The Long-term Influence of Coronary Bypass Grafts on Myocardial Infarction and Survival

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Approximately 1,000 coronary bypass procedures were performed at New York University between February 1968 and December 1973. This report reviews all elective operations performed for angina between 1968 and 1972, a total of 448 patients. In this five-year period the percentage of diseased arteries bypassed rose from 40% to 84%, and operative mortality decreased from 28% to less than 3%. There were a total of 28 operative deaths, mostly from myocardial infarction and low cardiac output. Operability was nearly 95%. The only fixed contraindication was chronic congestive failure. Over one-half of the patients had an abnormal ventriculogram, and there was some history of mild congestive failure in nearly 20%. Elevation of left ventricular end-diastolic pressure above 20 mm before operation was associated with a higher operative mortality, but the late mortality was similar to those with a normal preoperative end-diastolic pressure. In 383 surviving patients, angina was eliminated or greatly improved in 86%, unimproved in 12% and worse in 2%. Late angiograms were performed on 201 patients, studying a total of 445 venous grafts with an overall patency rate of 71%. Graft occlusion was sporadic and unpredictable, but over 90% of patients with multiple grafts remained with at least one patent graft. A late myocardial infarction occurred in 32 out of 420 patients surviving operation, and was fatal in eight. The cumulative incidence over a period of five years was 17%. Twenty-three deaths occurred following discharge from the hospital. Life-table analyses showed a five-year survival of 77% when all deaths were included, and a five-year cardiac survival of 81% when non-cardiac deaths were withdrawn alive at the time of death. The expected survival in a comparable population group without coronary disease was 92%, while data published by Sones of patients treated without operation showed a five-year cardiac survival of 66%. Current operative techniques have an operative mortality of 2–3% and a subclinical infarction rate of 5–10%. The ideal graft is yet evolving, but data with internal mammary artery grafts are most encouraging. A future goal should be a five-year graft patency of at least 80%. Because many infarcts probably develop from a relatively small decrease in coronary blood flow, either during rest or mild activity, the likelihood that future data will demonstrate a marked increase in longevity with bypass grafting is great.

THE FIRST CORONARY BYPASS operation was done at New York University in February 1968, an anastomosis of the internal mammary artery to the left anterior descending coronary. During 1968 and 1969 the procedure was cautiously applied to selected patients, but with the prompt relief of angina in most patients, the number of operations rapidly escalated to create the serious logistical question about how many bypass operations could be done annually with the institutional resources available. The decision was made to perform no more than 200–300 operations each year. This limit has been followed since 1970. Hence, the patients operated upon have been automatically selected to some degree as those most seriously disabled with angina, while those with lesser disability were either advised to be operated upon at another hospital, or else operation was not recommended.

By the end of 1973, over 1,000 bypass operations had been performed. For this analysis of late results, only the *elective* bypass operations for angina were considered from the first operation in February 1968 through December 1972, a total of 448 patients. Emergency procedures, operations for pre-infarction angina or myocardial infarction, and those combined with excision of ventricular scars and aneurysms or insertion of prosthetic valves, were excluded.

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* By invitation.

Methods

Indications for Operation

Operation was usually recommended for angina incapacitating the patient from normal activity despite the best medical therapy possible. This of course was a subjective decision influenced by the age, vocation and personality of the patient, as well as the experience of the referring physician. Operation was not advised on a prophylactic basis for angina controlled with medication or for the angiographic demonstration of occlusive disease in an asymptomatic patient. A prophylactic bypass was done only for the unusual condition of occlusive disease in the left main coronary artery, constituting less than 10% of operations performed.

Contraindications to Operation

Within the above criteria, an aggressive policy was pursued to evaluate the applicability and limitations of bypass. Virtually no fixed contraindications to operation were found except protracted congestive heart failure. Advanced age, diabetes, and hypertension were common but were not considered major contraindications. A large percentage of patients had varying degrees of injury of the left ventricle revealed on the ventriculogram, with elevation of end-diastolic pressure (Tables 2, 3), but unless chronic congestive failure was present, operation was recommended. With this aggressive policy, nearly 95% of patients considered candidates for operation were operated upon.[9]

Preoperative Evaluation

The two basic studies before operation were angiography and ventriculography. Significant obstruction was considered present on the angiogram when the diameter of the artery was narrowed more than 60–70%, representing a decrease in cross-sectional area greater than 75–80%. Neither the ability to opacify the artery beyond the obstruction, nor the size of the distal artery were consistently used as a criterion for operation. The ideal angiographic candidate, of course, was one in whom a 2 mm artery could be seen distally. However, a significant number of patients were operated upon in whom no major artery could be seen beyond the obstruction, or the artery distally seemed small, near 1 mm, but was found at operation to be 2 mm or larger. This varying ability to opacify arteries distal to an obstruction probably reflected the variation in amount of collateral circulation present. The only angiographic contraindication to operation was an artery with multiple areas of diffuse obstruction throughout its course. Fortunately this was rare.

