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RESEARCH ARTICLE

Comparative Study Between On-pump CABG & Off-pump CABG Regarding Neurological Outcome

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Abstract: ***Background***: Post-cardiac surgery, neurological dysfunction always has a great impact on the outcome, especially with an increasing number of elderly in need of coronary artery bypass surgery (CABG). Post-cardiac surgery, neurological dysfunction can be classified as Stroke, Encephalopathy, Neurocognitive dysfunction, and Seizures. Cerebral hypoperfusion and embolism lodging play a vast role in causing post-cardiac surgery neurological dysfunction. Off-pump CABG appears more innocent than conventional on-pump CABG in avoiding these risk factors. However, there is still an ongoing debate on this matter. The current study aims to compare the postoperative outcomes of on-pump CABG and off-pump CABG. ***Methodology:*** A prospective study including 50 patients who underwent an on-pump CABG and 50 patients who underwent an off-pump CABG, who were scheduled for elective first-time CABG, were chosen after applying propensity score matching to identify two groups with similar preoperative characteristics. The primary study endpoints were the occurrence of stroke or delirium, while the secondary endpoints were the achievement of complete revascularization, inotropic need, time to recover consciousness (ROC), re-exploration, the occurrence of postoperative neurocognitive dysfunction, and postoperative AF. ***Results:*** The incidence of early postoperative delirium was significantly lower in off-pump CABG ($P<0.01$). However, stroke and late postoperative neurocognitive dysfunction were slightly higher in on-pump CABG but without a statistically significant difference ($P>0.05$). Achieving complete revascularization was statistically significantly higher in the on-pump group. On the other hand, inotropic need, postoperative drainage, and atrial fibrillation (AF) were statistically significantly higher in the on-pump group versus the off-pump group. ***Conclusion***: In our experience, patients undergoing on-pump CABG were not exposed to a greater risk of significant stroke compared to the off-pump group. However, the off-pump technique appears to be promising in reducing post-operative delirium, post-operative AF and occurrence of low cardiac output early after surgery.

Keywords: Stroke, delirium, cognitive dysfunction, atrial fibrillation.

INTRODUCTION

Since the occurrence of postoperative neurological dysfunction is a devastating complication that has a great impact on the quality of a patient´s life, many studies have been carried out in the past decades aiming to scrutinize the underlying mechanisms causing post-operative cerebral injuries.

Altered cerebral perfusion, dislodging micro and macro emboli [1] due to aortic manipulations, inflammatory response [2], and cerebral venous obstruction [3] caused by cardiopulmonary bypass are directly condemned.

Developments in the cardiac surgery armamentarium, such as advancements in intraoperative monitoring of brain perfusion by Near Infrared Spectroscopy (NIRS) [4], detecting dislodged emboli by transcranial Doppler [5], and new techniques in Cardiopulmonary By-Pass (CPB), appear to improve the coronary artery bypass surgery (CABG) results and decrease complications. In the same context, off-pump CABG was rediscovered, reiterating the importance of avoiding CPB and decreasing the manipulation of the aorta whenever possible from the nineties.

Since then, many studies have been composed to compare on-pump CABG and off-pump CABG from different aspects, especially the incidence of neurological dysfunction after each. The current study aims to compare the postoperative outcomes of on-pump CABG and off-pump CABG, especially neurological deficits.

PATIENT AND METHODS

This is an observational retrospective comparative study that included 100 patients with ischemic heart disease (IHD) who underwent elective first-go CABG with no previous neurological deficit or significant carotid lesion necessitating intervention. Between May 2023 and August 2024, a total of 350 patients underwent CABG in a tertiary university-based center.

We excluded patients who have other cardiac diseases, mechanical complications post-myocardial infarction, and patients who are dialysis-dependent or have severe liver disease. Additionally, redo CABG, a history of previous stroke or neurological deficit, and emergent CABG procedures.

The final population that met our inclusion and exclusion criteria was 315 patients. Of this cohort, 185

patients received on-pump CABG & 130 patients received off-pump CABG. After matching using the propensity score model, 50 pairs were selected. Euro score and number of coronary vessels affected, presence of carotid lesions, aortic plaque burden are used to build the propensity score model as these are the main confounders that affect the postoperative outcomes.

