Reoperation for Coronary Atherosclerosis

Changing Practice in 2509 Consecutive Patients

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We analyzed trends in clinical, angiographic, and operative variables and documented long-term survival in 2509 consecutive patients who underwent reoperation for myocardial revascularization at The Cleveland Clinic during a 20-year period (1967 to 1987). The patients were grouped into four cohorts by year of surgery. This analysis showed that vein graft atherosclerosis has become the leading indication for reoperation, and patient age and interval between operations continue to increase. Mortality rates ranged from 2% to 5% and, despite increasing comorbidity, more extensive coronary atherosclerosis, and worse left ventricular function, the hospital mortality rate was 2.9% from 1985 to 1987. Perioperative new Q-wave myocardial infarction occurred in 7% to 8% of patients from 1967 to 1984 but decreased to 4% in the 1985 to 1987 period ($p = 0.04$). Internal thoracic artery graft usage in reoperations increased from 27% in the 1967 to 1978 period to 67% in the 1985 to 1987 period. Advanced age and presence of left main coronary artery disease adversely influenced late survival more consistently than other factors. Patients operated on in 1967 to 1978 had fewer risk factors, which explains their higher survival rate compared with more recent cohorts. Factors associated with improved 10-year actuarial survival included age younger than 65 years, mild angina, no major comorbidity, no left main coronary artery disease, good left ventricular performance, and an internal thoracic artery graft.

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IN THIS THIRD decade of direct myocardial revascularization, three determinants of outcome are acknowledged: the patient, the operation, and progression of coronary atherosclerosis. We know that the characteristics of the patient and the operation are changing.[1-3] As operative practices change, outcome analyses are necessary to base selection of therapy on documented efficacy. In coronary bypass surgery, primary end points are survival rates and late cardiovascular events. A coronary artery reoperation is one of these events.

We report (1) changing characteristics of patients undergoing coronary artery reoperations, (2) trends in early reoperation results, and (3) determinants of long-term survival and late cardiac events. This series of 2509 patients updates a report on coronary artery reoperation[4] by adding 1009 more consecutive patients who had a second operation from 1985 through 1987. This consecutive series of isolated reoperative coronary artery surgeries performed in one institution spans 20 years.

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Methods

Consecutive isolated coronary artery reoperation patients were identified; data on these 2509 patients were obtained from a computerized Cardiovascular Information Registry. All individual patient records were cross-checked with original computer entries and any discrepancies were resolved by the authors and recoded in the database. Patients with three or more coronary artery operations were excluded. The clinical, angiographic, and operative descriptions were defined previously.[5] Actuarial survival curves were computed according to the Kaplan–Meier method. Univariate comparisons for survival curves were calculated by the Wilcoxon test and all multivariate analyses were performed with Cox proportional hazard models.

The patients were grouped by the year of reoperation into four cohorts: 1967 to 1978, 436 patients; 1979 to 1981, 439 patients; 1982 to 1984, 625 patients; and 1985 to 1987, 1009 patients. Mean patient age at first and second isolated coronary operation and interval between operations were determined (Table 1). The interval between operations changed from a mean of 50 months in the first cohort to 101 months in the most recent cohort ($p = 0.0001$). The prevalence of reoperation in women increased through 1984 and then declined.

Angina was classified by New York Heart Association (NYHA) functional class I-IV. Diabetes, hypertension, and peripheral vascular disease were noted more frequently in the most recent group (1985 to 1987) compared with the earliest group (1967 to 1978) (Table 2). Severe coronary atherosclerosis was defined as a lesion that narrowed the arterial lumen by an estimated 50% or more.

TABLE 1. *Cohort Size, Gender, Mean Ages, and Interval Between Operations in 2509 Reoperation Patients*

Demographics	1967–1978 (n = 436)	1979–1981 (n = 439)	1982–1984 (n = 625)	1985–1987 (n = 1009)
Sex	38 (8.7%)	58 (13.2%)	91 (14.6%)	117 (11.6%)
Female	398	381	534	892
Male	(91.3%)	(86.8%)	(85.4%)	(88.4%)
Mean age at first operation (years)	49.1	50.3	51.2	52.5
Mean age at second operation (years)	52.3	56.3	58.2	60.9
Interval between operations (months)	50	72	84	101

The incidence of left main coronary artery narrowing increased from 51 cases (12%) in the first cohort to 253 (25%) in the most recent cohort ($p < 0.001$). Three-vessel disease, excluding patients with left main narrowing, increased significantly from 222 (51%) to 623 (62%) ($p < 0.001$) throughout the experience. Thus one- and two-vessel disease accounted for a decreasing percentage of patients over time.

