Interactive CardioVascular and Thoracic Surgery 22 (2016) 612–619
doi:10.1093/icvts/ivw005 Advance Access publication 16 February 2016

Cite this article as: Carmona P, Paredes F, Mateo E, Mena-Durán AV, Hornero F, Martínez-León J. Is off-pump technique a safer procedure for coronary revascularization? A propensity score analysis of 20 years of experience. Interact CardioVasc Thorac Surg 2016;22:612–19.

Is off-pump technique a safer procedure for coronary revascularization? A propensity score analysis of 20 years of experience

Paula Carmona[a], Federico Paredes[b,*], Eva Mateo[c], Armando V. Mena-Durán[b], Fernando Hornero[b] and Juan Martínez-León[b]

[a] Department of Cardiovascular-Anesthesia and Intensive Care, University Hospital La Fe, Valencia, Spain
[b] Department of Cardiac Surgery, General Hospital of Valencia, Valencia, Spain
[c] Department of Cardiovascular-Anesthesia and Intensive Care, University General Hospital, Valencia, Spain

* Corresponding author. Vicente Tormo Alfonso, 1. Apt 15, 46015 Valencia, Spain. Tel: +34-665855624; fax: +34-963131965; e-mail: feco_py@hotmail.com (F. Paredes).

Received 21 June 2015; received in revised form 29 November 2015; accepted 4 December 2015

Abstract

OBJECTIVES: We aim to describe our experience in coronary artery bypass grafting (CABG) with or without cardiopulmonary bypass by comparing intraoperative and postoperative outcomes.

METHODS: From January 1993 to June 2013, 3097 patients underwent consecutive emergency and scheduled CABG surgery. A total of 1770 patients underwent on-pump CABG (ONCABG) and 1327 off-pump CABG (OPCABG). A propensity score matching was performed to identify appropriate matched-pair patients; univariable and multivariable logistic regression analyses were performed to assess significant predictors of hospital and 30-day morbidity and mortality composite end-points. Morbidity composite end-point was defined as any renal, pulmonary, cardiovascular and neurological complication that occurred during hospital stay. We collected all-cause mortality data during the study period.

RESULTS: We identified 1004 patients in each group. There were no significant differences in thirty day mortality, 2.8 vs 3.8%, in OPCABG and ONCABG, respectively ($P = 0.21$). Cardiovascular, neurological, respiratory and renal complications were more frequent in the ONCABG group: 13.9 vs 8.7% ($P < 0.001$), 3.9 vs 2.2% ($P = 0.03$), 13.5 vs 7.5% ($P < 0.001$), 7.1 vs 5.3% ($P = 0.095$), respectively. The long-term all-cause mortality rate was 12.3 vs 12.9% in the OPCABG versus ONCABG group ($P = 0.42$), respectively. In both uni- and multivariable analysis preoperative renal failure, chronic obstructive pulmonary disease and ONCABG were independent predictors of mortality and morbidity composite end-points.

CONCLUSIONS: OPCABG is associated with less postoperative morbimortality and shorter hospital and intensive care unit length of stay. ONCABG resulted as an independent predictor of morbidity and mortality composite end-point. No statistically significant differences were observed in long-term all-cause mortality between groups.

Keywords: Coronary artery bypass graft • On-pump • Off-pump • Outcomes • Survival

INTRODUCTION

Coronary artery disease is the leading cause of cardiovascular morbidity and mortality in the general population [1]. In some severely-ill patients medical therapy confers a poor survival advantage relative to surgical revascularization. The goal of all surgical revascularization procedures is to perform a technical procedure with minimal morbidity and mortality, enhanced long-term survival and maximal freedom from recurrent symptoms and need for further revascularization procedures. On-pump coronary artery bypass graft (ONCABG) continues to be the gold standard to achieve these goals. Despite improved techniques and surgical experience, part of the morbidity related to CABG is caused by the cardiopulmonary bypass (CPB) [2], prompting off-pump coronary artery bypass graft (OPCABG). However, there are robust data in the literature suggesting that OPCABG is not superior to ONCABG regarding early outcomes and might be associated with inferior early and late graft patency rates and likely compromised long-term survival [3–5]. On the other hand, two recent large, international and randomized trials have shown no difference in 30-day and 1-year clinical outcomes between on- and off-pump surgery when performed by experienced surgeons [6, 7]. Complete off-pump procedures in the hands of highly trained teams appear to be associated with a reduced risk of early morbidity, such as stroke, wound and respiratory infections, as well as fewer transfusions and shorter hospital stay [8–10].

We aim to describe our experience in ONCABG versus OPCABG surgery comparing intraoperative and postoperative outcomes at 30-day and long-term all-cause mortality after 20 years of surgical experience in a single institution in which 45% of coronary revascularizations were performed under OPCABG.

