Review

Off-pump coronary artery bypass grafting: the myth, the logic and the science

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Summary

Coronary artery bypass grafting is a highly investigated surgical procedure and yet continues to attract rigorous research aimed at reducing observed and potential morbidity and mortality. Improvements in perioperative care, surgical technique and methods of attenuating the untoward effects of cardiopulmonary bypass have resulted in improved clinical outcome of on-pump myocardial revascularisation. The continuing drive to improve clinical outcome and compete with the ever-evolving non-surgical methods of myocardial revascularisation has provided the incentive for the rebirth of off-pump coronary artery bypass grafting (OPCAB). The appeal of avoiding cardiopulmonary pass with its direct and indirect physiological insult, the prospect of improved clinical outcomes, and the favourable economic impact gives OPCAB the potential of preference that may mark the dawn of a new era in our search for the optimal surgical strategy for the treatment of coronary artery disease. However, there are very genuine and serious concerns with this surgical technique. The logical appeal of OPCAB can only be validated by scientific scrutiny otherwise it would remain a myth.

This comprehensive review examines the "physiological cost" of cardiopulmonary bypass, the theoretical and clinical benefits of OPCAB, the concerns with this technique and strategies for maximizing the benefits. And in so doing, explore the myth, the logic and the science of this surgical technique.

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1. Introduction

Coronary artery bypass surgery before the era of cardiopulmonary bypass (CPB) was bedevilled by a limited understanding of the pathophysiology of myocardial ischemia, technical operative difficulty, and poor clinical outcome [1]. CPB sparked a monumental advance in cardiac surgery in the last 50 years that would otherwise be impossible. Today, coronary artery bypass grafting (CABG) and CPB are among the most scrutinized surgical techniques, and continue to evolve through research. The deleterious effects of CPB are well researched and the adverse clinical consequences clearly defined. Avoidance of CPB therefore, has the potential of obviating the clinical and 'sub clinical' manifestations of CPB-related morbidity, and it is this appeal that impelled the renaissance of off-pump coronary artery bypass grafting (OPCAB). OPCAB is currently the focus of scientific scrutiny and current medical literature contains a staggering amount of research related to this technique. Indeed, CABG has come full circle back to its pristine technique; on the beating heart!

This review gives a comprehensive, in-depth and critical appraisal of OPCAB with the purpose of exploring the logic, dispelling the myth, and providing a scientific paradigm using available literature.

2. On-pump CABG: a pyrrhic solution for coronary artery disease?

CPB brings relative technical ease to cardiac surgery, tremendously facilitating surgery inside, and on the surface of the heart. Unfortunately, in so doing it induces a whole-body inflammatory response that is capable of causing
devastating morbidity and mortality. The extent and severity of the deleterious effects of CPB has been severally described as ‘systemic inflammatory response syndrome’ (SIRS), ‘post-pump syndrome’ (PPS), ‘post-perfusion syndrome’ (PPS) and ‘adult respiratory distress syndrome’ (which actually refers to the respiratory component of a more generalized dysfunction). Although this phenomenon has been extensively investigated and continue to be the focus of ongoing research [2–12], there are still gaps in our understanding of the pathophysiology [9,10]. SIRS is a complex response resulting from the stimulation of both cellular and humoral normal defense mechanisms and involving several pathways. The triggers include surgical trauma, contact of blood with non-physiological surfaces in the CPB machine, ischemia and reperfusion injury. Activation of a cascade of physiological mechanisms involving the complement, coagulation, kallikrein, and fibrinolytic systems, and cellular interactions of leucocytes, platelets and endothelial cells result in the elaboration of mediators such as cytokines, nitric oxide, oxygen free radicals, the nuclear factor κB and cell adhesion molecules. The direct physiological insult from the CPB-related systemic inflammatory response has been associated with postoperative multi-organ dysfunction involving, cardiac [11], vascular [12,13], pulmonary [14], neurologic [15], renal [16], gastrointestinal [17] and haematologic [4] systems.

