Reduced risk of coronary artery bypass surgery for unstable angina during a 6-year period

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Abstract

Objective: To assess the risk of early death or acute myocardial infarction in patients undergoing isolated coronary artery bypass surgery for unstable coronary artery disease. Methods: Retrospective observational study of 853 patients operated on because of unstable coronary artery disease during 1990–1995. Results: There were 5.9% deaths and 13.0% nonfatal infarctions ≤ 30 days. These figures declined during the observation period and were 2.6% and 6.2%, respectively, in 1995. The relative risk of early death or myocardial infarction was 50% less during 1994–1995 than during 1990–1991, after multivariate adjustment for several patient risk factors. The risk of death or infarction was almost twice as high in patients ≥ 50 years than in those < 50 years of age. Multivariate analysis showed that aortic-cross-clamp time ≥ 60 min, previous bypass surgery, pre-operative heart failure, emergency surgery, worse Braunwald class and non-use of an internal mammary artery graft were associated with an increased risk of death or infarction. Early mortality was 3.4% (24/702) in unstable patients without symptoms of congestive heart failure, who were not operated on emergently after failed percutaneous coronary intervention and had not had previous cardiac surgery. Conclusions: We observed a marked reduction of the risk of early death or myocardial infarction after surgery for unstable angina during the 6-year period 1990–1995. The risk reduction was not explained from operations performed on patients with less risk and indicates improved peri-operative patient management.

Keywords: Coronary artery bypass surgery; Unstable angina; Risk factors

1. Introduction

Unstable coronary artery disease is currently a common cause of admission to hospital and urgent coronary revascularization. The pathophysiological mechanisms in unstable angina include plaque rupture, platelet aggregation and thrombus formation as precipitating events causing coronary artery obstruction and myocardial ischaemia [1]. Despite antithrombotic treatment to prevent further thrombus formation and myocardial infarction, many patients require urgent coronary artery angiography and subsequent revascularization because of persistent chest pain [2,3]. In many reports the risk of early death or acute myocardial infarction is higher after surgery for unstable coronary artery disease than after elective operations in patients with stable angina pectoris [4–8].

This retrospective analysis of patients operated on because of unstable coronary artery disease during a 6-year period was performed to assess the risk of early death or myocardial infarction in relation to year of surgery and patient variables.

2. Material and methods

2.1. Patients

During 1990–1995, 853 patients underwent isolated coronary artery bypass surgery at the Karolinska Hospital in Stockholm for unstable coronary artery disease. The mean age was 64 (range 28–84) years and there were 231 females (27%). Coronary angiography had been performed if the symptoms persisted after 24 h despite intense medical treatment. In 821 patients (96%), the indication for surgery was unstable angina pectoris. The operations were undertaken urgently and never more than a few days after angiography. In 32 patients (4%), an emergency operation was performed because of pain or ischaemic changes on the ECG after failed percutaneous coronary intervention. Previous bypass surgery had been performed in 44 patients
(5%), 98 (12%) had undergone elective percutaneous coronary intervention and 499 patients (59%) had had an acute myocardial infarction. Some further characteristics of the patients are listed in Table 1.

The symptoms on admission for surgery were classified according to Braunwald [9]. Patients who had experienced angina at rest despite medical treatment during the last month but not during the last 48 h were in Braunwald class II and those with angina at rest or within the last 48 h preceding the operation were in class III. Subgroup B patients had unstable symptoms, without any extracardiac condition causing the pain, whereas subgroup C patients had had an acute myocardial infarction within 2 weeks before the operation. Almost 90% of the patients had experienced chest pain during the preceding 2 days and about one-fourth of the patients had suffered an acute myocardial infarction within 2 weeks before surgery (Table 2).

Angiography demonstrated three-vessel disease in 515 patients (61%), two-vessel disease in 156 (18%) and one obstructed main coronary branch only, not suitable for percutaneous coronary intervention, in 27 patients (3%). A significant left main-stem stenosis was present in 155 patients (18%).

At the time of the operation all patients were being treated with acetylsalicylic acid 75–160 mg per day, 648 (76%) had heparin and 618 patients (72%) were receiving nitroglycerine infusion.

### 2.2. Operative techniques

The patients were operated on via a median sternotomy using cardiopulmonary bypass and moderate hypothermia at 32–34°C. The most common method of myocardial protection was cold crystalloid modified St. Thomas’ cardioplegia with procainamide 5 mmol/l given antegrade into the aortic root (n = 491). In 201 patients cold diluted blood cardioplegia was administered into the coronary sinus and in the remaining 161 patients various combinations of these two techniques were used. The distal coronary anastomoses were constructed first and the proximal vein anastomoses to the aorta sutured while rewarming the patient. The internal mammary artery was used in 782 patients (92%). There was a total of 3049 distal anastomoses, i.e. an average of 3.6 coronary anastomoses per patient. Median cardiopulmonary bypass and aortic cross-clamp times were 76 (range 14–368) min and 38 (range 7–181) min, respectively.

