ORIGINAL ARTICLE

A Randomized Comparison of Radial-Artery and Saphenous-Vein Coronary Bypass Grafts

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ABSTRACT

BACKGROUND

In the past decade, the radial artery has frequently been used for coronary bypass surgery despite concern regarding the possibility of graft spasm. Graft patency is a key predictor of long-term survival. We therefore sought to determine the relative patency rate of radial-artery and saphenous-vein grafts in a randomized trial in which we controlled for bias in the selection of patients and vessels.

METHODS

We enrolled 561 patients at 13 centers. The left internal thoracic artery was used to bypass the anterior circulation. The radial-artery graft was randomly assigned to bypass the major vessel in either the inferior (right coronary) territory or the lateral (circumflex) territory, with the saphenous-vein graft used for the opposing territory (control). The primary end point was graft occlusion, determined by angiography 8 to 12 months postoperatively.

RESULTS

Angiography was performed at one year in 440 patients: 8.2 percent of radial-artery grafts and 13.6 percent of saphenous-vein grafts were completely occluded (P=0.009). Diffuse narrowing of the graft (the angiographic "string sign") was present in 7.0 percent of radial-artery grafts and only 0.9 percent of saphenous-vein grafts (P=0.001). The absence of severe native-vessel stenosis was associated with an increased risk of occlusion of the radial-artery graft and diffuse narrowing of the graft. Harvesting of the radial artery was well tolerated.

CONCLUSIONS

Radial-artery grafts are associated with a lower rate of graft occlusion at one year than are saphenous-vein grafts. Because the patency of radial-artery grafts depends on the severity of native-vessel stenosis, such grafts should preferentially be used for target vessels with high-grade lesions.

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THE INTERNAL THORACIC ARTERY provides better long-term patency than does the saphenous vein as a conduit for coronary bypass, prompting cardiac surgeons to explore other arterial conduits. The radial artery was first used by Carpentier in 1971,[1] because of a number of potential advantages, including ease of harvesting, a low propensity for wound infection, a larger diameter than other arterial grafts, and a thick, muscular wall that facilitates the construction of an anastomosis. However, early experience suggested that radial-artery grafts were prone to spasm and functional occlusion, and their use was abandoned for many years.[2,3] The advent of drug therapy to prevent graft spasm and the adoption of newer harvesting techniques have revitalized interest in the radial artery as an additional arterial conduit,[4] although an observational study has raised questions regarding its long-term patency.[5]

To evaluate the potential role of the radial artery as a bypass conduit, we conducted a randomized trial to determine whether the patency rate of radial-artery grafts at 8 to 12 months exceeds that of saphenous-vein grafts. We used a study design that controlled for bias in the selection of patients and vessels.

METHODS

STUDY DESIGN

The study design has been described in detail elsewhere.[6] In brief, each patient received both a radial-artery graft and a saphenous-vein graft, but these were randomly allocated to two different coronary territories. Although the random assignment of grafts rather than patients precludes meaningful clinical comparisons, it serves to control for bias in patient and vessel selection and permits an unbiased comparison of the two types of grafts in terms of patency, the primary determinant of survival. Thus, the primary study objective was to compare the angiographic patency of radial-artery grafts with that of saphenous-vein grafts 8 to 12 months after surgery.

PATIENT POPULATION

Patients less than 80 years of age who were undergoing primary, isolated coronary bypass surgery on a nonemergency basis were eligible for the study if they had graftable triple-vessel disease and an estimated left ventricular ejection fraction greater than 35 percent. The target coronary vessels were the left circumflex and right coronary arteries, which had to be at least 1.5 mm in diameter, with proximal lesions causing narrowing of at least 70 percent of the diameter. Exclusion criteria included nonpalpable ulnar arteries or a positive Allen's test; an abnormal Doppler study or ultrasonographic study of the arms; or a history of vasculitis or Raynaud's syndrome, bilateral varicose veins or vein stripping, or conditions that affected the safety of follow-up angiography, as described elsewhere.[6] The study was approved by the research ethics committee at each participating center. All patients provided written informed consent.

