Myocardial revascularization in patients with severe ischemic left ventricular dysfunction. Long term follow-up in 141 patients


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Abstract

Objectives: The present study evaluates our experience with coronary bypass grafting in patients with EF ≤25%. Myocardial revascularization in this setting remains controversial because of concerns over operative mortality and morbidity and lack of functional and survival benefit. Materials and methods: One hundred and forty-one patients with coronary artery disease and left ventricular ejection fraction ≤25% underwent coronary artery bypass graft between January 1988 and December 1998. Mean age at operation was 63.3 years and 81.4% were male. The major indication for surgery was angina (114 patients, 80.8%). Ejection fraction (EF), left ventricular end diastolic pressure (LVEDP) and cardiac index (CI) were used to assess left ventricular function. The number of graft was 2.7 ± 1.6/patient. Internal mammary artery was used in 119 patients (84.3%). Intra aortic balloon pump was placed preoperatively in 25 patients (17.7%). Five operative risk factors were associated with a higher mortality: emergency, female sex, LVEDP, CI and NYHA class IV.

Results: The operative mortality was 7% (10 patients). Left ventricular ejection fraction (assessed post operatively in 83 patients) improved from 22.2% preoperatively to 33.5% post operatively (P < 0.001), mean end diastolic volume index fell from 98 to 83 ml/m² following surgery. Survival at 2, 5 and 7 years was respectively 84 ± 3%, 70 ± 4% and 50 ± 5%. Two variables were associated with increased long term survival: congestive heart failure (NYHA class lower than IV (P = 0.035) and cardiomegaly (P = 0.04) Conclusion: In patients with left ventricular dysfunction, myocardial revascularization can be performed relatively safely with good medium term survival and improvement in quality of life and in left ventricular function. Coronary artery bypass graft may be offered to patients with impaired ventricular function, but careful patient selection and management when considering these patients for operation should assess potentially reversible dysfunction. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Heart failure; Congestive; Coronary artery bypass

1. Introduction

Left ventricular function is an important predictor of hospital and late mortality following coronary artery bypass graft (CABG). Despite improvement in surgical technique, myocardial protection and postoperative care, surgical risk remains high and long-term survival is poor. Many studies [1–3] show that patients have better long term survival expectancy after coronary surgery than with continuous medical therapy and coronary bypass surgery is often the only available treatment that will improve symptoms and long-term survival because alternative treatments, such as transplantation, cardiomyoplasty and transmyocardial laser revascularization, are limited and the results of medical treatment are often unsatisfactory. This study evaluates short and long-term results after myocardial revascularization in patients with ejection fraction (EF) lower than 25%.

2. Patients and methods

Between January 1988 and December 1998, 141 patients whose preoperative EF was less than or equal to 0.25% underwent CABG. Patients undergoing CABG in combination with valvular surgery, left ventricular aneurysm resection, any other cardiac or aortic surgery, reoperation, arrhythmia surgery, angioplasty or thrombolytic therapy were excluded from this study.

Clinical, electrocardiographic and angiographic data are summarized in Tables 1 and 2. Mean age was 63 ± 8 years and ranged from 40 to 84 years. Thirty patients were over 70 (21%), and 10 were under 50 years old (7%). Twenty-six were women (18%). Hypertension was present in 48
patients (34%), diabetes in 29 (20%). Severe obesity was present in 11 patients (body weight ≥15% of the weight expected according to the patient’s height). Angina was present in 114 patients (80.8%), unstable angina was observed in 45 patients (31.9%). Symptoms of heart failure were present in 70 patients (50%). Thirty-nine patients were in NYHA class III and IV. History of hospitalization due to heart failure was present in 28 patients complicated by episodes of pulmonary oedema in 12. Sixty-three patients had experienced one or more myocardial infarctions before surgery. A mitral valve incompetence graded 1 (20 pts) or 2 (18 pts) was present preoperatively in 27% of the patients.

An exercise stress test was performed only in patients with stable angina. Preoperative echocardiography showed a mean left ventricular diastolic diameter of 62 mm (range 51–76), a mean left ventricular systolic diameter of 45 mm and shortening fraction of 0.23 ± 0.01. Evidence of reversible ischemia in the distribution of one or more major coronary arteries was assessed by dipyridamole thallium scintigraphy (15 patients) or dobutamine stress echocardiography (34 patients).

