

Long-term Results of Coronary Bypass Surgery

Analysis of 1698 Patients Followed 15 to 20 Years

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Between 1968 and 1975, 1698 patients underwent coronary artery bypass with autogenous saphenous vein and were followed for up to 20 years. Age at operation was 53.9 ± 8.4 years, and 1485 were men (88%). Angina was present in 1637 patients (96%). There was single-vessel disease in 306 patients (18%), double-vessel in 642 (38%), triple-vessel in 550 patients (32%) and left main stenosis in 200 (12%). Preoperative left ventricular quality was good in 1185 (70%), poor in 508 (30%), and unknown in five patients. Survival at 20 years was as follows: for single-vessel disease, 40%; double-vessel, 26%; triple-vessel, 20%; and left main, 25%. At 20 years of follow-up, 67% of surviving patients were asymptomatic and 26% were improved. Antianginal drug therapy consisted of nitrates in 49% of patients and beta-blockers in 26%. Graft patency at 0 to 5 years was 633 of 780 grafts (81%); at 6 to 10 years, 415 of 606 grafts (68%); at 11 to 15 years, 271 of 449 grafts (60%); and at 16 to 20 years, 65 of 140 grafts (46%). Coronary bypass reoperation was performed in 324 patients (19%) and survival of these patients was 62% compared to 37% for nonreoperation patients ($p < 0.05$). Cox analysis demonstrated that the major determinants of survival related to age at operation, extent of coronary disease, quality of ventricle, history of stroke, and preoperative congestive heart failure. At 20 years of follow-up of this early experience with coronary bypass, 76% of surviving patients had one or more patent grafts and the probability of freedom from reoperation was 0.62.

THIS REPORT CONTAINS information regarding the long-term clinical and angiographic outcome of coronary bypass surgery in a series of patients who have been the subject of ongoing prospective studies. Previous reports documented the 5-year,¹⁻⁴ 10-year,⁵ and 10- to 15-year^{6,7} follow-up results. The aim of this study was to present data for the 15- to 20-year follow-up interval.

Materials and Methods

Between 1968 and 1975, coronary bypass surgery was performed by one surgeon (G. C. Morris) on 1698 patients

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at Baylor College of Medicine and The Methodist Hospital. The preoperative clinical characteristics of the patients are summarized in Table 1 and the angiographic data in Table 2. Ejection fraction data were not available for most patients from this early experience, and therefore left ventricular function was defined as good if the left ventricular end-diastolic pressure was less than or equal to 15 mmHg and there was no akinetic or aneurysmal segment present on left ventriculography. Left ventricular function was considered to be poor if the end-diastolic pressure was more than 15 mmHg or there was an akinetic or aneurysmal segment. Previously we reported the results of an analysis of another group of 447 patients from our coronary database for whom preoperative ejection fraction, end-diastolic pressure, and the results of left ventriculography were available.⁶ In the 239 patients classified as having good ventricular function, the mean ejection fraction was $60\% \pm 1.25\%$ (\pm standard error). In the 208 patients classified as having poor function, the mean ejection fraction was $45\% \pm 0.9\%$. Thus, although not ideal, the classification used in this study did define two groups of patients with different prognoses.

The surgical procedures were all performed using a standardized technique. Autogenous long saphenous vein from the thigh was used for all bypasses. The veins were prepared by distension with room-temperature normal saline and then stored in saline at room temperature. Patients were placed on normothermic crystalloid prime cardiopulmonary bypass. The distal anastomoses were performed during a single period of normothermic aortic cross-clamping. The proximal anastomoses were performed during a period of partial aortic occlusion, with the empty beating heart supported by full-flow cardiopulmonary bypass. No antiplatelet agents were employed after operation.

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TABLE 1. *Clinical Characteristics Before Operation of 1698 Patients Who Underwent Saphenous Vein Coronary Bypass*

Parameter	Value
Age (yrs)	53.9 ± 8.4 (SD)
Sex	
Male	1485 (87%)
Female	213 (13%)
Angina pectoris	1637 (96%)
History of myocardial infarction	1030 (61%)
History of congestive failure	195 (11%)
History of stroke	47 (3%)
Obesity	606 (36%)
Smoking	1023 (60%)
Diabetes	255 (15%)
History of hyperlipidemia	985 (58%)
Blood pressure	
Systolic	136.9 ± 20.9 mmHg
Diastolic	82.8 ± 11.5 mmHg
Plasma cholesterol	246 ± 53 mg/dL
Plasma triglyceride	222 ± 138 mg/dL
Serum glucose	98 ± 41 mg/dL
Digoxin use	314 (18%)
Vasodilator use	1352 (80%)
Propranolol use	324 (19%)
Diuretic use	256 (15%)
Antiarrhythmic use	140 (8%)
Antihypertensive use	324 (19%)

After hospital discharge, follow-up of clinical status was assessed prospectively for all patients at regular intervals using a standardized questionnaire and supplemented by telephone inquiries to patients and their physicians.

