Regression of coronary disease after bypass surgery: Urban myth or common finding?

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Objectives: Coronary artery disease has been viewed as a relentless, progressive disease. We sought to describe the prevalence and distribution of regression of native vessel disease in coronary artery bypass patients and characterize its relationship with bypass grafting.

Methods: Among 619 patients who underwent bypass surgery in a radial artery trial, 405 had follow-up angiography available a mean of 6.2 ± 3.1 years (range, 0-14) after surgery. The percentage of diameter stenosis of each major native coronary vessel was reported by 3 cardiac specialists and classified into grades of nonflow limiting (0%-39%), moderate (40%-69%), flow limiting (70%-80%), severely stenosed (81%-99%), and occluded (100%). Native vessel disease regression was defined as decrease in 1 or more grades of stenosis between the pre- and postoperative angiograms.

Results: A total of 1742 native coronary arteries had preoperative stenosis of at least 40% and were included in the present analysis, receiving 753 arterial grafts and 391 saphenous vein grafts. Overall, the prevalence of disease regression was 19.7%, and 45% of patients demonstrated regression in 1 or more vessels. The presence of an arterial graft increased the likelihood of disease regression (21.3% compared with 16% for venous bypassed vessels, $P = .012$) as did the location in the left circulation (22.6% compared with 13.9% for the right circulation, $P < .001$) and having a flow-limiting (≥70%) lesion (21.9% compared with 9.8% for moderate lesions, $P < .001$).

Conclusions: Native coronary artery disease regression after coronary artery bypass grafting is common and affected by conduit type, vessel location, and lesion severity. Surgeons must consider these factors when assessing the requirement for bypass grafts in a borderline lesion. (J Thorac Cardiovasc Surg 2014;148:53-9)

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Atherosclerosis is generally viewed as a chronic, nonremitting disease associated with the formation of lipid-rich, fibroatheromatous plaques that compromise the coronary blood supply, leading to the clinical manifestations of angina and infarction. The past few decades have seen the advent of numerous pharmacologic agents aimed at inhibiting the formation of such plaques and halting the progression of existing lesions. More recently, several randomized controlled trials using imaging follow-up have provided convincing evidence that aggressive lipid-lowering therapy can retard the progression of coronary artery lesions[1-3] and promote disease regression[4-7] in patients with established coronary artery disease. Accordingly, the current guidelines recommend early and intensive lipid-lowering therapy to achieve very low target levels of cholesterol in high-risk secondary prevention patients.[8]

Changes in the anatomy and hemodynamics after coronary artery bypass grafting (CABG) can significantly affect the evolution of coronary atherosclerosis. Although angiographic disease regression has been evaluated previously, few of these studies included large numbers of surgical patients, and, to our knowledge, none have examined the complex relationships among native vessel disease behavior, conduit type, and patency. We sought to characterize the prevalence and distribution of native vessel disease regression in a cohort of patients who had undergone previous CABG and were angiographically followed up as a part of a randomized trial. We also assessed the influence of bypass grafting on native coronary artery disease regression.

METHODS

The present study was derived from the Radial Artery Patency and Clinical Outcomes (RAPCO) trial, the design of which has been previously reported.[9] The primary aim of the RAPCO trial was 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 (LAD) target. A total of 619 patients were enrolled in the RAPCO trial, and all patients underwent primary CABG using cardiopulmonary bypass.

Angiograms were randomly allocated at intervals of 1, 2, 5, 7, and 10 years, with the bulk weighted toward the second half of the follow-up

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CLAS = Cholesterol Lowering Atherosclerosis Study
HR = hazard ratio
LAD = left anterior descending artery
RAPCO = Radial Artery Patency and Clinical Outcomes

period, because this was anticipated to coincide with most graft failure events. Additional elective angiograms at 5 and 10 years were offered to all patients. Patients who had undergone at least 1 postoperative angiogram were included as a part of the present analysis, and, if more than 1 study was available, the most recent postoperative angiogram was used.

