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# Impact of off-pump coronary artery bypass grafting on survival: current best available evidence

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**Abstract:** The superiority of either off-pump (OPCAB) or on-pump (ONCAB) coronary artery bypass grafting (CABG) remains unclear despite a large body of literature evidence comparing the two approaches. The potential advantages of avoiding cardiopulmonary bypass (CPB), minimizing aortic manipulation and maintaining pulsatile flow may be associated with reduced inflammatory responses and embolic events. Numerous studies compared OPCAB with ONCAB and the cumulative data have been presented in meta-analyses of both randomized and observational studies. Although there is an abundance of data with respect to the operative morbidity and mortality and the short-term outcomes associated with these two strategies, not much is known about how they impact long-term survival and recurrence of myocardial ischaemic events. Recent studies and meta-analyses have focused on long-term survival and major secondary outcomes in OPCAB *vs.* ONCAB within the general population. Significant limitations in methodology, however, have raised concerns about the strength of several randomized trials with restrictive inclusion criteria that reduced the populations to those at low risk only, thus creating result bias. Here, we present a review of the best available evidence with a focus on long-term outcomes.

**Keywords:** Off-pump coronary artery bypass surgery (OPCAB); off-pump; long term; coronary artery bypass grafting (CABG); coronary by-pass grafting; review

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## Introduction

For decades, cardiac surgeons have performed coronary surgery with cardiopulmonary bypass (CPB) and cardioplegia-induced cardiac arrest, the on-pump technique (ONCAB), which provides a motionless and bloodless surgical field, this at the expense of potentially negative sequelae including blood trauma, activation of systemic inflammatory responses, non-pulsatile flow, aortic cannulation and clamping with possible embolization of air or atherosclerotic debris and systemic hemodilution (1).

Because of these detrimental aspects, ONCAB has been

challenged in recent years by off-pump coronary artery bypass surgery (OPCAB), which avoids the use of CPB. This has triggered a large number of randomized clinical trials (RCTs) and retrospective analyses addressing the clinical outcomes of the two techniques. There seems to be convincing evidence that OPCAB reduces the risk of early postoperative morbidity such as myocardial infarction, pulmonary dysfunction, abnormal renal function, atrial fibrillation, blood product transfusion, intensive care unit and hospital stay (2-14). However, concerns persist with respect to the impact of OPCAB on long-term mortality

and freedom from re-intervention (15-18) with some studies reporting a higher risk of incomplete revascularization and graft failure (19,20). Despite the potential benefits of OPCAB, recent data shows that only a minority of CABG operations worldwide (about 15% to 20%) are carried out with this technique (21).

Surgeons might be reluctant to commit to OPCAB because of concerns that the technique requires distal anastomoses to be performed on the beating heart, potentially compromising long-term graft patency. These concerns seem not to apply in large-volume centers and for surgeons who have crossed their learning curve (22,23).

## Methods

We conducted a literature search through PubMed, EMBASE, the Web of Science, the Cochrane Library and Google Scholar. No language, publication date or publication status was imposed. Suitable papers were individually analyzed and results were tabulated in a spreadsheet to categorize and organize the information. The main articles were presented as well in a table (Table 1).

## Results

### *A general view of recent randomized controlled trials*

The largest trials until now are the Randomized On/Off Bypass (ROOBY) trial (28) and the CABG Off or On Pump Revascularization Study (CORONARY) (29).

The ROOBY trial enrolled 2,203 patients from the Veterans Affairs (VA) system scheduled for urgent or elective CABG to either OPCAB or ONCAB. The primary long-term end point was a composite of death from any cause, a repeat revascularization procedure, or a nonfatal myocardial infarction within 1 year after surgery. The results showed a significantly higher rate of the composite long-term outcome with OPCAB when compared with ONCAB (9.9% *vs.* 7.4%; RR =1.33; 95% CI, 1.01–1.76; P=0.04). The 1-year patency rate of arterial grafts was lower in OPCAB (92.9%) than ONCAB (94.8%) although this difference was not statistically significant (P=0.13).