Sample size: The minimum calculated sample to be enrolled in the study is 50 patients undergoing an On-pump CABG and 50 patients undergoing an Off-pump CABG to achieve an effect size of 0.6 between-group comparisons. The sample was calculated using G-Power 3.1.9.7 software and based on prior data mentioned by Van Dijk et al. [6] that the mean overall postoperative change in neuropsychological tests among the Off-Pump Group versus On-Pump Group is 0.19 versus 0.13 respectively with assumed variation 0.1. Using a two-sided t-test at a Power of 80% and a level of significance of 5% and after adding a 10 % dropout rate.

Surgical techniques:

Each procedure was performed according to the surgeon's preference. Conduits were mainly LIMA to LAD and other SVG conduits to bypass other targeted vessels; sequential grafting and radial artery were sometimes used in both techniques. In on-pump procedures, a heart-lung machine with four roller pump heads on which a replaceable set is mounted. The set consists of a reservoir connected to a hollow membrane oxygenator. A common venous cannula is inserted in the right atrium to drain blood from the heart, and an arterial cannula is inserted in the distal ascending cannula to return oxygenated blood to the body. Hematocrit was maintained from 20% to 25% with pump flows of 2.0 to 2.5 L/min/m2 to maintain a mean arterial pressure of 50 to 70 mm Hg. The heart is arrested by warm blood cardioplegia infused into the ascending aorta by a separate cannula connected to a separate pump head. In off-pump procedures, heart stabilization was achieved with pericardial stay sutures, and the target vessel was stabilized with the aid of an epicardiac suction device. After coronary artery incision, an adequately sized intracoronary shunt (1.00 to 2.00 mm) was placed to minimize ischemia. Proximal anastomoses were performed in both techniques after applying the side biting clamp.

Definition of variables:

Stroke: neurological deficit of abrupt onset (aphasia, dysarthria, diplopia, or hemiparesis) caused by disturbance of cerebral blood supply that did not resolve in 24 hours.

Delirium or encephalopathy is an acute state of confusion and inattention, which may be accompanied by an altered level of consciousness and disorganized thinking.

Postoperative cognitive dysfunction is defined as a decline from the preoperative baseline cognition status after exposure to surgery and anesthesia. It affects one or more cognitive realms, such as attentiveness, behavior, memory, intellect, visual dimensions, motor dexterity, and management function.

Complete functional revascularization is achieved when at least one vessel of a caliber greater than 1.5 mm with stenosis > 70% is bypassed by a conduit to provide flawless blood supply in each vascular territory of the heart.

Complete anatomical revascularization assumes one graft for every significantly obstructed coronary artery

Low output syndrome after CABG: It is a clinical condition consisting of a spectrum of manifestations related to systemic hypoperfusion as (hypotension, cold extremities, and oliguria) and metabolic acidosis revealed as increased serum lactate levels (≥2 mmol/L for greater than 2 hours) treated by supporting the heart by inotropes and vasoactive agents or even mechanical supports as IAB.

Post-operative assessment

The intensivist performed the first post-operative neurological examination in the intensive care unit in the first 12 hours after admission to the ICU to check orientation about time, place, person, speech, memory function, and integrity of motor and sensory functions. CT brain was done if there was suspicion of any neurological affection according to neurologist advice. Montreal cognitive assessment test (MoCA) was used to examine patient performance in cognitive function of memory, done one day before surgery and on day three after transferring patient to the ward .

RESULTS AND OBSERVATIONS:

The current study included 100 patients with IHD who underwent elective first-go CABG. The mean study population age was in the middle age criteria in the 5th and 6th decades of age. The baseline characteristics are presented in **Table 1,** showing no differences in pre-operative variables. Operative details are shown in **Table 2.** On-pump CABG was associated with a higher number of distal anastomoses and a higher rate of completeness of revascularization. Post-operative complications are shown in **Table 3.** On-pump CABG carried a higher incidence of postoperative delirium (P<0.001), atrial arrhythmia (P=0.023)., LCOP syndrome (P=0.004), bleeding (P<0.001), post-operative packed RBCs transfusion (P<0.001).and the need for inotropes (P=0.005). The rate of stroke and postoperative cognitive dysfunction was slightly higher in the on-pump group but without statistical significance (P>0.05).

