Coronary Bypass Graft Fate and Patient Outcome: Angiographic Follow-Up of 5,065 Grafts Related to Survival and Reoperation in 1,388 Patients During 25 Years

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Objectives. We sought to examine, angiographically, the long-term fate of a large number of mainly venous coronary bypass grafts and to correlate graft patency and disease with patient survival and reoperation.

Background. Much is known about bypass graft patency and disease, but the precise relation between graft fate and patient outcome has not been substantiated and documented.

Methods. A total of 1,388 patients underwent a first coronary artery bypass graft procedure at a mean age of 48.9 years, 234 had a second bypass procedure at a mean age of 53.3 years, and 15 had a third bypass procedure at a mean age of 58.2 years during the 25-year period from 1969 to 1994. Most were male military personnel or veterans; 12% were ≤39 years old. Of 5,284 grafts placed, 91% were venous and 9% arterial. Angiograms were performed on 5,065 (98% of surviving) grafts early, on 3,993 grafts at 1 year and on 1,978 grafts at 5 years after operation; other examinations were also performed up to 22.5 years after operation, and 353 grafts were examined after ≥15 years. Grafts were graded for patency and disease. The status of all patients was known at the study's end.

Results. The perioperative mortality rate was 1.4% for an isolated first coronary bypass procedure, 6.6% for reoperation. Vein graft patency was 88% early, 81% at 1 year, 75% at 5 years and 50% at ≥15 years; when suboptimal grafts, graded B, were excluded from calculation, the proportion of excellent grafts,

graded A, decreased to 40% after ≥12.5 years. After the early study, the vein graft occlusion rate was 2.1%/year. Internal mammary artery graft patency was significantly better but decreased with time. Vein graft disease appeared by 1 year and the rate accelerated by ≥2.5 years, involving 48% of grafts at 5 years and 81% at ≥15 years; 44% of the latter grafts were narrowed >50%. Survival of all patients was 93.6% at 5 years, 81.1% at 10 years, 62.1% at 15 years, 46.7% (150 patients) at 20 years and 38.4% (25 patients) at 23 years after operation. Survival decreased as age increased, but curves approximated "normal" life expectancy for older patients. Survival curves at all ages showed a steeper decline after 7 years. The rate of reoperation increased between 5 years and 10 to 14 years, then decreased to stable levels. Coronary atheroembolism from vein grafts was the major cause of morbidity and mortality associated with reoperation. Vein graft patency and disease were temporally and closely related to reoperation and survival.

Conclusions. Coronary bypass graft disease and occlusion are common after coronary artery bypass grafting and increase with time. They are major determinants of clinical prognosis, specifically measured by reoperation rate and survival. Intraoperative graft atheroembolism was a major reoperation hazard. Reoperation is definitely worthwhile but entails identifiable risks that must be dealt with.

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The fate of coronary artery bypass grafts depends on many factors, including technical faults in harvesting, handling and fashioning the conduits; thrombosis; myointimal hyperplasia; fibrosis; and a rapidly progressing variety of atherosclerosis.

Nwasokwa (1) recently reviewed the extensive published data very well. The nature of our hospital permitted an attempt to correlate evolving graft morphology with clinical outcome through systematic sequential, selective, multiple plane angiographic studies. In 1978, we (2) described patency grading of 1,400 consecutive grafts early after operation and of 1,132 of these 1 year later. Subsequently, graft defects considered to be due to disease were also graded, and in 1986 we (3) reported on 1,179 vein grafts, each studied early and 1 and 5 years after operation. We (4) reported a similar study of 741 vein grafts examined in sequence >6.5 years (mean 9.6) after operation in 1991. Our principal findings were 1) Vein graft occlusion rates were ~11% early and ~50% late after operation. 2) Intimal irregularities appeared at 1 year and progressed to involve

some 75% of grafts late after operation. 3) As disease spread over the graft surface, lesions gained bulk and protruded into the lumen, resulting in graft stenosis or occlusion. 4) Disease increased relentlessly once it appeared, but some apparently healthy grafts were unexpectedly found to be diseased or occluded in later studies.

In the present report, we describe the angiographic appearance of 5,065 assorted coronary bypass grafts (91% venous, 9% arterial), not studied in specific sequences but each examined at least once during exactly 25 years. In addition, we have correlated bypass graft fate with reoperation rates and with patient survival, demonstrating that the clinical outcome of coronary bypass grafting depends primarily on graft integrity, and we have attempted to define the relation between this determinant and its consequences.

Methods

Institutional background. Coronary artery disease is the major nontraumatic cause of serious morbidity and mortality in Canadian military personnel. Myocardial revascularization began at the National Defence Medical Centre (NDMC), Ottawa, with the Vineberg procedure (5,6) in 1965, continuing with coronary artery bypass grafting from 1969 (7). However, operations requiring cardiopulmonary bypass required brief patient transfer to cardiac surgery facilities of the Ottawa Civic Hospital, which later became the University of Ottawa Heart Institute. Nevertheless, most postoperative care and all diagnostic and follow-up activities have taken place at NDMC (8). Military medical devolution and decentralization have recently led to major institutional downsizing (9), and this determined our series' end on December 31, 1994.

Patients. There were 1,388 patients; 79% were military personnel, only 12 were women. At the first coronary artery bypass graft procedure, the patients ranged in age from 27 to 79 years (mean 48.9), at the second bypass procedure from 32 to 83 years (mean 53.3) and at the third procedure from 45 to 71 years (mean 58.2). There were 167 patients (12%) ≤39 years old; 8 of these had a second operation by this age. A previous report (10) described results of coronary artery bypass grafting in 138 patients ≤39 years old. There were 954 patients (69%) aged 40 to 54 years and only 267 (19%) ≥55 years old. Thirty-five patients had had a previous Vineberg procedure. Since 1982, 159 patients have also undergone percutaneous transluminal coronary angioplasty of one or more coronary arteries or bypass grafts, 38 before and 121 after the bypass procedure. The angioplasty procedures were performed on 103 grafts, 95 venous; on 15 (16%) of the 95 for restenosis. Three patients underwent heart transplantation; all are currently surviving, one at 10 years after transplantation. The first coronary bypass operation was performed on December 18, 1969 and the last on December 14, 1994. All operations are reported and none performed elsewhere is included. The initial patient underwent reoperation in 1977 and 1993 and is currently well.