As systemic inflammatory response to CPB has the potential of engendering a constellation of clinical, biochemical and radiological manifestations of multi-organ dysfunction, attenuation of the complex multi-faceted response can have tremendous prognostic implications. To achieve this, and possibly eliminate the complications associated with CPB, many different modifications and refinements of the technique with and/or without pharmacotherapy continue to be the focus of evolving strategies. Heparin-coated circuits [18,19], pulsatile flow [20], normoxia [21], normothermia [22], biventricular bypass without an oxygenator [23], leukocyte and platelet depletion [24], and total minimal extracorporeal circulation [25] are some of the techniques reported. Pharmacological manoeuvres that have been utilized to decrease SIRS include corticosteroids [26,27], aprotinin [26,28], phosphodiesterase inhibitors [29], sodium nitroprusside [30], antioxidants [31], monoclonal antibodies for the inhibition of complement [32,33], neutrophil adhesion molecule blockade, and the inhibition of nuclear factor κB (NF-κB) [34–36]. Various combinations of these methods have been tried, however the experience with most of these strategies has not been entirely satisfactory [27,40,41] and SIRS still poses a postoperative management challenge. It has been suggested that these humoral and cellular responses may be genetically determined [10] which may explain the variability in clinical manifestation of morbidity [42].

Implicit in the technique of CPB is non-pulsatile flow and microemboli which also contribute to end-organ dysfunction. Ultimately some degree of end-organ dysfunction, often in the short-term and seldom in the long-term, seems to be the inevitable price to pay for on-pump CABG. However, this does not always translate into clinical morbidity, particularly if the patient is optimised perioperatively.

3. Off-pump CABG: theoretical advantages?

Even though beating heart coronary surgery predates CPB, it was rapidly off staged by on-pump CABG soon after the invention of the heart–lung machine. The perseverance of a few with OPCAB, mainly for economic reasons later became the credible base for the resurgence of interest. Favaloro [43], Trapp [44], Benetti [45] and Buffolo [46] and their associates made pioneering contributions to OPCAB. The major incentive for OPCAB is the avoidance of CPB and its adverse physiological effects.

3.1. Avoidance of cardiopulmonary bypass

It is logical to suppose that avoiding CPB would abolish the SIRS and its untoward physiological impact. Gu et al. [47] investigated the inflammatory response with OPCAB, and found that complement activation and consequently systemic inflammatory response occurred (due to surgical trauma) but the extent and severity were curtailed. Comparison with on-pump CABG confirms a limited and less severe form of inflammatory response. Strüber [48] and Matata [49] and their coworkers reported significant increases in the levels of specific biological markers of inflammation following on-pump CABG compared to OPCAB. The inflammatory indicators that were evaluated in both studies and their results are summarized:

- Activated complement factor 3a (C3a) demonstrated between 5- and 12-fold rise over the preoperative level after commencement of CPB, and minimal rise in the OPCAB patients.
- Prolinflammatory interleukin 8 (IL-8) increased 5-folds with CPB whilst the level was only slightly altered with OPCAB.
- Tumor necrosis factor α (TNF-α) peaked 24–48 h after CPB at a significantly higher value compared to OPCAB patients who had no increase. Tumour necrosis factor receptors 1 and 2 were elevated to three times their preoperative level only with CPB.
- Different markers tested in each study (interleukin 6 and plasma elastase) were significantly elevated with CPB. OPCAB patients showed a blunted response.

Additionally, the prospective randomised trial of Matata et al. [49], showed a disproportionate increase in the indicators of endothelial injury (sE-selectin) and oxidative stress (lipid hydroperoxides, protein carbonyls, protein nitrotyrosine) in favour of on-pump CAGB. Ascione and
Diegeler and colleagues [51] investigated SIRS in patients undergoing CABG, standard techniques of CPB were employed without cardioplegic arrest. In a comparative study, Diegeler and colleagues [51] investigated SIRS in patients who had one dose of 4,000,000 U of aprotinin before CPB, and OPCAB with full sternotomy and left anterior thoracotomy. The study failed to demonstrate a consistent pattern of change in the inflammatory markers (C3a, IL-8, and neutrophil elastase) after CPB for up to 24 hours, and a blunted ‘mirror-image’ response in the OPCAB group. In all these studies comparing off-pump and on-pump CABG, standard techniques of CPB were employed without cardioplegia. The anti-inflammatory pre-treatment with aprotinin may have influenced these findings.

