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Does Off-Pump Total Arterial Revascularization Without Aortic Manipulation Influence Neurological Outcome? A Study of 226 Consecutive, Unselected Cases

Dr. Patel

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Nirav C. Patel, D. Mark Pullan, Brian M. Fabri

The Cardiothoracic Centre Liverpool, Liverpool, UK

ABSTRACT

Background: Off-pump coronary artery bypass (OPCAB) is increasingly reported to have better post-operative outcomes than on-pump coronary artery bypass (ONCAB). Most series report OPCAB in selected cases and therefore the results of such studies are affected by selection bias. We report our series of consecutive, unselected OPCAB cases representing an entire coronary revascularization practice and its effect on neurological outcome.

Methods: Between January and December 2000, 226 consecutive OPCAB cases were performed. These were compared with 258 consecutive ONCAB cases performed by same surgeons historically. There were no significant differences in major demographic characteristics between the two groups. Postoperative outcomes including operation time, ventilation time, inotrope requirement, focal strokes, peak CKMB, length of hospital stay and mortality formed the basis of this study. All OPCAB patients had a median sternotomy approach. Left and right internal mammary arteries and radial arteries were used in varying combinations using composite and sequential grafting techniques to achieve revascularization and completely avoid aortic manipulation. ONCAB cases were performed employing conventional cardiopulmonary bypass techniques and using the left internal mammary artery and saphenous vein grafts as appropriate.

Results: OPCAB cases had significantly lower peak CKMB levels, operative time, length of hospital stay and number of grafts. There was a significantly lower incidence of permanent focal neurological events in OPCAB patients (0.4%, n = 1) compared to the ONCAB group (3.9%, n = 10, p = 0.012).

Conclusion: This study documents the safety of off pump total arterial revascularization without aortic manipulation as the routine technique for coronary bypass surgery. It also demonstrates a significant reduction in the incidence of focal strokes. We conclude that avoidance of both cardiopulmonary bypass and aortic manipulation are important factors in reducing the occurrence of neurological deficits.

INTRODUCTION

OPCAB has been increasingly reported to show better outcomes compared to ONCAB as regards to postoperative length of stay, inotrope usage, ventilation time, blood product usage, and cost effectiveness [Ascione 1999, Iaco 1999, Puskas 1999, Lancey 2000].

A focal neurological deficit following coronary artery bypass grafting still represents a most devastating complication. The mechanisms contributing to neurological deficit are multifactorial. The three major etiological factors include cerebral hypoperfusion, systemic inflammatory response and micro/macro embolism.

Recent studies examining cerebroprotective effects of OPCAB versus ONCAB procedures have yielded inconsistent results [Murkin 1999, Arom 2000, Deigeler 2000]. Unfortunately, the study groups in these reports are numerically small and not comparable. The aim of our study is (1) to establish the safety and efficacy of OPCAB total arterial revascualrisation as a routine procedure in a consecutive, unselected series representing an entire revascularization practice and (2) to assess its influence on neurological outcomes.

MATERIALS AND METHODS

The OPCAB group consisted of 226 patients under the care of two surgeons (BMF, DMP) at The Cardiothoracic Centre - Liverpool. These were consecutive patients undergoing surgical coronary revascularization between January 2000 and December 2000. Five additional patients in whom OPCAB was attempted and cardiopulmonary bypass was used due to hemodynamic instability were excluded from the study. These patients represented the entire coronary revascularization practice of the two surgeons including routine, urgent, emergency and redo operations.

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Address correspondence and reprint requests to: Dr. B.M. Fabri, FRCS Ed, Consultant Cardiac Surgeon, The Cardiothoracic Centre, Thomas Drive, Liverpool, UK, L143PE, Phone: +44 151 2932397, Fax: +44 151 2208573, Email: bmfabri@ukonline.net

The ONCAB group consisted of 259 patients performed consecutively by the same surgeons historically at the same institution and again represents the entire coronary revascularization practice of the two surgeons.

All OPCAB patients had a median sternotomy approach and all patients had total arterial revascularization without aortic manipulation. The left internal mammary artery was used in all the patients who needed grafting to the left coronary arterial system. The radial and/or right internal mammary arteries were used as a composite T-graft on the left internal mammary artery in order to avoid proximal anastamoses on the aorta. Sequential grafting was employed to achieve complete revascularisation. The target coronary artery was stabilized by using the Octopus II+ tissue stabilization system. (Medtronic, Inc., Minneapolis, MN). When appropriate, temporary proximal control of the artery was achieved with 4/0 Prolene suture buttressed with Teflon. After making a suitable arteriotomy an appropriate sized intracoronary shunt (Medtronic Clearview shunt, Medtronic, Inc., Minneapolis, MN) was introduced in almost all cases so as to maintain distal perfusion and to achieve a relatively bloodless field. Visualisation was aided with a humidified Carbon Dioxide blower (CTS Aires CO_2 Blower, Cardiothoracic Systems, Cupertino CA.). The 'T' graft was constructed first. Following this the anterolateral wall was revascularised followed by the circumflex territory and lastly the inferior wall. This sequence of anastomoses helps restoration of blood supply to more myocardium as the operation progresses. The radial artery was treated with phenoxybenzamine in heparinised blood bath to block alpha-receptors. Intravenous diltiazem was used peri-operatively and up to 12 hours post-operatively. All patients undergoing radial artery graft received oral calcium channel blockers from first post-operative day to one year post operative.

