Total arterial revascularisation: effect of avoiding cardiopulmonary bypass on in-hospital mortality and morbidity in a propensity-matched cohort

Ragini Pandey, Antony D. Grayson, D. Mark Pullan, Brian M. Fabri, Walid C. Dihmis

Department of Cardiothoracic Surgery, The Cardiothoracic Centre Liverpool, Thomas Drive, Liverpool L14 3PE, UK
Department of Research and Development, The Cardiothoracic Centre Liverpool, Thomas Drive, Liverpool L14 3PE, UK

Received 9 September 2004; received in revised form 19 October 2004; accepted 27 October 2004; Available online 14 November 2004

Abstract

Objective: The combination of total arterial revascularisation and avoidance of cardiopulmonary bypass may provide additional benefits to patients receiving complete arterial grafting with cardiopulmonary bypass. We performed a propensity-matched cohort study of complete arterial off-pump and on-pump coronary surgery and examined differences in in-hospital mortality and morbidity.

Methods: Three hundred and sixty patients who underwent off-pump coronary surgery with complete arterial grafting between April 1997 and September 2002 were matched to 360 patients who received coronary surgery with cardiopulmonary bypass and complete arterial grafting. To match off-pump with unique on-pump patients, logistic regression was used to develop a propensity score for off-pump surgery. The C statistic for this model was 0.79. Off-pump patients were matched to unique on-pump patients with an identical 5-digit propensity score. If this could not be done, we then proceeded to a 4-, 3-, 2-, or 1-digit match.

Results: Patient characteristics were well matched. There was no difference in in-hospital mortality between the groups. Off-pump patients were less likely to develop sternal wound infections compared to the on-pump group (2.5 versus 5.8%; \( P = 0.03 \)), and had significantly lower blood loss (675 versus 780 ml; \( P < 0.001 \)), red blood cell unit transfusion (8.6 versus 38.9%; \( P < 0.001 \)), enzyme rises (13 versus 23 U/l; \( P < 0.001 \)), inotrope support (11.9 versus 28.9%; \( P < 0.001 \)), and ventilation times (5 versus 8 h; \( P < 0.001 \)). Intensive care unit and hospital stay were also significantly lower in the off-pump patients.

Conclusions: Off-pump coronary surgery with complete arterial revascularisation can significantly reduce in-hospital morbidity and lengths of stay compared to conventional on-pump coronary surgery.

© 2004 Elsevier B.V. All rights reserved.

Keywords: Total arterial revascularisation; OPCAB; Coronary artery bypass surgery; Mortality; Morbidity; Propensity-matched

1. Introduction

The development of surgical techniques to further reduce the mortality and morbidity following coronary artery bypass grafting (CABG) are of great interest to cardiac surgeons. Two of these techniques include off-pump CABG (OPCAB) and total arterial revascularisation.

OPCAB is increasingly shown to have better outcomes by several institutions with regards to a reduction in morbidity [1-3]. A reduction in mortality has also been reported in many observational studies [2,3]. A recent randomised controlled trial by Puskas and colleagues found that OPCAB had similar in-hospital and 30-day outcomes, with a reduction in length of stay, reduced transfusion requirement, and less myocardial injury [4].

Total arterial revascularisation is associated with good graft patency rates and can potentially avoid the sequelae of vein graft atherosclerosis [5]. However, there are still some concerns about the immediate and short-term morbidity associated with total arterial revascularisation [6].

Avoiding the use of cardiopulmonary bypass and its adverse physiological consequences in the short-term together with the potential long-term beneficial effects of total arterial revascularisation seems to be ideal for myocardial revascularisation [7]. However, despite encouraging short and mid-term results the clinical advantages of OPCAB are attributed to selection bias and inclusion of patients with less severe coronary artery disease [8]. Concerns are also raised about completeness of revascularisation and quality of anastomosis [9,10].

We therefore, aimed to compare the in-hospital outcomes of 360 consecutive OPCAB operations with total arterial revascularisation to a propensity-matched group of patients undergoing on-pump CABG (ONCAB) with total arterial revascularisation.
2. Methods

2.1. Patient population and data

Between 1st April 1997 and 30th September 2002, 779 consecutive patients underwent OPCAB with total arterial revascularisation. Patients undergoing OPCAB that was incidental to heart valve repair or replacement, resection of a ventricular aneurysm or other surgical procedure were not included. Also excluded were patients who received alternative conduits to arterial grafting.

