery patency rates on the order of 92% at 1 year and 80% at 5 years.5 A recent prospective, randomized, multicenter trial (the Radial Artery Patency Study [RAPS]) confirmed these observational data, reporting significantly better perfect patency rates of radial artery compared with saphenous vein grafts 1 year postoperatively. However, the radial artery grafts had a significantly higher incidence of compromised flow states.6 At 5 years, 1 prospective randomized study showed no significant difference in patency rates between the right internal thoracic artery, radial artery, and saphenous vein grafts, although only 30% of the study group underwent angiographic assessment.7 Other studies have suggested inferior patency rates for radial artery grafts.8,9 Thus, ongoing doubt and debate remain regarding the efficacy of the radial artery as an aortocoronary conduit, with few robust data regarding the midterm patency rate of these grafts. In an editorial in Circulation earlier this year, Gardner, commenting on the 1-year results of RAPS, concluded, “Additional clarity about the usefulness and reliability of the radial artery bypass graft will have to come from late studies of radial
artery graft function, especially angiographic studies ≥5 years after CABG.\textsuperscript{10}

**Clinical Perspective p 2864**

The Radial Artery Versus Saphenous Vein Graft Patency (RSVP) trial presented here is a single-center, prospective, randomized clinical trial designed to compare 5-year patency rates of radial artery and saphenous vein aortocoronary grafts to a single coronary artery territory.

**Methods**

**Study Design**

The study was designed according to the Consolidated Standards of Reporting Trials (CONSORT) statement.\textsuperscript{11} All patients were scheduled to receive an aortocoronary bypass graft to a large epicardial coronary artery supplying the lateral wall of the left ventricle (usually a branch of the circumflex coronary artery). This vessel was identified angiographically and was deemed by the surgeon to have a proximal stenosis of >70%. The patients were randomized preoperatively to receive either a radial artery or a saphenous vein graft to this vessel. Randomization codes were obtained by use of a random number generator sequence and sealed in brown envelopes that were sequentially numbered. The first 100 patients were to be randomized in a ratio of 2:1 for radial artery to vein (these patients undergoing angiographic assessment first 100 patients were to be randomized in a ratio of 2:1 for radial artery to vein). The intention was to distend the conduit to a moderate supraphysiological pressure (1 mg/10 mL blood). The distal anastomoses were made to the angiographically ready for grafting.

Operative Procedure

The nondominant or left (depending on patient-physician preference) radial artery was harvested in the conventional manner.\textsuperscript{12} The saphenous vein was harvested in a routine fashion and gently distended with heparinized whole blood. The fascia on either side of the radial artery pedicle was divided radically,\textsuperscript{13} and the radial artery was distended with heparinized whole blood with verapamil added (1 mg/10 mL blood). The intention was to distend the conduit to a moderate supraphysiological pressure (∼200 mm Hg).\textsuperscript{14} Both conduits were then stored in the blood or blood/verapamil solutions until ready for grafting.

All grafts were constructed on cardiopulmonary bypass (“on pump”). The distal anastomoses were made to the angiographically identified stenosed epicardial coronary artery supplying the lateral wall of the left ventricle. All proximal anastomoses were constructed on the ascending aorta with 6/0 Prolene.

Postoperative Management

Postoperatively, all patients were started on aspirin (150 mg) and a course of oral diltiazem 60 mg 3 times daily for 6 weeks unless contraindicated by hypotension or bradycardia. Twenty-three patients with negative Allen’s test of the nondominant forearm were recruited preoperatively and underwent assessment of bilateral forearm function (soft touch and pinprick neural sensation, circumference, hand grip power, cyclical exercise fatigue) and blood flow measurements (forearm plethysmography).\textsuperscript{15}

**Follow-Up Angiography**

Follow-up angiography was scheduled for 5 years postoperatively. Ethics committee approval was given to intubate and view only the randomized (study) graft at follow-up unless there was a clinical indication for a full angiographic examination. All coronary angiograms were performed by a consultant cardiologist using 5F, 6F, or 7F angiographic catheters with Omnipaque contrast medium. Images were acquired digitally (Siemens AG, Erlangen, Germany) in 2 planes at an acquisition rate of 12.5 frames per second.