RANDOMIZATION AND STUDY PROCEDURES

Randomization was carried out in the operating room with the use of sealed envelopes, with stratification according to site and a randomly determined block size of four to six. Patients were randomly assigned to undergo surgery according to one of two strategies: radial-artery grafting to the circumflex territory and saphenous-vein grafting to the right coronary artery or radial-artery grafting to the right coronary artery and saphenous-vein grafting to the circumflex territory. With randomization performed within rather than between patients, each patient served as his or her own control for patient-level factors.

The internal thoracic artery was used to bypass the distribution of the left anterior descending coronary artery. Additional grafts were constructed as necessary. Single rather than sequential grafts were constructed; full details of the surgical technique have been previously reported.[7]

Postoperative Management and Follow-up

Patients received 325 mg of aspirin within six hours postoperatively and daily thereafter. Intravenous nitroglycerin was administered for 24 hours postoperatively. Treatment with vasoconstrictor agents was avoided whenever possible. Oral calcium-channel blockade was initiated on the first postoperative day and continued for six months. Study electrocardiograms were obtained preoperatively and on days 1 and 5 postoperatively. Patients were interviewed by telephone at one month, three months, six months, and yearly thereafter. If the patient had been hospitalized between interviews, in-patient records were obtained. All patients were questioned about the function of their hands and arms with the use of a modification of the Disabilities of the Arm, Shoulder and Hand questionnaire.[8]

Follow-up Angiography

Follow-up angiography was performed 8 to 12 months after surgery. Nitroglycerin was injected into each graft before filming. At least two orthogonal views each of the radial-artery graft and the control saphenous-vein graft were obtained, with continued exposure as required to visualize distal runoff and the size of the target bed.

END POINTS

The primary end point was the proportion of radial-artery and saphenous-vein grafts that were completely occluded at follow-up angiography. Complete occlusion was defined as the absence of visible opacification of the target coronary vessel (i.e., Thrombolysis in Myocardial Infarction [TIMI] flow grade 0).[9] Secondary angiographic end points included perfect graft patency (TIMI flow grade 3), angiographic stenosis of any degree (assessed visually), and the presence of diffuse narrowing of the graft to less than 1 mm in diameter but with a TIMI flow grade of at least 1 (the angiographic "string sign").

Follow-up angiograms were centrally reviewed by a committee of four experienced cardiologists. Each angiogram was independently adjudicated in a blinded fashion by two committee members, with a third review in the case of disagreement.

The following clinical events were recorded: death from any cause, perioperative myocardial infarction (occurring between 0 and 30 days), late myocardial infarction (occurring between 31 days and 1 year), additional cardiac surgery, and coronary angioplasty. Hand claudication and thenar paresthesia, complications potentially related to harvesting of the radial artery, were reported according to the diagnoses specified by a consultant neurologist. Because all patients received a study radial-artery graft, clinical events are reported for the entire study population only.

STATISTICAL ANALYSIS

Data from case-record forms were double entered to minimize errors. The primary comparison between the proportion of radial-artery grafts and that of saphenous-vein grafts that were occluded was performed on an intention-to-treat basis with the use of McNemar's test for paired proportional data. A P value of less than 0.048 was considered to indicate statistical significance, so as to achieve an overall level of 0.05 adjusted for a single interim analysis.

We calculated that the enrollment of 464 patients would provide the study with 80 percent power to detect a relative reduction of 40 percent in the rate of graft occlusion, from an estimated 12 percent with saphenous-vein grafting to 7.2 percent with radial-artery grafting, assuming a 20 percent within-patient correlation for graft occlusion, a two-tailed test, and an alpha value of 0.05. The sample size was increased to 561 patients to allow for the lack of follow-up angiography in approximately 20 percent of patients.

RESULTS

PATIENTS

Thirteen centers (12 in Canada and 1 in New Zealand) enrolled 561 patients between November 1996 and January 2001. Table 1 lists the baseline characteristics of the total study population and the 440 patients who underwent postoperative angiography. Patients who underwent follow-up angiography were generally representative of the entire study population, although fewer were over the age of 70 years (P=0.01). The severity of stenosis in native coronary vessels was similar in the target vessels for radial-artery grafts and saphenous-vein grafts, indicating that the randomization was balanced.

OPERATIVE DATA

Operative data are presented in Table 2. As described elsewhere,[7] a dilute solution of verapamil and papaverine was delivered into 92.3 percent of study radial-artery grafts to prevent spasm. Proximal anastomosis was achieved to the aorta in 98.4 percent of radial-artery grafts and 99.6 percent of saphenous-vein grafts.

