Should we consider off-pump coronary artery bypass grafting in patients with acute coronary syndrome?

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Abstract

A best evidence topic in cardiac surgery was written according to a structured protocol. The question addressed was whether off-pump coronary artery bypass (OPCAB) grafting should be considered as an alternative to the conventional on-pump surgery (ONCAB) in patients presenting with acute coronary syndrome (ACS) requiring emergency revascularization. Eighty-two papers were identified by a systematic search, of which nine were judged to best answer the clinical question. Of these, one was a randomized controlled trial and the remaining eight were retrospective observational studies. The author, journal, date, patient group, country of publication, relevant outcomes, results and study weaknesses were tabulated. In total, these nine studies included 3001 patients (n = 817 OPCAB, 2184 ONCAB) undergoing emergency revascularization in the setting of ACS. The timing between the onset of ACS and operative intervention ranged from 6 to 72 h. All cases were categorized as urgent/emergent according to the National confidential enquiry into patient outcome and death classification of intervention. Six studies included patients with preoperative cardiogenic shock; however the majority of patients were haemodynamically stable at the time of surgery. Three out of nine studies showed an improvement in 30-day mortality with OPCAB although the remaining six reveal no significant mortality benefit. No difference in long-term mortality was observed between the two techniques. OPCAB was associated with significantly fewer grafts per patient (six studies) and less complete revascularization (two studies). We conclude that whilst OPCAB may have a beneficial effect on 30-day mortality in haemodynamically stable patients undergoing emergency revascularization, there is a lack of high-quality data with clearly defined patient demographics. Future studies must ensure adequate preoperative matching between OPCAB and ONCAB groups and clearly categorize haemodynamic status, disease pattern and time to surgery in order to determine the patients in whom OPCAB may confer the greatest benefit.

Keywords: Cardiopulmonary bypass • Emergency surgery • Off-pump • Acute coronary syndrome • Mortality

INTRODUCTION

A best evidence topic was written according to a structured protocol. This protocol is fully described in the ICVTS [1].

THREE-PART QUESTION

In [patients presenting with acute coronary syndrome (ACS) requiring emergency coronary artery bypass graft (CABG)] is [off-pump coronary artery bypass, OPCAB] a safe alternative to [on-pump coronary artery bypass, ONCAB] in order to produce [optimal survival and lowest morbidity]?

CLINICAL SCENARIO

A 65-year old lady is admitted with central chest pain associated with anterior ST-elevation. She is transferred to the cardiac catheterization laboratory for primary angiography and intervention. A coronary angiogram revealed triple-vessel disease with complex stenosis of the left anterior descending artery. Although medical therapy improved her symptoms, balloon angioplasty failed to achieve a successful result. Transthoracic echo subsequently showed a hypokinetic anterior wall and an ejection fraction of 35%. As the cardiac surgeon on-call you are asked to consider her for emergency CABG and your trainee asks whether you would perform this case ‘off-pump’?

SEARCH STRATEGY

A literature search was performed using PubMed, Ovid, Embase and Cochrane databases using the terms ‘off-pump’, ‘coronary artery bypass grafting’ and ‘acute coronary syndrome (ACS)’. The search date was 1 May 2012.

