Review Article

Current outcomes of off-pump versus on-pump coronary artery bypass grafting: evidence from randomized controlled trials

Daniel Fudulu, Umberto Benedetto, Gustavo Guida Pecchinenda, Pierpaolo Chivasso, Vito Domenico Bruno, Filippo Rapetto, Alan Bryan, Gianni Davide Angelini

Bristol Heart Institute, University Hospitals Bristol, Bristol, UK

Contributions: (I) Conception and design: D Fudulu; GD Angelini; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Daniel Fudulu. Bristol Heart Institute, University Hospitals Bristol, Bristol, UK. Email: daniel.fudulu@bristol.ac.uk.

Abstract: Coronary artery bypass grafting remains the standard treatment for patients with extensive coronary artery disease. Coronary surgery without use of cardiopulmonary bypass avoids the deleterious systemic inflammatory effects of the extracorporeal circuit. However there is an ongoing debate surrounding the clinical outcomes after on-pump versus off-pump coronary artery bypass (ONCAB versus OPCAB) surgery. The current review is based on evidence from randomized controlled trials (RCTs) and meta-analyses of randomized studies. It focuses on operative mortality, mid- and long-term survival, graft patency, completeness of revascularisation, neurologic and neurophysiologic outcomes, perioperative complications and outcomes in the high risk groups. Early and late survival rates for both OPCAB and ONCAB grafting are similar. Some studies suggest early poorer vein graft patency with off-pump when compared with on-pump, comparable midterm arterial conduit patency with no difference in long term venous and arterial graft patency. A recent, pooled analysis of randomised trials shows a reduction in stroke rates with use off-pump techniques. Furthermore, OPCAB grafting seems to reduce postoperative renal dysfunction, bleeding, transfusion requirement and respiratory complications while perioperative myocardial infarction rates are similar to ONCAB grafting. The high risk patient groups seem to benefit from off-pump coronary surgery.

Keywords: Coronary artery bypass; off-pump coronary artery bypass (OPCAB); beating heart coronary artery bypass; outcome measure; randomized controlled trial (RCT); evidence

Submitted Jul 24, 2016. Accepted for publication Aug 24, 2016.
doi: 10.21037/jtd.2016.10.80
View this article at: http://dx.doi.org/10.21037/jtd.2016.10.80

Introduction

Despite a large body of evidence, there is an ongoing, controversial debate whether coronary artery bypass graft surgery should be performed with or without extracorporeal circulation. This intense debate is held between three schools of thought: the "pure", off-pump surgeons, the on-pump surgeons and the "selectivists" group that reserves off-pump surgery for selected cases only. Historically, the shift towards off-pump coronary artery bypass (OPCAB) grafting was proposed both to reduce the operation cost in developing countries but also to avoid the deleterious effects of the contact of blood with the artificial extracorporeal circuit (i.e., mainly the systemic inflammatory response and coagulopathy) (1-3). Furthermore, avoidance of aortic cannulation and minimisation of aortic manipulation would theoretically translate into reduced cerebral stroke, hence reduced morbidity and perioperative mortality (4). On the other hand, on-pump surgeons argue that the comfort of the bypass circuit results in a better anastomotic technique that translates into a more complete revascularization and

Table 1 Short term outcomes of OPCAB versus ONCAB

Author	Study design	Sample size	Short term survival
Deppe *et al.*, 2016 (3)	Meta-analysis of RCTs	49 RCTs, with a total of 16,718 patients	No 30-day mortality difference: 1.8% and 4.8% for OPCAB and 2.1% and 4.8% for ONCAB, odds ratio (OR), 0.86 or 0.97; 95% confidence interval (CI): 0.69–1.06 or 0.84–1.13
Diegeler *et al.*, 2013 (11)	RCT	In the GOPCABE trial, 2,539 patients underwent randomization to ONCAB versus OPCAB	No difference in death within 30 days 31/1,187 (2.6%) versus 34/1,207 (2.8%), OR, 0.92; 95% CI: 0.57–1.51; P=0.75
Kowalewski *et al.*, 2016 (1)	Meta-analysis of RCTs	36 RCTs, with a total of 15,531 subjects	No 30-day mortality difference: 2.04% (159/7,779) in the OPCAB group versus 2.45% (190/7,752) in the ONCAB group. No difference between the two techniques (OR, 0.88; 95% CI: 0.71–1.09; P=0.25)
Lamy *et al.*, 2012 (12)	RCT	The CORONARY trail enrolled 4,752 patients randomized to ONCABG or OPCAB	No significant difference in mortality between ONCAB and OPCAB at 30 days: 60 (2.5%) versus 59 (2.5%) respectively; HR, 1.02; 95% CI: 0.71–1.46
Møller *et al.*, 2012 (15)	Meta-analysis of RCTs	Cochrane systematic review of 86 trials (10,716 participants) were included	OPCAB increased all-cause mortality compared to ONCAB [189/5,180 (3.7%) versus 160/5,144 (3.1%); RR, 1.24; 95% CI: 1.01–1.53; P=0.04]. In the trials at low risk of bias the effect was more significant [154/2,485 (6.2%) versus 113/2,465 (4.6%), RR, 1.35; 95% CI: 1.07–1.70; P=0.01]
Taggart *et al.*, 2015 (13)	Post-hoc analysis of outcomes of ONCAB versus OPCAB from the Arterial Revascularization Trial (ART)	ART trial randomized 3,102 patients with multi vessel coronary artery disease to single internal mammary artery (IMA) or bilateral internal mammary arteries (BIMA)	Similar mortality rate at 30 days: 1.1% ONCAB and 1.3% OPCAB

OPCAB, off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; RCT, randomized controlled trial; RR, relative risk.

better graft patency (3).

Developed about 40 decades ago (5-7), OPCAB reached a plateau in Europe, accounting for nearly 15–20% of all coronary operations, while in Asia 60–100% of patients are offered coronary artery bypass grafting (2). A retrospective analysis of the Society of Thoracic Surgeons Adult Cardiac Surgery Database in USA revealed a decline in off-pump operations, currently being used in fewer than one out of five patients (8). The current review focuses on the main outcomes of on-pump coronary artery bypass (ONCAB) grafting versus OPCAB from randomized controlled trials (RCTs) (i.e., level I evidence). The main criticism of RCTs in this area, is the under powering because of recruitment of low risk patients but also because of the low mortality and morbidity of coronary artery bypass grafting that would require very large sample populations to detect a difference (4). Therefore, we will also be reviewing pooled data from recent, updated meta-analyses of randomized trials only. We selected in our review large sample size RCTs or large meta-analyses of RCTs to discuss the hard end-point outcomes but smaller trials were also included to discuss other outcomes.