Operations. Of the 1,637 coronary bypass procedures, 1,388 were first, 234 were second and 15 were third operations; 1,154 patients had only one bypass procedure, 219 had only two and 15 had three procedures. Fifteen percent of all operations were repeat procedures, but 17% of the patients had more than one procedure. We believe that <12 of our patients have had a repeat coronary bypass procedure elsewhere. The operations were performed by 11 surgeons; 1 performed 40% of the procedures and 4 colleagues collectively performed 54%. Normothermic anoxic cardiac arrest was used initially and cold potassium cardioplegia in the second half of the series. Coronary artery stenosis ≥50% was the indication for grafting. A total of 4,801 saphenous vein and 466 in situ internal mammary (internal thoracic) artery grafts were placed. The right gastroepiploic artery was utilized very late for six in situ grafts. There were four free internal mammary artery and three free inferior epigastric grafts. Expanded polytetrafluoroethylene conduits were used four times. Optimal use of internal mammary artery grafts was delayed; 90% of these grafts were placed after 1985 and 75% were placed at a first bypass procedure. Both internal mammary arteries were used in 12% of cases during 1985 to 1989 and in 23% of cases in the last 5 years, an important advance (11,12). Of internal mammary artery grafts, 67% were to the left anterior descending artery, 13% to its diagonal branches, 15% to marginocircumflex branches and 5% to right coronary artery branches. Adjuvant coronary endarterectomy was performed during 344 first operations and 23 reoperations; multiple endarterectomies were performed in 11% of these cases.

Complete revascularization was a constant aim. We (2) previously described 414 patients who had a mean of 3.3 grafts per primary operation before November 1976. In the present series, 3.4 grafts were placed at a first operation, 2.4 grafts at a second and 2.5 grafts at a third operation. Twenty-six percent of 5,284 grafts were to the trunk or branches of the right coronary artery, 27% were to the left anterior descending coronary artery, 19% to diagonal and 0.4% (19 cases) to septal branches and 28% to the marginocircumflex system. Proportionately fewer marginocircumflex grafts were placed at a second and fewer yet at a third operation. Most bypass grafts had a single distal anastomosis; we (13) have reported a disappointing experience with sequential grafts. Saphenous veins were harvested with minimal manipulation and held in papaverine/saline solution. *Full realization that patent but diseased vein grafts in situ pose major reoperation problems came slowly. This critically important (14) topic will be discussed later.*

Antiplatelet agents. Since 1969, we have given antiplatelet agents to all patients with coronary artery disease. Initially, we used dipyridamole and high dose aspirin, occasionally substituting sulfinpyrazone. Except in urgent cases, sulfinpyrazone, instead of aspirin, was used for 5 days before operation to decrease perioperative bleeding; the usual routine was reinstituted about 3 days postoperatively. Recently, dipyridamole has been given with aspirin only before angiography, and routine aspirin dosage is now conventional. These agents have not been evaluated formally.

Follow-up angiography. Examinations included two-plane left ventriculography and four-plane selective coronary and bypass graft angiography. Radiopaque thread rings marked aortic graft ostia. The Judkins technique was most often used, with 8F catheters (Cordis Corporation). A Judkins right coronary catheter was used for most aortic and many internal mammary artery intubations; the internal mammary artery catheter was frequently useful and the B1 (CB) catheter was sometimes invaluable. Graft occlusion was never inferred solely from difficulty in intubation; supporting coronary or aortic flood evidence was required for this determination.

We initially used meglumine diatrizoate as the contrast medium, later iopamidol. Selective vein graft angiography entails risk. We (15) previously reported coronary vein graft spasm 31 times in >10,000 selective opacifications; graft occlusion occurred in three patients, two of these sustaining nonfatal myocardial infarction. The sole death due to follow-up angiography in the present study (and in all our experience) was a result of fulminating anaphylaxis in a patient who had had four uncomplicated angiograms, also using meglumine diatrizoate, during the previous 12 years. Our mortality rate for all coronary angiography is an acceptable (16) 0.08%.

Graft angiograms and grading. Of the total of 5,284 grafts, 101 were lost to study because of perioperative death; the remaining 5,183 grafts were available for study, and 5,065 (98%) of these were examined early, 3,993 at 1 year and 1,978 at 5 years after operation. Our plan to repeat postoperative angiography every 5 years indefinitely was thwarted by lack of funds, although some patients returned repeatedly at their own expense for follow-up. Angiograms were obtained up to 22.5 years after operation. However, the number of vein grafts studied was <50 after 17.5 years, so those vein grafts examined at ≥15 years have been consolidated at 353, and internal mammary artery grafts examined at ≥5 years have been consolidated at 123. We (4) previously reported an unexpected increase in vein graft abnormality between 5 and 10 years postoperatively, "the 7.5 year phenomenon," thought to be due in part to "late" presentation of patients with covert symptoms at 5 years. Consequently, vein graft findings between principal quinquennial assessment points are assigned intermediately. Previous reports dealt with grafts that were all examined in a common temporal sequence. The present results relate to angiographic findings in all grafts at all examinations, and the number reported is thus greater.