Left ventricular performance, estimated subjectively, worsened in each succeeding cohort. In the earliest experience, normal left ventricular contraction was found in 263 (60%), but declined to 366 (36%) in the most recent experience ($p < 0.001$). In the latest cohort poor left ventricular function was found in 104 (10%) of patients. When left ventricular contraction before the first operation was compared to contraction before reoperation, 135 patients (31%) in the 1967 to 1978 cohort; 140 patients (31.9%) in the 1979 to 1981 cohort; 199 patients (31.6%) in the 1982 to 1984 cohort; and 219 patients (21.6%) in the 1985 to 1987 cohort lost previously normal left ventricular function in the interval between the two operations.

As in our previous reports on reoperations, patients were also grouped by angiographic indications for coronary artery reoperation. In addition to severe coronary arterial narrowing, the principal angiographic indications were graft closure, progressive atherosclerosis in coronary arteries (either previously grafted or ungrafted), or a combination of graft closure and progressive atherosclerosis (Table 3). Graft closure, either alone or combined with progressive atherosclerosis, increased from 197 cases (45%) in the first cohort to 854 (85%) in the last cohort ($p < 0.001$).

Early Results

The 1985 to 1987 cohort received significantly more grafts per patient and more complete revascularization than the 1967 to 1978 cohort. Internal thoracic artery grafts increased from 27% in the 1967 to 1978 cohort to 67% in the 1985 to 1987 group. Of 1313 patients (52.3%) who had internal thoracic artery grafts, 112 (8.5%) occurred in patients with previous internal thoracic artery grafting and 1201 (91.5%) occurred in patients without previous internal thoracic artery grafting. The number of grafts per patient increased from 1.5 to 2.8 throughout the four cohorts. Similarly complete revascularization increased from 222 (51%) to 779 (77%). The mortality and major morbidity rates, grouped by patient cohort, are shown in Table 4. The operative mortality rate ranged from 2% to 5% and was 2.9% in the last cohort. Hospital death was attributed mainly to ischemia/infarction, which accounted for 38 (74.5%) of 51 early deaths in the first three cohorts, compared with 18 (67%) of 27 deaths in the most recent cohort (not significant [NS]).

New Q-wave perioperative myocardial infarctions changed from 7% to 8% in the first three cohorts to 4% in the last cohort ($p = 0.007$). Return to the operating room for bleeding and blood transfusions occurred significantly less in the 1985 to 1987 experience compared with the 1967 to 1978 cohort. Neurologic, respiratory, and wound problems did not vary significantly with time.

A logistic regression analysis was used to determine operative risk factors. Twenty-three clinical angiographic or operative variables (listed in the Appendix) were tested by univariate analysis and 11 were significant at the $p < 0.05$ level. These risk factors were entered into a logistic

TABLE 2. *Incidence of Significant Comorbidity and Other Risk Factors in Reoperation Patients*

	1967–1978		1979–1981		1982–1984		1985–1987		
Clinical Characteristics	n	(%)	n	(%)	n	(%)	n	(%)	*p* value*
Severe angina (NYHA III or IV)	319	(73.2)	312	(71.2)	419	(67.0)	647	(64.0)	0.001
Diabetes	62	(14.2)	67	(15.3)	107	(17.2)	230	(22.8)	<0.001
Hypertension	117	(26.8)	143	(32.6)	205	(32.8)	353	(35.0)	0.002
Peripheral vascular disease	29	(6.7)	52	(11.8)	76	(12.2)	140	(13.8)	<0.001
Obesity	61	(14.0)	76	(17.3)	113	(18.1)	182	(18.1)	0.06
Cigarette smoking	123	(28.1)	94	(21.4)	133	(21.3)	237	(23.5)	0.06

* *p* value reflects difference between 1967–1978 and 1985–1987 cohorts.
NYHA, New York Heart Association.