Recently, the results of the CORONARY trial at 1 year have been published (29): authors compared OPCAB with ONCAB in 4,752 patients from 19 countries on 5 continents. They found no significant differences between groups at 1 year in the rate of the first co-primary outcome of death, nonfatal stroke, nonfatal myocardial infarction,

or nonfatal new renal failure requiring dialysis (HR =0.91; 95% CI, 0.77–1.07; P=0.24). The rate of repeat coronary revascularization at 1 year was 1.4% in the OPCAB group and 0.8% in the ONCAB group (HR =1.66; 95% CI, 0.95–2.89; P=0.07).

It is quite evident that there are notable differences between the two trials; CORONARY included more than twice as many participants than the ROOBY; furthermore, the participants in the CORONARY represented altogether a more heterogeneous group, whereas the ROOBY trial recruited patients exclusively from the VA system. The CORONARY specified a higher level of surgical ability at the beginning of the trial than was required in the ROOBY; each operation was performed by a surgeon who had more than 2 years of experience and had completed more than 100 cases of the specific technique (either OPCAB or ONCAB). In CORONARY, trainees were not allowed to be the primary surgeon. The rate of conversion from OPCAB to ONCAB was lower in CORONARY than in the ROOBY (7.9% *vs.* 12.4%), and the rate of repeat revascularization between 31 days and 1 year was also lower in CORONARY (0.7% in the OPCAB and 0.6% in the ONCAB *vs.* 4.6% and 3.4%, respectively). Interestingly, in CORONARY, the rate of the primary end point was lower in the OPCAB group than in the ONCAB group (11.5% and 13.2%, respectively; P=0.08), whereas in the ROOBY, the rate was lower in the ONCAB group (9.4% in the OPCAB group *vs.* 7.1% in the ONCAB group; P=0.08).

The most recent Cochrane Review on OPCAB versus ONCAB (30), which did not include the CORONARY trial, was strongly influenced by the results from the ROOBY trial and concluded that OPCAB did not confer any significant benefit compared with ONCAB in relation to mortality, stroke or myocardial infarction. The authors observed better long-term survival in the group of patients undergoing ONCAB. Based on the current evidence, they suggested ONCAB to continue to be the standard surgical treatment, and OPCAB to be acceptable when there are contraindications for cannulation of the aorta and CPB.

A previous meta-analysis of propensity score analyses published by Kuss *et al.* (12) showed results contrasting the Cochrane Review conclusions: a total of 35 out of 58 initially retrieved propensity score analyses were included, accounting for a total of 123,137 patients. The ROOBY trial was not enrolled in this meta-analysis. The estimated overall OR was less than 1 for all outcomes, favouring OPCAB. This benefit was statistically significant for mortality (OR =0.69; 95% CI, 0.60–0.75), stroke, renal failure, red blood

Table 1 Impact of OPCAB on long-term survival and outcomes: current best available evidence

