The Nature of Treatment Selection in Coronary Artery Disease: Experience with Medical and Surgical Treatment of a Chronic Disease

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The Nature of Treatment Selection in Coronary Artery Disease

Experience with Medical and Surgical Treatment of a Chronic Disease

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SUMMARY

This report presents our experience with the medical and surgical management of patients with coronary heart disease and uses this experience to document the role of a computerized medical information system in the long-term management of patients with a chronic disease. Of 781 consecutively evaluated patients, 402 were treated medically and 379 were treated with aortocoronary bypass surgery. At two years post-zero time, more than twice as many surgical survivors were pain free, but the survival was the same in the medical (83%) and surgical (85%) cohorts. The medically and surgically treated patients were compared with respect to 89 baseline characteristics. The cohorts were remarkably similar. Correction for baseline inequalities did not affect the fact that two-year survival was the same in both cohorts. One subgroup was identified in which surgically treated patients had a higher two-year survival. Other subgroups were identified in which therapy did not appear to affect two-year survival.

Additional Indexing Words:

Data bank Prognostic stratification Angina pectoris Aortocoronary bypass Follow-up studies

OUR THESIS is that comparison of the course of similar patients with a chronic disease following a variety of interventions is a valid procedure which can improve our ability to manage these patients and is a necessary step in the proper design of clinical trials. The validity of such comparison is based on the fact that, in chronic disease, therapeutic decisions tend to be random with respect to distant goals, and patients divided into subgroups on the basis of therapy are remarkably similar except for the fact that they have been treated differently. Until recently, we have been unable to readily catalog and recall the material which supports this thesis. The modern digital computer gives us this ability. The purpose of this paper is to present our experience with the medical and surgical management of patients with coronary artery disease. This experience illustrates that there is a tendency toward randomness in the method of management which has resulted in two groups of patients with coronary artery disease who are remarkably similar except that they have been treated differently: one group medically and the other surgically. These data can be used to define three subgroups of patients: one in which two-year survival is clearly improved by surgical management; one in which two-year survival is excellent regardless of the method of management; and one in which surgical mortality is high but two-year mortality is unaffected by the method of management.

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Methods

1. The Data Bank

The data bank used in this analysis consisted of 110

items of information on 781 consecutive patients with significant coronary artery disease who were evaluated at the Duke University Medical Center between August 1, 1969, and April 20, 1973. Significant coronary artery disease was defined as 70% or greater occlusion of at least one coronary artery. All but one patient evaluated had a history of ischemic pain and/or documented prior myocardial infarction. One patient had congestive heart failure and recurrent episodes of ventricular tachycardia but no ischemic pain and no evidence of myocardial infarction. Patients with coronary artery disease who had prior revascularization procedures elsewhere, congenital heart disease, idiopathic hypertrophic subaortic stenosis, or valvular disease other than mitral insufficiency thought to be secondary to ischemic heart disease were eliminated. The 89 parameters used to characterize the patients at zero time are shown in tables 1-3. Ideally, zero time would be the time at which a therapeutic decision was made.[1, 2] To approximate this ideal, we have defined zero time as the catheterization date for medically treated patients and as the surgical date for surgically treated patients. Sixty-five percent of patients were operated within one month of catheterization and all within four months.

Table 1

Prevalence of Characteristics Related to Chest Pain and Management of Chest Pain

	Prevalence (%)	
	Medical cohort	Surgical cohort
History of ischemic pain†	92	97
Type of pain*		
Typical angina	65	73
Atypical angina	27	25
Nonanginal	8	2
Course of pain†		
Stable	43	28
Improving	14	9
Progressing	43	63
Severity of pain*		
NYHA function class I	4	2
NYHA function class II	18	12
NYHA function class III	23	24
NYHA function class IV	55	62
Precipitators of pain		
Effort*	83	88
Meals	32	35
Temperature extremes	23	27
Emotional stress	52	52
Sexual intercourse	28	31
Rest	54	60
Sleeping*	44	52
Treatment of chest pain		
β-blocking agent†	30	43
Nitroglycerin†	70	84
Long-acting nitrates†	48	64

*Significant difference: $P < 0.05$.
†Significant difference: $P < 0.01$.
NYHA = New York Heart Association.