Postoperative cardiac catheterization was performed 1219 times in 818 of the 1698 patients. Results of these studies were also recorded on standardized data sheets. Vein grafts were classified as either patent or occluded. A vein graft was considered patent if it provided a communication of any size between the ascending aorta and the distal coronary artery. Patent grafts were further classified as either normal if there was no luminal irregularity causing greater than 20% stenosis or stenotic if there was greater than 20% stenosis.

The data from this study were entered into a custom database system written in MUMPS (Intersystems Inc. M/SQL [V5B.0-90-06B] resident on a DEC VAX/750 running VAX/VMS V5.3). The associations among discrete variables were analyzed by two-way contingency table analyses, and the statistical significance was calculated by the Pearson chi square test. The differences among groups were determined by analysis of variance for continuous variables and nonparametric methods for nominal data. Univariate analyses were performed also by means of Kaplan–Meier curves to estimate the influence of variables on the time-related probability of freedom from death or reoperation. The stepwise proportional hazards regression model of Cox was used to evaluate the influence of covariate factors on the survival interval. The BMDP Statistical Software 1990 (VAX/VMS) (BMDP Statistical Software Inc., Los Angeles, CA) package was used for all

statistical computation except Kaplan–Meier survival plots, which were generated by a custom routine validated against BMDP. Expected survival of these patients was calculated from the mortality rates presented in the 1970 United States Census for an age- and sex-adjusted population.^{8–11}

Results

A total of 3205 separate grafts were performed in 1698 patients, for a mean of 1.9 ± 0.6 grafts per patient. This resulted in the presence of residual disease after surgery in 471 of 1392 (33.8%) of the patients with multivessel coronary disease. Residual disease was considered to be present when one or more vessels with greater than 50% stenosis received no graft.

Perioperative deaths occurred in 85 patients (5%) within 30 days of operation.

Follow-up was 92.2% complete at 20 years. The mean follow-up interval was 15.2 ± 4.2 years for survivors, and the mean interval from operation to death in nonsurvivors was 8.6 ± 5.2 years.

Symptom status, work status, and current medication usage are summarized in Table 3. The results of evaluation of graft patency according to individual grafts are shown in Table 4. Overall graft patency in the 16- to 20-year interval was 46%. The numbers of patients with one or more patent grafts are shown in Table 5. Of the patients followed 16 to 20 years, 76% had one or more patent grafts. Analysis of the influence of various levels of cholesterol and triglycerides on vein graft patency were performed ($p > 0.05$ for differences in 20-year patency at different triglyceride levels). The triglyceride level did not influence graft patency. Patients with total cholesterol levels greater than 280 mg/dL had significantly lower graft patency in the 10- to 20-year interval (Fig. 1).

A total of 1016 deaths (60%) have occurred. This includes perioperative mortality. For sample of the general US population of 1970 adjusted for age and sex distribution,¹¹ 838 deaths (49.4%) would have been expected over the 20-year interval. Thus the observed to expected mortality ratio was 1.2 over the 20-year interval, an excess

TABLE 2. *Preoperative Coronary Angiographic and Left Ventriculographic Findings in 1698 Patients*

Factor	No. Patients (%)
Number of stenotic coronary arteries	
One artery	306 (18)
Two arteries	642 (38)
Three or four arteries	550 (32)
Left main artery	200 (12)
Quality of left ventricle	
Good	1185 (70)
Poor	508 (30)
Unknown	5 (0.3)

TABLE 3. Results of Clinical Follow-Up at 5-Year Intervals of the 1698 Patients

Factor	Interval			
	0-5 Years	6-10 Years	11-15 Years	16-20 Years
Relief of angina				
No. of responses	576	761	676	332
Asymptomatic	328 (57%)	406 (53%)	365 (54%)	221 (67%)
Improved	206 (36%)	286 (38%)	240 (36%)	86 (26%)
Same	34 (6%)	52 (7%)	38 (6%)	17 (5%)
Worse	8 (1%)	17 (2%)	33 (5%)	8 (2%)
Symptoms of heart failure	34/538 (6%)	70/658 (11%)	133/680 (20%)	103/334 (31%)
Work status				
No. of responses	531	643	660	321
Same	255 (48%)	248 (39%)	245 (37%)	82 (26%)
More	20 (4%)	41 (6%)	80 (12%)	17 (5%)
Less	64 (12%)	107 (17%)	192 (29%)	114 (35%)
None	192 (36%)	247 (38%)	143 (22%)	108 (34%)
Medication use (positive response/ total response)				
Digoxin	112/516 (22%)	168/646 (26%)	159/680 (23%)	56/322 (17%)
Vasodilator	118/512 (23%)	259/647 (40%)	298/685 (44%)	161/329 (49%)
Beta blocker	117/513 (23%)	213/640 (33%)	219/680 (32%)	83/322 (26%)
Antiarrhythmic	46/512 (9%)	82/637 (13%)	84/672 (13%)	48/321 (15%)
Oral hypoglycemic	1/3 (33%)	4/4 (100%)	7/121 (6%)	20/302 (7%)

mortality rate of about 20%. Cardiac causes of death predominated, accounting for 513 of all the 1016 deaths (50.5%). Cardiac deaths occurred from recurrent myocardial infarction (260 patients), progressive congestive heart failure (136 patients), or from arrhythmias (117 patients). Cancer accounted for 89 deaths and stroke for 51 deaths. The cause of death could not be determined in 199 patients. A large variety of other causes were responsible for the remaining deaths.