Definitions of bypass graft patency (2) and grades of disease (3) are summarized in Table 1. All grades relate to the worst appearance in four-plane views and were visually determined subjectively. Grades, assigned by four experienced cardiologists, have been reproducible (2-4,10,13,17).

Data handling and statistical methods. Information was examined in a computerized relational data base of our own design (produced by Neodyne Consulting Limited, Ottawa, Ontario, Canada). Life table and chi-square analyses were done by standard methods (18). We knew the survival status of

Table 1. Definitions of Graft Grades, Assessed by Four-Plane Angiography

Grade	Definition
Patency	
A	Excellent graft with unimpaired runoff
B	Stenosis reducing caliber of proximal or distal anastomoses or trunk to <50% *of the grafted coronary artery.* Overall graft B grade was determined by the lowest of the three specific site grades
O	Occlusion
Disease	
I	No intimal irregularity
II	Irregularity of <50% of estimated intimal surface
III	Irregularity of >50% of estimated intimal surface
HP	High profile lesion produces >50% *stenosis of graft*
LP	Low profile lesion produces <50% *stenosis of graft*

Grades A, B and O assess graft flow. Grades I, II, III, HP and LP reflect disease severity.

all patients on December 31, 1994 but have not attempted actuarial analysis by cause of death.

Results

Perioperative mortality; myocardial infarction. Perioperative mortality was defined as death from any cause during the entire stay at either hospital. Thirty-nine perioperative deaths yielded an overall mortality rate of 2.3%. However, 36 of the total group of 1,388 patients underwent coronary artery bypass grafting in association with another major cardiac procedure, such as valve replacement, and the mortality in this group was 11.1%. Excluding these 36, but including those who had coincident repair of ventricular aneurysm (6% of the remaining patients), the mortality rate was 1.4% for a first coronary bypass procedure. This rate increased to 6.6% for all reoperations, including 2 of 15 perioperative deaths for a third bypass procedure. We (10,17) have previously reported no perioperative deaths associated with a first bypass procedure in 118 patients with silent myocardial ischemia, and none in 138 patients ≤39 years old. There were no perioperative deaths for 167 first operations at ages ≤39 years in the present series.

Perioperative myocardial infarction was monitored only for reoperations. However, we (19) previously reported 56 infarctions (7.8%) complicating a first bypass procedure in 717 patients. The infarction was transmural in 23 (41%) of 56 of those patients and 2 of the 23 died; coronary endarterectomy increased the infarction rate by 170%. The incidence of infarction is probably similar for the present study.

Vein graft patency. In all, 4,801 vein grafts were fashioned and 4,592 of these were examined early, 3,706 at 1 year and 1,889 at 5 years after operation and some at other times. Table 2 lists patency grades. The patency rate was 88% early after grafting but decreased to 75% at 5 years and to 50% at ≥12.5 years. The venous graft occlusion rate was 2.1%/year after the early examination. Patency loses its cachet when grade B grafts are eliminated; grade A grafts decreased to 40% of the 580

Table 2. Vein Graft Patency Grades on Follow-Up Angiography (first, second and third operations combined)

	Early	1 Year	2.5 Years	5 Years	7.5 Years	10 Years	12.5 Years	≥15 Years
Total grafts examined	4,592	3,706	469	1,889	495	856	227	353
Graft grade								
A	3,728 (81%)	2,825 (76%)	303 (65%)	1,309 (69%)	238 (48%)	448 (52%)	90 (40%)	141 (40%)
B	299 (7%)	182 (5%)	29 (6%)	109 (6%)	60 (12%)	71 (8%)	21 (9%)	36 (10%)
A + B	4,027 (88%)	3,007 (81%)	332 (71%)	1,418 (75%)	298 (60%)	519 (60%)	111 (49%)	177 (50%)
O	565 (12%)	699 (19%)	137 (29%)	471 (25%)	197 (40%)	337 (40%)	116 (51%)	176 (50%)

Date presented are number (%) of grafts. Graft patency grades are defined in Table 1.

grafts examined at ≥12.5 years. Twelve percent of all patent grafts were graded B at ≥5 years. Early vein grafts were graded B primarily because of distal anastomotic defects, later mainly for graft trunk narrowing. At the early examination, the 8.2% incidence of B grades for marginal grafts was significantly higher (p < 0.05) than the 6.2% incidence rate for right, 5.8% for left anterior descending and 5.3% for diagonal vessels. This difference has been noted (2) previously, and may be due to technical difficulty with the distal anastomosis. Also confirming a previous observation (4), left anterior descending artery vein grafts were occluded early less often (p < 0.005) than were grafts to other vessels. This overall difference (p < 0.05) persisted at 1 and 5 years; even at 10 years, rates of occlusion of grafts to the left anterior descending and diagonal arteries were lower (p < 0.05) than for other grafts.

Arterial graft patency. Patency grades for internal mammary artery grafts are shown in Table 3. The 95% early internal mammary artery graft patency rate was better than the 88% rate for vein grafts, but 10% of the arterial grafts were grade B grafts. A learning curve effect may distort this number. During the 15 years to the end of 1984, 44 internal mammary artery grafts were examined early; 40 (91%) of these were patent and 4 (9%) were graded B. These grafts were fashioned by the most experienced surgeons. During the next 5 (learning) years 211 (93%) of 226 internal mammary artery grafts were patent, but 30 (13%) were grade B. In the 5 years to the end of 1994, 180 (97%) of 186 internal mammary artery grafts were patent, and only 11 (6%) were grade B. The B grades were usually assigned because of distal anastomotic internal mammary artery de-

Table 3. Internal Mammary Artery Graft Patency Grades on Follow-Up Angiography (first, second and third operations combined)

	Early	Intermediate	Late
Total grafts examined	456	320	123
Graft grade			
A	386 (85%)	267 (83%)	94 (77%)
B	45 (10%)	24 (8%)	4 (3)
A + B	431 (95%)	291 (91%)	98 (80%)
O	25 (5%)	29 (9%)	25 (20%)