Ventriculography was used to estimate the degree of injury of the left ventricle; a subjective decision based upon the extent of impaired contractility from previous infarction and fibrosis. Left ventricular end-diastolic pressure was also measured. More complicated methods of estimating left ventricular function, such as ejection fraction, were not used.

Operative Technique

Details of the operative technique have been described previously;[19] only certain points will be emphasized here. A standard cardiopulmonary bypass was used, with a Temptrol bubble oxygenator and DeBakey roller pumps. Pump prime was a non-blood balanced electrolyte solution, virtually identical to plasma, with 25 g/L of albumin. Perfusion was at a flow rate near $3L/m^2/min$, at 25–30 C. During perfusion mean blood pressure was kept *near that existing beforehand*, a technique employed regularly for the last three years and considered of particular importance in older patients with diffuse atherosclerosis and hypertension. Most anastomoses were performed during induced ventricular fibrillation. In recent years the heart has been periodically defibrillated during the procedure to permit monitoring of the electrocardiogram for any signs of ischemic injury. Periods of ischemia induced by clamping the aorta were progressively limited in extent, rarely using periods longer than 15 minutes and often avoiding clamping of the aorta altogether. A left ventricular vent was almost always used, with monitoring of the left atrial pressure. The duration of perfusion varied from one to more than four hours.

Before bypass was started, a segment of saphenous vein was removed from the lower thigh or upper leg and kept in a 4 C Plasmalyte solution. For the past two years the left internal mammary artery has been regularly used, with the most common procedure being a triple bypass with anastomosis of the left internal mammary artery to the anterior descending coronary, and vein grafts to the circumflex and right coronary arteries. Vein grafts were used however for most operations described in this report. During operation, an attempt was made to bypass almost all diseased arteries, performing a double or a triple bypass in most patients.

Certain points of operative technique should be emphasized. Currently most anastomoses are done end-to-side with interrupted or continuous 6–0 or 7–0 Prolene sutures. Following completion of the distal end-to-side anastomosis with a vein graft, the vein was carefully attached to the surface of the epicardium with sutures about 5 cm apart to curve the vein in a sinusoidal course over the surface of the heart, permitting a free range of motion during cardiac contractions. Straight grafts were avoided. Grafts to the right coronary artery were brought up over the right ventricle, while those to the circumflex were curved along the left atrial-ventricular groove and then across the right ventricular outflow tract and

up to the aorta. This avoided crossing the pulmonary artery. The aortic anastomoses were done with a simple 1 cm longitudinal aortotomy, performing an end-to-side anastomosis with continuous 6–0 Prolene. Meticulous care was taken to remove air from the vein grafts before flow of blood was started. Internal mammary artery anastomoses are currently done by dilating the artery with 30 mg of papaverine placed intraluminally beforehand, and then performing an end-to-side anastomosis with interrupted and continuous 7–0 Prolene sutures.

Following bypass, the rate of blood flow in each graft was measured with a flowmeter, finding a mean flow ranging from as small as 20–30 ml/min to as large as 60–80 ml per min. This, of course, varied primarily with the size of the artery grafted. Before closing the incision, the vein grafts were carefully covered with pericardium in the latter part of the series, as earlier observations indicated that adhesions were much more severe when mediastinal fat, rather than pericardium, was placed over the vein grafts.

Postoperative Care

The essentials of postoperative care were based upon continuous monitoring of the electrocardiogram and the O_2 and CO_2 concentrations in arterial and mixed venous blood. Blood samples were obtained through indwelling catheters left in a peripheral artery and the pulmonary artery at the time of operation. The basic objective was to maintain a PO_2 of 30 mm Hg or greater in the mixed venous blood, this level indicating an O_2 transport by the circulatory system which was adequate for body needs.[1] This method of postoperative monitoring has been regularly used for over 15 years. The most common causes of inadequate O_2 transport were cardiac failure, hypovolemia, or inadequate ventilation. Mechanical ventilation was usually done for a few hours following operation but seldom longer. Tracheostomy was rarely used. Infusions of blood and electrolyte solutions to adjust blood volume were monitored from left atrial or pulmonary artery diastolic pressure. If cardiac failure was present, small amounts of inotropic drugs, 1–2 mcg/min of isoproterenol or epinephrine, were given.

Anticoagulants were used following operation early in the series but not thereafter. Most patients were discharged from the hospital within nine to fourteen days after operation.

Late Management

Following discharge from the hospital, the patients returned under the care of their referring physician but were periodically seen in an out-patient cardiac clinic. As virtually all patients lived within the vicinity of New York City, followup examinations could be readily obtained. Repeat angiography six months following operation was routinely encouraged and accomplished in 201 of the 420 patients surviving operation (48%). In the summer and fall of 1973 a 96% followup of the 448 patients described in this report was accomplished by telephone or by questionnaire, seeing selected patients personally for an out-patient evaluation. Specific attention was given to the determination of the occurrence of angina, infarction, or death.

Statistical Methods

Survival and cumulative incidence curves were obtained by the product-limit life-table method of Kaplan and Meier.[12] When analyzing for the influence of bypass surgery on cardiac-related deaths, non-cardiac deaths were withdrawn alive at the time of death; similarly, when calculating the cumulative incidence of myocardial infarction for patients surviving operation, deaths not related to myocardial infarction were withdrawn alive at the time of death.