The results of Kaplan-Meier analysis of the influence of sex on survival probability is shown in Figure 2. Survival was similar for men and women. The influence of the number of vessels diseased before operation on survival is shown in Figure 3. The influence of quality of preoperative ventricular function on survival is shown in Figure 4. Figures 5 and 6 illustrate survival probability according to the simultaneous influence of quality of ventricle and the number of vessels diseased.

Kaplan-Meier analyses of the influence of plasma total

cholesterol, triglycerides, diabetes mellitus, and systolic blood pressure on 20-year survival probabilities demonstrated that neither the total cholesterol nor the triglyceride levels were predictive of survival (Figs. 7 and 8), whereas the presence of diabetes or a systolic blood pressure of at least 161 mmHg were associated with reduced survival (Figs. 9 and 10). A more detailed analysis of the influence of diabetes mellitus on 10- to 15-year survival rates in 212 of these patients has been reported previously.⁷ The age at operation was also a significant predictor.

The survival of the 471 patients with multivessel disease who had residual disease was compared with the remaining 911 patients who received a graft to each major coronary artery with a significant stenosis and thus had no residual disease. The survivals of patients with double-vessel disease and either no or one residual lesion are shown in Figure 11. Long-term survival was significantly lower in the presence of a residual lesion ($p < 0.05$).

The survival probabilities of patients with triple-vessel

TABLE 4. Results of 1975 Graft Evaluations from 1219 Studies in 818 Patients

Years (No. of Patients Cathed)	RCA	LAD	LCA	DIAG	Total
0-5 (418)					
No. patent/no. studied	214/271 (79%)	304/362 (84%)	99/122 (81%)	16/24 (64%)	633/780 (81%)
6-10 (333)					
No. patent/no. studied	138/207 (67%)	221/291 (76%)	54/96 (56%)	2/12 (17%)	415/606 (68%)
11-15 (236)					
No. patent/no. studied	86/156 (55%)	141/204 (69%)	39/79 (49%)	5/10 (50%)	271/449 (60%)
16-20 (232)					
No. patent/no. studied	21/42 (50%)	33/56 (59%)	11/26 (42%)	—	65/140 (46%)

Cathed, catheterized; RCA, right coronary artery; LAD, left anterior

descending coronary artery; LCA, left circumflex coronary artery; DIAG, diagonal.

TABLE 5. Analysis of the 818 Patients Who Underwent Postoperative Vein Graft Study According to the Presence or Absence of One or More Patent Grafts

Time to Most Recent Catheterization	At Least 1 Patent Graft	No Patent Grafts	Total Patients
≤31 days	37 (95%)	2 (5%)	39
1 month to 5 years	206 (88%)	29 (12%)	235
6–10 years	206 (79%)	56 (21%)	262
11–15 years	172 (78%)	48 (22%)	220
16–20 years	49 (79%)	13 (21%)	62
Total patients studied	670 (82%)	148 (18%)	818

disease are presented according to the extent of residual disease (Fig. 12). Both one and two residual lesions had a significant impact on late survival ($p < 0.005$).

Coronary bypass reoperation was performed in 324 (19%) of patients at a mean interval of $9.5 \pm$ years from initial operation. Perioperative mortality was 11.4% (37 patients). The probability of freedom from reoperation for all patients and the survival of the 324 patients after reoperation are shown in Figures 13 and 14. Reoperation was required for residual disease in 79 patients (27%) and progression of disease or graft failure in 244 patients (73%). The influence of reoperation on subsequent survival probability is shown in Figure 13, which provides a comparison of overall survival of the 1698 patients with the survival of all reoperated patients from the time of their first coronary bypass. The survival of the reoperated patients also is plotted from the time of their reoperation. Figure 14 illustrates the probability of freedom from coronary bypass reoperation for the 1698 patients over the 20-year interval. At 10 years the probability of freedom from reoperation was 0.87; at 15 years, 0.72; and at 20 years, 0.62.

Cox regression analysis was performed to evaluate the influence of preoperative and intraoperative variables on

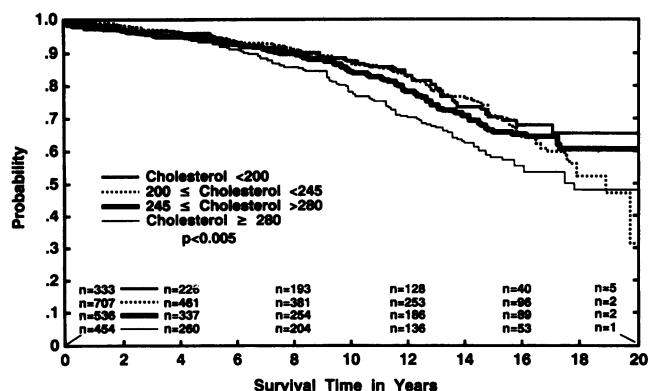


FIG. 1. Influence of various levels of total plasma cholesterol on the 20-year patency of saphenous vein grafts analyzed by the Kaplan-Meier technique. The number of patent grafts available for analysis at each interval are shown.