Data presented are number (%) of grafts. Because of the smaller number of internal mammary artery grafts, the grouping of follow-up data points differs from that used for vein graft patency in Table 2. Early = up to 6 months; Intermediate = 1 year and 2.5 years; Late = ≥5 years. Graft patency grades are defined in Table 1.

fects, but there were some lengthy trunk defects, little influenced by vasoactive drugs at angiography and perhaps due to operative trauma. Late internal mammary artery grade A grafts decreased to 77%, apparently not because of atherosclerosis. However, only 123 internal mammary artery grafts were examined late, mandating cautious interpretation of these results. Similarly, there were too few other arterial grafts for patency analysis, although five of six in situ right gastroepiploic grafts were impressively grade A and one was grade B in early selective angiograms.

Vein graft disease and fate. Atherosclerosis is rare in native internal mammary arteries (20) and was not found in internal mammary artery grafts. However, Table 4 shows intimal abnormalities appearing in vein grafts 1 year after operation and steadily increasing, until 239 (83%) of 288 patent grafts were diseased at ≥12.5 years. Curve B in Figure 1 reveals the suddenness of attack of vein graft disease after 2.5 postoperative years, and Table 4 shows that the incidence of the more extensive grade III disease outstrips that of grade II disease after 5 years. Furthermore, high profile lesions (producing stenosis ≥50%) were present in 106 (44%) of 239 diseased grafts and 37% of all patent grafts at ≥12.5 years, the steady increase with time seen in curve C of Figure 1. Increasing lesion bulk clearly complicated extension of disease in the mural plane. The interrelation of vein graft patency, disease and occlusion, the last two rising together in curves A and B of Figure 1, is obvious, as is the inexorable wastage of nondiseased patent grafts in curve D. The message is malign and powerful.

Survival after a first coronary bypass procedure. The survival data on all 1,388 patients after the first coronary artery bypass graft procedure, is shown in Table 5 and curve A of Figure 2. At 10 years, the proportion surviving was 81%, at 15 years 62%, at 20 years 47% and at 23 years 38% (25 survivors). The curve declines gradually to ~7 years postoperatively, with a steeper decline thereafter. The data are classified by age into the three panels of Figure 3, based on data in Table 5. All curve slopes increase at 5 to 7 years postoperatively. Survival times of patients ≤39 years old are better than those of older patients, particularly at ages ≥55 years. The panels display population life expectancy curves for comparable Canadian men (21). Survival data for subjects ≤39 years old are also plotted against comparable data reported by Gertler et al. (22) in a 1964, 15-year follow-up study of 91 medically managed patients <40 years old.

Table 4. Vein Bypass Graft Disease on Follow-Up Angiography (first, second and third operations combined)

	Early	1 Year	2.5 Years	5 Years	7.5 Years	10 Years	12.5 Years	≥15 Years
Patent grafts	4,027	3,007	332	1,418	298	519	111	177
Not diseased (I)	4,027 (100%)	2,812 (94%)	284 (86%)	731 (52%)	87 (29%)	119 (23%)	16 (14%)	33 (19%)
Diseased								
II	0	138 (5%)	32 (10%)	372 (26%)	82 (28%)	178 (34%)	30 (27%)	45 (25%)
III	0	57 (2%)	16 (5%)	315 (22%)	129 (43%)	222 (43%)	65 (59%)	99 (56%)
II + III	0	195 (7%)	48 (14%)	687 (48%)	211 (71%)	400 (77%)	95 (86%)	144 (81%)
High profile lesions								
Proportion of diseased grafts	0	19 (10%)	6 (13%)	291 (42%)	71 (34%)	125 (31%)	43 (45%)	63 (44%)
Proportion of patent grafts	0	19 (0.6%)	6 (2%)	291 (21%)	71 (24%)	125 (24%)	43 (39%)	63 (36%)

Data presented are number (%) of grafts. Disease grades are defined in Table 1.

Survival after reoperation. At 10 and 15 years after operation, the survival rate was 72% and 57%, respectively, for a repeat operation (curve B, Fig. 4), compared with 81% and 62%, respectively, for all operations (curve A, Fig. 2). Figure 4 shows the survival curves after the most recent bypass procedure of patients having only a primary procedure and of those having a reoperation. Early differences relate to perioperative mortality, but later disparities are slight, especially at >10 years. However, Figure 5 reveals the significant value of reoperation, when survival from the first bypass procedure, rather than from the last operation, is considered.

Indications for reoperation. Stable and unstable angina were equally represented in the groups with a first and a repeat bypass procedure. However, the incidence of unstable angina doubled before the second procedure and affected all 15 patients before the third procedure. Some 20% of patients did not have angina before either their first or second bypass procedure. In a previous series (17) of 723 consecutive operations, the incidence of asymptomatic patients was 16%. Differences between those asymptomatic patients and patients with

angina, including differences in long-term survival (23), were insignificant. Angiographic indications for reoperation in the present study were bypass graft failure in 80% of cases, failure combined with new native coronary disease in 12% and progression of native artery disease alone in 8%. Old grafts were occluded in 51% of cases. An ascending order of occlusion rate was seen in left anterior descending (41%), diagonal (46%), right (52%) and marginocircumflex (60%) coronary artery grafts. Fifty percent of patent grafts were healthy; disease was extensive (grade III) in 69% of the other 50%. High profile lesions (>50% graft stenosis) were seen in 51% of the grade II (moderate disease) grafts and in 67% of grade III (severe disease) grafts.