In the ONCAB group, standard cardiopulmonary bypass techniques were used with a median sternotomy approach. All the patients had the left internal mammary artery used along with saphenous vein grafts as appropriate. On completion of all distal anastamoses, the aortic cross-clamp was removed and the proximal were anatomoses constructed with the single application of a side-biting clamp. Normothermia was maintained and myocardial protection was achieved with antegrade induction followed by continuous retrograde perfusion of hyperkalemic blood.

Data was extracted from the cardiac surgical database and pre-, intra- and postoperative variables were collected for comparison between the two groups. Pre-operative group characteristics were compared using the modified Parsonnet and EuroScore risk models. The Parsonett risk model was modified to 0.51 of the original score as this reflects a more accurate prediction of mortality in our population in the North West of England [Wynne-Jones 2000].

The main outcome measure for our study was focal neurological deficit, defined as a new focal neurological event occurring post-operatively that persisted for >24 hours after its onset and was noted before discharge. We did not include transient ischaemic attacks, confused states, intellectual impairment and irritable states to avoid any subjective bias on neurological assessments. Resident and consultant medical staff made the diagnosis of focal neurological deficits.

Statistical analysis was performed with SAS for Windows Version 8. The patient and disease characteristics were compared with Chi-square or Wilcoxon ranks sum tests as appropriate. We used logistic regression analysis to quantify the effect of off-pump surgery on neurological deficit (expressed in terms of odds ratios – OR -, which approximates relative risk) and to adjust for potentially confounding variables. These variables included patient age, unstable angina, history of diabetes, prior CABG, history of vascular disease, history of pulmonary disease and history of neurological disease, which have been described as important determinants of neurological deficit [Newman 1996]. A P value of < 0.05 denoted statistical significance.

RESULTS

Preoperative group characteristics are shown in Table 1 (◎). There were no differences in preoperative characteristics between the two groups in terms of age, sex, extent of coronary disease, left ventricular ejection fraction, urgency of operation, hypertension, diabetes, respiratory disease, renal failure and previous cerebrovascular events. The body mass index was significantly higher in the OPCAB group. ($P = 0.003$). Risk stratification using the median EuroScore and modified Parsonnet scores did not show any statistically significant difference between the two groups.

Operative and postoperative characteristics of the groups are summarised in Table 2 (◎). Total operation time was 20 minutes shorter in the OPCAB group, which was highly significantly different to the ONCAB group ($p< 0.0001$). OPCAB patients had on an average one less bypass graft compared to the ONCAB group ($p<0.0001$). Median postoperative ventilation time was similar in both groups.

The incidence of peri-operative myocardial infarction was low (3.5%) in both groups and the use of inotropes and intra-aortic balloon counterpulsation was not significantly different between the two groups. Post-operative enzyme leak, as indicated by peak rise in Creatinine Phosphokinase-Mb fraction was significantly higher in ONCAB patients ($p<0.0001$).

Total post-operative blood loss was 140mls less in the ONCAB group, which was highly significant ($p<0.0001$). The incidence of re-exploration for bleeding was 1.76% in OPCAB patients compared to 0.7% in the ONCAB group, ($p = 0.89$).

There was no significant difference in the incidence of new atrial fibrillation between the two groups.

In hospital mortality was 3.1 % in the ONCAB group and 1.3% in the OPCAB group, which just failed to reach statistical significance ($p = 0.19$).

The incidences of other post-operative complications like renal failure, mediastinitis and gastrointestinal complications were very low in both groups.

The OPCAB patients stayed 2 days less in hospital compared to the ONCAB group ($p<0.001$). More than 78 % of patients in OPCAB group were discharged from hospital by seventh postoperative day compared to only 48% in ONCAB group.

There was a significantly higher incidence of focal neurological deficits in ONCAB patients (3.9%, $n = 10$) compared

Table 1. Continuous data is shown as median with range in brackets and categorical data as % with absolute numbers in brackets.

