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Does off-pump coronary artery bypass (OPCAB) surgery improve the outcome in high-risk patients?: a comparative study of 1398 high-risk patients

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Abstract

Objective: Although there has been some evidence supporting the theoretical and practical advantages of off-pump coronary artery bypass (OPCAB) over the conventional coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB), it has not yet been determined which group of patients would benefit most from it. It has been advocated recently that high-risk patients could benefit most from avoidance of CPB. The aim of this retrospective study is to assess the efficacy of the OPCAB technique in multi-vessel myocardial revascularization in a large series of high-risk patients. **Methods**: The records of 1398 consecutive high-risk patients who underwent primary isolated CABG at Harefield Hospital between August 1996 and December 2001 were reviewed retrospectively. Patients were considered as high-risk and included in the study if they had a preoperative EuroSCORE of ≥5. Two hundred and eighty-six patients were operated on using the OPCAB technique while 1112 patients were operated on using the conventional CABG technique with CPB. The OPCAB patients were significantly older than the CPB patients (68.1 ± 8.3 vs. 63.7 ± 9.9 years, respectively, $P < 0.001$). The OPCAB group included significantly more patients with poor left ventricular (LV) function (ejection fraction (EF) ≤30%) ($P < 0.001$) and more patients with renal problems ($P < 0.001$). **Results**: There was no significant difference in the number of grafts between the groups. The CPB patients received 2.8 ± 1.2 grafts per patient while OPCAB patients received 2.8 ± 0.5 grafts per patient ($P = 1$). Twenty-one (7.3%) OPCAB patients had one or more major complications, while 158 (14.2%) CPB patients ($P = 0.008$) developed major complications. Thirty-eight (3.4%) CPB patients developed peri-operative myocardial infarction (MI) while only two (0.7%) OPCAB patients developed peri-operative MI ($P = 0.024$). The intensive therapy unit (ITU) stay for OPCAB patients was 29.3 ± 15.4 h while for CPB patients it was 63.6 ± 167.1 h ($P < 0.001$). There were ten (3.5%) deaths in the OPCAB patients compared to 78 (7%) deaths in the CPB patients ($P = 0.041$) within 30 days postoperatively. **Conclusions**: This retrospective study shows that using the OPCAB technique for multi-vessel myocardial revascularization in high-risk patients significantly reduces the incidence of peri-operative MI and other major complications, ITU stay and mortality. Even though the OPCAB group included a significantly higher proportion of older patients with poor LV function (EF ≤30%) and renal problems, the beneficial effect of OPCAB was evident. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Off-pump coronary artery bypass surgery; Outcome; High-risk patients

1. Introduction

Although there has been an appreciable body of evidence supporting the theoretical and practical advantages of off-pump coronary artery bypass (OPCAB) over the conventional coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB), it has not yet been determined which group of patients would benefit from it [1]. It has been advocated recently that high-risk patients are the ones who would benefit most from avoidance of CPB [1–4].

The prospective randomized trials up to date, probably due to ethical considerations, have been recruiting relatively young cardiac surgical patients with relatively low surgical risk profiles and consequently showing either little or no substantial difference in the early clinical outcomes between OPCAB and CPB [5–7]. Therefore, observational reports, case-matched studies and retrospective series analyses are still useful to highlight the patient groups who would benefit from the avoidance of CPB [8].

The aim of this retrospective study is to assess the efficacy

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of the OPCAB technique in multi-vessel myocardial revascularization in a large series of high-risk patients.

2. Patients and methods

2.1. Clinical data collection

The records of 1398 consecutive high-risk patients who underwent primary isolated CABG at Harefield Hospital between August 1996 and December 2001 were reviewed retrospectively. Patients were considered to be high-risk and included in the study if they had a preoperative EuroSCORE of ≥5 on admission to the hospital.

Registry databases, medical notes and charts were studied for preoperative and postoperative data of the patients. Two hundred and eighty-six patients were operated on using the OPCAB technique while 1112 patients were operated on using the conventional CABG technique with CPB. The selection of the patients for either surgical technique (whether OPCAB or CPB) was done by the individual surgeons, and was completely based on their experience and preference. No randomization was involved in this cohort of patients.

2.2. Operative technique

2.2.1. Anaesthesia

Anaesthesia was induced using propofol 1–2 mg/kg, pancuronium 0.1 mg/kg and fentanyl 8–15 μg/kg, and was maintained by air/oxygen and propofol 2–3 mg/kg per h. Trans-esophageal echocardiography (TEE) was used for additional monitoring as required. For cases performed by the OPCAB technique, normo-thermia was maintained by using warm intravenous fluids, a heating mattress and a humidified airway, in addition to maintaining a warm operating theatre. A standby perfusionest with primed bypass circuit was available for all OPCAB cases.