TABLE 3. *Angiographic Indications for Reoperation and Corresponding Intervals Between Procedures*

	1967–1978		1979–1981		1982–1984		1985–1987	
Procedure	n	(%)	n	(%)	n	(%)	n	(%)
Graft closure	123	(28.2)	157	(35.8)	278	(44.5)	254	(25.2)
Mean interval (months)	25.6		48.3		66.2		83.1	
Progressive atherosclerosis	239	(54.8)	121	(27.6)	112	(17.9)	155	(15.4)
Mean interval (months)	63.2		93.5		111.2		113.3	
Combination of above	74	(17.0)	161	(36.7)	235	(37.6)	600	(59.5)
Mean interval (months)	45.4		79.6		91.2		105.6	

regression model and operative risk factors were determined: age ≥ 60 years, blood transfusion, three-vessel disease, left main coronary artery disease, current cigarette smoking, no internal thoracic artery graft at first operation, severe angina before reoperation (functional classes III and IV), interval greater than 60 months between operations, poor left ventricular function, and surgery during the period 1967 to 1978 (Appendix). Significance, relative risk, and confidence intervals were calculated.

Major complications in reoperation patients were compared with the first 1000 primary isolated coronary artery bypass patients, who were operated on from 1967 through 1987. These patients were grouped into cohorts corresponding to the patients in this reoperation series. Primary (n = 16,996) *versus* reoperation (n = 2509) incidences are as follows: mortality, 1.1% *versus* 3.2%; perioperative myocardial infarction, 2.1% *versus* 5.9%; return for bleeding, 4.8% *versus* 6.2%; respiratory complications, 2.0% *versus* 3.9%; stroke, 1.6% *versus* 1.8%; and wound complication, 1.6% *versus* 1.6%. Excluding stroke and wound complication, these differences were highly significant. Raw numbers are available in the Appendix. Median length of hospitalization and postoperative hospitalization period in days and by cohort were 1967 to 1978, 14 and 10; 1979 to 1981, 13 and 9; 1982 to 1984, 11 and 8; and 1985 to 1987, 11 and 8.

Late Results

The 2429 hospital survivors were followed for a mean of 72 months. The 1967 to 1978 group was followed for a mean of 140 months; the 1979 to 1981 group was followed for 96 months; the 1982 to 1984 cohort was followed for 70 months; and the 1985 to 1987 cohort was followed for 34 months. Incomplete follow-up occurred for 28 (1.1%) of patients, 17 from the first 1500 patients and 11 from the last 1009.

After an overall mean follow-up of 72 months, 1888 living patients were classified according to NYHA functional class as follows: class I, 1199 patients (64%); class II, 506 patients (27%); class III, 153 patients (8%); and class IV, 30 patients (2%). Fifty-six survivors were not classified at follow-up. We found that those who had mild angina, class I or II before reoperation, tended to remain class I or II more than did those who had severe angina before reoperation; this observation held true in all four cohorts. Of patients who were in classes I and II before reoperation, 619 (93%) were in classes I and II after reoperation and 44 (6%) were classed as III or IV. In contrast, of 1223 who were in classes III and IV before reoperation, 1086 (89%) were classed I or II after reoperation and 139 (11%) were III or IV ($p < 0.0001$).

Eight hundred ninety postreoperative coronary arteriograms were performed in 684 patients; only the last arteriogram after reoperation was reviewed. The mean interval between reoperation and the postreoperative coronary arteriogram was 58 months (SD = 44 months). Of 411 internal thoracic artery (ITA) grafts studied, 363 (88%) were patent and 932 (65%) of 1438 saphenous vein grafts were patent. Patency for anterior descending and diagonal grafts was as follows: ITA, 308 of 346 grafts (89%); and

