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On vs. off pump coronary artery bypass grafting: the next chapter

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Comment on: Lamy A, Devereaux PJ, Prabhakaran D, *et al.* Five-Year Outcomes after Off-Pump or On-Pump Coronary-Artery Bypass Grafting. *N Engl J Med* 2016;375:2359-68.

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Current guidance in the UK (1) (NICE guidelines) and the US (2) recommends the use of coronary artery bypass grafting (CABG) in the treatment of anatomically complex triple vessel disease. The UK also prefers CABG for the treatment of coronary artery disease in those >65 and those with diabetes (1), whilst the US recommends a heart team approach (2). Having made the decision to operate the next question that arises is whether to perform this with (on pump) or without (off pump) cardiopulmonary bypass. The attraction of off pump CABG is a reduction in the inflammatory response in combination with minimal aortic manipulation and avoidance of aortic cannulation, which may reduce the risk of stroke (3). However, many surgeons would argue that cardioplegic arrest provides the best conditions for optimal revascularisation (3,4). The debate as to which method is superior has been ongoing for the past 25 years.

There have been several meta-analyses that have pooled data from the numerous randomised clinical trials (RCTs) that have been conducted. A comprehensive Cochrane review published in 2012 reported that all-cause mortality was significantly increased in the off pump group whilst there were no differences in the incidence of myocardial infarction, stroke, renal insufficiency and coronary re-intervention (5). Since that time more RCTs have been conducted and this year there has been three fresh investigations of the data. Kowalewski *et al.* showed that there was a significant 28% reduction in the incidence of stroke in the off pump group, which was related to patient risk profile (6). Deppe *et al.* also found a reduced incidence

of stroke in the off pump group, whilst this group also had an increased need for revascularisation (4). The latest meta-analysis by Dieberg *et al.* reported a P value of 0.05 for the stroke comparison and only found a significant difference in the incidence of atrial fibrillation (7). Two limitations that affect each of these studies are the small size of many of the included RCTs and a concentration on short term (30 days) outcomes (4-7).

The four largest trials to date are CORONARY (n=2,375 off vs. 2,377 on) (8); DOORS (n=450 off vs. 450 on) (9); GOPCABE (n=1,271 off vs. 1,268 on) (10) and ROOBY (n=1,104 off vs. 1,099 on) (11). None of these studies showed a significant difference in the occurrence of death or stroke at or within 30 days of surgery (8-11) and the same was true for the incidence of myocardial infarction in CORONARY, DOORS and GOPCABE (8-10). A significantly higher early need for repeat revascularisation in the off pump group was measured in CORONARY and GOPCABE (8,10), whereas ROOBY measured no difference in the rate of repeat cardiac surgery (11). In short none of these major studies showed a difference in hard clinical outcomes between the off and on pump groups at 30 days.

Clearly answering the question of whether to operate off or on pump depends not only on 30 days outcomes but also on what happens in the longer term. Unfortunately, relatively few authors have published follow ups to their studies. For example, Luo *et al.* in their 2015 meta-analysis of RCTs with >6 months follow up only synthesised the results of four studies for mortality and only three

studies for incidence of myocardial infarction, stroke and revascularisation (12). Some caution might therefore be advised in the interpretation of the results. Nevertheless, the synthesised results showed that there was no difference in the incidence of mortality, myocardial infarction and stroke between the two groups; however, there was a significantly higher rate of revascularisation in the off pump group (12). It is noteworthy that the single 6 months follow up and the two 1-year follow ups discussed in this meta-analysis were from three of the large RCTs mentioned above (CORONARY, DOORS and GOPCABE) (12). It should also be noted that Luo *et al.* missed at least one study, namely that of Angelini *et al.* who pooled the follow up (1–3 years) results of two of their RCTs (13). The latter found no significant differences in the occurrence of cardiac or non-cardiac related events between the two groups (13). This included no significant difference in the number of patients who needed repeat cardiac catheterization (13).

One of the factors that predisposes to improved long-term survival is completeness of revascularisation, and a surrogate for this is the number of grafts placed (Adrian Marchbank, personal communication). In each of the four largest trials a significantly greater number of grafts were placed in the on pump group, although the difference in the number of grafts placed in each group was only 0.1–0.2 grafts (8–11). The CORONARY trial also reported the completeness of revascularisation where 278 patients were incompletely revascularised in the off pump group compared to 236 in the on pump group ($P=0.05$) (8). In spite of this mortality in the CORONARY study was not significantly different between the off and on pump groups at 30 days (8) and 1 year (14).

The paucity of follow up reporting, particularly regarding long term outcomes, makes the recent publication of the 5-year outcomes of the CORONARY trial very important (15). This was easily the largest of the RCTs to date, which enrolled a total of 4,752 patients from 79 hospitals in 19 different countries (8). There was very good matching of baseline characteristics including age, gender, clinical history, left ventricular ejection factor, and EuroSCORE grade (8). The primary outcome at 30 days was a composite of death, nonfatal stroke, nonfatal myocardial infarction and new renal failure. The results showed that there was no significant difference in the occurrence of the composite nor in any of its individual elements between the off and on pump groups (8) and this continued to be the case at 1 year (14). At the early time point significantly more of the off pump group had

required revascularisation compared to the on pump group; however, by the time 1 year had passed this difference had disappeared (14). Revascularisation was also amongst the outcomes analysed in the 5-year follow up alongside death, stroke, myocardial infarction and renal failure. In addition, Lamy *et al.* (15) also investigated cost and quality of life. There were no significant differences in the off compared to on pump group in any of the measured parameters. The authors do refer to four studies that have shown higher long term mortality or greater repeat revascularisation in the off pump group; however, all of these comparator studies were retrospective reviews of patient notes (15).

To date the CORONARY trial is the largest RCT comparing off pump *vs.* on pump CABG. It is also the only sizable trial to follow its participants through to 5-year post-operation, although a 6–8 years follow up in the pooled results of two small RCTs is noted (16). The CORONARY trial has consistently shown that there was no significant difference in hard clinical outcomes following either off or on pump CABG at 30 days, 1 year and 5 years post-operation. Consequently, with no hard clinical data in favour of one approach or the other, the decision as to whether to operate off or on pump may simply come down to the individual surgeon's preference.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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