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Comparison of on pump and off pump coronary surgery: risk factors for neurological outcome

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Abstract

Objective: Cerebrovascular accidents (CVA) are devastating complications after coronary artery bypass grafting (CABG). The reported incidence of neurological complications after conventional CABG (CCABG) is 3–6%. Off-pump coronary bypass grafting (OPCAB) has been associated in recent studies to a decreased morbidity and risk of perioperative stroke. Nevertheless, uncertainty still surrounds the relative benefits of OPCAB. We investigated whether, in our experience, OPCAB was associated with lower neurological morbidity than conventional CABG approach. **Methods:** Eight thousand and two patients underwent isolated CABG at our institution between January 1998 and January 2005. OPCAB operation was performed on 1415 patients. Data were prospectively collected. A multiple logistic regression analysis was used to evaluate the influence of the two different surgical techniques on the neurological outcomes. **Results:** Patients in the OPCAB group were significantly older (66.2 vs 63.5%, $p < 0.0001$), had a higher incidence of renal injury (5.4 vs 2.4%, $p < 0.0001$), and were more redo interventions (6.95 vs 1.53%, $p < 0.0001$). The CCABG patients were more urgent at operation (5.46 vs 3.26, $p = 0.0007$), were less hypertensive (57.6 vs 63% of the patients, $p = 0.0003$) more diabetics (22 vs 20.6%, NS), and had an ejection fraction less than 0.40 (10.4 vs 9.6%, NS). CVA incidence was similar in both groups (Type I outcome: OPCAB = 0.70% vs CCABG = 0.68%, $p = 0.91$; Type II outcome OPCAB = 0.70% vs CCABG = 0.83%, $p = 0.63$). **Conclusions:** In our experience patients undergoing CCABG were not exposed to a grater risk of neurological adverse events when compared to OPCAB patients.

Keywords: Off pump cardiac surgery; Cerebrovascular accidents; Neurological outcomes; Cardiopulmonary bypass

1. Introduction

Patients who undergo myocardial revascularization procedures are still exposed to the risk of major complications despite recent advances in cardiac surgical techniques. Stroke plays a major role as a complication of coronary artery bypass graft surgery. In the 1960s stroke was a common adverse event after coronary artery bypass grafting (CABG) with a rate of 9% [1]. Cerebral morbidity after CABG has largely been attributed to the use of cardiopulmonary bypass (CPB) [2]. Despite the improvement in surgical techniques and cardioplegic agents, along with the introduction of membrane oxigenators and in-line filtration, there is a persistent rate of major neurological sequelae after CABG, ranging from 0.8 to 5.2% [3–5]. Moreover, the incidence of minor neurological sequelae, such as postoperative cognitive decline, may still exceed 60% [3,6,7]. In these last years the attempts to demonstrate a cerebroprotective effect of beating heart coronary revascularization versus CPB showed inconsistent and often conflicting results [8]. Off-pump coronary bypass grafting (OPCAB) was introduced into our institute in 1997. We reviewed our database with the aim to identify the differences in the incidence of neurological complications after OPCAB and conventional CABG (CCABG) procedures.

2. Materials and methods

After IRB approval, a review of prospectively collected data entered into our computerized database identified a total of 8002 consecutive patients who had undergone isolated CABG between January 1998 and January 2005. Six thousand five hundred eighty-seven CABG were performed with CPB and 1415 CABG were performed without CPB. Patients were excluded from this study when undergoing concomitant CABG and other surgical procedures (valve replacement, ventricular aneurysm repair, carotid thromboendoarterectomy, etc.). Demographic, medical and perioperative variables were retrieved from the database. Data were collected of the following variables: age, gender, urgency of operation, prior cardiac operation, number of

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grafts performed, respiratory disease, diabetes, cerebrovascular disease, renal disease, degree of left ventricular ejection fraction. All the procedures were performed by the same group of cardiac surgeons who completed their 'learning curve' all along the study period and were considered all skilled and equally experienced in the technique of off-pump surgery. No strict criteria were followed to operate the patients with or without CPB, but the decision was up only to the attending surgeon. He freely decided if operate the patient off pump or on pump on the basis of his confidence with the technique, the coronary anatomy and the atherosclerotic aortic involvement. Preoperative transesophageal echocardiography of ascending aorta and intraoperative and gentle aortic palpation contributed in making the decision. No routine intraoperative epicardial scanning was performed. Postoperative neurological injury was the main considered outcome of this study.

