

Cite this article as: Sousa Uva M, Kolh P. The on-pump/off-pump saga: an enduring conundrum. *Eur J Cardiothorac Surg* 2015; doi:10.1093/ejcts/ezv399.

## The on-pump/off-pump saga: an enduring conundrum

Miguel Sousa Uva<sup>a</sup> and Philippe Kolh<sup>b,\*</sup><sup>a</sup> Department of Cardiothoracic Surgery, Hospital da Cruz Vermelha, Lisbon, Portugal<sup>b</sup> Department of Cardiovascular Surgery, University Hospital (CHU, ULg) of Liège, Liege, Belgium

\* Corresponding author. Department of Cardiovascular Surgery, University Hospital (CHU, ULg) of Liege, Sart Tilman B 35, 4000 Liege, Belgium. Tel: +32-4-3665196; fax: +32-4-3668318; e-mail: philippe.kolh@chu.ulg.ac.be (P. Kolh).

**Keywords:** Cardiopulmonary bypass • Coronary artery bypass grafting • Coronary artery disease • Internal thoracic artery • Off-pump surgery • Propensity score analysis

The aim of coronary artery bypass grafting (CABG) is to prolong life and reduce symptoms. However, when compared with percutaneous coronary intervention, CABG is a significantly more invasive operation, associated with a higher rate of early stroke. Off-pump CAB (OPCAB) brought the hope, about 25 years ago, that various CABG-related morbidities, and even perhaps mortality, would evaporate if cardiopulmonary bypass was to be eliminated. Yet, numerous risk-adjusted studies and large meta-analysis of propensity score-adjusted studies showed that this hoped superiority of OPCAB regarding mortality and several short-term outcomes did not materialize in large randomized trials [1, 2].

In this issue of the *European Journal of Cardiothoracic Surgery*, Deppe *et al.* [3] report the results of one of the largest meta-analyses of randomized controlled trials (RCTs) comparing OPCAB and on-pump CABG (ONCAB). In summary, the analysis was performed on 16 904 patients from 51 studies. There was no difference between the groups in the incidence of mortality, myocardial infarction (MI) or major adverse cardiac and cerebro-vascular events (MACCEs) at 30 days or at longest available follow-up. The incidence of mid-term graft failure [odds ratio (OR): 1.37; 95% confidence interval (CI): 1.09–1.72] and the need for repeat revascularization (OR: 1.55; 95% CI: 1.33–1.80) was increased after off-pump while on-pump surgery was associated with an increased occurrence of stroke (OR: 0.74; 95% CI: 0.58–0.95), renal impairment (OR: 0.79; 95% CI: 0.71–0.89) and mediastinitis (OR: 0.44; 95% CI: 0.31–0.62). There was a significantly lower volume of chest tube drainage and transfusion in the OPCAB group but a significantly lower number of distal anastomosis.

Meta-analyses are important tools in the generation of scientific evidence. However, they have several limitations. In the current meta-analysis, 22 among 51 (43%) studies included <100 patients [3]. Many of these randomized studies with limited population size had non-clinical end-points and ill-defined clinical outcomes, included much selected patients (reflected in a significantly higher mean ejection fraction in patients undergoing OPCAB), did not include risk-stratification and provided no information on surgical experience and important technical aspects, likely associated with results. As an example, lack of data regarding aorta manipulation prevents demonstration of larger OPCAB with no-touch aorta impact on stroke reduction [4].

Interestingly, meta-analyses can reach opposite conclusions, depending on inclusion criteria, quality of included studies, selected end-points, duration of follow-up and methodological issues. In a Cochrane review, Møller *et al.* [5] analysed 86 RCTs encompassing 10 716 patients and reported that OPCAB resulted in an increased all-cause mortality compared with ONCAB (3.7 vs 3.1%;  $P = 0.04$ ) and no significant difference in MI, stroke, renal insufficiency or coronary reintervention but significantly fewer distal anastomosis performed in the OPCAB group ( $P = 0.001$ ). On the other hand, Afilalo *et al.* [6] analysed 59 RCTs, encompassing 8961 patients and reported a significant 30% reduction in the occurrence of postoperative stroke with OPCAB (risk ratio: 0.70; 95% CI: 0.49–0.99) with no significant difference in mortality or MI.