Author, date and Journal	Title	Study population	Main outcomes	Key findings
Angelini et al. (21) [2009], <i>J Thorac Cardiovasc Surg</i>	Effects of on- and off-pump coronary artery surgery on graft patency, survival, and health-related quality of life: long-term follow-up of 2 randomized controlled trials	401 patients from two different prospective randomized controlled trials (BHACAS 1 and 2); 200 OPCAB (mean follow up: 6.3 years); 201 ONCAB (mean follow up: 6.4 years)	Survival Graft patency	No difference between ONCAB vs. OPCAB cohorts (HR = 1.24; 95% CI, 0.72–2.15; P=0.44) No difference in the likelihood of graft occlusion between OPCAB vs. ONCAB groups (OR = 1.00; 95% CI, 0.55–1.81; P>0.99)
Benedetto et al. (24) [2016], <i>J Thorac Cardiovasc Surg</i>	Off-pump versus on-pump coronary artery bypass surgery in patients with actively treated diabetes and multivessel coronary disease	Retrospective analysis of 2,450 actively treated diabetic patients undergoing OPCAB versus ONCAB (1,493 subjects were orally treated and 1,011 were on insulin) (1,253 OPCAB and 1,197 ONCAB); propensity score matching was used to compare the two matched groups; mean follow up: over 10 years	Survival; complete revascularization	OPACB did not significantly affect late mortality (HR = 1.08; 95% CI, 0.92–1.28; P=0.32). However, OPCAB with incomplete revascularization was associated with a reduced survival rate when compared to OPCAB with complete revascularization (HR = 1.82; 95% CI, 1.34–2.46; P=0.0002) and ONCAB with complete revascularization (HR = 1.83; 95% CI, 1.36–2.47; P<0.0001)
Di Mauro et al. (11) [2007], <i>Ann Thorac Surg</i>	Does off-pump coronary surgery reduce postoperative acute renal failure? The importance of preoperative renal function	Retrospective cohort study of 2,833 patients (normal renal function: 1,724; abnormal renal function: 160) (942 OPCAB and 942 ONCAB); mean follow up: 7.5 years	Survival Late outcomes	OPCAB provides better late outcomes in patients with normal creatinine preoperatively Surgical strategy does not affect late mortality in the overall population. Ten-year mortality ONCAB (7.0%) vs. OPCAB (5.3%) (HR = 1.3; 95% CI, 0.91–1.9; P=0.141)
Raja et al. (25) [2013], <i>Biomed Res Int</i>	Does off-pump coronary artery bypass grafting negatively impact long-term survival and freedom from reintervention?	Retrospective cohort study of 704 consecutive patients (single centre) (307 OPCAB and 397 ONCAB); follow-up: 10 years	Survival Need for repeat intervention	OPCAB compared with ONCAB does not adversely impact survival (HR = 0.91; 95% CI, 0.70–1.12; P=0.87) Freedom from re-intervention (HR = 0.93; 95%CI, 0.87–1.05) compared with ONCAB
Puskas et al. (3) [2011], <i>Ann Thorac Surg</i>	Off-pump and on-pump coronary artery bypass patency, myocardial ischemia, and freedom from reintervention: long-term follow-up	Prospective, randomized controlled trial (SMART); 297 patients (98 OPCAB and 99 ONCAB); mean follow up: 7.5 years	Long-term survival; graft patency; need for re-intervention	At 5-year follow-up, long term survival was statistically significant in favour of OPCAB (92.9% OPCAB vs. 81.8% CPB; P=0.02). However, by 7-year follow-up, this difference was no longer statistically significant (83.7% OPCAB vs. 73.7% CPB; P=0.09), and the two overall survival curves were not statistically different (P=0.33); other outcomes were similar between OPCAB vs. ONCAB

Table 1 (continued)

Table 1 (continued)

Author, date and Journal	Title	Study population	Main outcomes	Key findings
Kimmani et al. (26) [2016], <i>Ann Thorac Surg</i>	Long-term survival after off-pump coronary artery bypass grafting	Retrospective cohort study; single centre; 2,082 OPCAB and 2,082 ONCAB; median follow-up: 7.0 years	Long term survival	OPCAB group fewer in hospital cerebrovascular complications, mean number of grafts higher in the ONCAB, long-term survival was similar between groups
Hueb et al. (27) [2010], <i>Circulation</i>	Five-year follow-up of a randomized comparison between off-pump and on-pump stable multivessel coronary artery bypass grafting. The MASS III trial	Prospective, randomized controlled trial of 308 patients (155 OPCAB and 153 ONCAB); follow up: 5 years	Survival; graft patency	No difference in death, myocardial infarction or further revascularization was found between groups, number of grafts per patient was higher in the ONCAB
Robertson et al. (19) [2013], <i>J Thorac Cardiovasc Surg</i>	Complete revascularization is compromised in off-pump coronary artery bypass grafting	Retrospective cohort study of 1,285 patients (308 OPCAB and 308 ONCAB); follow up: 10 years	Long term survival; freedom from cardiac readmission	Complete revascularization and rate of total arterial grafting significantly higher in ONCAB, no difference in survival or freedom from cardiac cause and hospital readmission
Bakaeen et al. (16) [2013], <i>Ann Thorac Surg</i>	Off-pump may compromise long-term survival in a veteran population	Large, multicentre, retrospective review; total 65,097 patients (11,627 OPCAB and 53,468 ONCAB); follow up: 5 and 10 years	Survival (matched patients)	OPCAB vs. ONCAB (all-cause mortality): overall HR=1.06; 95% CI, 1.00–1.13; P=0.036; ONCAB may be associated with increased long-term survival
Filardo et al. (17) [2011], <i>Ann Thorac Surg</i>	Comparing long-term survival between patients undergoing off-pump and on-pump coronary	Retrospective cohort study, total 8,081 patients (732 OPCAB and 7,349 ONCAB); follow up: 5 and 10 years	Survival	Long-term survival following on-pump CABG is significantly greater; at 5 years: 77.4% OPCAB vs. 80.8% ONCAB (P<0.05); at 10 years: 54.7% OPCAB vs. 62.3% ONCAB (P<0.05)

