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Effect of avoiding cardiopulmonary bypass in non-elective coronary artery bypass surgery: a propensity score analysis

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Abstract

Objective: Non-elective coronary artery surgery (emergent/salvage or urgent) carries an increased risk in most risk-stratification models. Off-pump coronary surgery is increasingly used in non-elective cases. We aimed to investigate the effect of avoiding cardiopulmonary bypass on outcomes following non-elective coronary surgery. **Methods**: Of the 3771 consecutive coronary artery bypass procedures performed by five surgeons between April 1997 and March 2002, 828 (22%) were non-elective and 417 (50.4%) of these patients had off-pump surgery. Multivariate logistic regression was used to assess the effect of off-pump on in-hospital outcomes, while adjusting for treatment selection bias. Treatment selection bias was controlled for by constructing a propensity score from core patient characteristics, which was the probability of avoiding cardiopulmonary bypass. The C statistic for this model was 0.8. **Results**: Off-pump patients were more likely to be hypertensive, stable, had less extensive disease and better left ventricular function. The left internal mammary artery was used in 91.8% ($n = 383$) of off-pump patients compared to 79.3% ($n = 326$) of on-pump cases ($P < 0.001$). After adjusting for the propensity score, no difference in in-hospital mortality was observed between off-pump and on-pump (adjusted odds ratio (OR) 0.83 (95% confidence intervals (CI) 0.36–1.93); $P = 0.667$). Off-pump patients were less likely to require intra-aortic balloon pump support (adjusted OR 0.44 (95% CI 0.21–0.96); $P = 0.039$), less likely to have renal failure (adjusted OR 0.44 (95% CI 0.22–0.90); $P = 0.025$), and have shorter lengths of stay (adjusted OR 0.51 (95% CI 0.37–0.70); $P < 0.001$). Other morbidity outcomes were similar in both groups. **Conclusions**: In this experience, off-pump coronary surgery in non-elective patients is safe with acceptable results. Non-elective off-pump patients have a significantly reduced incidence of renal failure, and shorter post-operative stays compared to on-pump coronary artery bypass surgery.

Keywords: Off-pump; Coronary artery bypass surgery; Non-elective; Mortality; Morbidity; Risk adjustment

1. Introduction

Coronary artery bypass grafting (CABG) is the most widely performed surgery in the western world. For more than three decades, cardiopulmonary bypass (CPB) has been used by surgeons worldwide to achieve a still and bloodless operative field while performing intricate anastomoses. As time has passed, the results have improved tremendously, so much so that, in a predominant majority of the cases, CABG is now performed with minimal mortality risk [1]. This has resulted in an increase in the risk profile of patients being referred for CABG. While mortality figures have remained low, post-operative complications including stroke, renal failure and myocardial insufficiency continue to be a major cause for concern after CABG. CPB is believed to contribute to several of these problems [2].

In the last 15 years, CABG without CPB (OPCAB) has developed into a viable alternative to on-pump CABG (ONCAB). This was initially performed by Kolessov in the Soviet Union in 1967 [3] and a little later in the United States by Favaloro [4]. However, this was abandoned as the use of CPB and cardioplegia became routine. Interest in this technique recommenced towards the end of the 1980s and this received further impetus with a better understanding of

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the physiology of beating-heart surgery and technological advances, especially with regard to stabilizers and shunts.

While the results of OPCAB have been comparable to those of ONCAB with similar mortality rates, the major difference has been a lower incidence of many of the post-CABG complications in OPCAB patients as seen in several studies [5–7]. However, in many of these early studies, there was a strong patient selection bias as a result of which patients with a better risk profile were selected to under go OPCAB. As experience grew, more and more high-risk patients were accepted for OPCAB with similar results [8,9].

Non-elective CABG (urgent, emergent and salvage) carries an increased risk in most risk-stratification models, as was seen in a comparison analysis of six scoring systems by Geissler and colleagues [10]. We aimed to quantify the effect of avoiding CPB on outcomes in this subset of patients.

2. Methods

2.1. Patient population and data

Our study consisted of 3771 consecutive patients undergoing CABG surgery performed between April 1, 1997 and March 31, 2002 at two institutions (Cardiothoracic Centre – Liverpool and Manchester Royal Infirmary). Patients undergoing CABG that was incidental to heart valve repair or replacement, resection of a ventricular aneurysm or other surgical procedure were not included. These patients represented the entire coronary revascularisation practice of five surgeons (D.J.M.K., R.H., D.M.P., W.C.D., B.M.F.). All five surgeons have changed practice over the last 5 years, from performing almost all cases on-pump to now performing all cases off-pump. A total of 2943 (78%) patients received elective CABG and are excluded from the analysis, leaving 828 (22%) patients who underwent non-elective coronary surgery for our study population. The different surgical techniques used in these patients, off-pump and on-pump have already been published [11].