MATERIALS AND METHODS

This is a retrospective, observational cohort study of prospectively collected data from consecutive patients who underwent isolated CABG at the Consorcio Hospital General of Valencia between January 1993 and June 2013. The data collection was extracted from our database (PalexData®, Barcelona, Spain). Long term survival information was provided by the National Registry of Health Care System. The resulting base sample contained detailed clinical information on 3097 patients, of whom 1327 underwent OPCABG and 1770 underwent ONCABG. In order to reduce the effects of treatment selection bias and potential confounding factors, we used a propensity score matching analysis by building a binary logistic regression model with the main preoperative risk variables and comorbidities, which resulted in 1004 patients who underwent OPCABG matched with an equal number of patients who underwent ONCABG. Surgical procedure selection was at the discretion of the operating surgeon based on patients' comorbidities perceived as high risk for CPB and personal preferences. The procedures were performed by more than one surgeon and all of them have more than 10 years of experience and have been trained in OPCABG. Patients with concomitant cardiac procedures, such as valve replacement or repair, carotid endarterectomy or CABG reoperations were excluded. Long-term follow-up for all-cause mortality was obtained from Local and National Health Care System records.

Variables included in the model

- Age,
- Sex,
- Logistic EuroSCORE,
- Smoking habit,
- Obesity: body mass index >30,
- Hypertension: arterial hypertension under treatment,
- Dyslipidaemia: dyslipidaemia under treatment,
- Diabetes mellitus under insulin treatment,
- Past medical history of cerebrovascular accident (stroke or transient ischaemic attack),
- Chronic pulmonary disease: pulmonary disease under treatment with bronchodilators or corticoids,
- Clinical symptoms of stable or unstable angina,
- History of percutaneous coronary intervention in the past,
- History of coronary thrombolysis in the past,
- History of acute coronary syndrome in the 6 months before surgery,
- Implantation of an intra-aortic balloon pump prior to surgery,
- Chronic renal disease: defined as preoperative creatinine >2 mg/dl or need of renal replacement therapy,
- Peripheral arteriopathy with clinical symptoms of intermittent claudication in lower limbs, occlusion of over 50% in the carotid artery, amputation of any extremity due to arterial disease, prior surgery on the aorta or on lower limb arteries,
- Priority of the surgery: if the case was performed within the 24 h after the indication of surgery or later.

Definitions of outcomes

- In-hospital mortality included all deaths within 30 days of operation regardless where death occurred and all in-hospital deaths after 30 days among patients who had not been discharged after the index operation. The cause of death was recorded.
- Cardiovascular complications included myocardial infarction, atrio-ventricular block, new onset of atrial fibrillation and cardiogenic shock. A diagnosis of postoperative myocardial infarction was based on the presence of new Q waves, new wall motion abnormalities evidenced by echocardiography or coronary stenosis evidenced by coronary angiogram. Cardiogenic shock was defined as hypotension, cardiac index lower than 2.2 l/min or need of two or more inotropic drugs.
- Neurological complications included permanent or transient stroke, and episodes of delirium. Perioperative stroke was defined as any new temporary or permanent focal or global neurological deficit, in accordance with the published guidelines, within 30 days from operation or later than 30 days if still in hospital [11]. Temporary stroke included transient ischaemic attack, defined as fully reversible neurological deficit lasting less than 24 h and prolonged reversible ischaemic neurological deficits defined as events lasting more than 24 h and less than 3 weeks.
- Pulmonary complications included ventilation failure, reintubation, need of tracheotomy and pleural effusion requiring evacuation.
- Renal complications included acute renal failure, defined as the requirement of haemodialysis or an elevated creatinine level >2 mg/dl or an elevated creatinine level 50% or greater over the baseline preoperative value or >2 mg/dl.
- Infectious complications included pneumonia, septicaemia, sternal and leg wound infections, defined by positive culture and requiring antibiotic therapy.
- Composite end-point variable of morbidity was defined if any renal, pulmonary, cardiovascular and neurological complication occurred (as described earlier).
- A composite end-point variable of morbidity (renal, pulmonary, cardiovascular and neurological) and in-hospital mortality was included if any of those events defined above was present.
- Critical coronary artery disease was defined as a stenosis of greater than 50% of the lumen based on a preoperative coronary angiogram.
- Reintervention for bleeding.

Anaesthetic, surgical technique and postoperative management

Anaesthetic and surgical techniques were standardized for all patients. Patients undergoing ONCABG, CPB was instituted with the use of ascending aortic cannulation and a venous cannulation of the right atrium. CPB was carried out with non-pulsatile flow (in most cases), alpha-stat pH blood gas management, haematic cardioplegia with topical hypothermia, moderate systemic hypothermia (32–34°C) and pump flow rates to achieve a mean arterial pressure of 60–80 mmHg. The membrane oxygenator was primed with 1000 ml of crystalloid solution, 500 ml of Gelafundine® (B.Braun Melsungen AG, Melsugen, Germany), 250 ml of 20% mannitol and 5000 UI of heparin. Myocardial protection was achieved with intermittent hyperkalaemic antegrade and retrograde warm blood cardioplegia. For OPCABG, adjustable tissue stabilizer was used to expose the coronaries and provide stabilization that enhances visibility at the anastomotic site. During surgery heparin at 300 IU/kg for the ONCABG and 150 IU/kg for the OPCABG was administered. Activated clotting time was maintained over 480 s for ONCABG and over 300 s for OPCABG. The effect of heparin was reversed with protamine sulphate at a ratio of 1 : 1 after the distal anastomoses was finished in the OPCABG and after coming off-pump in ONCABG. In both techniques proximal anastomoses were performed with a partial occluding clamp in most patients. Postoperative management of all patients followed standard practice guidelines from surgery to discharge. This included admission to the intensive care unit (ICU) from the operating room, with subsequent transfer to a ward. In the ICU, patients were managed according to the unit protocol implementing fast-track extubation.