Definitions and data collection methods have been previously published [11]. Data was collected prospectively during the patient’s admission as part of routine clinical practice and entered into our cardiac surgery registry on the following variables: age, sex, body mass index, urgency of operation, prior cardiac surgery, Canadian Cardiovascular Society angina class, history of myocardial infarction, diabetes, hypercholesterolaemia, hypertension, peripheral vascular disease, cerebrovascular disease, respiratory disease, and renal dysfunction, as well as the extent of coronary disease, and left ventricular ejection fraction. The target-vessel and the type and number of grafts were also collected. Post-operative data collected included in-hospital mortality, re-exploration for bleeding, atrial arrhythmia, stroke, renal failure, sternal wound infection, highest creatine kinase-MB (CK-MB) release on post-operative day one, blood loss in the intensive care unit (ICU), duration of mechanical ventilation, use of inotropes, and length of stay at ICU and post-operative hospital stay.

In-hospital mortality was defined as death within the same hospital admission regardless of cause. All patients transferred from the base hospital to another hospital were followed up to confirm their status at discharge. Re-exploration for bleeding was defined as bleeding that required surgical re-operation after initial departure from the operating theatre. Post-operative atrial arrhythmia was defined as the occurrence of new atrial arrhythmia in the absence of pre-operative persistent or paroxysmal atrial arrhythmias. Post-operative stroke was defined as a new focal neurological deficit and coma states occurring post-operatively that persisted for >24 h after its onset and was noted before discharge. We excluded confused states, transient events and intellectual impairment from our study to avoid any subjective bias. Renal failure was defined as patients with a post-operative creatinine level greater than 200 µmol/l or patients requiring dialysis. Sternal wound infection was defined in accord with the published evidence-based guidelines by the Centres for Disease Control and Prevention [12].

2.2. Blood product requirements

Blood transfusion data was obtained from the local blood transfusion service, which is provided routinely on a monthly basis. These data consisted of date of request for platelets and number of units used, along with the number of red blood cell (RBC) and fresh frozen plasma (FFP) units used. The number of units used, if any, was calculated by summation across the patient’s post-operative stay [13].

2.3. Statistical analysis

In order to assess the effect of avoiding cardiopulmonary bypass, we performed a propensity-matched cohort analysis. OPCAB patients were propensity-matched with 450 unique patients who received total arterial revascularisation performed with cardiopulmonary bypass during the same time period between 1st April 1997 and 30th September 2002. To do this, logistic regression was used to develop a propensity score for OPCAB group membership [14]. The propensity score included age, sex, body mass index, diabetes, peripheral vascular disease, cerebrovascular disease, respiratory disease, renal dysfunction, as well as the extent of coronary disease, and left ventricular ejection fraction. The target-vessel and the type and number of grafts were also collected. Post-operative data collected included in-hospital mortality, re-exploration for bleeding, atrial arrhythmia, stroke, renal failure, sternal wound infection, highest creatine kinase-MB (CK-MB) release on post-operative day one, blood loss in the intensive care unit (ICU), duration of mechanical ventilation, use of inotropes, and length of stay at ICU and post-operative hospital stay.

In-hospital mortality was defined as death within the same hospital admission regardless of cause. All patients transferred from the base hospital to another hospital were followed up to confirm their status at discharge. Re-exploration for bleeding was defined as bleeding that required surgical re-operation after initial departure from the operating theatre. Post-operative atrial arrhythmia was defined as the occurrence of new atrial arrhythmia in the absence of pre-operative persistent or paroxysmal atrial arrhythmias. Post-operative stroke was defined as a new focal neurological deficit and coma states occurring post-operatively that persisted for >24 h after its onset and was noted before discharge. We excluded confused states, transient events and intellectual impairment from our study to avoid any subjective bias. Renal failure was defined as patients with a post-operative creatinine level greater than 200 µmol/l or patients requiring dialysis. Sternal wound infection was defined in accord with the published evidence-based guidelines by the Centres for Disease Control and Prevention [12].

Continuous variables are shown as median with 25th and 75th percentiles and comparisons were made with Wilcoxon rank-sum tests. Categorical variables are shown as a percentage and comparisons were made with χ² tests. In all cases a P value < 0.05 was considered significant. All statistical analysis was performed retrospectively with SAS for Windows Version 8.2.

3. Results

During the study time period, 5679 patients underwent CABG at our institution (987 OPCAB and 4692 ONCAB). Out of 779 patients who underwent OPCAB with total arterial revascularisation, we were able to successfully match 360 to unique ONCAB patients who also received total arterial revascularisation. Of these, 22 (6.1%) were 5-digit matches, 43 (11.9%) were 4-digit matches, 163 (45.3%) were 3-digit matches, 99 (27.5%) were 2-digit matches, and 33 (9.2%) were 1-digit match [15].