Non-elective cases include the following. (a) Urgent: patients who have not been scheduled for routine admission from the waiting list but who require surgery on the current admission for medical reasons. They cannot be sent home without surgery. (b) Emergency: unscheduled patients with ongoing refractory cardiac compromise. There should be no delay in surgical intervention irrespective of time of day. (c) Salvage: patients requiring cardiopulmonary resuscitation (CPR) en-route to theatre or prior to anaesthetic induction. CPR following anaesthetic induction is not included, so as to preclude elective patients who happen to 'crash' following induction [1,12].

Definitions and data collection methods have been previously published [13]. Data were 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 (BMI), urgency of operation, prior cardiac surgery, New York Heart Association (NYHA) functional class, Canadian Cardiovascular Society (CCS) 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. Procedural data was also collected on the use of cardiopulmonary bypass, type and number of grafts. Post-operative data collected included in-hospital mortality, myocardial infarction, re-exploration for bleeding, atrial arrhythmia, stroke, renal failure, duration of mechanical ventilation, intra-aortic balloon pump (IABP) support, and length of 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 comatose 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. Post-operative myocardial infarction was defined as a new Q-wave in two or more contiguous leads on an electrocardiogram or significant rise in cardiac enzymes combined with hemodynamic and echocardiographic signs of myocardial infarction.

2.2. Statistical methods

Continuous variables are shown as median with 25th and 75th centiles and categorical variables are shown as a percentage with 95% confidence intervals (CI). Comparisons were made with Wilcoxon rank sum tests and Chi-square tests as appropriate. Standard statistical tests were used to calculate odds ratios with 95% CI. The European System for Cardiac Operative Risk Evaluation (EuroSCORE) was derived to assess differences in patient case mix between off-pump and on-pump patients [14]. Logistic regression was used to adjust in-hospital outcomes for differences in patient and disease characteristics (treatment selection bias) [15].

Treatment selection bias was controlled for by constructing a propensity score [16]. The propensity score was the probability that a patient would receive off-pump coronary surgery, and included all the variables listed in Table 1

Table 1
Patient characteristics based on procedure performed

	Off-pump ($n = 417$)	On-pump ($n = 411$)	P-value
Age at operation (years)	66.0 (58.0–71.6)	64.0 (58.0–70.4)	0.19
Body mass index (kg/m^2)	26.7 (24.2–29.9)	26.4 (24.2–29.5)	0.39
Female sex (%)	30.5	24.6	0.058
NYHA class IV (%)	8.2	11.7	0.089
Angina class IV (%)	48.4	65.7	<0.001
Previous MI (%)	51.6	54.5	0.40
Diabetes (%)	18.2	15.3	0.27
Hypercholesterolaemia (%)	78.4	71.8	0.027
Hypertension (%)	52.5	43.3	0.008
Peripheral vascular disease (%)	13.7	13.1	0.82
Cerebrovascular disease (%)	10.3	6.6	0.053
Renal dysfunction (%)	3.8	2.4	0.25
Respiratory disease (%)	25.2	24.1	0.72
Ejection fraction < 30% (%)	10.6	15.1	0.049
Three vessel disease (%)	71.7	82.9	<0.001
Left main stenosis (%)	29.0	27.7	0.68
Prior cardiac surgery (%)	4.3	5.8	0.32
No. of grafts (n/patient)	3 (2–4)	4 (3–4)	<0.001
LIMA use (%)	91.8	79.3	<0.001
EuroSCORE	4 (2–6)	4 (2–7)	0.18

NYHA, New York Heart Association; MI, myocardial infarction; LIMA, left internal mammary artery; EuroSCORE, European system for cardiac operative risk evaluation. Continuous variables are shown as median with 25th and 75th centiles. Categorical variables are shown as a percentage.