### 2.3. Definitions and statistical methods

All patient charts were reviewed and information about deaths was obtained from the National Cause of Death Register, using the personal identification number. Early mortality was defined as death within 30 days of the operation. An infarction that had occurred within 2 weeks before the operation was included in the medical history as a previous acute myocardial infarction. An early acute myocardial infarction was defined as the appearance of a new Q wave or disappearance of an R wave in two or more adjacent leads which persisted after surgery and/or creatine kinase >20 μkat/l and aspartate aminotransferase (AST) >3 μkat/l with an AST/alanine aminotransferase ratio >2 within the first 48 h post-operatively. An autopsy was performed on all patients who died early and specimens were taken from the myocardium for microscopic examination. Information about patients with a non-fatal acute myocardial infarction after discharge from hospital and within 30 days of surgery (n = 10) was obtained from a myocardial infarction register covering the population of Stockholm. A reduced left ventricular function was defined as a markedly dilated ventricle, with one or more hypokinetic segments, on angiography or echocardiography with an estimated ejection fraction less than 30%. A history of heart failure was defined as pulmonary congestion on chest X-ray in the month before the operation requiring treatment with diuretics.
The relative risk of early death or an acute myocardial infarction was estimated crude and in multivariate analysis using Cox's proportional hazards regression [10]. The follow-up time was 30 days after the operation for all patients except in case of death or a myocardial infarction within this period, when the follow-up was terminated at the day of the event. In the multivariate analysis adjustment was made for age and other prognostic factors significantly associated with early death or myocardial infarction. Variables that did not influence the point estimate of relative risk when adjusted for in the multivariate analysis were excluded from the final model. The test of the hypothesis of no effect was assessed by using the Wald statistic. Estimates of relative risks were accompanied by asymptotic 95% confidence limits. In the multivariate analysis age was included in the models as a continuous variable and all other variables as dichotomous variables.

3. Results

3.1. Early mortality and myocardial infarction

Fifty of the 853 unstable patients (5.9%) died a median of 7 (range 1–30) days after the operation. Four of the early deaths among the unstable patients occurred after discharge from hospital. Eighty percent of the deaths were from cardiac causes (Table 3). Forty-seven of the deceased patients (94%) were in Braunwald class III, 17 of whom (36%) in Braunwald class IIIC had had an acute myocardial infarction within the last 2 weeks and 21 patients (42%) had had a recent history of congestive heart failure. Early mortality was 3.4% (24/702) in unstable patients without symptoms of congestive heart failure. Early mortality was 3.4% (24/702) in unstable patients without symptoms of congestive heart failure, who were not operated on emergently or had previous cardiac surgery.

An early myocardial infarction was documented in a total of 147 patients (17.2%), in 111 of whom (13.0%) the infarction was nonfatal. Altogether there were 161 cases (18%) of early death or non-fatal myocardial infarction.

Table 3
Underlying cause of death in 853 patients undergoing coronary artery bypass surgery for unstable coronary disease

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac causes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>36</td>
<td>72</td>
</tr>
<tr>
<td>Low cardiac output</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Non-cardiac causes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Infection</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

3.2. Early death and myocardial infarction in relation to time period and risk factors

The early mortality declined from 9.7% in 1990 to 2.6% in 1995. The corresponding figures for nonfatal early myocardial infarction were 13.9 vs. 6.2%. With univariate analysis the relative risk of early death or myocardial infarction was 50% less during 1994–1995 than during 1990–1991 (Table 4). This estimate was essentially unchanged when differences over time, in age, Braunwald class, previous cardiac surgery, emergency surgery and history of heart failure were taken into account. Thus, the improvement was not explained from operations performed on low-risk patients.

The risk of an early event was about twice as high in patients 50 years of age or more than in those less than 50 years. Five of the 21 patients (24%) 80 years of age or older died early or suffered a myocardial infarction. The risk was two and a half times higher if the aortic cross-clamp time exceeded 60 min than if the time was less than 30 in. The proportion of operations with aortic cross-clamp times longer than 60 min did not decrease, being 13.5% (27/200) during 1990–1991 and 16.0% (61/382) during 1994–1995. Previous bypass surgery, congestive heart failure before the operation, emergency surgery after failed percutaneous coronary intervention and a worse Braunwald class were associated with an increased risk of early death or a myocardial infarction. The rate of death or infarction was higher in patients who received retrograde blood cardioplegia than in those receiving antegrade crystalloid cardioplegia. A 1.5 times higher risk persisted after adjusting for patient variables. Taking into account differences in patient characteristics, a reduced left ventricular function, previous elective percutaneous coronary intervention, hypertension, previous acute myocardial infarction, gender, hyperlipidaemia, diabetes mellitus and the presence of left main-stem stenosis did not significantly influence the outcome.