Table 2

Prevalence of Zero Time Characteristics: Dichotomous Parameters

	Prevalence (%)	
	Medical cohort	Surgical cohort
Males	86	83
Patient status (private)	86	87
History of myocardial infarction	47	51
History of arrhythmias	19	17
History of congestive heart failure (CHF)	15	14
Severity of CHF:		
NHYA functional class I	16	25
NYHA functional class II	35	26
NYHA functional class III	21	29
NYHA functional class IV	28	20
History of hypertension	31	33
History of diabetes	14	14
History of obesity	40	46
History of smoking	71	71
History of hyperlipidemia	23	23
Family history of ischemic heart disease	49	45
History of cerebrovascular disease	2	2
History of peripheral vascular disease	4	5
History of menopause	5	7
History of hiatal hernia	8	12
History of gallbladder disease	4	6
Prior treatment with:		
Anticoagulants*	21	27
Digitalis	27	29
Diuretics*	21	26
Antiarrhythmics	12	12
Physical examination parameters:		
Xantholasma	3	3
Funduscopic exam normal	71	73
Tenderness	2	4
Rales	6	5
Precordial activity normal	86	89
Aterial gallop	54	57
Ventricular gallop	13	10
Murmurs:	31	31
Systolic ejection	33	29
Midsystolic*	20	12
Late systolic	11	7
Holsoystolic	12	11
Peripheral pulses absent	1	1
Peripheral bruits	10	9
Electrocardiographic parameters:		
Left ventricular hypertrophy	4	2
Antrior myocardial infarction	21	18
Diaphragmatic myocardial infarction	30	31
Lateral myocardial infarction	7	4
Left bundle branch block	2	2
Right bundle branch block	3	3
Nonspecific intraventricular conduction disturbance	3	2
Left axis deviation	10	9
Right axis deviation	1	1
Resting ST-T wave changes	49	45
Positive exercise test*	43	53

Table 2 (continued)

	Prevalence (%)	
	Medical cohort	Surgical cohort
Number of vessels with 70% or greater occlusion:		
One vessel	19	19
Two vessels	26	33
Three vessels	55	48
Left main coronary artery:		
Subtotal occlusion	9	11
Total occlusion	0	1
Left anterior descending coronary artery:		
Subtotal occlusion	56	56
Total occlusion	30	30
Left circumflex coronary artery:		
Subtotal occlusion	49	46
Total occlusion†	22	14
Right coronary artery:		
Subtotal occlusion	38	38
Total occlusion	38	38
Left ventriculogram normal:	46	50
Asynergy, apical	20	23
Asynergy, anterior	18	18
Asynergy, posterior	18	17
Diffuse abnormal pattern†	14	7
Aneurysm	5	3
Mitral insufficiency†	6	3
Heart size increased, chest film*	23	14

*Significant difference: $P < 0.05$.
†Significant difference: $P < 0.01$.

Table 3

Prevalence of Zero Time Characteristics: Continuous Parameters

	Mean ± standard deviation	
	Medical cohort	Surgical cohort
Age (years)	51 ± 9	51 ± 7
Duration of ischemic heart disease (mos.)	45 ± 48	46 ± 50
Frequency of chest pain (episodes/wk)*	13 ± 17	17 ± 21
Number of GTN (tablets/wk)	3 ± 5	3 ± 5
Weight (kgs)	77 ± 13	75 ± 14
Serum cholesterol	253 ± 51	252 ± 49
Fasting blood sugar	105 ± 23	104 ± 22
Pressures (mm Hg):		
Right atrial mean	5 ± 2	5 ± 2
Pulmonary artery diastolic*	11 ± 6	11 ± 4
Pulmonary capillary wedge	10 ± 5	9 ± 4
Left ventricular end-diastolic*	14 ± 7	12 ± 6
Aortic systolic	123 ± 22	123 ± 21
Aortic diastolic	74 ± 11	74 ± 11
A−VO_2 difference (vol. %)	5.1 ± 1.0	5.0 ± 0.8
Cardiac output (L/min)	5.2 ± 1.2	5.1 ± 1.1
Cardiac index (L/min/m²)	2.7 ± 0.6	2.7 ± 0.6
Ejection fraction*	39 ± 20	46 ± 15

*Significant difference: $P < 0.05$.
GTN = nitroglycerine; A-VO_2 = arterio-venous oxygen difference.

