Radial Artery Bypass Grafts Have an Increased Occurrence of Angiographically Severe Stenosis and Occlusion Compared With Left Internal Mammary Arteries and Saphenous Vein Grafts

Umesh N. Khot, MD; Daniel T. Friedman, DO; Gosta Pettersson, MD; Nicholas G. Smedira, MD; Jianbo Li, PhD; Stephen G. Ellis, MD

Background—The radial artery has been increasingly used in CABG. However, angiographic outcome data have been limited.

Methods and Results—We reviewed all coronary angiography procedures from February 1996 to October 2001 and selected patients with a radial artery bypass graft. Angiographic outcomes were divided into groups as (1) occluded, (2) severe disease (≥70% stenosis, or string sign), or (3) patent (<70% stenosis). Multivariable analyses determined predictors of severe disease or occlusion. A total of 310 patients had a radial artery graft. Mean follow-up after coronary artery bypass grafting was 565±511 days. Radial artery grafts had a patency rate of 51.3%, which was significantly lower than that for left internal mammary arteries (90.3%, P<0.0001) or saphenous vein grafts (64.0%, P=0.0016). Radial artery grafts had an occlusion rate of 33.7%, compared with 4.8% for left internal mammary arteries (P<0.0001), and had a severe stenosis rate of 15.1%, compared with 5.9% for saphenous vein grafts (P=0.0003) and 4.8% for left internal mammary arteries (P<0.0001). Women had a worse overall radial artery patency rate than men (38.9% versus 56.1%, P=0.025). A radial artery graft was the most powerful multivariable predictor of severe stenosis or occlusion (χ²=28.87, P<0.0001). Because of diseased radial artery grafts, 58 patients required subsequent percutaneous intervention, and 26 patients required repeat CABG.

Conclusions—In patients predominantly presenting with signs and symptoms of myocardial ischemia after CABG, radial artery grafts have lower patency rates than left internal mammary artery and saphenous vein grafts. Selective use of the radial artery is warranted, particularly in women. (Circulation. 2004;109:2086-2091.)

Key Words: angiography ■ bypass ■ revascularization ■ follow-up studies ■ surgery

The use of the internal mammary artery (IMA) as a conduit for CABG is arguably one of the most important advances in the treatment of coronary artery disease in the past 25 years. These arteries are associated with superior long-term angiographic patency compared with saphenous vein grafts (SVGs).1,2 Furthermore, their placement leads to a significant reduction in long-term mortality.1 Impressive results with the IMA have increased interest in other arterial conduits such as the gastroepiploic artery,3 the inferior epigastric artery,4 and the radial artery to achieve total arterial revascularization. Of these, the radial artery is currently the most popular. Initially described in 1973 by Carpentier et al,5 the radial artery was soon abandoned because reports documented dismal early angiographic outcomes.6 However, improvements in graft harvesting techniques, avoidance of mechanical dilation, new preservation methods, and the use of postoperative calcium channel blocker therapy to prevent early vasospasm led to a resurgence in the use of the artery as a bypass graft in the 1990s.7 Multiple institutions have documented that the radial artery can be used with acceptable morbidity and mortality4-10 and that early angiographic results in the modern era approach those of the IMA.7-13 This has led to a dramatic increase in the number of patients receiving radial artery bypass grafts. Yet, there are limited data on the later angiographic outcomes of these grafts. We, therefore, analyzed all patients with radial artery grafts undergoing coronary angiography at our institution between 1996 and 2001 to determine angiographic outcomes in this population.

Methods

Study Design
We reviewed all coronary angiography procedures at our institution from February 1996 to October 2001 and selected patients with a...
radial artery bypass graft. We collected basic demographic information, past medical history, reasons for angiography, calcium channel blocker use, and severity of stenosis being bypassed. The number and type of bypass grafts and the coronary artery anastomoses were noted. Each anastomosis was analyzed separately. Thus, for example, a patient with a sequential graft to 2 anastomotic targets would have the patency of each one analyzed individually. For patients who had undergone redo CABG, only the grafts and anastomoses from the most recent surgery were included in this analysis. The angiographic findings at the time of catheterization were categorized into 1 of 3 groups: (1) occluded, (2) severe disease (=70% stenosis, or string sign), or (3) patent (<70% stenosis). Occlusion was confirmed by an aortogram if a graft was unable to be selectively cannulated. In patients with multiple angiographic procedures, we selected the earliest study that documented a severely diseased (=70%) or occluded radial artery graft or the latest study if the radial artery graft was patent.