TABLE 4. *Mortality and Major Morbidity in Reoperation Patients*

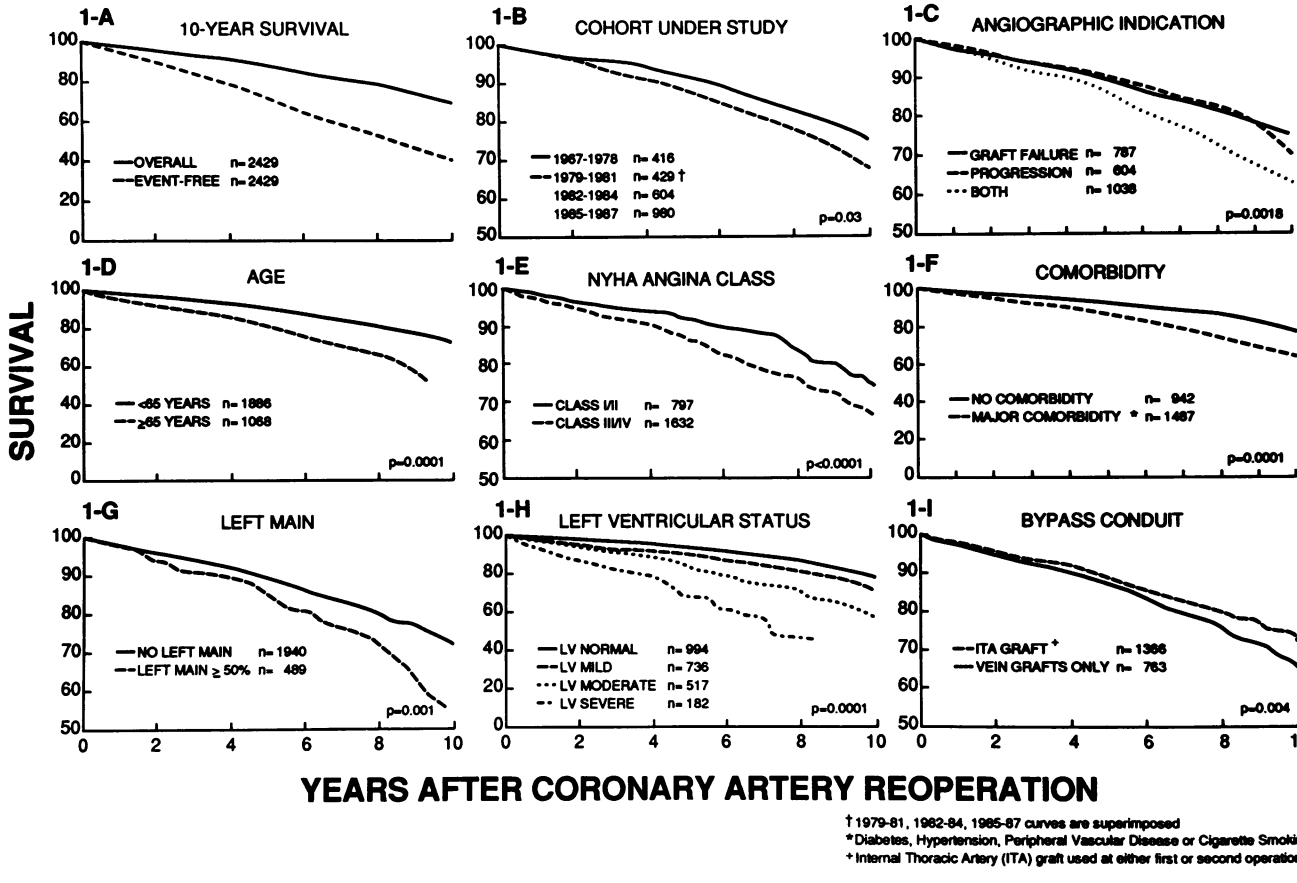
	1967–1978		1979–1981		1982–1984		1985–1987		
Mortality and Morbidity	n	(%)	n	(%)	n	(%)	n	(%)	*p* value
Operative mortality	20	(4.6)	10	(2.3)	21	(3.4)	29	(2.9)	NS
Perioperative myocardial infarction	29	(6.7)	29	(6.6)	50	(8.0)	41	(4.0)	.007
Return for bleeding	48	(11.0)	28	(6.4)	26	(4.2)	54	(5.3)	<.001
Blood transfusion (units)	8.0		2.5		2.0		2.7		<.0001
Neurologic deficit	8	(1.8)	8	(1.8)	16	(2.6)	14	(1.4)	NS
Respiratory dysfunction	25	(4.0)	6	(1.4)	34	(5.4)	42	(4.1)	NS
Wound complication	9	(2.1)	6	(1.4)	9	(1.4)	17	(1.7)	NS

NS, not significant.

vein grafts, 342 of 481 grafts (71%); compared with patency for right coronary artery: ITA, 11 of 14 grafts (79%); vein grafts, 286 of 464 (62%); and circumflex: ITA, 44 of 51 grafts (86%); vein grafts, 305 of 493 (62%).

