# Off-pump coronary bypass surgery for high-risk patients: only in expert centers?

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**Purpose of review**

Off-pump coronary artery bypass (OPCAB) grafting has been increasingly adopted in an effort to prevent deleterious effects of cardiopulmonary bypass, including the associated inflammatory response, global myocardial ischemia and the risks of aortic manipulation. In many studies, the greatest benefit of OPCAB has been in high-risk patients. This review will summarize the recent literature examining outcomes of OPCAB versus on-pump coronary artery bypass in high-risk subgroups, and will examine the safety of routine application of OPCAB in these patients.

**Recent findings**

Prospective randomized trials have shown that in comparison to on-pump coronary artery bypass, OPCAB reduces perioperative morbidity, but have failed to show a mortality benefit, owing to small sample sizes. However, numerous large retrospective series and meta-analyses have demonstrated a reduction in risk-adjusted mortality and morbidity with respect to the following outcomes: stroke, pulmonary function, renal function, atrial fibrillation, need for early reoperation, blood transfusion requirements, length of ICU and hospital stay, and hospital costs. An even greater benefit has been seen in the following high-risk patients: those with acute myocardial infarction, left ventricular dysfunction, previous history of stroke, renal insufficiency, women, elderly patients, and those undergoing reoperations.

**Summary**

Risk-adjusted outcomes are superior after OPCAB versus on-pump coronary artery bypass for mortality and numerous morbidity endpoints. This benefit is most easily demonstrated in high-risk patient populations.

**Keywords**

high-risk patients, off-pump coronary artery bypass, surgical revascularization

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## Introduction

As off-pump coronary artery bypass (OPCAB) has evolved over the past 2 decades, the procedure has gained popularity in many centers. However, despite favorable evidence from both prospective randomized trials and large retrospective series, the adoption of OPCAB has been variable both worldwide and in the United States, where the percentage of OPCAB has plateaued at approximately 20% (National Society of Cardiothoracic Surgeons Adult Cardiac Database Spring Report 2005). Due to local practice patterns and surgeon comfort level, some centers utilize OPCAB only in low-risk patients. The goal of this review is to summarize the recent literature comparing outcomes of OPCAB with conventional on-pump coronary artery bypass grafting [(CABG), ONCAB], with a particular emphasis on high-risk patient subgroups. In addition, the feasibility of routine application of OPCAB to high-risk patients in medium-volume and low-volume centers will be discussed.

## Comparison of off-pump coronary artery bypass versus on-pump coronary artery bypass in clinical trials

In recent years, outcomes of OPCAB versus ONCAB have been the focus of several prospective randomized trials and numerous nonrandomized studies, which have demonstrated the advantages of OPCAB in both low-risk and high-risk patients.

### Randomized clinical trials

Numerous randomized trials have been conducted over the last decade comparing outcomes of OPCAB and ONCAB [1–7]. In these studies, several important outcome measures have repeatedly favored OPCAB, including lower rates of blood transfusion, decreased

postoperative ventilator time, ICU length-of-stay (LOS), and hospital LOS. Serum markers of myocardial injury [2], systemic inflammation, and neuronal injury [4] have also been found to be lowered in patients undergoing OPCAB. In addition, several trials have demonstrated a benefit in terms of cost savings and resource utilization [3,4].

In early randomized trials of OPCAB versus ONCAB, completeness of revascularization and graft patency were questioned, as several studies indicated that fewer grafts were performed in OPCAB patients [7–9]. The number of grafts, however, is not an accurate measure of completeness of revascularization as it does not account for the number of diseased vessels, nor does it necessarily correlate with the incidence of adverse cardiac events [10]. In the Surgical Management of Arterial Revascularization Therapies (SMART) trial performed at Emory University, the more accurate index of completeness of revascularization (ICOR) was introduced [3]. ICOR was defined as number of grafts performed divided by the number of grafts determined to be ideal by the operating surgeon based on preoperative review of the coronary arteriogram prior to patient randomization. The ICOR was shown to be virtually identical in OPCAB and ONCAB. Several other recent randomized trials have corroborated this finding [5,6,11–14].

