

# Coronary Reoperations: Recurrence of Angina and Clinical Outcome With and Without Cardiopulmonary Bypass

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**Background.** We compared our experience of minimal tissue dissection and target vessel revascularization without cardiopulmonary bypass (CPB) with the standard procedure of total dissection of the heart and complete revascularization with CPB in patients who had elective reoperative coronary artery bypass grafting (redo-CABG).

**Methods.** We analyzed recurrence of angina and clinical outcome in 118 patients who had elective redo-CABG between January 1995 and April 2002. Seventy-four patients had redo-CABG with CPB, and 44 patients had redo-CABG without CPB.

**Results.** Perioperative outcome was comparable with regard to morbidity and mortality rates. At follow-up, the mean Canadian Cardiovascular Society score was  $1.3 \pm 0.6$  in patients who had redo-CABG with CPB and  $1.7 \pm 0.8$  in patients who had redo-CABG without CPB ( $p = 0.02$ ). At follow-up, patients who had redo-CABG with-

out CPB had a higher rate of recurrence of angina (log rank = 0.001) and higher use of nitrates ( $p = 0.015$ ). Target vessel revascularization was an independent predictor of recurrence of angina in younger patients (< 75 years;  $p = 0.012$ ) but not in the elderly ( $\geq 75$  years;  $p = 0.142$ ).

**Conclusions.** In elective redo-CABG patients, minimal tissue dissection and target vessel revascularization without cardiopulmonary bypass did not add significant benefit with regard to perioperative morbidity and mortality. The unsatisfactory relief of symptoms does not seem to justify target vessel revascularization by a less invasive approach. Therefore, this technique should be offered exclusively to patients at high risk with complete revascularization using CPB, such as the elderly.

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Reoperative coronary artery bypass grafting (redo-CABG) with cardiopulmonary bypass (CPB) currently accounts for 2% to 6% of all myocardial revascularization procedures [1, 2] and is associated with higher hospital morbidity and mortality rates than primary CABG [3-5]. Single-vessel redo-CABG without CPB can be performed safely and reduces the morbidity associated with conventional single-vessel redo-CABG [6]. Redo-CABG without CPB might prove to be more effective in reducing morbidity and mortality in a high-risk population, such as the elderly, who are generally more frail and have a diminished physiologic reserve compared with younger patients [7]. In elderly patients, redo-CABG with CPB is associated with higher hospital morbidity and mortality rates than primary CABG because these patients have more comorbidities [2-5]. Complete revascularization with the use of CPB remains the main object in primary CABG [8-10]. Target vessel revascularization without CPB is a promising option for selected high-risk patients who undergo primary CABG, predominantly because of lower perioperative mortality rates [11]. Few data exist, however, with regard to midterm and long-

term follow-up in these patients. Furthermore, an adverse effect of additional non-left anterior descending coronary artery stenoses in patients who had grafting only of the left internal thoracic artery to the left anterior descending coronary artery (LAD) called into question the long-term appropriateness of interventions whose strategy includes leaving unvascularized segments in territories not in the distribution of the LAD [12]. To date, the main object of redo-CABG is to relieve symptoms, as the survival benefit of the procedure has not yet been clearly demonstrated [9].

The aim of this retrospective analysis was to compare our experience of minimal tissue dissection and target vessel revascularization without CPB with the standard procedure of total dissection of the heart and complete revascularization with CPB in patients who had elective redo-CABG.

## Patients and Methods

### Patients

One hundred eighteen patients who had elective redo-CABG between January 1995 and April 2002 were included. Seventy-four patients had redo-CABG with CPB (< 75 years  $n = 43$ ;  $\geq 75$  years  $n = 31$ ), and 44 patients had

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Table 1. Patient Demographics

	With CPB (n = 74)	Without CPB (n = 44)	p Value
Age (yrs)	67.1 ± 7.7	66.9 ± 8.9	0.892
Diseased vessels (n)	2.7 ± 0.5	2.6 ± 0.6	0.298
Ejection fraction (%)	57 ± 11	53 ± 14	0.241
Time to previous CABG (yrs)	11.1 ± 5.7	12.0 ± 4.9	0.541
EuroSCORE	6.1 ± 2.7	6.7 ± 2.9	0.326
Parsonnet score	15.4 ± 1.2	15.0 ± 1.4	0.412

CABG = coronary artery bypass grafting; CPB = cardiopulmonary bypass.