Patients characteristics- preoperative	ONCAB (n = 259)	OPCAB (n = 226)	Significance
Age - years	64.4 (40-84)	64.3 (31-80)	NS
Sex- Females	19.3% (n = 50)	22.1% (n = 50)	NS
Left main stem stenosis	18.1% (n = 47)	23.8% (n = 54)	NS
Triple vessel disease	72.9% (n = 189)	69.9% (n = 158)	NS
Hypertension	45.6% (n = 118)	51.8% (n = 116)	NS
Diabetes	19.3% (n = 50)	20.7% (n = 47)	NS
Previous CVA	3.9% (n = 10)	6.6% (n = 15)	NS
Urgent/Emergency	20% (n = 52)	19.9% (n = 45)	NS
Redo	3.86% (n = 10)	3.98% (n = 9)	NS
COAD	23.9% (n = 62)	33.4% (n = 75)	NS
Renal failure	1.2% (n = 3)	3.1% (n = 7)	NS
Ejection fraction (30-50%)	35.5% (n = 92)	33.1% (n = 75)	NS
Ejection fraction (< 30%)	6.94% (n = 18)	9.7% (n = 22)	NS
Body mass index –kg/m2	26.9(22.1-34.4)	28.1(22.2-36.5)	0.0032
EuroScore	3 (0-8)	3(0-8)	NS
Modified Parsonnet Score	4(0-15)	5(0-17)	NS

to the OPCAB group (0.04%, n = 1) (p = 0.012). The relative risk reduction was almost nine fold (crude OR – 0.11; 95 % confidence interval: 0.01-0.87). The single OPCAB patient who had a focal neurological deficit developed minimal right-sided weakness 48 hours after the operation. Because the patients in each group had multiple variables that can also influence focal neurological deficits, we used multivariate analysis to assess the role of OPCAB as a technique in reducing the neurological complications. After simultaneously adjusting for age, unstable angina, history of diabetes, redo operation, previous history of cerebrovascular disease, history of peripheral vascular disease and history of respiratory disease, OPCAB remained a significant factor in reducing neurological deficits (adjusted OR = 0.08; 95% confidence interval: 0.01 – 0.70).

In the OPCAB group, 5 patients (2.16%) needed conversion to cardiopulmonary bypass due to hemodynamic instability after 'verticalization' of the heart. All these patients had coronary revascularization without aortic cross clamp on the beating heart. The techniques of avoiding aortic manipulation for proximal anastomoses were adhered to in all these patients. One patient suffered a peri-operative infarct and died on day 13.

DISCUSSION

The safety and efficacy of off-pump coronary revascularization has been reported by various authors [Iaco1999, Puskas 1999, Arom 2000, Lancey 2000]. All these reports represent retrospective case matched comparisons of off-pump versus conventional on-pump coronary revascularization. None of these reports represent an entire coronary revascularization practice subjected to a specific technique. In addition, total arterial revascularization was not performed in

Table 2. Continuous data is shown as median with range in brackets and categorical data as % with absolute numbers in brackets.

Patients characteristics- Operative and postoperative	ONCAB (n = 259)	OPCAB (n = 226)	Significance
Operative time-mins.	220 (170-300)	200 (155-265)	<0.0001
Number of grafts	4 (1-7)	3 (1-5)	<0.0001
Ventilation time hrs.	5(2-48)	5(2-20)	NS
Peri op MI	3.5%(n = 9)	3.5%(n = 8)	NS
Peak CKMB - IU	28 (0-425)	12 (0-774)	<0.0001
Post op atrial fibrillation	22.7% (n = 59)	24.3%(n = 55)	NS
Inotrope use	11.6% (n = 31)	9.7% (n = 22)	NS
IABP use	1.5% (n = 4)	2% (n = 5)	NS
Blood loss - mls.	590 (350-1160)	730 (360-1570)	<0.0001
Re exploration for bleeding	0.7% (n = 2)	1.76% (n = 4)	NS
Focal neurological deficit	3.9% (n = 10)	0.4% (n = 1)	0.012
Length of hospital stay - days	8 (1-57)	6 (2-42)	<0.0001
Hospitality mortality	3.1%(n = 8)	1.3%(n = 3)	NS

all patients involved in these study groups. We report on 226 consecutive, unselected OPCAB cases, representing 98% of the coronary revascularization programme of the individual surgeons. The control group (ONCAB) consisted of 259 consecutive, unselected cases performed by same surgeons historically. Because of the unselected nature of the study, the two groups showed no statistical differences in preoperative characteristics (Table 1). There was a tendency towards more patients with previous cerebrovascular history, renal failure on dialysis, chronic obstructive airway disease and poor left ventricular function in the OPCAB group but none reached statistical significance due to the small numbers involved.

In hospital mortality in the OPCAB group was 1.3% compared to 3.1% in the ONCAB patients (p = 0.194). Although not statistically significant, this trend has been the experience in most of the previous reports [Iaco1999, Puskas 1999, Arom 2000, Lancey 2000]. As the mortality of coronary revascularization is very low (1 - 3.5%) one would need thousands of patients to show any statistical difference.

