

Review Article

Off-Pump Coronary Artery Bypass Grafting Surgery : A Narrative Review

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Coronary Artery Bypass Grafting (CABG) Surgery is considered the standard treatment for revascularization in Coronary Artery Disease. The Off-Pump Coronary Artery Bypass Graft (OPCAB) which evades the use of Cardiopulmonary Bypass (CPB) became a popular CABG procedure, due to the adverse effect of CPB. Hypothetically, OPCAB may improve the rates of perioperative Myocardial Injury, Neurocognitive Impairment, Stroke and Mortality. However, some studies showed no superior outcomes for OPCAB compared to on-pump CABG. This study aims to evaluate the short-term and long-term outcomes of OPCAB versus On-Pump CABG. The results showed that OPCAB is probably a safe procedure for patients, especially for those with high-risk conditions. OPCAB procedure showed superior short-term outcomes in terms of Myocardial Infarction, Systemic Inflammatory Response, Postoperative Cognitive Dysfunction, Renal Failure, Stroke, Pulmonary Complication, Postoperative Transfusion, Hospital stay length and infection than On-pump CABG. However, regarding long-term outcomes, Off-Pump CABG had a higher rate of incomplete revascularization and repeat revascularization and a higher risk of long-term mortality as well as lower graft patency. Furthermore, the result showed that the higher experience of the surgeons in OPCAB improves the outcome of the Surgery.

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Key words : Off-Pump Coronary Artery Bypass Grafting Surgery, OPCAB, Short-term Outcomes, Long-term Outcomes.

Coronary Artery Disease (CAD) is the main reason for death Globally and AHA estimated that CAD leads to more than 360,000 deaths each year¹. Coronary Artery Bypass Grafting (CABG) considers the main standard treatment for CAD². The first CABG was done in the 1960s as the only treatment method for Ischemic Heart Disease³. Developments in Cardiopulmonary Bypass (CPB) have improved Cardiac Surgery; however, the non-physiological effect of CPB leads to organ dysfunction and tissue injury. In addition, cerebrovascular events related to CPB are a significant problem^{4,5}. As the number of patients undergoing CABG increases, solutions to reduce the alleged adverse effects of CPB due to aortic manipulation and clamping have been evaluated. Therefore, Off-Pump CABG (OPCAB) became popular in the 1990s⁶. In the United States, OPCAB peaked in 2002 and almost 25% of all CABG in operations were done Off-Pump⁶. In Japan, in 2000, and after the emersion of the stabilizer, OPCAB has become a prevalent practice for CABG, and now about 65% of CABG cases are done by OPCAB⁷.

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Editor's Comment :

- The comparison of Off-Pump CABG and On-Pump CABG has yielded mixed results.
- Off-Pump procedure is safer with lesser short term complications though long term outcomes like incomplete revascularization, repeat revascularization and poor graft patency is more in off pump revascularization.

After many years of using the OPCAB procedure and publishing many trials and meta-analyses about the benefits of this method, there is still controversy on the outcomes and advantages of Off-Pump CABG. The present review summarizes the most recent and relevant data about this method and evaluates the short-term and long-term outcomes of Off-Pump CABG.

MATERIALS AND METHODS

In this review study, all articles on Off-Pump Coronary Artery Graft surgery were evaluated from the year 2000 to 2021. Articles were searched through databases such as PubMed, Web of Science, Scopus, Google Scholar, Science Direct and Cochrane library using the keywords "Off-Pump Coronary Artery Graft Surgery", "OPCAB", "Short-term outcomes" and "long-term outcomes". A total of 167 articles were extracted in an initial search. After reviewing the abstract of these articles, finally, 68 articles that met the necessary criteria of the present review were selected and evaluated completely.

OPCAB in High-Risk Patients :

In a meta-analysis by Kowalewski, *et al*, it was shown that the odds of Cerebral Stroke are significantly decreased in OPCAB in comparison to conventional CABG in high-risk patients. Furthermore, they showed that there is a significant association between patients' risk profile and benefits from OPCAB in Myocardial Infarction (MI), Death and Cerebral Stroke, proposing that in high-risk patients, OPCAB must be toughly considered. Therefore, they concluded that OPCAB improves the short-term outcomes in high-risk patients⁸. In a prospective randomized trial study on 411 patients, it was found that OPCAB decreases primary mortality as well as morbidity in high-risk patients⁹.