redo-CABG without CPB (< 75 years  $n = 28$ ;  $\geq 75$  years  $n = 16$ ). In this retrospective study, emergency cases, patients with unstable angina as well as patients requiring other surgical options, such as transmyocardial laser revascularization, were excluded. The decision regarding which surgical strategy to use—minimal tissue dissection and target vessel revascularization without CPB or dissection of the entire heart and complete revascularization with CPB—was determined by the individual surgeon. A median sternotomy approach was used in all cases. In patients who had target vessel revascularization, we dissected the area of the target anastomosis and left the whole mediastinum undissected. If proximal aortic anastomotic sites were necessary, a small part of the ascending aorta was also dissected in order to apply a side-biting clamp. Preoperative patient characteristics (Table 1) include all features comprising the EuroSCORE, Parsonnet score, and the number of diseased vessels [13, 14].

#### Parameters of Clinical Outcome

In-hospital death, myocardial infarction, and stroke were defined as major adverse perioperative events. Perioperative myocardial infarction was defined as any new Q wave or loss of R in the electrocardiogram, significant increase in creatine kinase or creatine kinase-MB (creatinine kinase-MB > 40 U/L), or infarction validated at autopsy. Postoperative bleeding was defined as bleeding requiring reoperation. The systemic inflammatory reaction after CABG was defined by low blood pressure and increased heart rate, increased body temperature, leucocytosis, and tissue edema [15].

Minor adverse events were defined as wound infections or postoperative atrial fibrillation. We also recorded the number of bypass grafts, required units of blood, intubation time, and length of stay in the intensive care unit and in the hospital. We studied postoperative as well as long-term outcome.

#### Follow-Up

Endpoints were defined by means of survival, freedom from recurrence of angina (Canadian Cardiovascular Society [CCS] score), freedom from reinterventions as well as need for antianginal medication. All patients were seen in the outpatient clinic. The CCS score was determined according to the daily life activities of each patient. Follow-up was complete in all patients.

#### Completeness of Revascularization and Definition of the Culprit Lesion

Revascularization was considered incomplete when a territory was judged surgically nonreconstructable or when a suitable vessel was discarded. The decision regarding which lesion definitely was the culprit lesion was based on accurate clinical investigation including angiograms, electrocardiograms, and scan techniques.

#### Preoperative Graft Status

There were no significant differences with regard to patent, hemodynamically significantly stenosed (> 70%), or occluded grafts between the two groups. In patients who had CPB, the previous left anterior descending coronary artery (LAD) graft was a saphenous vein in 80.5% and a left internal mammary artery (LIMA) in 19.5%; in patients without CPB the LAD graft was a saphenous vein in 80.0% and a LIMA 20.0% ( $p = 0.694$ ). In patients with CPB, 27.4% of vein grafts were patent and 85% of these grafts showed hemodynamically significant stenoses; in patients without CPB, 25% of vein grafts were patent and 80% were stenosed ( $p = 0.154$ ). In patients with CPB, 80% of LIMA-to-LAD grafts were patent; in patients without CPB, 100% of LIMA-to-LAD grafts were patent ( $p = 0.532$ ). In patients with CPB, 25% of vein grafts to the circumflex system were patent, and 75% of these grafts showed hemodynamically significant stenoses; in patients without CPB, 32% of vein grafts were patent, and 90% of grafts were stenosed ( $p = 0.431$ ). In patients with CPB, 6% of vein grafts to the right coronary artery (RCA) were patent, and 67% of these grafts showed a subtotal occlusion; in patients without CPB, 7% of vein grafts were patent, and 50% of grafts were stenosed ( $p = 0.636$ ).

#### Statistical Analysis

Demographic, medical, intraoperative and postoperative data were collected on all patients. All clinical data are expressed as mean  $\pm$  standard deviation. Statistical analysis was performed using SAS statistical software. The Mann-Whitney test was used to calculate differences in continuous variables between the two groups. The  $\chi^2$  test was used to compare categorical variables. Survival analysis and freedom from recurrence of angina were calculated by means of Kaplan-Meier analysis (SAS Institute Inc., Cary, NC). Comparisons in Kaplan-Meier analysis were made using the log-rank test. A  $p$  value less than 0.05 was considered significant. Because of the paucity of events, multivariate logistic regression analysis was performed only with regard to recurrence of angina but not for cardiac-related mortality rate.