Table 1: Baseline characteristics among study participants.

	On pump (n = 50)		Off-pump (n = 50)		P-value	Sig.
	Mean/N	SD/%	Mean/N	SD/%		
Age	58.2	9.3	61.0	8.2	0.109	NS
Gender:						
- **Males**	40	80.0%	35	70.0%	0.248	NS
- **Females**	10	20.0%	15	30.0%		
Smoking	29	58.0%	29	58.0%	1.000	NS
DM	34	68.0%	31	62.0%	0.529	NS
HTN	34	68.0%	24	48.0%	0.043	**S**
COPD	14	28.0%	22	44.0%	0.096	**NS**
Classification of angina (CSS score):						
- **II**	16	32.0%	16	32.0%	0.236	NS
- **III**	13	26.0%	20	40.0%		
- **IV**	21	42.0%	14	28.0%		
NYHA classification for dyspnea:						
- **I**	32	64.0%	41	82.0%	0.129	**NS**
- **II**	12	24.0%	7	14.0%		
- **III**	6	12.0%	2	4.0%		
Previous PCI insertion	23	46.0%	23	46.0%		NS
Myocardial infarction within 90 days	15	30.0%	13	26.0%	0.656	NS
Atrial arrhythmias	0	0.0%	4	8.0%	0.117	NS
Right or Left carotid artery stenosis:						
- **< 50%**	42	84.0%	40	80.0%	0.603	NS
- **50%-70%**	8	16.0%	10	20.0%		
Peripheral arteriopathy	9	18.0%	15	30.0%	0.160	NS
Euro Score	1.2	0.6	1.4	0.8	0.202	NS
- Creatinine	1.3	0.5	1.6	0.9	0.056	NS
EF	54.8%	9.1%	55.5%	11.1%	0.746	NS
Mean number of affected vessels	3.7	0.91	3.5	0.78	0.217	NS

COPD: Chronic obstructive pulmonary disease, CSS: Cardiovascular Society Score, DM: Diabetes mellitus, EF: Ejection fraction, HTN: Hypertension, PCI: percutaneous coronary intervention, SD: Standard deviation. ***NS: Non-significant, S: Significant***

Table 2: Operative details among the two studied groups.

	On pump (n = 50)		Off-pump (n = 50)		P-value	Sig.
	Mean/N	SD/%	Mean/N	SD/%		
Operative time	5.5	0.9	4.0	0.7	**<0.001**	**S**
Mean number of distal anastomoses:	3.68	0.819	2.7	0.763	**<0.001**	**S**
Mean number of proximal anastomoses:	2.42	0.731	1.56	0.733	**<0.001**	**S**
Diagonal forsaken	5	26.3%	6	50.0%	0.255	NS
LCX forsaken	11	28.5%	14	29.8%	0.872	**NS**
RCA forsaken	1	2.4%	15	39.5%	**<0.001**	**S**
Achievement of Anatomical revascularization	37	74.0%	27	54.0%	**0.037**	**S**
Achievement of Functional revascularization	47	94.0%	35	70.0%	**0.002**	**S**

LCX: Left circumflex artery, RCA: Right coronary artery, SD: Standard deviation, ***NS: Non-significant, S: Significant***

Table 3: Clinical outcomes and complications among the two studied groups.