Operative mortality

The majority of the large RCTs to date failed to show a difference in early mortality between off-pump and on-pump surgery (1,3,9-13). One small sample size RCT by Fattouch *et al.* showed a reduced mortality in patients with ST elevation undergoing urgent/emergent off-pump coronary surgery compared to on-pump surgery (14). Deppe *et al.* in meta-analysis of RCTs on almost 16,900 patients found no difference in 30-day mortality. Kowalewski *et al.* in meta-analysis of over 19,000 patients demonstrated no significant difference in short term mortality (1). The evidence is summarised in *Table 1*.

Mid- and long-term survival

Angelini *et al.* pooled midterm follow-up outcomes from two

RCTs—Beating Heart against Cardioplegic Arrest Studies (BHACAS 1 and 2). The mean follow-up was 25.0 months for BHACAS 1, and 13.7 months for BHACAS 2. Combined all-cause mortality did not differ between patients in off-pump and on-pump groups [hazard ratio (HR), 0.57; 95% confidence interval (CI): 0.17–1.96] (16). A later study by the same group found no difference in long term survival up to 6–8 years between on-pump and off-pump coronary surgery (HR, 0.84; 95% CI: 0.58–1.24; P=0.39) (17). The Veterans Affairs Randomized On/Off Bypass (ROOBY) trial randomly assigned 2,203 of patients to either off-pump or on-pump. It was the first trial where off patients were recruited in based on the surgeon's experience (minimum number of 20 cases) though some argue that the learning curve extends beyond this set point (4). The primary long term (1 year) composite of death, repeat revascularization, non-fatal myocardial infraction was higher (9.9% *vs.* 7.4%, P=0.04) for the OPCAB group with no significant differences between the individual composite components. The sensitivity analysis revealed a trend toward more death from cardiac causes in the on-pump group (2.7% *vs.* 1.3%, P=0.03). A Cochrane systematic review of RCTs off-pump versus on-pump found an increased risk of death with off-pump in the long term (>30 days) follow-up studies [relative risk (RR), 1.34; 95% CI: 1.08–1.67; P=0.009] (15). Luo *et al.* in a recent meta-analysis of RCTs found no difference in patients with over 6 months' follow-up [odds ratio (OR), 1.02; 95% CI: 0.86–1.22; P=0.81] (18). The Coronary Artery Bypass Grafting Off- or On-Pump Revascularization Study (CORONARY) remains the largest RCT to date that recruited 4,752 patients (12,19). At 1 year the study reported no difference in primary composite of death, myocardial infarction, stroke, or new renal failure requiring dialysis. The primary outcome event had occurred in 288 participants (12.1%) in the off-pump group and 316 participants (13.3%) in the on-pump group (HR with the off-pump procedure, 0.91; 95% CI: 0.77–1.07; P=0.24). There was no significant difference between the rates of the individual primary outcome components. The 5-year long term outcomes from the CORONARY trial are still awaited (*Table 2*).

Graft patency, number of grafts and need for repeat revascularization

Graft patency

Graft patency was the primary endpoint in a RCT conducted by Puskas *et al.* on 200 patients. The authors found similar graft patency between off-pump and conventional surgery at 30 days (absolute difference, 1.3%; 95% CI: –0.66–3.31%; P=0.19) and 1 year (absolute difference, –2.2%; 95% CI: –6.1–1.7%; P=0.27) (20). Similarly, Magee *et al.* found no difference in vein patency or arterial graft patency at 1 year in 1,920 patients that completed angiographic follow-up (20). Lingaas *et al.* (21) reported no significant differences in arterial and vein graft patency in 120 patients randomized to OPCAB or ONCAB.

In contrast to previous studies, several trials reported poor graft patency for patients undergoing off-pump. Khan *et al.* found a poorer graft patency at 3 months for patient undergoing OPCAB (22). Houlind *et al.* found reduced graft patency in the OPCAB group compared to the on-pump group, on 481 patients that completed angiographic follow-up at 6 months (23). At 1 year follow-up, Widimsky *et al.* found a lower graft patency for the off-pump vein grafts while the arterial graft patency were similar for both arms (24). The ROOBY trial found a significantly lower graft patency in the off-pump group than in the on-pump group (82.6% *vs.* 87.8%, P<0.01) at 1 year (10). Similar results were found by Zhang *et al.* in a recent meta-analysis of 12 RCTs, on a total of 3,894 patients (4,137 grafts). Interestingly, the authors found an increased risk of occlusion of vein grafts but no difference in arterial graft patency [left internal mammary artery (IMA) and radial artery conduits] (25). In the longest follow-up study to date (up to 6 to 8 years) of patients recruited in two randomized trials comparing OPCAB to ONCAB, Angelini *et al.* demonstrated that 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). Furthermore, the authors found the graft occlusion to occur more likely at the distal anastomosis (OR, 1.11; 95% CI: 1.02–1.20) in both groups (17) (*Table 3*).

Number of grafts and repeat revascularization

Several trials demonstrated a reduced number of grafts performed in OPCAB arms and increased revascularization rates. The ROOBY trial demonstrated that the proportion of patients with fewer grafts than initially planned was higher in the off-pump arm than in the on-pump arm (17.8% *vs.* 11.1%, P<0.01) (10). Similarly, the Off-Pump versus On-Pump Coronary-Artery Bypass Grafting in Elderly Patients trial (GOCABE) trial (11) revealed that fewer grafts were