OPCAB, off pump coronary bypass; ONCAB, on pump coronary bypass; HR, hazard ratio; OR, odds ratio; CPB, cardiopulmonary bypass; CI, confidential interval.



cell transfusion ( $P<0.0001$ ), wound infection ( $P<0.001$ ), prolonged ventilation ( $P<0.01$ ), inotropic support ( $P=0.02$ ), and intra-aortic balloon pump support ( $P=0.05$ ). The odds ratios for myocardial infarction, atrial fibrillation, and reoperation for bleeding were not significant. These results agree with previous systematic reviews of randomized and nonrandomized trials (4).

### *Best available evidence for long-term survival*

The increasing availability of longer-term data now requires follow up analysis; recent studies and meta-analysis have focused on long-term survival and major secondary outcomes in OPCAB *vs.* ONCAB within the general population (31).

Our group has previously reported the results from two prospective, randomized, controlled trials the Beating Heart Against Cardioplegic Arrest Study (BHACAS) 1 and 2 trials (23): 401 participants were recruited overall, of whom 200 patients had OPCAB and 201 patients underwent ONCAB surgery. The patients were followed up for 6 to 8 years after surgical intervention to assess graft patency, major adverse cardiac-related events (MACEs), and health-related quality of life (HRQoL). Patency was assessed using multidetector computed tomographic coronary angiographic analysis with a 16-slice scanner. Two blinded observers classified the proximal, the body and the distal segments of each graft as occluded or patent. MACEs and HRQoL were obtained from questionnaires given to participants and family practitioners. The mean follow-up period for OPCAB and ONCAB survival was 6.3 and 6.4 years, respectively, and survival-free from MACEs or death was 5.4 and 5.2 years, respectively. The key findings (6 to 8 years after surgical intervention) are that there were no differences between the OPCAB and ONCAB groups in the hazard of death (HR =1.24; 95% CI, 0.72–2.15;  $P=0.44$ ) or survival free from MACEs or death (HR =0.77; 95% CI, 0.58–1.24;  $P=0.39$ ). Patency was studied in 199 out of 349 and HRQoL was studied in 299 out of 349 survivors. There was no evidence of attrition bias. The likelihood of graft occlusion was no different between OPCAB (10.6%) and ONCAB (11.0%) groups (OR =1.00; 95% CI, 0.55–1.81;  $P>0.99$ ). Graft occlusion was more likely at the distal than the proximal anastomosis (OR =1.11; 95% CI, 1.02–1.20).

More recently, our group reported a retrospective analysis of long term survival in actively treated diabetic patients undergoing OPCAB versus ONCAB (24). The final population consisted of 2,450 patients; of those, 1,493

subjects were orally treated and 1,011 were on insulin. OPCAB and ONCAB were performed in 1,253 and 1,197 patients respectively. Propensity score matching was used to compare the two groups. The results showed that OPCAB did not significantly affect late mortality (HR =1.08; 95% CI, 0.92–1.28;  $P=0.32$ ). However, OPCAB with incomplete revascularization was associated with a reduced survival rate when compared to OPCAB with complete revascularization (HR =1.82; 95% CI, 1.34–2.46;  $P=0.0002$ ) and ONCAB with complete revascularization (HR =1.83; 95% CI, 1.36–2.47;  $P<0.0001$ ). Di Mauro *et al.* (11) conducted a retrospective cohort study of 2,833 patients with multivessel coronary disease. Two analyses comparing OPCAB and ONCAB were created with respect to preoperative normal and abnormal renal function: one analysis included 1,724 (862 each group) out of 2,618 patients with normal preoperative creatinine ( $<1.5$  mg/dL), and the second analysis included 160 (80 each group) out of 215 patients with preoperative abnormal renal function; in both analyses matched groups were selected applying propensity score. Mean follow up was 7.5 years. Ten-year mortality did not show any significant difference between ONCAB (7.0%) *vs.* OPCAB (5.3%) (HR =1.3; 95% CI, 0.91–1.9;  $P=0.141$ ). The authors concluded that OPCAB provides better late outcomes in patients with normal creatinine preoperatively, but similar outcomes for those with abnormal creatinine levels. The occurrence of acute renal failure significantly impairs early and long-term mortality and the surgical strategy does not influence late mortality in the overall population.