Cardiac catheterization was carried out in all patients to assess ventricular function and coronary artery disease (Table 2). Preoperative EF of 25% or less, and left ventricular end diastolic volume index (LVEDVI) were calculated by area/length measurement on biplane ventricular cineangiography and planimetry. Wall motion score was determined and the degree of coronary stenosis was estimated from a review of at least two views of each coronary artery. Right heart catheterization was carried out and cardiac output measured. Left ventricular ejection fraction (EF), left ventricular end diastolic pressure (LVEDP) and cardiac index (CI) were used to assess left ventricular function (Table 2). Preoperative and postoperative angina and cardiac heart failure (CHF) were assessed according to the Canadian Cardiovascular Society and to the NYHA classifications.

Timing of surgery was classified as stable and unstable, urgent (less than 24 h after the coronary angiogram) and emergency (less than 12 h) [4]. Nineteen patients were operated on an urgent basis and 18 on an emergency basis. All patients with unstable angina were treated in ICU and received beta blockers, calcium blockers and IV nitroglycerin. Twenty-eight of the 49 patients presenting transmural infarction within 30 days before surgery had unstable angina.

Coronary angiography revealed triple vessel disease in 90 patients (63.8%), and left main coronary artery (LMCA) + right coronary disease in 21 patients (14.8%). Mean LVEDP was 22.3 mmHg, mean EF was 0.21, mean CI was 2.23 l/min/m² (Table 2). The mean interval between the last EF determination and surgery was 47 days. An intra aortic balloon pump (IABP) was inserted preoperatively in 25 patients, during surgery in nine and after surgery in 11 patients.

2.1. Surgical technique

Peripheral venous and arterial lines were inserted under local anaesthesia. The anaesthesia was balanced and used fentanyl citrate (25 μg/kg), midazolam and pancuronium bromide (0.1 mg/kg). A Swan–Ganz thermodilution catheter was introduced percutaneously through the internal jugular vein in all patients.

Membrane oxygenators were used in all patients. Cardiopulmonary bypass was performed in normothermia and blood was added to the clear priming volume to maintain a haematocrit higher than 20%.

2.1.1. Myocardial protection

Cold crystalloid cardioplegia was used from 1987 to 1989 on 43 patients (30%). Distal anastomoses were performed during cross clamp time and aortic anastomoses were carried out using tangential aortic clamping with the heart empty but beating. Since 1989, intermittent cold blood with warm reperfusion (45 patients) or continuous retrograde warm blood cardioplegia (53 patients) [5] have been used according to the surgeon’s preferences. All anastomoses were performed during cross clamp time. The average

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Preoperative clinical data</th>
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<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>Men</td>
<td>115</td>
</tr>
<tr>
<td>Body surface area</td>
<td>1.81 ± 0.2</td>
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<tr>
<td>Heart enlargement on chest X-ray</td>
<td>95</td>
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<tr>
<td>Hypertension</td>
<td>48</td>
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<tr>
<td>2 or more previous MI</td>
<td>63</td>
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<tr>
<td>Peripheral vascular disease</td>
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<tr>
<td>Diabetes mellitus</td>
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<tr>
<td>Dyslipidemia</td>
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<tr>
<td>Obesity</td>
<td>11</td>
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<td>Creatinine &gt;180 μmol/l</td>
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<tr>
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<tr>
<td>EKG abnormalities</td>
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<td>Arrhythmias</td>
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* LVEDP, left ventricular end diastolic pressure; IABP, intra aortic balloon pump.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Preoperative data</th>
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<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>21</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>22</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>2.3</td>
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<tr>
<td>Number of diseased vessels</td>
<td></td>
</tr>
<tr>
<td>1 vessel</td>
<td>4</td>
</tr>
<tr>
<td>2 vessels</td>
<td>35</td>
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<tr>
<td>3 vessels</td>
<td>90</td>
</tr>
<tr>
<td>4 vessels</td>
<td>12</td>
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<tr>
<td>Left main coronary artery disease</td>
<td>29</td>
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<tr>
<td>Preoperative IABP insertion</td>
<td>25</td>
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</table>
number of coronary arteries grafted was 2.7 ± 1.6. At least one internal mammary artery was used in 119 patients. A coronary artery endarteriectomy was performed in 11 patients (8%). Mean cross clamp time was 60 ± 19 min and mean CPB time was 95 ± 30 min. We never rushed to go off bypass. The heart was allowed to recover to the maximum extent with minimal pulmonary pressures and minimal inotropic support. Inotropes were required to wean 78 patients from CPB.