One or both study grafts were not placed in 17 patients owing to the presence of ungraftable coronary arteries in 4 patients, poor quality or length of the radial artery in 6 patients, poor vein quality in 2 patients, and various individual reasons in 5 patients. The protocol specified that these patients were to be excluded from the primary analysis because of protocol violations.

In 24 cases, a patient received both radial-artery and control saphenous-vein grafts but to the territory opposite that randomly allocated. The reasons for such crossovers were inadvertent error by the surgeon in the case of 19 patients and concern about the size or quality of the radial artery in 5 cases. In the analysis of the primary end point, all these

patients were analyzed according to the intention to treat rather than the treatment received.

POSTOPERATIVE MANAGEMENT

The majority of patients (94.1 percent) were discharged while taking a calcium-channel blocker, and this treatment was continued for three to six months in 90.0 percent of patients. Other medications at discharge included aspirin in 92.3 percent, other antithrombotic medications in 8.7 percent, lipid-lowering drugs in 66.7 percent, and beta-blockers in 70.6 percent of patients. At 12 months, 91.9 percent of patients were taking aspirin and 64.9 percent were taking a lipid-lowering drug.

ANGIOGRAPHY AT ONE YEAR

Follow-up angiography was performed in 440 of 561 randomized patients (78.4 percent). Reasons for not undergoing angiography included protocol violations in 17 patients (as described above), postoperative death before follow-up began in 8 patients, a new postoperative condition precluding the performance of research angiography in 19 patients, and late withdrawal of consent in 77 patients. In 9 of the 440 patients who underwent postoperative angiography, there was a clinical indication for the procedure. Angiography was performed a mean (±SD) of 4.7±2.4 months after surgery in these 9 patients and a mean of 10.9±4.3 months after surgery among the 431 patients who underwent angiography for research purposes alone.

PRIMARY ANALYSIS

The primary end point of complete graft occlusion occurred in 13.6 percent of saphenous-vein grafts and 8.2 percent of radial-artery grafts (60 of 440 vs. 36 of 440, P=0.009 by McNemar's test) according to the intention-to-treat analysis (Table 3). This corresponds to an absolute difference of 5.4 percent (95 percent confidence interval, 5.0 to 5.8 percent) and a reduction in the relative risk of graft occlusion of 40 percent (95 percent confidence interval, 28 to 52 percent) with radial-artery grafting, as compared with saphenous-vein grafting. When analyzed according to the treatment received, the results were nearly identical. In total, both study grafts were patent in 350 patients, both study grafts were occluded in 6 patients, only the radial-artery graft was occluded in 30 patients, and only the saphenous-vein graft was occluded in 54 patients.

The angiographic string sign was present in 7.0 percent of radial-artery grafts and 0.9 percent

Table 1. Clinical Characteristics of All Patients and Those Who Underwent Follow-up Angiography.*

Characteristic	All Patients (N=561)	Patients with Follow-up Angiograms (N=440)
Age — yr	61.0±8.5	60.8±8.4
Age >70 yr — no. (%)	111 (19.8)	61 (13.9)†
Nonelective surgery — no. (%)	196 (34.9)	145 (33.0)
Previous myocardial infarction — no. (%)	264 (47.1)	204 (46.4)
Female sex — no. (%)	75 (13.4)	57 (13.0)
CCS class of angina — no. (%)		
1	9 (1.6)	7 (1.6)
2	133 (23.7)	108 (24.5)
3	267 (47.6)	218 (49.5)
4	152 (27.1)	107 (24.3)
Congestive heart failure — no. (%)	18 (3.2)	12 (2.7)
Diabetes — no. (%)	148 (26.4)	115 (26.1)
Oral medication	114 (20.3)	93 (21.1)
Insulin	34 (6.1)	22 (5.0)
Hypertension — no. (%)	271 (48.3)	203 (46.1)
Dyslipidemia — no. (%)	375 (66.8)	303 (68.9)
Current smoking — no. (%)	104 (18.5)	76 (17.3)
Creatinine — μmol/liter‡	93.0±20.1	92.7±19.9
Peripheral vascular disease — no. (%)	50 (8.9)	32 (7.3)
Left ventricular grade — no. (%)§		
1	272 (48.5)	213 (48.4)
2	280 (49.9)	220 (50.0)
3	8 (1.4)	6 (1.4)
4	1 (0.2)	1 (0.2)
Target-vessel stenosis — no. (%)		
>50% Stenosis of left main coronary artery	49 (8.7)	42 (9.5)
Right coronary artery		
70–89% Stenosis	172 (30.7)	135 (30.7)
90–99% Stenosis	161 (28.7)	129 (29.3)
100% Stenosis	228 (40.6)	176 (40.0)
Circumflex artery		
70–89% Stenosis	247 (44.0)	188 (42.7)
90–99% Stenosis	200 (35.7)	153 (34.8)
100% Stenosis	114 (20.3)	99 (22.5)
Radial-artery target vessel		
70–89% Stenosis	222 (39.6)	169 (38.4)
90–99% Stenosis	174 (31.0)	135 (30.7)
100% Stenosis	165 (29.4)	136 (30.9)
Saphenous-vein target vessel		
70–89% Stenosis	197 (35.1)	154 (35.0)
90–99% Stenosis	187 (33.3)	147 (33.4)
100% Stenosis	177 (31.6)	139 (31.6)