Timing of reoperation and morbidity and mortality. The cumulative incidence of reoperation appears in curve D, Figure 2. The actual annual rate of reoperation (not displayed) increased significantly 5 years after the first coronary bypass procedure, plateaued at 10 to 14 years and then decreased to a lower but steady level. However, a repeat operation was performed in 31 patients within 6 months of the first bypass procedure, in 40 patients within 12 months and in 53 patients
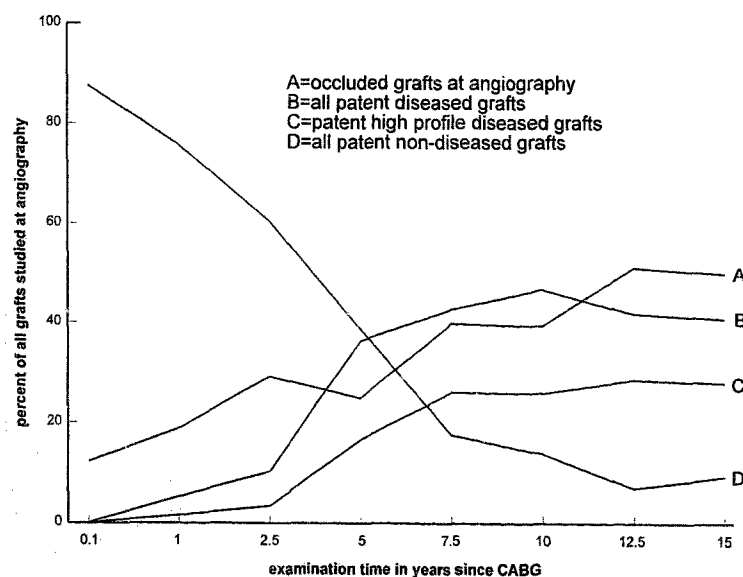

A=occluded grafts at angiography
B=all patent diseased grafts
C=patent high profile diseased grafts
D=all patent non-diseased grafts

Figure 1. Vein graft disease and occlusion. The graft occlusion rate was 2.1%/year after the first postoperative study. All categories of graft disease are included. High profile disease produces >50% graft stenosis. Note the increasing disease attack rate after 2.5 years. CABG = coronary artery bypass grafting.

Table 5. Survival After a First Coronary Artery Bypass Procedure Compared With That in the Series of Rahimtoola et al. (54) and in the Coronary Artery Surgery Study (CASS) (55)

	5 Years		10 Years		15 Years		20 Years		23 Years	
	No.	Survival	No.	Survival	No.	Survival	No.	Survival	No.	Survival
Present series: 1,388 patients (99% men, mean age 48.9 years)	1,226	93.6%	928	81.1%	556	62.1%	150	46.7%	25	38.4%
Age group										
≤39 years	154	95%	129	85%	86	68%	36	55%		
40 to 54 years	872	95%	693	84%	411	64%	98	46%		
≥55 years	200	85%	106	68%	9	47%	1	30%		
Rahimtoola et al.: late cohort, 1974 to 1988 (5,468 men, mean age of total cohort [7,026] 61.1 ± 9.9 years)		89%		74%		56%	(5)*	(38%)*		
CASS 1974 to 1979 (6,922 men, mean age 54.6 ± 8.5 years)	6,096	89%	4,921	73%	272	52%				

*Twenty-year value for entire 1969 to 1988 gender-unspecified cohort. Data presented are number of patients and survival rate.
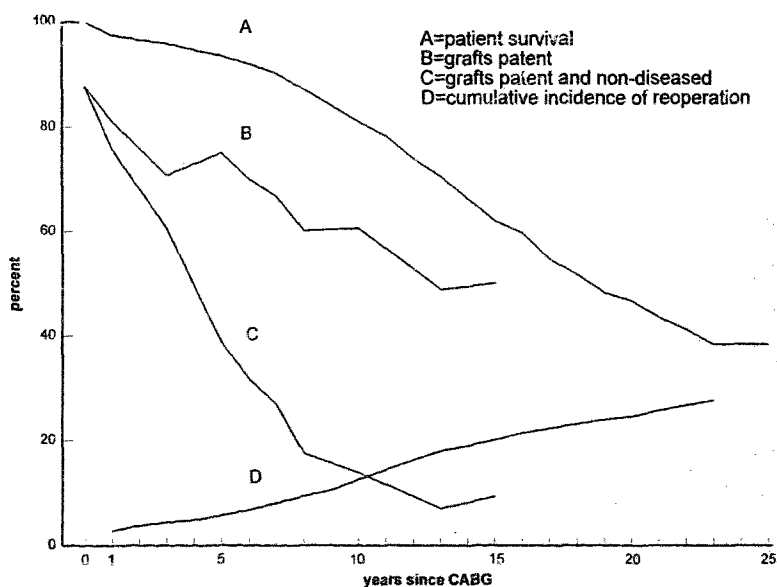
within 24 months. There were no (0%), one (2.5%) and two (3.8%) perioperative deaths in each of these groups, respectively. The early operations were mainly in the first years of the series. The perioperative mortality rate was 7.1% for reoperations after 24 months, but it was 11.8% (10 of 85) for those performed >10 years after the first operation.

The presence of diseased but patent grafts, particularly those with high profile lesions (>50% graft stenosis), increased reoperation morbidity and mortality. The incidence of myocardial infarction and perioperative death in patients with healthy or occluded grafts, or both, was insignificantly different from that in patients undergoing a first bypass procedure. However, the incidence increased fivefold in patients who underwent reoperation with one or more diseased patent grafts. Only 1 of 16 deaths related to reoperation was of noncardiac origin (pancreatitis with splenic vein erosion). However, 9 (60%) of

15 cardiac deaths were due to proved or strongly suspected intraoperative coronary atheroembolism. The latter was previously demonstrated (24) angiographically in a survivor of reoperation. In our patients who had a myocardial infarction, there was a highly significant correlation between graft disease with high profile lesions and atheroembolism. Eight of nine patients with a fatal infarction had grade III disease and all nine had high profile lesions. Twenty-one percent of myocardial infarctions that occurred at reoperation were fatal. Predictably, mortality rose with the interval between operations, correlating with the rising incidence of patent but diseased grafts. Perioperative deaths tripled as the interoperative interval increased from <5 years to 5 to 10 years and rose fourfold after 10 years.

