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Late Results of Surgical and Medical Therapy for Patients With Coronary Artery Disease and Depressed Left Ventricular Function

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Late survival and freedom from myocardial infarction were determined for 192 patients with coronary artery disease and depressed left ventricular ejection fraction at rest (≤35%) determined by biplane angiography who were evaluated between 1970 and 1977. Seventy-seven patients had coronary artery bypass grafting and 115 patients were treated medically and were considered surgical candidates. The medical and surgical groups were comparable in all baseline characteristics examined except frequency of three vessel disease and angina pectoris, which occurred in a significantly greater percent of the surgically treated patients ($p < 0.01$). Only three medically treated patients (2.6%) underwent coronary bypass grafting in the follow-up period.

Seven year actuarial survival was 63% in the surgical and 34% in the medical group ($p < 0.001$). Ninety-three percent of patients in the surgical group and 81% of those in the medical group were free of nonfatal myocardial infarction ($p = 0.01$), and 62 and 33%, respectively, were alive and free of myocardial infarction ($p < 0.001$) at 7 years. Significant differences in survival favoring surgical treatment were observed for the subsets of patients with an ejection fraction of 25% or less ($p = 0.0002$) and 26 to 35% ($p = 0.01$), and for the subsets with three vessel coronary disease ($p < 0.001$), normal left ventricular end-diastolic volume (≤100 ml/m²) ($p = 0.005$) and elevated end-diastolic volume (>100 ml/m²)($p = 0.001$). After adjustment for other important prognostic variables, the type of treatment remained significant in predicting the relative risk (medical to surgical) of mortality at 5 and 7 years (2.58 and 2.12, respectively).

These data corroborate the trends observed in several randomized trials of medical and surgical therapy in patients with abnormal left ventricular function. If hospital mortality for coronary artery bypass grafting is less than 5%, substantial benefit can be anticipated for the majority of patients with depressed ventricular function.

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Coronary artery bypass grafting has been conclusively shown in both observational studies and prospective randomized trials to be more effective than medical therapy in relieving the symptoms of angina pectoris and in improving the functional status of patients with significant coronary artery disease and preserved ventricular function. With the exception of patients with left main coronary artery disease, the results of randomized trials comparing the effect of medical and surgical therapy on survival and nonfatal coronary events are inconclusive (1–4). Only the European Coronary Surgery Study Group (3) demonstrated significantly increased survival in patients with three vessel disease treated surgically. These major studies have focused on patients without substantial impairment of left ventricular function: an ejection fraction greater than 30% in the Cooperative Study of Unstable Angina (1), greater than 25 to 30% in the Veterans Administration Cooperative Study (2), greater than 50% in the European Coronary Surgery Study (3) and greater than 35% in the Coronary Artery Surgery Study (CASS) (4). However, both the Veterans Administration Study and the CASS demonstrated trends in survival favoring surgical treatment in patients with three vessel coronary disease and moderate impairment of ventricular function (ejection fraction 25 to 50%).

Thus, the indications for coronary artery bypass grafting in such patients and those with more severe impairment of ventricular function remain incompletely defined. In view of the lack of sufficient data from randomized studies, we reviewed the results of surgical and medical therapy for a

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7 year period for patients with depressed ventricular function defined by the left ventricular ejection fraction and end-diastolic volume at rest. The principal outcome events examined were survival and freedom from nonfatal myocardial infarction.

Methods

Patient selection. Between January 1970 and December 1977, a total of 6,600 patients were prospectively entered into the Ischemic Heart Disease Registry at the University of Alabama Medical Center in Birmingham. This registry included all patients who had coronary arteriography at the medical center during this interval and the subset who underwent coronary artery bypass grafting. It also included patients having coronary artery bypass grafting who had preoperative coronary arteriography performed elsewhere. Stenoses of 50% or greater of the left main coronary artery and of the three major coronary arteries or their primary branches at angiography were considered significant. The patients were classified into three anatomic subsets: one, two and three vessel disease. Patients with isolated left main coronary artery stenosis were classified as having three vessel disease if the right coronary artery had a significant stenosis, and as having two vessel disease if it did not.

Biplane ventriculography was performed in approximately 1,500 of the 6,600 patients. Left ventricular volumes (end-systolic and end-diastolic) and left ventricular ejection fraction were calculated using the area-length method of Dodge et al. (5). Two hundred ten of these patients had significant coronary artery disease and ventriculograms suitable for analysis with a left ventricular ejection fraction of 35% or less; these constitute the study group. Patients with associated valvular heart disease, discrete areas of akinesia or dyskinesia of the left ventricle that might require excision, rupture of the ventricular septum, ascending aortic aneurysms or congenital cardiac lesions were excluded from the analyses.

Surgically treated patients. Seventy-seven of the 210 patients underwent coronary artery bypass grafting. Disabling angina pectoris was the most common indication for operation. Patients with little or no angina, with or without symptoms of congestive failure, but with areas of viable myocardium supplied by stenotic arteries were also operated on. Advanced age was not a contraindication to operation. The details of the anesthetic, intraoperative and postoperative management of patients having coronary artery bypass grafting at our institution during the study interval have been previously described (6).