**End Points**

The primary end point was the proportion of radial artery and saphenous vein grafts that were patent at 5 years. This was determined by independent review of the angiograms by 3 experienced observers. Two observers reviewed and graded the angiograms on 2 separate occasions. The graft was graded as either patent or completely occluded. Complete occlusion was defined as the absence of visible opacification of the study graft despite aortogram (Thrombolysis in Myocardial Infarction flow grade 0 to 3).\textsuperscript{16}

Additional secondary angiographic visual grading of the grafts was defined as follows: P1=perfect patency; P2=compromised flow states (stenosis at anastomoses or in the body of the graft) <50%; P3=compromised flow states >50%; P4=severe diffuse graft narrowing (string sign); and P5=total occlusion. The only robust clinical outcome assessed was mortality. All deaths were confirmed with reports from the UK death registry, which included date and cause of death.

**Statistical Analysis**

The study was powered at 80% to detect a 15% absolute difference in angiographic patency (ie, patent versus occluded) at 5 years. This was based on an estimate of saphenous vein graft patency to the circumflex of 75% at 5 years\textsuperscript{17,18} and a projected radial artery patency of 90%. With significance set at 5%, a total of 188 patients were required. Allowing for a 6% dropout, we aimed to recruit 100 patients in each arm.

Patient characteristics were compared between the 2 randomized groups for all patients and for the subgroup who underwent 5-year angiography; in addition, characteristics were compared for patients who did and did not undergo angiography. Fisher’s exact test was used for categorical variables, and Student’s t test was used for continuous variables. The primary analysis data percentages are expressed as the percent of patients who underwent angiography at 5 years. Data are presented as mean±SD. Results were analyzed with STATA 9.2 (Stata Corp, College Station, Tex).

The authors had full access to and take responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

**Results**

**Patients**

From 1998 to 2000, 142 patients were enrolled. The Table lists the clinical characteristics of the 142 patients enrolled and the 103 patients who underwent follow-up angiography. The target vessel stenosis was not significantly different between groups. The patient population undergoing reangiography had no systematic or significant differences compared with the patients who did not undergo reangiography except for a borderline difference in smoking status between groups who were randomized to saphenous vein (current, 5% versus 25%; ex, 68% versus 44%; never, 27% versus 22%; \(P=0.047\), angiography versus no angiography).
Operative Data
Patients randomized to radial artery and saphenous vein grafts received 3.3±0.7 (median, 3; range, 2 to 5) and 3.3±0.6 (median, 3; range, 2 to 4) grafts, respectively. Cardiopulmonary bypass time (96±28 and 95±28 minutes) and cross-clamp time (50±19 and 51±20 minutes) were the same for both groups. Thirty-day mortality was 0.7% (n=1); 1 patient in the saphenous vein cohort experienced a catastrophic stroke on postoperative day 3 and died on day 8. There was no difference in in-hospital morbidity except for delayed wound healing in the conduit harvest site, which was more common in the saphenous vein group (16% versus 5%; P=0.03). In the 23 patients studied, harvesting of the radial artery did not adversely affect subsequent forearm function or blood flow to a clinically significant degree 3.4±0.4 months postoperatively.15

Postoperative Medical Treatment
At 5 years, patients randomized to radial artery or saphenous vein grafts were taking equivalent amounts of cardiovascular medication, including aspirin, lipid-lowering drugs, angiotensin-converting enzyme inhibitors, β-blockers, and calcium channel antagonists, as prescribed by their primary physician. There were no significant differences between the groups.

Angiography at 5 Years
Follow-up angiography was performed in 103 of the 134 patients alive and not withdrawn from the study (77%; the Table). Angiography was performed a mean±SD of 67±10 and 68±12 months after surgery in those patients randomized to radial artery and saphenous vein grafts, respectively.

Primary Analysis
Graft occlusion (P5) occurred in 6 of 44 saphenous vein grafts and 1 of 59 radial artery grafts, corresponding to patency rates of 86.4% and 98.3% (P=0.04; Figure 1) and an absolute difference of 11.9% (95% CI, 5.6 to 18.2) between saphenous vein and radial artery grafts.

Secondary Analysis
Visual grading of the angiographic data is presented in Figure 2. Ten patients (23%) with patent vein grafts had graft disease graded P2 or P3. Five radial artery grafts graded P2 or P3 (8.5%) had anastomotic stenoses but remained patent with good flow and had no evidence of graft disease/atheroma/intimal proliferation. The string sign (P4) was present in 1 radial artery graft and 0 saphenous vein grafts.