Graft status after reoperation. All grafts in survivors of the bypass procedure were studied early. Of 406 vein grafts, 78%

Figure 2. Survival of all 1,388 patients after a first coronary artery bypass graft procedure, reoperations and graft fate. Standard actuarial methods were used to construct reoperation curve D, as for the survival curve A. Perioperative deaths are included. Note the change in the slope of curve A at ~7 years. This figure summarizes the study's findings.

39 & younger   **40 to 54**   **55 & older**

A=life expectancy 40 y old
B=survival of pt 39&less
C=Gertler data

A=life expectancy 48 y old
B=survival of pts 40 to 54

A=life expectancy 62 y old
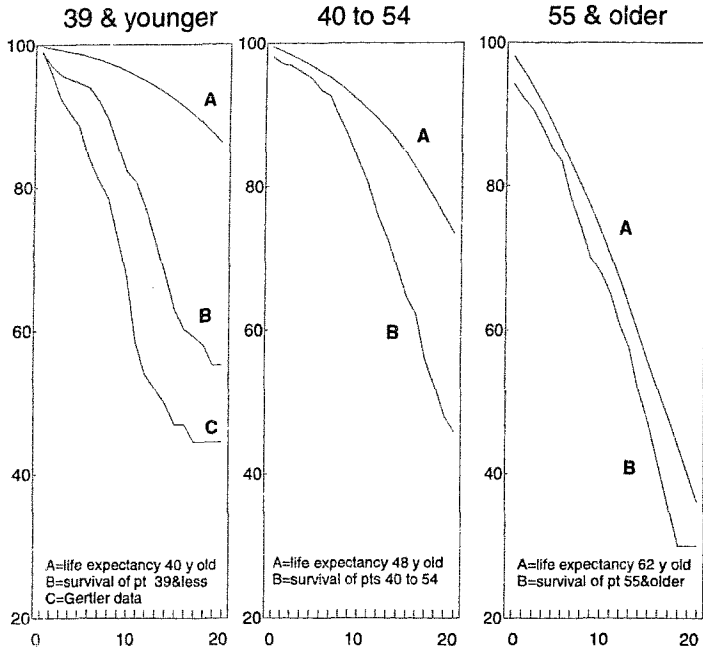B=survival of pt 55&older

Figure 3. Age-related survival after coronary artery bypass grafting. Data in present study (curve B) compared with age-matched life expectancy for Canadian men (21) (curve A) and with that of young men with coronary disease treated medically before 1964 described by Gertler et al. (22) (curve C). Note the change in curve B slopes at 5 to 7 years. pt = patient.

were grade A, 6% grade B (84% patent) and 16% were occluded. Of 111 internal mammary artery grafts, 81% were grade A, 12% grade B (93% patent) and 7% were occluded.

Graft fate and patient outcome. The interrelation between coronary bypass graft disease and occlusion, on the one hand, and reoperation and patient survival, on the other, is displayed in Figure 2, which summarizes the salient findings of this study.

Discussion

The 1978 editorial comment (25) that "graft occlusion is uncommon and most patients who do well do not undergo post-operative coronary angiography," was promptly challenged by the angiographic description (2) of a large number of consecutive coronary bypass grafts, with occlusion rates of 11%

early and 19% at 1 year after operation. The graft occlusion rate in the present study was 12% for 4,592 saphenous vein grafts and 5% for 456 internal mammary artery grafts early after operation, rising to 51% for vein grafts after 12.5 years and 20% at late internal mammary artery examinations. This is a considerable problem.

Bypass graft disease. Perioperative occlusion of bypass grafts may be due to thrombosis resulting from localized platelet dysfunction at the site of intimal damage, but it is later associated with atherosclerosis (14,26–37). Although pathologic changes are similar in both, venous bypass graft disease does not parallel in severity atherosclerotic progression in native vessels (14), as accelerated vein graft atherosclerosis is characterized by instability and the fragility of late lesions. Intimal damage is followed by smooth muscle proliferation, a

A=survival of 1154 patients having only primary CABG
B=survival of 234 patients having 249 repeat CABG

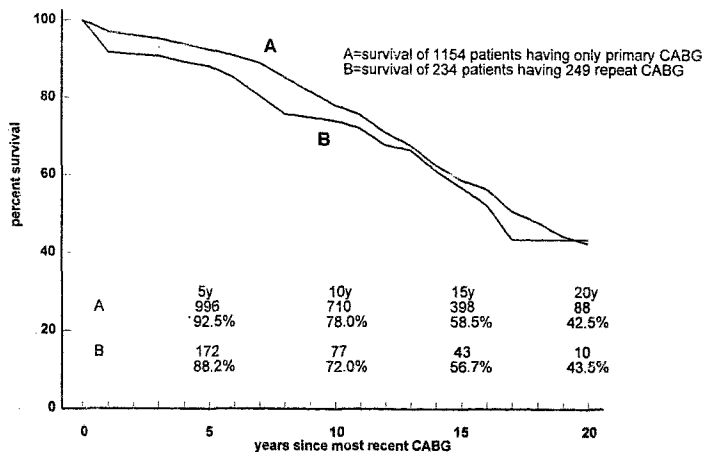|	5y	10y	15y	20y
A	996	710	398	88
	92.5%	78.0%	58.5%	42.5%
B	172	77	43	10
	88.2%	72.0%	56.7%	43.5%