Patients who died prior to surgery and patients who were not operated by six months were included in the medically treated cohort. Since January 1, 1971, all data have been recorded prospectively on a standardized form by a catheterization laboratory fellow. Data on patients evaluated prior to January 1, 1971, were recorded retrospectively on the same standardized form. All data were reviewed by at least one senior cardiologist. Chest X-ray, electrocardiographic and catheterization data, including the left ventriculogram and coronary angiograms, were reviewed the evening of the study by the entire senior staff of the cardiac catheterization laboratory. The remaining items of data in the data bank were treatment and follow-up information. Patients who were treated surgically had data as to the procedure performed and pre-, intra- and postoperative complications recorded by a data technician. These data were reviewed by a senior staff surgeon and a cardiologist. Follow-up, including life-death status and NYHA functional class for angina and congestive heart failure, were obtained at six, 12 and 24 months after zero time. These data were obtained by a staff cardiologist during a clinic visit or by a research associate by telephone. Follow-up was 99.5% complete: that is, the follow-up information at each interval for all patients was known in 99.5% of the instances in which the patient had reached the end of the appropriate interval. All data were entered into an interactive data analysis system[3, 4] by a data technician and corroborated by another data technician. There were 19 medically treated patients who were subsequently reevaluated and treated surgically. These patients were considered as medical patients until the date of surgery. Thereafter, they were considered as withdrawn from the medical cohort and followed as surgical patients.

2. Data Analysis

Patients were considered to be completely relieved of anginal pain if they had had chest pain prior to evaluation and had improved to NYHA functional class I at the follow-up interval. Seventeen patients who did not have chest pain prior to evaluation were not included in the analysis of relief of anginal pain. Complete relief of anginal pain was compared at six, 12 and 24 months using the Chi-square test.

Life table analysis[5] was performed to determine the survival rates for the medical and surgical cohorts. Differences in survival rates at six, 12, and 24 months post-zero time were tested for statistical significance, using the general linear model.[6] The proportion of each cohort evaluated during each six-month interval from August 1, 1969, to April 20, 1973, was compared to assure that the two cohorts were concurrent in time.

The medical and surgical cohorts were examined to determine the extent of baseline inequalities in the 89 zero time characteristics. Dichotomous parameters were compared, using the Chi-square test. Continuous parameters were compared, using the Students *t*-test. When an inequality was detected, survival rates were

recalculated for each value of that parameter to determine whether the relationship of survival rates of the medical and surgical cohorts was independent of that characteristic.[7] For example, survival rates were calculated in medical and surgical patients who had prior treatment with β-blockers and in medical and surgical patients who did not have prior treatment with β-blockers. Continuous parameters which were unequally distributed were dichotomized and survival rates recalculated in the same manner. For example, survival rates were calculated in the medical and surgical cohorts with left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg and in the cohorts with LVEDP greater than 15 mm Hg. Two-year survival rates were then compared again, using the Chi-square test.[8, 9]

The 89 zero time descriptors were analyzed, using both a multiple logistic[10] and a categorical logical tree method,[11] to determine which variables were effective discriminators between life and death. The three descriptors which were the most effective in discriminating between life and death were arteriovenous oxygen difference, the pattern of left ventricular contraction (as assessed by the ventriculogram), and the number of coronary vessels with significant obstruction. All patients were categorized as having:

1) one, two or three coronary vessels with greater than 70% occlusion, where a maximum of two was possible for the left coronary system;

2) normal or abnormal pattern of left ventricular contraction, where normal indicated the absence of areas of asynergy or ventricular aneurysm, and abnormal indicated the presence of a localized area of asynergy,[12] aneurysm or multiple areas of asynergy resulting in a diffusely abnormal contraction pattern; and

3) normal or abnormal arteriovenous oxygen difference, where normal was less than or equal to 5.5 volumes percent and abnormal was greater than 5.5 volumes percent.

The 12 subgroups which were defined by the interaction of these three effects are shown in table 4. These subgroups characterize a mild to severe spectrum of effects of coronary artery disease on the heart. The distribution of medically treated patients in the 12 subgroups was compared to that of the surgically treated patients using a Chi-square analysis. Life-table analysis was performed to determine the two-year survival rates for each subgroup and for the medical and surgical cohort in each of the 12 subgroups (table 4).