The other variables of CPB such as haemodilution, non-pulsatile flow, and aortic cross-clamping, which may act in concert with SIRS to increase postoperative morbidity, are eliminated by the avoidance of CPB. With the increased use of OPCAB in the treatment of coronary artery disease, the technique of CPB has come under rigorous investigation with a renewed enthusiasm at decreasing its harmful effects. A prospective randomised controlled trial comparing OPCAB with other SIRS-attenuation strategies is therefore warranted to determine if the amelioration of systemic inflammation is better with OPCAB.

3.2. Myocardial preservation

Adequate myocardial preservation is crucial in CABG operations. Preoperative resuscitation of ischemic myocardium enables recruitment of hibernating myocardium and forms an important component of any myocardial protection strategy. The intraoperative strategy varies (within physiological boundaries) as much from patient to patient as it is from surgeon to surgeon, to the extent that a good clinical outcome becomes the ultimate determinant of the optimal strategy. Even with the same surgeon, the strategy is adapted to the patient and clinical scenario that a prescriptive regimen is not standard. The objective of intraoperative myocardial preservation is to enable efficient myocardial energy management by reducing cardiac metabolic demands on the one hand, while improving myocardial oxygen supply and utilisation on the other [52].

In on-pump CABG, cardioplegia or cross-clamp fibrillation are conventional methods of intraoperative myocardial protection. Cardioplegia favourably affects myocardial energy metabolism but results in the alteration of both the intra- and extracellular milieu and, together with CPB, can precipitate changes in cardiac performance postoperatively [53]. Cross-clamp fibrillation can increase the endocardial viability ratio and lead to similar changes in cardiac function. In both strategies of myocardial protection, a period of global myocardial ischemia is followed by reperfusion with oxygen-rich blood predisposing to reperfusion injury which manifests as myocardial stunning and arrhythmias in the early postoperative period.

Since deliberate induction of global ischemia is unnecessary in OPCAB, it is logical to suppose that iatrogenic biochemical injury to the myocardium would not occur. More so, the blunted inflammatory response with avoidance of CPB is characterised by low production of IL-8 which is involved in myocardial injury [11]. In fact, Atkins et al. first suggested that OPCAB preserved cardiac function in 1984 [54]. In different prospective randomised studies, Ascione [55], Penttilä [56], Van Dijk [57], Czerny [58], Bennetts [59], and Masuda [60], and their collaborators reported minimal change in the biochemical markers of myocardial injury (troponin T and/or creatinine kinase-MB isoenzyme), and in some cases, better myocardial function after OPCAB compared to on-pump CABG. Changes in myocardial metabolism indicative of oxidative stress due to local ischemia when the target coronary artery is occluded to enable visualisation for distal anastomoses have been reported in OPCAB [49,61]. Compared to on-pump CABG, OPCAB is associated with better myocardial energy preservation, less oxidative stress and minimal myocardial damage [56,62]. However, emerging evidence suggests that intraoperative myocardial protection in OPCAB can provide an added advantage [63,64]. In their pioneering report, Trapp and Bisarya [44] gave an exquisite description of coronary perfusion and the instantaneous improvement in the ECG and blood pressure during OPCAB. Vassiliades et al. [65] compared active coronary perfusion using a perfusion pump, with passive perfusion by a cannula connected from the aorta to the graft, and no coronary perfusion, after the distal anastomosis in a randomised clinical trial. They found lower troponin I levels with active and passive coronary perfusion, but cardiac performance was better with active coronary perfusion. The use of intracoronary shunt during OPCAB has also been shown to preclude left ventricular dysfunction [66].

Reperfusion injury can occur from regional ischemia due to a combination of underlying coronary obstructive pathology, stabilization and anastomotic techniques, compounded by episodes of hypotension which precede revascularisation. The precarious normoxic and normothermic passive coronary perfusion may be insufficient to protect against myocardial damage in such clinical scenarios.

The concept of myocardial protection in OPCAB is less tedious. In most cases passive coronary perfusion with intracoronary shunts will suffice, but in the presence of heightened cardiac risk such as recent acute myocardial ischemia or infarction, and severely impaired left ventricular function active coronary perfusion is advantageous especially in multi-vessel revascularisation.

Myocardial protection during either method of myocardial revascularisation is an area of active research, and ongoing experiments focus on modifying endothelial...
response to vascular injury [67]. Some of the methods reported are the result of animal experiments investigating ischemic preconditioning, and include the use of L-arginine [68,69], prostaglandin E2 [70] and adenosine [71], and induction of heat stress proteins [72].