Results

Initial Results

The data for the five-year period (1968–1972) are tabulated in Table 1, showing the number of operations performed annually, the frequency of different types of bypass and the operative mortality. Two changes gradually occurred in the series, an increasing number of bypasses performed and a steady decrease in operative mortality. Before 1971 a triple bypass was seldom done because of lack of familiarity with the technique of grafting of the circumflex coronary, as well as the belief that a less extensive operation might be satisfactory.

TABLE 1. *Overall Experience*

Year	Total No. of Patients	Type of Surgery*	No. of Patients	Operative Mortality No. of Operative Deaths	Operative Mortality % Mortality
		SCB	11	2	
1968	14	DCB	3	2	28.6%
		TCB	—	—	
		SCB	6	0	
1969	31	DCB	22	2	6.5%
		TCB	3	0	
		SCB	12	0	
1970	73	DCB	58	8	10.9%
		TCB	3	0	
		SCB	23	0	
1971	152	DCB	59	6	6.5%
		TCB	70	4	
		SCB	21	0	
1972	178	DCB	63	1	2.2%
		TBC	94	3	

* SCB: single coronary bypass
DCB: double coronary bypass
TCB: triple coronary bypass

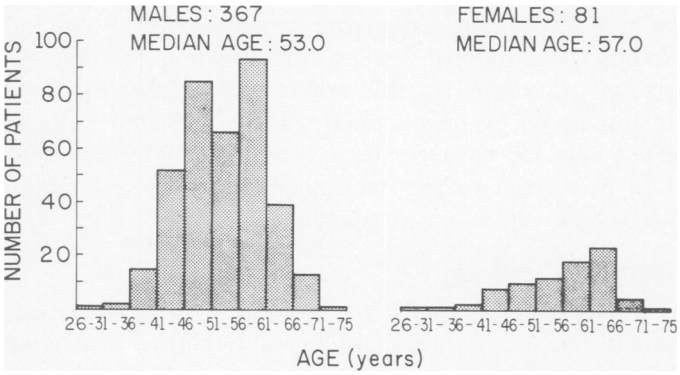

FIG. 1. Histograms of age by sex for 448 patients undergoing coronary bypass surgery between February 1968 and December 1972.

This policy was changed in 1971–1972 to where a triple bypass became the procedure most commonly performed, while a single bypass was rarely done. In the total of 448 patients, 170 had a triple bypass, 205 a double, and 73 a single.

A retrospective analysis of the number of bypass grafts inserted in comparison to the extent of arterial disease, single, double, or triple occlusive disease, was done for the entire period of five years. Between 1968 and 1970, the percentage of patients who had adequate grafts at operation gradually rose from 40 to 63%. During 1971 and 1972, with the increasing use of triple bypass, 84% of diseased arteries were grafted.

The operative mortality decreased from an initial high level of 28% in 1968 to 6% the following year. Since the end of 1971 it has remained less than 3%.

Patients ranged in age from 26 to 72 years (Fig. 1). Eighty-two per cent of the 448 patients were male, with a median age of 53, while 18% were female, median age 57.

Preoperative ventriculography found some impairment of ventricular function in approximately one-half of the patients (Table 2), while in 44% it was normal. There was a localized area of hypokinesis in 27%, a saccular aneurysm in 5%, and diffuse hypokinesia in 17%. Seven per cent of the patients had an inadequate ventriculogram. Corresponding with the frequency of impaired ventricular function was the finding that there was some history of congestive heart failure before operation,

TABLE 2. *Preoperative Left Ventriculogram in 448 Patients*

Description of LV	Number of Patients	%
Normal	199	44%
Diffuse Hypokinesia	76	17%
Local Hypokinesia	120	27%
Aneurysm	23	5%
Inadequate Ventriculogram	30	7%

TABLE 3. *Frequency of Late Death: Number of Grafts and Preoperative LVED*

No. of Grafts	LVED ≤ 12 No. of Patients	LVED ≤ 12 No. of Deaths	LVED 13–19 No. of Patients	LVED 13–19 No. of Deaths	LVED ≥ 20 No. of Patients	LVED ≥ 20 No. of Deaths
One	43	1	16	1	4	0
Two	100	3	49	5	18	0
Three	85	4	55	1	16	1
Totals	228	8 (3.5%)	120	7 (5.1%)	38	1 (2.5%)

usually either mild or intermittent, in about one patient in five (19%). The principal symptom was dyspnea on exertion. On the other hand, about one patient in six (16%) with normal ventricular function had some symptoms, usually dyspnea, consistent with transient congestive failure.