Medically treated patients. The coronary arteriograms of the remaining 133 patients were retrospectively reviewed to determine the suitability of the coronary arteries for bypass grafting using current criteria. Eighteen patients were excluded from further analysis because of the absence of two or more major coronary arteries or their primary branches which could accept grafts. The remaining 115 patients had two or more arteries suitable for grafting and constitute the medical group. The decision for initial surgical or medical therapy was made jointly by the attending physicians and the patients. The reasons for initial medical therapy in the 115 patients are listed in Table 1. Using our current criteria, all of the 18 patients who were originally classified as having unsuitable coronary artery anatomy were considered surgical candidates.

Baseline characteristics. The pertinent baseline, clinical and angiographic characteristics of the 77 surgical and 115 medical patients are shown in Table 2. Unstable angina was defined as recent onset of angina or a change in the pattern of pain (frequency, severity and duration), or onset of rest or nocturnal angina, or both, in the 3 months preceding angiography. Congestive failure was defined as exertional dyspnea plus paroxysmal nocturnal dyspnea, orthopnea or edema. A history of myocardial infarction required that the patients had been informed by a physician of a definite infarction or the presence of Q waves on the baseline electrocardiogram.

Follow-up. Follow-up information was obtained by yearly visits to an outpatient facility at our medical center or by telephone interview of the patients and their physicians at similar intervals. Follow-up information was available for 76 (99%) of the patients treated surgically and 112 (97%) of those treated medically. The mean duration of follow-up was 62 months in the surgical group and 45 months in the medical group. The causes of death were determined by postmortem examination when available, by death certificate or by a statement from the attending physician. The occurrence of nonfatal myocardial infarction was determined from a hospital record that showed a diagnosis of acute myocardial infarction and from electrocardiograms obtained at the annual follow-up visits using selected criteria from the Minnesota code (7).

Statistical methods. Comparisons of the surgical and medical groups were made using standard life table methods (8). Exposure was calculated from the time of cardiac catheterization in both groups. Fifty percent of the surgically

Table 1. Reasons for Medical (versus surgical) Therapy in the 115 Patients

	Patients	
	No.	%
Poor left ventricular function	62	54
Coronary anatomy unsuitable for surgery	18	16
Asymptomatic	16	14
Refused operation	14	12
Randomized (CASS)	5	4
Total	115	100

CASS = Coronary Artery Surgery Study.

Table 2. Baseline Characteristics of the Medically and Surgically Treated Patients

	Surgical (n = 77)	Medical (n = 115)	p Value
Clinical variables			
Mean age (yr)	54	54	NS
% Male	88	89	NS
% Angina	65	37	<0.001
% Unstable angina	52	29	<0.002
% Congestive failure	21	26	NS
% Previous myocardial infarction	92	88	NS
% Hypertension	38	47	NS
% Diabetes	12	9	NS
Hemodynamic Variables			
Mean ejection fraction (% ± SD)	0.27 ± 0.07	0.25 ± 0.07	NS
% Three vessel disease	64	57	<0.01
Mean number of diseased vessels	2.8	2.4	NS
% Left main coronary artery stenosis	3	0	NS

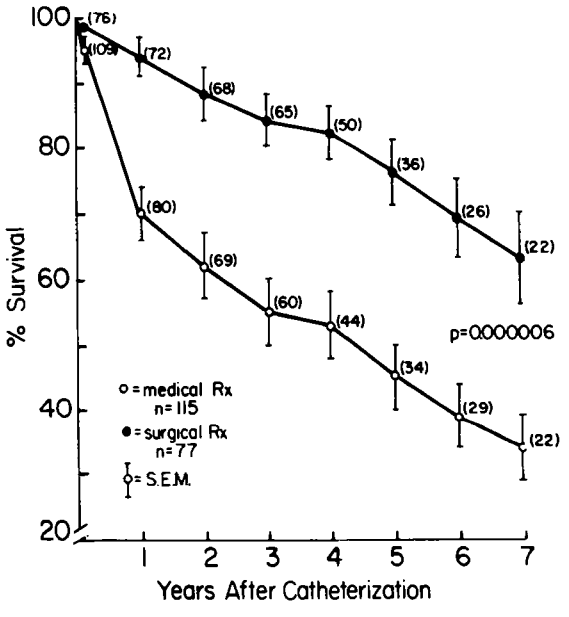
NS = not statistically significant ($p > 0.05$).

treated patients underwent coronary artery bypass grafting within 60 days of catheterization and 80% within 90 days; the median interval from catheterization to operation was 45 days. No patients for whom surgical treatment was advised died while awaiting operation. The problems related to retrospective comparisons of surgically and medically treated patients with coronary artery disease are well recognized and have been addressed in detail in recent publications from the Coronary Artery Surgery Study (CASS) (9,10). Because no patient in our study died while awaiting surgical treatment and a high percent of the surgically treated patients were operated on within 90 days of catheterization, use of the date of catheterization as the date of initial exposure for both groups appears justified.

Survival, freedom from nonfatal myocardial infarction and survival free of myocardial infarction (event-free survival) were determined for both groups. In the analyses of freedom from infarction, deaths were treated as censored observations (11). In the analyses of event-free survival, patients were withdrawn at the time of the first event (death or myocardial infarction). At the date of the last inquiry (April 1982), three of the medically treated patients had undergone coronary artery bypass grafting 25, 31 and 35 months, respectively, after catheterization. They were withdrawn from the medically treated group at these intervals.