Table 2 Midterm and long term outcomes of OPCAB versus ONCAB

Author	Study design	Sample size	Midterm and long term survival
Angelini *et al.*, 2002 (16)	Pooled analysis of two RCTs: Beating Heart Against Cardioplegic Arrest Studies (BHACAS 1 and 2)	BHACAS 1: 200 patients, 100 randomised to OPCAB and 100 to ONCAB; BHCAS 2: 200 patients, 101 randomised to OPCAB and 100 to ONCAB	Mean follow-up was 25.0 months standard deviation (SD): 9.1 for BHACAS 1 and 13.7 months SD: 5.5 for BHACAS 2. In the pooled survival estimates at 24 months there was no difference between combined all-cause mortality (HR, 0.57; 95% CI: 0.17–1.96)
Angelini *et al.*, 2009 (17)	Pooled analysis of two RCTs: Beating Heart Against Cardioplegic Arrest Studies (BHACAS 1 and 2)	BHACAS 1: 200 patients, 100 randomised to OPCAB and 100 to ONCAB; BHCAS 2: 200 patients, 101 randomised to OPCAB and 100 to ONCAB	Mean durations of follow-up for survival were 75.5 (SD, 20.6) and 76.7 (SD, 19.3) months for OPCAB and ONCAB; there were 23 and 29 deaths in each group, respectively. Cox regression showed no difference in survival rates between the two groups (HR, 1.24; 95% CI: 0.72–2.15; P=0.44)
Lamy *et al.*, 2013 (19)	Meta-analysis of RCTs	The CORONARY trial enrolled 4,752 patients randomized to ONCABG or OPCAB	No significant differences between the two groups in the composite end-point at 1 year and no difference in the death component: ONCAB 122 (5.1%) *vs.* OPCAB 119 (5.0%); HR, 1.03; 95% CI: 0.80–1.32
Luo *et al.*, 2015 (18)	Meta-analysis of RCTs	7 RCTs, 9,128 patients	No significant difference in all the long-term outcomes (over 6 months' follow-up), mortality, OR, 1.02; 95% CI: 0.86–1.22; P=0.81
Møller *et al.*, 2012 (15)	Meta-analysis of RCTs	Cochrane systematic review of 86 trials (10,716 participants) were included. Ten trials (4,950 participants) were considered to be low risk of bias	Post-hoc sensitivity analysis we compared trials with short-term follow-up (≤30 days) with trials with long-term follow-up (>30 days). In the trials with long-term follow-up the meta-analysis showed that OPCAB was significantly associated with increased risk of death (RR, 1.34; 95% CI: 1.08–1.67, P=0.009)
Shroyer *et al.*, 2009 (10)	RCT	The department of Veterans Affairs Randomized On/Off Bypass (ROOBY) randomized 2,203 patients to OPCAB versus ONCAB	The rate of the 1-year composite outcome was higher for OPCAB than for ONCAB (9.9% *vs.* 7.4%, P=0.04). The 1-year composite of death from cardiac causes was: OPCAB =93 (8.8%) and ONCABG =62 (5.9%), RR, 1.48; 95% CI: 1.09–2.02; P=0.01

OPCAB, off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; RCT, randomized controlled trial; CORONARY, Coronary Artery Bypass Grafting Off- or On-Pump Revascularization Study; OR, odds ratio; HR, hazard ratio; CI, confidence interval; RR, relative risk.

performed in the off-pump arm compared to on-pump arm. At 30 days, patients having OPCAB had a higher rate of repeat revascularization while at 1 year the revascularization rates remained similar. Similarly, the CORONARY trial showed fewer grafts performed in the off-pump group and higher early revascularization rate at 30 days, but at 1 year the revascularization rates were no longer different (12,19). A large meta-analysis of RCTs by Deppe *et al.* (3) showed increased early (30 days) revascularization in the off-pump group (*Table 4*).

Stroke and neurocognitive outcomes

Cerebral stroke is a major complication after coronary artery bypass grafting that increases mortality, morbidity and cost (27). Minimization of aortic manipulation (28) and avoidance of the extracorporeal circuit (29) reduce the risk stroke and cerebral embolization respectively. Therefore, OPCAB should offer better outcomes in this respect. The most prominent off-pump versus on-pump trials to date failed to show a reduction of stroke rates with use of OPCAB (10-12). Deppe *et al.* in the subgroup meta-analysis

Table 3 Graft patency outcomes

Author	Study design	Sample size	Graft patency investigation	Graft patency outcomes
Angelini *et al.*, 2009 (17)	Pooled analysis of two RCTs: Beating Heart Against Cardioplegic Arrest Studies (BHACAS 1 and 2)	BHACAS 1: 200 patients, 100 randomised to OPCAB and 100 to ONCAB; BHCAS 2: 200 patients, 101 randomised to OPCAB and 100 to ONCAB; 505 grafts were studied in 199 participants	Multidetector computed tomographic coronary angiographic analysis	Likelihood of graft occlusion was similar between OPCAB (10.6%) and ONCAB (11.0%) groups (OR, 1.00; 95% CI: 0.55–1.81; P>0.99). Mean durations of follow-up from the operation to multidetector computed tomographic coronary angiographic analysis were 85.1 months (SD, 4.8) and 85.8 months (SD, 4.7) for the ONCAB and OPCAB respectively
Houlind *et al.*, 2012 (23)	RCT	900 patients >70 years of age randomized to ONCAB or OPCAB surgery. A total of 481 patients underwent angiography at 6 months	Coronary angiography	In the ONCAB group, 549 (86%) of 650 grafts were patent, 38 (5%) were stenotic, and 63 (9%) were occluded. The difference between the proportion of patent grafts was statistically significant in favour of ONCAB group (P=0.01). The proportion of open left internal thoracic artery grafts was identical (e.g., 95% in both groups)
Khan *et al.*, 2004 (22)	RCT	50 patients ONCAB and 54 OPCAB. Follow-up angiographic data were available for 82 patients (39 patients ONCAB and 43 OPCAB)	Coronary angiography	The overall patency rate of ONCAB grafts was significantly higher than the patency rate of OPCAB grafts (98% *vs.* 88%, P=0.002). The patency rate was higher for all graft territories in the ONCAB group versus OPCAB
Lingaas *et al.*, 2006 (21)	RCT	120 patients were randomized to OPCAB or ONCAB	Coronary angiography	No difference in internal mammary artery (IMA) graft patency at 3 months: OPCAB 96% versus ONCAB 98% and 94% versus 96% after 12 months respectively. No difference in vein graft patency OPCAB 84% versus ONCAB 91% after 3 months and 80% versus 87% at 12 months respectively
Magee *et al.*, 2008 (20)	Follow-up of RCT	1-year angiographic follow-up was completed on 1,920 patients (4,736 grafts) of the PRoject of Ex-vivo Vein graft ENgineering via Transfection IV (PREVENT IV) a multicentre RCT of edifoligide to prevent vein graft failure from neointimal hyperplasia	Coronary angiography	Vein graft failure in ONCAB versus OPCAB patients was 25.3% versus 25.7% respectively (P=0.62) at 1 year. Failure of internal mammary artery grafts was similar
Puskas *et al.*, 2004 (26)	RCT	Randomized single-surgeon trial of 200 patients, unselected for coronary anatomy, ventricular function, or comorbidities. Follow-up was complete for 197 patients at 30 days; 185 at 1 year	Coronary angiography	Graft patency was similar for OPCAB and ONCAB at 30 days [absolute difference, 1.3%; 95% confidence interval (CI): −0.66–3.31%; P=0.19] and at 1 year (absolute difference, −2.2%; 95% CI: −6.1–1.7%; P=0.27)

Table 3 (*continued*)

Table 3 (*continued*)