Statistical analysis

Continuous data were expressed as mean ± SD, and categorical data were expressed as percentages. The Kolmogorov–Smirnov test was used to check for normality of data in the two groups before further analysis. Differences between OPCABG and ONCABG were compared with a χ^2 statistical test for categorical variables and T or Wilcoxon rank sum tests, as appropriate.

A propensity score matching was performed to identify appropriate matched-pair of patients (1 : 1) between groups by building a binary logistic regression model with the main preoperative risk variables and comorbidities defined as above. We performed a one-to-one matched analysis without replacement on the basis of the estimated propensity score of each patient. Table 1 presents all baseline characteristics of covariates under consideration for models. After propensity score matching, a general linear regression model with the pairs as random effects was used to test for differences between treatment groups. The goodness of fit of the method was evaluated by Hosmer–Lemeshow test ($P = 0.31$). The discriminative power of the model was evaluated by a receiver operating characteristic curve, contrasting the probability of belonging to the group of OPCABG according to logistic regression against the real location of each patient in each group and resulted in an area under the curve of 0.75 [95% confidence interval (CI) 0.70–0.89].

Stepwise univariable and multivariable logistic regression analysis was performed to assess independent predictors of the 30-day morbidity composite end-point (renal, pulmonary, cardiovascular and neurological complications) and the morbimortality composite end-point (mortality at 30 days and morbidity). A significance level of 0.2 was used to enter in the multivariable logistic regression analysis. Results are reported as percentages and odds ratio and 95% CIs. Overall survival was estimated by using the Kaplan–Meier method and was expressed as percentage. P-values are two-sided for the overall population, a value of 0.05 was considered statistically significant. Statistical analyses were performed with SPSS statistical software (version 18; IBM, corporation, Armonk, NY, USA).

RESULTS

Baseline characteristics of CABG patients are reported in Table 1. A total of 1327 patients underwent OPCABG and 1770 underwent

Table 1: Preoperative characteristics of the cohort and propensity matched patients

Clinical variables	Cohort			Propensity matched patients		
	ONCABG group (n = 1770)	OPCABG group (n = 1327)	P-value	ONCABG group (n = 1004)	OPCABG group (n = 1004)	P-value
Age (years)	63.18 ± 9.64	66.95 ± 10.59	<0.001	65.09 ± 8.90	65.60 ± 9.68	0.220
Gender						
Male	81.1%	20.2%	0.37	796 (79.3%)	800 (79.7%)	0.825
Female	18.9%	79.8%		208 (20.7%)	204 (20.3%)	
EuroSCORE I	4.47 ± 4.34	5.2 ± 5.02	<0.001	4.86 ± 3.91	4.68 ± 3.94	0.308
Angina						
Stable	58.3%	54.7%	0.077	555 (55.3%)	588 (8.6%)	0.137
Unstable	41.7%	45.3%		449 (44.7%)	416 (41.4%)	
Preop IABP	0.1%	0.2%	0.4	1 (0.1%)	2 (0.2%)	0.096
Renal failure						
No dialysis	5%	5.7%	0.354	48 (4.8%)	54 (5.4%)	0.542
Dialysis	0.5%	0.8%	0.319	6 (0.6%)	7 (0.7%)	0.781
Extracardiac arteriopathy	12.3%	17.4%	<0.001	154 (15.3%)	138 (13.7%)	0.311
COPD	11.3%	13.8%	0.11	135 (13.4%)	129 (12.8%)	0.692
Diabetes	43.6%	41.8%	0.321	418 (41.6%)	426 (42.4%)	0.923
Hypercholesterolaemia	58.4%	57%	0.716	575 (57.3%)	582 (58%)	0.752
HTA	59%	66.4%	<0.001	644 (64.1%)	634 (63.1%)	0.643
Obesity	14.7%	14.8%	0.511	158 (15.7%)	152 (15.1%)	0.711
Smoking	55.6%	54%	0.677	518 (51.6%)	558 (55.6%)	0.199
Previous AMI	44.7%	35%	<0.001	378 (37.6%)	385 (38.3%)	0.912
Previous PCI	6.9%	9.5%	0.007	78 (7.8%)	80 (8%)	0.868
Thrombolysis	0.2%	0.2%	1	3 (0.3%)	1 (0.1%)	0.306
Type of surgery						
Elective	65.4%	64.7%	0.379	646 (64.3%)	670 (66.7%)	0.260
Urgent	34.6%	35.3%		358 (35.7%)	334 (33.3%)	

HTA: hypertension; AMI: acute myocardial ischaemia; PCI: interventional percutaneous revascularization; Preop IABP: preoperative intra-aortic balloon pump; OPCABG: off-pump coronary artery bypass graft; ONCABG: on-pump coronary artery bypass graft; COPD: chronic obstructive pulmonary disease.

ONCABG. Compared with the ONCABG group, patients in the OPCABG group were older and had a statistically significant higher prevalence of hypertension, peripheral artery disease, history of previous myocardial infarction and previous interventional percutaneous revascularization ($P < 0.05$).

Of the total CAGB procedures performed, 42.8% were carried out using OPCAB during the study period.