Raja *et al.* (25) reported the results of a retrospective cohort study of 704 consecutive patients with multivessel disease; 307 patients had OPCAB and 397 underwent ONCAB. The 307 OPCAB patients were propensity score matched to 307 ONCAB patients. The follow-up at 10 years was 100%. Survival was similar for the two cohorts. After adjusting for clinical covariates, OPCAB did not emerge as a significant independent predictor of long-term mortality (HR =0.91; 95% CI, 0.70–1.12), readmission to hospital for cardiac cause (HR =0.96; 95% CI, 0.78–1.10), or the need for re-intervention (HR =0.93; 95% CI, 0.87–1.05). OPCAB compared with ONCAB did not adversely impact on survival or freedom from re-intervention at 10-year follow-up.

Puskas *et al.* (3) reported the results of their prospective, randomized controlled trial [The Surgical Management of Arterial Revascularization Therapies (SMART) trial], enrolling 297 unselected patients with multivessel CAD. Of

140 survivors, 87 volunteered to return after a minimum of 6.8 years (maximum, 8.4 years; mean, 7.5 years) for assessment of graft patency and myocardial ischemia. Age at follow-up ranged from 38 to 90 years (mean, 68 years). There were 26 deaths from all causes among OPCAB patients and 31 among ONCAB patients. Graft patency was similar between groups among 622 grafts assessed by angiography before hospital discharge (99% OPCAB *vs.* 97.7% ONCAB;  $P=0.22$ ), among 511 grafts assessed by angiography at 1 year (93.6% OPCAB *vs.* 95.8% ONCAB;  $P=0.33$ ), and among 190 grafts assessed by computed tomographic angiography at late follow-up (76% OPCAB *vs.* 83.5% ONCAB;  $P=0.44$ ). Twelve out of 34 OPCAB (35.3%) and 16 out of 39 ONCAB patients (41.0%) had any ischemia on positron emission tomography scanning ( $P=0.62$ ). Four OPCAB patients (11.8%) and 9 ONCAB patients (23.1%) had an ischemic region in excess of 10% of myocardium ( $P=0.21$ ). At late follow-up, recurrent angina had occurred in 11 of 43 (25.6%) OPCAB patients and 5 of 44 (11.4%) ONCAB patients ( $P=0.09$ ). Percutaneous re-intervention had been performed at the discretion of blinded local cardiologists in 1 of 43 (2.3%) OPCAB patients and 1 of 44 (2.3%) ONCAB patients ( $P=1.0$ ). No patient in either group has undergone repeat CABG. The authors concluded that OPCAB and ONCAB were associated with similar early and late graft patency, incidence of recurrent or residual myocardial ischemia, need for re-intervention, and long-term survival.

Kirmani *et al.* (26) recently presented the results of a retrospective cohort study of patients undergoing isolated CABG at a single centre. A total of 8,055 patients were identified, with a median follow-up of 7.0 years. Propensity score matching was performed on the basis of demographic variables and two groups of 2,082 patients for both OPCAB and ONCAB were obtained. The results showed that in the OPCAB group, there were significantly fewer in hospital cerebrovascular complications (0.5% *vs.* 1.1%;  $P=0.017$ ), and mean length of stay was shorter (7.6 *vs.* 8.1 days;  $P<0.0001$ ). The mean number of grafts was higher in the ONCAB group ( $3.28\pm 0.94$  *vs.*  $3.10\pm 1.10$ ;  $P<0.0001$ ). The authors concluded that despite a lower mean number of grafts, long-term survival after OPCAB was not inferior to long-term survival after ONCAB ( $P=0.167$ ).

Hueb *et al.* (27) reported the results of a prospective, randomized controlled trial (MASS III) of 308 patients undergoing CABG. Of those patients, 155 underwent OPCAB and 153 had ONCAB. The follow-up was at 5 years. Primary composite end points were death,

myocardial infarction, further revascularization (surgery or angioplasty), or stroke. After 5-year follow-up, the primary composite end point was not different between groups (HR =0.71; 95% CI, 0.41–1.22;  $P=0.21$ ). The number of grafts per patient was higher in the ONCAB than the OPCAB group (2.97 *vs.* 2.49 grafts/patient;  $P=0.001$ ). The authors concluded that no difference was found between groups in the primary composite end point at 5-year follow-up. Although OPCAB surgery was related to a lower number of grafts and higher episodes of atrial fibrillation, it had no significant implications related to long-term outcomes.