Figure 4. Survival after repeat (B) versus primary (A) coronary artery bypass grafting (CABG). Perioperative deaths are included. Survival times are from the most recent procedure. Year, number of survivors and percent survivors are listed.

complex interaction between endothelium and platelets, the presence of lipids in "foam cells," and the appearance of plaques, that differ in character by degree of fibrosis, lipid deposition, thrombosis and, occasionally, late calcification. Late thrombosis may occur (38) in vein grafts with nonatherosclerotic intimal hyperplasia, but it is uncommon. Thrombus forms slowly or suddenly after a "plaque accident" (plaque rupture) (39,40) in a coronary artery or bypass graft (41,42). Atheroembolism occurs spontaneously or with cardiovascular manipulation at reoperation (36,43), leading to coronary occlusion (24), often lethal. Results of graft biopsies and autopsy studies attest to the frequency of atherosclerosis in older grafts; lesions have been noted (34) in 71% of grafts examined 6 to 12 years postoperatively.

Early angiographic findings are problematic. Myointimal hyperplasia and thrombus may present diagnostic difficulties (26). Our attribution of atherosclerosis to vein graft irregularities seen 1 year after operation (4) has been questioned (27), and the condition has been ascribed to localized myointimal hyperplasia. Nevertheless, vein graft atherosclerosis before 1 year has been described histologically (30,31). However, high profile defects were seen at 1 year in only 0.5% of patent grafts in an earlier series (4) and in 0.6% of patent grafts in the present study. We have chosen to use consistent criteria to interpret angiographic findings, which are similar at earlier and later times. We believe that attribution to atherosclerosis of changes observed in sequential angiograms accords with general pathologic and angiographic opinion. Grondin et al. (44) have provided excellent descriptive terms, including "irregular wall," "plaque," "conventional stenosis," "spur diaphragm" and "cauliflower". Sequential study pictures of "low profile" disease, which proliferates in the mural plane, evolving to heaped up "high profile" obstructive lesions, similar to the angiographic atherosclerotic progression in native coronary arteries, have supplemented these observations.

A 1974 Montreal Heart Institute report (45) noted presciently that "the attrition rate [of these grafts] may be progressive. Therefore, it is imperative to obtain long-term angiographic follow-up in patients with coronary vein grafts. Such studies may help determine the fate of the saphenous vein in the aorto-coronary position. . . ." These words highlight the extensive studies in this field from other centers, particularly the work done in Cleveland, Montreal and Houston (14,33,35–38,43–53). Our projects have differed only in focus, and the results are in accord with and complement those of others.

Bypass graft fate. Our internal mammary artery grafts did better than vein grafts in the short term (patency rate 95% vs. 88%) but less well in the long term, when the proportion of grade A internal mammary artery grafts decreased from 85% early to 77% late. The striking decrease in grade B grafts from 10% early to 3% late, coincided with the increase to an occlusion rate of 20% at ≥5 years. However, the limited long-term data in Table 3 may not justify didactic conclusions.

A technical defect, usually at the distal anastomosis, is probably the most important factor in perioperative bypass
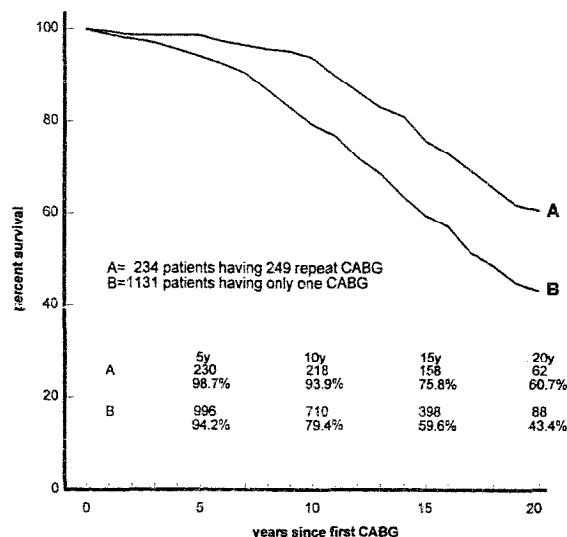

Figure 5. Overall survival of patients having more than one coronary artery bypass graft procedure. This graph includes all patients surviving the first bypass procedure and compares the *overall survival from the first bypass procedure* of the 234 patients (group A) who had a later reoperation, with that of the 1,131 patients (group B) who had only one bypass procedure. Those who died perioperatively at the first bypass procedure are excluded, because they were not at risk for reoperation. Reoperation mortality appears in the curve for group A at the approximate times that might be expected from reoperation times, noted in the text. It appears that overall survival from the time of the first bypass procedure is enhanced in patients (group A) undergoing reoperation.

graft occlusion. B graft grades were assigned (2–4) early after operation in 80% to 90% of cases because of distal defects. Our previously reported 1-year occlusion rate for grade B grafts (2) was 24% compared with 6% for grade A grafts, so grading is prognostically potent. Later vein graft occlusion reflects developing graft atherosclerosis, but it may occur unexpectedly (3,4). Five years after operation, 50% of the patent vein grafts were diseased; this rate increased to 83% at ≥12.5 years, with almost 50% of the lesions producing >50% graft stenosis.

Survival. Our survival data are displayed in Figures 2 to 5. Comparison with results reported (53–55) in other long-term studies is hindered by differences in patient age and other disparities. For instance, only 6.3% of the patients of Rahimtoola et al. (54) were ≤44 years old, whereas 12% in our series were ≤39 years old, with a wider discrepancy at later ages. Nevertheless, allowing for study differences but taking account of gender, our survival rates appear superior; Table 5 compares our results with those from Portland, Oregon (54) and a recent Coronary Artery Surgery Study (55) series. Figure 3 attests that our young surgically treated patients fared better at every stage than did those in the study of Gertler et al. (22) in the era before coronary artery bypass grafting. The closer approximation of patient and general population survival curves with increasing age is striking in Figure 3. Paradoxically,

survival time after bypass grafting is longer for younger than for older patients, but the latter gain life expectancies closer to the "normal" for their ages; however, this is surely a multifactorial phenomenon. There may also be several reasons for the apparently significant benefit of reoperation, surprisingly revealed in Figure 5. This phenomenon was shown in Figure 13 of Lawrie et al. (53) but was not discussed. Perhaps unknown preselection factors favor those patients who survive to reoperation.