After propensity score analysis, 1004 pairs of patients were matched. In the matched cohorts, no significant differences between the two groups for any covariate were observed (Table 1). The average grafts performed was higher in the on-pump group, 3.50 ± 0.96 vs 2.87 ± 0.99 ($P < 0.001$). No significant differences in anterior territory revascularization (left anterior descending and diagonal arteries) were found, 98 vs 97.6% ($P = 0.54$) in ONCABG versus OPCABG, respectively. The lateral and postero-inferior wall were significantly less revascularized in the OPCABG versus ONCABG: 64.5 vs 79.2% ($P < 0.001$) and 60.6 vs 76.3% ($P < 0.001$), respectively. A statistically significant difference was found when we compared the number of grafts in the OPCABG group if surgery was performed during the initial 10 years of surgical experience versus the last 10 years (2.7 ± 1 vs 3.1 ± 0.9, respectively, $P < 0.001$).

There were no significant differences in mortality between groups, 2.8 vs 3.8% in OPCABG versus ONCABG, respectively ($P = 0.21$). Concerning clinical outcomes: cardiovascular 13.9 vs 8.7% ($P < 0.001$), neurological 3.9 vs 2.2% ($P = 0.03$), respiratory 13.5 vs 7.5% ($P < 0.001$) and renal complications 7.1 vs 5.3% ($P = 0.95$) were more frequent in the ONCABG group (Table 2).

ICU and hospital length of stay (LOS) were longer in the ONCABG group: 4.1 ± 2.6 vs 3.4 ± 2.3 days ($P < 0.001$) and 9.7 ± 5.8 vs 7.8 ± 4.1 days ($P < 0.001$), respectively.

Causes of mortality are reported in Table 3.

The mean follow-up period was 7.4 ± 4.3 years for OPCABG and 9.4 ± 4.2 years for ONCABG ($P < 0.001$). The long-term record for all-cause mortality was 12.3 vs 12.9% in the OPCABG versus ONCABG group, respectively ($P = 0.42$) (Fig. 1).

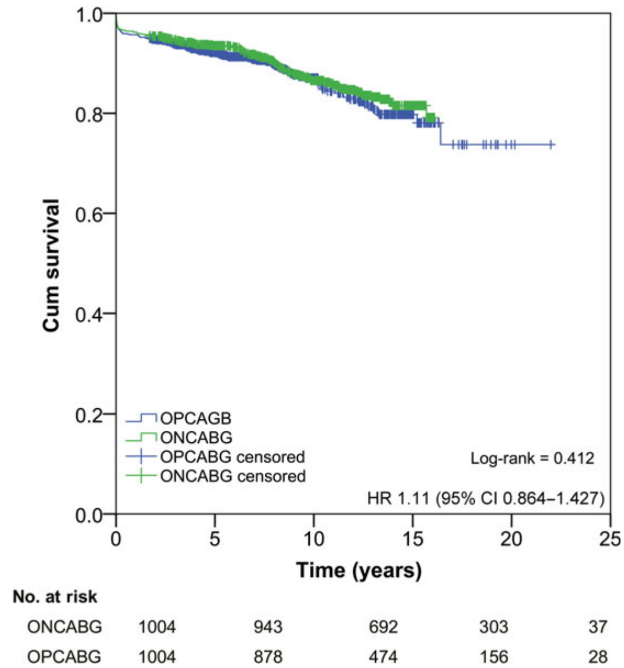

Figure 1: Cumulative survival. OPCABG: off-pump coronary artery bypass graft; ONCABG: on-pump coronary artery bypass graft; CI: confidence interval.

Table 2: Postoperative clinical outcomes in propensity matched patients

Clinical outcomes	Cohort			Propensity matched patients		
	ONCABG group (n = 1170)	OPCABG group (n = 1327)	P-value	ONCABG group (n = 1004)	OPCABG group (n = 1004)	P-value
Thirty day mortality	52 (2.9%)	61 (4.6%)	0.01	28 (2.8%)	38 (3.8%)	0.210
Haemodynamic complications	224 (12.7%)	122 (9.2%)	0.007	140 (13.9%)	87 (8.7%)	0.001
Heart failure	18 (1.53%)	14 (1.05%)		8 (0.8%)	9 (0.9%)	
Auriculo-ventricular block	5 (0.3%)	3 (0.2%)		4 (0.4%)	2 (0.2%)	
AMI				3 (0.3%)	4 (0.4%)	
Atrial fibrillation	188 (10.6%)	89 (6.7%)		124 (12.4%)	71 (7.1%)	
Cardiogenic shock	13 (1.1%)	15 (1.2%)		1 (0.1%)	1 (0.1%)	
Neurological complications	63 (3.6%)	31 (2.3%)	0.05	39 (3.9%)	22 (2.2%)	0.026
Stroke	14 (0.8%)	6 (0.5%)		8 (0.8%)	5 (0.5%)	
Transitory stroke	10 (0.6%)	3 (0.3%)		7 (0.7%)	2 (0.2%)	
Delirium	27 (1.6%)	9 (0.7%)		24 (2.4%)	15 (1.5%)	
Respiratory complications	250 (14.1%)	107 (8.1)	<0.001	136 (13.5%)	75 (7.4%)	<0.001
Atelectasis	28 (1.6%)	9 (0.7%)		17 (1.7%)	10 (1%)	
Pleural effusion	131 (7.4%)	47 (3.5%)		70 (7%)	34 (3.4%)	
Pneumothorax	28 (1.6%)	13 (1%)		15 (1.5%)	11 (1.1%)	
Respiratory failure	51 (4.3%)	28 (2.1%)		34 (3.4%)	20 (2%)	
Renal complications	116 (6.6%)	71 (5.4%)	0.16	71 (7.1%)	53 (5.3%)	0.09
Reintervention for bleeding	53 (3%)	43 (3.2%)	0.6	35 (3.5%)	23 (2.3%)	0.109
Infectious complications	65 (5.5%)	30 (2.2%)	0.02	48 (4.8%)	34 (3.4%)	0.09
Surgical wound	10 (0.9%)	10 (0.6%)		24 (2.4%)	20 (2%)	
Pneumonia	51 (4.3%)	16 (1.2%)		23 (2.3%)	12 (1.2%)	
Urinary	3 (0.2%)	2 (0.2%)		1 (0.1%)	1 (0.1%)	
Bacteraemia	1 (0.1%)	2 (0.2%)		0	1 (0.1%)	