Similar results were demonstrated by Robertson *et al.* (19) in a retrospective cohort study of 1,285 patients. Following propensity-score matching for baseline characteristics, they reviewed the results of 308 patients undergoing OPCAB compared with 308 patients who had ONCAB. Survival and readmission for cardiac causes were monitored for up to 10 years postoperatively, with a median follow-up period of 5.9 years. The frequency of complete revascularization was significantly different between the 2 groups (OPCAB, 79.2% *vs.* ONCAB 88.3%;  $P=0.002$ ). The OPCAB group had a significantly higher rate of total arterial grafting (OPCAB, 66.6% *vs.* ONCAB, 49.7%;  $P=0.001$ ). No difference was seen in 8-year survival or freedom from cardiac cause and hospital readmission between the 2 groups.

Bakaeen *et al.* (16) recently published the results of their large multicentre retrospective review of all primary isolated CABG procedures performed at VA hospitals during a 13.5-year period. Their objective was to compare risk-adjusted long-term survival between patients who underwent ONCAB *vs.* OPCAB. Using VA Continuous Improvement in Cardiac Surgery Program, they identified all VA patients ( $n=65,097$ ) who underwent primary isolated CABG from October 1997 to April 2011. The primary outcome measure was all-cause mortality. A greedy-match algorithm using the propensity scores matched 8,911 OPCAB with 26,733 ONCAB patients.

For the matched cohort, the median follow-up was 6.7 years (interquartile range, 3.72–9.35 years). Risk-adjusted mortality did not differ significantly between the OPCAB and ONCAB groups at 1 year (4.67% *vs.* 4.78%; RR =0.98; 95% CI, 0.88–1.09) or 3 years (9.21% *vs.* 8.89%; RR =1.04; 95% CI, 0.96–1.12). However, risk-adjusted mortality was higher in the OPCAB group at 5 years (14.47% *vs.* 13.45%; RR =1.08; 95% CI, 1.02–1.15) and 10 years (25.18% *vs.* 23.57%; RR =1.07; 95% CI, 1.03–1.12). Overall, the hazard ratio for OPCAB *vs.* ONCAB was 1.06

(95% CI, 1.00–1.13;  $P=0.04$ ).

They concluded that OPCAB may be associated with decreased long-term survival.

Filardo *et al.* (17) published a retrospective cohort study of 8,081 consecutive patients; 732 patients had OPCAB, 7,349 underwent ONCAB. A propensity-adjusted model controlling for preoperative risk factors identified by the Society of Thoracic Surgeons (STS) and other preoperative clinical and nonclinical details was used to assess adjusted long-term mortality differences between OPCAB and ONCAB. Their results showed that ten-year unadjusted survival was 54.7% (95% CI, 47.2–61.6%) in OPCAB patients and 62.3% (95% CI, 60.9–63.8%) in ONCAB patients. The log-rank test ( $P=0.012$ ) indicated a significantly higher risk of death in OPCAB patients. After adjustment, the risk of death remained significantly higher in the OPCAB patients (HR =1.18; 95% CI, 1.02–1.38). The authors concluded that for multivessel coronary disease, ONCAB might be preferable to OPCAB given that it may achieve a more complete and durable revascularization.

Takagi *et al.* (15) recently published the results of a meta-analysis including 5 randomized controlled trials and 17 observational studies, enrolling a total of 104,306 patients. A pooled analysis of all 22 studies demonstrated a statistically significant 7% increase in long-term all-cause mortality with OPCAB relative to ONCAB (HR =1.07; 95% CI, 1.03–1.11;  $P=0.0003$ ). Although a pooled analysis of 5 randomized trials (1,486 patients) demonstrated a statistically nonsignificant 14% increase in mortality with OPCAB relative to ONCAB (HR =1.14; 95% CI, 0.84–1.56;  $P=0.39$ ), another pooled analysis of 17 observational studies (102,820 patients) demonstrated a statistically significant 7% increase in mortality with OPCAB relative to ONCAB (HR =1.07; 95% CI, 1.03–1.11;  $P=0.0004$ ). The authors concluded that OPCAB is likely associated with worse long-term (>5-year) survival compared with ONCAB.