Ten-year survival curves for the entire series and specific subsets are shown in Figure 1. Ten-year actuarial survival was 69.3% for those discharged alive after reoperation. The patients operated on in the initial experience, 1967 to 1978, enjoyed a significantly higher 10-year survival compared with patients in the next three cohorts. However a comparison of clinical, angiographic, and operative characteristics among the cohorts indicates that the 1967 to 1978 series was composed of lower-risk patients with respect to age, extent of coronary atherosclerosis, and left ventricular function. Patients who were operated on because of graft failure and progression of native vessel atherosclerosis had significantly lower 10-year survival rates, as did patients older than 65 years compared with younger patients. Patients with severe angina, any major comorbidity, severe left main coronary artery narrowing, moderate-to-poor left ventricular performance, and those who did not have an internal thoracic artery graft at either operation had significantly lower 10-year actuarial survival compared with their counterparts. The 10-year survival rate for women was 62.7%; for men it was 69.3% (NS).

Descriptors of late outcome varied from cohort to cohort, but left main coronary artery narrowing of 50% or more and left ventricular dysfunction consistently affected late survival throughout the entire experience. Significant variables are listed by cohort in the Appendix.



FIGS. 1A–I. (A) Ten-year actuarial survival and event-free survival rates for 2429 hospital survivors were 69.3% and 41.2%, respectively. (B) The earliest group, 1967–1978, enjoyed a significantly higher 10-year survival rate, 74.5%, than the first three cohorts, whose curves are virtually superimposed and reach 67.4% at 10 years. (C) Analysis of longevity by angiographic indication group shows that patients reoperated on for graft failure or progressive atherosclerosis had a better ($p = 0.0018$) 10-year survival rate than patients who experienced both progression and graft failure, 75.5% and 70.4% *versus* 63.4%, respectively. (D) Patients younger than 65 years before reoperation had a significantly better 10-year survival rate, 72.0%, than their older counterparts, 50.8% ($p = 0.0001$). (E) Survival rate by NYHA angina functional class shows I–II achieved 69.1% and III–IV 63.5% ($p < 0.0001$). (F) Comorbidity was defined as diabetes, hypertension, peripheral vascular disease, and cigarette smoking. Those with no comorbidity had a 10-year survival rate (77.1%) significantly greater than those with one or all comorbid conditions (63.7%) ($p = 0.0001$). (G) The presence or absence of left main coronary artery narrowing ≥ 50% significantly influenced 10-year survival rate, 71.9% *versus* 55.2% ($p = 0.001$). (H) Left ventricular performance before reoperation, stratified subjectively, demonstrated a wide range of 10-year survival rates: normal function 77.4%, mild impairment 70.3%, moderate dysfunction 56.4%, and severe impairment 45.1%. The survival difference between normal and poor performance is significant ($p = 0.0001$). (I) The performance of an internal thoracic artery graft either at the first or second operation affected long-term survival rate (72.6%) compared with vein grafts at both operations (65.5%) ($p = 0.004$).

Discussion

Among the first 1000 consecutive patients who had myocardial revascularization each year from 1971 to 1978, 3% had been reoperated on at our institution or elsewhere within 5 years of the first procedure. At 10 years 12% had undergone reoperation and by the 12th postoperative year, 17% had undergone reoperation.[6] This estimated incidence of reoperation at year 15 rises to 30% (95% confidence interval, 29% to 32%).

Many factors intervene after operation, and not all fit statistical analysis. Progression of atherosclerosis is unpredictable and depends on heredity and serum lipid concentrations. The rate of reoperation is also influenced by age, left ventricular function, and comorbidity. The choice of conduits used in the first operation modifies the rate of reoperation significantly. The higher patency and relative freedom from graft atherosclerosis found in the patients who underwent internal thoracic artery bypass significantly reduces the reoperation rate.[7,8] Previously we surveyed the first 1000 isolated primary coronary bypass patients operated on annually from 1971 to 1978. Of the measurable clinical, angiographic, and operative variables, use of vein grafts was the single greatest determinant of reoperation. Percutaneous transluminal coronary angioplasty doubtless spares some patients from reoperation, but quantitatively this protection and its effect are not yet known.