Anaesthesia was induced by the administration of fentanyl, sodium thiopental and maintained with sufentanyl and propofol. Muscle relaxation was accomplished by the administration of pancuronium (0.1 mg/kg) or vecuronium (0.1 mg/kg). At the end of the procedures, all patients were transferred to the intensive care unit.

Non pulsatile cardiopulmonary bypass was conducted in standard fashion using a membrane oxygenator (Affinity, Medtronic) with mild hypothermia (32—34 °C). A standard adult extracorporeal tubing set was used incorporating a 40 μm arterial catheter filter. The flow rate was maintained at approximately 2.0 l/min/m^2, with a mean arterial pressure of 55—65 mmHg and a haemodilution to maintain a haematocrit of at least 22% during CPB. Myocardial protection was achieved by means of intermittent antegrade and retrograde cold blood cardioplegia. Proximal saphenous veingraft (SVG) anastomoses were performed using a partial side clamp technique.

During OPCAB, distal anastomoses were performed with the use of stabilizing retractors and coronary shunts. In the most recent years, a stabilizing suction device was used to simplify the exposition especially of the lateral and inferior wall (Octopus System, Medtronic, Minneapolis, MN).

Proximal anastomoses were performed using a partial occlusion clamp.

2.1. Definitions

Preoperative renal insufficiency was defined as a serum creatinine $\geq$ 2.26 mg/dL. This value, corresponding to 200 μmoles/L, is reported by the 'European System for cardiac operative risk evaluation' (EuroSCORE) as the cut off for renal insufficiency [9]. Pulmonary disease was defined as a documented obstructive pulmonary disease on therapy. The Tuman score is the score used to establish the mortality risk profile for cardiac surgical patients and was applied in our institution till 2001 [10]. With the development of the EuroSCORE, the European System for Cardiac Operative Risk Evaluation in 1999 [9], we started to use it since 2002. Then we stratified all the patients of our database in three levels of risk of mortality: high — medium — low risk, according to their respective scores, as illustrated in Table 1. The classification of neurological outcomes was made in two categories, according to Roach criteria [3]: Type I outcome was defined as postoperative fatal or non-fatal stroke, transient ischemic attack (TIA), or stupor or coma that persisted more than 72 h after surgery. Type II outcome was defined as a new deterioration in intellectual function, confusion, agitation, disorientation, memory deficit or seizure without evidence of focal injury. Anaesthesiologist and neurologist medical staff made the diagnosis of neurological deficits. In patients with a previous history of stroke, a new cerebrovascular event was diagnosed if new neurological findings or prolonged worsening of their pre-existing neurological deficits were observed.

Table 1
Preoperative risk profile

Low risk patients	⇨	EuroSCORE 1—4	Tuman score 1—5
Medium risk patients	⇨	EuroSCORE 5—8	Tuman score 6—9
High risk patients	⇨	EuroSCORE $\geq$ 9	Tuman score $\geq$ 10

2.2. Statistical analysis

Continuous variables are expressed as mean ± standard deviation and categorical variables are shown as a percentage. Comparisons were made with the Student's *t*-test for the continuous variables and with the χ^2 or the Fisher's exact test for the categorical variables. The variables considered are listed in Appendix A. Our study was not a randomised prospective clinical trial, but a retrospective observational study, therefore many important differences potentially affecting the neurological outcome are expected in patients undergoing the two surgical procedures. All the factors that differed significantly between on- and off-pump patients were then included in a multivariate logistic regression model, in order to compute adjusted odds ratios (OR) and 95% confidence intervals.

A p value less than 0.05 was considered statistically significant. All statistical analysis was performed with SAS statistical package (North Carolina statistical software).

3. Results

3.1. Patients characteristics

One thousand four hundred fifteen patients (18%) underwent off-pump CABG and 6587 patients (82%) underwent on-pump CABG between January 1998 and January 2005. Till 2001 OPCAB was performed on 897 patients (15% of the patients). In the last period (2002—2004) the percentage of OPCAB patients remarkably increased (25% of the patients), maybe due to the major confidence of the attending surgeons with this technique.

The two groups of patients were similar with respect to the percentage of patients at low and medium risk score, the frequency of history of diabetes and the similar ejection fraction (Table 2). No significant differences were noted between the two groups with regard to the duration of surgery, postoperative ventilation, bleeding and ICU stay (Table 3).

