Risk factors among patients undergoing repeat aorta-coronary bypass procedures

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Abstract:

It is estimated that as many as 7% of patients who have an aorta-coronary bypass operation will require a second bypass procedure within 10 to 12 years. Using information from the Milwaukee Cardiovascular Data Registry, we matched 166 men who underwent two coronary bypass operations at least 6 months apart, between 1968 and 1981, with 428 patients who had a single procedure. Patients were matched according to date of operation and left ventricular wall motility function for analysis of risk factors for repeat operation. Elevated triglyceride levels were found to be the strongest risk factors associated with reoperation. In addition, both younger age and less complete revascularization during the first operation were significant predictive factors of repeat operation. The results suggest that efforts to reduce plasma triglyceride levels and ensure adequate revascularization may significantly reduce the need for repeat coronary bypass.

Article:

It has been estimated that the number of aorta-coronary bypass procedures performed in the United States rose from 24,000 to 169,000 between 1971 and 1982.[1-3] Though some studies have suggested that the palliative effects of bypass grafting may be no different from those of medical therapies, especially in less severe disease,[4,5] the widespread success of surgical treatment in reducing or eliminating angina in patients with coronary artery disease has largely accounted for this dramatic increase.[6-8] However, a portion of these patients (3% to 7%) have temporary or minimal relief and have a second procedure performed at some later date.[9,10] If these patients could be identified before the first bypass operation, steps could be taken to reduce the likelihood of a second surgical procedure. This in turn would result in lower health care costs, less stress for patients and their families, and reduced risks of surgical mortality or complications.

The study presented here used case-control techniques to identify risk factors for a second aorta-coronary bypass procedure among male patients in the Milwaukee Cardiovascular Data Registry.

Methods

Patient population. The patient population for this study was drawn from the more than 14,000 patients who underwent coronary bypass operations at St. Luke's Hospital, Milwaukee, Wisconsin, from 1968 through 1981 and are included in the Milwaukee Cardiovascular Data Registry. A case-control design was used to compare risk factors between patients who had a repeat bypass operation (cases) and control patients who had only a single procedure during the same time period. To be eligible for the study, patients had to be male and to have undergone one or two aorta-coronary bypass operations within the 14 year time frame of this study. Patients were not eligible if any of the following surgical procedures were performed concurrently with or after either bypass operation: (1) valve replacements or commissurotomies, (2) aneurysm resections, (3) septa' defect repairs, or (4) surgical treatment for peripheral vascular disease.

The study was approved by the Institutional Review Committee of the Medical College of Wisconsin. Informed consent was obtained from all patient before their participation.

Table I. *Comparisons between patients with two bypass operations (cases) and control patients with one operation**

Factors	Cases (n = 166) Mean	Cases (n = 166) SD	Controls (n = 428) Mean	Controls (n = 428) SD	p Value
Age at first operation	49.9	6.8	53.4	7.7	0.01
Occlusion score	181.7	55.9	189.3	55.0	0.14
Obesity index	3.8	0.4	3.8	0.4	0.41
No. of initial grafts	2.3	1.0	2.9	1.2	0.01
Cholesterol (mg/dl)	276.3	61.2	258.8	48.6	0.01
Triglyceride (mg/dl)	278.4	230.8	214.4	177.4	0.01
HDL cholesterol (mg/dl)	41.3	10.6	44.0	12.4	0.16
	(n = 80)		(n = 190)		
LVEDP (mm Hg)	10.6	5.4	10.9	4.7	0.53
Hypertension (%)	21.1	40.9	30.4	46.0	0.02
Diabetes (%)	11.5	31.9	11.7	32.2	0.94
Chest pain—all types (%)	73.5	44.3	75.4	43.1	0.64
Angina (%)	68.1	46.8	68.3	46.6	0.96
Exercise index	43.6	37.4	40.0	32.4	0.51
Smoking history	3.4	1.3	3.4	1.3	0.78
Alcohol (oz/wk)	5.2	6.6	4.4	5.2	0.35
	(n = 48)		(n = 230)		
Type A behavior	2.0	1.5	2.0	1.3	0.75
	(n = 46)		(n = 220)		
Myocardial infarction (%)	59.6	49.2	49.3	50.1	0.02
Revascularization index†	135.6	78.5	163.2	78.0	0.01

Legend: HDL, High-density lipoprotein. LVEDP, Left ventricular end-diastolic pressure. SD, Standard deviation.
*Controls were matched to cases according to date of first operation (within 6 months) and left ventricular function.
†(No. of grafts/occlusion score) × 10,000.

