# Off-Pump CABG: A Review

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**Abstract**

Off-pump coronary artery bypass grafting is a newly resurgent technique because of the constant endeavour to make surgery safer for the patients. This method eliminates the use of cardiopulmonary bypass thus avoiding an unphysiological state and reducing the cost involved in the use of this circulatory support system. The rationale appears sound. In the following few pages, I will scan the mass of literature available to analyse if this rationale is substantiated by evidence. Based on what I have found, I conclude it is a definite addition to our armamentarium with great potentials but has its own limitations and needs to be applied with clinical judgement.

## INTRODUCTION

Coronary artery bypass surgery (CABG) is the commonest operation in the western world and its demand in the developing countries is likely to increase very much in the future[1]. The risk of CABG increases with the increasing age of patients, their co-morbid factors and referral of patients for surgery after multiple attempts of percutaneous intervention. The cost of the operation has become prohibitive especially in the developing world because of the cost of import of various materials required for the conventional CABG using cardiopulmonary bypass (CPB). Innovative surgeons and the enterprising industry strived together to address this twin concern of risks and cost of conventional CABG culminating in the development of Off pump CABG (OPCAB). In the following few pages the history, rationale, technique, systemic changes and comparative results, indications, limitations and contraindications of OPCAB will be discussed.

## HISTORY

Even though CABG was reported to have been performed without CPB as an emergency procedure earlier [2], the first planned CABG recorded is credited to Kolesov of Russia[3]. He anastomosed the left internal mammary artery (LIMA) to left anterior descending artery (LAD) without CPB and angiographic verification in 1964. Because of the technical difficulties and concerns about patency of the anastomosis, CABG was performed on CPB, which provided a still avascular field. The pump was considered an absolute requirement for CABG [4,5] for the next 2 decades during which a large number of conventional CABG was performed and the techniques were perfected. However, the limitations of the CPB were also recognised and the reports of Buffolo [6], Benetti [7] and Calafiore[8] prompted a resurgence of interest in OPCAB. However, doyens like Cooley[9] have expressed concern about the quality of the anastomosis done on beating heart. The impact of newer developments in stabilisation, blood scavenging during surgery, anaesthesia and supportive measures needs to be studied in future.

## RATIONALE

Conventional CABG performed on cardiopulmonary bypass was the standard of care for nearly 25 years. Great improvements in outcome were achieved by systematic research in the field of anaesthesia and perfusion apart from refinements in surgical techniques. Despite these developments a sort of flattening of the curve of improvement was noticeable. Basic research in perfusion revealed various harmful effects of extracorporeal circulation. Cardiopulmonary bypass is an unphysiological state involving alterations in hemorheology, exposure of blood to non-endothelial surfaces triggering various enzyme cascades such as complement, kinins, coagulation systems and fibrinolytic systems, protein denaturation, alteration in thermal regulation etc. There is a great perturbation of the homeostasis leading to various organ dysfunctions thus accounting for the postoperative morbidity. Hence the attempts to do away with CPB. Another reason was the cost of equipments used for CPB. These imported materials were prohibitively costly especially for the developing world. So it is not without reason that the early reports of success with OPCAB emanated from the developing world.

## DEFINITIONS

A host of abbreviations have sprung up due to various modifications of techniques. Some of the common terminologies are explained below.

Minimally Invasive CABG (MICAS): This refers to all techniques of CABG wherein there is no use of CPB. It also includes operations involving lesser incisions than a standard full median sternotomy.

Minimally invasive Direct CABG (MIDCAB): This is usually restricted to LIMA-LAD anastomosis done through a short incision in the fourth left intercostal space and entering the pericardium through the bed of excised cartilage.

Left Anterior Small Thoracotomy (LAST): The chest is entered through 4th or 5th intercostal space. Pleural cavity is entered and LIMA dissected.

Off-Pump CABG (OPCAB): This is the approach most commonly used today. Multivessel grafting is done through a standard median sternotomy.