Author	Study design	Sample size	Graft patency investigation	Graft patency outcomes
Shroyer *et al.*, 2009 (10)	RCT	The department of Veterans Affairs Randomized On/Off Bypass (ROOBY) randomized 2,203 patients to OPCAB or ONCAB. Out of 2,127 patients who underwent coronary artery bypass grafting at 12 months, 1,371 (64.5%) had follow-up angiograms: 1,335 had angiograms at the 12-month and 36 patients had an interim angiogram	Coronary angiography	Rate of graft patency was significantly lower in the OPCAB than OPCAB group (82.6% *vs.* 87.8%, P<0.01). There was a lower rate lower rate of patency of saphenous-vein grafts in the OPCAB patients than in the ONCAB (76.6% *vs.* 83.8%, P<0.01). The patency rate for left internal thoracic-artery pedicle grafts to the left anterior descending artery were similar (95.3% for OPCAB and ONCAB 96.2%, P=0.48). There were fewer grade A grafts (excellent graded graft) in OPCAB (89.0%) *vs.* ONCAB (93.2%, P=0.01)
Widimsky *et al.*, 2004 (24)	Follow-up of RCT	1-year follow-up of 255 patients from the PRAGUE-4 trial that randomized 400 consecutive nonelected cardiac surgery to ONCAB (n=192) and OPCAB (n=208)	Coronary angiography	Arterial graft patency after 1 year was 91% in both groups. Vein graft patency was 59% ONCAB versus 49% OPCAB (P= not significant) but graft patency per patient was lower in the OPCAB: 0.7 patent anastomosis per patient versus 1.1 patent anastomosis in the ONCAB group (P<0.01)
Zhang *et al.*, 2014 (25)	Meta-analysis of RCTs	12 RCTs, for a total of 3,894 and 4,137 grafts performed during OPCAB and ONCAB	Computed tomographic angiography or coronary angiography	Increased risk of occlusion of all grafts (RR, 1.35; 95% CI: 1.16–1.57) and saphenous vein grafts (RR, 1.41; 95% CI, 1.24–1.60) in the OPCAB group. No significant difference in graft occlusion of IMA (RR, 1.15; 95% CI, 0.83–1.59) and radial artery grafts (RR, 1.37; 95% CI, 0.76–2.47) between OPCAB and ONCAB

OPCAB, off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; RCT, randomized controlled trial; OR, odds ratio; HR, hazard ratio; RR, relative risk.

Table 4 Repeat revascularisation and number of grafts outcomes

Author	Study design	Sample size	Repeat revascularisation and number of grafts outcomes
Deppe *et al.*, 2016 (3)	Meta-analysis of RCTs	49 RCTs, with a total of 16,718 patients	OPCAB was associated with a 1.9-fold increased risk of repeat revascularization at 30 days (OR, 1.87; 95% CI: 1.13–3.11; P=0.0191)
Diegeler *et al.*, 2013 (11)	RCT	In the GOPCABE trial, 2,539 patients underwent randomization to ONCAB versus OPCAB	Repeat revascularization at 30 days was higher for OPCAB: 15/1,187 (1.3%) *vs.* ONCAB: 5/1,207 (0.4%), OR, 2.42; 95% CI: 1.03–5.72; P=0.04. Repeat revascularization at 1 year was similar for OPCAB: 36/1,179 (3.1%) versus ONCAB: 24/1,191 (2.0%), OR, 1.52; 95% CI: 0.90–2.54; P=0.11
			The average number of coronary anastomoses was lower (2.7%) in the OPCAB group versus the ONCAB group (2.8%), P<0.001. The proportion of patients with fewer grafts than planned was higher in the OPCAB (34.0% *vs.* 29.3% in the on-pump group) and the proportion of patients having more grafts than planned was lower in OPCAB group (10.2% *vs.* 16.7%)
Lamy *et al.*, 2013 (19)	RCT	The CORONARY trial enrolled 4,752 patients randomized to ONCABG or OPCAB	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)
Shroyer *et al.*, 2009 (10)	RCT	The department of Veterans Affairs Randomized On/Off Bypass (ROOBY) randomized 2,203 patients to OPCAB versus ONCAB	Revascularization between 30 days and 1 year after surgery were similar: 49 (4.6%) for OPCAB versus 36 (3.4%) for ONCAB, absolute percentage difference =1.2 (95% CI: −0.5–2.9), relative risk (RR) =1.35 (95% CI: 0.88–2.05), P=0.18. Significant difference between OPCAB (2.9±0.9) and ONCAB groups (3.0±1.0) in the average number of grafts performed, P=0.002
			The proportion of patients with fewer grafts than originally planned was significantly higher in OPCAB group compared to ONCAB (17.8% *vs.* 11.1%, P<0.01)

OPCAB, off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; RCT, randomized controlled trial; CORONARY, Coronary Artery Bypass Grafting Off- or On-Pump Revascularization Study; OR, odds ratio; HR, hazard ratio; CI, confidence interval.

of 13 trials found no difference in stroke rates between OPCAB or ONCAB (3). However, the recent meta-analysis by Kowalewski *et al.* on 40 RCTs found OPCAB to be associated with a significant 28% reduction in odds of cerebral stroke (OR, 0.72; 95% CI: 0.56–0.92; P=0.009; I^2=0%) (1).

Several studies suggested neurocognition to be more related to aortic manipulation rather the use of extracorporeal circulation (30,31). The ROOBY trial demonstrated no difference in neurophysiological outcomes between off or on-pump groups (10). Similarly, three other randomized trials (32-34) and two systematic reviews of RCTs (35,36) failed to show any benefit with OPCAB in terms of neurocognitive function (*Tables 5*,*6*).

Postoperative renal dysfunction

The ROOBY trial found no significant difference between OPCAB and ONCAB, in terms of renal failure requiring dialysis (10). The CORONARY trial found the use of OPCAB to significantly reduce acute kidney injury (28.0% *vs.* 32.1%; RR, 0.87; 95% CI: 0.80–0.96; P=0.01) (12). The GOPCABE trial found no difference between off-pump or on-pump in new renal-replacement therapy required at 30- or 1-year which was part of the primary composite endpoint (11). In a subgroup meta-analysis of 1,571 patients from 25 trials, Deppe *et al.* found OPCAB to reduce the absolute risk of renal dysfunction by 2.1% (OR, 0.79; 95% CI: 0.71–0.89; P<0.0001) but no difference in the new onset of renal replacement (3) (*Table 7*).