(C statistic $= 0.8$) [17]. Once the propensity score is constructed for each patient, there are three ways of using the score for comparisons: matching, stratification, and multivariable adjustment. Due to the small sample size available to us for this study, we have decided to use multivariable adjustment because matching would have reduced the study size even further and stratification can be difficult to interpret. The propensity score is then included along with the comparison variable (off-pump or on-pump) in a multivariable analyses of outcome producing adjusted odds ratios as shown in Table 4. The propensity score adjusts for the treatment selection bias, which is evident in Table 1, between one group versus another. Using a propensity score as the sole means for adjusting outcomes was preferable due to the low number of events in our study and provides better adjustment for those factors driving treatment selection; the overall effect is more complete risk adjustment [16]. In all cases a P-value of less than 0.05 was considered significant. All statistical analysis was performed retrospectively with SAS for Windows Version 8.2.

3. Results

Overall, 417 (50.4% (95% CI 46.9–53.8)) patients received off-pump coronary surgery, while 411 (49.6% (95% CI 46.2–53.1)) patients underwent CABG with cardiopulmonary bypass.

Table 1 lists patient and disease characteristics based on the procedure performed. There were no differences between patients characteristics with respect to age, sex, body mass index, severity of dyspnoea, previous myocardial infarctions, diabetes, peripheral vascular disease, cerebrovascular disease, respiratory disease, renal dysfunction, left main stem stenosis, prior cardiac surgery and the EuroSCORE. Patients receiving off-pump coronary surgery were less likely to have severe angina ($P < 0.001$), poor ejection fraction ($P = 0.049$), less extensive coronary disease ($P < 0.001$), and fewer distal anastomoses ($P < 0.001$). However, off-pump patients were more likely to be hypercholesterolaemic ($P = 0.027$), hypertensive ($P = 0.008$), and receive the left internal mammary artery ($P < 0.001$).

The distribution of urgent, emergency and salvage work by the procedure performed are shown in Table 2, which shows that both groups were well matched.

Off-pump patients were more likely to have a shorter post-operative length of stay (median 7 days (25th and 75th centiles: 5–8)) compared to on-pump patients (median 7 days (25th and 75th centiles: 6–11); $P < 0.001$). Almost 50% of ONCAB patients stayed longer than 7 days compared to just under 33% of OPCAB cases.

In-hospital outcomes by procedure performed are shown in Table 3 (crude) and Table 4 (adjusted for the propensity score). There was no association between avoiding cardiopulmonary bypass and in-hospital mortality, re-exploration for bleeding, atrial arrhythmia, and peri-operative myocardial infarction in either univariate or multivariate analyses.

Off-pump was associated with significantly shorter mechanical ventilation, and incidence of post-operative strokes in the univariate analyses. However, after adjusting for the propensity score in the multivariate analyses these differences disappeared.

Table 2
Priority of surgery based on procedure performed

	Off-pump ($n = 417$)	On-pump ($n = 411$)	P-value
Urgent (%)	90.4	88.1	
Emergency (%)	9.1	10.7	
Salvage (%)	0.5	1.2	0.37[a]

Categorical variables are shown as a percentage.
[a] Chi-square test for trend.

The incidence of post-operative renal failure was significantly lower in patients receiving off-pump coronary surgery in both the univariate and multivariate analyses (adjusted odds ratio (OR) 0.44, $P = 0.025$). The incidence of mild renal impairment (creatinine > 200 μmol/l) is 2.4% (95% CI 1.2–4.4) for off-pump patients compared to 6.3% (95% CI 4.5–9.2) for on-pump patients ($P = 0.006$), while the incidence of acute renal failure (dialysis support) was 1.4% (95% CI 0.6–3.2) in off-pump patients compared to 1.5% (95% CI 0.6–3.3) in on-pump patients ($P = 0.979$).

Of the patients who developed mild renal impairment during the post-operative course, the average preoperative serum creatinine level was 112 μmol/l (minimum 85 μmol/l and maximum 133 μmol/l). Off-pump patients were also less likely to need IABP support (adjusted OR 0.44, $P = 0.039$) and have lengths of post-operative stay > 7 days (adjusted OR 0.51, $P < 0.001$).

In the salvage group, in-hospital mortality, myocardial infarction, stroke, renal failure, and ventilation requirements were all significantly higher. However, there were no significant differences between whether the procedure was performed on-pump or off-pump, although this is from a very small sample size (five on-pump cases with one death and two off-pump with one death), and therefore no conclusions can be drawn.

4. Discussion

We have analysed the practices of five surgeons based at the two institutions over a 5-year period, during which all of them have changed their practice from predominantly performing ONCAB to OPCAB now. While patients undergoing ONCAB are more likely to be males, have CCS Class IV angina, with poor left ventricular functions and more extensive coronary artery disease, those receiving OPCAB were more likely to be females, hypercholesteraemic and hypertensives with better left ventricular functions. While the OPCAB group received fewer grafts, they were more likely to receive the left internal mammary artery (LIMA) graft to the left anterior descending artery (LAD) (Table 1). There is no significant difference in distribution of urgent, emergent and salvage cases in the two groups (Table 2). Although there are significant differences between off-pump and on-pump characteristics, overall, both groups were well matched according to the EuroSCORE risk stratification model (Table 1).

