Should obese patients undergo on- or off-pump coronary artery bypass grafting?

Mark Pullan, Bilal H. Kirmani, Thomas Conley, Aung Oo, Matthew Shaw, James McShane and Michael Poullis*

Liverpool Heart and Chest Hospital, Liverpool, UK

* Corresponding author. Liverpool Heart and Chest Hospital, Thomas Drive, Liverpool L14 3PE, UK. Tel: +44-0151-2281616; fax: +44-0151-293-2254; e-mail: mpoullis@hotmail.com (M. Poullis).

Received 10 September 2013; received in revised form 21 January 2014; accepted 18 February 2014

Abstract

OBJECTIVES: To determine if on- or off-pump coronary artery bypass grafting (CABG) makes a difference to in-hospital mortality and long-term survival in obese patients.

METHODS: Analysis of consecutive patients on a validated prospective cardiac surgery database was performed for patients undergoing isolated CABG. Obesity was defined as a body mass index (BMI) >30 kg/m². Uni- and multivariate analyses were performed for in-hospital mortality and long-term survival. A propensity analysis was also performed.

RESULTS: The overall mortality rate was 2.1% (N = 284) for all cases, N = 13 369. The mortality rate for obese patients (N = 4289) was 2.3%, and for non-obese patients (N = 9080) it was 2.0%, P = 0.4. The median follow-up was 7.0 (interquartile range 4.1–10.1) years. Univariate analysis identified that in-hospital mortality was significantly lower in obese patients undergoing off-pump CABG; P = 0.01. No significant difference existed with regard to non-obese patients; P = 0.55. Kaplan–Meier survival analysis identified that off-pump CABG was associated with improved survival in obese patients; P = 0.01. Multivariate analysis of non-obese patients did not identify on- or off-pump CABG as a significant factor determining in-hospital mortality or long-term survival. Multivariate analysis of obese patients identified off-pump CABG as being associated with significantly reduced in-hospital mortality (odds ratio [OR] 0.56, 95% confidence interval [CI] 0.34–0.93, P = 0.03), and significantly improved long-term survival (hazard ratio 0.81, 95% CI 0.67–0.98, P = 0.03). In-hospital mortality and long-term survival were significantly affected by the era of surgery, regardless of patients’ BMI. Propensity matching of non-obese patients (N = 6088, 1:1 matching) did not identify on- or off-pump CABG as a significant factor determining in-hospital mortality or long-term survival. Propensity matching of obese patients (N = 2980, 1:1 matching) identified on-pump CABG as a significant factor determining in-hospital mortality (OR 0.50, 95% CI 0.26–0.98, P = 0.04), but having no effect on long-term survival.

CONCLUSIONS: Univariate, multivariate and propensity matching suggest that obese patients undergoing CABG have reduced in-hospital mortality if they undergo revascularization with the off-pump technique.

Keywords: Obesity • Off pump • Coronary • Mortality • Survival

INTRODUCTION

Numerous studies examine the effect of obesity on in-hospital mortality and long-term survival with variable conclusions [1–6]. Obesity can be defined as a body mass index (BMI) >30 kg/m² [4]. As obesity has an increasing incidence in the western world [7], the optimum management of these patients undergoing coronary artery bypass grafting (CABG) is important.

To date, few studies have examined the effect of off-pump cardiac surgery and obesity [1, 8]. These studies identified off-pump CABG as being equivalent to on-pump with regard to in-hospital mortality and long-term survival; however, both were small studies.

We undertook a retrospective analysis in a unit with a long-standing interest in off-pump CABG with regard to the effect of obesity on in-hospital mortality and long-term survival.

METHODS

Local institutional review board permission was granted for this retrospective study. The characteristics of the study population are summarized in Table 1. The study cohort was from 1 April 1997 to 30 March 2012. Only patients undergoing first-time isolated coronary artery bypass surgery were included. Obesity was defined as a BMI >30 kg/m². Off-pump conversions were analysed ‘on an intention-to-treat’ basis, and so were classified as off-pump procedures. Preoperative renal failure was defined as a preoperative serum creatinine >200 μmol/l or the need for preoperative dialysis.
Table 1: Pre-, peri- and postoperative characteristics of patients in the study group (N = 13 369)