2.2.2. Approach and exposure

A standard midline sternotomy incision is used to expose the heart. The pericardium is opened using an inverted T-shaped incision following the harvest of the internal thoracic arteries (ITAs). Opening the right pleural space creates a space for the rotated and vertically placed heart to minimize haemodynamic compromise when performing the operation off-pump. This is followed by an evaluation of the status of coronary arteries and the required lengths of the conduits.

2.2.3. The CPB technique

Anticoagulation was achieved using 250 units/kg of heparin. The activated clotting time was maintained above 480 s. Heparin was reversed by protamine at the end of the procedure. CPB was instituted with a single right atrial cannula and an ascending aorta perfusion cannula. Standard bypass management included membrane oxygenators, arterial line filters, non-pulsatile flow of 2.4 l/min per m^2, and a mean arterial blood pressure greater than 50 mmHg. Myocardial protection was achieved with intermittent cold blood cardioplegia (4:1 blood to crystalloid ratio).

2.2.4. The OPCAB technique

Anticoagulation was achieved using 150 units/kg of heparin. The activated clotting time was maintained above 250 s. The heart is stabilized using a suction/irrigation tissue stabilization system (Octopus® 3 Medtronic Inc., Minneapolis, MN). One deep pericardial retraction suture is placed at the posterior fibrous pericardium very close and medial to the most proximal part of the inferior vena cava (IVC). It acts as a lever that helps the surgeon manipulate and rotate the heart to vertical and lateral positions along with the Octopus®. Coronary shunts are not routinely used, unless grafting large or non-collateralized coronary arteries.

2.3. Statistical analysis

Numerical variables are presented as the mean ± standard deviation for both patient groups and compared using Student's *t*-test or the Mann–Whitney test where appropriate. Patient characteristics and postoperative complications are compared using the Fisher exact test or the χ^2 test where appropriate. Small values of P (<0.05) indicate a significant difference.

3. Results

3.1. Preoperative characteristics

The preoperative characteristics of both groups of patients are listed in Table 1. The OPCAB patients were significantly older than the CPB patients (68.1 ± 8.3 vs. 63.7 ± 9.9 years, respectively, $P < 0.001$). The OPCAB group included significantly more patients with poor left ventricular (LV) function (ejection fraction (EF) ≤30%) ($P < 0.001$) and less patients with good LV function ($P = 0.009$). The OPCAB group also included more patients with renal problems ($P < 0.001$).

The renal problems included renal impairment (Cr ≥200 μmol/l) and acute or chronic renal failure. Cerebrovascular disease included transient ischaemic attacks (TIA) and cerebrovascular accidents (CVA). Peripheral arterial disease included acute or chronic ischaemia of the upper or lower limbs. Respiratory problems included asthma and chronic obstructive airway disease (COAD) requiring active treatment at the time of the operation.

3.2. Operative characteristics

There was no significant difference in the number of grafts between the groups. The CPB patients received 2.8 ± 1.2 grafts per patient while OPCAB patients received 2.8 ± 0.5 grafts per patient ($P = 1$). The distribution of distal anastomoses to the various vascular territories of the

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Table 1
Preoperative characteristics[a]

Variable	CPB		OPCAB		P value
	N = 1112	%	N = 286	%	
Female gender	200	18	56	19.6	NS
Operative priority					
Elective	733	66	205	71.7	NS
Urgent	289	26	57	19.9	NS
Emergency	90	8	24	8.4	NS
LV function (EF)					
> 50%	733	65.9	163	57	0.009
31–49%	272	24.5	63	22	NS
0–30%	107	9.6	60	21	< 0.001
Current congestive cardiac failure	145	13	34	11.9	NS
Recent MI (within 30 days)	189	17	37	12.9	NS
Diabetes (tablet controlled + insulin-dependent)	200	18	60	21	NS
Hypercholesterolaemia	582	52.3	142	49.6	NS
Hypertension	606	54.5	148	51.7	NS
Renal problems	26	2.3	20	7	< 0.001
Respiratory problems	150	13.5	34	11.9	NS
Cerebrovascular disease	96	8.6	19	6.6	NS
Peripheral arterial disease	120	10.8	26	9.1	NS
Preoperative IABP	81	7.3	29	10.1	NS

[a] LV, left ventricle; EF, ejection fraction; MI, myocardial infarction; IABP, intra-aortic balloon pump; NS, non-significant.

heart was not significantly different between the two groups and is presented in Table 2. For the CPB patients, the cumulative bypass time was 71.7 ± 38.9 min and the cumulative aortic cross-clamp time was 32.4 ± 25.6 min.