Table 3 reveals the crude outcomes analysed in this study in both the groups. Patients having OPCAB seem to do better on most counts including lower stroke rate ($P = 0.047$), renal failure ($P = 0.015$), lesser need for intra-operative IABP ($P = 0.002$), shorter post-operative in-hospital stay ($P < 0.001$) and fewer patients requiring ventilation longer than 24 h ($P = 0.011$).

After adjusting for differences in patient case-mix (propensity score), we found that off-pump patients still had a lower incidence of renal failure ($P = 0.025$) and need for intra-operative IABP support ($P = 0.039$). Their in-hospital stay tends to be shorter as well ($P < 0.001$). Although there is a lower incidence of peri-operative myocardial infarction (MI) and stroke with fewer deaths in the OPCAB group, these differences are not significant.

Chamberlain et al. have recently published an observational study, evaluating the effectiveness of OPCAB in high-risk patients, where they found a significantly lower incidence of need for IABP, transfusion requirements, pulmonary complications and shorter intensive care unit and in-hospital stays in the OPCAB group. They were unable to demonstrate any difference in the incidence of peri-operative MI, renal complications, infective complications or new atrial fibrillation (AF). They did not demonstrate any

Table 3
Post-operative data based on procedure performed

	Off-pump ($n = 417$)	On-pump ($n = 411$)	Odds ratio (95% confidence intervals)	P-value
In-hospital mortality (%)	3.6	3.9	0.92 (0.45–1.89)	0.82
Myocardial infarction (%)	2.6	2.4	1.09 (0.46–2.59)	0.85
Stroke (%)	0.7	2.4	0.29 (0.08–1.06)	0.047
Atrial arrhythmia (%)	26.4	23.6	1.16 (0.85–1.59)	0.36
Renal failure (%)	3.8	7.8	0.47 (0.25–0.87)	0.015
Re-exploration for bleeding (%)	4.6	2.9	1.59 (0.76–3.31)	0.22
Ventilation > 24 h (%)	5.3	10.0	0.50 (0.29–0.86)	0.011
IABP support (%)	2.9	7.8	0.35 (0.18–0.69)	0.002
Post-operative stay > 7 days (%)	32.8	49.9	0.49 (0.37–0.65)	< 0.001

IABP, intra-aortic balloon pump.

Table 4
Post-operative data based on procedure performed adjusted for the propensity score

	Off-pump ($n = 417$)	On-pump ($n = 411$)	Odds ratio (95% confidence intervals)	P-value
In-hospital mortality (%)	3.5	3.9	0.83 (0.36–1.93)	0.67
Myocardial infarction (%)	2.2	2.8	0.72 (0.26–1.98)	0.52
Stroke (%)	0.9	2.0	0.36 (0.08–1.53)	0.17
Atrial arrhythmia (%)	26.8	23.2	1.30 (0.89–1.88)	0.16
Renal failure (%)	4.1	7.3	0.44 (0.22–0.90)	0.025
Re-exploration for bleeding (%)	4.4	3.0	1.72 (0.73–4.04)	0.22
Ventilation > 24 h (%)	6.1	8.8	0.58 (0.31–1.08)	0.088
IABP support (%)	3.6	6.4	0.44 (0.21–0.96)	0.039
Post-operative stay > 7 days (%)	35.0	46.9	0.51 (0.37–0.70)	<0.001

significant in-hospital survival benefit [8]. Hernandez and co-workers in the Northern New England Cardiovascular Disease Study Group were also unable to show any significant difference in outcomes in a multicentre OPCAB versus ONCAB comparison, except for a lower incidence of post-operative AF and an almost significant difference in the use of intra and post-operative IABP. The patients in the OPCAB group had a lower median in-hospital stay [9]. Another recent study by van Dijk et al. on behalf of the Octopus study group, showed less blood loss in the OPCAB group and thus less requirement for blood products. They also demonstrated a shorter in-hospital stay [18].