Table 5 Stroke outcomes

Author	Study design	Sample size	Stoke outcomes
Deppe *et al.*, 2016 (3)	Meta-analysis of RCTs	Subgroup analysis of 13 RCTs of 'high quality' RCT	Incidence of stroke was similar: 1.5% for OPCAB and 1.8% for ONCAB (OR, 0.86; 95% CI: 0.65–1.13; P=0.3146)
Diegeler *et al.*, 2013 (11)	RCT	In the GOPCABE trial, 2,539 patients underwent randomization to ONCAB versus OPCAB	No significant difference stroke rates in the primary composite end-point: OPCAB: 26/1,187 (2.2%) versus ONCABG 32/1,207 (2.7%), OR, 0.83; 95% CI: 0.50–1.38; P=0.47 and at 1 year: OPCAB: 41/1,179 (3.5%) versus ONCABG 52/1,191 (4.4%), OR, 0.79; 95% CI: 0.53–1.19; P=0.26
Kowalewski *et al.*, 2016 (1)	Meta-analysis of RCTs	40 RCTs, with a total of 15,829 participants	OPCAB significantly reduced (by 28%) the odds of stroke compared with CABG (OR, 0.72; 95% CI: 0.56–0.92; P=0.009)
Lamy *et al.*, 2012 (12)	RCT	The CORONARY trail enrolled 4,752 patients randomized to ONCABG or OPCAB	No significant difference in stroke rates in the primary outcome at 30 days: OPCAB: 24 (1.0%) versus ONCAB: 27 (1.1%), HR, 0.89; 95% CI: 0.51–1.54
Shroyer *et al.*, 2009 (10)	RCT	The department of Veterans Affairs Randomized On/Off Bypass (ROOBY) randomized 2,203 patients to OPCAB versus ONCAB	No significant difference in stroke rates between groups: OPCAB: 14 (1.3%) versus ONCAB: 8 (0.7%). RR, 1.75; 95% CI: 0.74–4.14; P=0.28

OPCAB, off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; RCT, randomized controlled trial; CORONARY, Coronary Artery Bypass Grafting Off- or On-Pump Revascularization Study; OR, odds ratio; HR, hazard ratio; CI, confidence interval; RR, relative risk.

Table 6 Neurocognition outcomes

Author	Study design	Sample size	Neurocognition outcomes
Ernest *et al.*, 2006 (32)	RCT	107 patients randomized to OPCAB or ONCAB; 11 standardized neuropsychological tests done before surgery, at 2 and 6 months after surgery	Less OPCAB had impairment of verbal fluency at 6 months. The rest of the cognitive test results did not differ between groups
Hernandez *et al.*, 2007 (33)	RCT	201 patients undergoing no emergent isolated revascularisation randomized to OPCAB or ONCAB. 19-test neurocognitive tests administered at baseline, discharge, and 6 months	No difference at discharge (discharge versus preoperative: RR, 0.83; 95% CI: 0.65–1.07) or at 6 months (6 months versus preoperative: RR, 0.94; 95% CI: 0.70–1.28)
Kennedy *et al.*, 2013 (35)	Meta-analysis of RCTs	13 RCTs that included a total of 2,405 patients; seven psychometric tests administered	No significant differences were found between OPCAB and ONCAB in the early (P range, 0.21–0.78) or late (P range, 0.09–0.93) postoperative period
Marasco *et al.*, 2008 (36)	Meta-analysis of RCTs	Eight trials incorporating 892 patients fulfilled all the inclusion criteria	No differences in outcomes in the five neurocognitive tests assessed (Rey Auditory Verbal Learning, Grooved Pegboard, Trail A and B, and Digit Symbol)
Shroyer *et al.*, 2009 (10)	RCT	The department of Veterans Affairs Randomized On/Off Bypass (ROOBY) randomized 2,203 patients to OPCAB versus ONCAB	No difference in the battery of 11 tests between the ONCAB and OPCAB
van Dijk *et al.*, 2007 (34)	RCT	The Octopus Study, a randomized 281 patients to OPCAB or ONCAB. Ten standardized neuropsychological tests administered at 5 years follow-up	No difference in cognitive decline: 62 (50.4%) of 123 in the OPCAB and 59 (50.4%) of 117 in the ONCAB had cognitive decline (absolute difference, 0%; 95% CI, −12.7–12.6%; P>0.99)

OPCAB, off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; RCT, randomized controlled trial; CI, confidence interval; RR, relative risk.

Table 7 Renal function outcomes

Author	Study design	Sample size	Renal function outcomes
Deppe *et al.*, 2016 (3)	Meta-analysis of RCTs	1,571 patients (12.0%) reported in 25 trials had a renal dysfunction	OPCAB associated with absolute risk reduction of 2.1% for renal dysfunction after coronary artery bypass surgery (OR, 0.79; 95% CI: 0.71–0.89; P<0.0001); incidence of new-onset renal replacement therapy was 1.3% OPCAB and 1.7% for ONCAB, P=0.0945
Diegeler *et al.*, 2013 (11)	RCT	In the GOPCABE trial, 2,539 patients underwent randomization to ONCAB versus OPCAB	No difference in new renal failure requiring dialysis within the primary composite at 30 days OPCAB: 29/1,187 (2.4%) *vs.* ONCAB: 37/1,207 (3.1%), OR, 0.80; 95% CI: 0.49–1.29; P=0.36 and at 1 year: OPCAB: 34/1,179 (2.9%) *vs.* ONCAB: 42/1,191 (3.5%), OR, 0.82; 95% CI: 0.52–1.28; P=0.37
Lamy *et al.*, 2012/2013 (12,19)	RCT	The CORONARY trail enrolled 4,752 patients randomized to ONCABG or OPCAB	No difference in new renal failure requiring dialysis within the primary composite at 30 days OPCAB: 28 (1.2%) *vs.* ONCAB: 27 (1.1%) and at 1 year: OPCAB: 30 (1.3%) *vs.* ONCAB: 31 (1.3%)
Shroyer *et al.*, 2009 (10)	RCT	The department of Veterans Affairs Randomized On/Off Bypass (ROOBY) randomized 2,203 patients to OPCAB versus ONCAB	No difference in renal failure requiring dialysis: OPCAB: 9 (0.8%) *vs.* ONCAB: 10 (0.9%), RR, 0.90; 95% CI: 0.37–2.20; P=0.82

OPCAB, off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; RCT, randomized controlled trial; CORONARY, Coronary Artery Bypass Grafting Off- or On-Pump Revascularization Study; OR, odds ratio; CI, confidence interval; RR, relative risk.