In Kerendi, *et al* study it was revealed that the risk-adjusted outcomes for mortality and morbidity endpoints in high-risk patient populations were superior after OPCAB versus On-Pump CABG¹⁰. The result of Rastan, *et al* study on high-risk patients demonstrated that patients with reduced left ventricular function and multi-risk patients benefit from OPCAB in terms of perioperative mortality and morbidity. Furthermore, in patients with major extracardiac risk factors, OPCAB reduced the rate of Perioperative Stroke. In individuals with Pulmonary or renal Dysfunction, OPCAB resulted in a reduction in the failure of the organ. OPCAB resulted in a lower need for transfusion in high-risk populations¹¹.

Morbidity and Mortality after OPCAB :

In a study on 118,140 CABG procedures, that 11,717 cases of them were OPCAB, the use of the OPCAB method was related to a reduction in risk-adjusted operative mortality from 2.9% with the On-Pump method to 2.3% in the OPCAB group. Also, the risk-adjusted morbidity rate was reduced from 14.15% with On-Pump CABG to 10.62% in OPCAB group¹². Bittner, *et al* evaluated 57 multivessel diseases OPCAB cases for 2 years and reported that Off-Pump CABG can be done with rational low morbidity and mortality in high-risk patients¹³. Vettath, *et al* also showed that Off-Pump CABG resulted in an improvement in the mortality rate over time¹⁴. Takagi, *et al* studied eight medium- to large-size RCTs including 8780 patients with long-term follow-up OPCAB versus on-pump CABG and revealed that OPCAB rises long-term (5 years or more) mortality in comparison to On-Pump CABG (ONCAB)¹⁵. In another study, they demonstrated that OPCAB is related to an increase in very long-term, 10 years and more, all-cause mortality in comparison to ONCAB¹⁶.

OPCAB and Systemic Inflammatory Response :

The systemic inflammatory response is probable after CABG using CPB which comprises the

complement and Leukocyte activation, pro-inflammatory cytokines releasing Nitric Oxide metabolism changes, and an increase in the free radical's Oxygen production that may lead to organ dysfunction and coagulation conditions¹⁷. Schulze, *et al* showed that the OPCAB revascularization process and not using CPB significantly diminishes the Systemic Inflammatory Response Syndrome and the need for primary catecholamine. This can help to the improvement of Organ Function, also improvement of recovery from surgery¹⁸. Neshar, *et al* study demonstrated that Serum cytokine levels (IL-6, IL-8 and IL-10) in the OPCAB method were lower in comparison to the on-pump method¹⁹. In another study, OPCAB attenuated the systemic release of IL-8 and IL-10, whereas no difference was seen in the release of IL-6, CRP and Neutrophils. Signs of cytokine uptake were seen in the Lungs by OPCAB²⁰. In Meng, *et al* study, the analyses presented that the concentration of IL-10 was significantly lower after OPCAB in comparison to on-pump CABG. But, for IL-6 and IL-8 no significant differences were observed in the two groups²¹.

Postoperative Cognitive Dysfunction in OPCAB :

Cerebral Dysfunction including Postoperative Cognitive Dysfunction (POCD), delirium and stroke after Cardiac Surgery remains a devastating problem, especially in the older age group. They may happen as a result of cerebral emboli, inflammation, or hypoperfusion²².

In Sun *et al.* study, a Meta-analysis of 13 randomized controlled trials on 2326 patients it was demonstrated that the occurrence of POCD was significantly lower following OPCAB than On-Pump in 1-2 weeks and at 3 months after Surgery²³. In a study by Szwed, *et al*, it was shown that anaortic OPCAB significantly reduced the rate of postoperative cognitive dysfunction and delirium compared to conventional OPCAB²⁴. Schmitz, *et al* also found that postoperative neurocognitive function significantly improves by OPCAB²⁵. In another study, Off-pump CABG decreased postoperative Neuropsychological dysfunction in elderly cases in comparison to on-pump CABG²⁶. However, in Lund, *et al* study, long-term cognitive function after OPCAB was similar to on-pump coronary Artery Bypass Grafting Surgery²⁷. Similarly, Marasco *et al* meta-analysis indicated no significant neurocognitive advantage while using OPCAB in comparison to on-pump CABG²⁸.

Postoperative Renal Dysfunction and OPCAB :

Postoperative Renal Dysfunction is a significant complication of CABG and is associated with the

patient's clinical condition, CPB-related events, renal hypoperfusion, hypotension, hypothermia, microemboli, and stimulation of the inflammatory response^{29,30}. According to Umit, *et al* study, the Off-Pump CABG offers excellent renal protection and a significantly lower risk of Renal Dysfunction compared with conventional CABG³¹. Abu-Omar *et al* in a study on 1580 patients showed that Off-pump CABG is associated with a decrease in postoperative renal damage³². Rocha, *et al* reported that OPCAB is related to improving in-hospital renal outcomes in patients with moderate renal failure, but is not related to the long-term cumulative occurrence of end-stage renal failure which needs permanent Dialysis³³.

