Predictors of Operative Mortality for Coronary Bypass Grafting in Patients with Ischemic Heart Disease

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Predictors for operative mortality (OM) were studied in 172 consecutive patients (pts) undergoing coronary artery grafts (CAG) for angina pectoris.

Seventy-eight pts had Class IV angina; of the 147 patients given propranolol, 41 were gradually withdrawn from propranolol and finally discontinued 24 hours before surgery, and 106 were abruptly withdrawn from propranolol 24 hours before CAG; 20 pts had left main coronary disease; 156 pts had cardio-pulmonary bypass (CPB) time shorter than 20 minutes, and 16 pts had a CPB longer than 120 minutes.

The operative mortality was 5.2% (9/172) for the entire group. Class IV angina (OM 7%), abrupt propranolol withdrawal (OM 6.6%), left main coronary artery disease (OM 25%), and CPB longer than 120 minutes (OM 50%), all significantly increased OM. These variables were interdependent, however, as many pts belonged to several predictor categories, combinations of predictors were examined, in order to more accurately predict the risk of individual pts. The combination of left main coronary artery disease and CPB longer than 120 minutes; and Class IV angina and CPB longer than 120 minutes were significantly associated with higher operative mortality.

We conclude that Class IV angina, abrupt propranolol withdrawal, left main coronary artery disease and prolonged CPB are potent, interdependent predictors of OM in pts undergoing CAG. Consideration of these predictors, alone and in combination, allows effective prediction of OM for CAG in patients with stable angina pectoris.

INTRODUCTION

Coronary artery bypass surgery is now a widely used approach to the treatment of arteriosclerotic heart disease in selected patients. A few studies have suggested short-term relief of angina [1–3] and an increase in longevity [4]. Further follow-up is necessary before the effects of the operation can fully be evaluated.

In this report we present an analysis of clinical, anatomic, hemodynamic and operative factors affecting operative mortality in 172 consecutive patients. These patients underwent cardiac catheterization and coronary artery bypass grafts without associated surgical procedures at Yale-New Haven Hospital from July 1974 to June 1975. Data on each patient were prospectively collected and analyzed to identify those preoperative factors which could predict the immediate outcome of individual patients.

METHODS

From July 1974 to June 1975, 172 consecutive patients underwent cardiac catheterization and coronary bypass grafts for treatment of angina pectoris refractory to medical therapy. Diagnostic cardiac catheterization consisted of pressure measurements, cardiac output determination, single plane ventriculogram and selective coronary cinearteriography, all performed by standard techniques.
Coronary artery lesions of greater than 70 percent obstruction were classified as significant. Coronary artery disease was recorded as one, two or three vessel disease. Left main coronary artery disease (LMCD) was considered equivalent to disease of the proximal left anterior descending artery and proximal left circumflex artery. Diffuse disease of a coronary artery was determined by the presence of several lesions with greater than one cm in length and more than 70 percent narrowing of the arterial lumen. The right anterior oblique left ventriculogram was analyzed for calculation of ejection fraction according to the method of Greene [5], and for the presence of mitral regurgitation.

Coronary artery surgery was performed within three weeks following cardiac catheterization in all patients. In one group of patients, no propranolol therapy was used preoperatively; in a second group, propranolol doses were gradually decreased (during a mean period of three days) and finally discontinued 24 hours prior to surgery; and in a third group, propranolol was abruptly discontinued 24 hours before surgery. Coronary artery bypass grafts were performed using saphenous veins to graft the posterior descending artery and marginal branch of the left circumflex coronary artery. The left internal mammary artery was used whenever possible to graft the left anterior descending artery. Dissection of the internal mammary arteries from the chest wall and proximal anastomoses of saphenous vein grafts were both accomplished without cardiopulmonary bypass. Sidebiting clamps were employed for proximal anastomoses of saphenous vein to the aorta. Distal anastomoses were done on full cardiopulmonary bypass with the heart in ventricular fibrillation; aortic cross-clamping was used only when a dry field could not be obtained by local occlusion of the coronary artery. Revascularization was considered "incomplete" if grafts were not placed in every diseased coronary branch. For the purpose of this study, operative mortality was defined as death occurring up to six weeks after surgery was performed. The period of six weeks was selected because it appeared to be the natural cut-off point between early and late mortality.