Table. Clinical Characteristics of All Patients at Randomization and Those Who Underwent Follow-Up Angiography

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (n=142)</th>
<th>Patients With Angiographic Follow-Up (n=103)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RA (n=82)</td>
<td>SV (n=60)</td>
</tr>
<tr>
<td>Age, y</td>
<td>58±6</td>
<td>59±7</td>
</tr>
<tr>
<td>Male/female, n (%)</td>
<td>79/3 (96/4)</td>
<td>58/2 (97/3)</td>
</tr>
<tr>
<td>Smoking status, n (%)</td>
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<td></td>
</tr>
<tr>
<td>Current</td>
<td>14 (17)</td>
<td>6 (10)</td>
</tr>
<tr>
<td>Ex</td>
<td>52 (63)</td>
<td>37 (62)</td>
</tr>
<tr>
<td>Never</td>
<td>16 (20)</td>
<td>17 (28)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>15 (18)</td>
<td>10 (17)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>46 (56)</td>
<td>32 (53)</td>
</tr>
<tr>
<td>Hypercholesterolemia, n (%)</td>
<td>63 (77)</td>
<td>52 (87)</td>
</tr>
<tr>
<td>Previous MI, n (%)</td>
<td>45 (55)</td>
<td>29 (48)</td>
</tr>
<tr>
<td>Target vessel stenosis, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70% to 89%</td>
<td>45 (55)</td>
<td>28 (47)</td>
</tr>
<tr>
<td>90% to 99%</td>
<td>22 (27)</td>
<td>18 (30)</td>
</tr>
<tr>
<td>100%</td>
<td>15 (18)</td>
<td>14 (23)</td>
</tr>
</tbody>
</table>

RA indicates radial artery; SV, saphenous vein; and MI, myocardial infarction.

Figure 1. Graft patency at 5 years. There was a significant difference in patency (P=0.04). Black bars indicate patent grafts; hatched bars, blocked grafts.
Survival

The 5-year survival rate was 94.4%, with no significant difference in survival between the 2 groups.

Discussion

In this single-center randomized study of aortocoronary bypass grafts to a single coronary territory, the angiographic patency of radial artery grafts at 5 years was significantly superior to that of saphenous vein grafts. This is the first trial to report the systematic repeat angiographic study of radial artery grafts at 5 years in a randomized trial. The radial artery grafts were significantly superior to the saphenous vein grafts in terms of both absolute patency and perfect patency. This study demonstrates the relatively frequent (23%) occurrence of occlusive disease in the body of patent vein grafts at 5 years. This was absent in the radial artery grafts. However, a number of the latter (n=5) were prone to suboptimal anastomoses. These stenoses were not severe and did not adversely affect overall graft patency at 5 years. When such a stenosis was present at the 3-month angiography (n=3), there was no progression in narrowing at 5 years. If anything, there was a tendency for the degree of stenosis to be less severe. Therefore, radial artery grafts, like internal thoracic artery grafts, are free of late graft attrition, at least by 5 years.

Enrollment in the trial did not reach the proposed total of 200 patients. The reasons for this were multifactorial. For logistical reasons, a firm date was chosen on which recruitment would end. By this date, 142 patients had been enrolled. The imbalance in the numbers between the 2 arms of the study was a result of the randomization strategy (ie, 2:1 for radial artery to vein for the first 100 patients and then 1:2 for the remainder) and the incomplete enrollment of the second group of 100 patients. The randomization strategy was intentional because, at the time of trial design, there were concerns regarding the clinical safety and early patency of radial artery grafts. Therefore, the aim was to have a sufficient number of patients with radial artery grafts in the 3-month angiography cohort to address these concerns.1–3 Given the results, we do not believe that the failure to recruit 200 patients affects the message of this trial. In fact, the ability to detect a statistical significance in such a small study indicates a clinically important difference.

The trial design was prescriptive, enrolling a relatively low-risk patient population concentrating on a single coronary artery territory. The vessel to be grafted was identified angiographically and confirmed at the time of surgery. As a result of patients declining the invitation to return for restudy, only 103 of the eligible patients (77%) underwent reangiography at 5 years. This rate of angiography is comparable to previous trials of this type of coronary artery surgery.6 The patient population undergoing reangiography had no significant systematic differences compared with the trial population as a whole (the Table).

There has been marked variability in the reported early and midterm patency of radial artery grafts.5 This is unlikely to be due to inherent biological differences between the radial arteries and is more likely to reflect technical issues. We therefore outlined in the Methods section details of the harvesting and implantation techniques of the radial artery. Radical division of the fascia enclosing the radial artery, followed by moderate supraphysiological distention, facilitates the use of the radial artery from a technical standpoint. We have previously shown that supraphysiological distention to the degree used causes a 70% to 80% loss of contractility of radial artery rings in vitro, thus reducing the propensity of the radial artery to spasm. This may reduce the risk of early postoperative spasm in this muscular artery. No incidence of clinically important hypoperfusion in the grafted territory was recorded in the patients with radial artery grafts. Endothelial injury may potentially affect the in vivo physiology of the graft and subsequent graft patency. However, we have previously reported that the radial artery grafts implanted in the study have preserved endothelial function in vitro.14 Clearly, this degree of distention did not adversely affect the patency of these grafts at 5 years.