Other perioperative complications

The current literature debating about perioperative morbidity related to OPCAB or ONCAB focuses on the following clinical outcomes: low cardiac output, perioperative myocardial infarction, infection rates, bleeding and reintervention rates, length of stay, ventilation time and rates of atrial fibrillation. The ROOBY trial demonstrated no difference in reoperation for bleeding, new mechanical support or mediastinitis (10). In the CORONARY trial, the use of OPCAB reduced perioperative transfusions (50.7% *vs.* 63.3%; RR, 0.80; 95% CI: 0.75–0.85; P<0.001), reoperation for perioperative bleeding (1.4% *vs.* 2.4%; RR, 0.61; 95% CI: 0.40–0.93; P=0.02), acute kidney injury (28.0% *vs.* 32.1%; RR, 0.87; 95% CI: 0.80–0.96; P=0.01), and respiratory complications (5.9% *vs.* 7.5%; RR, 0.79; 95% CI: 0.63–0.98; P=0.03). Two large meta-analyses of RCTs (1,3) found no difference in myocardial infraction rates between ONCAB or OPCAB. In the meta-analysis by Deppe *et al.* (3), the incidence of low cardiac output and infection were reduced with use off-pump. Furthermore, the number of patients needing transfusion and the chest tube drainage was significantly reduced in the in the off-pump group, but with no difference in re-thoracotomy rates. In the same meta-analysis (3) there was no difference in atrial fibrillation rates between off-pump versus on-pump, contrary to a smaller, previous meta-analysis of RCTs (37) (*Table 8*).

High-risk patients

Most of the available evidence for the high risk patient is focused on several high risk groups: left ventricular dysfunction, renal impairment, left main stem disease, old age, stroke, re-do coronary artery bypass grafting, chronic lung disease, emergency surgery and patients with an European system for cardiac operative risk evaluation (EuroSCORE) of >5 (1). In a RCT of 411 high risk patients (EuroSCORE ≥6), OPCAB was found to reduce mortality and morbidity at 30 days (38). Similarly, a smaller RCT by Hlavicka *et al.* of 206 patients with EuroSCORE ≥6 found a significantly higher incidence of the combined endpoint (all-cause deaths, stroke, myocardial infarction, or renal failure requiring new haemodialysis) in the ONCAB group at 30 days, while at 1 year there was no significant

Table 8 Perioperative morbidity outcomes

Author	Study design	Sample size	Perioperative morbidity outcomes
Deppe *et al.*, 2016 (3)	Meta-analysis of RCTs	16,904 patients from 51 RCTs	ONCAB associated with increased risk mediastinitis. OPCAB was associated with a reduction of the length of ventilation, the length of ICU stay and the length of hospital stay, less transfusion requirements and less chest tube drainage. Rethoracotomy rates, myocardial infarction rates and atrial fibrillation rates were normal
Kowalewski *et al.*, 2016 (1)	Meta-analysis of RCTs	15,733 from 43 RCTs	No significant reduction in MI rates
Lamy *et al.*, 2012 (12)	RCT	The CORONARY trail enrolled 4,752 patients randomized to ONCABG or OPCAB	OPCAB at 30 days reduced the rates of blood-product transfusion, reoperation for perioperative bleeding, acute kidney injury and respiratory complications
Shroyer *et al.*, 2009 (10)	RCT	The department of Veterans Affairs Randomized On/Off Bypass (ROOBY) randomized 2,203 patients to OPCAB versus ONCAB	No difference between OPCAB or ONCAB in 30-day complication rates: cardiac arrest, coma, repeat cardiac surgery, reoperation for bleeding, new mechanical support, mediastinitis, tracheostomy

OPCAB, off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; RCT, randomized controlled trial; CORONARY, Coronary Artery Bypass Grafting Off- or On-Pump Revascularization Study.

difference between the two groups (39). In the large meta-analysis of RCTs by Kowalewski *et al.*, the main finding was a significant linear relationship between the risk profile and the beneficial effect of OPCAB (1). A randomized study of patients with preoperative non-dialysis-dependent renal insufficiency by Sajja *et al.* demonstrated that ONCAB adversely affects renal function compared to the off-pump group (40). Two large RCTs on elderly populations failed to show any mortality or morbidity benefit with use OPCAB (11,23). Masoumi *et al.* reported significantly lower rates of mortality, morbidity, balloon-pump support, inotropic usage, gastrointestinal bleeding, renal dysfunction, reintubation, intensive care and hospital stay reported patient with a poor ejection fraction (≤35%) in patients randomly assigned to OPCAB or ONCAB (41). In the RCT by Fattouch *et al.* patients undergoing emergency OPCAB had a reduction in early mortality (14) while the late mortality did not differ compared to conventional surgery (42). Several retrospective studies found a benefit in using off-pump techniques in other high risk groups such as: females (43) or reoperative coronary artery bypass grafting (44). Overall, the weight of randomized data for the high risk patient undergoing coronary surgery shows a clear benefit from OPCAB as demonstrated by other landmark retrospective studies (45) or large meta-analyses of non-randomized trials (46) (*Table 9*).

Conclusions

The current evidence synthesised from RCTs demonstrates comparable early and late survival for both off-pump and conventional coronary artery bypass grafting. However, patients undergoing OPCAB grafting appear to have fewer coronary anastomoses and increased repeat revascularisation rates. Some studies suggest poorer vein graft patency but comparable midterm arterial conduit patency. In contrast, a long term follow-up study found no difference between venous and arterial graft patency pooled randomised data shows a reduction in stroke rates with use off-pump techniques. OPCAB grafting seems to reduce postoperative renal dysfunction, bleeding, transfusion requirements and respiratory complications while perioperative myocardial infarction rates remain unchanged. The high risk patient groups seem to benefit from off-pump coronary surgery.