Statistical Methods

Contingency table chi-square (χ²) [6] was used to examine the possible relationship of each study factor to operative mortality. Although the factors relating to operative mortality were not necessarily independent influences, they were initially examined one at a time and then in combinations. Statistical significance was attributed to a P value of less than 0.05.

When information on some preoperative clinical characteristic of a patient was not available, that patient was not included in the analysis of that variable.

Characteristics of Patients

The average age of the patients was 55.4 years (range 31 to 76), and 78 percent (134/172) were male. Associated peripheral disease was present in 24 patients (14 percent); diabetes mellitus in 24 patients (14 percent); and lipid abnormality in 47 patients (31 percent). Other characteristics included: family history of ischemic heart disease in 108 patients (66 percent); hypertension in 57 patients (33 percent); obesity [7] in 90 patients (54 percent); and smoking history in 138 patients (80 percent). In addition, there were one hundred and two patients with remote myocardial infarction (59 percent) and nine with recent myocardial infarction, occurring less than three months prior (5 percent). Nine patients (5 percent) had angina pectoris Class I NYHA; 24 (14 percent) had Class II; 61 (35 percent) had
TABLE 1
Characteristics of Patients by Medical History and Physical Examination

| Characteristics                        | Total Patients (no.) | Patients with Characteristic (no.) | (%) |
|---------------------------------------|----------------------|-----------------------------------|-----|
| Peripheral Vascular Disease           | 170                  | 24                                | 14  |
| Diabetes Mellitus                     | 170                  | 24                                | 14  |
| Lipid Abnormality                     | 151                  | 47                                | 31  |
| Family History                        | 164                  | 108                               | 66  |
| Hypertension                          | 171                  | 57                                | 33  |
| Obesity                               | 167                  | 90                                | 54  |
| Remote Myocardial Infarction          | 172                  | 102                               | 59  |
| Recent Myocardial Infarction          | 172                  | 9                                 | 5   |

Anginal Status

Class I 172 9 5
Class II 172 24 14
Class III 172 61 35
Class IV 172 78 45

Congestive Heart Failure

172 26 15

β-Adrenergic Therapy

No Therapy 172 25 14
< 160 mg. q.d. 172 56 32
≥ 160 mg. q.d. 172 91 53

Class III; and 78 (45 percent) had Class IV. Congestive heart failure was present in 26 patients (15 percent), and only 25 patients (14 percent) had not received beta blocking therapy (Table 1).

TABLE 2
Characteristics of Patients by Chest X-ray and Cardiac Catheterization

| Characteristic                      | Total Patients (no.) | Patients with Characteristic (no.) | (%) |
|-------------------------------------|----------------------|-----------------------------------|-----|
| Cardiac Enlargement                 | 172                  | 32                                | 19  |
| LVEDP*                              |                      |                                   |     |
| ≤ 12 mm Hg.                         | 172                  | 93                                | 54  |
| 13-17 mm Hg.                        | 172                  | 41                                | 24  |
| ≥ 18 mm Hg.                         | 172                  | 38                                | 22  |
| Ejection Fraction                   |                      |                                   |     |
| ≥ 0.60                              | 172                  | 109                               | 63  |
| 0.30-0.59                           | 172                  | 62                                | 36  |
| < 0.30                              | 172                  | 1                                 | 1   |
| Mitral Regurgitation                | 172                  | 22                                | 13  |
| Number of vessels diseased          |                      |                                   |     |
| One                                 | 172                  | 22                                | 13  |
| Two                                 | 172                  | 44                                | 26  |
| Three                               | 172                  | 106                               | 62  |
| Left Main Coronary Artery Disease   | 172                  | 20                                | 12  |

*Refers to left ventricular end-diastolic pressure.
Cardiac enlargement, (CT ratio > 50 percent) measured by standard upright chest x-ray, was present in 32 patients (19 percent); normal left ventricular end-diastolic pressure (≤ 12 mm Hg) was recorded in 93 patients (54 percent); and normal ejection fraction (≥ 60 percent) in 109 patients (63 percent). Mitral regurgitation documented by left ventriculography was present in 22 patients (13 percent). Coronary arteriography in this group of patients revealed 22 patients (13 percent) with single vessel disease; 44 patients (26 percent) with double vessel disease; and 106 patients (62 percent) with triple vessel disease. Left main coronary artery narrowing was documented in 20 patients (12 percent), (Table 2).