Differences in the baseline characteristics of the patients in the two groups were analyzed using chi-square techniques for discrete variables and the two sample *t* test for continuous variables. The observed differences in survival and freedom from infarction between the surgical and medical groups were tested by the log rank (Mantel-Hantzel chi-square) test. The proportional hazards method of Cox (12) was used to adjust for covariates of survival. Analyses of end point events adjusted for the covariates angina, unstable angina, ejection fraction, left ventricular end-diastolic volume, year of catheterization, number of vessels diseased and type of treatment were performed for the 5 and 7 year intervals using likelihood ratio tests and compared with the chi-square distribution. The survival and event-free survival curves for all patients (Figs. 1 to 12) extend to 7 years. The dashed lines at the ends of these curves in Figures 3, 6 and 10 encompass an interval in which there were no deaths. The vertical bars represent the standard error.

Figure 1. Cumulative survival of the 77 surgically treated and 115 medically treated (Rx) patients. Numbers in parentheses are the patients alive at the end of that interval. Seven year survival rates were 63 and 34%, respectively. SEM = standard error of the mean.



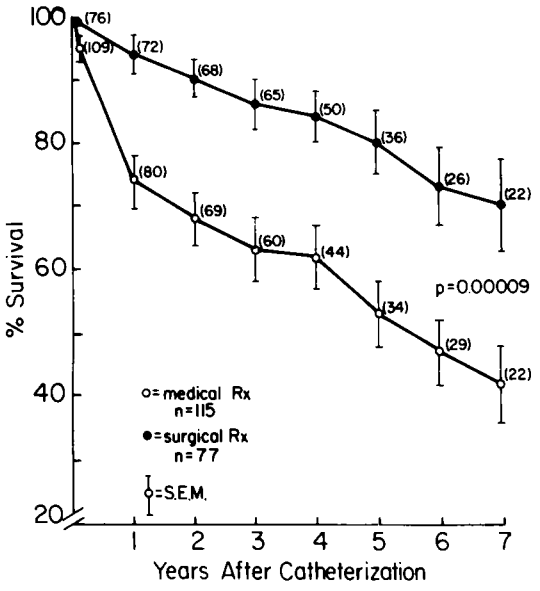


Figure 2. Cumulative survival of the 77 surgically treated and 115 medically treated patients excluding deaths from causes other than cardiovascular disease. Seven year survival rates were 70 and 42%, respectively.

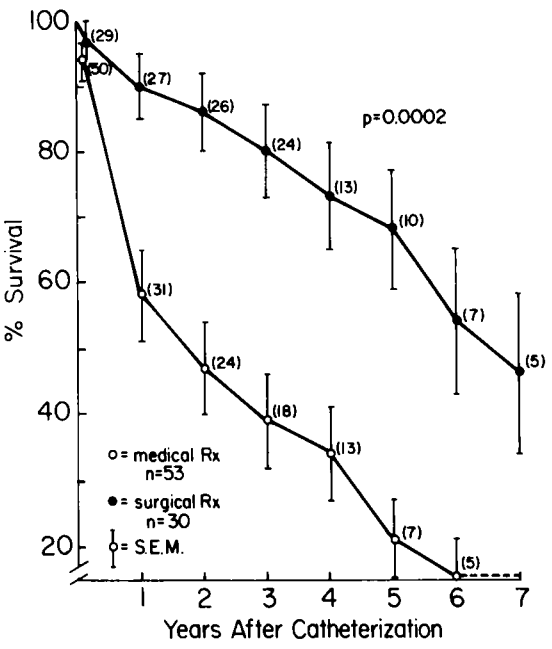


Figure 3. Cumulative survival of 30 surgically treated and 53 medically treated patients with an ejection fraction of 25% or less. Seven year survival rates were 46 and 15%, respectively.

Results

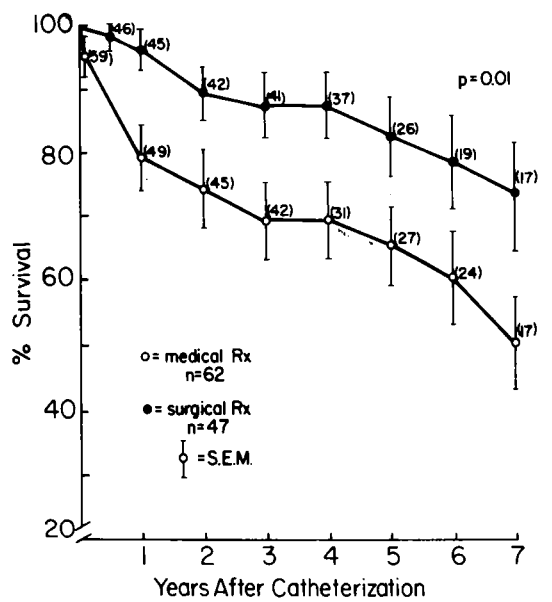
Survival

Overall survival. There was 1 hospital death among 77 surgically treated patients (1.3%). This patient had three vessel disease and an ejection fraction of less than 25%. The cumulative survival rates of the 77 patients treated surgically and the 115 patients treated medically are shown in Figure 1. The 5 year survival rate was 76 and 45%, and the 7 year rate was 63 and 34% for the surgical and the medical groups, respectively ($p < 0.001$). When deaths from causes other than cardiovascular disease were excluded, respective survival at 5 years was 80 and 50% and at 7 years 70 and 42% for the surgical and the medical groups ($p < 0.001$) (Fig. 2). Sudden death (death within 24 hours of onset of symptoms) occurred in 9 (11.8%) of the 76 surgically treated hospital survivors and in 27 (23.5%) of the 115 medically treated patients ($p = 0.04$).