The left ventricular end-diastolic pressure was measured in 91% of patients and found elevated in 42% (Tables 3, 4). The relationship between end-diastolic pressure, the number of grafts inserted at surgery, and operative and late deaths is shown in Tables 3 and 4. Mild elevation of end-diastolic pressure (13–19 mm Hg) had no significant influence on operative mortality (2.4%) when compared with normal end-diastolic pressure (3.4%); but an end-diastolic pressure above 20 mm Hg was associated with a significantly greater mortality (22.4%) (Table 4). However, an elevated end-diastolic pressure before operation did not indicate a serious prognosis for those patients surviving operation (Table 3). The three-year survival for patients surviving operation was virtually identical for those with an elevated end-diastolic pressure as compared with those in whom it was normal, approximately 92%.

There were a total of 28 operative deaths in the overall series of 448 patients (Table 5). Most were due to either myocardial infarction or a low cardiac output. The incidence of subclinical infarction following operation was low, probably in the range of 6–10%. This incidence has been found in two consecutive series of patients studied.[4,18] Such infarcts usually produced no hemodynamic signs but were detected from either the electrocardio-

TABLE 4. *Operative Mortality: Number of Grafts and Preoperative LVED*

No. of Grafts	LVED ≤ 12 No. of Patients	LVED ≤ 12 No. of Deaths	LVED 13–19 No. of Patients	LVED 13–19 No. of Deaths	LVED ≥ 20 No. of Patients	LVED ≥ 20 No. of Deaths
One	43	0	17	1	5	1
Two	107	7	50	1	23	5
Three	86	1	56	1	21	5
Totals	236	8 (3.4%)	123	3 (2.4%)	49	11 (22.4%)

TABLE 5. *Operative Deaths in 448 Patients**

Cause of Death	No. of Patients	Time of Death (days)
Myocardial Infarction	8	1-26
Low Output Syndrome	7	1-24
Arrhythmia	3	1-10
Miscellaneous†	10	1-38
Total	28	1-38

* Within 30 days or never left hospital (only one patient was > 30 days)
† Technical Factors: 5
Infection: 2
CVA: 1
Pulmonary Embolism: 1
Sup. Mesenteric Artery Thrombosis: 1

TABLE 6. *Status of Angina in 383 Patients Following Operation*

Status of Angina	Number of Patients	% of Total
Symptomatic Improvement No angina: 215 (57%) Less angina than preop: 114 (29%)	329	86%
Angina Equal to Preop	48	12%
Angina Worse than Preop	6	2%

gram or from serum enzyme concentrations following operation.

Late Evaluation

Relief of Angina. Information regarding status of angina was available on 383 of 420 patients surviving operation (Table 6). Angina was either completely relieved or significantly improved in 329 patients, 86% of the entire group. It was considered unimproved, equal to that before operation, in 12% and actually worse than before operation in 2%. Usually any type of chest pain was interpreted as possible angina, so the actual frequency of angina may be overestimated, being confused with complications of the sternotomy incision such as fracture of costal cartilages and similar musculoskeletal disorders.

Angiographic Studies of Graft Patency. As mentioned earlier, coronary angiography was strongly recommended on a routine basis 6–12 months following operation. However, asymptomatic patients were naturally reluctant to have angiography again; so this could not be done in many patients. Forty-eight per cent of the group of 420 patients surviving operation were restudied, a total of 201 patients. Frequently the angiograms were done because of reappearance of angina. When angina returned after being absent, it was almost always found that either a graft was occluded or severely narrowed. Very rarely was disease in another artery found as the explanation. Almost never were all of the grafts inserted found to be normal.

Seventy per cent of the angiograms were done within the first year after operation, usually 6–12 months afterward, 19% between one and two years, and the remaining 11% at a later time. Almost all of the significant angiographic data are with venous bypass grafts. Only limited data are available in this 1968–1972 group regarding patency of internal mammary artery grafts though results thus far indicate a patency rate well above 90%. The results are shown in Table 7. Thirty-six single bypass grafts were studied, finding a patency rate of 81%. With 86 double bypass grafts, 51% had both grafts patent, 41% only one patent, while 8% had both occluded. Overall patency in this group for all vein grafts inserted was 72%. Seventy-nine patients with a triple bypass were studied. Thirty-eight per cent of these had all three grafts patent, 34% had two patent, 24% had one patent, while only 4% had all three occluded. Hence, this group was similar to the double bypass group, with an overall patency of 69% for all vein grafts inserted.

These data probably represent some of the lowest patency rates that can be expected with vein grafts, for at operation an aggressive policy was pursued of attaching grafts to most arteries explored, even those diseased and as small as 1 mm internal diameter. It was realized that such grafts might well occlude but rather than simply ligate an artery or attempt to suture the arteriotomy, a graft was usually attached once an arteriotomy had been made. This policy, of course, resulted in a greater frequency of thrombosis and a lower patency. Data were not available to correlate patency rate with such significant factors as diameter of the coronary artery (1.0, 2.0 mm, or greater) or with the rate of flow through the graft afterward.[23]

In the 201 patients studied there were only 17 in whom no grafts were patent. Of these 17, only three had no

TABLE 7. *Patency of Venous Grafts Found on Angiography 6-24 Months After Operation*