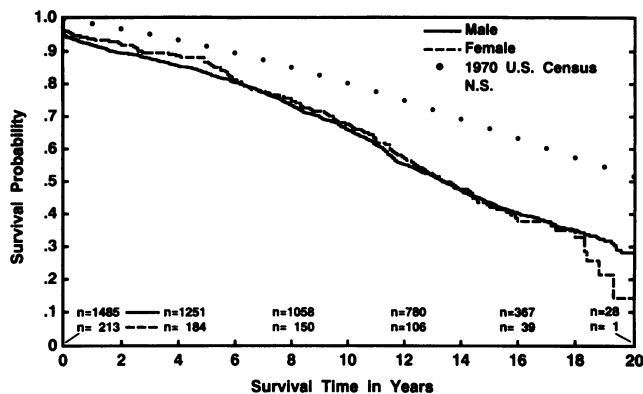


FIG. 2. Comparison of the survival probabilities (Kaplan-Meier) of 1485 men and 213 women after coronary bypass surgery. Survival was similar at all intervals for men and women. ($p > 0.05$ for differences). The expected survival for an age and sex adjusted sample of the general population is shown for comparison on this and subsequent figures. (See text for details of methods used to derive this population.)

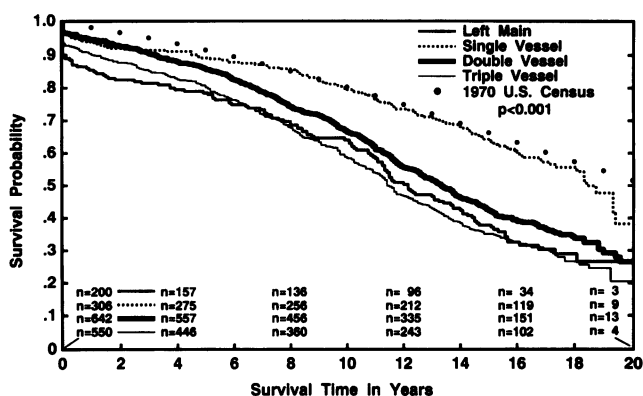


FIG. 3. Survival probabilities of 1698 patients according to the extent of coronary disease before operation.

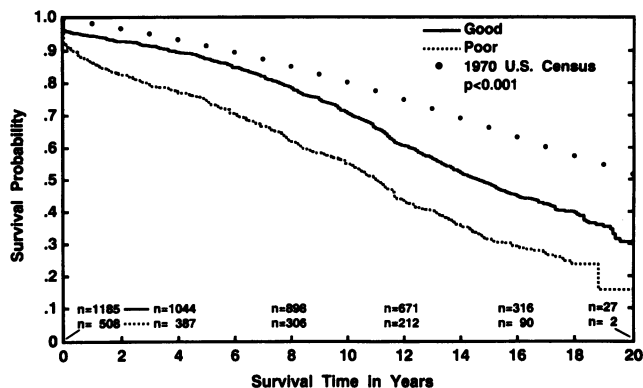


FIG. 4. Survival probabilities of 1698 patients according to the quality of left ventricular function before operation. (See text for definitions of good and poor left ventricular function.)

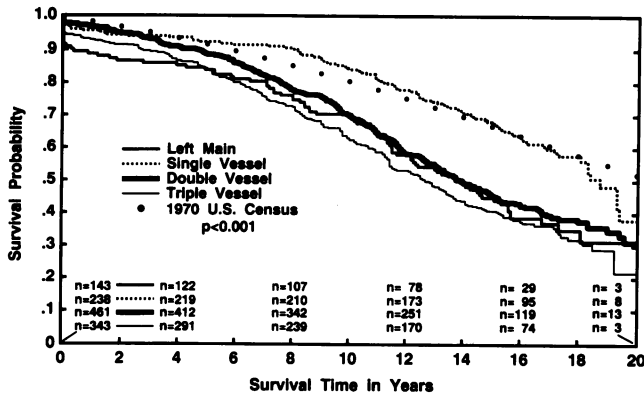


FIG. 5. Survival probabilities of 1185 patients with good left ventricular function according to the number of vessels diseased.

