

# Neurological Complications of On-Pump versus Off-Pump Coronary Artery Bypass Graft Surgery

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**Running Title:** Neurological Complications of On-Pump versus Off-Pump CABG

**Abstract:** **Background:** Neurological complications following cardiac surgery are serious, debilitating and, sometimes, life-threatening. **Objective:** Assessment of neurological complications following on and off pump coronary artery bypass graft surgery. **Methods:** We evaluated 441 consecutive patients undergoing cardiac surgery at the Service of Cardiac Surgery at the American Hospital from January 2012 October 2016. Patients were intervened following two different procedures: on-pump by pass (ONCABG) surgery or off-pump bypass surgery (OPCABG). The recorded and analyzed data were as following: preoperative status, including age, sex and comorbidities; intraoperative factors, including surgery type and time of surgery, duration of cardiopulmonary bypass, duration of aortic cross clamping, hypothermia, need for blood transfusions; and post operative outcomes, including neurological complications, type and time of neurological complications, period of intensive care unit treatment. **Results:** Of all 441 patients, 338 underwent OPCABG and 103 underwent ONCABG surgery. There were no significant differences between the groups in terms of age, gender and stroke risk factors. Nevertheless the patients undergoing ONCABG surgery presents a significantly higher prevalence of arrhythmia and prior stroke history. Moreover, more patients of the ONCABG group were treated in emergency conditions. As a result, the off-pump technique presented better neurological outcomes in terms of less stroke complications (4.4% vs. 14.6%,  $p<0.001$ ), less encephalopathic complications (4.1% vs. 14.6%,  $p<0.001$ ), less seizure complications (2.1% vs. 7.8%,  $p=0.045$ ) and lower in-hospital mortality (1.8% vs. 6.8%,  $p=0.008$ ). **Conclusion:** In our observational study, the off-pump CABG surgery was associated with lower neurological complications compared to the on-pump CABG surgery.

**Keywords:** On-pump coronary bypass grafting (ONCABG); off-pump coronary bypass grafting (OPCABG); stroke; encephalopathy; in-hospital mortality.

## 1. Introduction

Coronary artery bypass grafting (CABG) is one of the most common surgeries performed by the cardiac surgeons. Cardiac surgery became more feasible in the late 1930s with the development of the heart-lung machine by Dr. John Gibbon which enabled cardiopulmonary bypass (CPB) (1)

In 1950, at McGill University in Montreal, QC, Canada, Vineburg and Buller were the first to implant the internal mammary artery (IMA) into the myocardium to treat cardiac ischemia and angina (2)

Benetti, Calafiore, and Subramian in 1973 completed anastomoses on a beating heart. (3)

The principle of the CABG is to re-establish perfusion to the myocardium and there are different approaches to accomplish that. The first factor considered is the utilization of cardiopulmonary bypass (CPB) or on pump surgery and the second is without CPB, off pump.

With the development of cardiopulmonary bypass and cardioplegia, most CABG was performed on pump. However, interest in off-pump coronary artery bypass (OPCAB) surgery had resurgence in the 1990s. Benneti et al and Buffallo et al published their results of nearly 2000 OPCAB patients showing operative safety (4) (5)

Standard CABG employs a midline incision through the sternum, placement of the patient on coronary bypass, arrest of the heart with cardioplegia. Off pump CABG is without use of the cardiopulmonary bypass. This procedure is called "beating heart surgery" and take consideration because is meant to avoid morbidity and mortality associated with cardiopulmonary bypass (systemic inflammatory response, cross clamping of the aorta). This technique is chosen for the patients with contraindications for conventional CABG, as those with extensive ascending aortic atheromatosis and aortic calcifications. Comparison between these two revascularization techniques is still hot point of debate for outcomes regarding morbidity, complication, and graft patency. OPCABG is performed at 15-20% of all CABG in

the developed world, but in the developing world and Far East is performed over 80% of cases.

The incidence of postoperative CVA after CABG ranges from 1.4% to 3.8% (6), hypo perfusion (7) and female sex (8)

## 2. Methods

This study is a prospective control analytic study that was conducted in order to assess the neurological complications between on and off pump coronary artery bypass grafting (CABG) techniques. The study was conducted at the American Hospital Tirana from January 2012 to October 2016. Patients were intervened following two different procedures: on-pump by pass (ONCABG) surgery or off-pump bypass surgery (OPCABG).

All patients included in the study were subjected to full demographical and medical history (age, sex, comorbidities, previous TIA, CVA, previous myocardial infarction or PCI), routine laboratory investigations, imaging study before surgery that includes carotid duplex and arterial duplex on both limbs for arterial graft.

Also are prescribed variable related to the procedure (on or off pump, emergent or elective surgery, time of cross clamping of the aorta, time of cardiopulmonary bypass, circulatory arrest, need for blood transfusions).

Exclusion criteria were cases of mixed surgeries, as for example CABG and valve surgery or CABG and carotid endarterectomy.