Reoperation. Seventeen percent of our patients had one or more reoperations. The cumulative incidence (Fig. 2), is smaller than in some series, perhaps because of longstanding efforts to achieve optimal myocardial revascularization (3.3 grafts/patient undergoing a first bypass procedure before 1977). High rates of reoperation in the first 2 years after a first bypass procedure during our early experience were due to concern for maximal planned surgical benefit, which persuaded us to reoperate frequently for essentially angiographic indications. Some reoperations might well have been delayed. Happily, except for 2 of 53 patients, both with major clinical problems, no patient died who underwent reoperation before 24 months. Lack of coronary angioplasty was another incentive for reoperation; 83% of 40 reoperations within 12 months of a first bypass procedure were done before angioplasty was available to us.

The perioperative mortality rate five times greater for repeat than for primary operations is a matter of grave concern. We recognize the high risk of myocardial infarction and death due to coronary atheroembolism (36,56,57) at reoperation and know that minimizing these events requires meticulous surgical technique illuminated by precise information on graft status. The handling and disposition of old grafts at reoperation (49,57) is a topic of inestimable importance. Loop et al. (49) have reported reducing the perioperative mortality rate to <3%, and this is an admirable therapeutic goal.

Care of the bypass graft. Because first causes are as yet unalterable, optimal control of risk factors for atherogenesis must be ensured. Smoking is a major problem. We (58) reported that men continuing to smoke after coronary artery bypass grafting had a significantly greater disposition to graft atherosclerosis and occlusion than did nonsmokers; 67% of those patients smoked before operation and only 50% had stopped smoking 5 years later. Voors et al. (59) have clearly demonstrated the clinical consequences. The smoking habit is hard to curb. Of 138 military patients ≤39 years old who underwent coronary artery bypass grafting (10), 88%, or twice the proportion in the Canadian Armed Forces study (60), smoked before operation and only slightly <50% had stopped 5 years later. Control of dyslipidemia may be better, because new drugs have changed the odds significantly. Scandinavian Simvastatin Survival Study (61), Pravastatin Limitation of Atherosclerosis in the Coronary Arteries I (62) and West of Scotland Coronary Prevention Study Group (63) (pravastatin) studies herald a major therapeutic advance. However, optimal utilization of therapy may be the greater challenge (64,65). With respect to other drugs, we have given agents affecting platelet behavior to all patients undergoing coronary surgery

since 1969 but have not done a systematic study. Conventional long-term anticoagulant therapy in patients with inoperable graft disease seems to have been useful, and we believe that this treatment option deserves its present attention. Finally, we are certain that a dedicated follow-up program of risk factor control and early detection of complications is invaluable. Unfortunately, the necessary resources are increasingly hard to find.

The conduit. Internal mammary artery grafts, particularly from both the left and the right artery together, have come into common use quite slowly, but they improve survival (12,66–68). The right gastroepiploic artery (69,70) will probably also prove to be a valuable long-lasting conduit. Our experience with 109 right gastroepiploic artery Vineberg implants (7) and a very few, but splendid, bypass grafts has been excellent. We are dubious about the inferior epigastric artery and cannot comment on the radial arteries as conduits. Synthetic conduits have not proved themselves in any hands. Perhaps a superb new fabric awaits discovery, but this seems unlikely. The supply of arteries is limited and vein grafts will be with us for a long time yet.

Technicalities. Shiley Incorporated (71) recently warned that the identity of the person welding outlet struts to valve flanges was a "new" risk factor for prosthetic cardiac valve failure. Concern for the human variable, led us, in 1983, to examine the early patency rates of 424 coronary bypass grafts fashioned by five senior surgeons during 1981 to 1982. There was no significant difference in overall graft patency for the five surgeons, but there were surprising internal variations. The most striking was a grade O (occlusion) graft incidence rate of 17% (16 of 94) juxtaposed with a 1% incidence rate of B grades for Surgeon X, when the incidence rate of B grades for his four colleagues was 5% to 7% (20 of 330). Furthermore, Surgeon X had 88% to 92% A ratings for right, left anterior descending and marginocircumflex artery grafts, but there were 9 occlusions (56%) without any B grades, in 16 grafts to diagonal vessels. These branches are fairly accessible and usually less important than the parent trunk. We concluded that some differences in operative results probably occurred because of the heavy responsibility for surgical residency training in a teaching hospital. This is a problematic topic, especially in a time of surgical "report cards" (72,73), and it may need to be addressed formally.

The bottom line. A quarter-century of efforts in our institution to alleviate coronary stenosis with coronary artery bypass grafting have yielded morbidity, mortality and increased life expectancy results at least as good as those reported by others. However, all the early promise of coronary bypass grafting has not been fulfilled, and an insidiously deadly variety of atherosclerosis progressively chokes most vein grafts and, in the end, extinguishes their benefit. The clinical consequences are evident. Arterial grafts offer better results but have limited potential. Many difficult problems in coronary bypass grafting remain to be addressed. They include optimal timing of intervention, selection of the best conduits, methods of ensuring technical excellence, control of disease risk factors, moni-

toring of long-term graft integrity, prompt detection of those requiring reoperation and, not least, methods of ensuring that reoperation b as safe as possible.

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