* Plus–minus values are means ±SD. CCS denotes Canadian Cardiovascular Society.
† P=0.01.
‡ To convert values to milligrams per deciliter, divide by 88.4.
§ According to this scale, a grade of 1 indicates an estimated global left ventricular ejection fraction (LVEF) of 50 percent or more, a grade of 2 an LVEF of 35 to 49 percent, a grade of 3 an LVEF of 20 to 34 percent, and a grade of 4 an LVEF of less than 20 percent.

Table 2. Operative Data on All Patients and Those Who Underwent Postoperative Angiography.*

Variable	All Patients (N=561)	Patients with Postoperative Angiograms (N=440)
No. of distal anastomoses	3.8±0.7	3.8±0.7
Proximal aortic anastomosis — no. (%)		
Radial artery	552 (98.4)	433 (98.4)
Saphenous vein	559 (99.6)	438 (99.5)
Blood cardioplegia — no. (%)	467 (83.2)	365 (83.0)
Study dose of papaverine delivered — no. (%)	518 (92.3)	407 (92.5)
Time in operating room — min	234±58	233±55
Duration of cardiopulmonary bypass — min	97±26	97±26
Duration of cross-clamping — min	73±26	74±25
Use of antifibrinolytic agents — no. (%)	100 (17.8)	79 (18.0)

* Plus–minus values are means ±SD. There were no significant differences between patients who underwent angiography and the study group as a whole.

of saphenous-vein grafts (31 of 440 vs. 4 of 440, P=0.001). Target coronary-vessel lesions with stenosis of 90 percent or greater, as compared with those with stenosis of 70 percent to 89 percent, were associated with a lower rate of occlusion of the radial-artery graft (Table 3) and a lower rate of the string sign in radial-artery grafts (3.7 percent vs. 12.4 percent, P<0.001). The relative patency of either radial-artery or saphenous-vein grafts did not depend on the bypassed native vessel.

Among patients with patent study grafts, some degree of angiographic stenosis was present at the proximal anastomosis in 21.4 percent of radial-artery grafts and 11.1 percent of saphenous-vein grafts (75 of 350 vs. 39 of 350, P<0.001). Some degree of angiographic stenosis was present in the graft body in 5.7 percent of radial-artery grafts and 12.3 percent of saphenous-vein grafts (20 of 350 vs. 43 of 350, P=0.003). There was no significant difference in the incidence of angiographic evidence of stenosis at the distal anastomosis between radial-artery grafts (49 of 350, or 14.0 percent) and saphenous-vein grafts (62 of 350, or 17.7 percent).

ADVERSE EVENTS

One patient required readmission because of infection at the site at which the radial artery was harvested. One patient had a hand-questionnaire score greater than 18, implying clinically significant functional limitation. Thirty-two patients (5.7 percent) reported moderate-to-severe symptoms of thenar paresthesia or numbness at 1 month, and this number had decreased to six (1.1 percent) at the 12-month follow-up assessment. Ten patients (1.8 percent) reported moderate-to-severe weakness of the hand at 1 month, and this number had decreased to five (0.9 percent) at the 12-month follow-up assessment. No patient reported hand claudication or ischemia. There were no reports of adverse events during follow-up angiography.