Indeed, short of individual patient data collection, meta-analyses are only as good as the included studies and the most refined statistical techniques cannot account for large heterogeneity and eliminate all possible sources of bias. A major problem with RCTs, in surgery, is that findings can be hampered by differential expertise bias. In particular, a volume–outcome relationship in OPCAB surgery has been demonstrated, with hospitals and surgeons in the highest percent OPCAB volume quartile displaying adjusted mortality and morbidity rates significantly lower when compared with ONCAB, whereas results in the lowest quartile of experience were similar [7]. Expertise-based randomized trials, where surgeons perform only the procedure in which they have expertise, have been proposed as a potential solution to enhance the validity of surgical RCTs.

Critical appraisal of all forms of scientific evidence, including meta-analysis, is at the core of recommendations for patient management. The present meta-analysis confirms previous data showing that OPCAB reduces selected short-term adverse events and stroke with comparable mortality, MI and MACCE rates, but with increased mid-term graft failure and need for repeat revascularization. Increased saphenous graft occlusion after off-pump surgery has also been reported in a recent meta-analysis, without affecting internal thoracic artery patency [8]. The continued debate over the best method for myocardial revascularization will now focus on the trade-off between reduced early morbidity including stroke versus potentially reduced graft patency and its impact on late survival and quality of life. To conclude, the recent

2014 ESC/EACTS guidelines on myocardial revascularization state that (i) OPCAB should be considered for sub-groups of high-risk patients in high-volume off-pump centres (level of evidence B) and (ii) OPCAB and/or no-touch on-pump techniques on the ascending aorta are recommended in patients with significant atherosclerotic disease of the ascending aorta in order to prevent perioperative stroke (level of evidence B) [9].

## REFERENCES

- [1] Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E *et al.* Effects of off-pump and on-pump coronary-artery bypass grafting at 1 year. *N Engl J Med* 2013;368:1179–88.
- [2] Diegeler A, Börgermann J, Kappert U, Breuer M, Böning A, Ursulescu A *et al.* Off-pump versus on-pump coronary-artery bypass grafting in elderly patients. *N Engl J Med* 2013;368:1189–98.
- [3] Deppe AC, Arbash W, Kuhn EW, Slottosch I, Scherner M, Liakopoulos OJ *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* 2015; doi:10.1093/ejcts/ezv268.
- [4] Misfeld M, Brereton RJ, Sweetman EA, Doig GS. Neurologic complications after off-pump coronary artery bypass grafting with and without aortic manipulation: meta-analysis of 11,398 cases from 8 studies. *J Thorac Cardiovasc Surg* 2011;142:e11–7.
- [5] Møller CH, Penninga L, Wetterslev J, Steinbrüchel DA, Gluud C. Off-pump versus on-pump coronary artery bypass grafting for ischaemic heart disease. *Cochrane Database Syst Rev* 2012;3:CD007224.
- [6] Afilalo J, Rasti M, Ohayon SM, Shimony A, Eisenberg MJ. Off-pump vs. on-pump coronary artery bypass surgery: an updated meta-analysis and meta-regression of randomized trials. *Eur Heart J* 2012;33:1257–67.
- [7] Konety SH, Rosenthal GE, Vaughan-Sarrazin MS. Surgical volume and outcomes of off-pump coronary artery bypass graft surgery: does it matter? *J Thorac Cardiovasc Surg* 2009;137:1116–23.
- [8] Zhang B, Zhou J, Li H, Liu Z, Chen A, Zhao Q. Comparison of graft patency between off-pump and on-pump coronary artery bypass grafting: an updated meta-analysis. *Ann Thorac Surg* 2014;97:1335–42.
- [9] Kolh P, Windecker S, Alfonso F, Collet JP, Cremer J, Falk V *et al.* 2014 ESC/EACTS guidelines on myocardial revascularization. *Eur J Cardiothorac Surg* 2014;46:517–92.