Beating-Heart CABG (BHCABG): This refers to any procedure done on a beating heart not supported with CPB.

Beating Heart on Pump (BHOP): When circumstances favour the use of CPB, the procedure is done on pump without aortic clamping to avoid manipulating aorta and global myocardial ischemia

## TECHNIQUES

No attempt is made to go into the various practical hints of how to do OPCAB. There are a few important concerns in performing OPCAB. The constant motion of the heart interferes with making the anastomosis. So various ingenious devices have been developed to reduce this motion. Pharmacological methods to reduce the contractility were tried and given up. At present varieties of stabilisers are used to immobilise a limited segment of the heart where the anastomosis is in progress. These stabilisers use either mechanical compression or suction or both to achieve this. Another problem is blood in the operative field. This is circumvented by either “snares” which pinch the vessel to reduce the bleeding or by “shunts” which are placed across the site of anastomosis to allow perfusion distally and prevent spillage of blood. The added advantage of shunts is the avoidance of distal ischemia during the period of anastomosis. Sometimes gas (CO2) blowers are used to wash off the blood from the site. The third concern is the hemodynamic alterations during positioning of the heart to access different regions. Various strategies like volume loading, vasopressors and Trendelenburg positioning are employed to prevent the hypotension associated with cardiac retraction. Peroperative Trans-Oesophageal Echocardiography has revealed the changes in ventricular function [10,11] associated with positioning of the heart. Since right ventricular dysfunction appears to be a limiting factor Right Ventricular Assist Devices (RVAD) [12] are under evaluation.

## SYSTEMIC CHANGES IN CABG

The systemic inflammatory response syndrome, neurological, myocardial, renal, pulmonary and haematological alterations during the surgery are to be considered in this section.

## SYSTEMIC INFLAMMATORY RESPONSE

Inflammation is a normal response to injury. The injury is likely to be more when CPB is used. Various markers of inflammation have been studied. Wan[13] reported significantly lower release of Interleukins in the off-pump group. Diegler[14] noted a significantly increased release of complement factors and TNF alpha-receptors in CPB group. Several reports[15, 16, 17] are available with similar conclusions. However, this does not mean that inflammatory response is completely eliminated by avoiding CPB. Fransen et al[18] measured various markers like bactericidal permeability increasing protein, interleukin 6, lipopolysaccharide binding protein and C- Reactive protein in 8 patients in CPB group and 8 patients in OPCAB group. They found that the acute phase reactants were present in both the groups but the neutrophil activation was more in the CPB group. This establishes clearly that inflammatory response is not entirely due to CPB and is predominantly due to tissue trauma, which is inseparable from any surgery. Menasche[19] observed that this difference in the degree of inflammation in between the two groups might be clinically relevant in patients with renal failure, severe left ventricular dysfunction and major extracardiac co-morbidities.

## NEUROLOGICAL FUNCTION

Gross neurological deficits following cardiac surgery have become rare due to developments in perfusion, anaesthesia, monitoring and surgical techniques. However subtle neuropsychological changes develop in 20-60% of patients[20, 21]. The cognitive dysfunction may persist in 25-30% of patients at 8 weeks after the operation and diminish only slightly at one year[22]. The causes of these neurological events are multifactorial. It could be microembolisation,