Three subgroups were defined for further analysis. Subgroup F was the only subgroup in which the two-year survival was significantly higher in the surgical cohort. The remaining subgroups were clustered into a low risk and high risk subgroup. Subgroups with a two-year survival of greater than 85% were considered low risk. Subgroups with a two-year survival of less than 85% were considered high risk. The low risk subgroup contained all patients with one-vessel disease (A,D,G,J), patients with two-vessel disease and a normal left ventriculogram (B,H), and patients with three-vessel disease, a normal ventriculogram and a normal arteriovenous oxygen difference (C). The high risk subgroup contained patients with two-vessel disease and an abnormal ventriculogram (E,K) and those with three-vessel disease and an abnormal arteriovenous oxygen difference (I,L). Because arteriovenous oxygen difference and/or the pattern of left ventricular contraction were not available in 11 patients, the subgroups contain only 770 of the 781 patients. The three subgroups were subjected to the same analysis as the total population. Survival rates were calculated and compared. The medical and surgical cohorts of each subgroup were examined for inequalities and reevaluated as described above.

Since it appeared that surgical therapy improved the survival of subgroup F, the cineangiograms of all patients in this subgroup were reviewed to determine if the vessel distal to the occlusion appeared to be sufficiently patent to accept a graft. Each of the distal vessels was graded as good, poor, or absent. The reviewers did not know whose cineangiograms they were reviewing and were unaware of the patient's treatment program or survival data.

Table 4

Subgroups Defined by Interaction of A-VO_2 Difference, Left Ventricular Contraction and Number of Vessels Diseased

Subgroup	A-VO_2 D	LVC	Number	Two-year survival (%) Total	Medical	Surgical
A (86)	≦5.5	NORM	1	94	95	93
B (105)	≦5.5	NORM	2	97	100	95
C (121)	≦5.5	NORM	3	89	89	88
D (36)	≦5.5	ABN	1	90	100	82
E (60)	≦5.5	ABN	2	83	82	83
F (169)	≦5.5	ABN	3	83	76	90
G (18)	>5.5	NORM	1	100	100	100
H (20)	>5.5	NORM	2	95	100	90
I (18)	>5.5	NORM	3	71	86	60
J (8)	>5.5	ABN	1	86	71	100
K (35)	>5.5	ABN	2	61	59	61
L (94)	>5.5	ABN	3	65	61	71

A-VO_2 D = arteriovenous oxygen difference; LVC = left ventricular contraction pattern by angiogram, where NORM = normal and ABN = abnormal. Number = number of vessels with 70% or more occlusion. The numbers in parentheses under Subgroup indicate the number of patients in each subgroup.

Results

1. Results in the Total Population

The data concerning relief of anginal pain in the medical and surgical cohorts are seen in table 5. More surgical patients experienced complete relief of anginal pain at each interval ($P < 0.001$). At two years post-zero time, more than twice as many surgical survivors were pain free.

The interval survival data of both medical and surgical patients are seen in table 6. Life-table

Table 5

Relief of Anginal Pain (Pain-free Patients)

	Medical cohort	Surgical cohort
6 month interval*	81/346 (23%)	215/312 (69%)
12 month interval*	52/246 (21%)	163/262 (62%)
24 month interval*	26/102 (26%)	78/147 (53%)

*$P < 0.001$.

The numerators indicate the number of patients who were pain free at the end of each interval. The denominators indicate the number of survivors of each interval.

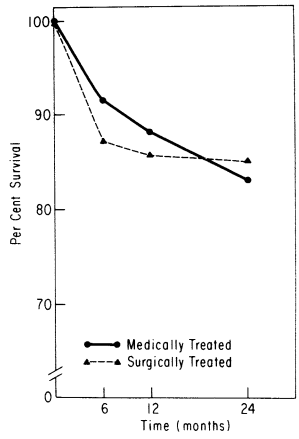

Figure 1

Survival in coronary artery disease.

analysis of these data resulted in survival curves shown in figure 1. There was a definite difference between the medical and surgical curves ($P < 0.025$). The difference was due entirely to the early surgical mortality. At two years post-zero time, there was no difference in the survival of medically and surgically treated patients.

There were 402 patients in the medical cohort and 379 in the surgical cohort. Table 1 shows the prevalence of 14 baseline characteristics related to pre-zero time anginal pain and its management. Nine of these characteristics were unequally distributed between the medical and surgical cohorts. Surgical patients had more severe chest pain and they were more likely to have been treated with β-blockers, nitroglycerin, and long-acting nitrates.