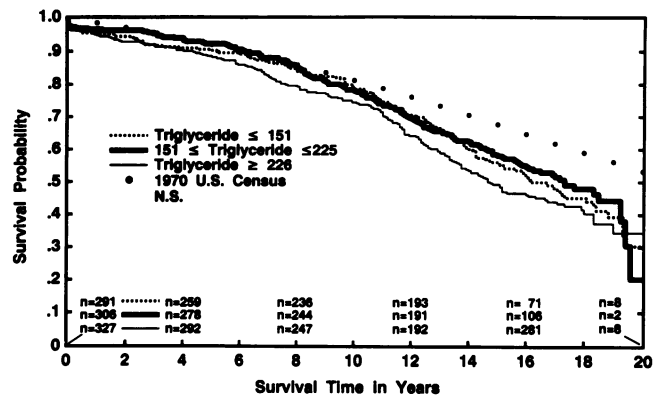


FIG. 8. Influence of the plasma triglyceride level on 20-year survival. Triglyceride levels are in mg/dL. There were no significant differences in survival probabilities.

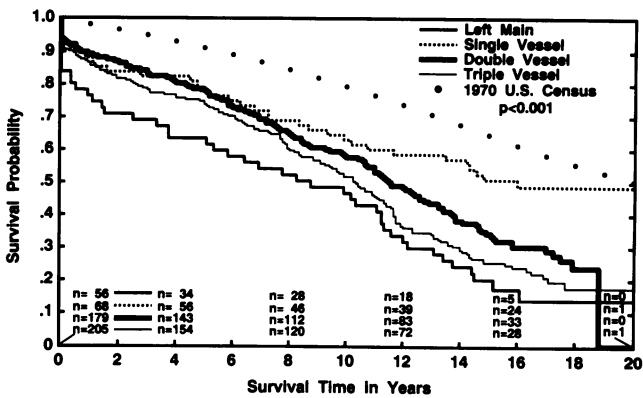


FIG. 6. Survival probabilities of 508 patients with poor left ventricular function according to the number of vessels diseased.

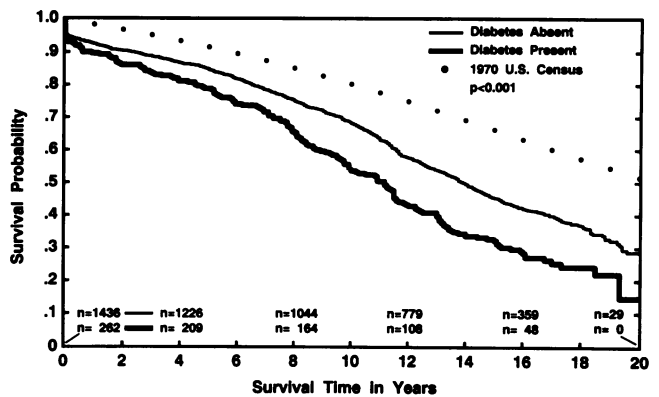


FIG. 9. Influence of diabetes mellitus on the 20-year survival probability of 1698 patients, of whom 262 were diabetic.

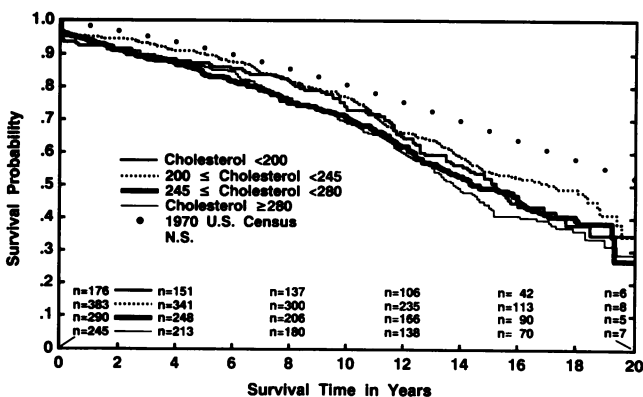


FIG. 7. Influence of total cholesterol (mg/dL) on the 20-year survival of 1094 patients for whom cholesterol data was available. There were no significant differences in survival ($p > 0.05$).

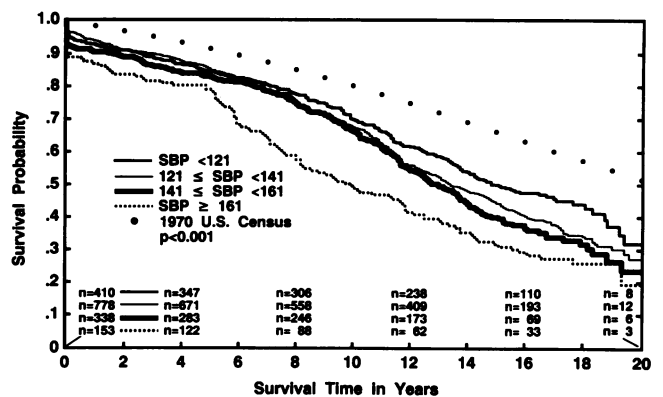


FIG. 10. Influence of level of systolic blood pressure (SBP) in mmHg before operation on 20-year survival probability.

overall survival (Table 6). Many variables had some independent predictive value, in part due to the large number of patient-years available for analysis. The most important variables, however, related to the extent of cor-

onary disease and factors associated with the quality of left ventricular function. The risk factors of age, systolic hypertension, diabetes mellitus, and a history of preoperative stroke were also important predictors.