All angiograms were reported independently by 3 coronary specialists. Graft failure was defined as occlusion, greater than 80% stenosis or string sign, and was recorded with any pathologic findings at the proximal or distal anastomoses. Any disputed findings were further assessed by a fourth independent observer. The severity of native vessel disease was similarly assessed by the 3 observers, with the native vessels divided into proximal, mid, and distal sections, and the location and percentage of diameter stenosis recorded. The overall severity of stenosis was taken as the greatest value from the 3 segments and the mean of the 3 estimations by the cardiac specialists. In addition to the percentage of stenosis, the lesions were ascribed a grade, which we used to group the lesions of similar severity or functional significance. We had noted a pattern whereby observers consistently classified the same lesions with a particular percentage, depending on whether the lesion was non–flow-limiting (grade 0), moderate (grade 1), flow-limiting (grade 2), severe or subtotally occlusive (grade 3), or totally occlusive (grade 4). Grade 0 represented 0% to 39% stenosis; grade 1, 40% to 69%; grade 2, 70% to 80%; grade 3, 81% to 99%; and grade 4, total occlusion. This grading scale allowed for the assessment of disease regression only, which significantly affects coronary perfusion. The vessels recorded were the left main stem, LAD and each diagonal branch, left circumflex and each obtuse marginal branch, right coronary artery, posterior descending artery, and posterolateral branch. Each of these formed a unique data point.

The severity of disease within each native coronary vessel was compared on the preoperative and postoperative angiograms and the duration of imaging follow-up was recorded. A change in the severity of the stenosis was recorded, together with the presence, conduit type, and patency of any graft to the vessel. A decrease of at least 1 grade was defined as regression of native vessel disease. If a native vessel lesion changed by more than 1 grade, the angiograms were reviewed to check that the same lesion had been compared.

As a part of the trial protocol, the patients received annual telephone and clinical follow-up from a trained research nurse for at least 10 years after surgery, and clinical data such as diabetes, hypertension, smoking status, and symptom control were collated. Lipid studies were obtained by a review of the external pathology databases and general practitioner records, and all results dating back to the operation date were acquired, if possible. A graph of lipid measurements against time was compiled for each patient and the area under the curve calculated. This was then divided by the duration in years between the date of the first and last readings to obtain the annualized average lipid exposure. This calculation was repeated for each of the lipid subfractions, and all values are in mmol/L, unless specified otherwise. The cholesterol measurements were filtered to include only the readings taken within 3 months of surgery and within 3 months of the angiogram date; thus, only the measurements that might have influenced event occurrence (either graft failure or regression of native vessel disease) were incorporated into the calculations.

All patients agreed to the surgery, angiograms, annual telephone follow-up, and surgical reviews. The Austin Hospital Human Research Ethics Committee approved the RAPCO protocol (project no. H95/086), and additional approval was gained for the present project as a substudy (project no. H2006/02690).

Statistical Analysis

Statistical analyses were performed using Statistical Package for Social Sciences software (SPSS, Chicago, Ill). Dichotomous variables were analyzed using Pearson's chi-square 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 graft failure and disease regression. Disease regression was also assessed using the Kaplan-Meier method, and the log-rank test was used to test for differences between groups.

RESULTS

Of the 619 patients originally enrolled in the RAPCO trial, 405 patients had follow-up angiograms available at an average of 6.2 ± 3.1 years (range, 0-13.7) after surgery. Of the remainder, 176 patients were not due to undergo angiography because the RAPCO trial was not yet completed, and a small proportion had died before angiography or refused to undergo their assigned angiography, usually because they were well in the earlier years after surgery. A total of 6077 individual lipid measurements were obtained. From these angiograms, 3816 native coronary vessels were examined, and 1742 were found to have preoperative stenosis of at least 40% and were included as a part of the regression analysis. These vessels received 753 mixed arterial grafts and 391 saphenous vein grafts, bypassing a total of 1523 native vessels, because some grafts backfilled more than 1 coronary artery.

Prevalence and Distribution of Native Vessel Disease Regression

Overall, 182 patients (44.9%) demonstrated regression in at least 1 native coronary vessel, with an average of 0.85 regressing lesions per patient. The frequency of native vessel disease regression per patient is listed in Table 1.

The baseline characteristics of the regressing and nonregressing coronary vessels are listed in Table 2. Native coronary lesions were more likely to exhibit regression in female patients and in those with diabetes. This association with diabetes was confirmed on multivariate analysis (hazard ratio [HR], 1.56; $P = .001$; see Table 3).

The prevalence of disease regression by coronary vessel territory, bypass status, graft type, and graft patency is listed in Table 4. Of all native coronary vessels that originally exhibited at least 40% stenosis on their preoperative angiogram, 19.7% demonstrated regressive disease on the follow-up angiogram. The overall distribution of disease regression was 15.7% for the LAD, 24.6% for the left circumflex, 11.8% for the right coronary artery, 24.4% for the diagonal branches, 29.2% for the obtuse marginal