4. OPCAB: areas of concern

The wide variation in adoption rate of OPCAB within one institution of 1–96% in a 6-year period portrays the extreme disposition of surgeons with the practice of OPCAB [73]. Over the years, OPCAB has generated widespread interest and attracted varied response in the cardiac community and beyond [74–81]. The reinvention of this technique has introduced a different set of genuine concerns that need to be addressed convincingly.

4.1. Haemodynamic changes

Exposure of the coronary artery target sites requires the heart to be lifted, rotated, dislocated and displaced producing a distortion of cardiac geometry and consequently haemodynamic fluctuations frequently occur. As a result, the early reports of OPCAB described single or double grafts limited to anterior target sites. The corrective measures for these haemodynamic changes include volume loading, trendelenberg positioning, and displacement of the heart into the opened right pleura, use of inotropes, vasopressors, vasodilators, intraaortic balloon pump, and right heart circulatory support [82,83]. These measures together with temporary suspension of cardiac manipulation often suffice to restore good haemodynamics, but occasionally severe and prolonged deterioration unresponsive to corrective measures occur. This is described as haemodynamic collapse or failure, and is usually associated with evidence of acute myocardial ischemia and accounts for most conversions to on-pump, which ranges from 0 to 11% in most series [73,84–86].

The iatrogenic haemodynamic changes that occur during OPCAB and the underlying mechanisms have been investigated and characterized [85,87–90] (Table 1). There is a decrease in stroke volume, mean arterial pressure, cardiac output and, an increase in the atrial pressures, ventricular end diastolic pressures and pulmonary arterial pressure. The mechanisms identified include significant regional systolic dysfunction, restrictive diastolic filling, compression of the ventricles and myocardial ischemia. These changes are severe for the positioning for circumflex and posterior descending arteries. There is an acute decrease in ventricular performance which is usually transient and reversible, and the haemodynamic sequel well tolerated.

The haemodynamic impact of myocardial stabilization systems has been elucidated. Animal experiments have shown that mechanical stabilisation during OPCAB invokes only a minimal and reversible decrease in cardiac output due to compression, and negligible tissue injury [91]. Mueller et al. found no change in the haemodynamics during exposure of the posterior and anterior wall arteries, and only marginal change for the lateral wall artery with a ‘no compression’ technique [92]. It has been suggested that the use of left ventricular apical suction device for cardiac positioning provokes less haemodynamic instability compared with pericardial retraction sutures [93].

The fluctuations in the haemodynamics that occur during OPCAB can usually be successfully corrected without causing a significant adverse impact on the end-organ function, especially neurological function. However, it is speculated that a steep trendelenberg positioning by increasing the internal jugular venous pressure, can compromise cerebral perfusion [94]. When haemodynamic collapse occurs, the prognosis is probably guarded. Vassiliades and colleagues [86] reported a good outcome in more than 90% of patients converted to on-pump because of haemodynamic collapse, but Lacò et al. [75] observed high mortality and complication rates in a patient group converted to CPB for haemodynamic, electrophysiological and technical reasons.

4.2. Handling of the heart

The heart arrested by cardioplegia is usually flaccid, easy to handle and position to obtain optimum exposure for the distal anastomosis. On the contrary, the beating heart is not collapsible, difficult to hold in position and provides a constantly moving target, and therefore threatens to
compromise the finesse required for distal anastomosis. Pharmacological agents such as β-blockers to reduce the heart rate, deep pericardial retraction sutures or retrocardiac swabs/slings or left ventricular apical suction device to present the heart and coronary artery to the surface, and mechanical restrain of target sites with a stabilization device to abolish active percussion, are some of the methods used to overcome this technical challenge. The past 5 years have seen a rapid increase in the manufacture of different types of mechanical cardiac stabilisation devices contrived and designed to address this challenge of OPCAB. Two stabilisation systems: compression (such as Genzyme Immobilizer) and vacuum or suction (such as Medtronic Octopus) stabilisers, are in common use and compare fairly well in effectiveness. What the compression stabilisers lose in haemodynamic compatibility, is gained in a steadier operating field [75]. These devices leave a limited temporary superficial bruising on the heart, without causing a significant rise in markers of myocardial injury. All graftable coronary targets can be reached using mechanical myocardial stabilisation during coronary bypass surgery without CPB [58].