Postoperative Pulmonary Dysfunction and OPCAB:

One of the prevalent difficulties after CABG is pulmonary complications associated with surgical procedures, anaesthesia procedure effects, and Cardiopulmonary bypass pump³⁴.

A study by Staton *et al.* reported that OPCAB was associated with a greater decrease in postoperative respiratory compliance compared to the on-pump method. Moreover, OPCAB resulted in superior gas exchange and earlier extubation³⁵. According to Raja *et al.* study, based on available evidence from RCTs, OPCAB reduces Postoperative Pulmonary Dysfunction and is more effective than On-Pump CABG for Chronic Obstructive Pulmonary Disease (COPD) patients³⁶. Silva, *et al* study also revealed that patients in the OPCAB group had higher improvement in pulmonary function after Surgery than On-Pump group³⁷. However, in Montes, *et al* study Off-pump CABG in comparison to the On-Pump method did not result in important protection from postoperative pulmonary dysfunction³⁸.

OPCAB and Postoperative Arterial Fibrillation :

Postoperative Atrial Fibrillation (AF) is a common arrhythmia that happens after CABG. OPCAB is considered to be a less invasive technique and is believed to reduce the rate of AF, however, there is inconsistency in obtained data. Athanasiou, *et al* demonstrated a reduction in the occurrence of postoperative AF with Off-Pump CABG techniques. However, they suggested that the results should use with caution²⁹. Lewiki *et al.* reported no difference between the incidence of AF after OPCAB and ONCAB surgeries. Böning *et al.* also showed no alteration in the rate of postoperative AF by using OPCAB³⁹. In the Junior, *et al* study, Off-pump CABG did not decrease the occurrence of postoperative AF. They also defined age >70 years old and preoperative AF as risk factors

for postoperative AF⁴⁰.

Incomplete Revascularization in OPCAB :

In this Cohort Ji, *et al* on 1,349 patients with a triple-vessel lesion, the occurrence of Off-Pump incomplete revascularization was 19.9%⁴¹. In a report on 41,139 patients with the left main and three-vessel lesion, the rate of incomplete revascularization in 6,367 OPCAB patients was about 29.0%⁴². In a SYNTAX trial by Head, *et al*, the incomplete revascularization rate was 36.8% after OPCAB⁴³. Another study including 7,427 OPCAB cases and 7,128 on-pump CABG cases demonstrated that the incomplete revascularization rate of the Off-Pump method was 13.3%⁴⁴.

Repeat Revascularization and OPCAB :

Takagi, *et al* analysis showed that OPCAB may raise the rate of repeat revascularization by 38% over ONCAB⁴⁵. In a meta-analysis study by Zhou, *et al*, it was found that OPCAB increases the rate of repeat revascularization in comparison to ONCAB at 1-year follow-up, but not at 5-year follow-up⁴⁶.

Graft Patency After OPCAB :

Hattler *et al.* study demonstrated significantly lower graft patency for OPCAB than On-Pump CABG⁴⁷. Parolari, *et al* study in a meta-analysis of randomized studies showed a reduction in postoperative graft patency of Coronary Artery Bypass Grafts done by OPCAB methods⁴⁸. Another study by Houliind, *et al* found that graft patency after Off-Pump CABG was lower than the On-Pump method even with heparinization protocols⁴⁹. However, Puskas, *et al* reported that graft patency was similar for OPCAB and on-pump CABG at 30 days and one year⁵⁰. Hu, *et al* also revealed no significant differences in graft patency between OPCAB and ONCAB GROUPS in Triple Vessel Coronary Artery Disease patients⁵¹.

Conversion in OPCAB :

Regardless of the popularity of OPCAB and its benefits, in a small number of patients, conversion to on-pump CABG may be required due to reasons including hemodynamic disturbance, physical difficulty in grafting, ischemia, or arrhythmias. Chakravarthy *et al.* reported that conversion in OPCAB is related to significant mortality raise. Increased left ventricular end-diastolic pressure, women's gender and pre-operative need for Intra-aortic balloon are indicators of amplified mortality risk in conversion⁵². According to Tariq, *et al* study, emergency conversion from OPCAB to on-pump is the most disastrous occurrence leading to higher morbidity and mortality. Conversion as a result of

arrhythmias was the main cause (rate: 9%) and patients with higher New York Heart Association status and Chronic Obstructive Pulmonary Disease had a higher risk of emergency conversion. Therefore, they suggested that the decision for OPCAB should be made with caution for each patient⁵³. In Keeling, *et al* study, intra-operative conversion from OPCAB to on-pump was reported to be a morbid incident. They recommended that elective ONCAB should be selected for those with a higher risk for conversion. They also found that older age, preoperative intraaortic balloon pump placement, ejection fraction <35%, increasing number of involved vessels, Heart Failure and emergent procedural condition were independent markers for conversion⁵⁴.