Our study also confirms the importance of the severity of target vessel stenosis on the patency of arterial grafts as reported by Desai et al.6 The single radial artery graft occlusion occurred in a patient in whom the radial artery had been incorrectly grafted to a vessel that had a minor stenosis on the original coronary arteriogram. Similarly, the presence of the string sign occurred in a patient in whom, retrospectively, the target vessel had a moderate rather than severe stenosis.
The significant difference in patency between radial artery and saphenous vein grafts was not achieved because of a particularly high attrition rate of the saphenous vein grafts. Complete occlusion of saphenous vein grafts in this study at 5 years occurred in 13.6% compared with a 13.6% rate of occlusion at 1 year in the RAPS® study and a predicted rate of occlusion at 5 years, based on the literature at the time of trial design, of 25%.17,18 Thus, despite a good patency rate for saphenous grafts in our trial at 5 years, there was still a significant superiority of the radial artery grafts. One possible explanation for the difference in patency rates between this study and some other published data in this field may depend on the surgical strategy within our unit, which is an intention to graft only those vessels with important flow-limiting stenoses rather than those with more moderate disease. In this trial, almost half of the target vessels were occluded or had a stenosis of >90%. Published data suggest that this strategy may be associated with improved arterial graft patency.19–21

There are a number of limitations of this study, including its relatively small size, the lack of enrollment of the total planned number of patients, and an imbalance in numbers between the 2 arms of the trial. The failure to achieve complete angiographic follow-up at 5 years is a limitation but is comparable to other studies of this type in this field. There was a marked preponderance of men randomized into this trial. This was not by design. Exclusion criteria such as Raynaud’s syndrome and poor quality or varicose veins were more common in the female population. At the time of recruitment into the trial, there were still concerns regarding safety in terms of early morbidity and mortality using the radial artery, and a number of female patients were excluded because of equivocal Allen’s tests. In addition, we have found in a number of clinical trials that female patients have been less willing to be randomized.22 Thus, the conclusions of this study can be directly applied only to male patients, who form the large majority of patients undergoing surgical revascularization, and are applicable only by inference to females. However, it is pertinent to note that other studies have suggested that the patency benefits of radial arteries over vein grafts are even more marked in women than in men.19–21 The preparation methods for the grafts differ but reflect the real world in terms of graft preparation. The supraphysiological distension of the radial grafts, while attenuating early spasm, induces endothelial injury14 and, if anything, would be expected to adversely affect long-term patency. We did not believe it to be ethical to distend vein grafts in this manner. Despite these limitations, we believe that there is a very clear message from the data: The radial artery is a superior aortocoronary bypass graft to branches of the circumflex coronary artery with flow-limiting stenoses compared with the saphenous vein. In fact, the patency rates achieved for the radial artery grafts in this study are comparable to patency rates described for left and right internal thoracic artery grafts. We believe that our study provides evidence to support a significant change in clinical practice in terms of the choice of conduit in coronary artery bypass surgery.

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Disclosures
None.

References
CLINICAL PERSPECTIVE

Recent publications highlight the ongoing role for and importance of coronary artery bypass surgery in the interventional management of ischemic heart disease. There is still debate as to the role of radial artery grafts in this procedure. As Gardner stated last year in an editorial in *Circulation*, “Additional clarity about the usefulness and reliability of the radial artery . . . will . . . come from late studies of radial artery graft function especially angiographic studies ≥5 years after CABG” (Gardner TJ. Searching for the second-best coronary artery bypass graft: is it the radial artery? *Circulation*. 2007;115:676–680). This small randomized trial is the first to report such data. It is important to note the good 5-year patency (86%) that can be achieved in the modern era with saphenous vein grafts. The radial artery patency rate at 5 years was excellent (98%), significantly superior to that of saphenous vein grafts and comparable to internal mammary artery patency. Another important finding was the complete absence of occlusive graft disease in the radial grafts. In addition to previous 1-year data from this and other radial artery trials, we believe that these 5-year patency rates and the absence of graft disease should substantially change clinical practice, with much more widespread and acceptable use of the radial artery as an aortocoronary bypass graft.

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