Table 2 shows the prevalence of 58 historical, comorbid, physical examination, electrocardiographic, coronary anatomy, and angiographic parameters. There were eight characteristics which were unequally distributed between the medical and surgical cohorts. More surgically treated patients had prior treatment with anticoagulants and positive exercise tests. There were more medically treated patients who had prior treatment with diuretics, who had midsystolic murmurs, total occlusion of the left circumflex coronary artery, diffusely abnormal contraction pattern, mitral insufficiency, and an enlarged heart on the chest film.

Table 3 shows the mean and standard deviation of 17 continuous parameters. Four of these parameters were statistically different in the two cohorts. Surgical patients had more frequent chest pain, lower pulmonary artery diastolic and left ventricular end-diastolic pressures, and higher ejection fractions.

Correction for these 21 zero time inequalities did not affect the two-year survival rates which remained the same in the medical and surgical cohorts.

2. Results in Subgroups

The distribution of medically treated patients in the 12 subgroups was similar to that of the surgically treated patients ($\chi^2 = 9.5$, $df = 11$, $P > 0.5$).

Interval survival data for subgroup F—patients with three-vessel disease, a normal arteriovenous oxygen difference and an abnormal left ventriculogram—are shown in table 7. The life-table analysis

Table 6

Interval Survival Data for the Total Group

	Medical cohort				Surgical cohort			
			Withdrawn				Withdrawn	
	Alive	Dead	NRAD*	Lost	Alive	Dead	NRAD*	Lost
6 months	359	34	6	3	320	49	10	0
12 months	268	11	78	2	269	5	45	1
24 months	109	12	147	0	155	1	113	0

*NRAD = not reached anniversary date. These are patients who have not yet reached the end of the interval or medically treated patients who were treated surgically prior to the end of the interval.

Table 7

Interval Survival Data for Subgroup F ($A\text{-}VO_2D \leqq 5.5$; number of occluded vessels = 3; abnormal left ventricular contraction)

	Medical cohort			Surgical cohort		
	Alive	Dead	Withdrawn*	Alive	Dead	Withdrawn*
6 months	82	13	1	64	7	2
12 months	47	4	31	48	0	16
24 months	16	2	29	21	0	27

*See table 6.

Table 8

Interval Survival Data: Low Risk Subgroup (Subgroups A, B, C, D, G, H, J, table 4)

	Medical cohort			Surgical cohort		
	Alive	Dead	Withdrawn*	Alive	Dead	Withdrawn*
6 months	187	5	6	181	14	6
12 months	149	1	37	155	2	24
24 months	54	2	93	88	1	66

*See table 6.

survival curves for the medically and surgically treated cohorts of this subgroup are shown in figure 2. Surgical patients clearly had a higher survival than medical patients ($P < 0.028$). There were zero time inequalities in the prevalence of prior treatment with long-acting nitrates, systolic ejection murmurs, total occlusion of the left circumflex coronary artery, and diffusely abnormal left ventricular contraction pattern. Correction for these inequalities did not affect the relationship of the survival rates in the medical and surgical cohorts: the two-year survival was higher in the surgical cohort in every case. The two-year survival rates were no longer statistically different when the patients had not had prior treatment with long-acting nitrates, when the patients had systolic ejection murmurs (SEM), when the patients did not have SEM, when the patients did not have total occlusion of the left circumflex coronary artery or when the patients did not have a diffusely abnormal left ventricular contraction pattern. The two-year survival rates remained statistically different when the patients had had prior treatment with long-acting nitrates, when they did have total occlusion of the left circumflex coronary artery or when they did have diffusely abnormal left ventricular contraction patterns. There was no difference in the distribution of patients with no, one, two or three good distal vessels.

Interval survival data for the low risk subgroup are shown in table 8. Life-table analysis survival curves for the medically and surgically treated cohorts of the low risk subgroup are shown in figure 3. Survival in both cohorts was high. There was no significant difference in the two-year survival rates. There were zero time inequalities in the prevalence of 20 of the 89 baseline characteristics. Correction for these inequalities failed to alter the relationship of the survival rates in the medical and surgical cohorts. The two-year survival rates remained the same in the medical and surgical cohorts.

Interval survival data for the high risk subgroup are shown in table 9. Life-table analysis survival curves for the medically and surgically treated cohorts of the high risk subgroups are shown in figure 4. There was a high early mortality in the surgically treated cohort but the two-year survival was not different from the two-year survival in the medically treated cohort. There were zero time inequalities in the prevalence of 23 of the 89 baseline characteristics. Correction of these inequalities did not alter the poor survival in both cohorts.