4.3. Quality of distal anastomosis

Performing vascular anastomoses on small arteries on a beating heart can be a daunting and frustrating adventure, and so far, no available method of target vessel stabilisation can achieve a steady bloodless field comparable to a cardioplegically arrested heart. This was a major concern with OPCAB [95,96,97]. The beating heart with a bloody operating field poses a major challenge to delicate tissue handling, and casts a shadow of uncertainty about the quality of the distal anastomosis. Also, the use of coronary snares has a potential of causing endothelial dysfunction with a predisposition to thrombosis which can compromise the distal anastomosis. In fact it has been suggested that OPCAB has lower patency rates [98]. However, with the application of effective target vessel stabilisation, and efficient visualisation systems the early and mid-term patency of OPCAB is encouraging [99,100] and comparable to on-pump CABG [101–107]. Jatene et al. [104] showed that the introduction of epicardial stabilisation system resulted in a commanding improvement in early postoperative patency rates. Puskas [106] and associates reported an impressive patent rate of 98.8% at the time of hospital discharge. Five of 421 grafted vessels were occluded, and three of these were related to preoperative hypercoagulability states.

4.4. Incomplete myocardial revascularisation

Early reports of OPCAB in the literature were uniformly consistent in the low number of grafts per patient [44,46]. The selection of patients with mainly single-vessel disease may, in part, explain this finding. But the persistence of lower average number of grafts in later comparative studies [108,109] places OPCAB in a contentious position which detracts from its potential benefits [77]. In their retrospective study, Gundry and colleagues [108] reported a significantly lower mean number of grafts, and a two-fold increase in cardiac re-intervention rate during a 7-year period with off-pump performed without cardiac stabilisation, compared to on-pump CABG. This finding has been corroborated by other reports [58,109], and exemplifies incomplete revascularisation with OPCAB. Effective cardiac retraction, stabilisation and visualisation systems with patient positioning enables grafting of all graftable targets [58,110] making complete myocardial revascularisation (CMR) attainable in OPCAB [111,112], and this has been demonstrated in a recent prospective randomised study [113]. However, incomplete myocardial revascularisation with OPCAB is still reported in retrospective studies [58,105,114]. Technical difficulties due to small calibre of target vessels or their intramyocardial course, poor exposure of target sites, precarious intraoperative haemodynamic state, electrophysiological instability and inexperience of the surgeon are some of the reasons for incomplete myocardial revascularisation [58,114]. The concept of revascularisation of “ischemic zones” in OPCAB [81] is an anecdotal evidence of incomplete myocardial revascularisation and while this may be accepted for a high risk elderly patient, it may not be appropriate for the majority of patients requiring myocardial revascularisation.

5. OPCAB: the outcome

The clinical benefit of avoiding cardiopulmonary has attracted many studies. While there are many retrospective studies reporting on the outcome of OPCAB, few randomised trials have been conducted to investigate these findings.

5.1. Safety

Morbidity and mortality rates are commonly accepted as indicators of the safety of a surgical procedure, but unfortunately they do not take into account intraoperative variables and technical difficulties that may be potentially fatal. This is nowhere more relevant than in OPCAB. But for the lack of a better alternative, these quantifiable markers of surgical outcome are still used to assess the safety of surgical operations.

There is burgeoning evidence that OPCAB is safe in a select group of patients [109,115,116], and the selection criteria are constantly expanding [117]. The rates of morbidity and mortality compare well with on-pump CABG [57,118], and some retrospective studies even report better outcomes [75,119]. Further evaluation in a prospective
randomised study of comparable groups of patients is necessary.

5.2. High surgical risk patients

OPCAB has been demonstrated to offer prognostic advantage over on-pump CABG in patients with exaggerated surgical risk from complicated coronary artery disease and/or debilitating co-morbidities [109,120–124]. More importantly, the preoperative optimization of high risk patients plays a crucial role in determining the clinical outcome for both methods of myocardial revascularisation.