As with other reports [Bouchard 1998, Arom 2000, Lancey 2000], we noted a significantly lower peak creatinine phophokinase Mb fraction in the OPCAB group. Contrary to other reports, in our experience inotrope requirements [Ascione 1999, Boyd 2000], use of intra-aortic balloon pump [Puskas 1998] and the incidence of perioperative myocardial infarction [Bouchard 1998, Arom 2000], were similar in the two groups.

Similarly, although lower rates of atrial fibrillation have been reported [Arom 2000, Boyd 2000] in OPCAB patients this was not our experience.

Less post operative bleeding in off-pump patients, reducing blood transfusion requirement, has been reported [Calafiore 1998, Puskas 1998, Arom 1999, Ascione 1999] as has the decreased incidence of reoperation for bleeding [Ascione 1999, Arom 2000]. In contrast, we experienced on an average 140mls more drainage in OPCAB patients (p<0.0001). Re-exploration for bleeding was very low in both groups (0.7% for ONCAB versus 1.7% for OPCAB; p = 0.89). The increased drainage in our experience can be explained on the basis of exclusive use of arterial conduits and intravenous infusion of calcium channel blockers postoperatively causing vasodilatation and increased capillary bleeding from internal mammary artery harvesting site.

As shown by others [Arom 1999, Arom 2000, Lancey 2000], total operating time was shorter in off-pump patients. This is partly related to the time required to institute and wean from cardiopulmonary bypass as well as to the lower number of grafts performed in OPCAB patients. The OPCAB group had, on an average, one distal anastomoses less than the ONCAB patients (median graft rate of 3 vs 4; p<0.0001). Other reports [Iaco 1999, Arom 2000, Lancey 2000, Czerny 2001] share a similar experience. We believe that avoidance of cardiopulmonary bypass is a crucial strategy that allows quicker recovery leading to early discharge from hospital. Most other authors [Iaco 1999, Puskas 1999, Arom 2000, Lancey 2000] report similar findings.

Our conversion rate to cardiopulmonary bypass was extremely low (2.16% - n = 5) even though there was no case selection. Other reports show conversion rates ranging from 2.9% [Iaco 1999] to 22% [Czerny 2001] and have been associated with worse outcome. We attribute our low conversion rate to an improved stabilization technique (Octopus II+) and a better understanding of cardiovascular pathophysiology in off-pump revascularization. We believe that our routine use of intracoronary shunts is an important technical factor that avoids myocardial ischaemia during grafting leading to less hemodynamic instability.

The most favourable outcome observed in this report was a significant reduction in focal neurological deficit. Several authors have reported improved neurological outcomes in off-pump coronary surgery when compared to on-pump techniques [Murkin 1999, Diegeler 2000, Ricci 2000]. The report of Ricci et al. showed a significant reduction of cerebrovascular strokes in octogenarians in the off-pump group. However, the on-pump group was not comparable in terms of major risk factors. Reports by Diegeler and Murkin showed a significant reduction in neurocognitive impairment in off-pump patients in small randomised controlled trials. However, others have not reported improved neurological outcome when comparing off-pump versus on-pump patients [Iaco 1999, Arom 2000, Lancey 2000]. These groups still manipulated and side clamped the aorta despite not using cardiopulmonary bypass. Our study groups are comparable in terms of risk factors for stroke and thus the improvement in neurological outcome is a true one. Logistic regression analysis after adjusting for major stroke risk variables shows a reduction in odds ratio (crude OR-0.11; 95 % confidence interval: 0.01-0.87) (adjusted OR = 0.08; 95% confidence interval: 0.01-0.70). We believe that this signifies that, in our experience, the higher the preoperative risk of stroke the more marked improvement in outcome with off-pump revascularization. The role of micro and macro embolism in neurological impairment has been well documented [Pugsley 1994, Blauth 1995, Waters 2000]. We believe avoiding cardiopulmonary bypass and more importantly avoiding aortic manipulation reduces micro and macro embolism. By employing composite and sequential anastomotic techniques we can achieve complete arterial revascularization without aortic manipulation.

As all the patients in OPCAB group did not have any aortic manipulation it is difficult to conclude from our study independent effect of avoiding aortic manipulation or avoiding cardiopulmonary bypass on neurological outcomes. But we certainly can conclude that avoidance both does improve neurological outcomes.

The non-randomized, retrospective nature of this study is a limitation that can be criticised. We have tried to limit any bias by comparing unselected, consecutive series. The other criticism of our study is lack of follow-up data, especially of long-term outcome data in the OPCAB patients. This is being undertaken and will form part of a further report.

In conclusion, we have documented the safety of off-pump total arterial revascualrisation as a routine procedure. The improvement in neurological outcome is attributable to avoidance of cardiopulmonary bypass and aortic manipulation.

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