No. of Grafts Inserted	Total No. of Patients	No. of Grafts Patent 0	1	2	3	Overall Patency Rate
One	36	7 (19%)	29 (81%)	—	—	81%
Two	86	7 (8%)	35 (41%)	44 (51%)	—	72%
Three	79	3 (4%)	19 (24%)	27 (34%)	30 (38%)	69%

Note: 92 and 96% of patients with two and three grafts inserted respectively, had at least one graft patent.

angina. Nine felt that their angina had improved somewhat but remained to a significant degree. In the others, angina was either equal in severity or worse than that before operation. Previous studies have found a high inverse correlation between patency of vein grafts following operation and the persistence or recurrence of angina.[8]

Cardiac Function. The influence of bypass grafting on impaired cardiac function is not the purpose of this report, but in general, little influence of bypass grafting on cardiac function could be discerned in the 201 patients studied.[21] Unfortunately, patients with impaired ventricular function showed little change after bypass grafting, neither improving nor deteriorating. The failure to improve was discouraging, probably due to irreversible injury, but the lack of further deterioration raised the question of whether the insertion of bypass grafts had prevented further injury.[16]

Late Myocardial Infarction. Myocardial infarction occurred in 32 of the 420 patients surviving operation during the period of observation, and was fatal in eight. The cumulative incidence of late myocardial infarction is shown in Fig. 2, increasing to about 17% five years after operation. Figure 3 shows the five-year probability of surviving without myocardial infarction to be 73%.

Late Mortality. There were a total of 23 deaths following discharge from the hospital (Table 8). By comparison, there were 28 operative deaths, most occurring in 1968–1970; so the largest mortality in the series was at the time of operation, giving an overall operative mortality of 6%. As mentioned earlier, since the end of 1971 the operative mortality has remained less than 3%. The causes of late deaths are shown in Table 8.

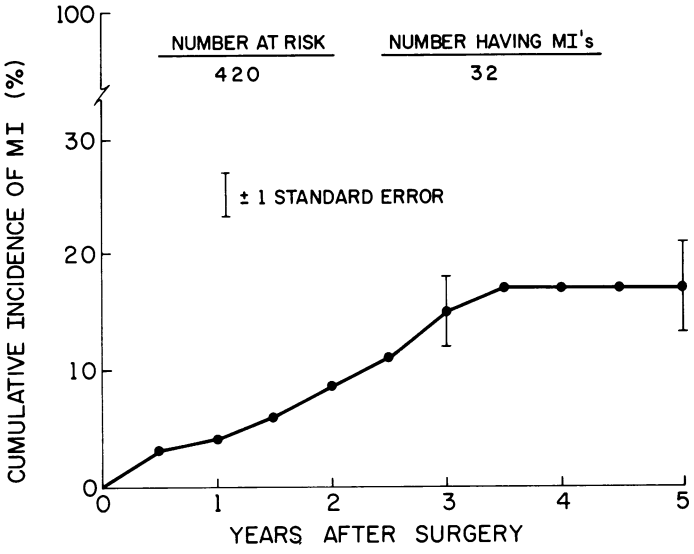

FIG. 2. The cumulative incidence of myocardial infarction in five years following surgery in patients surviving operation. Patients not experiencing myocardial infarction who died were withdrawn alive at the time of death.

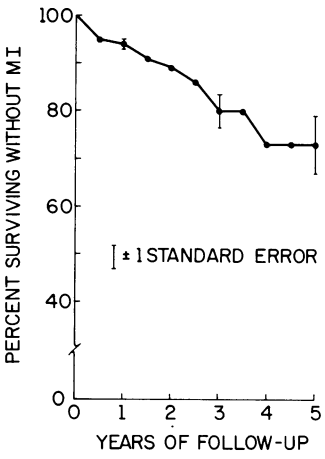

FIG. 3. Five-year survival without myocardial infarction. The curve shows that patients surviving operation had a 73% chance of living five years without myocardial infarction.

Figure 4 shows that when all deaths are included, including operative deaths and deaths from non-cardiac causes, the five-year survival is 77%. If 15 non-cardiac deaths are withdrawn alive at the time of death, the five-year survival is 81%. The expected five-year survival for this study group based on U.S. Population Life Tables (1965) is 92%. Also shown in Fig. 4 is the five-year survival of a group of patients reported by Sones who had coronary disease confirmed by angiography, either single, double, or triple disease, but were not operated upon. The five-year survival was 66%.[2]

The question of bypass grafting for single vessel disease has been particularly scrutinized because this group has the most favorable prognosis with conservative management. It is significant that in this series there were no operative deaths whatsoever following a single bypass graft in the last four years of the study. Four patients died at a later time. The cause of death in one was from non-cardiac causes, while in the other three it was due to disease in other vessels. In no instance was death due to failure of the single bypass graft. Hence, the operative hazard of a single bypass graft is extremely small and the likelihood of sustained benefit great.