Cases. "Cases" were selected from patients in the registry who had two bypass operations at least 6 months apart. This interval was believed to represent the minimum time needed to assure that the subsequent operation was not a direct consequence of the first one and that possible risk factors had time to affect any physiologic mechanisms leading to the recurrent symptoms prompting the repeat procedure. A total of 166 patients met all of the eligibility criteria for cases. The time between the first and second operation for these patients ranged from 6 to 139 months with a median of 73 months.

Control patients. Initially, 3,740 men were eligible for the control group, after surgical exclusions identical to those for the cases were made. From this group, only the 3,269 patients reported alive over the entire duration of the study were selected and matched to cases according to date of operation (± 3 months) and wall motility. Matching according to date of operation was necessary because of the considerable improvements in surgical technique over the past 20 years, which might have obscured risk factor associations. Matching according to wall motility was done to reduce the possibility of bias from any tendency to select patients with a stronger left ventricular function for repeat operations. A total of 428 control patients were successfully matched to cases, with between one and five controls for each case (mode = 3). Eighty percent of the cases had two or three controls.

Variables. The prognostic variables used in this study included seven composite indices to measure obesity, coronary occlusion, ventricular wall motility, exercise habits, smoking history, type A behavior (coronary-prone), and degree of revascularization at the initial bypass operation. The obesity index is a measure combining both weight and height (weight/height^2).[11] Occlusion score is based on angiographic interpretation of coronary artery occlusion originally suggested by Rowe, Thomsen, and Stenlund,[12] with a score of 0 indicating no occlusion and 300 total occlusion.[13] Wall motility, for which control patients were matched to cases, was graded on a scale of 1 to 6, with 1 denoting normal function and 6 denoting aneurysms or severe dyskinesia of at least two segments of the walls of one or both ventricles.[13] The exercise index is a composite of patient responses to three items on the Cardiovascular Data Questionnaire, which were used to create a scale from 1 (least exercise) to 600.[14] The smoking history scale ranges from 1 (never) to 5 (heavy).[15] Type A behavior, described and used by Young and colleagues,[16] is an index of degree of time-preoccupied behavior ranging from 1 (lowest) to 6 (highest). The seventh index used is revascularization index (RI); which was determined by dividing the number of grafts used in the bypass operation by the occlusion score, multiplied by a constant: RI = (number of grafts/occlusion score)X 10^4. Although completeness of revascularization is frequently mentioned in the literature, quantitative criteria for the extent of revascularization are generally lacking. Sometimes the term is used to refer to vessels with greater than 50% occlusion that were not grafted,[17] but this meaning does not describe whether the whole heart was adequately revascularized. The index described here and used in this study represents an original attempt to quantitatively characterize completeness of revascularization in this group of patients.

Table II. *Results of multiple logistic regression analysis for predictive factors of two bypass operations*

Factor	Coefficient	Standard error	p Value
Triglyceride	0.002	0.0009	0.02
No. of grafts	−0.391	0.1240	0.01
Age at first operation	−0.045	0.0162	0.01
Cholesterol	0.003	0.0024	NS
Hypertension	−0.080	0.1320	NS
Myocardial infarction	0.110	0.1190	NS
Constant	0.723	1.090	

Legend: NS, Not significant.