Further revascularization procedures performed within 90 days of catheterization were noted. If a patient underwent percutaneous intervention to the radial artery graft itself or to the coronary artery originally bypassed by a severely diseased or occluded radial artery graft, then percutaneous intervention was noted. If a patient underwent repeat CABG to the coronary artery originally bypassed by the radial artery graft, then CABG was noted. The Institutional Review Board of the Cleveland Clinic Foundation approved the research protocol.

Statistical Analysis
Continuous variables are expressed as mean±SD and categorical variables as percentages. Comparisons were made between left IMA (LIMA) grafts, right IMA (RIMA) grafts, SVGs, and radial artery grafts with regard to overall patency, severe stenosis, and occlusion rates. Multivariable logistic regression analysis was performed on the entire cohort of grafts to determine predictors of severely diseased or occluded grafts. Predictors selected by this analysis were then used in ordinal logistic regression for repeated measures (SAS PROC GENMOD) for comparison of grafts. Variables included time since CABG, type of graft (LIMA, RIMA, SVG, and radial artery), graft target vessel (left anterior descending, left circumflex, and right coronary artery), redo CABG, smoking, diabetes mellitus, hypertension, hyperlipidemia, age, and gender. Similarly, multivariable analysis with proportional hazard survival analysis was performed on radial artery bypass grafts to determine predictors of severe disease or occlusion with the identical variables, except type of graft was excluded. Predictors were selected with bootstrap aggregating with reliability of 50% or above. Kaplan-Meier curves evaluated patency rates over time. Log-rank tests compared the Kaplan-Meier estimates of event rates between bypass graft types. Univariate analysis was conducted on calcium channel blocker use and severity of the proximal stenosis bypassed by the radial graft to determine if they were predictors of severe disease or occlusion. Proximal stenosis severity was categorized as <70%, 70% to 99%, and occluded. Comparison of patency between genders was done with Fisher’s exact test on the basis of single measurements from individual patients. P<0.05 was statistically significant.

Results
Characteristics of Patients and Bypass Grafts
A total of 35 536 angiographic procedures from 27 211 individual patients were reviewed. A total of 310 patients had a radial artery graft. Baseline demographics are shown in Table 1.

Angiographic Outcomes
The LIMA and RIMA were associated with the best overall relative patency rate (Figure 1). Radial artery grafts had the lowest overall patency of the 4 graft types owing to high rates of severe disease and occlusion (P<0.0001 compared with LIMA). The rate of occlusion for radial artery grafts was similar to that for the SVG (P=0.28), although overall patency rates were significantly lower than with SVGs (P=0.0016) owing to a high incidence of severe disease among radial artery grafts (P=0.0003 compared with SVG). Radial artery grafts had the lowest patency rates when
anastomosed to either the left circumflex coronary artery or the right coronary artery.

Kaplan-Meier curves are shown in Figure 2. Radial artery grafts had the lowest cumulative patency rates and were significantly worse than all other bypass graft types ($P<0.0001$ compared with LIMA and RIMA, and $P=0.0001$ compared with SVG).

The patency rate of the radial artery bypass graft was significantly worse in women than in men (38.9% versus 56.1%, $P=0.025$). Women and men had different patterns of radial artery disease, with women having higher rates of occlusion (53.7% versus 27.1%, $P<0.0001$) but lower rates of severe disease (7.4% versus 16.9%, $P=0.095$).

Predictors of Severe Disease or Occlusion

A total of 305 patients with 1004 grafts had complete data for multivariate analysis in the entire cohort of grafts. The presence of a radial artery graft was the most significant multivariate predictor of severe graft disease and occlusion in the entire cohort ($\chi^2=28.87$, $P<0.0001$; Table 2). Other significant predictors included the presence of an SVG ($\chi^2=10.61$, $P=0.0011$) and anastomosis to a non–left anterior descending coronary artery ($\chi^2=5.23$, $P=0.022$). A total of 304 patients with 392 radial artery grafts had complete data for multivariate analysis in the radial artery cohort. When multivariate analysis was performed on the radial artery bypass grafts, the significant predictors of severe disease or occlusion were anastomosis to a non–left anterior descending coronary artery ($\chi^2=6.27$, $P=0.012$), female gender ($\chi^2=4.01$, $P=0.045$), and absence of diabetes mellitus ($\chi^2=3.72$, $P=0.054$).
Calcium channel blockers were administered early after surgery in 191 patients and were not administered to 37 patients. In 82 patients, calcium channel blocker use could not be determined either because the original surgery was performed outside of our institution (n=50) or because we were unable to obtain information about calcium channel blocker use from the medical record (n=32). Among the 228 patients with 305 radial artery anastomoses with data, calcium channel blocker use was not a significant univariate correlate of severe stenosis or occlusion (P=0.65). With increasing proximal stenosis severity (<70% versus 70% to 99% versus occluded), there was an increase in patency rates of radial artery grafts from 44.4% (24 of 54) to 49.5% (106 of 214) to 60.5% (49 of 81). However, this relationship was not statistically significant (P=0.133).