SEARCH OUTCOME

Eighty-two papers were found of which nine [2-10] provide the best evidence for this topic. A summary is presented in Table 1.
<table>
<thead>
<tr>
<th>Author, date, journal and country Study type</th>
<th>Patient group</th>
<th>Outcomes</th>
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<tr>
<td><strong>Locker et al. (2000), Eur J Cardiothorac Surg, Israel [7]</strong> Retrospective observational study</td>
<td>Seventy-seven patients with evolving ACS (within 48 h of symptom onset). 40 OPCAB (CS 38%) 37 ONCAB (CS 46%) Patient selection based on surgeons’ preference. Feasibility for ‘off-pump’ was determined by the vessel size (&gt;1.5 mm for OPCAB), and on the number of vessels to be grafted</td>
<td>Grafts per patient In-hospital mortality Late survival (1 and 4 years) Angina recurrence Re-operation</td>
<td>Operative mortality: Lower in the OPCAB group (2/40 vs 9/37, P = 0.01) Early mortality was still statistically lower in the OPCAB group when controlling for preoperative patient covariates (P = 0.00279, OR [6.12, 95% CI 1.21–30.83])</td>
<td>Conclusions: Disappointing short-term and no long-term survival benefit with OPCAB OPCAB may be better than ONCAB in ACS where OPCAB is technically possible Limitations: Small number, non-randomized trial 40% of OPCAB patients received single graft 8% OPCAB received graft to circumflex branch</td>
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<td><strong>Ochi et al. (2003), Ann Thorac Cardiovasc Surg, Japan [9]</strong> Retrospective observational study</td>
<td>Seventy-two patients with ACS undergoing emergency CABG within 24 h of admission: 25 OPCAB (CS 12%) 47 ONCAB (CS 23.4%) OPCAB selection: mostly &gt;75 years poor renal function suitable coronary anatomy OPCAB excluded in haemodynamic instability unless stable with IABP</td>
<td>Operative mortality Grafts per patient Postoperative angiographic patency Postoperative target vessel revascularization</td>
<td>In-hospital mortality: No difference between OPCAB and ONCAB (12% vs 8.5%, P = 0.69) Grafts per patient: Fewer with OPCAB (P = 0.0001) Postoperative angiographic patency: 100% in OPCAB (not recorded in ONCAB) Zero conversion rate No target vessel revascularization in either group</td>
<td>Conclusions: OPCAB not associated with increased mortality can be performed safely and effectively in selected patients with ACS requiring emergency CABG Limitations: Small number. No late mortality. Non-randomized. Patients requiring fewer grafts selected for OPCAB to avoid incomplete revascularization</td>
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<td><strong>Kerendi et al. (2005), Ann Thorac Surg, USA [6]</strong> Retrospective observational study</td>
<td>Six hundred and fourteen patients undergoing emergency CABG for ACS (STS criteria): 44 OPCAB (CS 13.6%) 570 ONCAB (CS 13.2%) OPCAB selection: Excluded: salvage operation, CPR on route to theatre OPCAB considered where haemodynamically stable with medical therapy or IABP</td>
<td>Mortality MACCE Completeness of revascularization</td>
<td>MACCE reduced with OPCAB (6.8 vs 21.1% ONCAB, P = 0.038) Operative mortality: No significant difference between OPCAB and ONCAB (0.0 vs 6.3%, P = 0.168) Completeness of revascularization (CR): Less grafts per patient with OPCAB (1.25 ± 0.07 vs 1.51 ± 0.03, P = 0.0003) After 2001 no difference in CR (P = 0.759) was observed OPCAB patients received fewer blood transfusions (65.9 vs 84.9%, P = 0.004) Significantly shorter ICU stay with OPCAB (1.47 vs 3.20 days, P = 0.016)</td>
<td>Conclusions: OPCAB safe and effective in haemodynamically stable patients undergoing emergency revascularization Limitations: Small OPCAB group—underpowered to detect mortality differences Non-randomized. Selection bias (ONCAB patients more severe pattern of disease)</td>
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<td>Biancari et al. (2008), Ann Thorac Surg, Finland [2]</td>
<td>Three hundred and fifteen patients with ACS requiring nitrates till arrival in theatre included: 161 OPCAB (CS not included) 153 ONCAB (CS not included) Haemodynamically unstable patients excluded. Surgeons selected techniques based on the patients’ condition and individual preference. Where target not reachable the procedure was converted to on-pump beating heart</td>
<td>30-day mortality</td>
<td>In-hospital mortality: No difference between OPCAB and ONCAB (3[1.9%]/6[3.9%], P = 0.33)</td>
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<td>Fattouch et al. (2009), J Thorac Cardiovasc Surg, Italy [4]</td>
<td>Randomized, blinded trial One hundred and twenty-six patients within 72 h of STEMI: 61 OPCAB (CS 22%) 65 ONCAB (CS 17%) Exclusions: mechanical complications of MI Preoperative CPR CS for &gt;24 h Moderate/severe ischaemic MR</td>
<td>In-hospital mortality</td>
<td>In-hospital mortality: No difference between OPCAB and ONCAB groups (1[1.65%] vs 5[7.7%], P = 0.4) Lower in patients undergoing surgery &lt;6 h from onset of symptoms (P = 0.0026) No late mortality was observed in either group at last follow-up (2–68 months)</td>
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<td>Darwazah et al. (2009), Asian Cardiovasc Thorac Ann, Israel [5]</td>
<td>Seventy-nine patients presenting within 24 h of ACS requiring emergency revascularization (STS criteria):</td>
<td>In-hospital mortality</td>
<td>In-hospital mortality: Similar between OPCAB and ONCAB (4[8.9%] vs 5[14.7%], P = 0.42)</td>
<td>Conclusions: OPCAB performed better than predicted EuroSCORE. OPCAB may confer improvements in</td>
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Late mortality (4 years): No difference between OPCAB and ONCAB (95.4% vs 94.1%) Number of distal anastomoses significantly less with OPCAB (P = 0.0001) Fewer blood transfusions in OPCAB group (P = 0.005) MACCE: No significant difference between OPCAB and ONCAB (P = 0.63) Conclusions: OPCAB may improve short-term morbidity and mortality in patients undergoing emergency revascularization for STEMI OPCAB may be of particular benefit in patients presenting within 6 h of ACS and in those with CS |
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<td>Grafts per patient Short- and long-term morbidity</td>
<td>Late mortality (&gt;1 year): No difference between groups (410.3% vs 310.7%, P = 0.95). No significant difference in 5-year survival</td>
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RESULTS