Perioperative or postoperative myocardial infarction was defined as the appearance of a new Q wave with an elevation of the CK MB isoenzyme higher than 50 U/l or more than 8% of total CK.

Follow-up was complete for all patients. Information was obtained from the patient interview and examination or by phone calls to the physician or the cardiologist. Postoperative follow-up included clinical assessment and serial transthoracic echocardiography.

In case of death during long-term follow-up the mode and causes of death were obtained from relatives and/or referring physicians.

### 2.2. Data analysis

Statistical analysis were performed using Fischer’s exact test or student’s test when appropriate. A P-value less than 0.05 was considered significant. A number of variables which might affect mortality were assessed by univariate analysis before being entered into a stepwise logistic regression model. Late survival was calculated according to Kaplan Meier actuarial survival curves and also correlated retrospectively to preoperative features.

### 3. Results

Operative mortality was 7% (10 patients). The causes of death were cardiogenic shock in five patients (with ventricular arrhythmia in two), multi-organ system failure in four (one myocardial infarction) and mediastinitis in one. The mean interval between death and the procedure was 7.9 days (range 1–22). The most common postoperative complications were arrhythmias, pneumonia and low cardiac output diagnosed when inotropic drugs were required for longer than 30 min to maintain systolic blood pressure higher than 90 mmHg and a CI lower than 2 l/min⁻¹ m², or when IABP was required to maintain the hemodynamic condition (Table 3). Mean duration of postoperative hospitalization for survivors was 11 days.

Five preoperative risk factors were associated with an increased operative mortality: patients with elevated LVEDP ≥ 23 mmHg (operative mortality 20 vs. 2.7%, P ≤ 0.03), a cardiac index lower than 2.3 l/min/m² (mortality 15 vs. 2%, P ≤ 0.05), NYHA functional class 4 (operative mortality 29 vs. 3%, P ≤ 0.002), female sex (mortality 19 vs. 4%, P ≤ 0.02) and emergency operation (mortality 25 vs. 6%, P ≤ 0.04). Patients with elevated LVEDP and decrease cardiac index had a mortality rate of 25%. Advanced age, left main coronary artery lesions, longer CPB time, myocardial protection modalities were not predictors of outcome. NYHA class IV, female sex and emergency were entered in the stepwise logistic regression with odd ratios of 9.7 for NYHA class IV, 4.8 for female sex and 4.2 for emergency operation.

#### 3.1. Long term survival

Mean follow-up was 38 months (12–108). No patient was lost to follow-up. There were 30 late deaths. Late deaths were related to heart failure in 15 patients, to sudden deaths in seven, and to non-cardiac-related causes in eight. Survival was 84 ± 3% at 2 years, 70 ± 4% at 5 years and 50 ± 5% at 7 years (Fig. 1). Most patients were reassessed in a lower CCS and NYHA class 6–12 months after surgery (Fig. 2). Nearly all patients were free from angina, only seven had mild symptoms. Four patients remained in NYHA class IV, of whom two received heart transplantation. All patients were left on medication including diuretics, vasodilators, aspirin or anticoagulants in case of atrial fibrillation.

Exercise capacity of the patients increased after surgery from 51 to 81 W (P < 0.01).

Transthoracic echocardiography was performed in 82

![Fig. 1. Actuarial survival curve after CABG in low ejection fraction patients (n = 141).](image-url)
patients between 6 and 9 months postoperatively. Mean ejection fraction improved from 22.2 to 33.5% \((P < 0.001)\). A reduction in left ventricular volume was also observed; mean end diastolic volume index fell from 98 to 83 ml/m² following surgery \((P < 0.001)\). Sixty-nine percent of the patients who preoperatively had mitral insufficiency had a reduction of the severity of regurgitation. Patients with angina as the primary indication of surgery showed a mean ejection fraction increase of 13.2 vs. 6.4% in patients with cardiac failure \((P = 0.02)\). Similar results were obtained categorizing patients on the basis of preoperative end diastolic volume index. Patients with end diastolic volume index >95 ml/m² showed a mean ejection fraction increase of 5.1 vs. 12.1% in patients with end diastolic volume index <95 ml/m². Our study revealed two factors associated with a significant increase of long term survival after CABG for patients with EF ≤ 0.25: cardiomegaly (cardiothoracic ratio >0.55 on chest X-ray) \((P = 0.04\) for logrank test) and NYHA class lower than IV \((P < 0.001)\).