Continuous variables are shown as median with 25th and 75th percentiles and comparisons were made with Wilcoxon rank-sum tests. Categorical variables are shown as a percentage and comparisons were made with χ² tests. In all cases a P value < 0.05 was considered significant. All statistical analysis was performed retrospectively with SAS for Windows Version 8.2.

<table>
<thead>
<tr>
<th>Financial year</th>
<th>OPCAB (n = 360)</th>
<th>ONCAB (n = 360)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997/1998</td>
<td>1</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>1998/1999</td>
<td>7</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>1999/2000</td>
<td>36</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>2000/2001</td>
<td>133</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>2001/2002</td>
<td>116</td>
<td>117</td>
<td></td>
</tr>
<tr>
<td>2002/2003 (upto September 2002)</td>
<td>67</td>
<td>68</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

OPCAB, off-pump coronary artery bypass grafting; ONCAB, on-pump coronary artery bypass grafting; *χ² test for trend.
The median number of grafts was 3 (25th and 75th percentiles, 2 and 3) in both OPCAB and ONCAB groups ($P = 0.62$). The target vessels grafted and the types of grafts used are shown in Table 3.

There were no significant differences between OPCAB and ONCAB patients in in-hospital mortality rate, stroke, renal failure, atrial arrhythmia, re-exploration for bleeding, or FFP and platelet transfusion (Table 4).

Table 3 shows that OPCAB patients had a significantly lower sternal wound infection rate, CK-MB level, post-operative blood loss, RBC transfusion requirement, inotrope support, ventilation times, and ICU and post-operative lengths of stay. There was a statistically significant difference in ICU and post-operative lengths of stay, despite the median values being the same in both groups, due to differences in distributions, with ONCAB patients having a higher interquartile range (Table 4).

4. Discussion

Though still to be determined, the combination of OPCAB and total arterial revascularisation has the potential to offer many advantages. Apart from the absence of long-term studies, the issues that concern most cardiac surgeons is the feasibility of total arterial OPCAB, increased technical demands, the completeness of revascularisation and the quality of distal anastomosis. Once these problems are surmounted the question still remains whether the results are at least equivalent if not advantageous as compared to ONCAB with total arterial revascularisation.

Reports have been published that not only show the feasibility of OPCAB total arterial revascularisation but also an equivalent graft patency in the short term [16]. Some studies have also shown reduced hospital stay and morbidity with OPCAB total arterial revascularisation [17]. However these benefits have been attributed to selection bias [8].

Muneretto and associates published a randomised control trial in 2003 which examined OPCAB as a technique for total arterial myocardial revascularisation [7]. They concluded that this technique did not compromise the completeness of revascularisation and significantly reduced mechanical ventilation support, and the duration of ICU and post-operative stay.

In this study we have attempted to reduce any potential bias by enrolling 360 consecutive OPCAB patients and comparing them to a propensity-matched group of ONCAB patients. This matching resulted in two groups where not only is the number of grafts the same but there is also no difference in the location of the target vessel.

Having established that complete arterial revascularisation is feasible one might still wonder about the quality of anastomoses. Unfortunately, post-operative coronary angiography to examine graft patency, though ideal, is not always practical or feasible.
Increased CK-MB is associated with worse outcome after CABG [18]. Trends towards higher mortality were observed in patients with CK-MB levels >3-5 times normal. This was seen as early as 30-days after the procedure study. At 1 year in patients with normal CK-MB as compared to those with 5 fold rise in CK-MB the respective rates of death was 1 versus 10% and of myocardial infarction was 1 versus 12% [19]. In this study we have demonstrated a significantly higher enzyme rise in the ONCAB group as compared to the OPCAB patients, with a significantly higher proportional of patients with CK-MB of more than 5 times the upper limit of normal range (Roche, reference range 5-24 U/l at 37 °C). Myocardial protection using cardioplegia is in reality an exercise in myocardial damage limitation. Global ischaemia induced by cross clamping still results in a degree of myocardial necrosis. Indeed OPCAB surgery also results in some myocardial ischaemia, but this is regional as opposed to the global insult caused by cross clamping. The use of intracoronary shunts aims to reduce the extent of ischaemia and the amount of myocardial necrosis, although the evidence for this is somewhat debatable.