ONCABG: on-pump coronary artery bypass graft; OPCABG: off-pump coronary artery bypass graft; AMI: acute myocardial ischaemia.

Table 3: Causes of 30-day mortality

Causes of mortality	ONCABG group (*n* = 1170)	OPCABG group (*n* = 1327)	ONCABG group (*n* = 1004)	OPCABG group (*n* = 1004)
Cardiovascular	19 (1.1%)	27 (2%)	13 (1.3%)	17 (1.7%)
Infectious	10 (0.8%)	11 (0.8%)	5 (0.5%)	8 (0.8%)
Neurological	4 (0.2%)	4 (0.3%)	3 (0.3%)	4 (0.4%)
Renal	7 (0.4%)	2 (0.2%)	3 (0.3%)	0 (0%)
Respiratory	12 (0.7%)	14 (1.1%)	4 (0.4%)	8 (0.8%)
Massive bleeding	0 (0%)	1 (0.1%)	0 (0%)	1 (0.1%)

ONCABG: on-pump coronary artery bypass graft; OPCABG: off-pump coronary artery bypass graft.

Table 4: Univariable analysis for morbidity composite outcome

Variable	Composite outcome morbidity		
	B	OR (95% CI)	*P*-value
EuroSCORE I	4.3	78.5 (1.65–3729.6)	0.02
COPD	0.43	1.55 (1.17–2.05)	0.002
Dyslipidaemia	−0.14	0.86 (0.70–1.05)	0.16
Peripheral vascular disease	0.23	1.26 (0.95–1.68)	0.09
Coronary percutaneous revascularization preop	−0.28	0.75 (0.50–1.12)	0.16
Chronic renal failure	0.92	3.12 (2.01–4.62)	0.0001
Dialysis preop	0.92	2.51 (0.84–7.52)	0.09
Carotid stenosis	1.52	4.57 (2.10–9.93)	0.001
Ejection fraction <45%	0.17	1.19 (1.06–1.34)	0.003
Redo	0.36	1.43 (0.82–2.50)	0.20
CPB	0.64	1.90 (1.54–2.33)	0.001

COPD: chronic obstructive pulmonary disease; CPB: cardiopulmonary bypass; preop: preoperatively; OR: odds ratio; 95% CI: 95% confidence interval.

Table 5: Univariable analysis for mortality and morbidity composite outcome

Variable	Mortality and morbidity composite outcome		
	B	OR (95% CI)	*P*-value
EuroSCORE I	4.14	63.1 (1.36–2909.92)	0.03
COPD	0.48	1.62 (1.23–2.17)	0.0001
Dyslipidaemia	−0.21	0.8 (0.66–0.98)	0.03
Peripheral vascular disease	0.23	1.26 (0.96–1.65)	0.87
Previous ACS	0.15	1.16 (0.95–1.42)	0.13
Chronic renal failure	1.14	3.12 (2.09–4.67)	0.0001
Dialysis preop	1.47	4.36 (1.42–13.40)	0.01
Carotid stenosis	1.41	4.27 (2.05–8.87)	0.0001
Ejection fraction <45%	0.20	1.23 (1.09–1.38)	0.001
Redo	0.51	1.67 (0.97–2.87)	0.06
CPB	0.58	1.79 (1.47–2.19)	0.0001

COPD: chronic obstructive pulmonary disease; CPB: cardiopulmonary bypass; ACS: acute coronary syndrome; Preop: preoperatively; OR: odds ratio; 95% CI: 95% confidence interval.

Table 6: Multivariable analysis for morbidity composite outcome

Variables	Mortality and morbidity composite outcome		
	B	OR (95% CI)	*P*-value
CBP	0.71	2.05 (1.64–2.55)	0.0001
COPD	0.41	1.51 (1.14–2.00)	0.004
Chronic renal failure	1.00	2.72 (1.52–4.88)	0.001
Ejection fraction <45%	0.17	1.18 (1.05–1.34)	0.005

COPD: chronic obstructive pulmonary disease; CPB: cardiopulmonary bypass; OR: odds ratio; 95% CI: 95% confidence interval.