CLINICAL END POINTS

Clinical follow-up information was available for all study patients for the first year (Table 4). The one-year survival rate was 98.6 percent (553 of 561 patients). Nonfatal perioperative myocardial infarction occurred in 9.8 percent of patients (55 of 561). The infarct location was in the territory of the radial-artery graft in 3.2 percent of patients, the control saphenous-vein graft in 3.0 percent, and internal-thoracic-artery grafts in 2.8 percent and was indeterminate in 0.7 percent of patients.

No patient underwent cardiac surgery a second time. Among four patients who underwent percutaneous coronary intervention, intervention was performed on one radial-artery graft at the proximal anastomosis, on two control saphenous-vein grafts, and on one native coronary artery distal to the insertion of a control saphenous-vein graft. At one year, the overall rate of the composite end point of death from cardiac causes, nonfatal myocardial infarction, or repeated revascularization was 11.6 percent.

DISCUSSION

In this large, randomized, multicenter clinical trial, radial-artery bypass grafts had a higher rate of patency at one year than did the usual saphenous-vein graft, thus establishing radial-artery grafts as a second arterial conduit for targets other than the left anterior descending coronary artery. Previous studies have established the superiority of the left internal thoracic artery over saphenous-vein grafts for revascularization of the left anterior descending coronary artery.[10] A recent observational series showed reduced patency of the radial-artery graft as compared with that of other conduits.[5] However, that study did not use standardized surgical methods and concurrent pharmacotherapy, randomized controls, or routine angiographic follow-up, leading to potential bias in ascertainment and follow-

up. In contrast, our study relied on a randomized design with routine angiographic follow-up. The study design was novel in that each patient received both the study radial-artery graft and the control saphenous-vein graft, thereby avoiding inherent bias regarding patient selection. Since the target vessel was randomly assigned, the effect of target-vessel location on graft patency could be analyzed independently. Grafting to either the left circumflex or right coronary territory did not influence patency in this study.

The relationship between the severity of proximal native-vessel stenosis and arterial-graft patency has been previously reported for internal-thoracic, gastroepiploic, and radial-artery grafts in retrospective studies.[11-13] Certain characteristics of the radial artery, including the increased wall thickness and the density and organization of myocytes, may increase the propensity of this artery for spasm when there is decreased or competitive flow.[14] Accordingly, we placed the radial artery in demanding situations by stipulating that the proximal target-vessel stenosis exceed 70 percent. Despite this inclusion criterion, a decrement in performance of radial-artery grafts was still evident in the form of higher rates of both occlusion and the angiographic string sign when they were used to bypass less severely stenotic target lesions. Fortunately, investigators have shown that inducible ischemia is uncommon in myocardial territories supplied by grafts with an angiographic string sign.[15] The patency of these grafts may also improve late in follow-up, as native-vessel stenosis progresses.[16]

There were rare complications of harvesting of radial arteries in our study. A previous, larger study involving the harvesting of nearly 4000 radial arteries for coronary bypass grafting reported similarly low rates of complications of the hand and arm.[17]

The incidence of occlusion in the control saphenous-vein graft at one year was 13.6 percent, consistent with previous studies of the patency of saphenous-vein grafts showing one-year occlusion rates between 10 and 15 percent.[18-20] Follow-up of patients with vein grafts has revealed a substantial incidence of atherosclerotic changes in the graft body, leading to hemodynamically significant stenoses at 10 years, with angiographic evidence of patency in only 50 to 60 percent of grafts[21] — a rate that is sharply lower than late patency rates of more than 95 percent for the left internal thoracic artery.[22,23] The increased incidence of angiographic stenoses in vein-graft bodies, as compared with radial-artery–graft bodies in our study, suggests that even during a one-year follow-up period, atherosclerotic changes are more apparent in vein grafts. Given the natural history of accelerated atherosclerosis in vein grafts, we speculate that the su-

Table 3. Angiographic End Points.