<table>
<thead>
<tr>
<th>Preoperative</th>
<th>Operative, n (%)</th>
<th>Postoperative, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.9 (9.0) [18–90]</td>
<td>10.4 (9.0) [18–61]</td>
</tr>
<tr>
<td>Female (%)</td>
<td>2620 (19.6)</td>
<td>12 (0.3)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.4 (4.3) [16–61]</td>
<td>42 (0.5)</td>
</tr>
<tr>
<td>Obese, n (%)</td>
<td>9080 (67.9)</td>
<td>1286 (91.9)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>187 (0.14)</td>
<td>3.3 (0.95) [1–7]</td>
</tr>
<tr>
<td>Critical preop state</td>
<td>17 (0.13)</td>
<td>10.762 (80.5)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4906 (36.7)</td>
<td>2433 (18.2)</td>
</tr>
<tr>
<td>Preop dialysis</td>
<td>54 (0.4)</td>
<td>174 (1.3)</td>
</tr>
<tr>
<td>Preop IABP</td>
<td>174 (1.3)</td>
<td>7981 (59.7)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6537 (48.9)</td>
<td>4198 (31.4)</td>
</tr>
<tr>
<td>Preop PCI</td>
<td>1818 (13.6)</td>
<td>1190 (8.9)</td>
</tr>
<tr>
<td>Status, n (%)</td>
<td>856 (6.4)</td>
<td>10 (0.13)</td>
</tr>
<tr>
<td>Elective</td>
<td>4.7 (2.6) [0–80.4]</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Urgent</td>
<td>2.2 (10.1) [0–703]</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Emergency</td>
<td>9.5 (11.7) [0–381]</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Log EuroSCORE</td>
<td>4.7 (2.6) [0–80.4]</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Graft number</td>
<td>3 [1–6]</td>
<td>12 (13.1)</td>
</tr>
<tr>
<td>LIMA</td>
<td>12.286 (91.9)</td>
<td>0.3 (12)</td>
</tr>
<tr>
<td>No. of grafts</td>
<td>3.3 (0.95) [1–7]</td>
<td>1.0 (10.1)</td>
</tr>
<tr>
<td>Off-pump conversion, n (%)</td>
<td>12 (0.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Obese</td>
<td>12 (0.3)</td>
<td>12 (0.3)</td>
</tr>
<tr>
<td>Non-obese</td>
<td>42 (0.5)</td>
<td>42 (0.5)</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>109 (32) [16 to &gt;600]</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Graft number</td>
<td>3 [1–6]</td>
<td>3 [1–6]</td>
</tr>
<tr>
<td>Postoperative, n (%)</td>
<td>30.3 (54) [0–931]</td>
<td>0 (0)</td>
</tr>
<tr>
<td>CK-MB</td>
<td>30.3 (54) [0–931]</td>
<td>0 (0)</td>
</tr>
<tr>
<td>ITU LOS (days)</td>
<td>2.2 (10.1) [0–703]</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hospital LOS (days)</td>
<td>9.5 (11.7) [0–381]</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Mortality</td>
<td>284 (2.1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Median follow-up (years)</td>
<td>7.02</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Continuous variables are shown as mean (SD) [range]. Categorical variables are shown as n (%). Critical preoperative state was as defined by the EuroSCORE risk system. BMI: body mass index; MI: myocardial infarction; PVD: peripheral vascular disease; IABP: intra-aortic balloon pump; PCI: percutaneous coronary intervention; LIMA: left internal mammary artery; CPB: cardiopulmonary bypass; CK-MB: creatinine kinase myocardial isoenzyme—units/l; ITU LOS: intensive care length of stay.

(as per the EuroSCORE I scoring system). Risk factors incorporated in EuroSCORE I were defined as per the scoring system. Creatinine kinase muscle–brain isoenzyme (CK-MB) was measured in all patients. Continuous variables are presented as means (standard deviation [SD]) [range].

Off-pump technique

We utilize deep pericardial stitches, and the Trendelenburg position for grafting the back of the heart. An Octopus stabilizer (Medtronic, Minneapolis, MN, USA) was used for all cases. Haemodynamic instability and electrocardiogram changes of ischaemia were countered by heart repositioning, volume loading if appropriate and intra-aortic balloon pump insertion where necessary. Inotropic support was very rarely utilized during the grafting, but vasconstrictor administration was common. Intracoronary shunts were utilized for all anastomoses. We routinely utilize end-tidal CO₂ monitoring during the off-pump technique as a marker of cardiac output when the heart is positioned for intermediate, obtuse marginal and posterior descending artery grafting.

Outcome measures

Primary outcomes were in-hospital mortality and long-term survival. As previously described, the national strategic tracing service in the UK was utilized to track patients’ long-term survival [9–11].