Table 7: Multivariable analysis for mortality and morbidity composite outcome

Variables	Mortality and morbidity composite outcome		
	B	OR (95% CI)	*P*-value
CBP	0.684	1.982 (1.599–2.451)	<0.001
COPD	0.458	1.581 (1.200–2.451)	0.001
Chronic renal failure	0.938	2.555 (1.428–4.689)	0.002

COPD: chronic obstructive pulmonary disease; CPB: cardiopulmonary bypass; OR: odds ratio; 95% CI: 95% confidence interval.

In both uni- and multivariable analysis, preoperative renal failure [odds ratio (OR) 2.5 (1.4–4.68)] chronic obstructive pulmonary disease [OR 1.58 (1.2–2.4)] and ONCABG [OR 1.9 (1.5–2.4)] were independent predictors of morbidity and morbimortality composite end-points (Tables 4–7).

DISCUSSION

CABG can be performed with or without CPB. However, the preferable technique is unclear and the results are controversial.

Our study, based on a large cohort of patients, shows that OPCABG is a safe technique for patients with ischaemic heart disease and is associated with a non-inferior morbidity and mortality and shorter length of ICU and hospital stay. However, the number of grafts performed is higher in the ONCABG and the lateral and postero-inferior walls are significantly less revascularized in the OPCABG group. ONCABG was found to be an independent predictor of morbidity composite end-point and mortality and morbidity composite end-point.

Despite the continuous evolution, CPB has potential harm as a result of physiological processes and can result in tissue damage and organ dysfunction. As the interest for OPCABG has been gradually increasing, several concerns have been raised and authors are still trying to answer if OPCABG reduces hospital morbidity and mortality, if OPCABG has the same outcomes especially regarding security, long-term survival and quality of grafts and if it is possible to perform the full revascularization using OPCABG [12].

Murzi *et al.* [13] studied after propensity score matching 584 pairs of patients undergoing OPCABG and ONCABG. They observed lower in-hospital mortality (0.5 vs 2.9%, P= 0.01), lower incidence of stroke (0 vs 0.9%, P = 0.02), postoperative renal dysfunction (4.9 vs 10%, P = 0.001), pulmonary complications (10.2 vs 16.6%, P = 0.002) and fewer infectious complications (3.5 vs 6.2%, P = 0.03) in OPCABG compared with ONCABG. They also observed less atrial fibrillation (20.6 vs 26.8%, P = 0.01) and less inotropic support (38 vs 46.5%, P = 0.03) in the off-pump patients.

Liu *et al*. [14] in a recent propensity score analysis of 54 matched-pair patients demonstrated lower incidence of postoperative myocardial infarction and similar mortality and major complications in both groups. Our results are consistent with data reported [13, 14] and, in our propensity matched groups, we also observed less cardiovascular, neurological and pulmonary complications. We also demonstrated less infectious and renal complications, albeit without statistical significance probably due to sample size and low number of events. The haemodynamic instability that may occur while performing revascularization on a beating heart is proposed as the main reason for not using the OPCABG technique. As technology has evolved with new stabilization tools and the experience of the surgical team and haemodynamic management have been improved, this complication might have been reduced [15]. It may explain the reduced cardiovascular, pulmonary and neurological complications reported in our data after 20 years of experience. Consistent with our data, CPB has been reported to be an independent predictor of in-hospital mortality [13].

Furthermore, an randomized controlled trial (RCT) of patients over 75 years old randomized to ONCABG and OPCABG did not find any significant difference with respect to a composite outcome of death, stroke, myocardial infarction or new renal replacement therapy at 30 days and at 12 months. However, repeat revascularization occurred more frequently in the OPCABG [7]. Similarly, meta-analysis of RCT and observational studies did not find significant improvements in early mortality and morbidity in the off-pump group [16] and in a 1-year follow-up [17].

Although many studies showed that early mortality of OPCAB is comparable with the one obtained with the use of CPB, the results related to the medium and long term are even more controversial. By assessing the follow-up between 1 and 3 years of 401 patients who participated in two RCTs (BHACAS I and II) Angeli *et al.* [18] observed that survival free of cardiac events, including death, was similar in surgeries with and without CPB. A similar result was observed in the MASS III [10] study after 5 years of follow-up, with a trend towards greater survival in patients undergoing surgery without CPB, which reached significance in the fifth year of follow-up, but with no significant difference in the seventh year.

Some the most important concerns related to long-term outcome are the early graft patency and the quality of anastomoses in the beating heart with the off-pump technique. A recent meta-analysis by Moller *et al*. [5], which included 86 trials with a total of 10 716 participants, showed that OPCABG increased all-cause mortality compared with ONCABG (3.7 vs 3.1%, P = 0.04) and resulted in fewer distal anastomoses (MD −0.28; P < 0.0001). In addition, they did not demonstrate any significant benefit regarding myocardial infarction, stroke, renal insufficiency or coronary reintervention in the off-pump group. Similarly, Hattler *et al*. [19] and Takagi *et al*. [20] showed a significantly lower patency rate for grafts and less effective revascularization in the OPCABG group. At 1 year after surgery, patients with less revascularization had higher adverse event rates [19].