hypoperfusion or alteration in blood-brain barrier[23, 24]. A prospective randomised study from Bristol Heart institute[25] compared the S100 protein release and neuropsychological outcome at 12 weeks between a group of 30 patients in conventional CABG and an equal number of OPCAB. They concluded that the biochemical damage in the brain is more in CPB patients but the clinical status at 12 weeks was no different. They surmise that the subtle brain damage as evidenced by increased S100 protein release may not be relevant in low and moderate risk patients but their importance in high risk patients of advanced age and pre-existing neurological deficits need to be evaluated. Another report [26] also corroborates this finding. Two recent reports[27, 28] contradict this finding by observing better preservation of neuropsychological function in the OPCAB group. Patel[29] compared three groups of patients viz: 1210 patients on CPB, 520 by OPCAB with aortic manipulation and 597 patients by OPCAB without aortic manipulation and demonstrated by multiple logistic regression analysis that CPB and not aortic manipulation is a risk factor for focal neurological deficit. Stamou et al[30] compared 2320 OPCAB patients with 8069 on-pump patients and found that the on-pump patients are 1.8 times more likely to suffer a stroke compared to OPCAB patients. An editorial[31] written in 1999 opined that avoidance of neurological events should not be an excuse for resorting to OPCAB if it is traded for lesser revascularisation. With more reports coming in of equal degree of revascularisation in both groups, this opinion may need to be revised. Murkin[32] feels epiaortic scanning will be very useful to plan aortic manipulation during surgery and influence the neurological outcome. The areas of loose atheromatous plaques, which are likely to embolise by manipulation of aorta are better picked up by this technique than by transesophageal echo. Digital palpation of aorta is the least reliable but sadly the most practised method to assess the aorta.

## MYOCARDIAL FUNCTION

In the conventional CABG, there is invariably global myocardial ischemia. Cardiac Troponin I is considered to be a specific marker of myocardial injury[33]. Wan13 and Ascione[34] found a significantly higher release of Troponin I in CCABG. CK-MB also is found to be higher in on-pump patients. In clinical practice, we have found the need for inotrope to be less in OPCAB patients[35]. The superior myocardial preservation in OPCAB patients may be due to elimination of global myocardial ischemia and better subendocardial blood flow because of the beating heart with pulsatile blood flow and less myocardial tension.

## RENAL FUNCTION

Mean urinary creatinine excretion decreases significantly during CPB in contrast with OPCAB group[36]. A prospective study by Loef et al[37] demonstrated more renal dysfunction in CPB group. The deleterious effects of CPB on renal function are found to be more relevant in the high-risk group of patients with pre-existent renal dysfunction and Diabetes[38]. In a study of 3250 consecutive patients from Bristol[39], 253 patients were identified with a preoperative serum creatinine of more than 150 micromoles/L. 202 were operated on pump and 51 were OPCAB. They concluded that OPCAB reduces the likelihood of acute renal failure in these patients with non-dialysis dependent renal failure. However, a recent randomised study from Netherlands[40] did not find the renal function any different at the end of 1 month of surgery in between the two groups.

## PULMONARY FUNCTION

Pulmonary dysfunction following cardiac surgery is multifactorial in origin being ascribed to anaesthesia, surgical trauma, CPB and various drugs used during surgery. OPCAB eliminates the component of CPB induced inflammatory cascades. So, it is logical to expect a better lung function in the postoperative period. The reduced usage of blood products in OPCAB may also add to the beneficial effect. However, a prospective randomised study on pulmonary gas exchange[41] observed a similar degree of pulmonary dysfunction. A study from Oxford[42] evaluated the effects of CPB and use of internal mammary artery on respiratory dysfunction and found no significant difference. A more recent report from Turkey[43] compared conventional CABG and OPCAB and MIDCAB in patients with COPD and found that OPCAB produced less reduction of FEV1 measured at 1-month follow up. Kochamba et al[44] compared the gas exchange, lung compliance and shunting in a prospective randomised study and found that there was no difference in gas exchange and compliance but shunting was less in the OPCAB group. So at present the evidence is in favour of causes other than CPB to be important in producing pulmonary changes. Resorting to OPCAB for the sake of preserving lung function is not yet supported by available literature.