TABLE 8. *Causes of Late Death in 420 Patients Surviving Operation*

Cause of Death	Number of Patients	Time of Death Postop (months)
Myocardial Infarction	8	1½ 37
CHF	2	12½ and 33
Arrhythmia	1	3
Death Related to Operation	4	3 46
Miscellaneous*	8	1 33
Total	23	1 46

* Miscellaneous: Infection: 3 CVA: 1 Suicide: 2 Cancer: 1 Pulmonary Insufficiency: 1

In Table 9 the 15 late cardiac deaths are analyzed in relation to two questions: whether all diseased arteries were bypassed at the original operation and the status of the grafts on late angiograms. Unfortunately the crucial data of graft patency at the time of death is unknown in seven of the 15. Hence, definite conclusions cannot be made. It may be significant however, that there are only two patients in the group of late deaths, in whom all three grafts inserted were found patent on subsequent angiography. One of these died 20 months after angiography; so the subsequent development of a graft complication could not be excluded.

Discussion

Operative Considerations

Operative Mortality. As shown in Table 1, operative mortality steadily decreased from an initial high level of 28% in 1968 to the low level of 2.2% in 1972. This decrease was primarily related to changes in operative technique, not to patient selection. The only patients excluded were those with chronic congestive failure after initial experiences had shown both a prohibitive mortality and failure of significant improvement in survivors. However, patients with substantial injury of the left ventricle from previous infarction were consistently operated upon. As shown in Table 2, approximately half of the patients had significant signs of cardiac injury beforehand, in many of whom the end-diastolic pressure was elevated (Table 4).

The principal factors improving operative mortality can only be estimated as these evolved gradually. These are probably the avoidance of long periods of cardiac ischemia, maintenance of a normal blood pressure during operation, decompression of the left ventricle with monitoring of the left atrial pressure during operation, and meticulous avoiding of air embolism. The low mortality has not been related to a short perfusion time, for periods of perfusion of two to three hours have been common with a triple bypass, and a perfusion even for four hours has had little morbidity.

The frequency of operative infarction was measured only in selected samples, but was well under 10%. The absence of a high operative risk in patients with serious impairment of ventricular function may be partly due to the low frequency of operative infarction. Patients with extensive injury of the left ventricle are probably much more vulnerable to operative infarction than those with a normal ventricle beforehand.

As mentioned earlier, impaired ventricular function and an elevated end-diastolic pressure was not associated with a high late mortality (Table 3). This supports the policy of operation upon such patients, realizing that ventricular function will probably not improve but further injury may be prevented. Similar data have been reported by others.[13,16] Actually, a strong thesis can be made for operation upon such patients, for the reserve of functioning left ventricular muscle has already been seriously compromised. Such patients are much less able to withstand loss of additional muscle from a future infarction than those with a normal ventricle.

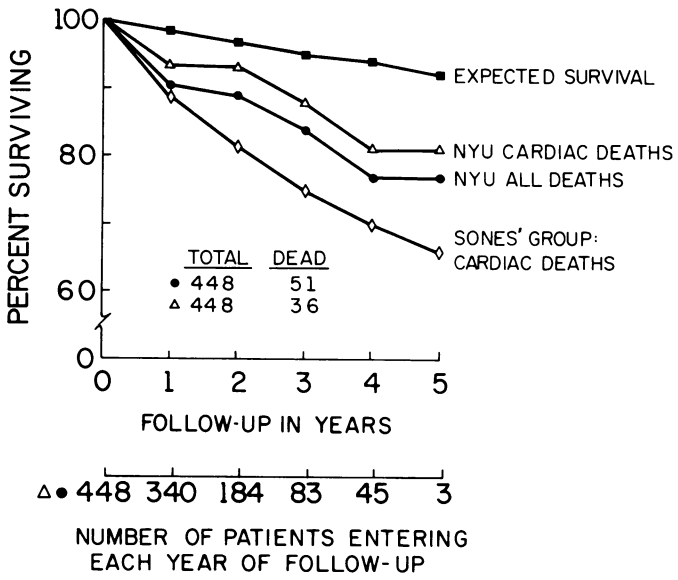

FIG. 4. Life-table survival curves. Expected survival is determined for the same age-sex-race composition as the group under study using U.S. Life Tables for 1965. Survival curves for cardiac deaths (NYU and Sones' group) considered non-cardiac deaths as withdrawn alive at the time of death. Cardiac deaths included deaths due to myocardial infarction, congestive heart failure, arrhythmia, low output syndrome and reoperation for coronary bypass.

TABLE 9. *Relation of Late Cardiac Deaths to Adequacy of Operation and Graft Patency*

Cause of Death	Adequacy of Operation	Graft Patency
1. Arrhythmia	Yes	unknown
2. CHF*	No	unknown
3. CHF	Yes	3/3
4. MI†	Yes	1/3
5. MI	Yes	unknown
6. MI	Yes	unknown
7. MI	Yes	unknown
8. MI	Yes	unknown
9. MI	No	unknown
10. MI	No	1/2
11. MI	Yes	3/3
12. Death related to reop	Yes	1/3
13. Death related to reop	Yes	occluded
14. Death related to reop	No	occluded
15. Death related to reop	Yes	occluded

* CHF: congestive heart failure
† MI: myocardial infarction

As shown in Table 1, a double or a triple bypass was performed on most patients. However, as mentioned earlier, experiences with a single bypass graft were particularly favorable. There was no mortality in the last four years, and no late deaths resulted from failure of the single grafts. Hence, although the five-year mortality for non-surgical patients with single vessel disease reported by Sones is only 14.6%,[2] the outlook following a single bypass graft may be even more favorable.