Effect of angiographic variables. *Ejection fraction.* Thirty surgically treated patients and 53 medically treated patients had an ejection fraction of 25% or less (mean ± SD = 19.6 ± 5.2 and 18.4 ± 5.2, respectively)(p = NS). Survival at 5 years was 68% for the surgically treated patients and 21% for the medically treated patients; at 7 years these rates were 46 and 15%, respectively ($p = 0.002$) (Fig. 3). For the 47 surgically treated patients and 62 medically treated patients with an ejection fraction between 26 and 35% (mean ± SD = 31.1 ± 3.3 and 30.5 ± 3.2, respectively) (p = NS), the respective 5 year survival rates were 82 and 64%, and the 7 year rates 73 and 50% ($p = 0.01$)(Fig. 4).

Ventricular volume. Left ventricular volume determinations with normalization for body surface area were available for 74 (96%) patients in the surgical group and 105 (91%) of those in the medical group. A left ventricular end-

Figure 4. Cumulative survival of the 47 surgically treated and 62 medically treated patients with an ejection fraction between 26 and 35%. Seven year survival rates were 73 and 50%, respectively.



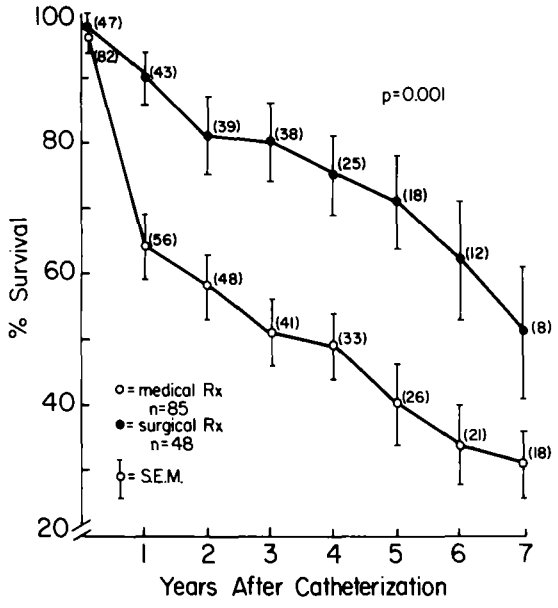


Figure 5. Cumulative survival of the 48 surgically treated and 85 medically treated patients with an abnormally elevated left-ventricular end-diastolic volume (>100 ml/m^2 of body surface area). Seven year survival rates were 51 and 31%, respectively.

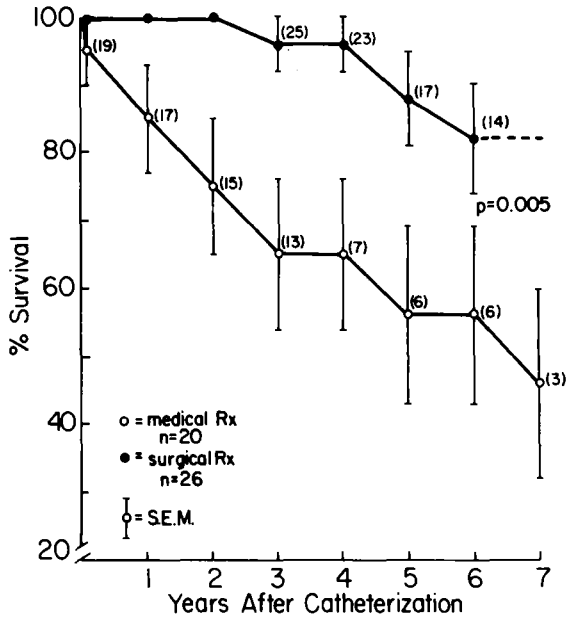


Figure 6. Cumulative survival of the 26 surgically treated and 20 medically treated patients with a normal left ventricular end-diastolic volume. Seven year survival rates were 88 and 56%, respectively.

diastolic volume of 100 ml/m^2 body surface area or less was considered normal. Forty-eight (65%) surgically treated patients and 85 (81%) medically treated patients had an abnormal end-diastolic volume (mean ± SD = 145 ± 42 and 150 ± 47 ml/m^2, respectively)(p = NS). Survival rates at 5 years were 71% for the surgical group and 40% for the medical group and at 7 years, 51 and 31%, respectively (p = 0.001)(Fig. 5). For the 26 patients treated surgically, and the 20 patients treated medically with a normal end-diastolic volume, survival at 5 years was 88 and 56%, and at 7 years 82 and 46%, respectively (p = 0.005)(Fig. 6).