## HAEMATOLOGICAL CHANGES

Several studies have shown a significantly less blood loss and therefore lesser use of blood products in OPCAB patients. The reexploration rate also is less. The reasons for

this are many. The damage to the formed elements of blood by contact activation in extracorporeal circulation is avoided. The dose of heparin used is approximately half of the dose used for CPB. The target Activated Clotting Time (ACT) for CPB is more than 400 secs but in OPCAB cases it is maintained at about 250 secs. The hypothermia associated with CPB promotes coagulopathy. There is a report[45] of procoagulant activity after OPCAB, which may cause early graft thrombosis.

## COMPARATIVE STUDIES

Some of the issues to be considered in the evaluation of OPCAB are Safety, Cost, Adequacy of revascularisation, patency of the grafts and long-term outcome. There is a surfeit of reports in current literature about OPCAB and the above issues will be answered by gleaning at a few of them. Most of these reports are retrospective non-randomised observational studies. The findings in the earlier phase of this operation are not comparable to the situation at present because OPCAB performed in the beginning of this era is a totally different operation compared to what is practised at present. The state of the art stabilisers have made this operation very much easier, safer and reproducible by any surgeon with average skills. So I will restrict this analysis of papers to those published in the last 4 years.

Iaco from the Calafiore group in Italy[46] reported in 1999 their experience comparing 472 cases off-pump with 290 on-pump cases and concluded that there was no difference in primary endpoints (mortality, peri operative myocardial infarction, stroke and other major complications). But those done off-pump had fewer complications especially when they were females, aged more than 70 years or having unstable angina. They found a significant difference in secondary endpoints such as blood drainage, blood usage, ICU and hospital stay. The mean number of grafts was 2.3± 0.8 and 3.1± 1.0 in the off and on pump respectively. The same group[47] reported in 2001 a comparison of 919 patients done off-pump with 924 patients done on-pump and found that CPB was a risk factor for early mortality and peri operative MI both at univariate analysis and stepwise logistic regression analysis. Arom[48] compared 350 OPCAB patients with 3171 on-pump patients. They found both procedures equally safe and a trend of increased angina and reinterventional procedures in OPCAB group at short-term follow-up of 1 year. On comparison of results in the high-risk group, there was a significant reduction in complications in the OPCAB group. The retrospective study of Puskas[49] compared 200 off-pump with 1000 on-pump cases. They found that off-pump procedure reduces hospital cost, length of stay and morbidity with a significantly less revascularisation rate in OPCAB. The angiographic study of OPCAB cases showed a patency rate of 98.8% with 100% patency of all the 163 LIMA grafts. Plomondan et al[50] studied retrospectively the data of the Department of Veteran Affairs continuous improvement in cardiac surgery program. They noted that the off-pump approach reduced the risk-adjusted mortality and morbidity by comparing the records of 680 OPCAB patients with 1733 on-pump cases (0.52 and 0.56 multivariable odds ratios for off-pump versus on-pump, respectively $p<0.05$).

Using The Society of Thoracic Surgeons National Adult Cardiac Surgery Database, Cleveland et al[51] studied the records of 118,140 on-pump cases and 11,717 OPCAB cases done in 126 experienced centres in USA. The risk-adjusted mortality was 2.9% for on-pump and 2.3% for OPCAB ($p<0.001$). The OPCAB approach reduced major complications from 14.15%to 10.62%($p <0.0001$). This improvement in outcome is noted despite the fact that the study includes the results of centres performing as little as 20 OPCAB cases per year. When the experience of larger centres is compared, the results may show a wider difference. However, the completeness of revascularisation in the OPCAB group is not available in this study. In contrast, another multicentric study from Northern New England does not find any significant superiority with off-pump technique. Hernandez et al[52] compared 1741 OPCAB patients with 6126 on-pump patients done in four centres. They did not find any difference in mortality, stroke, mediastinitis, or bleeding despite the fact the on-pump group consisted of more patients with ejection fraction of <40% or be urgent or emergent operations. The need for IABP was less in the OPCAB group. Atrial fibrillation was significantly less in OPCAB group. Magee et al[53] conducted a review of results of two major hospitals in Dallas and Washington. They compared 6466 patients done on pump with 1983 OPCABs. The mortality in the on-pump group was higher (3.5vs 1.8%) despite a lower predicted risk. Meherwal et al[54] analysed the results in the high-risk group by comparing 1075 OPCAB with 2312 on-pump patients. The study demonstrated that OPCAB can be performed safely in this group of patients but failed to show any significant superiority with this technique in contrast with the findings of Arom[48] .A recent report[55] of 1 year follow-up study in the New England Journal of Medicine failed to show any difference in outcome but for a 14% cost-savings in the OPCAB group.