	On pump (n = 50)		Off-pump (n = 50)		P-value	Sig.
	Mean/N	SD/%	Mean/N	SD/%		
Re-exploration	2	4.0%	3	6.0%	1.000	NS
Amount of bleeding (ml)	473.0	163.3	295.0	116.6	< 0.001	**S**
Amount of Packed RBCs used	2.6	1.0	1.8	0.7	< 0.001	**S**
Adrenaline usage	36	72.0%	22	44.0%	0.005	**S**
Nor adrenaline usage	20	40.0%	14	28.0%	0.205	NS
Other inotropes usage	3	6.00%	1	2.0%	0.617	NS
Length of ICU stay (days)	4.0	1.2	2.8	1.1	<0.001	**S**
Highest level of urea (mg/dl)	42.9	23.8	31.2	25.8	0.021	**S**
Highest level of creatinine (mg/dl)	2.2	1.1	1.7	1.1	0.014	**S**
Highest level of ALT (IU/L)	51.8	41.1	35.3	13.8	0.008	**S**
Highest level of AST (IU/L)	57.9	27.3	42.4	11.3	<0.001	**S**
Need for post-operative dialysis	4	8.0%	2	4.0%	0.678	NS
Atrial arrhythmias	18	36.0%	8	16.0%	0.023	**S**
Ventricular arrhythmia	4	8.0%	3	6.0%	1.000	**NS**
IAB	2	4%	0	0	1.000	**NS**

Low CO syndrome	36	72%	22	44%	0.004	**S**
Postoperative MI	3	6.0%	2	4.0%	1.000	NS
Time to regain consciousness (h)	11.2	27.8	3.7	1.8	0.060	NS
Mechanical ventilation time	17.4	30.4	7.8	4.4	0.031	**S**
Pulmonary complications	15	30.0%	5	10.0%	0.012	**S**
Stroke	3	6.0%	2	4.0%	1.000	NS
Lethal coma	1	2.0%	0	0%	1.000	NS
Delerium	13	36%	4	8.0%	<0.001	**S**
seizures	3	6.0%	2	4.0%	1.000	NS
Cognitive dysfunction	12	25.0%	7	14.3%	0.184	NS
Superficial wound infection	8	16.0%	7	14.0%	0.779	NS
Deep wound infection	3	6.0%	2	4.0%	1.000	NS
Mortality	2	4.0%	1	2.0%	1.000	NS

ALT: alanine transaminase, AST: aspartate transaminase, CO: Cardiac output, IAB: Intra-aortic balloon, ICU: Intensive care unit, MI: Myocardial infarction, RBC: Red blood corpuscles, SD: Standard deviation.

DISCUSSION

Coronary artery bypass grafting (CABG) is a common procedure for multivessel coronary artery disease. It can be performed on-pump, using a heart-lung machine, or off-pump, with the cardiac muscle beating [6].

Neurological deficits occur among CABG patients such as delirium and strokes. Stroke occurs in up to 3% of CABG patients, impacting quality of life and increasing mortality with rates varying based on patient characteristics and surgical type [6].

In our study, as patients were recruited after applying propensity score matching, there was no statistically significant difference between both groups regarding preoperative criteria except for hypertension, whose incidence was higher in the on-pump group, reflecting population characteristics.

The present study documented a statistically significant (P-value <0.001) increased number of grafts and increased percentage of full anatomical revascularization in the on-pump group compared to the off-pump group. This aligns with numerous studies that reported a significantly higher rate of achieving full revascularization in the on-pump group [7,8].

Similar studies agree that OPCAB has a higher incidence of RCA forsaken [9,10]. This may be due to heart elevation during right system grafting, which leads to venous and pulmonary impairment and distortion of atrioventricular valve geometry.

As in many previous studies [3,4], this study showed no statistically significant difference in the incidence of reoperation for bleeding or tamponade between the On Pump CABG (ONCAB) and On Pump CABG (OPCAB) groups, although there is a statistically significantly higher amount of postoperative bleeding in the ONCAB versus OPCAB groups. Studies attributed the higher need for blood transfusion in ONCAB to hemodilution and hemolysis [11].

Our study showed the merit of the OPCAB technique in preserving hepatic and renal function postoperatively. This finding goes hand in hand with similar studies [12,13] documenting that patients, especially those with mild to moderate renal affection preoperatively, benefit the most from OPCAB.

The present study emphasized the role of the OPCAB technique in reducing postoperative LCOP and consequently reducing the need for inotropes and dosage per case when administered. This is in concordance with multiple analytical studies [14,15]. This may be due to the fact that ONCAB is associated with a higher degree of myocardial injury [16]. LCOP has been accused of increasing the rate of stroke post-CABG by two to three folds [17].