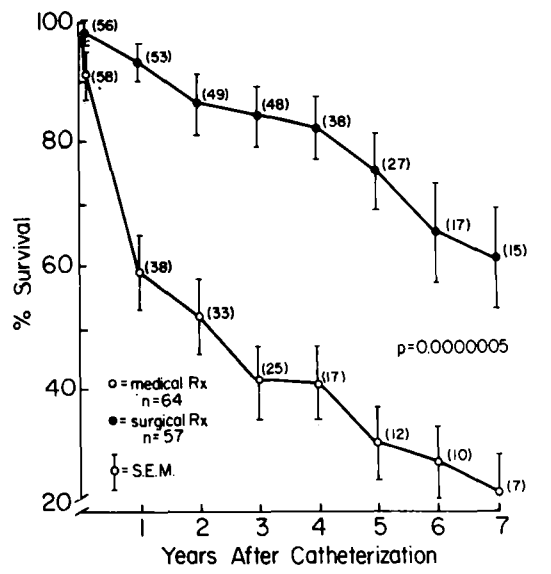
Extent of coronary artery disease. Fifty-seven patients in the surgical group and 64 in the medical group had three vessel disease. Survival at 5 years was 75 and 31% and at 7 years 61 and 25%, respectively, for the two groups (p < 0.001)(Fig. 7).

Myocardial Infarction

Nonfatal infarction. Follow-up information on the incidence of nonfatal myocardial infarction was available for 75 (97%) patients in the surgical group and 103 (90%) of those in the medical group. Fifteen patients (3 in the surgical group and 12 in the medical group) had one or more infarctions. None of the infarctions in the surgical group occurred in the early postoperative period. At both 5 and 7 years, 93% of patients in the surgical group and 81% of those in the medical group were free of nonfatal infarction (p = 0.01)(Fig. 8).

Infarction-free survival. Survival free of myocardial infarction at 5 years was 75% for the entire surgical and 43% for the entire medical group, and at 7 years was 62 and 33%, respectively (p < 0.001) (Fig. 9). For the subset of patients with an ejection fraction of 25% or less, the 5

Figure 7. Cumulative survival of the 57 surgically treated and 64 medically treated patients with three vessel disease. Seven year survival rates were 61 and 25%, respectively.



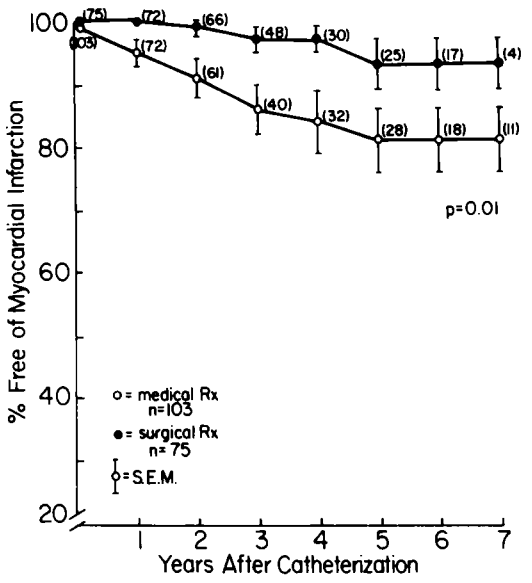


Figure 8. Cumulative incidence of freedom from nonfatal myocardial infarction for 75 surgically treated and 103 medically treated patients with available follow-up information. Seven year rates were 93 and 81%, respectively.

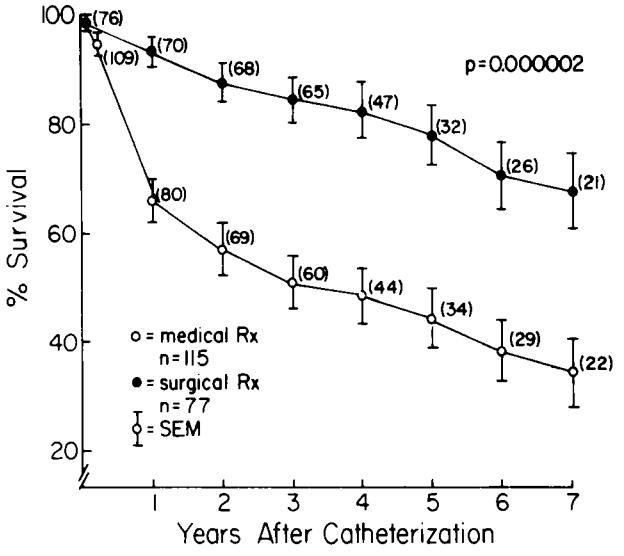


Figure 9. Cumulative survival free of nonfatal myocardial infarction for the 77 surgically treated and 115 medically treated patients. Seven year survival rates were 62 and 33%, respectively.

year event-free survival rates were 68 and 21%, and the 7 year rates were 46 and 15%, respectively ($p = 0.0003$) (Fig. 10). For the subset with an ejection fraction between 26 and 35%, the 5 year event-free survival rates were 82% in the surgical group and 65% in the medical group, and at 7 years were 73 and 50%, respectively ($p = 0.02$)(Fig. 11). For the 57 patients in the surgical group and the 64 patients in the medical group with three vessel coronary disease, the respective event-free survival rates were 75 and 31% at 5 years and 61 and 23% at 7 years ($p < 0.001$)(Fig. 12).