Analysis

Univariate. Kaplan–Meier survival curves were constructed for obese and non-obese patients undergoing isolated on- or off-pump CABG. The log-rank test was utilized to test significance.

Multivariate. Long-term survival was assessed by stepwise Cox regression analysis. In-hospital mortality was assessed by stepwise logistic regression analysis. The entry criterion was P < 0.05, and the removal criterion was P > 0.1, for multivariate analysis. Covariates analysed included on- or off-pump grafting, age, sex, BMI, renal impairment as defined above, diabetes, ejection fraction, respiratory dysfunction, peripheral vascular disease and left internal mammary artery (LIMA) usage.

Propensity analysis. Logistic regression for group membership of those who underwent off-pump CABG was used to calculate the propensity score for 1:1 matching. Nearest neighbour matching without replacement with a caliper of 0.2 was utilized. Variables used in the propensity match included age, sex, BMI, renal failure as defined above, diabetes, ejection fraction, respiratory dysfunction, peripheral vascular disease and LIMA usage. A dotplot of standardized mean differences (Cohen’s d) for all covariates before and after matching was produced. Cox survival curves plotted at the mean of the covariates post-propensity matching were created.

Era of surgery

Owing to the long period of study of our cohort, we performed an era of surgery analysis. This was performed in two different ways: by dividing the study group into two equal time periods and by using a sequential time index starting with the first case.

Statistical software

All statistical analyses other than the propensity matching were performed with MedCalc for Windows (version 12.1.4, MedCalc Software, Mariakerke, Belgium). The propensity matching was performed with SPSS (version 20.0 for Windows; SPSS, Inc., Chicago, IL, USA), SPSS Statistics Integration Plug-In for R, and R 2.12.2.
RESULTS

Study population

The overall mortality rate was 2.1% (N = 284) for all cases, N = 13 369. The mortality rate for obese patients was 2.3% (N = 4289), and for non-obese patients it was 2.0% (N = 9080). The mortality rate for off-pump CABG (N = 4462) was 1.8%, and for on-pump CABG (N = 8907) it was 2.3%. The median follow-up was 7.0 (interquartile range 4.1–10.1) years.

Univariate analysis

In-hospital mortality (Fig. 1) was significantly lower in obese patients undergoing off-pump CABG; P = 0.01. No significant difference existed in non-obese patients, P = 0.55. No significant difference existed between mortality for obese and non-obese patients undergoing off-pump CABG; P = 0.3. Kaplan–Meier survival for the effects of on- or off-pump CABG in non-obese (P = 0.7) and obese (P = 0.01) patients is shown in Fig. 2A and B. No significant difference existed between the graft number in the off-pump group in obese and non-obese patients (P = 0.1); however, in the on-pump group obese patients received significantly fewer grafts than non-obese patients (mean graft number 3.5 vs 3.6); P < 0.001.

Multivariate analysis

Non-obese patients (BMI <30 kg/m²). Logistic regression (receiver operating curve [ROC] 0.79, Hosmer–Lemeshow P = 0.20) identified age, ejection fraction, preoperative renal dysfunction, female sex, preoperative respiratory dysfunction, operative priority and era of surgery as significant factors determining in-hospital mortality (Table 2). On- or off-pump CABG was not identified as a significant factor.

Cox regression (Harrel’s c statistic 0.71) identified age, diabetes, ejection fraction, hypertension, previous cerebrovascular event, preoperative renal dysfunction, no LIMA used, CK-MB release, preoperative respiratory dysfunction, operative priority, era of surgery, recent MI and critical preoperative state, as significant factors determining long-term survival (Table 3 and Fig. 3A). Off-pump surgery was not identified as being a significant factor.

Obese patients (BMI >30 kg/m²). Logistic regression (ROC 0.78, Hosmer–Lemeshow P = 0.90) identified off-pump CABG as being associated with significantly reduced in-hospital mortality. Age, diabetes, ejection fraction, female sex, era of surgery, preoperative respiratory dysfunction, critical preoperative state and operative priority were also identified as significant factors determining in-hospital mortality (Table 2).

Cox regression (Harrel’s c statistic 0.71) identified off-pump CABG, age, diabetes, ejection fraction, renal dysfunction, operative priority, era of surgery, LIMA non-usage and respiratory dysfunction, as significant factors determining long-term survival (Table 3 and Fig. 3B).