Surgical technique and procedure:

**On pump surgery.** All operations were performed through a median sternotomy. Standard techniques of CPB were used. Both antegrade and retrograde blood cardioplegia cannulas were placed. The aorta was cross-clamped; Full heparinization was used. The distal anastomoses were first performed, followed by the proximal anastomoses. Heparin was reversed following weaning from the CPB. The LIMA to LAD graft was used, where possible.

**Off pump surgery:** All operations were performed through a median sternotomy. The order of grafting was the LIMA to LAD, followed by other vessel conduits. The Octopus tissue stabilizer (Medtronic, Octopus Tissue Stabilizer) was used to stabilize the beating heart to perform distal anastomoses. Coronary shunts were used to maintain target vessel haemostasis.

### Anaesthetic procedure:

Non-pulsatile CBP at the flow rate 2.0-2.4 L/min/m<sup>2</sup> was established using a roller pump (Sarns 8000) the mean arterial pressure 65-90mm Hg. Preservation of the myocardium is realized with antegrade cardioplegia with cold crystalloids (4°C). Cardioplegia is repeated every 30 minutes during the cross clamping. After the cardiopulmonary bypass all the blood was gathered and retransfused if is well tolerated by the patient. The procedure

is realized at mild hypothermia 32-34°C. Off pump procedure is realized at normothermia.

After a systematic neurological examination, stroke was defined as a motor-sensory deficit localized to a focal region of the brain, with or without a decreased levels of consciousness, and encephalopathy as a decrease or fluctuations in the level of consciousness, with cognitive deterioration, in the absence of focal motor deficits, after recovery from anaesthesia. (These definitions are adaptations of those accepted by the Society of Thoracic Surgeons.) (9).

### Neurological complication diagnosis:

Diagnosis of CVA firstly is made by surgery team then after confirmed by the neurologist based on the clinical evaluating and imaging. Patient with neurological symptoms underwent at the brain imaging.

### Brain imaging:

Non-contrast Cranial CT (Siemens sensation 64 detectors) or MRI (Siemens Avanto I-st Class). MRI was also performed (using DWI, GRE, T1-weighted, T2-weighted and FLAIR sequences) in the patients in whom CT revealed nothing abnormal. All the neuroimaging studies were analyzed by an expert neuroradiologist. Ischemic lesions were diagnosed considering the mechanism (atherotrombotic, cardioembolic, hypoperfusion/hypoxia) and taking into account the cerebral vascular territory. Seizures are described by typology.

The patients that had previous TIA or CVA are evaluated by the neurologist before the surgery and after the surgery. For patients with postoperative CVA were prescribe time of stroke. For patients with neurological complication are evaluated for the days spend at stupor and coma and was used CGS (Glasgow coma scale). Was prescribed time in the ICU, hospital history, mortality. Death from stroke included those patients where death was determined to be the direct result of the stroke or from stroke-related complications. This included sepsis with subsequent respiratory failure due to aspiration, hemodynamic collapse due to pulmonary embolism, brain death due to cerebral edema or herniation.

## 3. Results

A total of 441 patients were enrolled in our study, of which 338 underwent off-pump CABG surgery and 103 underwent on-pump CABG surgery. Demographics and baseline data, including differences between patients undergoing off-pump or on-pump CABG surgery, are outlined in Table 1. In brief, there was no significant difference between groups in terms of age, gender, body mass index, and prevalence of diabetes, hypertension, dyslipidemia, kidney failure, smoking and drinking, positive history for myocardial infarction or transient ischemic attack. Nevertheless, patients undergoing off-pump procedures had a lower prevalence of arrhythmia (13.0% vs. 26.2%,  $p$  0.001) and lower positive history of prior stroke (0.9% vs. 3.9%,  $p$  0.033). Importantly, the off-pump technique was employed less in emergency surgery, with only 15.1% of the off-pump cases being emergent interventions, while 36.9% of the on-pump cases were emergent intervention,  $p$  <0.001.

**Table 1:** Baseline Data of the CABG Surgery Patients

Variable	Off-Pump (n = 338)	On-Pump (n = 103)	p-value
Age (years)	63.4 ± 8.9	64.8 ± 8.6	0.152
Males (%)	79.9	77.7	0.548
BMI (kg/m <sup>2</sup> )	26.7 ± 3.6	26.3 ± 3.6	0.349
Diabetes (%)	45.0	45.6	0.907
Hypertension (%)	76.0	74.8	0.794
Dyslipidemia (%)	74.0	74.8	0.872
Smoking (%)	56.8	64.1	0.191
Alcohol (%)	28.7	28.2	0.915
Arrhythmia (%)	13.0	26.2	0.001
Kidney Failure (%)	5.9	9.7	0.182
History for Myocardial Infarction (%)	8.0	11.7	0.253
History for Transient Ischemic Attack (%)	1.5	3.9	0.131
History for Stroke (%)	0.9	3.9	0.033
Emergency Surgery (%)	15.1	36.9	<0.001
Values are means (SD), percentages (%), or medians (95% range).			