Of the 147 patients given propranolol, 41 (28 percent) were gradually withdrawn from propranolol and finally discontinued 24 hours before surgery; and 106 patients (72 percent) were abruptly withdrawn from propranolol 24 hours before coronary artery surgery. The daily dose of propranolol was less than 160 mg in 56 patients (32 percent) and more than 160 mg in 91 patients (53 percent). For one hundred fifty-six patients (91 percent) the cardiopulmonary bypass (CPB) time was shorter than 120 minutes. Seventy-three patients (42 percent) underwent complete revascularization; 27 had single bypass graft; 86 had double grafts; and 59 had triple or more grafts.

RESULTS

The overall operative mortality for this group of patients was 5.2 percent (nine deaths among 172 consecutive patients). None of the patients died on the operative day; seven patients died within the first week, and one in the fourth week and one in the sixth week postoperatively. Six of these deaths were attributed to perioperative myocardial infarction as documented by serial electrocardiograms and/or autopsy; one due to ventricular fibrillation without anatomical documentation of acute myocardial necrosis; and two others due to non-cardiac causes.

Factors Related to Operative Mortality

Four factors appeared to be related to operative mortality (OM): angina pectoris Class IV NYHA; abrupt propranolol withdrawal; left main coronary artery disease; and cardiopulmonary bypass time longer than 120 minutes. Patients with angina pectoris Class IV showed a significantly higher mortality than those with angina pectoris Class III or less (7 percent, 7/78 vs. 2.0 percent 2/94 [p < 0.05]). Patients in whom propranolol therapy was abruptly discontinued 24 hours prior to surgery had a risk of dying which was more than two times as great (6.6 percent) as those in whom propranolol therapy had been gradually reduced over a three-day period and finally discontinued 24 hours before surgery (2.4 percent). Patients with left main coronary artery disease (LMCD) sustained operative risks 10 times greater than those patients without LMCD (25 percent vs. 2.6 percent [p < 0.001]), as seen in Table 3. Finally, patients whose CPB time was longer than 120 minutes showed a mortality of 50 percent, a figure which is significantly higher than that of patients with CPB time shorter than 120 minutes (Table 4). For all 16 patients with CPB time longer than 120 minutes, severe diffuse distal disease was present in arteries receiving bypass grafts.

An analysis of other probable preoperative risk factors for operative mortality by contingency table chi-square ($\chi^2$) showed that operative mortality was not related to age, sex, peripheral vascular disease, diabetes mellitus, lipid abnormality, family
TABLE 3
Risk Factors as Related to Operative Mortality

| Factors                        | Total Patients | Number of Patients | Percent Mortality | P Value |
|--------------------------------|----------------|--------------------|-------------------|---------|
|                                |                | With Factor | Without Factor | With Factor | Without Factor |         |
| Angina Class IV                 | 172            | 78         | 94            | 7.0        | 2.0         | <0.05   |
| Propranolol Therapy             |                |            |               |            |              |         |
| Abrupt Withdrawal               | 147            | 106        | 41            | 6.6        | 2.4         | <0.05   |
| Left Main Coronary Artery Disease| 172           | 20         | 152           | 25.0       | 2.6         | <0.001  |

TABLE 4
Operative Mortality: Duration of Cardiopulmonary Bypass

| Group       | Total Patients | Deaths |
|-------------|----------------|--------|
|              | Number | Percent |
| < 90 min.   | 119 | 0 | 0 |
| 90–119 min. | 37 | 1 | 2.7 |
| ≥ 120 min.  | 16 | 8 | 50.0* |
| All Groups  | 172 | 9 | 5.2 |

*p < 0.001

history of ischemic heart disease, hypertension, obesity, smoking habits, previous myocardial infarction, congestive heart failure, heart size, left ventricular end-diastolic pressure, ejection fraction, or mitral regurgitation, or number of diseased vessels (except for left main coronary artery disease). In addition, this analysis of operative factors indicated that neither the number of grafts nor the completeness of revascularization had any effect upon operative mortality.