OPCAB and Surgeons' Experience :

The important role of Surgeons' experience in OPCAB was highlighted frequently by professionals in the field. Benedetto, *et al* showed that mortality was reduced after OPCAB when done by high-volume surgeons in high-volume OPCAB centers and in contrast the mortality risk increased when OPCAB was done by surgeons in low-volume centers⁵⁵. In the Glance *et al.* study it was found that for On-Pump CABG Surgery, higher surgeon case volumes are related to lower rates of mortality⁵⁶. In another study by Chen, *et al*, it was shown that by Increasing the experience of a surgeon the rate of blood transfusion was reduced by about 33%⁵⁷. Hsu, *et al* evaluated the proficiency of surgeons for OPCAB by the following quality indicators, the revascularization index, and the conversion rate. They reported that a revascularization index of ≥ 1.4 and a conversion rate of $\leq 5\%$ show the proficiency of surgeons for OPCAB⁵⁸. Hemil, *et al* reported that the occurrence of emergency conversion during OPCAB has reduced with raising surgeons' experience; however, in these patients, the rate of morbidity remained unaffected⁵⁹.

Short-term Outcomes of OPCAB :

In a meta-analysis, by Reston, *et al* the results showed that rates of perioperative myocardial Infarction, Reoperation for bleeding, Renal failure, Stroke and Mortality were lower after OPCABG than after CABG. They also showed a decrease in hospital stay length, AF and wound infection related to OPCABG, however, the differences were not statically significant⁶⁰. In a study by Elmahrouk, *et al* on 450 patients, it was found that the rate of early postoperative AF and Renal Failure was decreased in the Off-Pump group. But, no statistically significant difference was observed in neurologic complications, AMI, or early mortality between Off- or On-Pump groups⁶¹. Gao, *et al* evaluated the short-term outcome

in 318 high-risk patients who underwent CABG and found that the OPCAB group had significantly decreased ventilator support time, Postoperation ICU time, operative mortality and morbidity⁶². Guan, *et al* performed a meta-analysis and systematic review on 32,354 patients and reported a significant benefit from OPCAB in terms of 30-day mortality, MI, stroke, renal failure, Infection, Pulmonary complication, Postoperative transfusion, and reoperation bleeding. They showed no significant difference in AF and Neurological Dysfunction⁶³. Kowalewski, *et al* performed a meta-analysis on 100 studies (19,192 patients) and demonstrate a significant decrease in the odds of cerebral stroke in the OPCAB group compared with on-pump CABG⁸.

Long-term Outcomes of OPCABG :

In Luo, *et al* study on seven RCTs and 9,128 patients, in long-term follow-up OPCAB had a significantly higher rate of revascularization (OR=1.45; p=0.04) than on-pump CABG⁶⁴. Chikwe *et al.* evaluated long-term results on 6,950 who underwent Off-Pump CABG and reported a rise in repeat revascularization, incomplete revascularization and mortality at 10 years in comparison to ONCAB⁶⁵. A meta-analysis by Takagi, *et al* on 22 studies, and more than 100,000 patients, disclosed that OPCAB is probably related to worse long-term survival (5 years or more) compared with ONCAB⁶⁶. In another study on 13 studies including 13,234 patients, Off-pump CABG increased the risk of all-cause death and repeat bypass surgery at long-term, more than 4-year follow-up⁶⁷. In a study on 5,203 patients by Kim, *et al* it was reported that for overall mortality, patients who underwent Off-Pump CABG had a significantly higher risk of mortality (HR: 1.43; p<0.0001) in comparison to those who underwent ONCAB⁶⁸.

CONCLUSION

OPCAB is probably a safe substitute for On-Pump CABG for patients, especially with high-risk conditions. OPCAB procedure showed superior short-term outcomes in terms of Myocardial Infarction, renal Failure, Stroke, Pulmonary Complication, Postoperative Transfusion, Hospital stay length and Infection than On-Pump CABG. Also, it was shown that the OPCAB revascularization process significantly diminishes the systemic inflammatory response syndrome. In addition, OPCAB significantly reduced the rate of early postoperative cognitive dysfunction compared to conventional OPCAB. However, regarding long-term outcomes Off-Pump CABG had a higher rate of incomplete revascularization and repeat revascularization and a higher risk of long-term mortality

as well as lower graft patency. Furthermore, the result showed that the higher experience of the surgeons in OPCAB improves the outcome of the surgery.

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