### Need for Further Revascularization

Fifty-eight patients required percutaneous intervention to a severely diseased or occluded radial artery graft or to the coronary artery originally bypassed by the radial graft. Twenty-six patients required repeat CABG to the coronary artery originally bypassed by the radial artery graft.

**Discussion**

The present study of 310 patients with 398 radial artery anastomoses constitutes one of the largest angiographic follow-ups in patients with radial artery bypass grafts. We have shown that in patients predominantly presenting with recurrent signs or symptoms of myocardial ischemia after CABG, radial artery grafts are associated with a high rate of both occlusion and severe flow-limiting disease. In fact, radial artery graft results were dramatically inferior to IMA bypass grafts and even inferior to SVGs. Although both genders had poorer angiographic outcomes with the radial artery graft, women particularly had very high rates of occlusion.

The present results are in significant contrast to the widespread belief that radial artery grafts have a high rate of patency. The seminal report by Acar et al. documented 100% angiographic patency 3 weeks after surgery and 94% patency after 9 months. Multiple studies have replicated these findings, which indicates that early angiographic patency with radial artery grafts in the modern era consistently exceeds 90% and is similar to results achieved with the IMA. In addition to these reports, the increasing acceptance of the radial artery has been based on 2 studies with angiographic results, both with 5 years of follow-up. In one, angiography in 50 patients with 64 radial grafts revealed a patency rate of 83%. In the other, 61 patients with 62 radial grafts were studied, which yielded an 87% patency rate. Superficially, these reports contradict the present findings; however, these and other long-term angiographic studies largely consisted of patients without symptoms or evidence of myocardial ischemia. Among the 14 symptomatic patients in the first study and 15 patients in the second study, the patency rates were considerably lower: 64% and 73%, respectively. In addition, a recent larger study of 109 patients who underwent cardiac catheterization for symptoms of ischemia showed an overall patency rate of the radial artery graft of only 75.1% at a mean follow-up of 2.3 years.

Improvements in harvesting techniques and postoperative administration of calcium channel blockers were expected to lead to improved results with the radial artery, yet we are concerned that these technical advances and pharmacological therapies have merely delayed the ultimate poor outcome with these grafts. The exact mechanism for the observed high rate of radial artery graft failure is not known. The propensity for the radial artery to vasospasm is well documented, and it has been speculated that this vasospasm leads to early graft failure. However, the increased vasoreactivity of the denervated radial artery diminishes with time, and we therefore doubt that this is the cause of the graft failure seen in the present study. Furthermore, the present study showed no relationship between calcium channel blocker use and the risk of severe stenosis or occlusion. Similarly, discontinuation of the calcium channel blocker diltiazem 1 year after CABG failed to lead to an increase in the incidence of radial artery occlusion. The development of intimal hyperplasia in the radial artery is believed to be a cause of graft failure, although the present study is unable to confirm or refute this hypothesis. We are also concerned that the development of graft arteriosclerosis may be a contributing factor. In contrast to the IMA, which is almost universally without arteriosclerosis, severe arteriosclerosis of the radial artery sufficient to make the graft unusable has been documented in as many as 5% of patients, and the prevalence of less severe arteriosclerosis is much higher, being as high as 50% in diabetic patients. Therefore, more intensive preoperative evaluation of the radial artery for arteriosclerosis may be required. Finally, patency of the radial artery may be dependent on maintenance of a high level of blood flow. In fact, previous studies with the radial artery graft stipulated target-artery conditions to maintain a high level of blood flow. In situations in which this does not occur (less than critical native coronary stenosis or right coronary artery), the radial artery may be more prone to graft occlusion. The present study does support this mechanism in part, because the patency rate was much lower with anastomoses to non–left anterior descending artery.
targets. However, the severity of native-vessel stenosis had a modest and statistically insignificant effect on graft patency.