In our study, we did not observe significantly higher 30-day mortality in the OPCABG group but we found fewer distal anastomoses performed and an inferior revascularization rate in the inferior and posterior wall. However, we observed an increase in the mean number of grafts performed over the years, which also could explain our good global outcomes with the OPCABG technique. Indeed, our short- and long-term all-cause mortality was not different between groups despite the fact that the number of grafts initially was lower in OPCABG. It is noteworthy that revascularization of anterior territory was not different between groups.

In the latest meta-analysis by Takagi and Umemoto [21] which included 22 studies, the number of grafts per patient and the index of completeness of revascularization was significantly greater for the ONCABG group. Previously, Takagi *et al*. had demonstrated a statistically significant 37% reduction in follow-up mortality with complete revascularization compared with incomplete revascularization (heart rate, 0.63; 95% CI, 0.53–0.75; P < 0.00001) [3]. Furthermore, they demonstrated a statistically significant 7% increase in long-term (more than 5 years of follow-up) all-cause mortality with OPCABG. However, the pooled analysis of five randomized trials demonstrated a statistically non-significant 14% increase in mortality with OPCABG. In contrast, we had a mean follow-up of 7.4 years and we did not observe differences in all-cause mortality.

This finding of worse long-term survival after OPCABG relative to ONCABG might be strengthened by the results from another meta-analysis by Takagi *et al*. [3, 22] and Moller *et al*. [5].

Proponents of OPCAB have suggested that earlier studies which data have been included in the meta-analysis did not use modern stabilizers, heart-positioning devices or intracoronary shunts and the surgical and anaesthesiologist's experience was inadequate. In large randomized trials involving OPCABG surgeons who had at least 2 years of experience and who had performed at least 100 procedures, there was no difference in death, mortality or major adverse cardiac events between OPCABG and ONCABG surgery [6, 23].

In our hospital, an explanation for good outcomes might be due to the fact that OPCABG is a routine procedure, in which all professionals are consistently involved. Moreover, specific protocols for intraoperative anticoagulation therapy, postoperative antiplatelet therapy, perioperative anesthetic management and availability of immediate cardiopulmonary bypass if needed have been developed. Cardiac surgeons are experienced in OPCABG and outcomes have improved substantially from the beginning of OPCABG procedures to date.

Study limitations

This is a retrospective observational analysis of our institutional database and has the limitations of the available collected information and the bias inherent to a retrospective study. Although patient selection bias is sought to be solved with a propensity score matching, the fact that the decision to perform a procedure is based sometimes in the perceived high comorbidity for CPB might introduce bias difficult to be controlled in this study. However, some of our surgeons performed routinely all the procedures under OPCABG. The learning curve and its impact on selection bias have not been assessed in the study. The heterogeneous enrollment over time in both groups is also a limitation due to the fact that changes in standard of care could also have had an impact on our outcomes, which we could not correct for with propensity score matching.

We used the number of grafts to analyse revascularization but not the definition of complete revascularization specifically for every patient or any other completeness of revascularization index. This feature could have introduced a selection bias. Moreover, the trends towards more grafts over time in the OPCABG could have been a source of bias. The impact on morbidity and mortality is unclear although we do not observe differences over time.

Even though the multivariable logistic regression identified the use of CPB as an independent predictor of morbidity and morbimortality, we included major and non fatal cardiovascular, neurological, renal and pulmonary morbidity to increase sensitivity to the effect of CBP.

Our 30-days follow-up for complications and mortality is clearly a limitation due to the fact that any fatal event immediately after this period might have been related to the surgery and we could have missed this event.

Although long-term follow-up was achieved for all patients in our series and deaths were comprehensively recorded, we could not define the precise cause of death for every patient. Differences in cardiovascular death between groups could not be determined. Although no statistically significant differences were observed in long-term all-cause mortality between groups, differences in overall survival between both can still not be excluded.

We did not collect the data of the reconversion rate on an emergency basis, which has also been shown to increase morbidity and mortality.

We did not collect the postoperative bleeding and the transfusion rate data, which might have been proven to be predictors of worse outcomes and could be different in both techniques.

In conclusion, our study indicates that both coronary revascularization techniques are safe options and OPCABG. We could not show statistically significant differences in outcomes between both of them. However, OPCABG is associated with less postoperative morbimortality and shorter hospital and ICU LOS. OPCABG may be an alternative when there are contraindications for cannulation of the aorta or for CPB. Long-term follow-up showed no differences in all-cause mortality despite the reduced number of grafts performed in the OPCABG during the first years of study.

It would be important for cardiac surgical societies to develop guidelines for the practice of OPCAB and establish criteria for surgeon training, patient selection, institutional requirements, standardization of operative techniques and postoperative management to guarantee short- and long-term outcomes for OPCABG comparable with ONCAB, which remains the gold standard for coronary surgical revascularization.

Conflict of interest: none declared.

REFERENCES

[1] Kolh P, Windecker S, Alfonso F, Collet JP, Cremer J, Falk V *et al*. 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur J Cardiothorac Surg 2014;46:517–92.

[2] Warren OJ, Smith AJ, Alexiou C, Rogers PL, Jawad N, Vincent C *et al*. The inflammatory response to cardiopulmonary bypass: part 1—mechanisms of pathogenesis. J Cardiothorac Vasc Anesth 2009;23:223–31.

[3] Takagi H, Watanabe T, Mizuno Y, Kawai N, Umemoto T. A meta-analysis of adjusted risk estimates for survival from observational studies of complete versus incomplete revascularization in patients with multivessel disease undergoing coronary artery bypass grafting. Interact CardioVasc Thorac Surg 2014;18:679–82.