There is some evidence that patients with in-hospital graft occlusion have higher peak CK-MB values as compared to patients with patent grafts. This has been shown by Holmvang et al. who angiographically studied graft patency in all patients irrespective of symptoms [20]. Although a cut-off value for enzyme rise was not identified, patients with in-hospital, angiographically proven occluded grafts had higher peak enzyme levels. While a significant enzyme rise does not necessarily translate into occluded grafts, the difference does indicate a greater level of myocardial necrosis in the ONCAB group. We and others [4,21] have shown that post-operative CKMB is less in OPCAB patients as compared to the ONCAB group. This is also supported by the finding that post-operative inotrope use was lower in OPCAB patients (Table 4).

The use of bilateral internal mammary arteries (BIMA) has been weakly associated with a higher rise in CK-MB as compared to single internal mammary arteries [22]. In our study in the OPCAB total arterial group the percentage of BIMA use was 16.7% as compared to 20.8% in the ONCAB group (P=0.15). Although the use of BIMA is marginally higher in the ONCAB group, this did not reach a statistically significant difference, therefore, we believe this cannot explain entirely the significantly higher CK-MB levels seen in this group of patients.

Higher rates of sternal wound infection in patients with multiple arterial grafts used, especially BIMA, has been previously shown [23]. Therefore, identifying surgical techniques to help reduce this risk when using total arterial revascularisation is essential.

In this report we have shown a significantly lower rate of sternal wound infection in the OPCAB group as compared to the ONCAB group. Cardiopulmonary bypass is known to induce a degree of immununospression and make the patient more susceptible to infection [24]. Previously we have reported that an increased duration of mechanical ventilation is a significant risk factor for sternal wound infection [23]. The use of blood products especially platelets are also known to increase the risk of infection [25]. In this study mechanical ventilation times and blood loss in OPCAB was significantly less. Though the lower blood loss did not translate into reduced re-exploration rates it definitely reduced the transfusion requirement and most probably has prevented the associated untoward effects of blood transfusion. Our findings of fewer sternal infections in OPCAB patients can therefore be attributed to the reduced need for mechanical ventilation and blood usage as well as the avoidance of cardiopulmonary bypass.

Despite reports of higher morbidity and lengths of stay with arterial revascularisation [6] this study has shown that, reduced ICU stay and earlier discharge can be achieved when cardiopulmonary bypass is avoided. A finding which is supported by the randomised controlled trial by Muneretto [7].

There are some limitations which need to be considered when drawing conclusions from this report. The first is that it is an observational study and therefore could have some degree of selection bias. The retrospective nature of the study cannot account for unknown variables affecting the outcomes that are not correlated strongly with the variables used in the propensity-matching. Although, propensity score adjustment is no substitute for a properly designed randomised control trial, retrospective comparisons with propensity-matching are more versatile and may be more widely acceptable than randomised control trials [14]. A further limitation is that the time period of the OPCAB and ONCAB operations is significantly different; therefore, this report could be biased by a time-effect. We can also not rule out the potential for surgeon-bias when examining certain outcomes such as blood product use and inotropic support. The differences between OPCAB and ONCAB patients cannot be fully explained by the significant difference in blood loss or myocardial injury shown in our study. However, randomised control trial evidence suggests OPCAB can significantly reduce blood product use [4] and myocardial damage [7]. A final limitation is that we have only examined short-term in-hospital outcomes. Long-term graft patency and the need for subsequent revascularisation will be of great interest as our experience grows.

In conclusion, OPCAB total arterial revascularisation is feasible and can be performed with the same risk of mortality as ONCAB total arterial revascularisation. In this propensity-matched population of OPCAB patients with total arterial revascularisation our experience shows added benefit seen as a reduction in the rate of sternal wound infection, the need for inotropic support, ventilation times, blood loss, transfusion requirements as well as shorter ICU and in-hospital stay. Long-term follow-up is necessary to assess the further benefits of arterial graft usage.

Acknowledgements

We would like to acknowledge the co-operation given to us by all the Consultant Cardiac Surgeons at the Cardiothoracic Centre-Liverpool: Mr John A.C. Chalmers, Mr Walid C. Dihmis, Mr Brian M. Fabri, Miss Elaine M. Griffiths, Mr Neeraj K. Mediratta, Mr Richard D. Page, Mr D. Mark Pullan, Mr Abbas Rashid, and Mr W. Ian Weir. We would also like to thank Miss Janet Deane who maintains the quality and ensures completeness of data collected in our Cardiac Surgery Registry.
References