End Point	Radial-Artery Graft (N=440)	Saphenous-Vein Graft (N=440)	P Value
	no./total no. (%)		
Graft occlusion (TIMI flow grade 0)	36/440 (8.2)	60/440 (13.6)	0.009
70–89% Stenosis of native vessel	20/169 (11.8)*	25/154 (16.2)†	
≥90% Stenosis of native vessel	16/271 (5.9)	35/286 (12.2)	
TIMI flow grade			
1	15/440 (3.4)	2/440 (0.5)	—
2	3/440 (0.7)	1/440 (0.2)	—
3	386/440 (87.7)	377/440 (85.7)	—
0, 1, or 2	54/440 (12.3)	63/440 (14.3)	0.37
Angiographic string sign	31/440 (7.0)	4/440 (0.9)	0.001
Catheter-tip spasm	50/440 (11.4)	11/440 (2.5)	0.001
Nonocclusive graft stenosis on angiography			
Proximal anastomosis			
0%	275/350 (78.6)	311/350 (88.9)	<0.001‡
1–30%	56/350 (16.0)	32/350 (9.1)	
31–70%	12/350 (3.4)	5/350 (1.4)	
71–99%	7/350 (2.0)	2/350 (0.6)	
Graft body			
0%	330/350 (94.3)	307/350 (87.7)	0.003‡
1–30%	14/350 (4.0)	29/350 (8.3)	
31–70%	4/350 (1.1)	11/350 (3.1)	
71–99%	2/350 (0.6)	3/350 (0.9)	
Distal anastomosis			
0%	301/350 (86.0)	288/350 (82.3)	0.15‡
1–30%	34/350 (9.7)	39/350 (11.1)	
31–70%	8/350 (2.3)	14/350 (4.0)	
71–99%	7/350 (2.0)	9/350 (2.6)	

* P=0.03 for the comparison of radial-artery grafts with native-vessel stenosis of 90 percent or more with radial-artery grafts with native-vessel stenosis of 70 to 89 percent.

† P=0.24 for the comparison of saphenous-vein grafts with native-vessel stenosis of 90 percent or more with saphenous-vein grafts with native-vessel stenosis of 70 to 89 percent.

‡ The P value is for the binary comparison, with the use of the McNemar test, of the absence of stenosis with any stenosis in pairs of radial-artery and saphenous-vein grafts at the specified site in the 350 patients without any occluded grafts.

Table 4. Clinical Outcomes among the 561 Patients.

Outcome	30 Days	31 Days–1 Year	Total
	number of patients (percent)		
Death	4 (0.7)	4 (0.7)	8 (1.4)
Death from cardiac causes	3 (0.5)	2 (0.4)	5 (0.9)
Nonfatal myocardial infarction*	55 (9.8)	1 (0.2)	56 (10.0)
Repeated coronary surgery	0	0	0
Coronary angioplasty	0	4 (0.7)	4 (0.7)
Composite end point†	58 (10.3)	7 (1.2)	65 (11.6)

* Values include perioperative myocardial infarctions, defined by the presence of persistent, new pathologic Q waves on the postoperative electrocardiogram; and late myocardial infarctions, defined by the presence of new Q waves or typical changes in ST-T waves without Q waves on the postoperative electrocardiogram.

† The composite end point consisted of death from cardiac causes, nonfatal myocardial infarction, and any repeated revascularization procedure.

periority of radial-artery conduits over vein grafts may be even greater at 5 and 10 years of follow-up. A small observational study recently showed a 10-year patency rate of 91 percent for radial-artery grafts.[24] Five-year angiographic follow-up of patients in our trial is currently under way.

Although our study was designed to include patients at low risk for radial-artery atherosclerosis, inadequate size or quality of the radial artery precluded its use in six patients. Concern about the size or quality of the radial artery caused the surgeon to deviate from the randomized target vessel in an additional five patients. The incidence of an inadequate radial artery owing to atherosclerotic changes would probably be higher in the general population of candidates for coronary bypass, particularly among patients with severe peripheral vascular disease.

In conclusion, radial-artery grafts had a higher rate of patency than saphenous-vein grafts at one year in this multicenter trial. Surgeons can confidently use the radial artery as a second arterial bypass graft, particularly in patients with severe native-vessel stenosis.