Improvement in Angina. As noted in many reports, the immediate response after operation in the majority of patients is either elimination or striking improvement in angina. This was true in 86% of this group (Table 6). Angina of course is a subjective sensation, difficult to evaluate with precision, but is the principal symptom of myocardial ischemia. As mentioned earlier, once angina disappeared after operation, its reappearance at a later time almost always indicated stenosis or occlusion of a previously functioning graft. Progression of atherosclerosis in arteries without significant disease at the original operation was an uncommon cause.

Patency of Vein Grafts. The overall patency of vein grafts was 71%, 315 out of 445 grafts studied (Table 7). It was striking, however, that the occlusion of vein grafts was sporadic, and few patients, only 4–8% of those undergoing double or triple bypass grafting, were unfortunate enough to occlude all grafts inserted. Hence, the likelihood of a patient remaining with at least one functioning graft for two years after operation was well over 90%. The recent report by Grondin and associates[10] of serial angiographic studies one to three years after operation showed that most occlusive changes developed in the first year after operation, with patency rates three years following grafting being similar to those one year after operation.

A detailed analysis of the cause of vein graft closure is beyond the scope of this report, but certain observations seem pertinent. The occurrence of segmental occlusion, with comparatively normal segments proximally and distally, is suggestive of a local injury from either trauma at the time of procurement of ischemia during preservation. Szilagyi[22] has emphasized that warm ischemia time for vein grafts may be important because of the smooth muscle in the wall of the vein. This forms the basis of our current practice of keeping vein grafts in a 4 C balanced electrolyte solution until used. The role of adhesions in obstructing grafts was impressive in some patients with a chronic pericarditis which obliterated all grafts within a few months. Reoperation upon several such patients found two distinct findings. First, adhesions were often severe where the grafts were not covered by pericardium but left free in the pericardial cavity, while segments of the graft covered by pericardium were unusually free of adhesions. Following this observation, grafts have been covered with pericardium in almost all patients. The second observation was that straight grafts were peculiarly vulnerable to intermittent tension from the cyclic contraction and relaxation of the heart, with the grafts stretching in diastole and relaxing in systole. A few patients showed a striking proliferation of collagen when adhesions permitted intermittent tugging on the graft, similar to formation of a keloid in a surgical incision crossing a joint. Subsequent to this observation, grafts have been placed in a curved, sinusoidal fashion over the epicardial surface, carefully attaching them with sutures five cm apart. The apposition of lymphatics in the adventitia of the vein graft to those in the epicardium is an additional theoretical advantage.

Grafting combined with endarterectomy was disappointing in a few patients, and subsequently has been almost abandoned. Grafting a vessel as small as 1 mm, with a flow rate of 20 ml or less, was also disappointing and is probably of limited value. A side-to-side anastomosis to these small arteries is now being explored.

Though not the purpose of this report, results with anastomosis with the internal mammary artery to the anterior descending were quite encouraging. This operation was originally developed at New York University by Green and Tice in 1968.[20] During the past two to three years, this artery has been used in over 80% of patients operated upon.[11] Double internal mammary grafts however have not been widely used.

Late Myocardial Infarction and Death. As mentioned earlier, only 32 out of 420 patients surviving operation subsequently developed a myocardial infarction during the period of observation (Fig. 2). A life-table analysis of these data found the probability of surviving five years without an infarction to be 73% (Fig. 3). The overall five-year survival of 77%, including both operative deaths and deaths from non-cardiac causes, (Fig. 4), is most encouraging as it compares to an expected 92% for a similar U.S. population group. If deaths from non-cardiac causes are excluded, the five-year survival is 81%. The best available data for comparison of our results with non-surgical therapy are those of Bruschke and Sones at the Cleveland Clinic, who found, in a consecutive group of 590 cases of coronary disease not operated upon, that the five-year cardiac mortality was 34%, or a survival of 66% (Fig. 4).[2] They reported a five-year cardiac mortality of 15% for single vessel disease, 38% for double vessel disease, and 54% for triple vessel disease. Comparison of the overall five-year cardiac survival of 81%, in our series, with that of Sones' overall five-year cardiac survival of 66%, although favorable, is nevertheless probably adversely influenced by the fact that most patients in our series had double or triple coronary disease. A more precise statistical comparison would be to compare

single, double and triple coronary disease treated by surgical or nonsurgical methods. Furthermore, the surgical results now being obtained will probably show much better long-term results because of improvements in operative technique. A more complete bypass operation is being performed, grafting nearly 85% of all diseased vessels, and the operative mortality is much less, under 3%. Probably the frequency of subclinical infarction is similarly decreased.