In order to better predict operative mortality in individual patients, combinations of risk factors were also examined. Two combinations appeared to be associated with a significantly higher operative mortality: CPB time longer than 120 minutes and LMCD; and CPB time greater than 120 minutes and angina pectoris IV (Fig. 1). Other combinations of risk factors were not significantly related to operative mortality.

DISCUSSION

Coronary artery bypass surgery offers great promise for symptomatic treatment of ischemic heart disease [1–4, 8]. At the present, data concerning the benefits of direct myocardial revascularization have been amply documented [1–3]. However, long-term results are not widely available [4] because this operation has only been performed for a relatively short period of time. Reluctance to recommend this surgery is partially related to the risk of open heart surgery. This study addresses the identification of those particular factors which affect operative mortality after coronary bypass surgery. Clinical, anatomic, hemodynamic and operative charac-
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Left Main Coronary Artery Disease

| Cardiopulmonary Bypass Time | N = 10 | N = 6 |
|-----------------------------|--------|-------|
| < 120 min                   | 40%    | 67%   |

| N = 142 | N = 14 |
|---------|--------|
| 0%      | 7%     |

Angina

| Classes I–III | N = 6 | N = 10 |
|---------------|-------|--------|
| Cardiopulmonary Bypass Time | 17%  | 70%    |

| N = 88 | N = 68 |
|--------|--------|
| 1.1%   | 0%     |

FIG. 1. Combined risk factors as related to operative mortality: Left Main Coronary Artery Disease versus Cardiopulmonary Bypass Time; Severity of Angina versus Cardiopulmonary Bypass Time. Numbers refer to total patients having both factors, percentage to mortality in each group.
teristics of the patients were analyzed. The overall operative mortality of 5.2 percent compares favorably with the range of 2.3 to 12 percent reported in 15 other surgical series [4, 8–12].

Four factors were found to be significantly associated with operative mortality: (1) angina pectoris Class IV NYHA; (2) abrupt propranolol withdrawal 24 hours prior to surgery; (3) left main coronary artery disease; and (4) cardiopulmonary bypass time longer than 120 minutes. The operative risk for individual patients with angina Class IV was four times greater than those patients with functionally less severe angina. Reports on the significance of severity of angina symptoms are conflicting; some authors report that severity of angina is a very important risk factor, while others do not find that severe angina significantly increases operative mortality [15–23]. It must be pointed out, that objective measurements of angina pectoris severity are not available; and this fact may explain in part the lack of agreement in the findings of different medical centers. Furthermore, medical therapy with beta blocking agents may change the functional classification for angina pectoris in individual patients. However, it is not clear that all published series are comparable concerning the use of beta blocking agents. Our patients were on optimal medical management at the time that they were classified according to their angina symptoms.

In the 106 patients in whom propranolol was withdrawn abruptly 24 hours prior to surgery, the mortality was 6.6 percent (7/106); while in the 41 patients in whom propranolol doses were gradually reduced over an average of three days and then finally discontinued 24 hours before surgery, the operative mortality was 2.4 percent [1/41 (p < 0.05)]. In the 25 patients in whom propranolol was not used at all preoperatively, the operative mortality was 4.0 percent (1/25). Seven patients died in the abrupt propranolol withdrawal group: six after sustaining a myocardial infarction (first postoperative week), and one after a cerebrovascular accident (first postoperative week). One patient died in the gradual propranolol withdrawal group due to non-cardiac cause (bleeding peptic ulcer, fourth postoperative week). One patient died in the group which did not receive propranolol before surgery (sudden ventricular fibrillation, sixth postoperative week). A number of observers have recently reported that in some patients with severe coronary artery disease symptoms, abrupt propranolol withdrawal can cause rebound angina and even fatal myocardial infarction [24–28]. These observations are, to date, anecdotal and controlled studies have not been reported. However, if the discontinuation of propranolol were responsible for the induction of myocardial infarction, a role for the drug in the prevention of myocardial necrosis in patients with coronary artery disease might be implied. Myocardial infarction as complication of sudden propranolol withdrawal appears to be related to a diminished drug effect which leaves the myocardium suddenly unprotected against stress, rather than to residual pharmacological effects of the drug [29]. However, because the drug is known to have a depressive action upon myocardial contractility, some authors have stressed that it should be discontinued [30] before anticipated myocardial revascularization to avoid increased morbidity and mortality in the early postoperative period. Our observations clearly indicate that abrupt withdrawal of propranolol increased the risk for coronary bypass grafting by a factor of two. Patients in whom propranolol therapy was suddenly withdrawn were chosen, depending upon the clinical preferences of the referring physician. In addition, they did not differ significantly with respect to known clinical, anatomic, or operative descriptors.
Left main coronary artery disease (LMCD) has been associated in several other studies with increased operative mortality in coronary artery bypass grafting [9, 15, 31-33]. The mortality of 25 percent for patients with LMCD observed in this study compares with that reported by several series [9, 15, 31-33]. The number of diseased coronary vessels were not associated with a higher mortality. However, patients with left main coronary disease had higher operative mortality than those patients without left main coronary disease; suggesting that the severity of coronary disease may, indeed, play an important role in operative mortality.