#### Results

##### Perioperative Outcome

Perioperative mortality rates were comparable (with CPB 4.2% versus without CPB 2.2%,  $p = 0.277$ ). In this series of patients who had redo-CABG there were three perioperative deaths in the group that had redo-CABG with

Table 2. Clinical Outcomes

	With CPB	Without CPB	<i>p</i> Value
Death (%)	4.2	2.2	0.277
Myocardial infarction (%)	5.4	2.7	0.374
Stroke (%)	0	0	
Wound infections (%)	3.8	2.7	0.326
Atrial fibrillation (%)	34.6	13.8	0.021
Blood units ( <i>n</i> )	2.1 ± 1.4	1.8 ± 1.4	0.154
Duration of operation (min)	294 ± 53	198 ± 62	0.002
Intubation time (h)	20.1 ± 22.4	5.2 ± 4.7	0.004
Reexploration for bleeding ( <i>n</i> )	2	2	0.636
Intensive care unit stay (days)	1.7 ± 8.6	1.5 ± 12.5	0.840
In-hospital stay (days)	13 ± 8	14 ± 7	0.708

CPB = cardiopulmonary bypass.

CPB and one perioperative death in the group that had redo-CABG without CPB. Reasons for death were myocardial infarction in 3 patients (with CPB *n* = 2, without CPB *n* = 1; *p* = 0.374) and septic shock in 1 patient (with CPB *n* = 1, without CPB *n* = 0; *p* = 0.573). All patients who died perioperatively had a left ventricular ejection fraction below 30%. Perioperative adverse cerebrovascular events were not observed in this series. A significant systemic inflammatory response developed in 4 patients (with CPB *n* = 3, without CPB *n* = 1; *p* = 0.646). Minimal tissue dissection did not lead to fewer bleedings in patients without CPB. There were two reexplorations in each group because of bleeding. The mean intensive care unit stay was comparable (with CPB 1.7 ± 8.6 days, without CPB 1.5 ± 12.5 days; *p* = 0.840). The incidence of minor adverse perioperative outcomes is shown in Table 2. Patients who had redo-CABG without CPB had fewer perioperative episodes of atrial fibrillation compared with patients who had redo-CABG with CPB (*p* = 0.021).

#### Completeness of Revascularization

Of the patients who had CPB, 92% had complete revascularization, as could be expected by our strategy to perform complete revascularization in this group. In the group who had redo-CABG without CPB, only 27% of patients had complete revascularization, as could be also expected by our strategy of target vessel revasculariza-

Table 3. Coronary Territories Grafted

	With CPB	Without CPB	<i>p</i> Value
Complete revascularization (%)	92	27	0.001
Number of grafts	2.8 ± 0.9	1.3 ± 0.5	0.0001
Left anterior descending artery (%)	86	81	0.493
Diagonal branches (%)	32	3	0.001
Circumflex artery (%)	79	8	0.001
Right coronary artery (%)	76	38	0.001
Conversion to CPB (%)		0	

CPB = cardiopulmonary bypass.

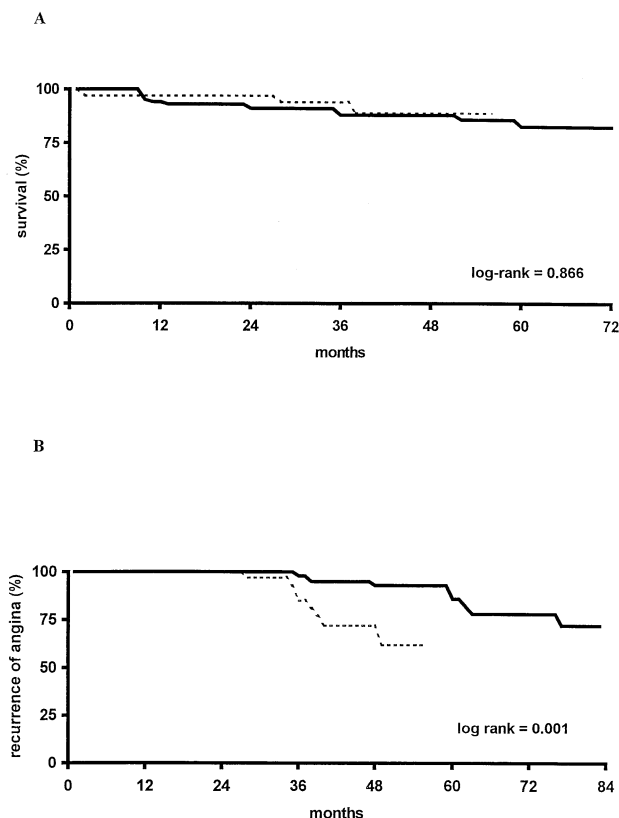


Fig 1. Survival (A) and recurrence of angina (B) in patients with and without cardiopulmonary bypass. Solid line = patients with CPB; dashed line = patients without CPB.

tion. The average number of grafts and the distribution of myocardial territories grafted are shown in Table 3.