4. Discussion

Early and long-term survival rates of patients with impaired ventricular function, undergoing CABG are related to the different criteria characterizing this function. We used LVEF, LVEDP and CI to assess left ventricular function in these patients \([6]\). Many studies have concluded that CABG in such patients is effective and able to provide a better prognosis than medical treatment \([1–4, 7–9]\). Alderman et al. \([1]\) reported a 5 year survival rate of 43% for the medical group compared with 63% for the surgical group. Nevertheless, operative mortality rate was 1–2% in patients with normal left ventricular EF, compared to 6.9% in patients with impaired left ventricular function.

4.1. Operative mortality

The surgical problem may be to reduce the mortality in patients with CAD associated with poor left ventricular function. In series conducted on patients with ejection fraction lower than 20, 25 or 30%, operative mortality rates ranged from 4.7 to 15% \([4, 10–12]\). Increased operative mortality after surgery in patients with low ejection fraction has previously been associated with several factors (advanced age, female gender, obesity, emergency, severity of coronary artery disease, preoperative cardiac failure, ventricular arrhythmias, low cardiac index, elevated end diastolic pressure, renal failure). Christakis et al. \([4]\) found five operative risk factors for groups with EF ≥ 0.40 and EF between 0.20 and 0.40: age, sex, LMCA stenosis, redo, emergency. For EF ≤ 0.20, urgency of operation was the only risk factor. Goor \([7]\) found cardiomegaly as a significant risk factor, no death occurring in patients with a normal-sized heart. Louagie et al. \([11]\) found that obesity was a significant risk factor (two-thirds of the patients who died were obese). In the present series, operative mortality was 7%, indicating that coronary revascularisation can be performed with an acceptable operative risk in this subgroup of patients.

4.2. Intraaortic balloon pump

We tend to use IABP rapidly in patients who require high doses of inotropic agents and also frequently in the preoperative period for patients when maximal medical therapy has failed or for patients with LMCA + RC disease. In recent years, a number of published studies \([12, 13]\) have expanded the potential clinical applications of IABP, to include high risk patients who undergo CABG. Dietl et al. \([12]\) undertook a 5-year retrospective analysis of 163 consecutive CABG patients with severe ventricular dysfunction \((EF \leq 25\%)\). Thirty seven patients had received IABP support preoperatively, while 126 did not. The 30-day mortality rate was 2.7% among patients receiving preoperative IABP vs. 11.9% in the non-preoperative IABP group \((P < 0.005)\). This increased survival when using preoperative counterpulsation support was particularly evident among patients undergoing reoperation, patients in NYHA functional class III or IV and in those who had experienced a recent myocardial infarction or with LMCA stenosis \([13]\).

Our study indicates that the combination of EF, LVEDP
and CI more accurately characterizes the operative risk of CABG in patients with poor left ventricular function, than EF alone [6]. It focuses on coronary surgery in patients with EF ≤ 0.25. The only long-term series [14], a group of 140 patients with 22% operative mortality, was expanded to 232 patients with 41% survival at 5 years and 14% at 10 years. Lansman et al. [10] presented a survival of 88% at 1 year which declines continuously, particularly after 3 years, to 34% at 6 years. Four significant predictors of long-term survival after CABG for patients with EF of 0.20 or less were: chief complaint of pain only, unstable angina, Canadian and NYHA class lower than IV.

4.3. Mitral insufficiency

The incidence of ischemic mitral insufficiency (IMR) in patients undergoing coronary bypass surgery varies between 4 and 7% [15,16]. In patients with severe left ventricular dysfunction, IMR incidence has been reported to reach 43% [17]. Dilatation of the mitral annulus is present in all cases and is the only mechanism of regurgitation in 50% of the patients [15]. There is no general agreement in the literature regarding the surgical attitude. In the presence of IMR, hospital mortality for coronary bypass grafting alone increases from between 3% and 6.5% up to 15 to 33% when CABG is associated with mitral valve repair or mitral valve replacement. Furthermore, 5-year mortality is increased two-fold in patients with moderate/severe IMR who have had only coronary revascularization [15,16,18]. In the present study 38 pts had IMR (grade 1 in 30 patients; grade 2 in 18). In grade 2 patients, IMR remained unchanged, but survival showed a 3-year freedom from cardiac death of 58% compared with 88% in patients without IMR In grade 1 patients, the observation that mild IMR is corrected by myocardial revascularization [15] was confirmed in the present study. Indeed, 69% of the patients who preoperatively had IMR, had a reduction of the severity of the regurgitation. These data encourage a conservative attitude toward surgery for concomitant low-grade IMR (grade 1 and 2), restricting it to severe regurgitation.