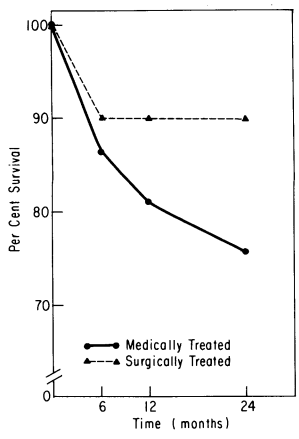

Figure 2

Survival in coronary artery disease in subgroup F ($AVO_2 D \leqq 5.5$; Left ventricular contraction, abnormal; number of occluded vessels, 3). The two-year survival of surgically treated patients is significantly higher than that of medically treated patients ($P < 0.028$).

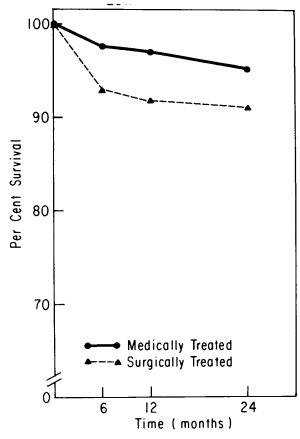

Figure 3

Survival in coronary artery disease in low risk subgroup.

Table 9

Interval Survival Data: High Risk Subgroup (Subgroups E, I, K, L, table 4)

	Medical cohort			Surgical cohort		
	Alive	Dead	Withdrawn*	Alive	Dead	Withdrawn*
6 months	87	15	1	73	24	2
12 months	70	6	11	64	3	6
24 months	37	8	25	44	0	20

*See table 6.

Discussion

Cornfield[13] has discussed the use of a national registry of patients with ischemic heart disease who have undergone coronary angiography in evaluating the effects of therapy. This paper extends the usefulness of this concept by demonstrating that the characteristics of patients treated in different ways by a variety of doctors in a medical center are very similar. These results confirm our thesis that comparison of concurrent but differently treated patients with a chronic illness gives information which is useful in determining the role of a therapeutic intervention. The comparison is particularly useful when the therapy focuses on distant goals. Although there are several excellent studies of the natural history of patients with angina pectoris,[14, 15, 16] these studies may not help the doctor with the long-term therapy of the individual patient. The doctor has no way of rapidly discerning the prognosis of patients similar to his patient or the effect of treatment on this prognosis. Because the doctor does not have information to define the characteristics of the patients who will benefit two years later from the therapy and he does not know the characteristics of the patients who will show evidence of harm two years later, he has to focus on a short-term goal such as the relief of pain. There is abundant information that aortocoronary bypass surgery is associated with complete relief of angina for an average of up to 12 months in from 62 to 92% of operative survivors.[17, 18, 19, 20] He hopes that the relief of pain is tightly coupled to other desirable effects, including prolongation of life. If the relief of the pain is not closely coupled to survival, the treated and untreated groups will have the characteristics of a randomly selected group when examined with survival as the endpoint. Our study shows that the relief of anginal pain is not closely coupled to survival. At two years post-zero time, almost twice as many surgical survivors are pain free, but the survival of the medically and surgically treated patients is identical.

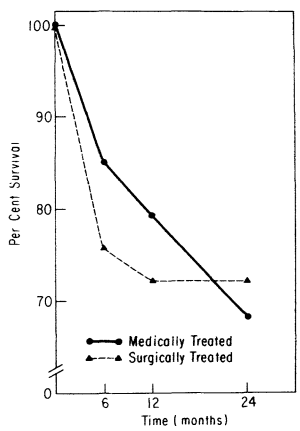

Figure 4

Survival in coronary artery disease in high risk subgroup.

The medically and surgically treated patients are surprisingly alike (tables 1-3). All but four of the 17 statistically significant baseline inequalities in dichotomous parameters are of the order of 10% or less. The four differences in the continuous baseline characteristics likewise may not be large enough to be of physiologic importance. Seventeen of the 21 statistically significant differences between the cohorts fall into two categories. One of these, pain and treatment to control pain (table 1, and chest pain frequency, table 3), relate to the interplay between the heart and the nervous system of the patients and their doctors. The variables in this category measure the amount of distress caused by the acute symptom, chest pain. The other category includes factors thought to be associated with increased immediate risk if one therapy, surgery, is applied. Fewer of the surgically treated patients have enlarged hearts, a diffusely abnormal pattern of left ventricular contraction, mitral insufficiency, elevated left ventricular end-diastolic and/or pulmonary artery diastolic pressures or a low ejection fraction. The treatment decision is clearly based on the physician's desire to relieve an acute symptom without excessive immediate mortality. By examining survival in cohorts with and without the unequally distributed zero time characteristics, we determine that these characteristics either do not affect survival or else affect survival in the same manner in medically and surgically treated patients.