The other factor found to affect operative mortality was duration of cardiopulmonary bypass (Table 4). Mortalities for patients on bypass for less than 90 minutes, 90-119 minutes, and for 120 minutes or greater were 0 percent (0/119), 2.7 percent (1/37), and 50 percent (8/16), respectively. All 16 patients whose cardiopulmonary bypass time was longer than 120 minutes presented diffuse disease of one or more coronary vessels. These coronary arteries received grafts with great technical difficulty, thereby prolonging the CPB time to undesirable levels. The only difference found between patients with cardiopulmonary bypass time longer than 120 minutes and those with less than 120 minutes, was the presence of severe, diffuse distal coronary disease in those patients with prolonged cardiopulmonary bypass (> 120 minutes). Therefore, it appears that the severity and extent of coronary atherosclerosis rather than the duration of cardiopulmonary bypass determines the operative risk of an individual patient. No relationship was found between operative mortality and such factors as heart failure, heart size, left ventricular end-diastolic pressure and ejection fraction, despite data in the literature to the contrary [15, 18, 34, 35]. The reason that depressed ejection fraction and other measures of impaired left ventricular function were not significant risk factors in our study is that most patients with impaired left ventricles either had the additional procedure of mitral valve replacement or aneurysm surgery. Patients with these combined procedures do not appear in the present study.

Statistical analysis of the interdependence of risk factors has been included in the results section because those factors which do relate to operative mortality do not necessarily represent independent risks. Such analysis has demonstrated that two combinations of factors appear to be associated with a high surgical mortality: first, left main coronary artery disease with cardiopulmonary bypass time longer than 120 minutes; and second, angina pectoris Class IV with cardiopulmonary bypass duration greater than 120 minutes.

The combination of LMCD and CBP time longer than 120 minutes carries a mortality of 67 percent, while the absence of the combination carries no mortality (Fig. 1). The combination of angina pectoris Class IV and CBP time longer than 120 minutes showed a mortality of 70 percent; and when angina was less severe than Class IV and the CBP time was under 120 minutes, the mortality was only 1.1 percent (Fig. 1). These findings suggest, again, that the severity and extent of coronary artery disease and its clinical presentation, mainly severity and extent of angina pectoris, are the most important determinants of operative mortality.

**Clinical Implications**

Our data suggest the following clinical conclusions. First, patients on full medical therapy with angina pectoris Class IV NYHA are at four times greater risk for coronary bypass surgery. If these patients require a prolonged cardiopulmonary bypass time during cardiac surgery, their risk increases over fifty times. In this
study, the prolonged cardiopulmonary bypass time was usually attributed to the presence of diffuse disease of the grafted vessel or vessels. Second, patients with LMCD are 10 times at greater risk than those without LMCD. If the CPB time for these patients during surgery extends longer than 120 minutes, their risk increases significantly.

Finally, abrupt propranolol withdrawal appears to play a very important role in operative mortality. Patients in whom propranolol therapy was stopped suddenly showed a significantly higher mortality than those patients in whom propranolol was gradually tapered and finally discontinued 24 hours before surgery.

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