3.3. Postoperative morbidity

Peri-operative myocardial infarction (MI) was diagnosed when one of the following was observed: (1) new Q waves in the electrocardiogram (ECG); (2) CK-MB >50 with ECG changes; or (3) creatine kinase-MB >70 without ECG changes. Atrial fibrillation was identified by cardiac monitoring and confirmed by 12-lead electrocardiography (ECG).

We defined the term ‘major complications’ to include peri-operative MI, pulmonary oedema or adult respiratory distress syndrome (ARDS), septicaemia, CVA (permanent stroke), and renal dysfunction requiring haemofiltration or haemodialysis. Twenty-one (7.3%) OPCAB patients had one or more major complications, while 158 (14.2%) CPB patients ($P = 0.008$) developed major complications. Thirty-eight (3.4%) CPB patients developed peri-operative MI while only two (0.7%) OPCAB patients developed peri-operative MI ($P = 0.024$). Twenty-three (8%) OPCAB patients developed low cardiac output (LCO) in the post-operative period compared to 146 (13.1%) CPB patients ($P = 0.024$). There was no statistically significant difference between the two groups with regard to other complications as evident from the data listed in Table 3.

The intensive therapy unit (ITU) stay for OPCAB patients was 29.3 ± 15.4 h while for CPB patients it was 63.6 ± 167.1 h ($P < 0.001$), which meant that OPCAB patients stayed in ITU for a significantly shorter duration. Unfortunately, we could not show a similar significant

Table 2
The distribution of distal anastomoses between the various vascular territories of the heart

Vascular territory[a]	CPB		OPCAB		P value
	N = 3139	%	N = 812	%	
Anterior territory	1346	42.9	376	46.3	NS
Lateral territory	954	30.4	230	28.3	NS
Posterior territory	839	26.7	206	25.4	NS

[a] Anterior territory: includes left anterior descending and diagonal arteries; lateral territory: includes circumflex and marginal arteries; posterior territory: includes posterior descending and right coronary arteries.

Table 3
Postoperative outcome[a]

Variable	CPB		OPCAB		P value
	N = 1112	%	N = 286	%	
30-day mortality	78	7	10	3.5	0.041
Major complications	158	14.2	21	7.3	0.008
MI	38	3.4	2	0.7	0.024
Renal dysfunction	47	4.2	8	2.8	NS
PO/ARDS	36	3.2	5	1.7	NS
Septicaemia	23	2.1	6	2.1	NS
CVA	14	1.3	0	0	NS
Atrial fibrillation	257	23.1	66	23	NS
Re-operation	58	5.2	12	4.2	NS

[a] MI, myocardial infarction; PO, pulmonary oedema; ARDS, adult respiratory distress syndrome; CVA, cerebrovascular accident.

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Table 4
Postoperative outcome in patients with EF ≤30%

Variable	CPB		OPCAB		*P* value
	N = 107	%	*N* = 60	%	
Postoperative inotrope use	49	45.8	23	38.3	NS
IABP insertion[a]	18	16.8	8	13.3	NS
Ventilation >24 h	86	80.4	35	58.3	0.004
30-day mortality	9	8.4	2	3.3	NS

[a] IABP, intra-aortic balloon pump.

difference in the hospital stay between the groups due to the nature of our institution being a tertiary referral centre. We refer cases requiring long convalescence back to their local general hospitals. The hospital stay was 10.2 ± 8.5 days for the OPCAB group and 11.1 ± 19.3 days for the CPB group ($P = 0.4$).

3.4. Postoperative mortality

We defined the '30-day mortality' as death within the 30 days following the operation. There were ten (3.5%) deaths in the OPCAB patients compared to 78 (7%) deaths in the CPB patients ($P = 0.041$) within 30 days postoperatively.

The ten OPCAB deaths included two due to cardiac causes, four due to septicaemia, three due to multi-organ failure (MOF) and one due to respiratory failure. The 78 CPB deaths included 32 due to cardiac causes, 19 due to MOF, 13 due to septicaemia, six due to CVA, two due to respiratory failure and six due to gastrointestinal tract (GIT) causes such as pancreatitis, mesenteric infarction and peptic ulcer bleeding/perforation.

3.5. Poor LV function

The sub-group analysis of patients with poor LV function (EF ≤30%) presented in Table 4 shows that there were significantly less OPCAB patients requiring ventilation for >24 h. The two sub-groups were not different otherwise in the rest of the postoperative outcomes or 30-day mortality.