Table III. *Estimated relative risks for repeat bypass operation, upper versus lower quintile for each risk factor*

Factor interval	Relative risk	95% Confidence limit
Triglyceride levels (<90 vs. > 210 mg/dl)	1.68	1.10-2.62
Age at first operation (< 40 vs. > 65 yr)	1.97	1.22-3.19
No. of grafts at first operation (1 vs. 6)	2.39	1.39-4.11

Other prognostic variables included age at first bypass operation, alcohol consumption, presence of anginal or other chest pain, histories of diabetes, hypertension, or myocardial infarction, and fasting levels of plasma cholesterol and triglycerides. Cholesterol and triglyceride values were determined by routine procedures under quality control by the Lipid Standardization Program of the Center for Disease Control in Atlanta, Georgia. Although some data are available on high-density lipoproteins (HDL), this factor was not routinely measured in this study until 1975 and therefore is available for only a limited number of patients.

Statistics. Statistical analysis was performed on bivariate and multivariate levels. Differences in means between cases and controls were tested by pooled t tests. Maximum likelihood estimates of possible predictor variables as functions of a second bypass procedure were made with a logistic regression model. The relative risks for repeat operation were calculated on the basis of the logistic regression coefficients.

Results

Bivariate analysis. A number of significant differences between patients having single or repeat coronary bypass operations were revealed in the bivariate analysis (Table I). Patients who underwent two bypass operations (cases) were younger and had significantly fewer grafts at first operation than the patients having one procedure (controls). The first-operation RIs of patients having repeat operations were also significantly lower than those of controls, which indicates that cases received fewer initial bypasses even after adjustment for occlusion scores. However, there was not a significant difference in occlusion scores between the cases and their controls.

Plasma triglyceride and cholesterol levels were both higher for cases, and a higher percentage of these cases had had a myocardial infarction before the first bypass operation. However, significantly fewer cases were hypertensive at the time of the first operation.

No significant differences were observed for the other variables measured, including obesity, exercise, smoking, alcohol intake, type A behavior, diabetes, chest pain (all types), and angina. Although controls had slightly higher HDL levels than cases, the difference was not statistically significant. Information on three variables—cholesterol, alcohol intake, and type A behavior—was not available on all patients, and the appropriate numbers are indicated in Table I.

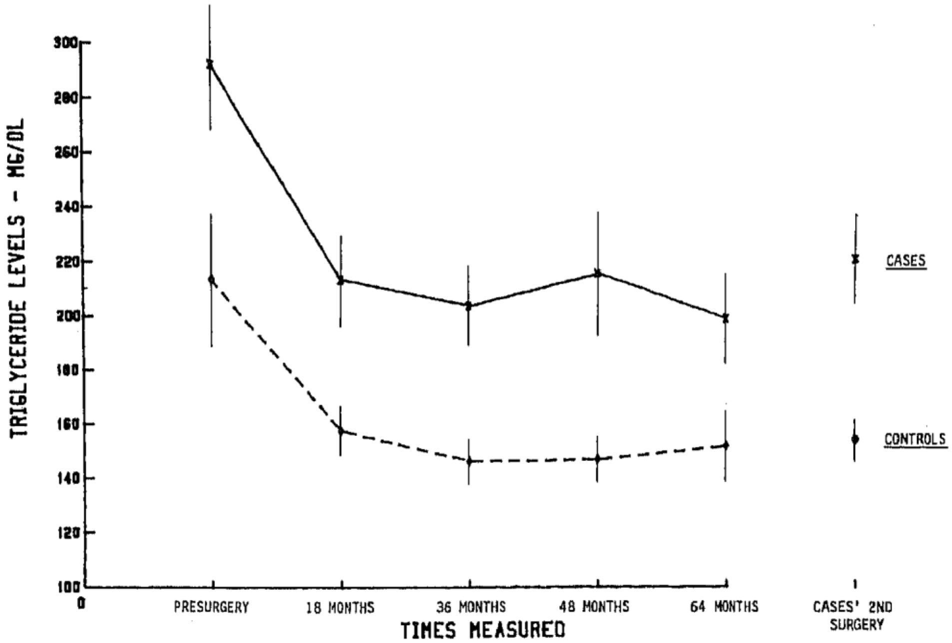

Fig. 1. Triglyceride levels for cases and matched controls before the operation and 18, 36, 48, and 64 months after the first operation. *Vertical lines* represent standard errors.