The findings of this meta-analysis must be interpreted with caution as the results are strongly influenced by the ROOBY trial (28) which, as already mentioned, has received a lot of criticism and has several important limitations.

## Discussion

There has been increasing interest in OPCAB over the last two decades on the basis of the clinical advantages attributed to avoiding CPB during CABG. The most notable merits, as suggested by several observational

studies, included avoiding embolic stroke caused by invasive aortic manipulation and reducing coagulopathy and renal dysfunction (2–14). However, the expected benefit on long term survival is still debated. To date, results of the largest randomized trials are limited to within 1 year of surgery and the long term comparative data regarding clinical outcomes between the 2 strategies are currently unavailable (28,29).

Despite initial enthusiasm, concerns have been raised regarding the risk of incomplete revascularization and higher rate of graft failure with OPCAB. These potential drawbacks have been related to poorer long term survival after OPCAB reported in sporadic studies (16,17).

Incomplete revascularization of patients with multivessel coronary artery disease is an independent risk factor for increased long-term mortality after CABG (32) and has been related to inferior cardiac survival after 5 years of follow-up compared with complete revascularization (33). The criticism regarding completeness of revascularization with OPCAB seems no longer valid in the current era as technology to securely perform multivessel OPCAB has improved significantly; in fact, the majority of evidence from randomized trials suggests at least equivalent completeness of revascularization with OPCAB and ONCAB (3,8,29,30). It is interesting to note that in those trials where OPCAB was associated with incomplete revascularization it is impossible to determine myocardial viability in the territory left ungrafted, because myocardial viability studies were not used, so the significance of a reduced number of grafts in the OPCAB cohort is uncertain. Moreover, none of the trials or studies reporting incomplete revascularization provides an explanation for failure to completely revascularize the OPCAB group.

In our review, most of the available comparisons found similar survival rates after OPCAB *vs.* ONCAB, especially when OPCAB is performed in high volume centres, thus supporting the view that OPCAB is as effective as ONCAB in terms of late survival. It should be underlined that substantial variability between the studies in terms of risk profile, selection criteria and expertise of surgeons limits the generalizability of any conclusions. The frequency of complete revascularization reported by different studies comparing OPCAB and ONCAB is strongly influenced by relative experience with each technique of the reporting centre and surgeon, highlighting once more the importance of a learning curve as well as case load. These differences can also have an impact on the final completeness of revascularization achieved by multicentre randomized trials.

Graft failure is one of the major determinants of clinical



prognosis after CABG. There has been considerable concern among surgeons and cardiologists that the higher technical difficulty of OPCAB might translate into less precise anastomoses and subsequently reduced graft patency (34). A precipitous learning curve, distractions caused by cardiac motion or pulmonary insufflations, and performing the anastomoses on a moving target have been considered as factors accountable for poorer graft patency after OPCAB (35). Interestingly, the concerns about suboptimal graft patency over the last years have been largely influenced by the results of the ROOBY trial (28), whose findings have been strongly criticised since the 53 participating surgeons enrolled on average only eight patients per year during the study period and had unacceptably high conversion rates to on-pump surgery (12%) and incomplete revascularization (18%). Moreover, in 60% of the cases a junior resident was the primary surgeon. Another unrecognized confounder that contributed to poor graft patency in the ROOBY trial was the concomitant use of endoscopic vein harvesting (EVH) in 1,471 patients (ONCAB =907 and OPCAB =564). The incidence of a patient having 1 or more occluded saphenous vein grafts on follow-up angiography was 41.3% in the EVH group, compared with 28.0% in the open vein harvesting (OVH) group ( $P<0.0001$ ). Since ROOBY trial was recruiting at a time when EVH was not being widely practiced, the poor vein graft patency secondary to EVH can be attributed to the learning curve and relative inexperience of the vein harvesters. Poor conduit quality, an unavoidable consequence of the learning curve for EVH, has been found to be a significant predictor of early graft failure (36).

## Conclusions

In view of the increasing risk profile of patients currently referred to coronary artery bypass surgery and potential benefit from OPCAB in reducing operative morbidity, current evidence suggest that OPCAB should still be considered a valuable strategy. Undoubtedly, better results using the OPCAB technique are achieved by specialised groups completely committed to this surgical technique. OPCAB is more technically complex and completeness of revascularization is strongly influenced by surgeon and centre volume and expertise.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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