OPCAB patients were more likely to be older than CCABG patients (21.08 vs 9.28% over 75 years, $p < 0.0001$), were

Table 2
Univariate comparisons between patient characteristics based on procedure performed

	OPCAB (n = 1415)	On-pump CABG (n = 6587)	p Value
Age at operation (years)	66.2 ± 9.4	63.5 ± 8.9	<0.0001
Percent of patients ≥ 75 years	21.08	9.28	<0.0001
Female sex (%)	19.5	17.1	0.03
Weight (kg)	74.3 ± 12.2	74.7 ± 11.7	0.25
1st period of operations[a], (no. of patients), (% of patients of 1st period)	897 (15.%)	5076 (85%)	<0.0001
Second period of operations[b], (no. of patients), (% of patients of 2nd period)	518 (25.2%)	1511 (75%)	<0.0001
Prior cardiac surgery (%)	6.95	1.53	<0.0001
Emergent procedure (%)	3.26	5.46	0.0007
Low preoperative risk (%)	73.2	67.7	0.071
Medium preoperative risk (%)	23.3	22.7	0.067
High preoperative risk (%)	3.33	8.49	<0.0001
Hypertension (%)	62.9	57.6	0.0003
Diabetes (%)	20.6	22	0.24
COPD (%)	11.1	9	0.0134
Renal failure[c] (%)	5.4	2.4	<0.0001
Prior cerebrovascular disease (%)	8.02	6.34	0.0215
Previous MI (%)	49.3	53.8	0.0023
Ejection fraction (mean ± SD)	56.9 ± 10.8	56.3 ± 11.2	0.096
Ejection fraction ≤ 40% (% of patients)	9.61	10.44	0.37

Continuous variables are shown as mean ± standard deviation. Categorical variables are shown as a percentage. CABG: coronary artery bypass grafting. OPCAB: off-pump cardiopulmonary bypass. COPD: chronic obstructive pulmonary disease.
[a] January 1998–December 2001.
[b] January 2002–January 2005.
[c] Preoperative creatininemia > 2.2 mg/dl.

more COPD cases, have more preoperative cerebrovascular diseases and have a higher incidence of renal dysfunction (5.4 vs 2.4%, $p < 0.0001$) (Table 2). A total of 6.95 percent of the OPCAB patients had undergone prior cardiac procedures compared to 1.53% of the CCABG patients ($p < 0.0001$). The most frequent preoperative disease was hypertension: 4683 patients were hypertensive (59% of all the patients). One thousand seven hundred thirty-nine patients had diabetes, with 650 (52%) on oral medications, 320 (25%) diet-controlled, and (23%) insulin-dependent. The high-risk patients had undergone more frequently on pump surgery (Table 2). The CCABG patients were more likely to have diabetes (22 vs 20.6%) and a depressed ejection function (10.4 vs 9.6% of the patients) but the differences were not significant.

3.2. Neurological outcome

Adverse cerebral outcomes occurred in 173 patients (2.16 percent). Type I outcome occurred in 1.34% of the patients: 3 died of cerebral injury, 69 had non-fatal strokes, and 36 had TIAs. Type II outcome occurred in 0.82 percent of the patients: 50 had deterioration of intellectual function at discharge and 15 had seizures. CVA incidence was similar in both groups (Type I outcome: OPCAB = 1.4 vs CCABG = 1.54%, p = 0.91; Type II outcome OPCAB = 0.70 vs CCABG = 0.83%, p = 0.63) (Table 3). The multiple logistic regression analysis failed as well to demonstrate a significant benefit of the off-pump compared to the on-pump procedure for both the two outcomes when all the cohort of patients was considered (type I outcome: on pump versus off pump OR = 1.014, p = 0.9641; type II outcome: OR = 1.247, p = 0.5607). The multivariate analysis showed that male gender, high risk score and renal failure increased the risk for type I outcome (Table 4) while only preoperative MI increased the risk for type II outcome (Table 5). Remarkably, the neurological outcome did not significantly change throughout the study period nevertheless the improved surgical practice (Tables 4 and 5).

4. Discussion

Stroke is a serious devastating complication after coronary surgery and deeply modifies the short and long-term prognosis of cardiac surgery. The mechanisms that contribute to poor neurological outcome have been well documented. Cerebral embolization with macro- and micro emboli has been shown to be the most commonly, CPB related, involved mechanism [11].