Highly statistically significant increased incidence of postoperative atrial arrhythmias in the on-pump group

when compared with the off-pump group, endorsing many studies that describe a significantly more frequent AF in on-pump CABG compared to off-pump CABG [18,19]. Many factors intrinsic to CPB, such as atrial cannulation, increased inflammatory response, and oxidative stress, seem to play a role [20]. Large studies and meta-analyses focused on the association between postoperative AF and increased cerebrovascular accidents, strokes, and cognitive decline [21,22].

This study revealed a substantially obvious, about to reach statistical significance, increased time to regain consciousness in the on-pump group when compared with the off-pump group. This finding goes with other studies, as the off-pump CABG surgery was associated with early recovery of consciousness [23].

In our study, there is a growing incidence of patients developing delirium more often in the on-pump group than in the off-pump group. Additionally, multivariate logistic regression analysis detected off-pump surgery as an independent surrogate of decreasing the incidence of post-CABG delirium [24].

Some neurological studies hypothesize that delirium might be a manifestation of TIA or a minor stroke not diagnosed due to unusual presentation and rapid symptom regression. Therefore, avoiding the CPB and decreasing manipulation of the aorta in off-pump CABG may lead to regression of postoperative delirium [25]. Recent studies, such as ours, reported insignificant differences between ONCAB and OPCAB regarding postoperative stroke [26,27]. In contrast, studies concerned with high-risk patients assumed a lower stroke rate in off-pump CABG, especially with patients having atheromatous disease of ascending aorta [28]. Zhao et al., by ranking treatments according to their comparative effectiveness for reducing stroke rate, demonstrated that AN-AORTIC OPCAB was the superior technique, and lastly came the conventional ONCAB method [29].

Our study failed to show a statistically significant higher ratio of postoperative cognitive dysfunction in any of the two groups. This comes concordant with numerous studies where there was no difference in neurocognitive state after on-pump surgery compared to off-pump surgery [30-32]. On the other hand, different studies reported less neurocognitive impairment in off-pump patients, especially in the early postoperative period [33,34]. Sun et al. showed that perfusion of specific brain regions (including the bilateral occipital, cerebellar, thalami, and left temporal lobe) was reduced after ONCAB but remained unchanged after OPCAB [35]. Liu et al., in a prospective observational study, found a significantly higher number of micro-emboli in patients undergoing ONCAB compared with OPCAB. Still, the two groups had no significant difference regarding POCD [36]. This controversy between the studies may be attributed to variations in used cognitive tests, different definitions of cognitive impairment, and different assessment times.

Limitations: The limited number of patients in both groups with disadvantages related to statistical significance and short follow-up duration are limiting factors. Also, our institution does not routinely perform intraoperative epi-aortic ultrasound, transcranial Doppler, and other advanced monitoring facilities.

CONCLUSION

Avoiding the CPB and transaortic cross-clamp in Off-pump surgery can reduce the generated micro-emboli, inflammatory response, and AF, leading to a lower incidence of cerebrovascular accidents. This is reflected clinically as a shorter duration to regain consciousness and a lower rate of postoperative delirium.

Further clinical directions:

Future studies should scrutinize an aortic off-pump CABG and compare it with other techniques. Clampless devices, including Heartstring II , have been developed to avoid partial clamping of the aorta during proximal anastomosis, and longer follow-up and direct comparison with other techniques are needed.

Declarations

Availability of data and material: The data supporting this study's findings are available on request from the corresponding author. The data are not publicly available as they contain information that could compromise the privacy of research participants.

Authors' contributions: Prof. Dr Mohammed Hagrass generated ideas, and revised the manuscript. Assistant prof Dr Abdallah Nosair, interpreted the data, and revised the manuscript.,. Michael Boulos, collected, analyzed the data, and wrote the manuscript. Dr Omar and Dr John, interpreted the data, and wrote and revised the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate: The study protocol was reviewed and permitted by the institutional research and ethics committee (Code: MD-197-2023). After the participants were adequately briefed on the study's goals, their written informed consent was obtained. The subject was free to withdraw from the study at any moment; participation was entirely voluntary. In accordance with the Declaration of Helsinki, all steps of data collecting, entry, and analysis were conducted in a highly confidential and private manner.

Competing interests: Authors declare no conflict of interest is present.

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