Acute myocardial infarction and depressed left ventricular function constitute a high surgical risk with on-pump CABG, because the myocardial damaging effects of CPB and the often cumbersome and, inefficient intraoperative myocardial protection do not prevent immediate postoperative cardiac dysfunction [52,125,126]. OPCAB achieves comparatively better outcomes in patients who have myocardial revascularisation soon after recent AMI [127,128]. Mohr et al. [129] reported a mortality of 1.7% with 1- and 5-year actuarial survival rates of 94.7 and 82.3%, respectively, in a series of 57 patients in which 56% had emergency surgery within 48 h of acute myocardial infarction and some were in cardiogenic shock. OPCAB decreases the operative risk in the presence of impaired left ventricular function [130,131].

Preoperative renal impairment is an independent predictor of poor prognosis after on-pump CABG [132]. OPCAB preserves renal function better than on-pump CABG [62,133], and available evidence favours the preferential use of OPCAB for patients with chronic renal failure for a better early clinical outcome [134].

Patients with coexisting chronic obstructive airway disease derive better early clinical benefit from CABG performed without CPB compared with on-pump surgery [116,135], although in low-risk patients, OPCAB induces impairment of the mechanics of the respiratory system, lung and chest wall similar to on-pump CABG [136].

Elderly patients are considered high risk surgical patients because of their reduced functional capacity and the presence of co-morbidities. Correspondingly, the outcome of on-pump CABG in this group is characterized by increased morbidity and mortality [137–139]. Interestingly, OPCAB has been shown to improve the clinical outcome in this growing population of surgical patients [140–143]. Specifically, the incidence of stroke, perioperative myocardial infarction, duration of mechanical ventilation, blood transfusion, length of intensive care and hospital stay, and mortality are decreased.

It would be expected that the advantages of retrograde cardioplegia in reoperative CABG on-pump, which is not available in OPCAB, would confer favourable prognostic implications. On the contrary studies are reporting less adverse outcomes with avoidance of CPB [144–146]. Probably, the combination of this method with minimal surgical access and limited intrapericardial dissection without extensive cardiac manipulation, employed in these studies may contribute to the improved results. Further research is needed to clarify this.

5.3. Intermediate and low-risk surgical patients

Growing confidence in the techniques of OPCAB and the favourable influence on clinical outcome has provided the impetus for extension of this approach to intermediate and low-risk patients [117,147,148]. A randomised clinical trial [57] comparing the clinical outcome at 1 month between OPCAB and on-pump CABG in low-risk patients, found no difference except for less blood product usage in the OPCAB group. After 1 year, the freedom from death, stroke, myocardial infarction, and coronary re-intervention for both techniques were similar (90.6% on-pump versus 88% OPCAB), and there was no difference in graft patency rates (93% on-pump versus 91% OPCAB) [149]. Compared with percutaneous transluminal coronary angioplasty with stenting, a prospective randomised trial of single-vessel left anterior descending coronary artery stenosis found OPCAB performed through a small left anterior thoracotomy, to substantially decrease the incidence of major adverse cardiac and cerebrovascular events, severity of recurrent angina and need for anginal medication, and target vessel re-intervention [148].

5.4. Postoperative morbidity

It has been suggested that CPB is a risk factor for postoperative morbidity and mortality [150], and a better clinical outcome reported with OPCAB [150–152]. On the other hand, prospective randomised clinical trials have not found any significant difference in morbidity and mortality between the two techniques [57,113,153]. However, both prospective and retrospective studies have reported a reduction in the need for mechanical ventilation [45,154], postoperative blood loss and need for transfusion [153,155,156], postoperative complications [114,141,157], length of intensive care and hospital stay [152,158], and consequently the cost of treatment [159], with OPCAB. A synopsis of the morbidity reported in large retrospective studies is illustrated in Table 2.

CPB has been described as an independent predictor of impaired cognitive brain function after CABG [160,161]. By avoiding micro- and macro-emboli from the CPB circuit, and manipulation of artheromatous aorta at cannulation and cross-clamping, OPCAB causes less impairment of neurocognitive function [151–163]. In a prospective randomised trial, Diegeler et al. [164] demonstrated a significantly low level of the neurobiochemical marker protein S-100, and low number of high intensity transit signals in the middle cerebral artery with transcranial Doppler ultrasound during OPCAB, with a clinical correlate of 0% postoperative neurocognitive impairment, as opposed to 90% with
on-pump CABG. Zamvar et al. [165] reproduced similar clinical results in another randomised clinical trial. Although it has been reported that the risk of stroke is lowered by OPCAB [166,167], this has not been reproduced in a randomised study. Repeated side-clamping of the aorta at normal systemic pressure for proximal anastomoses in OPCAB creates one of the mechanisms by which on-pump CABG causes embolic stroke. Complete avoidance of aortic manipulation may be advantageous in this regard.