Although the number of women in the present study is small, their results raise concerns about the use of radial artery grafts in this population. The exact reason for their poorer outcome is not known, and there has been limited research on the specific outcomes of women with these bypass grafts. Mong et al. have shown that radial arteries from women are more sensitive to vasoconstrictors and less sensitive to vasodilators than are radial arteries from men. In addition, women have smaller radial artery lumens, even when one controls for the smaller overall size of their arteries compared with men.

The present study provides an important window into the future of patients who have received a radial artery bypass graft. The return of symptoms or signs of myocardial ischemia after CABG is typically delayed for 5 years after surgery. In one study, only 18% of patients had ischemia after 5 years, but this increased to >39% at 10 years and 62% at 15 years. In addition to progression of native coronary artery disease, the return of symptoms occurs because of a high rate of SVG occlusion during this time period. The hope of arterial revascularization was to achieve an improved long-term conduit patency rate to extend this asymptomatic period and, importantly, to reduce long-term mortality. Although this paradigm has clearly been true for the LIMA, it may not be for the radial artery. The observed high rate of radial graft stenosis and occlusion in symptomatic patients is of concern because it suggests that the natural history of these grafts is similar to that of the SVG. Because most radial artery grafts have been placed in the past 5 years, we have yet to see the complete natural history in these patients.

The present study has a number of limitations. Our results are confounded by selection bias, because predominantly patients with symptoms or signs of recurrent ischemia were studied. Thus, the low radial artery graft patency may reflect the high-risk nature of the population studied rather than any intrinsic tendency for this graft to fail. However, the LIMA bypass graft can effectively serve as a control given its extensive prior angiographic validation. If the radial artery were truly equivalent to the LIMA, the patency rates should be similar irrespective of the population studied. However, radial artery patency was considerably inferior to the LIMA and even worse than the SVG. In addition, despite the limitations of this design, it has been widely used in previous studies, including those that have established the superiority of the LIMA to the SVG. The poor results of the radial graft may be due to its predominant use as a free graft from the aorta compared with the typically in situ LIMA. However, RIMA grafts, which were typically free grafts (Table 1), had a significantly higher patency rate than radial artery grafts, which indicates that it is the nature of the graft that is the issue rather than style in which the graft is placed. In contrast to previous studies that limited radial artery placement to high-grade stenoses with good distal runoff, the present study reflects a “real-life” use of the radial artery because the decision to use a radial graft was done at each surgeon’s discretion. Thus, our results may reflect less stringent criteria for radial artery bypass use. We also could not account for selection bias in the placement of radial artery grafts because they may have been preferentially placed on secondary targets with poor runoff or to targets with subcritical stenoses with resulting competitive flow. However, poor patency rates were noted even when bypassed to the left anterior descending artery or to coronary arteries with high-grade proximal stenoses. It is also important to not confuse the relative patency rates shown in the present study of patients with predominantly signs and symptoms of myocardial ischemia with the absolute patency rates of radial artery grafts as a whole. Finally, the present study reflects a single-center experience; therefore, confirmation from other centers will be required.

We have reevaluated our approach to total arterial revascularization in patients undergoing CABG. Not all arterial grafts are equivalent, and for now, a bilateral IMA remains the standard for long-term angiographic patency and long-term mortality reduction. However, a bilateral IMA can lead to considerable morbidity, especially in patients with diabetes, obesity, or chronic obstructive pulmonary disease. In these populations and in redo CABG, the radial artery can still be used as a conduit, noting that its long-term patency is likely similar to that of the SVG. The radial artery also should bypass critically narrowed arteries, according to data from other institutions.

The ideal of total arterial revascularization has been based on the presumption that all arterial grafts are associated with superior long-term patency compared with the SVG. The present data indicate that in patients predominantly presenting with recurrent signs or symptoms of myocardial ischemia, the radial artery is associated with a high rate of severe stenosis and occlusion. Our data suggest that radial artery bypass grafts are unlikely to approach the patency rates of IMAs. Therefore, selective use of the radial artery is warranted, particularly in women.

Acknowledgments

Funding for this study was provided by Dr Umesh N. Khot and by the Departments of Cardiovascular Medicine and Cardiothoracic Surgery at the Cleveland Clinic Foundation.

References


Radial Artery Bypass Grafts Have an Increased Occurrence of Angiographically Severe Stenosis and Occlusion Compared With Left Internal Mammary Arteries and Saphenous Vein Grafts

Umesh N. Khot, Daniel T. Friedman, Gosta Pettersson, Nicholas G. Smedira, Jianbo Li and Stephen G. Ellis

_Circulation._ 2004;109:2086-2091
doi: 10.1161/01.CIR.0000127570.20508.5C

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/109/17/2086

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/