Multivariate Analyses

Data from 179 of the 192 patients were analyzed using the proportional hazards model of Cox (12) at 5 and 7 year intervals. After adjustment for other important prognostic variables, the type of treatment (surgical or medical) remained statistically significant in predicting the relative risk of mortality at 5 and 7 years (Table 3). The relative risk (medical to surgical therapy) was 2.58 at 5 years and 2.12 at 7 years. Adjustment of ventricular volumes to calculated body surface areas did not alter the results.

Discussion

Role of left ventricular dysfunction. Left ventricular function is the most important independent predictor of survival for patients with coronary artery disease treated nonsurgically (13,14). It is also an important predictor of in-

Table 3. Cox Regression Analysis and Proportional Hazard Functions

Covariates	5 Year Coefficients		7 Year Coefficients	
	Treatment Excluded	Treatment Included	Treatment Excluded	Treatment Included
Angina	0.148	0.160	0.185	0.200
Unstable angina	0.337	0.292	−0.513	−0.483
Ejection fraction	−0.028	−0.028	−0.025	−0.026
Ventricular end-diastolic volume	0.006	0.005	0.005	0.005
Year of catheterization	1.007	0.074	−0.076	−0.054
Number vessels diseased	0.438	0.465	0.293	0.310
Treatment (medical, surgical)		−0.949		−0.753
Test for overall model	χ^2 = 32.6	χ^2 = 38.8	χ^2 = 30.9	χ^2 = 35.7
(degrees of freedom)	(6)	(7)	(6)	(7)
Test that treatment is significant	χ^2 = 6.13		χ^2 = 4.76	
p Value	0.013		0.029	
Relative risk (medical to surgical)	2.58		2.12	

JACC Vol. 5, No. 5
May 1985:1036–45

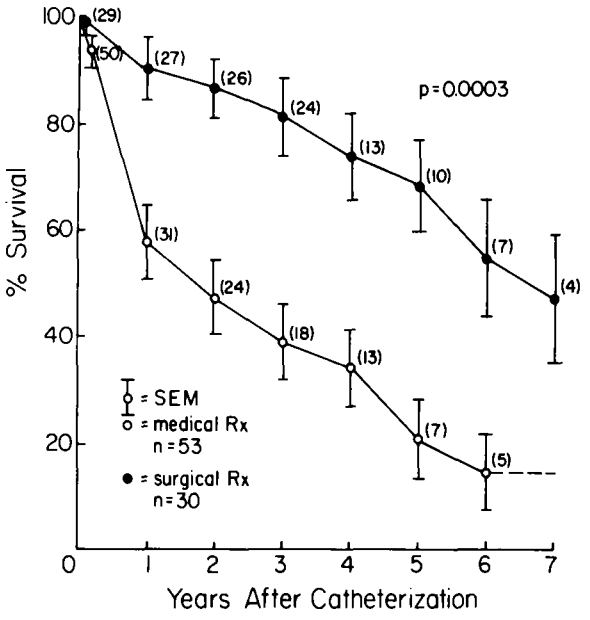


Figure 10. Cumulative survival free of nonfatal myocardial infarction for the 30 surgically treated and 53 medically treated patients with an ejection fraction of 25% or less. Seven year survival rates were 46 and 15%, respectively.

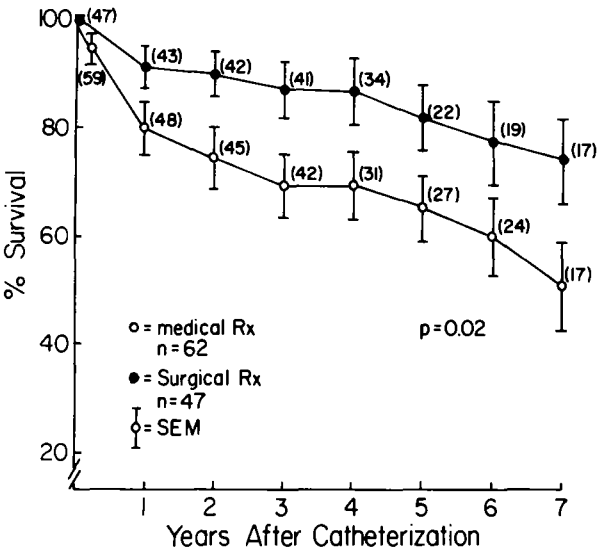


Figure 11. Cumulative survival free of nonfatal myocardial infarction for the 47 surgically treated and 62 medical treated patients with an ejection fraction between 26 and 35%. Seven year survival rates were 73 and 50%, respectively.

hospital and late mortality after coronary artery bypass grafting (15–18). Rest left ventricular ejection fraction and left ventricular wall motion score are two variables that have been used to quantitate the severity of left ventricular dysfunction. An ejection fraction at rest of 25% or less and a left ventricular wall motion score of 17 to 30 (normal = 5) have been associated with poor long-term survival in patients treated medically and are more powerful predictors of survival than is the extent of coronary artery disease (4).

Assessment of the relative efficacy of medical and surgical therapy of coronary artery disease can be best accomplished by prospective randomized trials. To date, no such trials have been performed in patients with substantially impaired ventricular function using left ventricular ejection fraction or some other precise descriptor of ventricular function such as the wall motion score. The randomized portion of the Coronary Artery Surgery Study (CASS) contains a subset of patients with three vessel disease and left ventricular ejection fraction between 35 and 49% for whom a trend (not statistically significant) in favor of surgical treatment was observed (4).