#### Multivariate Logistic Regression Analysis

Target vessel revascularization was the only independent factor predicting recurrence of angina. This finding was observed only in patients younger than 75 years old (*p* = 0.012), whereas target vessel revascularization had no predictive value with regard to recurrence of angina in the elderly (*p* = 0.142).

#### Follow-Up

The mean follow-up period in patients with CPB was 50 ± 23 months compared with 34 ± 15 months in those without CPB (*p* = 0.0001). Kaplan-Meier analysis revealed similar mortality rates in both groups, with a cardiac-related mortality rate of 1.4% in the CPB group compared with 5.4% in the group without CPB (log-rank = 0.09). The non-cardiac-related mortality rate was 4.2% in the CPB group versus 2.7% in the group without CPB (*p* = 0.102; Fig 1A).

Kaplan-Meier analysis revealed a higher rate of recurrence of angina in patients without CPB (13.2% with CPB versus 24.2% without CPB; log rank = 0.001) (Fig 1B). At the time of follow-up, mean CCS score in patients who had redo-CABG with CPB was lower (1.3 ± 0.6 with CPB versus 1.7 ± 0.8 without CPB; *p* = 0.02). After redo-CABG

without CPB, patients had a higher use of nitrates (8.9% with CPB versus 29.6% without CPB;  $p = 0.015$ ). After redo-CABG with CPB, 1 patient had coronary angiography and percutaneous transluminal coronary angioplasty of a venous bypass graft to the right coronary artery 6 months postoperatively.

#### *Analysis With Regard to Different Age Groups*

Kaplan-Meier analysis revealed a higher rate of recurrence of angina in patients younger than 75 years old, who were operated on without CPB (10.0% with CPB versus 33.2% without CPB; log rank = 0.0009). Mean CCS score was also higher ( $1.3 \pm 0.6$  with CPB versus  $1.7 \pm 0.8$  without CPB;  $p = 0.02$ ). After redo-CABG without CPB, patients younger than 75 years also had a higher use of nitrates (8.9% with CPB versus 29.6% without CPB;  $p = 0.015$ ).

At follow-up, recurrence of angina in elderly patients was 16.0% with CPB and 13.3% without CPB ( $p = 0.243$ ). Mean CCS score was  $1.5 \pm 0.8$  with CPB and  $1.6 \pm 0.7$  without CPB ( $p = 0.432$ ). There were no rehospitalizations because of cardiac causes. Use of nitrates was comparable (8.7% with CPB versus 14.3% without CPB;  $p = 0.542$ ).

#### **Comment**

In this unselected series of consecutive patients who had elective redo-CABG, our results indicate that minimal tissue dissection and target vessel revascularization without CPB did not add any significant benefit with regard to perioperative morbidity and mortality rates. The relief of symptoms during follow-up was unsatisfactory. Despite a shorter follow-up period in these patients, CCS class and use of nitrates were higher.

Despite technical improvements and increased surgical experience, the risks of reoperation still exceed those of primary cardiac operation [6,16]. Mortality and morbidity rates are higher than at primary operation in most reported series and vary from 2.7% to 16.7% [6,17,18]. Our mortality rate of 4.2% in patients who had redo-CABG with CPB is therefore acceptably low. Allen and coworkers [6] reported a mortality rate of 16.7% in 12 patients who had redo-CABG with CPB. Stamou and coworkers [16] reported a mortality rate of 10% in 41 patients who had redo-CABG with CPB. In the series of Allen and coworkers [6], mean left ventricular ejection fraction in patients with CPB was lower than in our study (40% versus 57%). Sixty-six percent of patients in their analysis were urgent or emergent cases [16]. We excluded urgent and emergent patients from our analysis. Because left ventricular ejection fraction and urgent procedures remain strong predictors of early and late outcome after CABG, the difference in left ventricular ejection fraction as well as the exclusion of emergent cases might explain our diverging results in perioperative mortality.