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APPENDIX

The members of the Radial-Artery Patency Study Group are as follows (all institutions are in Canada unless otherwise specified): Executive Committee — S.E. Fremes, E.A. Cohen, C.D. Naylor, N.D. Desai, R. Feder-Elituv; Manuscript Committee — N.D. Desai, E.A. Cohen, C.D. Naylor, S.E. Fremes; Steering Committee — S.E. Fremes, E.A. Cohen, C.D. Naylor, M. Carrier, G. Cote, D. Doyle, O. Gleaton, R. Masters, L. Higginson, L. Errett, K. Watson, S. Lichtenstein, R. Carere, M.L. Myers, D. Almond; Participating Cardiologists — D. Almond (Victoria Hospital, London, Ont.), C. Buller (University of British Columbia, Vancouver), F. Charbonneau (McGill University, Montreal), E.A. Cohen (University of Toronto, Toronto), C. Constance (McGill University, Montreal), G. Cote (Montreal Heart Institute, Montreal), J. Ducas (Health Sciences Centre, Winnipeg, Man.), O. Gleeton (Hôpital Laval, Sainte-Foy, Que.), L. Higginson (University of Ottawa Heart Institute, Ottawa), L. Schwartz (University of Toronto, Toronto), W. Tymchak (University of Alberta Hospital, Edmonton), R. Watson (University of Toronto, Toronto), G. Devlin (Waikato Hospital, Hamilton, New Zealand); Data Committee — N.D. Desai, H.R. Mallidi, R. Feder-Elituv (all at University of Toronto, Toronto); Statisticians — J.P. Szalai, M. Katik, K. Sykora, A. Kiss (all at University of Toronto, Toronto); Angiographic Committee — E.A. Cohen, J. Dubbin, S. Radhakrishnan, A. Adelman (deceased), L. Schwartz (all at the University of Toronto, Toronto); Clinical End-Points Committee — Z. Sasson (University of Toronto, Toronto), P. Dorian (University of Toronto, Toronto), K. Teoh (McMaster University, Hamilton, Ont.); Electrocardiogram Committee — G. Newton, Z. Wullfart, R. Myers, E. Crystal (all at the University of Toronto, Toronto); Data and Safety Monitoring Committee — S. Brister, C. Morgan, S. Logan (all at the University of Toronto, Toronto); Investigators (the number of patients recruited is in parentheses): Hôpital Laval, Sainte-Foy, Que.: D. Doyle (2), D. Desaulniers (2), R. Baillot (1), G. Raymond (6), M. Lemieux (6), P. Cartier (deceased) (2); Institute de Cardiologie de Montreal, Montreal: R. Cartier (2), M. Carrier (6), Y. Leclerc (1); London Health Sciences Center — University Campus, London, Ont.: A. Menkis (4), D. Boyd (24), R. Novick (2); London Health Sciences Center — Victoria Campus, London, Ont.: M.L. Myers (20); Montreal General Hospital, Montreal: D. Shum-Tim (1), J.F. Morin (48); Sunnybrook and Women's College Health Sciences Centre, Toronto: B. Goldman (14), C. Cutrara (32), G. Bhatnagar (39), S.E. Fremes (108), G.T. Christakis (43), L. Abouzhar (16); Health Sciences Centre, Winnipeg, Man.: D. Del Rizzo (10); St. Michael's Hospital, Toronto: D. Bonneau (6), D. Latter (23), L. Errett (11); Toronto General Hospital, Toronto: C. Peniston (4), H. Scully (1), R. Weisel (22), R.J. Cusimano (1), S. Brister (3), T. Ralph-Edwards (1), T. Yau (9); University of Alberta Hospital, Edmonton: E. Gelfand (8), P. Penkoske (2); University of Ottawa Heart Institute, Ottawa: F. Rubens (26); Vancouver Hospital and Health Sciences Centre, Vancouver, B.C.: G. Fradet (25), L. Burr (14), D. Thompson (2); Waikato Hospital, Hamilton, New Zealand: R. Ullal (14); Site Coordinators — M. Aleggretti, A.M. Powel, H. Brochu, R. Feder-Elituv, R. Fox, L. Lepicq, G. Keuen, C. Jessina, S. Finlay, E. Reeves, A. MacDonald, M. El-Tawil, L. Paul, M.A. James, L. Verreault, B. Weller, C. Nacario, J. Wilson, D. Penny, F. Denis, A. Munoz, L. Montebruno.

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