Era of surgery analysis

In-hospital mortality and long-term survival were significantly affected by the era of surgery, regardless of patients’ BMI (Tables 2 and 3), respectively.

Figure 1: Univariate comparison of in-hospital mortality for obese and non-obese patients undergoing on- or off-pump surgery. In-hospital mortality was significantly lower in obese patients undergoing off-pump CABG; P = 0.01. No significant difference existed between mortality for obese and non-obese patients undergoing off-pump CABG; P = 0.3. CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass.

Figure 2: Kaplan–Meier survival for (A) non-obese (P = 0.7), and (B) obese patients (P = 0.01).
Propensity analysis

Separate propensity analyses were performed for obese and non-obese patients.

Non-obese patients (BMI <30 kg/m²). Propensity matching of patients with a BMI <30 kg/m² resulted in patients being matched 1:1 with regard to on- or off-pump CABG (N = 6088). The median logistic EuroSCORE after matching was 3.1 (25th–75th percentile 1.7–5.9) for the off-pump cohort, compared with a median risk of 2.8 (25th–75th percentile of 1.5–5.1) for the on-pump cohort; P = 0.0003 (Mann–Whitney test—independent samples). A dotplot of standardized mean differences (Cohen’s d) for all covariates before and after matching for on- or off-pump CABG is shown in Fig. 4A. Overall multivariate imbalance testing after matching was not significant; P = 0.31.

Logistic regression (ROC 0.91, Hosmer–Lemeshow P < 0.001) identified preoperative renal impairment, female gender, ejection fraction and era of surgery as significant factors determining in-hospital mortality (Table 2). Off-pump CABG, age, BMI, diabetes, preoperative respiratory dysfunction, LIMA usage and peripheral vascular disease were not identified as significant factors.

Cox regression (Harrell c statistic 0.70) identified age, BMI, renal failure, diabetes and ejection fraction as significant factors determining long-term survival (Table 3 and Fig. 5A). Off-pump CABG, peripheral vascular disease and female sex were not identified as significant factors.
Obese patients (BMI >30 kg/m²). Propensity matching of patients with a BMI >30 kg/m² resulted in patients being matched 1:1 with regard to on- or off-pump CABG (N = 2980). The median logistic EuroSCORE after matching was 2.5 (25th–75th percentile 1.4–4.8) for the off-pump cohort, compared with a median risk of 2.6 (25th–75th percentile of 1.4–4.9) for the on-pump cohort; P = 0.72 (Mann–Whitney test—独立 samples). A dotplot of standardized mean differences (Cohen’s d) for all covariates before and after matching for on- or off-pump CABG is shown in Fig. 4B. Overall multivariate imbalance test after matching was not significant; P = 0.4.

Logistic regression (ROC 0.9, Hosmer–Lemeshow P < 0.001) identified off-pump CABG as being associated with significantly reduced in-hospital mortality. Poor ejection fraction, female sex and era of surgery were also identified as significant factors determining in-hospital mortality (Table 2). Age, BMI, peripheral vascular disease, renal impairment, diabetes, ejection fraction, LIMA usage and respiratory dysfunction were not identified as significant factors.

Cox regression (Harrell c statistic 0.7) identified age, BMI, peripheral vascular disease, preoperative renal impairment, diabetes, ejection fraction and LIMA non-usage as significant factors determining long-term survival (Table 3 and Fig. 5B) (survival plotted at the mean of the covariates). Off-pump CABG, female sex and era of surgery were not identified as significant factors.

**DISCUSSION**

Off-pump CABG results in a significantly lower in-hospital mortality rate in obese patients. A propensity analysis confirmed the
multivariate analysis results. After propensity matching, the survival advantage of off-pump CABG in obese patients disappeared.

Obesity is defined by the World Health Organization (WHO) as a BMI >30 kg/m² and can be subdivided into Class I obesity (BMI 30.0–34.9), Class II obesity (BMI 35.0–39.9) and Class III obesity (BMI >40.0) [12]. Additionally, any BMI ≥35 can be classified as severe obesity, a BMI ≥40–44.9 as morbid obesity and a BMI ≥45 as super obesity [12]. We did not have enough patients to subanalyse these subgroups without potentially incurring a statistical error due to a lack of power. Previous work examining the effect of off-pump surgery in overweight patients was hindered by a small study size and may have been underpowered [1,8].