Multivariate analysis. Logistic regression analysis provided maximum likelihood estimates of the probability of a repeat coronary bypass operation (Table II). Variables with significant bivariate associations with second operations were included in the logistic regression equation, except for RI, because the relationship of number of grafts to second operation was independent of occlusion scores. Three variables continued to demonstrate significant associations with repeat coronary bypass according to this logistic model: the plasma triglyceride level before the first operation, the number of grafts performed at the first operation, and age at the first operation.

The estimated relative risks and corresponding confidence intervals of a second bypass operation for these three significant risk factors are shown in Table III. The risks are based on comparisons between the highest and lowest quintiles of triglyceride levels, age at the first operation, and number of grafts at the first operation. The risks range from 1.68 for elevated plasma triglyceride levels to 2.39 for fewer grafts at first operation.

Significant differences between cases and controls in triglyceride levels after the initial operation were also observed (Fig. 1). Although striking reductions in triglyceride levels occurred for both cases and controls immediately after the initial bypass operation, levels among patients destined to have a repeat operation (cases) never dropped to the levels of the patients having a single operation (controls). The higher triglyceride levels among cases persisted for at least as long as 64 months after the initial operation, which was the length of follow-up for this study. It should be noted that cases had their repeat operation at varying times after the initial procedure, and the comparisons in Fig. 1 are between cases who had not yet had a repeat operation and their respective controls. When comparisons between cases and controls were made for the time of the second operation for cases (± 3 months), regardless of time since the initial operation, the difference in triglyceride levels was still greater than 66 mg/dl (221.67 mg/dl for cases versus 155.06 mg/dl for controls, $p < 0.01$). These values are indicated on the far right in Fig. 1.

Discussion

Of the three factors that were associated in this study with a significantly higher risk of a second bypass operation, two—triglyceride levels and number of grafts at the first operation—provide opportunities for intervention aimed at reducing this risk.

Plasma triglyceride levels of men who had two bypass operations were significantly higher than those of their matched controls, both before the initial operation and throughout the 64 month postoperative period. Previous studies have also suggested that elevated plasma lipid levels may be associated with the development of atherosclerotic lesions in the vein graft.[17,18] These levels could be managed by dietary or pharmacologic intervention, particularly to lower levels after the first operation.

This study also found that men requiring a repeat bypass procedure received significantly fewer grafts during their initial operation, which suggests less complete revascularization. Though this finding has also been reported before,[13,17-19] matching according to date of operation in this study effectively eliminated the possibility of bias contributed by the use of greater numbers of grafts in recent years as the bypass technique has improved. That cases had significantly fewer grafts at the first operation, even after adjustment for occlusion scores, appears to confirm the inadequacy of initial revascularization among some patients. This risk factor could be minimized if graft placements were made to achieve maximum revascularization, particularly when a patient is relatively young or has elevated preoperative triglyceride levels.

Age is the single risk factor in this study that cannot be changed, but the inverse association between age at first operation and risk of a second bypass operation may reflect other factors, perhaps associated with life-style or family history, in addition to a likelihood of selection against older patients for repeat operations. Significant age differences at the time of their first bypass operation between patients who eventually underwent second operations and those who did not has also been seen in other studies.[13,18,20,21] Early onset of vascular disease may indicate higher risks for the continued progression of disease after the initial bypass procedure. The younger person is also more likely to be employed and to engage in other activities that symptoms of coronary heart disease would greatly restrict. An older, less active person may be less likely to submit to the additional risk, stress, and expense that a second operation would entail.

These results give evidence that at least three factors contribute to increased risk of a second bypass operation. Knowledge of these factors may provide a basis for identifying those patients who are at higher risk and for taking steps to reduce that risk. Further investigations will undoubtedly extend and clarify these findings to enable more precise estimates of risk to be made and more efficient targeting of preventive strategies.
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