The risk of death or infarction was less than half in patients who received an internal mammary artery graft than in those who did not. The reason for not using an internal mammary artery was a redo procedure in 34% (24/71 patients). A reduced risk associated with use of an internal mammary artery persisted after multivariate correction for factors such as repeat bypass procedure, emergency surgery and heart failure.

4. Discussion

This study shows a substantially improved early prognosis after coronary artery bypass surgery in patients operated on because of unstable angina pectoris. We included patients in Braunwald class II or worse and not patients in Braunwald class I, who had new onset of angina or aggravating symptoms the month before the operation. Although
such patients were frequently encountered they could not be identified retrospectively.

Our results concern a subset of patients undergoing an isolated bypass operation with a relatively short aortic cross-clamp time. We analyzed the combined adverse end-point, early mortality or non-fatal myocardial infarction as markers of major myocardial damage following surgery for unstable coronary disease. Eighty percent of the early deaths were from cardiac causes and autopsy was performed to verify if the cause was an early myocardial infarction. Louagie et al. found that low cardiac output caused 69% of hospital deaths in patients operated on for unstable angina [7]. We included all deaths, since there might have been patients who died in the operating room, in whom the myocardial damage was too recent to be detected at the autopsy [11]. Furthermore, cardiac causes may have contributed to the fatal outcome in patients listed to have stroke or infection as the underlying cause of death. We chose to include every patient who died within the first post-operative month and used both enzyme and electrocardiographic criteria to detect an acute myocardial infarction. Therefore our rate of peri-operative myocardial infarction was higher than if only infarctions diagnosed in survivors the first post-operative day were included. In a literature review there were no consistent definitions and the reported rate of peri-operative myocardial infarction ranged from 4 to 17% [6].

The risk increased with age and longer aortic cross-clamp time. A long cross-clamp time often reflects more extensive coronary disease, the need for multiple distal anastomoses and technical difficulties. In our analysis, history of chest pain within 2 days and an acute myocardial infarction within 2 weeks increased the risk of early death or a myocardial infarction associated with the operation. Wasvary and co-workers found that the clinical condition of the patient and the left ventricle predicted outcome rather than the timing of the operation after an acute myocardial infarction [12]. In other reports, early year of surgery, urgent surgery, female gender, increasing age, aortic cross-clamp time, depressed left ventricular function, reoperation, number of diseased
vessels, pre-operative intra-aortic balloon pumping, left main stenosis and pre-operative myocardial infarction increase the risk of early death after surgery for unstable angina [7,13,14].

Our observational study was not designed to evaluate the impact of different methods of cardioplegia. There was no randomization of the different techniques and at each operation the surgeon selected the preferred method of cardioplegia. In a recent randomized trial there were no differences in mortality and morbidity between antegrade crystalloid and retrograde blood cardioplegia [15]. In critically ill patients the internal mammary artery was not dissected and also, it was not inserted at redo procedures, which partly explains the observed higher risk when only vein grafts were used. The mammary artery in addition to its excellent patency rate has the advantage that myocardial reperfusion is instituted immediately, in contrast to vein grafts that first must be anastomosed to the aorta. In the Society of Thoracic Surgery Database, operative mortality was significantly less in patients having at least one mammary artery graft than in those with only vein grafts, except for in patients more than 70 years of age requiring reoperations [16]. Furthermore, Seargent and co-workers have found that use of arterial grafts significantly reduce the risk of both peri-operative and late myocardial infarction [17].

The 50% reduced risk of early mortality or non-fatal myocardial infarction during a 6-year period could not be explained by patient selection and was present after multivariate correction for patient risk factors. Limitations of our analysis included factors that could not be evaluated in the absence of valid information such as skill of the surgical team, development of the anaesthesiological management, and improved pre-operative medical treatment and haemodynamic monitoring.

In conclusion, the incidence of adverse events, early mortality or early non-fatal myocardial infarction declined substantially during a 6-year period after bypass surgery in patients with unstable coronary artery disease. This improvement could not be explained by changes in patient risk factors during the study period, and indicates an improved peri-operative management.

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References