Our institution has been routinely performing off-pump CABG for 14 years. The surgeons who perform off-pump surgery in our institution have all performed over 300 cases and have an off-pump CABG rate of over 98%, and a conversion rate of <2% as part of their routine and urgent practice. In addition, all our anaesthetists are full-time cardiothoracic specialists.

The average logistic EuroSCORE of the off-pump group was significantly higher than the on-pump group. The finding that off-pump CABG was associated with a reduced in-hospital mortality and improved long-term survival despite having a significantly higher baseline risk profile implies that the result is real. The addition of propensity matching resulted in the differences in EuroSCOREs between the on- and off-pump groups becoming non-significant. Despite this, off-pump CABG was associated with reduced in-hospital mortality in obese patients.

We have not presented any morbidity data for the obese patients. The increased incidence of morbidity in obese patients undergoing CABG has been published previously [4].

Arterial grafting strategy has been advocated to improve the long-term outcome post-CABG [13,14]. Very few obese patients undergo bilateral internal mammary artery grafting. We have a number of patients who have undergone composite arterial grafting with the LIMA and the radial as a T-graft. Subanalysis failed to identify composite grafting as a significant factor determining in-hospital mortality or long-term survival.

Multivariate analysis identified off-pump CABG as a significant factor determining long-term survival in obese patients. The statistically significant difference in EuroSCOREs between the on- and off-pump groups identified the possible need for propensity matching, to match the unmatched groups. We are unable to explain why off-pump surgery is associated with reduced operative mortality, but this did not translate into improved long-term survival.

Defining why off-pump CABG may be beneficial in obese patients is not possible in this study. We speculate that cardiac and non-cardiac factors may explain our findings.

(i) CK-MB released following CABG was significantly higher in the on-pump group (37 vs 17, P < 0.001). CK-MB is a known risk factor for in-hospital mortality [10].

(ii) Deep sternal wounds following CABG are significantly more common in obese individuals [15]. These deep infections are associated with increased hospital mortality and reduced long-term survival [15,16]. Our data confirmed this series (obese rate 1.7%, non-obese rate 0.7%, P = 0.0004); however, in obese patients on- or off-pump CABG made no difference to sternal wound infections in our series.

(iii) Renal failure requiring dialysis is associated with increased in-hospital mortality and reduced long-term survival [9]. Our data confirm this (dialysis associated with an odds ratio of death of 8.5, P < 0.0001, and a hazard ratio for survival of 5.4, P < 0.0001); however, we found that obesity was not associated with an increased rate of postoperative renal failure (P = 0.2), but on-pump surgery was P = 0.0003.

(iv) Obesity has been described as a significant factor determining operative length in thoracic surgery [17]. The bypass time for obese patients in our study was significantly longer than for non-obese patients (101 vs 97 min, P = 0.001). Increased cardiopulmonary bypass (CPB) time is a known adverse parameter with regard to in-hospital mortality and long-term survival [18].

(v) Diabetes is a known risk factor for atherosclerosis. The CABG operative procedure does not affect this ongoing process. In our series, obese patients had an incidence of diabetes of 52%, compared with non-obese patients who had an incidence rate of 30%.

(vi) Obese patients may be hypoperfused during cardiopulmonary bypass due to errors in the predicted flow rate [19]. Hypoperfusion generates tissue hypoxia, which upon reperfusion results in an inflammatory reaction, which is frequently termed ‘an inflammatory reaction to CPB’.

(vii) Obesity, via leptins and adipokines, is thought to play an important role in the inflammatory response [20–22]. To date, no work exists in cardiac surgery defining the link between the inflammatory response to bypass and obesity. We did not collect any inflammatory markers for this study.

LIMITATIONS

We present a single-institution retrospective study and it should be interpreted as such due to the inherent errors associated with this methodology. We do not have any long-term morbidity data for our study cohort; however, our study is large and has extended follow-up, which was 100% complete. We did not have enough patients to subanalyse patients with a BMI >35 or 40 kg/m² without potentially incurring a statistical error due to a lack of power. Dialysis is a poor marker of renal dysfunction post-CABG, and we do not have creatinine data for all patients postoperatively.

CONCLUSIONS

Univariate, multivariate and propensity matching suggest that obese patients have reduced in-hospital mortality post-CABG if they undergo revascularization with the off-pump technique.

Conflict of interest: none declared.

REFERENCES


Bastard JP, Maachi M, Lagathu C, Kim MJ, Caron M, Vidal H et al. Recent advances in the relationship between obesity, inflammation, and insulin resistance. Eur Cytokine Netw 2006;17:4–12.