The impact of OPCAB on atrial fibrillation is not clear, as the results of clinical studies are inconsistent. While some studies, observational [73,168] and randomised [169] report a decreased incidence, other comparative studies [150,170,171] and randomised trials [57] showed no difference with on-pump CABG. The effect of avoiding CPB on myocardial electrophysiology is not known, and remains to be determined.

The early experience with OPCAB was bedraggled by incomplete revascularisation and consequently higher incidence of major adverse cardiac events and re-intervention [75,108,109]. Hirose [172] and Calafiore [111,150] and their collaborators found a comparatively lower incidence of major adverse cardiac events and re-intervention with OPCAB, when equivalent extent of myocardial revascularisation, Table 2

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<td>30.8</td>
<td>53.8</td>
<td>57.3</td>
<td>53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reop. bleed</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>OPCAB (%)</td>
<td>2.07</td>
<td>1.9</td>
<td>1.8</td>
<td>3.2</td>
<td>1.7</td>
<td></td>
</tr>
<tr>
<td>ONCAB (%)</td>
<td>2.8</td>
<td>3.4</td>
<td>2.3</td>
<td>2.3</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>Prolonged vent</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>NS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPCAB (%)</td>
<td>4.13</td>
<td>4.6</td>
<td>2.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ONCAB (%)</td>
<td>6.51</td>
<td>10.5</td>
<td>3.5</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>LOS (days)</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>NS</td>
<td>P &lt; 0.001</td>
<td>NS</td>
</tr>
<tr>
<td>OPCAB</td>
<td>4.2</td>
<td>6.14</td>
<td>5.95</td>
<td>7.7</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>ONCAB</td>
<td>4.9</td>
<td>6.97</td>
<td>7.33</td>
<td>7.4</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Mortality</td>
<td>P = 0.016</td>
<td>P &lt; 0.0001</td>
<td>P &lt; 0.001</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>OPCAB (%)</td>
<td>1.4</td>
<td>2.31</td>
<td>1.8</td>
<td>3.1</td>
<td>1.4</td>
<td>0.5</td>
</tr>
<tr>
<td>ONCAB (%)</td>
<td>3.1</td>
<td>2.93</td>
<td>3.8</td>
<td>2.5</td>
<td>2.3</td>
<td>1.2</td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; AMI, acute myocardial infarction; ARF, acute renal failure; CVA, cerebrovascular accident; LOS, length of hospital stay; ONCAB, on-pump coronary artery bypass grafting; Prolonged vent., prolonged mechanical ventilation; Reop. bleed, reoperation for bleeding.

a Risk-adjusted studies.

b Propensity matched cohort study.
which is a substrate for recurrent angina, myocardial infarction, coronary re-intervention and cardiac death, OPCAB may be associated with a higher failure rate in the mid- to long-term.

The rates of specific complications with OPCAB have been reported to be similar to or higher than on-pump CABG in some studies. Gommes et al. [173] reported the occurrence of vasoplastic syndrome in four out of 1014 patients (0.4%). Unfortunately the preoperative details of the patients were not stated. Musleh and colleagues [174] did not find any advantage with OPCAB in the rate of gastrointestinal complications. However, the OPCAB patient group had more risk factors such as previous gastrointestinal surgery, gastric ulcer, smoking, hypertension, and renal dysfunction. Chavanon et al. [175] reported a high incidence of iatrogenic ascending aortic dissection with OPCAB. Side-clamping the aorta at high systemic pressures especially in hypertensive patients can increase this risk.

5.5. Mortality

OPCAB does not increase the early mortality [75,109,168,171]. In fact, a reduction in mortality has been reported in some retrospective studies [150,152]. Mack and associates [73] showed that the introduction of OPCAB in an institution brought about a progressive fall in early mortality. However, the operative mortality was higher with occasional OPCAB operators.

The rates of morbidity and mortality reported in most early observational studies, and case-matched and risk-adjusted comparisons showed lower mortality with OPCAB [73,116,124,151,166,172]. The bias introduced by the selection of patients with less extensive coronary artery disease for OPCAB may explain this finding, as the results of randomised studies have failed to show any difference in mortality rates between off- and on-pump CABG [57,113,153].