4.4. Quality of life

The present study and others [19–22] show a significant improvement in both angina and heart failure status, not only objectively (EF 22.2 vs. 33.5%) but also large enough to be of clinical relevance. Patients with angina as the main symptom were significantly more likely to improve their left ventricular ejection fraction after surgery. These findings are consistent with the concept that preoperative angina predicts a good result, but its absence is not necessarily associated with a poor result. Ischemic dysfunction may be reversible or not [4,9,17], the degree of reversibility probably determining which patients will respond favourably to CABG [4,16–19]. Potentially reversible dysfunction should be assessed when considering CABG for patients with poor left ventricular function (ischemic or hibernating myocardium) [9,20,21]. Our findings suggest that CABG in patients with impaired left ventricular function is indicated when predominant signs of myocardial ischemia (angina) are present and coronary revascularization is possible. Additional factors include wall motion improvement in response to nitrates or catecholamine infusion, thallium scanning and metabolic viability as indicated by positron emission tomography [23]. Patients with symptoms of cardiac failure in the absence of angina but with cardiac viability had satisfactory results in terms of survival, symptoms relief and improvement of ventricular function. On the other hand, unsatisfactory results were obtained in patients with marked chronic left ventricular dysfunction. Cardiac transplantation [24] would be the best treatment for these patients, if their age permitted.

References


Appendix A. Conference discussion

Dr A. Arifi (Hong Kong, China): My question is that when you assess the risk factors, I see you haven’t mentioned ischemic time. I think your average graft is about two grafts in this study, two to three grafts, and your ischemic time was 60 minutes, and I think having a patient with an ejection fraction of 25% is not very uncommon, but having a mortality of 7%, I think that is too much, and I feel that an ischemic time of 60 minutes may be a reasonable factor for this. What do you think about that?

Dr Bouchart: We don’t have a control group to assess that, but the 60 minutes we used to do all the anastomosis during cross-clamp time. So it is quite a longer cross-clamp time.

Mr S. Large (Cambridge, UK): I think the previous speaker was a little hard on you. I think these are very commendable results in a very challenging group of patients. The area I am very interested in, tackling patients like this as well, is the use of arterial grafts. I see that you only used arterial grafts in 40%, in other words, the minority. Like you, I am very reluctant to use arterial grafts here because of concerns about the requirement for inotropic drive and subsequent arterial vasospasm leading to myocardial ischaemia. My worry is that they might actually be a risk factor for death.

Dr Bouchart: It may be. We used arterial grafts essentially in the younger age group, and at the beginning we used saphenous vein grafts for the first two or three years systematically for those patients, but after ’91 we used at least the LIMA to the LAD like for older patients, and for the younger age group, that means patients below 60, we used arterial graft, although I must recognize that 50% survival at five years may be a good indication for doing only one mammary and vein graft.

Mr Large: Let me be more specific. Do you use the radial graft here?

Dr Bouchart: Yes. I think about four patients.

Mr Large: Okay. Concerns surround the use of a vasodilator for radial artery patency. So often these patients present with a very challenging problem of continued expression of preoperative vasodilation from drugs for their heart failure, particularly ACE. The early postoperative period can be very trying, requiring pressors. I am very nervous about the use of pressors plus vasodilators in radial arteries. Is this a practice you are going to promote?

Dr Bouchart: We didn’t have the feeling that there was trouble with the radial arteries in those patients, although I didn’t really specifically look into this data, but it is not our feeling. We put the radial artery in diltiazem just after harvesting and try to put them on calcium blocker as soon as possible, but of course for those patients it is really difficult to put them on a calcium blocker in the OR.

Mr S. Ashraf (Swansea, UK): Out of your 7% mortality, how many patients did have preoperative balloon?

Number two, have you changed your practice now? Do you put more preoperative balloon in the really poor LV function group?

Dr Bouchart: Repeat the question.

Mr Ashraf: Out of your 7% mortality, how many of those patients had preoperative balloon?

Dr Bouchart: The balloon pump did not show up as a risk factor for death.

Mr Ashraf: All balloon patients survived, did they?

Dr Bouchart: No. Two patients with balloon died but the others did well. So I think we can be really liberal in putting balloon pump preoperatively in these very high risk patients.