All nine studies conclude that OPCAB may be performed safely in haemodynamically stable ACS patients. Locker et al. retrospectively reviewed 77 patients (40 OPCAB, 37 ONCAB) with evolving ACS (<48 h). OPCAB was associated with lower in-hospital mortality \((P = 0.015)\), but late mortality (6–66 months) was higher \((P = 0.0066)\) and fewer distal anastomoses \((P = 0.0001)\) were performed.

Ochi et al. [9] studied 72 ACS patients (25 OPCAB, 47 ONCAB). OPCAB was selected in patients with poor renal function and ONCAB in those with haemodynamic instability. Operative death and in-hospital mortality were found to be similar using both the techniques; however, OPCAB was associated with fewer grafts per patient. Multivariate logistic regression revealed cardiogenic shock (CS) as the only significant predictor of in-hospital mortality.

Kerendi et al. [6] analysed 544 ACS patients (44 OPCAB, 500 ONCAB) undergoing emergency CABG. A higher proportion of ONCAB patients had critical left main stem stenosis. No difference was seen in in-hospital mortality, re-operation, postoperative myocardial infarction (MI), cerebrovascular accident, sternal wound infection, renal failure requiring haemodialysis or respiratory failure requiring reintubation; however, the combined incidence of these end-points was significantly lower with OPCAB. OPCAB patients received less blood transfusion and had a shorter intensive care unit (ICU) stay. Fewer grafts per patient were performed with OPCAB.

Biancari et al. [2] studied 314 patients (161 OPCAB, 153 ONCAB), and showed a lower 30-day mortality \((P = 0.04)\) and risk of major adverse cardiac events (MACE) \((P = 0.0009)\) with OPCAB (adjusted for logistic EuroSCORE). However, again OPCAB resulted in significantly fewer grafts per patient.

In their randomized controlled trial, Fattouch et al. [4] demonstrate a lower in-hospital mortality with OPCAB \((P = 0.04)\), although no difference in late mortality. All patients achieved completeness of revascularization (CR) with no difference in grafts per patient. OPCAB patients had less re-operation for bleeding \((P = 0.02)\), shorter duration of inotropic support \((P = 0.001)\), mechanical ventilation \((P = 0.006)\), ICU \((P = 0.01)\) and hospital stay \((P = 0.02)\).
Darwazah et al. [3] retrospectively studied 79 patients (45 OPCAB, 34 ONCAB). OPCAB patients had a worse pre-morbid state including lower LVEF and higher EuroSCORE. Operative and mid-term mortality was similar between groups; however, OPCAB was associated with less CR ($P = 0.001$) and ONCAB patients had less recurrent angina and improved long-term symptom control.