6. OPCAB: the future—maximizing the benefits

The techniques of OPCAB are constantly undergoing refinement and many areas of potential benefit are vigorously explored. Increasing number of surgeons are expanding their OPCAB practice and offering many more patients this technique of myocardial revascularisation [118,158]. Notwithstanding, in many centres it is still the operation performed by a select group of surgeons for the select group of patients.

CMR should not be accepted as a trade-off for the benefits of avoiding CPB. Because of the perilous clinical consequences of incomplete myocardial revascularisation [108,109,176,177] any method of surgical revascularisation adopted should strive as much as the clinical scenario permits, to achieve complete revascularisation. The technological advance with OPCAB makes this a practical possibility and it should be pursued in order to offset the uncertainty that clad long-term clinical outcomes. Patient selection is therefore important, and should be ongoing intra-operatively. In this context, the institution of CPB to achieve CMR, even in the absence of haemodynamic collapse or acute myocardial ischemia may be justified.

Advances in OPCAB technology and adoption of creative techniques [178,179] will help to maximize the benefits of OPCAB. Concepts and budding practices like complete avoidance of the aorta (no touch technique) [179,180], atraumatic anastomotic connection [181,182], complete arterial revascularisation [113,172], sutureless anastomosis [183,184], and ultrashort hospital stay [158] will gain wider acceptance. As more low-risk patients undergoing OPCAB have on-table or early extubation, CABG may tend to become less intensive care-dependent.

OPCAB promotes innovative revascularisation strategies. Perfusion-assisted direct coronary artery bypass (PADCAB), a strategy adopted during OPCAB to perfuse the myocardium at suprasystemic pressures and deliver vasoactive drugs and cardioprotective agents like adenosine locally, enhances myocardial protection particularly in multi-vessel revascularisation and poor cardiac risk patients, and facilitates CMR [185].

A new philosophy of avoiding the ventilator as well as the pump seems to interest some OPCAB enthusiasts. With on-table and early extubation becoming routine with OPCAB, some surgeons are now exploring the feasibility of complete avoidance of the ventilator during surgery (awake coronary artery bypass grafting) [186].

OPCAB is frequently performed through minimal or limited surgical access thereby combining its advantages with those of MIDCAB. The beneficial impact of this practice has already been alluded to [144–146,148].

The rapid spread of OPCAB has also exerted a commanding influence on on-pump CABG, and will continue to provide the driving force for innovative practice. Rigorous research into reducing CPB-related complication continues, with clinical studies reporting reduced post-operative morbidity, less use of surgical resources and consequently reduced length of ITU and hospital stay [187,188].

The complimentary roles of both techniques of myocardial revascularisation will be better appreciated and established by the results on multi-centre, prospective randomised controlled clinical trials.

7. Conclusions

The advance that has been made in the surgical management of coronary artery disease has placed us in a vantage position of judging the outcome of our management techniques not only by morbidity and mortality incurred, but
also by the potential of our treatment modality to cause harm. This is why OPCAB has generated renewed, widespread and sustained interest. The resurgence of OPCAB has also ignited a keen enthusiasm in the refinement of CPB techniques and the management of on-pump CABG patients. In most practices, OPCAB is paradoxically dependent on, and guaranteed by the presence of the CPB machine. Therefore the two techniques should be regarded as complimentary, and the advance of one technique will tend to improve the practice of the other. With the encouraging early- to mid-term results demonstrated with OPCAB, the prospect is promising. However, there are still unanswered questions and concerns. We await the results of ongoing prospective randomised controlled trials, the results of long-term patency rates, and rates of major adverse cardiac events, and coronary re-intervention with OPCAB. OPCAB is establishing itself alongside on-pump CABG as a complementary method of surgical revascularisation. Further research into various aspects of the surgical approach is needed before firm conclusions can be reached.

Mythology captivates the gullible.
Logic impresses the simple.
Science, the gnawing of the inquisitive mind relies on proof.
Both mythology and logic motivated pioneer physicians. But science guides current practice.
OPCAB has journeyed through the past and now, by science shall take its place.

References


[60] Masuda M, Morita S, Tomita H, Kurisu K, Nishida T, Tominaga R, Yasu H. Off-pump attenuates myocardial enzyme leakage but not...