Similar to concerns surrounding the number of grafts, graft quality and patency were questioned in the early OPCAB experience due to the inherent technical demands of off-pump anastomoses. Early and late angiographic graft patency has been evaluated in several randomized trials. Whereas one study found a lower graft patency in OPCAB patients at three moths [11], several others have demonstrated equivalent early [4,15] angiographic patency in randomized patients undergoing OPCAB versus ONCAB. Two of these trials used both arterial and venous conduits whereas one was a randomized trial utilizing all arterial grafts [4]. Furthermore, Widimsky *et al.*, Nathoe *et al.*, and Puskas *et al.* have shown equivalent angiographic graft patency at 1 year [7,14,16]. Although not a randomized OPCAB trial, Magee *et al.* [17••] recently reported the 1-year angiographic results of the Prevent IV trial, which also showed equivalent patency between OPCAB and ONCAB. Graft patency has been demonstrated in the long-term as well. Angelini *et al.* [18••] recently presented 7-year follow-up of a randomized trial of OPCAB and ONCAB, including graft patency as detected by computed tomography of coronary angiography. Overall long-term graft patency was outstanding with no difference between ONCAB (89.4%) and OPCAB (89.0%) [18••].

### Nonrandomized trials

Although data from randomized trials provide the most accurate evidence, some end points, including mortality, stroke, and renal failure occur relatively infrequently in patients undergoing isolated CABG. As a result, the randomized trials conducted have been underpowered to demonstrate a significant difference in these endpoints. With respect to these important outcome measures, several large propensity-matched retrospective series and meta-analyses have provided compelling evidence in favor of OPCAB.

The 2004 International Society for Minimally Invasive Cardiothoracic Surgery (ISMICS) consensus conference on OPCAB versus ONCAB resulted in several class I, level A recommendations in all patients undergoing surgical revascularization. The conclusions supported OPCAB as a safe alternative to ONCAB with equivalent mortality and quality-of-life and decreased risk of perioperative morbidity including duration of ventilation, ICU and hospital LOS, and resource utilization [19]. In addition, the evidence (class IIa, level B) suggested that OPCAB should be considered to reduce mortality, perioperative morbidity, and resource utilization in high-risk patients (including those with Euroscore greater than 5, age greater than 75, diabetes, renal failure, left ventricular dysfunction, left main disease, and patients undergoing reoperation) [19].

Recently, a large retrospective analysis of 49 830 patients from the New York state registry reported risk-adjusted outcomes after isolated OPCAB versus ONCAB surgery was done through sternotomy. OPCAB had significantly lower 30-day mortality, as well as a lower incidence of postoperative stroke and respiratory failure. Three-year follow-up revealed that OPCAB patients had a higher rate of repeat revascularization, but survival was equivalent between the two groups [20•]. A similar intention-to-treat analysis of 42 477 patients from the Society of Thoracic Surgeons National Adult Cardiac Surgery database showed a reduction in risk-adjusted mortality, stroke, perioperative myocardial infarction (MI), renal failure, mediastinitis, need for reoperation, atrial fibrillation, and prolonged ventilation among OPCAB patients [21••].

## Evidence in high-risk patients

Much of the prospective data referenced above has focused on low-risk or a mixed group of patients. However, most proponents of OPCAB share the perception that its greatest benefit may be seen in high-risk patients. This is important, as patients referred for surgical revascularization are increasingly older with greater comorbidities. Accordingly, there has been a greater emphasis in the recent literature comparing high-risk

subgroups undergoing OPCAB versus ONCAB. As referenced above, the ISMICS consensus conference revealed an overall mortality benefit for high-risk patients undergoing OPCAB with the greatest benefit being in the following patients: Euroscore more than 5, left ventricle (LV) dysfunction, and atherosclerotic aortic disease. Perioperative morbidity was further reduced in the following subgroups: age more than 75 years, diabetes, renal failure, left main disease, reoperations, and chronic lung disease [19]. In addition to this meta-analysis, there has been an abundance of recent data favoring OPCAB in the following high-risk subgroups.

#### Acute myocardial infarction and nonelective coronary artery bypass grafting

The safety and feasibility of OPCAB in emergency situations has been confirmed in several series [22–27]. Recently, Fattouch *et al.* [22] reported the results of a prospective trial, randomizing patients with acute ST elevation MI (within 48 h of infarction) to OPCAB versus ONCAB. Their findings indicate that OPCAB had a significantly lower mortality, fewer patients with low cardiac output syndrome, decreased ventilator time, and decreased ICU and hospital LOS [22]. Rastan *et al.* [24] similarly found reduced morbidity and mortality when cardioplegic arrest was avoided in a comparison of patients with acute coronary syndrome undergoing ONCAB with cardioplegic arrest versus beating heart CABG (including both OPCAB and beating heart on CPB). In a propensity-matched analysis of 5760 patients undergoing nonelective CABG, Stamou *et al.* [28] reported a reduction in LOS, and lower rates of postoperative renal failure, need for IABP, and re-exploration for bleeding among OPCAB patients.