Table 9 Outcomes in the high risk patients

Author	Study design	Sample size	Outcomes
Lemma *et al.*, 2012 (38)	RCT	411 patients, 203 randomized ONCAB and 208 patients to OPCAB, European system for cardiac operative risk evaluation (EuroSCORE) of 6 or more	Rate of the composite primary end-point (operative mortality, myocardial infarction, stroke, renal failure, reoperation for bleeding and adult respiratory distress syndrome within 30 days after surgery was significantly lower (unadjusted P=0.009, adjusted P=0.010) in the OPCAB (5.8% *vs.* 13.3%)
Hlavicka *et al.*, 2016 (39)	RCT	PRAGUE-6 randomized 206 patients, with an additive EuroSCORE ≥6, to OPCAB (n=98) or ONCAB (n=108)	ONCAB associated with a significantly higher incidence of primary combined end-point versus OPCAB (20.6% *vs.* 9.2%, P=0.028; HR, 0.41; 95% CI: 0.19–0.91) in the first 30 days, but not after 1 year (30.8% *vs.* 21.4%, P=0.117; HR, 0.65; 95% CI: 0.37–1.12)
Kowalewski *et al.*, 2016 (1)	Meta-analysis of RCTs	Meta-analysis included 100 studies, with a total of 19,192 subjects. Meta regression taking into account the risk profile of the patient (EuroSCORE)	Significant relationship between patient risk profile and benefits from OPCAB demonstrated in all-cause mortality (P<0.01), myocardial infarction (P<0.01), and cerebral stroke (P<0.01)
Sajja *et al.*, 2007 (40)	RCT	116 patients with preoperative non-dialysis-dependent renal insufficiency randomized to OPCAB or ONCAB	ONCAB significantly associated with adverse renal outcome (P<0.000)
Diegeler *et al.*, 2013 (11)	RCT	In the GOPCABE trial, 2,539 patients, aged >75 years, underwent randomization to ONCAB versus OPCAB	No difference between in OPCAB or ONCAB in the incidence of the primary end-point at 30 days: (7.8% *vs.* 8.2%; odds ratio, 0.95; 95% CI: 0.71–1.28; P=0.74) or 1 year (13.1% *vs.* 14.0%; HR, 0.93; 95% CI: 0.76–1.16; P=0.48)
Houlind *et al.*, 2012 (23)	RCT	900 patients >70 years of age randomized to ONCAB or OPCAB surgery	At 30 days, proportion of patients experiencing the primary composite end-point was 10.2% for ONCAB and 10.7% for OPCAB. Implied risk difference of 0.4% (with a 95% CI: −3.6–4.4), P=0.83. At 6-month follow-up, mortality was 4.7% for ONCAB compared to 4.2% for OPCAB (P=0.75)
Masoumi *et al.*, 2008 (41)	RCT	124 patients undergoing coronary artery bypass grafting with poor ejection fractions ≤35% were randomly assigned to OPCAB or ONCAB	Mortality, morbidity, balloon-pump support, inotropic usage, gastrointestinal bleeding, renal dysfunction, reintubation, as well as intensive care and hospital stay, were significantly lower in the OPCAB. The incidence of perioperative myocardial infarction did not differ between groups
Fattouch *et al.*, 2009 (14)	RCT	138 STEMI patients undergoing ONCAB (66 patients) or OPCAB (63 patients)	Hospital mortality was 7.7% (5 patients) in the ONCAB and 1.6% (1 patient) in the OPCAB (P=0.04). Statistical significant difference favouring OPCAB in terms of: incidence of low cardiac output syndrome (P=0.001), time of inotrope drugs support (P=0.001), time of mechanical ventilation (P=0.006), reoperation for bleeding (P=0.04), intensive care unit stay (P=0.01), in-hospital stay (P=0.02)

OPCAB, off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; RCT, randomized controlled trial; CI, confidence interval; HR, hazard ratio.

Acknowledgements

The study was supported by the British Heart Foundation and the NIHR Bristol Cardiovascular Biomedical Research Unit.

Footnote

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

References

1. Kowalewski M, Pawliszak W, Malvindi PG, et al. Off-pump coronary artery bypass grafting improves short-term outcomes in high-risk patients compared with on-pump coronary artery bypass grafting: Meta-analysis. J Thorac Cardiovasc Surg 2016;151:60-77.e1-58.
2. Taggart DP. Replacement of the aortic root with a pulmonary autograft. N Engl J Med 1994;330:1615-6.
3. Deppe AC, Arbash W, Kuhn EW, et al. Current evidence of coronary artery bypass grafting off-pump versus on-pump: a systematic review with meta-analysis of over 16,900 patients investigated in randomized controlled trials†. Eur J Cardiothorac Surg 2016;49:1031-41; discussion 1041.
4. Greason KL, Sundt Iii TM. Myocardial Revascularization without Cardiopulmonary Bypass. In: Cohn LH. editor. Cardiac Surgery in the Adult. 4th edition. New York: The McGraw-Hill Companies, 2012:505-22.
5. Trapp WG, Bisarya R. Placement of coronary artery bypass graft without pump oxygenator. Ann Thorac Surg 1975;19:1-9.
6. Buffolo E, Andrade JC, Succi JE, et al. Direct revascularization of the myocardium without extracorporeal circulation. Description of the technic and preliminary results. Arq Bras Cardiol 1982;38:365-73.
7. Ankeney JL. Off-pump bypass surgery: the early experience, 1969-1985. Tex Heart Inst J 2004;31:210-3.
8. Bakaeen FG, Shroyer AL, Gammie JS, et al. Trends in use of off-pump coronary artery bypass grafting: Results from the Society of Thoracic Surgeons Adult Cardiac Surgery Database. J Thorac Cardiovasc Surg 2014;148:856-3, 864.e1; discussion 863-4.
9. Hattler B, Messenger JC, Shroyer AL, et al. Off-Pump coronary artery bypass surgery is associated with worse arterial and saphenous vein graft patency and less effective revascularization: Results from the Veterans Affairs Randomized On/Off Bypass (ROOBY) trial. Circulation 2012;125:2827-35.
10. Shroyer AL, Grover FL, Hattler B, et al. On-pump versus off-pump coronary-artery bypass surgery. N Engl J Med 2009;361:1827-37.
11. Diegeler A, Börgermann J, Kappert U, et al. Off-pump versus on-pump coronary-artery bypass grafting in elderly patients. N Engl J Med 2013;368:1189-98.
12. Lamy A, Devereaux PJ, Prabhakaran D, et al. Off-pump or on-pump coronary-artery bypass grafting at 30 days. N Engl J Med 2012;366:1489-97.
13. Taggart DP, Altman DG, Gray AM, et al. Effects of on-pump and off-pump surgery in the Arterial Revascularization Trial. Eur J Cardiothorac Surg 2015;47:1059-65.
14. Fattouch K, Guccione F, Dioguardi P, et al. Off-pump versus on-pump myocardial revascularization in patients with ST-segment elevation myocardial infarction: a randomized trial. J Thorac Cardiovasc Surg 2009;137:650-6; discussion 656-7.
15. Møller CH, Penninga L, Wetterslev J, et al. Off-pump versus on-pump coronary artery bypass grafting for ischaemic heart disease. Cochrane Database Syst Rev 2012;(3):CD007224.
16. Angelini GD, Taylor FC, Reeves BC, et al. Early and midterm outcome after off-pump and on-pump surgery in Beating Heart Against Cardioplegic Arrest Studies (BHACAS 1 and 2): a pooled analysis of two randomised controlled trials. Lancet 2002;359:1194-9.
17. Angelini GD, Culliford L, Smith DK, et al. 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. J Thorac Cardiovasc Surg 2009;137:295-303.
18. Luo T, Ni Y. Short-term and Long-term Postoperative Safety of Off-Pump versus On-Pump Coronary Artery Bypass Grafting for Coronary Heart Disease: A Meta-analysis for Randomized Controlled Trials. Thorac Cardiovasc Surg 2015;63:319-27.
19. Lamy A, Devereaux PJ, Prabhakaran D, et al. Effects of off-pump and on-pump coronary-artery bypass grafting at 1 year. N Engl J Med 2013;368:1179-88.
20. Magee MJ, Alexander JH, Hafley G, et al. Coronary artery bypass graft failure after on-pump and off-pump coronary artery bypass: findings from PREVENT IV. Ann Thorac Surg 2008;85:494-9; discussion 499-500.
21. Lingaas PS, Hol PK, Lundblad R, et al. Clinical and