Natural history and observation studies. In the absence of randomized trials, useful information may be obtained from natural history and observational studies provided that the relevant clinical and angiographic variables of the groups under study are documented. A summary of the results of nonoperative therapy in five published (10,14,19–21) series of patients with a left ventricular ejection fraction of 35% or less is shown in Table 4. Despite similar degrees of left ventricular dysfunction, the patients in these series differed in other important characteristics. Patients with left ventricular aneurysm were included in some series and excluded in others. Not all patients in each series were considered suitable candidates for bypass grafting. The number of patients who crossed over to surgical therapy during the follow-up intervals, primarily because of worsening symptoms (usually angina pectoris), varied from 9 to more than 33%. Because patients managed nonoperatively who have "progressive" symptoms have been shown by Harris et al. (19) to have a higher ischemic death rate in the early years after diagnosis than that of patients with "nonprogressive" symptoms, withdrawal from the medical group of substantial numbers of patients whose symptoms worsen may yield more favorable survival curves for the remaining patients. These curves will not accurately reflect the true natural history of the patients originally under study. These and possibly other undetected differences could account for the widely differing survival rates observed and, as emphasized by Mock et al. (14), demonstrate the unsuitability of such survival data for comparison with the survival of groups of patients with similar degrees of left ventricular dysfunction treated surgically.

In the present study, all patients in the medical group were considered suitable candidates for bypass grafting. The patients in the medical and surgical groups were evaluated and treated concurrently by the same physicians and surgeons during the 7 year interval. Patients who were be-

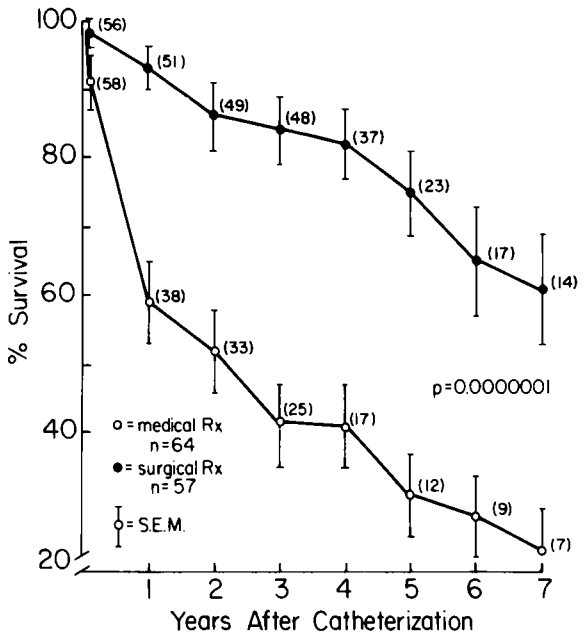


Figure 12. Cumulative survival free of nonfatal myocardial infarction for the 57 surgically treated and 64 medically treated patients with three vessel coronary disease. Seven year survival rates were 61 and 23%, respectively.

lieved to have a ventricular aneurysm or scar that would require excision were excluded. Only three patients (2.6%) in the medical group underwent bypass grafting in the follow-up interval, and they each had received medical therapy for at least 2 years. Thus, the survival data of our medical group may be more representative of the natural history of patients with severely depressed left ventricular function than those from the previously published series.

Baseline characteristics. In our study, differences in the baseline characteristics of the medically and surgically treated patients did exist. The surgically treated patients had a significantly greater prevalence of angina, unstable angina and three vessel disease. Similar differences were observed by Vlietstra et al. (17), Faulkner et al. (20) and the CASS investigators (10) for patients in the nonrandomized registry portion of the study with an ejection fraction of 35% or less who had medical or surgical therapy. In the CASS (10), when these and other covariates were adjusted by multivariate analysis, surgical treatment was shown to significantly improve survival. Similarly, in our study, surgical therapy was a significant independent predictor of survival in the multivariate analyses (Table 3). Furthermore, when patients with threee vessel disease were compared, survival was significantly greater in the surgical group (Fig. 7). It is possible that other undetected differences exist between our medical and surgical groups which could have biased selection of patients for one or the other form of therapy and affected survival. However, the major prognostic variables currently recognized as significant were considered simultaneously in the analyses of survival, and the results were consistent throughout the period of follow-up.

Hospital mortality. Hospital mortality for the surgical group was low (1.3%). However, this was a nonconsecutive series of patients, since other patients with left ventricular dysfunction that was not quantitated by biplane ventriculography were operated on during the period of study. Data from the CASS (18) for 5,024 patients operated on between

Table 4. Previous Studies on Survival of Medically Treated Patients With Depressed Ventricular Function

	No. of Patients	Ejection Fraction (%)	Inclusion of Patients With Ventricular Aneurysm	Suitability of all Patients for Bypass Grafting	Cross-Over Rate (%)	Cumulative Survival (%)		
						4 Year	5 Year	6 Year
Harris et al. (19) 1967 to 1978	152	<25*	Yes	No	10	44	38	33
Faulkner et al. (20) 1969 to 1975	70	<30	No	No	†	7	†	†
Alderman et al. (21) 1973 to 1978	48	≤35	No	†	†	†	20	†
Mock et al. (14) (CASS) 1975 to 1979	909	<35	†	No	>33	58	52‡	†
Alderman et al. (10) (CASS) 1975 to 1979	420	<35§	Yes	Yes	9	61‖	54	46

*Estimated (diffusely abnormal contractions); †not stated; ‡unpublished data; §plus wall motion score ≥12; ‖survival curve adjusted for other prognostic variables.