Our observational data in this report indicate that vein graft atherosclerosis is the leading cause of reoperation, more than progressive coronary atherosclerosis *per se*. Late graft closure, particularly after the fifth postoperative year, relates to vein graft atherosclerosis. This statement relies on demonstration of lesions in the conduit by angiography or a visual impression at surgery. Old conduits were removed infrequently for examination, but angiographic and microscopic observations correlate consistently.

The interval before reoperation continues to lengthen and, for patients in our 1985 to 1987 cohort, the mean duration before reoperation was approximately 9 years. As the frequency of left internal thoracic artery grafts to the anterior descending coronary artery increase and expanded use of thoracic arterial conduits gains favor, reoperation rates may decline and intervals between operations may lengthen further. Other factors that may decrease these rates include less traumatic vein preparation,[9,10] use of antiplatelet agents,[11,12] cessation of cigarette smoking,[13] and reduction of serum lipids.[14,15]

Trends in Patient Characteristics

A slightly reduced prevalence of severe angina before reoperation in the most recent cohort (1985 to 1987) compared with the earliest cohort (1967 to 1978) is probably due to improved antianginal therapy and possibly to liberalization of selection criteria. Comorbidity in the form of diabetes, hypertension, obesity, and peripheral vascular disease rose in the reoperation candidates during the interval surveyed, which reflects patient age and lengthening interval between operations. Women did not become more frequent reoperation candidates over time.

Nearly all patients had multivessel disease, but left main narrowing of 50% or more was seen significantly more often (25%) in reoperation than in primary surgical candidates (average, 10% to 12%). Twenty-five to thirty per cent of reoperation patients lost previously normal left ventricular function in the interval between operations.

We reported previously that vein graft failure was the most frequent angiographic reason for reoperation. In most cases late vein graft failure relates to atherosclerosis in the vein conduit. Internal thoracic artery graft atherosclerosis necessitating reoperations is rare.

Evolution of Technique

Changes in technique in 20 years involve (1) techniques of reentry, (2) myocardial protection, and (3) blood conservation. The gas-powered oscillating saw has replaced older re-entry techniques. Myocardial protection has changed from normothermic arrest to core cooling with cold potassium cardioplegia. Cardioplegic solutions were used in all patients in the last cohort, compared with 16%, 80%, and 97% in the first, second, and third cohorts, respectively. Beginning in 1988 this technique of crystalloid cardioplegia was supplanted by blood cardioplegia and, in early 1989, we began an antegrade and retrograde (coronary sinus) delivery protocol[16] for most reoperation candidates. Blood conservation in the form of a regionally heparinized blood processing system, retrieval of all oxygenator blood, and transfusion of shed blood after operation[17,18] have significantly reduced transfusion requirements. Because 20% of blood transfusions may result in some adverse effect,[19] we infer that some morbidity has been avoided.

These three advances in technique allow greater time for exposure and complete revascularization. Retrograde cardioplegia cools the subendocardium more than does antegrade cardioplegia delivery and is especially suited for left ventricular regions involved with a totally obstructed coronary artery.[20] Rather than dissection of the beating heart, mobilization of the adhered left ventricle is facilitated by administration of cardioplegia first. Previous patent internal thoracic artery grafts must be identified and temporarily occluded. A patent atherosclerotic vein graft is best managed by a no-touch technique followed by early division near the distal anastomosis. A new graft is then attached to that artery first so that regional cooling is preserved. The trend toward arterial grafting is shown by new internal thoracic artery graft

usage, which rose from 27% in the 1967 to 1978 period to 67% of cases in the 1985 to 1987 period.

Results in the 1985 to 1987 Cohort

Patients in this latest cohort had significantly fewer perioperative new Q-wave infarctions. This finding is attributed to routine use of cardioplegia solutions and early defunctionalization of patent, atherosclerotic vein grafts. The reduction in transmural myocardial infarction rates occurred in a significantly older patient group who had more diabetes, hypertension, peripheral vascular disease, three-vessel disease, left main lesions, vein graft atherosclerosis, and worse left ventricular performance compared with the first three cohorts. After the initial experience from 1967 to 1978, mortality and other morbidity rates generally declined in this reoperation experience, but these rates were significantly higher than complications related to the first surgery.