Kaya et al. retrospectively studied 198 ACS patients (142 OPCAB, 56 ONCAB) undergoing emergency revascularization. [5] ONCAB patients were either haemodynamically unstable, or had evidence of coronary artery disease. OPCAB patients had a lower EuroSCORE ($P < 0.001$), underwent surgery sooner after symptom onset (<6 h: OPCAB 76.1%; ONCAB 60.7%), and more commonly received one to two grafts ($P < 0.001$). OPCAB resulted in a shorter operation time ($P < 0.001$), ICU ($P < 0.05$) and hospital stay ($P < 0.001$). In-hospital mortality was similar between the two groups ($P = 0.69$).

Martinez et al. studied 136 patients (68 OPCAB, 68 ONCAB) [6]. In-hospital mortality was similar between OPCAB and ONCAB ($P = 0.63$). However, ventilation time ($P = 0.03$), pulmonary complications ($P = 0.04$), inotropic requirement ($P = 0.002$), blood transfusion ($P < 0.0001$) and postoperative pacing requirement were lower with OPCAB. Again, OPCAB resulted in less CR ($P = 0.002$).

Ben-Gal et al. performed both an unmatched and propensity-matched analysis of 1375 patients (231 OPCAB, 1154 ONCAB; propensity matched: 220 OPCAB, 660 ONCAB) [10]. Whilst propensity-matched OPCAB patients received fewer grafts than ONCAB (2.8 ± 1.2 vs 3.4 ± 1.03; $P < 0.001$), no difference was seen in 30-day or late mortality by either analysis method. Furthermore, although fewer non-Q wave MI and bleeding events were seen with OPCAB at 30-days; no difference was seen in MI, stroke, acute kidney injury or MACE in either the short- or long-term. Unplanned re-intervention was significantly higher at 30 days with OPCAB ($P = 0.001$; PM: $P = 0.02$) although no difference was observed at 1 year.

**CLINICAL BOTTOM LINE**

The ‘gold-standard’ treatment for most patients presenting with ACS is primary PCI of the culprit coronary vessel. Where emergency CABG is required, OPCAB is theoretically ideal as it preserves coronary flow, avoids global myocardial ischaemia and reduces ischaemia-reperfusion injury. Its main limitation in ACS is maintaining the haemodynamic stability during cardiac manipulation, which may necessitate conversion or produce less CR. We sought to identify whether OPCAB conferred a mortality benefit in patients requiring emergent CABG in the setting of ACS.

Three [2, 4, 7] of nine studies showed a lower early mortality with OPCAB; however, the remaining six observed no mortality benefit [3, 5, 6, 8, 9]. No studies showed a difference in late mortality (>1 year) between OPCAB and ONCAB. Six studies [5-10] found OPCAB to be associated with fewer grafts per patient and two [3, 8] observed less CR with OPCAB. Whilst no differences in long-term mortality were demonstrated, the effect of incomplete revascularization on other long-term outcomes such as angina recurrence, escalation of medical therapy and target vessel revascularization is yet to be fully evaluated.

Several limitations must be considered when interpreting this evidence. First, eight of nine studies are non-randomized and the sample size is small resulting in insufficient statistical power to detect mortality differences. Second, variable selection criteria, surgeon-specific morbidity, preoperative state and time to surgery may have an unmeasurable effect on short- and long-term outcomes.

In summary, provisional results suggest that OPCAB in the setting of ACS may carry lower or at least equal 30-day mortality to ONCAB. However, there is currently insufficient evidence to determine the effect of less complete revascularization on long-term outcomes. Future studies must ensure adequate preoperative matching between OPCAB and ONCAB groups, and clearly categorize haemodynamic status, disease pattern and time to surgery in order to determine the patients in whom OPCAB may confer the greatest benefit.

**Conflict of interest:** none declared.

**REFERENCES**