Patients who have primary CABG without CPB are thought to have a smoother early postoperative course and a shorter hospital stay compared with patients who have primary CABG with CPB [19]. Furthermore, pri-

mary CABG without CPB is associated with less myocardial injury [20], reduced cytokine response [21], and less neurologic injury by avoiding cross-clamping of the ascending aorta [22]. Recent reports also indicated that redo-CABG without CPB significantly reduced morbidity and mortality rates compared with redo-CABG with CPB [7, 16]. Stamou and colleagues [16] reported a mortality rate of 1% in 91 patients who had redo-CABG without CPB. Allen and associates [6] reported a mortality rate of 4.3% in 23 patients who had redo-CABG without CPB. Other groups also reported mortality rates well below 5% [7, 16]. This is in line with our mortality rate of 2.2%; however, we are aware that our study clearly lacks statistical power to draw definite conclusions with regard to improved perioperative survival.

The incidence of redo-CABG has increased because of the increase in the number of patients who have had primary CABG, many of whom had their first CABG when routine use of the LIMA was not widely advocated [6]. Even in the current era, reoperation, impaired left ventricular function, impaired renal function, and advanced age continue to be independent predictors of increased operative risk and mortality [23,24]. Additionally, the incidence of myocardial infarction after redo-CABG is higher than at primary operation in most reported series and varies from 6.4% to 8.1% [17, 18]. In our series the incidence of perioperative myocardial infarction was acceptably low (5.4% in patients with CPB and 2.7% in patients without CPB). Difficulties with myocardial protection secondary to progression of native arterial disease and occluded vein grafts, as well as embolization from atheromatous vein grafts, have been defined as the main factors responsible for increased risk of perioperative myocardial infarction [25-27]. Two recent analyses found that failure to use retrograde cardioplegia is an independent predictor of morbidity and mortality [26, 27]. Our standard technique of retrograde blood cardioplegia might explain our low rate of myocardial infarction in these patients.

In our series, however, the rate of recurrence of angina, use of nitrates, and CCS score were significantly higher in younger patients after redo-CABG without CPB, although mean follow-up time was shorter than for patients who had redo-CABG with CPB. Completeness of revascularization was an independent predictor of recurrence of angina. This may be attributed to the strategy of target vessel revascularization in this group, which resulted in many patients being underrevascularized. It seems likely that with a longer follow-up period, differences with regard to recurrence of angina in our series might increase. These findings are in contrast to those reported by Allen and coworkers [6]. In that study, redo-CABG without CPB had a length of event-free survival similar to that of redo-CABG with CPB [6]. However, only patients with single-vessel disease were included, and the mean follow-up period was only 12 months. Transmyocardial laser revascularization has emerged as a useful alternative treatment modality in patients with a limited coronary bed who are suffering from recurrence of angina [28]. Though providing symp-

tomatic benefit and improving exercise tolerance in highly selected patients [29], concomitant transmyocardial laser revascularization was not included in this analysis to maintain homogeneity between both groups.

At follow-up in our series, despite fewer grafts, angina recurrence rate, use of nitrates, and CCS score were comparable in elderly patients after redo-CABG with and without CPB. In the elderly, completeness of revascularization did not predict occurrence of angina. However, follow-up was shorter in patients after redo-CABG without CPB than in redo-CABG with CPB. Therefore it remains to be shown whether, when follow-up is longer, these findings remain similar in both groups or whether patients experience adverse outcome after redo-CABG without CPB as a result of unrevascularized segments in territories that are not in the distribution of the LAD.

The main limitation of this study is the small sample size. In terms of recurrence of angina, potential imbalances were corrected for in the multivariate model but not for cardiac-related mortality rate because of the paucity of events. Because the decision regarding which surgical strategy to use—minimal tissue dissection and target vessel revascularization without CPB or dissection of the entire heart and complete revascularization with CPB—was determined by the surgeon, this study is certainly limited by the fact that we investigated nonrandomized patient groups. Importantly, follow-up is shorter in patients without CPB, but even after this short follow-up period, relief of symptoms was significantly worse in younger patients who had target vessel revascularization without CPB. We presume that this difference will increase over time. In the elderly who had CABG without CPB, however, follow-up was short and must be longer to determine whether there is worsening of symptoms or a trend toward adverse survival in this group. Finally, the lack of angiographic follow-up has precluded a comparison between early and late graft patency between the groups.

Taking these limitations into account, we conclude that in this unselected series of consecutive patients who had elective redo-CABG, minimal tissue dissection and target vessel revascularization without CPB did not add significant benefit with regard to perioperative morbidity and mortality. The unsatisfactory relief of symptoms does not justify target vessel revascularization by a less invasive approach. Therefore, this technique should be offered exclusively to patients at high risk of complete revascularization with CPB and cardioplegic cardiac arrest, such as the elderly.

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