Most of the findings in our study are in agreement with the findings in the above-mentioned reports. However, one significant difference has been the benefit of OPCAB over ONCAB in terms of incidence of renal outcomes. Although there is no difference in the two groups for dialysis post-operatively and pre-operative renal dysfunction is higher in OPCABs, the ONCAB patients seem to have a significantly higher incidence of renal impairment with serum creatinine > 200 μmol/l. This contributed to a longer ITU or high dependency unit stay and longer in-hospital stay. Using a threshold definition of more than 200 μmol/l of post-operative serum creatinine for renal failure may imply that some patients had a trivial baseline increase in serum creatinine resulting in a classification of renal failure. However, all our patients classified as post-operative renal failure, without requiring dialysis, had a baseline serum creatinine increase of 67 μmol/l. This is comparable with the findings of Mangano and colleagues [19] who regarded anyone with a serum creatinine increase of 62 μmol/l or more over baseline as having clinically significant renal failure.

While none of the studies showed any significant benefit of OPCAB with regards to renal outcomes, there have been several studies in the literature demonstrating the reno-protective effect of OPCAB [20,21]. Peri-operative renal dysfunction represents a significant and potentially lethal complication of CABG. The causes for this are multi-factorial, including the use of CPB, peri-operative cardio-vascular instability, non-pulsatile flow, hypothermia and various toxins generated during CPB. Hence, it seems reasonable to assume that avoiding CPB would reduce the incidence of renal complications.

A recent study at one of our institutions, (Grayson and colleagues, Cardiothoracic Centre – Liverpool, unpublished work), found that non-elective cardiac surgery patients were 2.63 times more likely to develop post-operative renal failure. This study suggests that avoiding CPB, in non-elective cases, could reduce the incidence of renal failure (adjusted OR 0.44, $P = 0.025$). Baumgartner and colleagues were able to show a similar reduction in the incidence of renal complications after OPCAB [22].

Interestingly we were unable to show a statistically significant reduction in post-operative stroke when avoiding CPB in non-elective cases, although the stroke rate was lower in off-pump patients (0.9% versus 2.0%, $P = 0.165$). We have shown in previously published studies that off-pump surgery can significantly reduce the incidence of neurological deficits in patients undergoing CABG [11,23]. Failure to achieve significance may be due to the relatively smaller number of patients analysed in this report.

There are some limitations which may effect the conclusions drawn from our study. These include variables not measured such as the quality of the coronary vessels, which is important in selecting the type of surgery and in determining the outcome, and selection bias resulting from the operating surgeon's decision to perform the procedure off-pump or on-pump. For this to effect our conclusions by a significant amount, the variables used in the propensity score (e.g. diabetes, age, sex) would have to be uncorrelated with the variables not measured (e.g. quality of coronary vessels or distal coronary disease), but we do not believe that this is likely. This study also does not take into account long-term outcomes for these patients (e.g. graft patency and quality of life); such outcomes will be of great interest as our experience grows.

The most important limitation is that the study is spread over 5 years and most patients in the ONCAB group are from the early part of the study period, while most belonging to the OPCAB group are from the later part of the study period. Hence, they may represent two different patient populations. Also, the OPCAB group includes patients from the period during the 'learning curve' of each surgeon maybe indicating a degree of selection bias. However, we have compared the outcomes of the ONCAB patients of the five surgeons to their own OPCAB results, thus accounting for any variation due to the surgeon factor. Also, the two patient groups are well comparable in terms of patient characteristics and pre-operative variables despite the temporal differences. In addition, we have used multivariate logistic regression analysis, incorporating these patient characteristics in a propensity score to account for any significant differences in the two groups. However, it is important to note that the propensity score cannot adjust for any changes that may have occurred in policy, which may influence our outcomes.

Propensity score adjustment is no substitute for a properly designed randomized controlled trial. The retrospective nature of the study cannot account for the unknown variables affecting the outcome that are not correlated strongly with measured variables. On the other hand, retrospective comparisons with propensity score adjustment are more versatile and may be more widely acceptable than randomized control trials [16].

In conclusion, our experience across the practice of five surgeons, shows that the results of OPCAB are at least as good, if not better than their own ONCAB results for this group of high-risk patients undergoing non-elective CABG. While the outcomes in terms of crude in-hospital mortality are similar in the two groups, patients undergoing OPCAB seem to have fewer morbid events after surgery. The patients undergoing OPCAB tend to have fewer renal complications, which as a group are a significant cause for morbidity and mortality in the post-CABG patients. The need for intra-operative IABP is also less in the OPCAB patients. This is a significant finding for this group of patients, many of whom are likely to be unstable and haemodynamically compromised. OPCAB may also have economical benefits due to the shorter in-hospital stay.

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