All the papers referred to above are retrospective and observational studies. In the era of evidence-based medicine, we need to analyse our results and arrive at a conclusion based on accepted scientific methods. A randomised control trial will be the answer. But, there are a lot of practical difficulties in this method. OPCAB is not a standardised procedure. There are a lot of variations in the practice of this technique. Since the overall incidence of complications following CABG have come down remarkably the minimum required number of patients in both arms of the study will have to be in the order of many thousands. I will cite a few randomised studies, albeit in small numbers. Czerny et al[56] studied 40 low-risk patients assigned randomly to each arm. They had a high conversion rate to CPB of 22.5%. 65% of OPCAB and 85% of on-pump patients received complete revascularisation. There was no difference in the primary endpoints (death, stroke, M.I.) or in incidence of AF, bleeding, ICU and hospital stay. Apart from the small number and low-risk patients this study was done at an early stage of OPCAB experience of the team as mentioned by the authors. This is a serious limitation of this study. Van Dijk et al[57] of the Octopus study group published a multicenter randomised study involving 281 patients. There was no difference in primary endpoints. Both groups had complete revascularisation. Blood was used in 3% of OPCAB and 13% of on-pump patients ($p<0.01$). Release of CPK-MB was 41% less in OPCAB ($p<0.01$). At 1 month follow-up patients in both groups did equally well. The Beating Heart against Cardioplegic Arrest Studies is a randomised study from United Kingdom on 401 patients[58]. Mortality and completeness of revascularisation were similar. They observed a significant difference in the incidence of inotrope requirement, drainage, blood usage, arrhythmias, intubation time, chest infection, ICU and Hospital stay. At follow-up of 29.3± 7.4 months, they did not observe any difference in late mortality, cardiac related events or coronary re-interventions.

## CONCLUSIONS

Based on available evidence, it is clear that OPCAB is safe and practical with comparable midterm outcomes. The results are reproducible by any average surgeon. The claim that this technique completely eliminates all the problem areas of CABG is unfounded. The painting of CPB as the most horrendous villain in Post-CABG complications is not substantiated well. There is a definite trend towards lesser morbidity especially in high-risk groups even if not statistically proven uniformly. The myocardial necrosis is significantly less with OPCAB. The neurological complications may not differ unless OPCAB is done with a “no-aortic manipulation” technique. This method is definitely contraindicated in acutely unstable patients, in irritable hearts with frequent arrhythmias, heavily calcified arteries, very deeply placed intramyocardial vessels, grossly dilated hearts and in diffusely diseased small vessels. The rate of application of this technique will vary according to the experience, judgement, adventurousness and bias of the surgeon. It is important to realise that if the patient's interest will be better served by resorting to on-pump method, the conversion to CPB must be done electively without waiting for acute deterioration of hemodynamics to precipitate an emergent conversion. Ego and bigotry to persist with off-pump method in the face of adverse clinical situations is a betrayal of faith that the patient has placed in the surgeon and should not be misconstrued as courage or heroism on the part of the surgeon.

Even though randomised trials are not yet available to prove any superiority of this technique, it should be practised in all patients where its benefit is likely. Till we get the results of large studies done scientifically, we will not know whether off-pump bypass surgery is a step forward, backwards, or sidewards[59].

## CORRESPONDENCE TO

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