#### Left ventricular dysfunction

Two recent comparisons of OPCAB and ONCAB in patients with LV dysfunction (defined as ejection fraction $<35\%$) revealed a reduction in perioperative morbidity in OPCAB patients, specifically with respect to ICU LOS, respiratory failure, need for intotropes, and need for intraaortic balloon counterpulsation (IABP) [29,30]. Youn *et al.* [30] also showed similar 6-year survival rates (88% in OPCAB versus 72% in ONCAB) and freedom from major adverse cardiovascular events.

#### Reoperative coronary artery bypass grafting

In a propensity-matched comparison of reoperative OPCAB versus ONCAB, Morris *et al.* [31] reported a significant reduction in overall postoperative complications, atrial fibrillation, blood transfusion, and hospital LOS. Mishra *et al.* similarly demonstrated a reduction in need for prolonged ventilator and inotropic support, and shorter ICU and hospital LOS in favor of redo OPCAB [32]. Vohra *et al.* [33] found that OPCAB patients were less likely to need IABP support, had a shorter duration of ventilation, and despite having less number of grafts performed ($3 \pm 0.08$ in ONCAB versus $2 \pm 0.06$ in OPCAB) had similar 5-year survival rates (87% in ONCAB versus 95% in OPCAB).

#### Elderly patients

In a retrospective analysis of octogenarians undergoing OPCAB versus ONCAB, Nagpal *et al.* [34] found similar rates of perioperative MI, renal dysfunction, and mortality. OPCAB patients, however, have a significantly lower incidence of stroke (1.5% OPCAB versus 7.6% ONCAB) and prolonged ventilation [34]. Jensen *et al.* [35] evaluated 3-month neurocognitive outcomes in elderly patients (mean age 76 years) in a randomized trial of OPCAB versus ONCAB. In this study, no difference was seen in stroke rate or cognitive outcome as evaluated by four different neuropsychological tests [35]. In contrast, in a meta-analysis of nine clinical trials examining the incidence of stroke in patients over the age of 70, Athanasiou *et al.* [36] found a benefit in OPCAB group with an odds ratio of 0.38 [95% confidence interval (CI), 0.22–0.65]. Panesar *et al.* [37] performed a similar meta-analysis of OPCAB versus ONCAB in elderly patients (>70 years), and found a reduction in mortality, stroke, and atrial fibrillation in the OPCAB group. This benefit was even more pronounced in octogenarians with respect to stroke and mortality [37].

#### Patients with cerebrovascular disease

Halkos *et al.* [38] recently examined the impact of preoperative neurological events [defined as previous stroke or transient ischemic attack (TIA)] on postoperative stroke in 14 279 patients undergoing isolated OPCAB versus ONCAB. OPCAB was associated with a reduced risk of stroke in patients with no previous neurological event (1.1% OPCAB versus 1.9% ONCAB, $P < 0.001$). In patients with a history of preoperative neurological event, a postoperative stroke or TIA occurred in 3.5% of OPCAB patients compared with 5.6% of ONCAB patients ($P = 0.059$) [38]. Mishra *et al.* [39] performed a propensity-matched comparison of OPCAB versus ONCAB of 6991 patients with atheromatous aortic disease and found a significant decrease in in-hospital mortality (1.4 versus 3.3%; $P < 0.001$) and stroke incidence (0.50 versus 0.97%, $P = 0.05$), with OPCAB being the only independent predictor of decreased stroke rate.

#### Off-pump coronary artery bypass versus on-pump coronary artery bypass in women

It has long been recognized that women are at a greater risk of morbidity and mortality than men undergoing CABG. We recently reported our institutional results of 11 413 consecutive patients undergoing isolated CABG over an 8-year period. Among these patients, women undergoing ONCAB were at significantly greater risk of death, stroke, and MI compared with men. Women

undergoing OPCAB, however, had statistically similar results to men, suggesting that OPCAB reduced the gender discrepancy in these outcomes [40]. Similar findings were seen in a larger intention-to-treat analysis of 42 477 patients from 63 North American institutions identified from the Society of Thoracic Surgeons (STS) national database [21••].