As shown in Table 2, a total of 29 patients (6.8%) were complicated by post-surgery stroke, of which 27 cases (6.1%) of ischemic stroke and 3 cases (0.7%) of hemorrhagic stroke. Of the all documented strokes, 15 cases occurred in the ONCABG group (14.6%) and 15 cases occurred in the OPCABG group (4.4%), thus associating the off-pump technique with a 3.3-fold lower chances of post-surgery stroke,  $p < 0.001$ .

All three cases of hemorrhagic strokes occurred in the ONCABG group, while the OPCABG group presented no hemorrhagic stroke.

Moreover, the OPCABG group presented lower cases of post-surgery encephalopathy with only 14 cases (4.1%), while 15 cases (14.6%) occurred in the ONCABG,  $p < 0.001$ .

Likewise, seizures occurred significantly less in the OPCABG group, 7 cases (2.1%), than in the ONCABG group, 8 cases (7.8%),  $p = 0.045$ .

In-hospital mortality was also significantly lower in the OPCABG group, 6 cases (1.8%), comparing to the ONCABG group, 7 cases (6.8%),  $p = 0.008$ . While no significant difference between groups in terms of mortality during the follow-up period could be observed, (data not shown).

**Table 2:** Neurological Complications

Variable	Off-Pump (n = 338)	On-Pump (n = 103)	p-value
Stroke	4.4	14.6	<0.001
Hemorrhagic stroke	0.0	2.9	NS
Encephalopathy	4.1	14.6	<0.001
Seizures	2.1	7.8	0.045
In-hospital mortality	1.8	6.8	0.008
Follow-up mortality	1.8	2.9	NS
Values are percentages (%). NS – not significant.			

## 4. Discussion

The incidence of postoperative CVA after CABG ranges from 1.4% to 3.8 % ( 6)

Risk factors include age, previous stroke, diabetes mellitus, hypertension (9), hypo perfusion (7) and female sex (8).

Afilalo et al. published a meta-analysis of fifty nine trials including nearly 9000 patients, comparing on-pump CABG and OPCAB. Postoperative CVA was significantly reduced by 30% in the OPCAB group (risk ratio (RR) 0.70, 95% CI: 0.49–0.99). (10)

Kuss and colleagues analyzed 38 propensity matched studies of 123,137 patients and reported highly clinically and statistically significant benefits for off pump surgery for mortality [odds ratio (OR) 0.69; 95% CI, 0.60–0.75] and stroke (OR 0.42; 95% CI 0.33–0.54) as well as renal failure, prolonged ventilation ( $P < 0.01$ ), inotropic support ( $P = 0.02$ ), intra-aortic balloon pump support ( $P = 0.05$ ), wound infection ( $P < 0.001$ ), and red blood cell transfusion ( $P < 0.0001$ ). (11)

Puskas and colleagues analyzed the STS database of 42,471 patients matched for 32 clinical risks and reported that OPCABG resulted in significant reductions in the risk of death, stroke, MI and major adverse cardiovascular events (12).

But other studies showed no significant differences between two techniques.

The ROOBY results (randomized on/off bypass) trial was published, reporting the outcomes for 2,203 patients (99% men) at 18 Veterans Affairs Medical Centres. Neuropsychological outcomes were not different between the groups, and graft patency was higher in the on-pump group (87.8% versus 82.6%;  $P=0.01$ ) at 12 months.

Another randomized trial, The Coronary Trial (the CABG Off or On Pump Revascularization Study) (13) which review 4752 patients and GOPCABE trial (German Off-Pump CABG Trial in Elderly Patients (14), with 2539 patients, found that there was no significant difference in overall death, MI, stroke, new renal dialysis or repeat revascularization in any of the trials.

Muller and colleagues, in a Cochrane review, have analyzed 86 randomized trials, involving 10,716 patients. OPCABG resulted in an increased all-cause mortality compared to ONCABG (3.7% versus 3.1%  $p = 0.04$ ). Also they found that there was no significant difference in myocardial infarction, stroke, renal insufficiency or coronary reintervention between the two techniques but that OPCABG resulted in fewer distal anastomoses with a mean reduction of 0.28 grafts ( $p < 0.001$ ). (15)

OPCABG will only reach its full potential to reduce the risk of neurological injury if a true no-touch aortic technique is used. While avoidance of cannulation and cross-clamping of the aorta by itself reduces aortic manipulation and the risk of embolic debris the placement of vein grafts to the ascending



aorta increases the risk. In a meta-analysis of 11,398 patients from eight studies, Misfield and colleagues reported that the relative risk of neurological injury was 0.46 (95% confidence intervals 0.29–0.72;  $p = 0.0008$ ) when there was complete avoidance of any aortic manipulation (16)

Like in several other studies, in our study, off pump CABG, is shown to be safe, effective and with less neurological complications. The reason for that is avoidance of cardiopulmonary bypass, cross clamp of the aorta and use of sequential anastomosis, also the experience of our surgeons on the off pump technique. One other cause is that emergency CABG are realised with on pump technique, and those patients present with higher risk for complication.

## 5. Conclusion

In our observational study, the off-pump CABG surgery was associated with lower neurological complications compared to the on-pump CABG surgery

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