Our data show that surgery does not affect the over-all two-year survival. The group collected under the diagnosis of coronary artery disease is composed of patients in all different stages of the disease. One might have predicted that surgery would be helpful at some stage, harmful at some

stage, and make no difference at another stage in terms of two-year survival. If the good effects are cancelled out by the bad effects, the over-all effect would be no change, and this is just what happened.

When the descriptors of the patients at zero time are used to stratify the patients into more homogeneous subgroups, we again note that the distribution of medically and surgically treated patients within each subgroup is not different from that which we would expect by chance. We are able to determine that the two forms of treatment may have different effects in different subgroups. The patients with a normal arteriovenous oxygen difference, disease in three vessels, and a localized area of disturbance in ventricular contraction appear to have a higher two-year survival when treated surgically. These patients are theoretically at high risk for myocardial infarction and death within two years. One would anticipate that the presence of severe three-vessel disease is the milieu for myocardial infarction. The presence of localized ventricular disease demonstrates that this milieu is being translated into muscle disease and the presence of a normal arteriovenous oxygen difference shows that the muscle disease is still localized. One may further speculate that this situation is one in which successful bypassing would have the best chance to show its effect on survival within two years. Another subgroup, the low risk subgroup, does relatively well with either treatment. The third subgroup, the high risk subgroup, has a high immediate surgical mortality ($>20\%$), but within two years, the medical mortality is so high that there is no difference between the two cohorts.

These subgroups have implications which could help us improve our ability to manage patients with ischemic heart disease. Patients in subgroup F may have a longer survival as well as more relief of chest pain if treated surgically. Patients in the low risk subgroup may be at too early a stage in the course of their disease to receive maximal benefit from surgical treatment at this time. Patients in the high risk subgroup may be willing to risk high surgical mortality for the possibility of functional improvement. Although it is possible that some unknown factor may be accounting for these results, we have no choice but to use information such as this until better information becomes available.

Better information is not likely to become available unless data such as these are collected prior to designing randomized clinical trials. Randomized trials are costly, both in terms of money and manpower. The demonstration of differences in survival depends on the magnitude of the differences and the size of the population. Assuming survival rates similar to those illustrated in figure 1, the demonstration that the two-year surgical survival (85%) is higher than the medical survival (83%) would require about 100,000 patients. If patients with only one-vessel disease were randomized, one would also be unlikely to demonstrate a difference in two-year survival. It is possible that at five to ten years post zero time the difference will be greater and could be detected with fewer patients. It is clear that a randomized trial involving the total stable angina population will require either many patients or many years of follow-up and probably both. On the other hand, the apparent higher survival of the surgical cohort in subgroup F could be substantiated within three to five years by randomizing about 200 patients.

We have focused on only one long-term outcome: two-year survival. Our intent is not to say that only one group of patients with angina should be treated surgically. It is likely that, as we focus on more distant goals, other subgroups will emerge which have a higher survival if treated surgically. We will certainly be able to sharpen our characterization of those patients who should be operated to increase two-year survival. It should be pointed out that our presentation has frozen time. We have presented the results as if an irrevocable decision has to be made at one point in time. In fact, at a referral center, this is unfortunately often true. Coronary artery disease is a chronic disease. Ninety-five percent of the patients who were in the low risk subgroup and were treated medically will survive two years. Their disease will have progressed. In several years, many of them may benefit in terms of two-year survival from aortocoronary bypass. Similarly, the management of chronic disease is a dynamic process. The question is not whether the patient should be treated medically or surgically but what is the best treatment at a particular time and is there a time when the treatment should be altered. It may turn out that surgery can be done too early or too late in the course of the disease. The construction of the data bank and its use in clinical practice to predict two-year survival shows the power of the system. It is clear that the data bank approach and the ability to compare cohorts in similar subgroups extends the doctor's ability to manage patients by allowing him to focus on distant goals.

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