Should all moderate coronary lesions be grafted during primary coronary bypass surgery? An analysis of progression of native vessel disease during a randomized trial of conduits

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Objective: Whether to graft a moderately stenosed coronary vessel remains debatable. We investigated whether grafting such vessels is warranted based on angiographic evidence of disease progression.

Methods: Of 619 patients who underwent on-pump coronary artery bypass grafting in an ongoing, randomized radial artery trial, 405 have at least 1 follow-up angiogram at a mean of 6.2 ± 3.1 years (range, 0-14 years) after surgery. Percent diameter stenosis in each major native vessel was reported by 3 cardiac specialists and classified as either moderate (40%-69%) or severe (≥70%) stenosis. Progression of native vessel disease and graft patency were determined by comparison of pre- and postoperative angiography.

Results: A total of 3816 native vessels and 1242 bypass grafts were analyzed, of which 386 moderate preoperative lesions were identified, 323 of which were grafted. In all territories, grafted vessels had greater risk of disease progression than ungrafted equivalents (43.4% vs 10.5%, $P < .001$). Moderate lesions were more likely than severe lesions to remain unchanged on follow-up angiography (52.6% vs 31.1%, $P < .001$). Only 1 in 7 moderate lesions in the right coronary artery exhibited significant progression during follow-up if left ungrafted, whereas the likelihood of progression in left-sided counterparts approached 50%. Arterial and vein grafts to left-sided moderately stenosed vessels had excellent patency (83% and 77% at 8 years, respectively), which was not matched by right-sided grafts ($P = .051$). Placement of a graft for a moderate lesion was associated with significantly greater incidence of disease progression, most marked in the right coronary territory.

Conclusions: The greater risk of progression of left-sided moderate lesions, and high graft patency rates when bypassed, suggests that the balance of clinical judgment lies in favor of grafting moderate left-sided lesions. In the right coronary system, however, a lesion is likely to remain moderate if left ungrafted and, with a low risk of progression, it may be reasonable to leave these vessels undisturbed. (J Thorac Cardiovasc Surg 2013;145:140-9)

ACD

Recent trials and database analyses of long-term outcomes following coronary revascularization have reinforced the place of coronary artery surgery as the gold standard therapy for multivessel disease.[1] Most patients referred for surgery have severe disease unsuitable or unfavorable for percutaneous intervention. Many of these patients will also have 1 or more moderate lesions, with luminal stenosis estimated around 50%, and surgeons frequently have to decide whether such vessels require bypass grafting. Studies of the assessment of fractional flow reserve in moderate lesions, largely used to guide requirement for placement of coronary stents, have suggested that the majority are not flow limiting in their moderate state,[2] so the decision to graft is based primarily upon anticipation of further progression to greater severity.

The choice that the surgeon must make depends, in essence, on 3 judgments: the likelihood of progressing to severe stenosis or occlusion, the likelihood of the lesion remaining static or regressing, and the outcome (patency) of a graft placed to such a moderate lesion (which in itself depends on the conduit used and location of the target artery). This decision is likely affected by other factors, such as how many other severe lesions require grafting or which other cardiac procedures need to be performed, because containment of the cardiopulmonary bypass or aortic crossclamp time and total operative time may be a priority in practice, and there may not be adequate conduit to bypass every diseased vessel.

Existing data on which the surgeon must make these judgments is conflicting, and much of the data predate modern secondary prevention therapy, such as the widespread use of statin and antiplatelet therapy. In some studies, follow-up angiography may have been prompted by recurrence of symptoms, which may result in a bias and

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CASS = Coronary Artery Surgery Study
DEFER = Deferral of Percutaneous Coronary Intervention study
FAME = Fractional Flow Reserve Versus Angiography for Multivessel Evaluation study
FFR = fractional flow reserve
PCI = percutaneous coronary intervention
PNVD = progression of native vessel disease
RAPCO = Radial Artery Patency and Clinical Outcomes trial

overestimation of the incidence of graft failure or progression of native vessel disease (PNVD).

In an attempt to provide contemporary data to inform this decision, we sought to compare pre- and postoperative angiograms undertaken as part of a randomized trial of arterial and venous conduits, with a program of protocol-driven angiography up to 10 years after surgery, in conjunction with regular surgical and cardiologic follow-up. The fate of moderate lesions in these patients offers some insight that may inform the decision making of the surgeon today.

METHODS

This study derives from the Radial Artery Patency and Clinical Outcomes (RAPCO) trial, the design of which has been published elsewhere.[3] The primary aim of RAPCO is to assess the long-term patency and clinical outcomes of the radial artery, right internal thoracic artery, and saphenous vein when grafted to the largest non–left anterior descending artery target. The RAPCO Trial enrolled a total of 619 patients for coronary bypass surgery using cardiopulmonary bypass, and all patients received the gold standard in situ left internal thoracic artery to the left anterior descending artery.