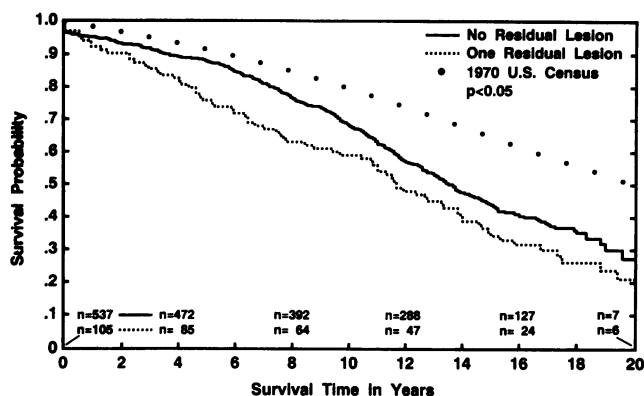


FIG. 11. Survival probabilities of patients with double vessel disease according to the presence or absence of a residual lesion.

A total of 918 peripheral vascular procedures were performed on 638 (38%) patients during the follow-up interval.

Discussion

This early experience with coronary bypass surgery differs in several notable respects from current practice. Most patients were operated on before the availability of beta-blocking agents, and none were treated before operation with calcium channel-blocking agents. These factors, combined with anesthetic techniques that were still evolving, led to significant problems with hemodynamic instability before institution of cardiopulmonary bypass in many of the higher-risk patients.

There were a small number of grafts performed per patient (1.9) compared with our current practice of performing three to four grafts per patient in most cases of multivessel disease. The saphenous vein was used exclusively, whereas now at least one internal mammary bypass is performed in more than 80% of patients.

No hypothermic or cardioplegic myocardial protection

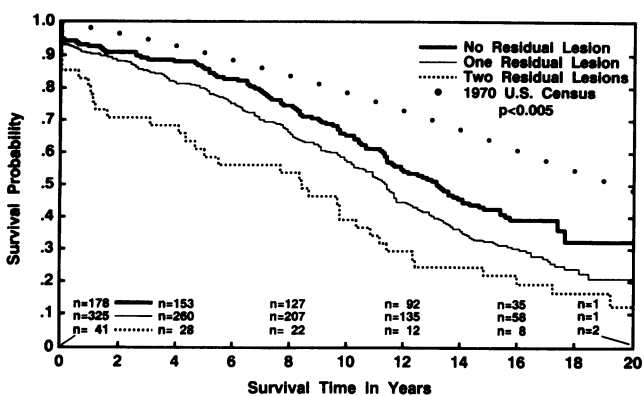


FIG. 12. Survival probabilities of patients with triple vessel disease according to whether one or two residual lesions were present.

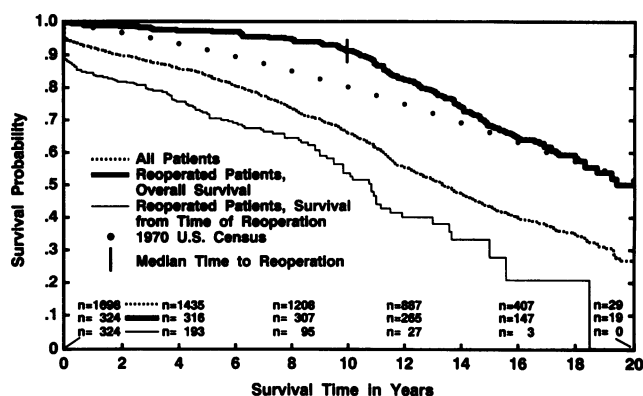


FIG. 13. Survival probability of 324 patients who underwent coronary reoperation. A comparison is provided for both survival from the first coronary bypass operation and for survival from the time of reoperation.

was used. Although this had little impact on the results in patients with good preoperative left ventricular function, patients with severely impaired ventricles and multivessel coronary disease experienced significant perioperative mortality from left ventricular dysfunction.

Despite these problems, most of the patients have done well over the 15- to 20-year follow-up interval. Analysis of the impact of the coronary bypass on clinical status and survival has become more complicated as the follow-up interval has lengthened, because most surviving patients are now older than 70 years and, like the rest of their peer group, have retired and become more sedentary. Furthermore to survive over such a long follow-up interval, it is likely that, in the 15- to 20-year survivors, characteristics of their coronary disease and graft function have provided them with this outcome, in contrast to the fate of the nonsurviving patients. Thus it is difficult to assess how many of the changes in activity levels documented in Table 3 are due to self-selection for survival, aging alone, and how many are due to their coronary disease.