[4] Takagi H, Goto SN, Watanabe T, Mizuno Y, Kawai N, Umemoto T. A meta-analysis of adjusted hazard ratios from 20 observational studies of bilateral versus single internal thoracic artery coronary artery bypass grafting. J Thorac Cardiovasc Surg 2014;148:1282–90.

[5] Moller CH, Penninga L, Wetterslev J, Steinbruchel DA, Gluud C. Off-pump versus on-pump coronary artery bypass grafting for ischaemic heart disease. Cochrane Database Syst Rev 2012;3:CD007224.

[6] Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E *et al*. Effects of off-pump and on-pump coronary-artery bypass grafting at 1 year. N Engl J Med 2013;368:1179–88.

[7] Diegeler A, Borgermann J, Kappert U, Breuer M, Boning A, Ursulescu A *et al*. Off-pump versus on-pump coronary-artery bypass grafting in elderly patients. N Engl J Med 2013;368:1189–98.

[8] Sedrakyan A, Wu AW, Parashar A, Bass EB, Treasure T. Off-pump surgery is associated with reduced occurrence of stroke and other morbidity as compared with traditional coronary artery bypass grafting: a meta-analysis of systematically reviewed trials. Stroke 2006;37:2759–69.

[9] Keeling WB, Kilgo PD, Puskas JD, Halkos ME, Lattouf OM, Guyton RA *et al*. Off-pump coronary artery bypass grafting attenuates morbidity and mortality for patients with low and high body mass index. J Thorac Cardiovasc Surg 2013;146:1442–8.

[10] Hueb W, Lopes NH, Pereira AC, Hueb AC, Soares PR, Favarato D *et al*. Five-year follow-up of a randomized comparison between off-pump and on-pump stable multivessel coronary artery bypass grafting. The MASS III Trial. Circulation. 2010;122(11Suppl):S48–52.

[11] Edmunds LH Jr, Clark RE, Cohn LH, Grunkemeier GL, Miller DC, Weisel RD. Guidelines for reporting morbidity and mortality after cardiac valvular operations. Ad Hoc Liaison Committee for Standardizing Definitions of Prosthetic Heart Valve Morbidity of The American Association for Thoracic Surgery and The Society of Thoracic Surgeons. J Thorac Cardiovasc Surg 1996;112:708–11.

[12] Rodrigues AJBÉP, Alves Tubino PV. On-pump versus off-pump coronary artery bypass graft surgery. What do the evidences show? Rev Bras Cir Cardiovasc 2013;28:531–7.

[13] Murzi M, Caputo M, Aresu G, Duggan S, Miceli A, Glauber M *et al*. On-pump and off-pump coronary artery bypass grafting in patients with left main stem disease: a propensity score analysis. J Thorac Cardiovasc Surg 2012;143:1382–8.

[14] Liu P, Wang F, Ren S, Lin F, Yang Y, Fan X *et al*. A propensity score analysis on the effect of on-pump versus off-pump coronary artery bypass grafting for patients with coronary artery disease. J Thorac Dis 2014;6:838–44.

[15] Lazar HL. Should off-pump coronary artery bypass surgery be abandoned: a potential solution. J Thorac Cardiovasc Surg 2014;148:2475–6.

[16] Wijeysundera DN, Beattie WS, Djaiani G, Rao V, Borger MA, Karkouti K *et al*. Off-pump coronary artery surgery for reducing mortality and morbidity: meta-analysis of randomized and observational studies. J Am Coll Cardiol 2005;46:872–82.

[17] Feng ZZ, Shi J, Zhao XW, Xu ZF. Meta-analysis of on-pump and off-pump coronary arterial revascularization. Ann Thorac Surg 2009;87:757–65.

[18] Angelini GD, Taylor FC, Reeves BC, Ascione R. Early and midterm outcome after off-pump and on-pump surgery in Beating Heart Against Cardioplegic Arrest Studies (BHACAS 1 and 2): a pooled analysis of two randomised controlled trials. Lancet 2002;359:1194–9.

[19] Hattler B, Messenger JC, Shroyer AL, Collins JF, Haugen SJ, Garcia JA *et al*. Off-pump coronary artery bypass surgery is associated with worse arterial and saphenous vein graft patency and less effective revascularization: results from the Veterans Affairs Randomized On/Off Bypass (ROOBY) trial. Circulation 2012;125:2827–35.

[20] Takagi H, Matsui M, Umemoto T. Off-pump coronary artery bypass may increase late mortality: a meta-analysis of randomized trials. Ann Thorac Surg 2010;89:1881–8.

[21] Takagi H, Umemoto T. Worse long-term survival after off-pump than on-pump coronary artery bypass grafting. J Thorac Cardiovasc Surg 2014; 148:1820–9.

[22] Takagi H, Mizuno Y, Niwa M, Goto SN, Umemoto T. A meta-analysis of randomized trials for repeat revascularization following off-pump versus on-pump coronary artery bypass grafting. Interact CardioVasc Thorac Surg 2013;17:878–80.

[23] Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E *et al*. Off-pump or on-pump coronary-artery bypass grafting at 30 days. N Engl J Med 2012;366:1489–97.