Table 3
Univariate comparisons of operative and postoperative patient characteristics between OPCAB and on-pump CABG

	OPCAB (n = 1415)	On-pump CABG (n = 6587)	p Value
No. of grafts performed	1.7 ± 0.9	3.05 ± 0.8	0.0001
Duration of surgery (hours)	5.08 ± 1.2	5.06 ± 1.8	0.83
Postoperative ventilation (hours)	14.7 ± 16.4	14.8 ± 26.01	0.95
Bleeding (ml/24 h)	758.9 ± 568.3	762.1 ± 524.7	0.88
ICU stay (days)	2.43 ± 2.7	2.44 ± 2.9	0.96
Type I (no. of patients)	20 (1.4%)	88 (1.54%)	0.91
Type II (no. of patients)	10 (0.70%)	55 (0.83%)	0.63

Continuous variables are shown as mean ± standard deviation. Categorical variables are shown as a percentage.

Table 4
Multiple logistic regression testing preoperative risk factors for neurologic outcome Type I

Preoperative risk factors	Odds ratio	95% Confidence intervals	*p* Value
On-pump CABG versus OPCAB	1.014	0.55–1.86	0.9641
Age	1.013	0.98–1.04	0.4188
Weight	0.976	0.95–0.99	0.0427
Male gender (vs female)	2.340	1.08–5.05	0.0306
Period (II[a] vs I[b])	0.659	0.37–1.17	0.1552
Prior cardiac surgery	1.312	0.39–4.31	0.6546
Emergent procedure	0.913	0.27–3.02	0.8822
Medium versus low risk score	1.603	0.88–2.89	0.1176
High versus low risk score	2.220	1.04–4.71	0.0379
Hypertension	1.471	0.86–2.49	0.1510
Diabetes	0.954	0.53–1.71	0.8743
COPD	1.539	0.74–3.17	0.2437
Renal failure	3.093	1.39–6.83	0.0053
Prior cerebrovascular disease	1.063	0.45–2.49	0.8893
Previous MI	1.164	0.68–1.97	0.5735
Ejection fraction $\leq$ 40%	1.119	0.55–2.27	0.755

[a] January 2002–January 2005.
[b] January 1998–December 2001.

Atherosclerotic disease of the ascending aorta has been thought to contribute significantly to the release of emboli during aortic manipulation and clamp application during CABG [12]. Air/fat embolism, haemodynamic fluctuation, cerebral hyperthermia, and systemic inflammatory reaction are other physiologic derangements elicited by CPB contributing to neurological damage as well [3,13]. A lot of studies investigated CVA determinants in large cohort of patients to identify the variables that have a clinical influence towards stroke rate. The presence of an atherosclerotic ascending aorta has been reported as the most significant marker for adverse cerebral events [13]. Among the other preoperative variables, advanced age, hypertension, carotid disease, previous stroke, depressed left ventricular ejection fraction (<40%), diabetes mellitus, preoperative surgery, and chronic renal failure are all identified as independent determinants for stroke [4,14,15]. The length of CPB (CPB time longer than 2 h) [4,14,15], the need for intraoperative haemofiltration, high transfusion requirements, perioperative intra aortic balloon pump (IAPB), postoperative arrhythmia and atrial fibrillation [14] seem to be the intra and postoperative independent determinants for stroke. The off pump surgery shows in several recent studies a trend to a better outcome in terms of mortality, myocardial infarction and stroke [4,12,14,16–18]. Avoidance of CPB reduces systemic inflammatory response and eliminates the risk of atheroma dislodgement following ascending aortic cannulation and aortic cross clamping. However, the risks associated with partial aortic side clamping persist in OPCAB surgery [12]. Furthermore, haemodynamic fluctuations that may present during cardiac manipulations could determine temporary brain hypoperfusion especially in patients with associated cerebrovascular disease. The real benefits of off-pump surgery compared to on pump surgery are still uncertain. The randomized prospective trials are few and not always show significant advantages from on-pump surgery [19,20]. Meta-analysis of the observational [21] or prospective [22] studies were also performed but they did not show definite results as well. A few studies showed no statistical differences in terms of in-hospital and 30-day outcomes, but OPCAB achieved shorter length of stay, reduced transfusion requirements, less myocardial injury [19] while other authors documented a reduction in postoperative patency of the grafts performed during OPCAB procedures [18].