Despite these problems relief of symptoms, as described

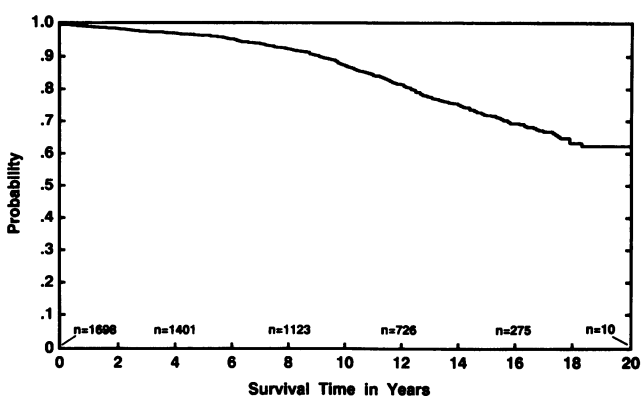


FIG. 14. Probability of freedom from coronary bypass reoperation for the 1698 patients over a 20-year period.

TABLE 6. Results of Cox Regression Analysis for Factors Predictive of Overall Mortality Rate

Variable	Beta	SE (B)	Level	RR (95% CI)	χ^2	p Value
Left main disease	0.6585	0.1264	Absent	1.0	27.15	<0.0001
			Present	1.9 (1.5, 2.5)		
Age at operation	0.0209	0.0041	0	1.0	25.43	<0.0001
			Per year	1.02 (1.01, 1.03)		
Systolic blood pressure	0.0066	0.0015	0	1.0	20.48	<0.0001
			Per mmHg	1.007 (1.003, 1.010)		
Number of vessels diseased	0.3803	0.1049	1 or less	1.0	20.17	<0.0001
			2 vessels	1.5 (1.2, 1.8)		
			3 or more	1.7 (1.3, 2.1)		
Preoperative CHF	0.5199	0.1208	Absent	1.0	16.04	0.0001
			Present	1.5 (1.2, 1.8)		
Diabetes	0.3347	0.0841	Absent	1.0	15.85	0.0001
			Present	1.4 (1.2, 1.6)		
Preoperative stroke	0.6616	0.1680	Absent	1.0	15.51	0.0001
			Present	1.9 (1.4, 2.7)		
Preoperative myocardial infarction	0.2494	0.0707	Absent	1.0	12.46	0.0004
			Present	1.3 (1.1, 1.5)		
Ventricular quality	0.2499	0.0715	Good	1.0	12.22	0.0005
			Poor	1.3 (1.1, 1.5)		
Preoperative digoxin	0.2817	0.0871	Absent	1.0	10.45	0.0012
			Present	1.3 (1.1, 1.6)		
Assoc valve surgery	1.6296	0.5809	Absent	1.0	7.87	0.0050
			Present	5.1 (1.6, 15.9)		
Isolated CABG	-0.4569	0.1666	No	1.0	7.52	0.0061
			Yes	0.63 (0.46, 0.88)		
Preoperative diuretic use	0.2459	0.0908	Absent	1.0	7.34	0.0067
			Present	1.3 (1.1, 1.5)		
Residual disease	0.1702	0.0847	Absent	1.0	4.04	0.0446
			Present	1.2 (1.0, 1.4)		

B, beta; SE (B), standard error; RR, relative risk; CI, confidence interval;

χ^2 , chi square; CHF, congestive heart failure; Assoc, associated; CABG, coronary artery bypass graft operation.

by the patients, has been persistently good. Freedom from angina has been well maintained, but at the same time there has been a progressive increase in the use of various forms of coronary vasodilators, including calcium channel-blocking agents. The most important change in symptoms has been the significant increase in the number of patients reporting symptoms of congestive heart failure. Whether this is due to true congestive heart failure secondary to progressive deterioration of left ventricular function or is a manifestation of the left ventricular hypertrophy and diastolic dysfunction seen in coronary disease could not be determined in this study.

We have not observed the marked deterioration in symptom relief reported by Campeau et al.¹² of 3.7% per annum. Our results are similar to those of Schaff et al.¹³

There are few reports of long-term survival data with which to make comparisons with our own study. In the randomized European Coronary Surgery Study¹⁴ the overall survival at 12 years of follow-up was 70.6% \pm 5.8% for surgically treated and 66.7% \pm 5.3% for medically treated patients. This study was restricted to patients with reasonably good preoperative left ventricular function. Our group of patients with good left ventricular function achieved a survival rate of 60.6% at 12 years.

The Veterans Administration Coronary Artery Bypass Cooperative Study Group¹⁵ reported that, at a follow-up

interval of 11 years, the survival probability for single-vessel disease treated medically was 0.65 and for surgically treated patients was 0.70. At 11 years the survival probability of our surgically treated patients with single-vessel disease was 0.76. For double-vessel disease our survival was 0.61 at 11 years, compared with a VA medical rate of 0.69 and operative rate of 0.55. For triple-vessel disease, the VA survival probability was 0.50 for medical and 0.56 for surgical treatment, compared with our surgical result of 0.54.

Proudfit et al.¹⁶ reported on the 15-year survival of a medically treated 'surgical candidate' group of 386 patients. The 15-year survival rates were, for single-vessel disease, 57% to 61%; double-vessel disease, 23% to 30%; and triple-vessel disease, 17% to 30%. The corresponding figures at 15 years for our surgical patients are 0.63, 0.42, and 0.35.