Patients receive annual telephone and clinical reviews for at least 10 years after surgery. Using a second random assignment, protocol-directed angiograms were allocated at intervals of 1, 2, 5, 7, and 10 years, with the bulk weighted to the second half of the follow-up because this was anticipated to coincide with the majority of graft occlusion events. In addition, elective angiograms at the 5- and 10-year marks were offered to all patients. All angiograms are reported independently by 3 coronary specialists. Graft failure is defined as occlusion, >80% stenosis, or string sign, and is recorded along with any pathologic findings at the proximal or distal anastomoses. Any disputed findings are assessed further by a fourth independent observer. Severity of native vessel disease is assessed similarly by the 3 observers, with the native vessels divided into proximal, mid, and distal sections, and the location and percent stenosis recorded. The latter is recorded in the database as the mean of the 3 estimations. In addition to the percent stenosis, lesions have been ascribed a grade that we have used to group lesions of similar severity or functional significance, because we noted a pattern with which observers consistently classify the same lesions with a particular percentage, depending on whether the lesion is nonflow limiting (grade 0), moderate (grade 1), flow limiting (grade 2), severe or subtotally occlusive (grade 3), and totally occlusive (grade 4). Grade 0 is 0% to 39% stenosis, grade 1 is 40% to 69%, grade 2 is 70% to 80%, grade 3 is 81% to 99%, and grade 4 represents total occlusion. Vessels recorded were the left main stem, left anterior descending and each diagonal branch, circumflex and each obtuse marginal branch, right coronary, posterior descending, and posterolateral branch. Computerized quantitative assessment was not performed as part of the trial, because this was intended to be a pragmatic study replicating real-life practice, in which computerized quantitative assessment is not used widely in Australia.

All patients in RAPCO who have undergone at least 1 postoperative angiogram were included in this study, and each of their coronary artery branches formed a unique data point. By researching the database, the severity of each native vessel lesion was compared in the preoperative and postoperative angiograms (or most recent postoperative angiogram when more than 1 exists), and the duration of imaging follow-up was calculated. Change in severity of the stenosis was recorded together with the presence, type, and patency of any graft to the vessel noted. Change of more than 1 grade, or to occlusion, was defined as PNVD. If a native vessel lesion changed by >1 grade, the angiograms were reviewed to check that the same lesion was being compared. Similarly, any incidence of regression was reviewed.

Statistical analysis was performed using SPSS software (SPSS Statistics 19; IBM Corporation, Somers, NY). Dichotomous variables were analyzed using the Pearson χ^2 test, and continuous variables were analyzed using the Student t test. The Cox proportional hazards regression model was used to assess for independent predictors of disease progression. Graft patency was estimated by the Kaplan-Meier method and the log-rank was test used to test for differences between groups.

All patients consented to the surgery, angiograms, annual telephone follow-up, and surgical reviews. The RAPCO protocol was approved by the Austin Hospital Human Research Ethics Committee (project no. H95/086). Further approval was gained for this project as a substudy within RAPCO (December 3, 2008, project no. H2006/02690).

RESULTS

Of the 619 patients originally enrolled in RAPCO, 405 had undergone at least 1 protocol, elective or symptom-directed angiogram, postoperatively. Mean duration of follow-up was 6.17 years (range, 0-14 years). A total of 3816 native coronary artery branches were identified, of which 386 contained at least 1 moderate lesion on the preoperative angiogram (40%-69% stenosis), and 1356 vessels were significantly stenosed (defined as flow limiting or severe stenosis, luminal diameter narrowed by $\geq$70%). Patients received 800 arterial grafts and 442 saphenous vein grafts, functionally bypassing a total of 1940 native coronary vessels, as some grafts backfilled more than 1 coronary artery branch. Grafting of undiseased vessels occurred when grafts were placed to healthy distal branches in the presence of isolated proximal disease in the common stem—for example, in isolated left main stem stenosis.

Change in Native Vessel Disease

Table 1 shows the likelihood of progression, regression, or stability of a moderate or severe coronary lesion on follow-up angiography. In the overall cohort of native vessels (ranging from no stenosis to complete occlusion preoperatively), rates of progression, regression, and stability were 27.2%, 9.0%, and 63.8%, respectively. Severe lesions (stenosis $\geq$ 70%) were at higher risk of progressive atherosclerosis (46.7% vs 36.3%, P <.001) and were less likely to