radiologic outcome of off-pump coronary surgery at 12 months follow-up: a prospective randomized trial. Ann Thorac Surg 2006;81:2089-95.
22. Khan NE, De Souza A, Mister R, et al. A randomized comparison of off-pump and on-pump multivessel coronary-artery bypass surgery. N Engl J Med 2004;350:21-8.
23. Houlind K, Kjeldsen BJ, Madsen SN, et al. On-pump versus off-pump coronary artery bypass surgery in elderly patients: results from the Danish on-pump versus off-pump randomization study. Circulation 2012;125:2431-9.
24. Widimsky P, Straka Z, Stros P, et al. One-year coronary bypass graft patency: a randomized comparison between off-pump and on-pump surgery angiographic results of the PRAGUE-4 trial. Circulation 2004;110:3418-23.
25. Zhang B, Zhou J, Li H, et al. Comparison of graft patency between off-pump and on-pump coronary artery bypass grafting: an updated meta-analysis. Ann Thorac Surg 2014;97:1335-41.
26. Puskas JD, Williams WH, Mahoney EM, et al. Off-pump vs conventional coronary artery bypass grafting: early and 1-year graft patency, cost, and quality-of-life outcomes: a randomized trial. JAMA 2004;291:1841-9.
27. Puskas JD, Winston AD, Wright CE, et al. Stroke after coronary artery operation: incidence, correlates, outcome, and cost. Ann Thorac Surg 2000;69:1053-6.
28. Calafiore AM, Di Mauro M, Teodori G, et al. Impact of aortic manipulation on incidence of cerebrovascular accidents after surgical myocardial revascularization. Ann Thorac Surg 2002;73:1387-93.
29. Bowles BJ, Lee JD, Dang CR, et al. Coronary artery bypass performed without the use of cardiopulmonary bypass is associated with reduced cerebral microemboli and improved clinical results. Chest 2001;119:25-30.
30. Hammon JW, Stump DA, Butterworth JF, et al. Single crossclamp improves 6-month cognitive outcome in high-risk coronary bypass patients: the effect of reduced aortic manipulation. J Thorac Cardiovasc Surg 2006;131:114-21.
31. Hammon JW, Stump DA, Butterworth JF, et al. Coronary artery bypass grafting with single cross-clamp results in fewer persistent neuropsychological deficits than multiple clamp or off-pump coronary artery bypass grafting. Ann Thorac Surg 2007;84:1174-8; discussion 1178-9.
32. Ernest CS, Worcester MU, Tatoulis J, et al. Neurocognitive outcomes in off-pump versus on-pump bypass surgery: a randomized controlled trial. Ann Thorac Surg 2006;81:2105-14.
33. Hernandez F Jr, Brown JR, Likosky DS, et al. Neurocognitive outcomes of off-pump versus on-pump coronary artery bypass: a prospective randomized controlled trial. Ann Thorac Surg 2007;84:1897-903.
34. van Dijk D, Spoor M, Hijman R, et al. Cognitive and cardiac outcomes 5 years after off-pump vs on-pump coronary artery bypass graft surgery. JAMA 2007;297:701-8.
35. Kennedy ED, Choy KC, Alston RP, et al. Cognitive outcome after on- and off-pump coronary artery bypass grafting surgery: a systematic review and meta-analysis. J Cardiothorac Vasc Anesth 2013;27:253-65.
36. Marasco SF, Sharwood LN, Abramson MJ. No improvement in neurocognitive outcomes after off-pump versus on-pump coronary revascularisation: a meta-analysis. Eur J Cardiothorac Surg 2008;33:961-70.
37. Cheng DC, Bainbridge D, Martin JE, et al. Does off-pump coronary artery bypass reduce mortality, morbidity, and resource utilization when compared with conventional coronary artery bypass? A meta-analysis of randomized trials. Anesthesiology 2005;102:188-203.
38. Lemma MG, Coscioni E, Tritto FP, et al. On-pump versus off-pump coronary artery bypass surgery in high-risk patients: operative results of a prospective randomized trial (on-off study). J Thorac Cardiovasc Surg 2012;143:625-31.
39. Hlavicka J, Straka Z, Jelinek S, et al. Off-pump versus on-pump coronary artery bypass grafting surgery in high-risk patients: PRAGUE-6 trial at 30 days and 1 year. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2016;160:263-70.
40. Sajja LR, Mannam G, Chakravarthi RM, et al. Coronary artery bypass grafting with or without cardiopulmonary bypass in patients with preoperative non-dialysis dependent renal insufficiency: a randomized study. J Thorac Cardiovasc Surg 2007;133:378-88.
41. Masoumi M, Saidi MR, Rostami F, et al. Off-pump coronary artery bypass grafting in left ventricular dysfunction. Asian Cardiovasc Thorac Ann 2008;16:16-20.
42. Fattouch K, Runza G, Moscarelli M, et al. Graft patency and late outcomes for patients with ST-segment elevation myocardial infarction who underwent coronary surgery. Perfusion 2011;26:401-8.
43. Puskas JD, Kilgo PD, Kutner M, et al. Off-pump techniques disproportionately benefit women and narrow the gender disparity in outcomes after coronary artery bypass surgery. Circulation 2007;116:I192-9.
44. Mishra YK, Collison SP, Malhotra R, et al. Ten-year

experience with single-vessel and multivessel reoperative off-pump coronary artery bypass grafting. J Thorac Cardiovasc Surg 2008;135:527-32.
45. Puskas JD, Thourani VH, Kilgo P, et al. Off-pump coronary artery bypass disproportionately benefits high-risk patients. Ann Thorac Surg 2009;88:1142-7.
46. Kuss O, von Salviati B, Börgermann J. Off-pump versus on-pump coronary artery bypass grafting: a systematic review and meta-analysis of propensity score analyses. J Thorac Cardiovasc Surg 2010;140:829-35, 835.e1-13.

Cite this article as: Fudulu D, Benedetto U, Pecchinenda GG, Chivasso P, Bruno VD, Rapetto F, Bryan A, Angelini GD. Current outcomes of off-pump versus on-pump coronary artery bypass grafting: evidence from randomized controlled trials. J Thorac Dis 2016;8(Suppl 10):S758-S771. doi: 10.21037/jtd.2016.10.80