Proudfit also noted that the main predictors of 15-year survival identified by Cox regression analysis were the presence of two- or three-vessel disease, hypertension, symptoms for more than 5 years, abnormal electrocardiographic (ECG) findings, evidence of peripheral vascular disease, and an end-diastolic pressure greater than 30 mmHg.

The deleterious influence of residual disease was recognized early in our experience with coronary bypass.^{1,2,4}

The adverse influence of failure to revascularize all major graftable vessels has continued through the 15- to 20-year interval. As shown in Figures 11 and 12, the 15-year survival probability for patients with completely revascularized double-vessel disease was 0.43, compared with 0.34 for incompletely revascularized patients. For triple-vessel disease the effect was even greater, with a survival probability of 0.42 for no residual lesion, 0.32 for one residual lesion, and 0.22 for two residual lesions.

Other authors have reported similar findings with regard to the adverse influence of residual disease on survival.¹⁷⁻²⁴ An additional benefit of more complete revascularization has been improved relief of angina and exercise tolerance after surgery.²⁵⁻²⁷

These long-term data continue to demonstrate that it is important to ensure that all stenosed major epicardial coronary arteries receive a bypass graft. Currently the average number of grafts placed is 3.4 per patient.

The other factor critically important to the long-term success of the operation is the behavior of the saphenous vein grafts. In our own experience we have documented a steady rate of attrition of graft patency of 2% to 3% a year (Table 4).^{1-7,28,29}

Despite this attrition and the small number of grafts performed in each patient, 79% of patients (Table 5) had at least one patent graft in the 16- to 20-year interval.

In earlier reports we documented the occurrence of intimal proliferation³⁰ and later, atherosclerosis³¹ in the saphenous vein grafts. Whereas progression of coronary disease appears to have had a minor role in vein graft occlusion in our experience,^{1,6} vein graft atherosclerosis now has emerged as the major threat to the long-term patency of the vein grafts. This is consistent with data from other long-term studies³²⁻³⁴ showing progressive degeneration of vein grafts with time.

The cause of these changes remain unknown. Some authors consider hyperlipidemia-induced lipid uptake by the vein wall to be the dominant event.³³ Our own data has consistently failed to demonstrate significant differences in the total cholesterol, triglyceride, or lipoprotein levels of patients with normal or abnormal grafts late after operation, except in patients with very severe hypercholesterolemia.^{29,31}

We believe that intraoperative manipulation of the saphenous veins may cause trauma to the intima and media that leads to changes ultimately culminating in the late onset of graft atherosclerosis. Our studies on human saphenous vein suggest that vein preparation with saline solution should be abandoned and replaced with a balanced salt solution containing albumin.^{35,36} Our data are consistent with the results of many other studies, which we recently reviewed at length.³⁶

Initially in this experience, reoperation was required for correction of residual disease. Subsequently the major

cause of reoperation has been vein graft failure. The reoperation rate was 1% per annum up to 9 years of follow-up, but thereafter increased to 2.5% per annum. However this rate has remained stable during the 10- to 20-year interval. Similar rates of reoperation have been noted for this same interval by other authors.³⁷ A substantial reduction in the reoperation rate to less than 0.5% per annum has been noted in more recent experience. As reported by others, our patients after reoperation had long-term survival rates comparable to other nonreoperated patients.^{38,39}

It was of interest to note that age at operation, diabetes mellitus, systolic hypertension, and a history of stroke all continued to be significant predictors of overall survival. Over a 20-year period, it is evident that patients aged 60 to 70 years will ultimately have a survival disadvantage compared with patients aged 50 years. As we have reported previously,⁷ diabetic patients experienced excess mortality from cardiac, renal, and stroke events. The role of systolic hypertension as a risk factor for cardiovascular mortality has received increasing attention in recent years.⁴⁰⁻⁴² In this study it was a relatively powerful independent predictor of death.

Notably absent as a risk factor predictive of death was the total serum cholesterol level. These findings are consistent with those of the Framingham study, which showed no association of level of cholesterol with mortality for men over 50 years of age.⁴³

Changes in practices that should lead to enhanced long-term results among patients currently undergoing coronary bypass surgery include improved preoperative and intraoperative patient stabilization, better vein graft preparation techniques, and the liberal use of one or both internal mammary arteries. The use of perioperative and long-term aspirin therapy has favorably affected early and intermediate graft function and has important experimentally demonstrated effects on vein graft lipid metabolism.

The results of this study further emphasize the need for sustained intensive medical supervision of these patients and treatment of all controllable risk factors. The role of intensive lipid lowering in these patients is not yet established.

The significant proportion of patients dying from arrhythmias suggests that greater attention needs to be given to the management of patients who manifest serious arrhythmias in the preoperative or perioperative intervals or during the long-term follow-up interval. Such patients may benefit from more intensive evaluation, including electrophysiology studies.

Given the foregoing, it is highly probable that patients now undergoing coronary bypass will have more favorable long-term results than those of the 1698 patients in this study.

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