Our analysis aimed at determining the impact of the surgical choice – on-pump and off-pump surgery – on neurological outcome. Our data are in agreement with findings in few reports as that one of Karthik et al. [23] and Hernandez et al. [24]. Those studies were unable to demonstrate a protective effect of OPCAB surgery in neurological outcome. Also the only prospective randomized controlled trial large enough to have statistical power, Van Dijk et al, did not detect any significant difference in postoperative stroke [25]. On the other hand Bucerius et al. [14] reported that OPCAB surgery was the only variable associated with a lower incidence of neurological impairment. He did not find older age as independent factor of stroke and he explained the lower incidence of stroke in the OPCAB group by avoidance of aortic cannulation and subsequent decreased risk of embolization. Our multivariate analysis showed older age not associated to an increase of neurological risk as well. Off pump surgery in our series of patients failed to show a better neurological outcome when compared to conventional technique, and this may be explained because our off pump surgical technique did not remove the need for aortic manipulation and OPCAB were always done with side clamping of aorta for proximal anastomosis. Surprisingly in our analysis male gender resulted as a risk factor for worse neurological outcome, and this has not been reported by any author as far as we know. Our analysis revealed that high preoperative risk values and especially preoperative renal impairment were the strongest correlating factors for neurological complications (OR = 2.2 and OR = 3.09 respectively). Interestingly no factors were associated to a major risk for neurological outcome type II except for previous MI. This is a retrospective non-randomised study and has therefore several limitations. First of all a selection bias due to aortic atherosclerosis cannot be excluded, since the coronary anatomy and ascending atherosclerosis influenced the surgeons' choice for OPCAB or on pump surgery. Moreover the patients' characteristics differed in some important points and this could have influenced the results even though a multi-

Table 5
Multiple logistic regression analysis of preoperative risk factors for neurologic outcome Type II

Preoperative risk factors	Odds ratio	95% Confidence intervals	*p* Value
On-pump CABG versus OPCAB	1.247	0.59–2.62	0.5607
Age	1.033	0.99–1.07	0.0724
Weight	0.981	0.95–1.00	0.1586
Male gender (vs female)	1.626	0.67–3.90	0.2776
Period (II[a] vs I[b])	0.909	0.48–1.69	0.7638
Prior cardiac surgery	<0.001	<0.001–>999.99	0.9797
Emergent procedure	0.937	0.21–4.04	0.9310
EuroSCORE	0.917	0.57–1.45	0.7136
Hypertension	0.735	0.41–1.30	0.2904
Diabetes	1.467	0.79–2.72	0.2249
COPD	0.347	0.08–1.44	0.1460
Renal failure	1.556	0.46–5.23	0.4749
Prior cerebrovascular disease	1.115	0.39–3.15	0.8367
Previous MI	1.932	1.10–3.66	0.0438
Ejection fraction $\leq$ 40%	0.996	0.97–1.02	0.7563

[a] January 2002–January 2005.
[b] January 1998–December 2001.

variate analysis has been utilized to point out the risk factors for a worse neurological outcome. On the other hand it is very difficult to conduct prospective randomised trials in this field because the neurological outcomes have a low incidence in the average patient population, and consequently a great number of patients should be enrolled to reach a statistical power. Secondly, no screening neuropsychological tests were performed before or after surgery to evaluate cognitive impairment and the diagnosis of postoperative type II outcome was based only on the neurological clinical evidence. Finally, given that our database is limited to in-hospital data, the long term implications of neurological adverse events after hospital discharge remain unknown.

Nevertheless this study takes into account a great number of patients and has the important characteristic of all the retrospective studies to represent the clinical daily life. After 7 years of beating heart surgery we wanted to evaluate if this surgical technique truly apported some benefits to our practice, especially on neurological outcome, compared to the traditional on-pump surgery. Our results suggest that patients with coronary artery disease can be operated on either on-pump or off-pump with the same neurological morbidity.

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Appendix A

List of patient variables considered in analyses

Age	Continuous (years)
Age $\geq$ 75-years old	Dichotomous
Female gender	Dichotomous
Renal failure	Creatinine value $\geq$ 2.2 mg/dl
Chronic obstructive	Forced expiratory volume in 1 s
Pulmonary disease	(FEV_1), 75% of predicted value, air PO_2 Lower than 60 mmHg or chronic medical treatment
Diabetes	Medical treatment for hyperglycaemia at rest
Previous cardiac	Previous coronary or valve operation surgery
Previous CVA	History of previous cerebrovascular accident With or without persistent neurological defect
Urgency	Any condition that requires immediate surgery
Ejection fraction (EF)	Continuous
Ejection fraction $\leq$ 40%	Dichotomous
EuroSCORE and Tuman score	Systems of cardiac operating risk evaluation