10-year Survival

Actuarial 10-year survival for each cohort and the composite series, *i.e.*, all 2509 patients, reveals the following. (1) Patients reoperated on in the initial experience, 1967 to 1978, showed significantly higher survival and event-free survival rates. Higher survival in this initial cohort occurred because of their significantly younger age, less extensive coronary artery disease, and better left ventricular performance before reoperation. (2) We found a significant adverse effect on longevity in patients 65 years or older compared with younger patients, severe angina before reoperation, left main disease of 50% or more compared with lesser or no left main lesion, severe left ventricular dysfunction, reoperation for both graft closure and progressive atherosclerosis, saphenous vein grafts only at both operations, any or all of the major forms of comorbidity (diabetes, hypertension, peripheral vascular disease, and current cigarette smoking). Of the conditions constituting comorbidity, peripheral vascular disease alone showed the greatest adverse influence on 10-year survival. We found no significant difference in long-term survival whether the patient was operated on for graft closure *or* for progressive atherosclerosis, and gender differences had no effect. As descriptors of late outcome, left main narrowing of 50% or more and left ventricular dysfunction worsened the prognosis more consistently than other variables for individual cohorts.

Functional Status

Angina relief is acknowledged to be less after reoperation compared with the first operation.[4,21] We presume that diffuse coronary atherosclerosis and left ventricular impairment underlies this consistent finding. Noteworthy in this report is the finding that patients with no angina or mild angina before reoperation tended to remain in NYHA functional class I or II (mean follow-up, 72 months), whereas those in classes III and IV before operation may achieve a long-term asymptomatic status but are more likely to have recurring severe angina compared with patients who had mild angina or no symptoms before reoperation.

Postreoperative angiography was reserved almost exclusively for patients with recurring symptoms. We found vein graft patency of 65% and internal thoracic artery patency of 88% after a mean of 58 months; these rates are lower than those found 5 years after the first operation.

Coronary artery reoperations are undertaken for angina or ischemia related mainly to three-vessel or left main coronary artery disease. The interval between operations has lengthened throughout this experience and now approaches 9 years. Vein graft atherosclerosis has become the major angiographic indication for reoperation.

A comparison of the 1985 to 1987 patients with earlier cohorts reveals a higher-risk population of candidates for reoperation. Advancing age, increased comorbidity, more three-vessel and left main coronary artery disease, and greater left ventricular dysfunction are documented in the most recent group. Improved myocardial protection permits wider use of the internal thoracic artery, more grafts per patient, and consequently more complete revascularization.

Operative risk is related to age and left main coronary artery disease more than any other factors. Hospital mortality rate has consistently been less than 5%. Myocardial protection accounts for a significant reduction in new Q-wave perioperative myocardial infarction, which constitutes the single greatest improvement in recent history of isolated coronary artery operations. Further advances in myocardial protection will provide the key to greater safety in these increasingly frequent procedures.

Survival is influenced by patient age, medical status, and angiographic findings before reoperation. Those who received an internal thoracic artery graft to the anterior descending artery, either at the first or the second operation, fared significantly better than those with vein grafts only.

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Appendix

TABLE 5. *Variables Tested for Operative and Late Risk*

1. Age (years): <65, ≥65
2. Sex
3. Interval between operations: months <60, ≥60
4. Internal thoracic artery graft at first operation (no, yes)
5. Internal thoracic artery graft at second operation (no, yes)
6. Angiographic reason for reoperation (progressive atherosclerosis, graft failure, combination of progressive atherosclerosis and graft failure)
7. Obesity (no, yes)
8. Hypertension (no, yes)
9. Diabetes (no, yes)
10. Peripheral vascular disease (no, yes)
11. Cigarette smoking (no, yes)
12. Preoperative angina NYHA functional class (I, II, III, IV)
13. Congestive heart failure (no, yes)
14. Extent of disease: (one, two, three, left main)
    1/2 *versus* 3/left main
15. Left ventricular function (normal/mild, moderate/severe)
16. Referral (internal, external)
17. Units of blood: units (0, >0)
18. Cohort (1967–1978, 1979–1981, 1982–1984, 1985–1987)
19. Total number of grafts per patient at reoperation
20. Total number of grafts per patient at first operation
21. Completeness of revascularization at reoperation
22. Prereoperative cholesterol value
23. Prereoperative triglycerides value