August 1975 and December 1978 showed a hospital mortality rate of 2.5% for 404 patients with an ejection fraction of 39% or less and 4.7% for 107 patients with an ejection fraction of 29% or less. These data were obtained from 15 centers of varying size and distribution in North America, including the University of Alabama in Birmingham, and are probably most representative of the results of bypass grafting during that time period. As emphasized by Alderman et al. (10), hospital mortality for the subset of patients with an ejection fraction of 35% or less must not exceed the 7% value observed in the CASS registry to demonstrate a significant difference in survival in favor of surgical treatment. With current operative techniques, including the use of hypothermic cardioplegia for intraoperative myocardial protection which was used infrequently before 1977 (6), hospital mortality for elective coronary artery bypass grafting in this subset of patients with left ventricular dysfunction (ejection fraction ≤35%) should not exceed 5%.

Prognostic value of ejection fraction. The severity of left ventricular dysfunction as assessed by the left ventricular ejection fraction had an adverse effect on survival in both the medically and surgically treated groups (Fig. 3 and 4). Similar differences were observed in the CASS nonrandomized registry of patients with an ejection fraction of 35% or less treated medically and surgically (10). In every subset examined in our study and in the CASS, the surgically treated patients had a higher survival rate. The differences were statistically significant, however, only for the subset of patients with an ejection fraction of 25% or less (CASS and our study) and in our study for the subset with an ejection fraction between 26 and 35%.

A major uncertainty regarding the use of depressed left ventricular ejection fraction as an indicator of impaired left ventricular function is the inability of this variable to differentiate myocardium that is depressed because of reversible ischemia from myocardium depressed by fibrosis from previous infarction. Furthermore, these conditions may coexist in the same patient. More sensitive tests for the detection of reversibly ischemic myocardium, such as measurement of ejection fraction during exercise or scintigraphic studies to distinguish between ischemia and fibrosis, were not available in the early years of the study and were used only selectively in the later years, resulting in insufficient numbers for statistical comparison. Elevated end-diastolic volume may be a more specific indicator of the presence of myocardial fibrosis in patients with coronary artery disease than is the ejection fraction at rest, and in univariate analyses it has been associated with poor long-term survival (13). In our study, the late survival rate of both medically and surgically treated patients with an elevated left ventricular end-diastolic volume was lower than that for the corresponding patients with a normal end-diastolic volume (Fig. 5 and 6). Significantly greater survival of the surgically treated patients with an elevated end-diastolic volume suggests that bypass grafting may be beneficial in patients with substantial left ventricular fibrosis. The specific mechanism for this beneficial effect is unknown, but it may relate to the prevention or delay of additional myocardial fibrosis afforded by the bypass grafts.

The survival of patients with depressed ejection fraction and three vessel coronary disease treated medically was lower than that of the medically treated group as a whole (Fig. 1 and 7). The difference in survival between medically and surgically treated patients in this subgroup was highly significant (Fig. 7). In the randomized portion of the CASS (10), the difference in survival between medically and surgically treated patients with three vessel disease and a lesser degree of left ventricular dysfunction (ejection fraction 35 to 49%) followed up for 5 years approached statistical significance ($p = 0.063$).

The incidence of nonfatal myocardial infarction was significantly lower in the surgically treated group (Fig. 8). Survival free of myocardial infarction was greater for the surgically treated patients with both moderate and severe depression of ventricular function and for the subset with three vessel disease (Fig. 10 to 12).

Therapeutic implications. Our data confirm the findings of previous studies which indicate that left ventricular function is an important predictor of survival in patients with coronary artery disease treated medically or surgically. In all subsets of patients we examined, survival of surgically treated patients was significantly greater than that of medically treated patients. In addition, there was a significantly lower incidence of nonfatal myocardial infarction in the surgically treated groups. Relief of symptoms was not assessed in this study. The nonrandomized CASS registry (10) compared patients with poor left ventricular function treated medically and surgically and found that patients with the predominant symptom of angina were relieved of their symptoms to a greater extent with surgical therapy. There was no greater relief of symptoms of heart failure with surgical therapy. Other reports (19,22–24) of surgical therapy in similar patients have documented substantial relief of angina. Relief of symptoms of congestive failure and improvement in left ventricular ejection fraction at rest and after exercise have been less consistently observed after bypass grafting (19,23,25,26).

Conclusion. If coronary artery bypass grafting can be accomplished with an operative risk of less than 5% in patients with depressed ventricular function, survival and freedom from nonfatal myocardial infarction will be enhanced when compared with medical therapy. It is unlikely that randomized trials comparing the two forms of therapy in patients with depressed ventricular function will be con-

ducted. Until such studies are done and the results known, we believe that coronary artery bypass grafting should be applied to this subset of patients if two or more of the major coronary arteries or their major branches are suitable for grafting and if the operative mortality does not exceed 5%. Patients with symptoms of heart failure without angina and with a diffusely, poorly contracting left ventricle (ejection fraction <10 to 15%) appear to be the only exception. The great majority of patients with angina or without symptoms should derive substantial benefit from bypass grafting.

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