In patients developing either a late myocardial infarction or dying from cardiac causes several possibilities can be considered. If all diseased major coronary arteries were effectively grafted, death would represent a failure of bypass grafts. It seems significant that this apparently occurred in only *two* patients in the entire group of 448, both of whom had triple bypass grafts which were subsequently found patent on late angiography. The other general possibility to consider is whether the diseased coronary arteries had effective bypass grafts at the time of deaths. An ineffective bypass could result from either an incomplete operation initially or from late failure of a previously functioning graft. A third possibility is the development of additional occlusive disease in arteries with physiologically insignificant disease at the time of operation. As mentioned earlier, these possibilities are briefly considered in tabular form in Table 9, but few conclusions can be reached as the status of the grafts was unknown at the time of death in seven patients.

Long-term Considerations

1. Indications for Operation. At present there are widely varying approaches to the use of bypass grafting for coronary disease, ranging from bypass grafting for asymptomatic patients following angiographic demonstration of severe stenosis to those who employ grafting only as a last resort or virtually not at all. This series includes predominantly those with severe angina not responding to medical therapy. It seems unlikely that everyone with occlusive coronary disease should require a bypass graft because of the great capacity of many individuals to develop collateral circulation. The crucial question of course is whether or not a patient can develop adequate collateral circulation around an area of occlusion. Clearly many cannot, or otherwise there would not be such a high fatality rate from coronary artery disease. This widely varying capacity of patients to develop collateral circulation is partly responsible for the broad range of clinical syndromes in coronary disease.

2. Harm from Bypass Grafting. The operative risk of bypass grafting has decreased to a surprisingly low level, less than 3% in many centers, indicating its great safety. The occurrence of operative infarction in some series as high as 20%, is distressing and surely can be eliminated with a better understanding of cardiac physiology during bypass. The frequency of infarction has been small in specific groups in this series, but the future goal should be a frequency well under 5%. Apart from operative injury, the theoretical hazard with a bypass graft is inhibition of the development of collateral circulation. In addition, several studies have found that closure of a proximal area of stenosis is accelerated because of change in flow rate. Hence, a graft may not only accelerate the progression of a proximal stenotic lesion but at the same time inhibit the development of collateral circulation. Theoretically, then, if a graft becomes occluded, a patient might be even worse than without operation, having occluded his stenotic artery without developing collateral circulation. Clinically, this has been quite unusual. Apparently graft closure, when it does occur, is at a slow enough rate to permit development of a collateral circulation. Relatively few patients who have occluded previously inserted grafts have required reoperation.

3. Prevention of Myocardial Infarction with Bypass Grafting. The frequent occurrence of a fatal myocardial infarction either during sleep, rest, or mild physical activity, rather than during intense physical activity, suggests that relatively small changes in blood flow may precipitate infarction in an area of severely ischemic myocardium. A common finding at autopsy following a fatal "heart attack" is extensive occlusive disease but no acute change, such as hemorrhage into an atherosclerotic plaque, which might explain the sudden death. Thrombosis in an area of stenosis may be found in some patients, but Roberts has recently published an intriguing hypothesis that the thrombus may develop as a *consequence* of infarction rather than causing it.[17]

The probability that a small decrease in coronary blood flow, in the range of 50–100 ml/min, may precipitate myocardial infarction indicates that a bypass graft to a critical ischemia area could have a profound influence on preventing infarction and prolonging life.

4. Future Goals. At present two major goals for future studies seem clear. First, the objective should be to develop a method of coronary bypass grafting that will produce a consistent patency rate of at least 80% five years after operation. This has been achieved by several investigators with venous bypass grafts for femoral-popliteal disease over the past 15 years; so this goal is theoretically attainable.[5,6] It appears that an arterial graft has a much better probability of remaining patent, but a comparison of long-term results between arterial and venous grafts is not yet available. Possibilities such as the use of a radial artery or the splenic artery have been explored by some investigators.[3,7] If a patency rate of 80% for five years can be achieved, it seems highly probable from the data presented in this report that

significant prolongation of life and protection from myocardial infarction can be achieved. Answers will come primarily from comparative prospective studies of medical and surgical therapy, preferably randomized. A nonrandomized comparative study has recently been published by McNeer and Rosati, analyzing nearly 90 variables in 402 patients treated medically and 379 patients treated surgically. A particularly ominous prognosis was found in patients with triple disease and an abnormal ventriculogram, with a two-year mortality between 61% and 76% with medical therapy.[15] For disease groups to be comparable, certain specifications seem crucial. An angiogram must obviously be obtained. Otherwise the great overlap in clinical syndromes between single, double and triple coronary disease makes comparative data almost impossible. A second consideration is the presence of symptoms, for there is widespread individual variation in the ability to develop collateral circulation. A patient who becomes asymptomatic after occlusion of a major artery by development of adequate collateral circulation is surely not comparable to one who remains symptomatic from occlusion of a similar artery because collateral circulation is inadequate. Hence, the need exists for randomized studies of comparable patients. Such studies are currently being developed by the National Institutes of Health. Only by objective comparison of such data over a period of years can decisions be made regarding the immense logistical question of widespread use of bypass grafts for coronary disease in the mildly symptomatic or asymptomatic patient.

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