#### Patients with renal failure

Preoperative renal insufficiency is a significant predictor of postoperative renal failure and mortality in patients undergoing CABG [41]. In multiple studies, OPCAB has been shown to reduce morbidity and mortality in patients with normal renal function [42,43], those with renal dysfunction not yet on hemodialysis [44] as well as those with end-stage renal failure on dialysis [45]. In a prospective randomized trial of patients with preoperative renal insufficiency, Sajja *et al.* [44] demonstrated that OPCAB was beneficial with decreased postoperative serum creatinine values and increased glomerular filtration rate compared to ONCAB. Dewey *et al.* [45] showed improved operative mortality in favor of OPCAB among patients with dialysis-dependent renal failure; this early benefit, however, did not translate into improved long-term survival.

## Adoption of off-pump coronary artery bypass in high-risk patients

Despite the abundance of evidence favoring OPCAB in high-risk patients, many centers and individual surgeons have not fully embraced the technique. For various reasons, including the technical demands of off-pump anastomoses and concern over graft quality and long-term patency, the majority of CABG patients in the United States and worldwide are still performed with CPB. However, as patients undergoing CABG become older with more associated comorbidities, the unrealized benefits of OPCAB will become greater.

Although it may be more technically challenging than ONCAB, OPCAB can be adopted into routine practice safely without compromising clinical outcomes. In our experience, OPCAB was gradually incorporated into routine practice first by applying the technique to low-risk patients with normal ventricular function and limited comorbidities. As our proficiency with OPCAB developed, more and more high-risk patients needing surgical revascularization were considered as candidates for OPCAB [46]. Currently, at our institution, over 80% of all isolated CABG procedures are performed off-pump. Adoption of OPCAB has been aided by the development of improved techniques and devices for cardiac positioning and coronary stabilization as well as enhanced intraoperative patient management by our anesthesiology colleagues.

Most surgeons currently in practice were not trained in OPCAB during residency and have subsequently learned the technique after completion of their formal training. In contrast, residents currently going through training programs are becoming more proficient in OPCAB. As indicated by a recent survey of US cardiothoracic residents, though only 20% of CABG cases in the United States are being performed off-pump, approximately 50% of residents feel that they are well trained in performing OPCAB (Thoracic Surgery Residents Association 2008 In-training exam survey). Several European studies [47–49] have also examined the feasibility of training residents in OPCAB, with the conclusion that it can be done safely with outcomes equivalent to procedures performed by attending surgeons. As these current residents enter the workforce, it should follow that facility with OPCAB techniques should become more widespread. In addition to improved resident education and instruction, there are now enhanced opportunities for postgraduate training in OPCAB. On-line e-training modules (http://www.ctsnet.org/sections/learningcenter/lms/index.html) and the increasing use of surgical simulators will allow proficiency in OPCAB to develop without posing additional risk to patients in the operating room. Advances by industry have also helped broaden the application of OPCAB. When first attempting OPCAB, many established surgeons did not have the benefits of the current suction positioning and stabilization devices. The current generation of these devices has helped alleviate many of the technical and hemodynamic challenges facing surgeons during OPCAB and have allowed revascularization in higher risk patients to be performed safely off-pump.

Much of the evidence presented in this review has come from centers that have developed proficiency in OPCAB and routinely utilize the technique for most patients. In Japan, for example, 61% of all cases in 2005 were performed off-pump with an overall mortality of 0.6%; this included high-risk patients such as octogenarians and those requiring more than four grafts [50]. In contrast, OPCAB can also be performed safely by those who utilize the technique less frequently, as evidenced by Canadian analyses of outcomes in the province of Ontario [51,52]. These results indicate that though only 11% of CABG patients in 2000–2001 were performed off-pump, in-hospital and 1-year outcomes of OPCAB were similar to those of ONCAB [51].

## Conclusion

In summary, though there is a learning curve with OPCAB, the technique can be adopted safely without placing patients at increased risk. By first applying the technique to low-risk patients who need fewer grafts and gradually evolving toward routine application of OPCAB in all patients, the learning curve can be managed safely.

Abundant prospective and retrospective data suggest that patient benefit from OPCAB is most dramatic in high-risk patients. We propose that OPCAB should be routinely available in all cardiac surgical centers, particularly as the surgical patient population becomes increasingly high-risk.

## References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 647–648).


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