TABLE 6. *95% Confidence Intervals for the Relative Risk Estimates: Multivariate Model of Operative Risk by Cohort and Overall*

Risk Factors	1967–1978 20/438	1979–1981 10/439	1982–1984 21/623	1985–1987 29/1009	1967–1987 80/2509	Relative Risk	95% Confidence Interval
Left ventricular dysfunction	0.02			0.05	0.02	1.7	1.1–2.8
Age (decade)		0.03	0.02	0.002	0.0009	1.7	1.2–2.3
Current cigarette smoking				0.01	0.01	1.9	1.1–3.1
Left main narrowing ≥ 50%	0.002		0.0001		0.0001	6.9	2.6–18.3
Three-vessel disease					0.05	2.6	1.007–6.7
Blood transfused (units)					0.02	2.1	1.1–3.8
Angina NYHA class III/IV					0.02	2.1	1.1–3.7
Interval in months > 60	0.004				0.02	2.1	1.1–4.0
No ITA at first operation					0.04	2.3	1.03–5.2
Cohort 1967–1978					0.002	2.7	1.5–5.0

NYHA, New York Heart Association. ITA, internal thoracic artery.

TABLE 7. *95% Confidence Intervals for the Relative Risk Estimates: Multivariate Model of Long-term Survival*

Risk Factors	1967–1978	1979–1981	1982–1984	1985–1987	1967–1987	Relative Risk	95% Confidence Interval
Left ventricular dysfunction	0.01	0.0001	0.0001	0.0001	0.0001	1.9	1.6–2.3
Age	0.0001	0.002	0.003	0.001	0.0001	1.04	1.03–1.05
Diabetes		0.0001			0.0001	1.6	1.3–1.9
Current cigarette smoking	0.02	0.0006			0.0001	1.5	1.3–1.9
Hypertension	0.0001	0.01			0.0002	1.4	1.2–1.7
Left main narrowing ≥ 50%		0.001			0.0001	2.0	1.5–2.7
Three-vessel disease		0.02			0.0001	1.6	1.3–2.1
New Q-wave myocardial infarction	0.007	0.0001			0.002	1.6	1.2–2.3
Angina NYHA class III/IV			0.0009		0.003	1.4	1.1–1.7
Peripheral vascular disease		0.01			0.001	1.5	1.2–2.0
Interval in months > 60		0.02			0.006	1.003	1.001–1.005
No ITA at first operation	0.005			0.002	0.03	1.5	1.09–1.9

NYHA, New York Heart Association. ITA, internal thoracic artery.

TABLE 8. *Primary* Versus *Reoperation Mortality and Morbidity*

Mortality and Morbidity	Primary* (n = 16,996) (n)	(%)	Reoperation (n = 2509) (n)	(%)	p value
Operative mortality	240	1.1	80	3.2	<0.0001
Perioperative myocardial infarction	415	2.1	148	5.9	<0.0001
Bleeding	891	4.8	155	6.2	<0.0001
Respiratory insufficiency	377	2.0	98	3.9	<0.0001
Neurologic deficit	294	1.6	46	1.8	NS
Wound complication	302	1.6	41	1.6	NS

* First 1000 cases annually from 1971 to 1987.

DISCUSSION

DR. O. WAYNE ISOM (New York, New York): The contributions by the Cleveland Clinic in the surgical treatment of coronary disease over the past quarter of a century have certainly been monumental and the reports over the years have been enlightening to all of us. I appreciate the opportunity to review the manuscript in detail before the meeting.

I have five questions combined with a few comments. The first is: Was there a reason that the cohorts were divided up into an 11-year period between 1967 and 1978 and a 3-year period between 1979 and 1981, and 2-year periods between 1982 and 1984 and between 1985 and 1987? Was there some specific change in technique in these particular periods, or was there a change in composition of the surgeons during that period, or perhaps was this just an arbitrary decision to divide them up into equal numbers even though the last group is higher?

The second question is that in all groups operated on between 1967 and 1987, the mean age at first operation ranged between 49 and 52. The mean age in the second operation, in the last two groups was between 58 and 60.