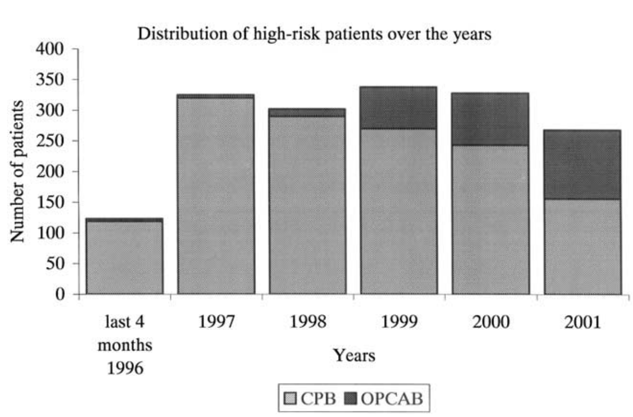

Fig. 1. The relation between CPB and OPCAB in high-risk patients over the years.

4. Discussion

This retrospective comparative study shows that using the OPCAB technique for multi-vessel myocardial revascularization in elevated and high-risk patients significantly reduces the incidence of peri-operative MI and other major complications, ITU stay and mortality when compared to CPB. Even though the OPCAB group included a significantly higher proportion of older patients with poor LV function (EF ≤30%) and renal problems, the beneficial and protective effects of OPCAB were evident.

The initial application of OPCAB in the early nineties was mainly directed to highly selected and relatively low-risk surgical patients [9]. Since then there has been a growing body of evidence suggesting many potential advantages of the OPCAB technique over the conventional CPB technique in different groups of high-risk patients [10,11]. Therefore, it seems that the referral pattern, and consequently, the cardiac surgical practice has come round full circle and the OPCAB technique has become more commonly used in patients presenting with preoperative risk factors and co-morbidities that make them more susceptible to the hazardous effects of the CPB [12].

We have recently shown that conversion to non-selective application of OPCAB does not increase morbidity nor necessitate a change of practice [13]. Furthermore, encouraged by our previous reports on the favourable outcome of the OPCAB technique in elderly and emergency patients [14,15], we have expanded the use of the OPCAB technique to all high-risk cardiac surgical patients with satisfactory clinical and angiographic results. This is presented in Fig. 1 which shows the gradual increase in the OPCAB practice for high-risk cases in relation to CPB practice over the last 5 years, growing from 3.3% in the last 4 months of 1996 to 41.8% in 2001.

The theoretical and practical disadvantages of the CPB and the accompanying cardioplegic arrest have been widely described including myocardial injury [16], systemic inflammatory response that could contribute to multi-organ damage [17] and more need for blood and blood product transfusion [10,18]. The avoidance of these disadvantages could be the rationale behind the protective effects of OPCAB on the vital organs including the heart [19], the kidney [20] and the brain [21] and consequently offer a better outcome in high-risk patients who might have less reserve in these vital organs to start with.

Indeed, the data from the present study support this concept as we found that OPCAB significantly reduces peri-operative MI, major morbidity, ITU stay and mortality in this group of high-risk patients. These data conform to those of another retrospective study on a series of consecutive high- and low-risk patients where CPB was found to be an independent risk factor for higher mortality, peri-operative MI and major early complications [22].

The difference in concept between the regional ischaemia caused by OPCAB and the global ischaemia caused by CPB

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with aortic cross-clamping might explain the myocardial protective effect of the OPCAB technique as evident from the low incidence of MI in this study and other previous studies [22]. Undoubtedly, these findings made OPCAB a safe alternative technique for surgical treatment of patients with recent acute MI [23], and also ruled out some theoretical contraindications on the use of OPCAB in patients with critical left main stem disease [24].

Interestingly, in our study there was no difference in the average number of total grafts between the two groups, which rules out the possibility of incomplete revascularization in the OPCAB patients that was previously suggested by others and allows for better matching and comparison of the two patient groups [3,11,25]. Furthermore, the absence of a difference in the distribution of distal anastomoses to the various vascular territories of the heart reduces the possible bias that could be involved in the selection of the procedure. However, the lack of an objective means of graft function assessment, i.e. flow measurement, is considered as a limitation of this study in comparing the two techniques in terms of the patency of the anastomoses.

Indeed, the study is limited by its retrospective non-randomized nature. It would be ideal to have a prospective randomized study design for high-risk patients, restricted only to surgeons who are adequately experienced in both techniques. However, the currently available randomized studies involve relatively low-risk cardiac patients, and therefore are not very likely to show a substantial difference in the outcome especially considering the relatively small numbers of patients that can be recruited [5–7]. For these reasons, retrospective comparative studies are still of some value in high-risk patients who are likely to benefit most from the OPCAB technique and this consequently shows up in terms of saving economic resources [26,27].

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