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Lessons from the trials

# Off-pump coronary artery bypass grafting (OPCABG): the beginning of the end?

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Since the early descriptions of off-pump coronary artery bypass grafting (OPCABG) more than three decades ago,[1] debate has continued about its relative potential merits or disadvantages in comparison to on-pump CABG (ONCABG). Proponents argue that OPCABG reduces the damaging effects of cardiopulmonary bypass, particularly in higher risk patients, whilst sceptics maintain that it is actually inferior to the "gold standard" ONCABG with less effective revascularisation and inferior graft patency. Consequently while the numbers of OPCABG have plateaued at around 15–20% of all CABG in the developed world, in the developing world and Far East the proportion of OPCABG is over 80% of all cases.

Two new large randomised trials have helped inform and settle some components of the debate.[2,3,4] Before examining these trials in detail, however, it may be particularly useful to summarize the current state of knowledge defined in the two most definitive meta-analyses to date. Afilalo and colleagues performed a meta-analysis of nine randomised trials of ONCABG and OPCABG.[5] The study included 8,961 patients and reported that, while there was no significant difference in mortality and myocardial infarction between the two techniques, there was a clinically and statistically significant 30% reduction in the occurrence of post-operative stroke with OPCABG (RR = 0.7 95% CI 0.49–0.99). In contrast, in a Cochrane review, Moller and colleagues[6] analysed 86 randomised trials involving 10,716 patients and reported that OPCABG resulted in an increased all-cause mortality compared to ONCABG (3.7% versus 3.1% $p = 0.04$). They additionally reported that there was no significant difference in myocardial infarction, stroke, renal insufficiency or coronary reintervention between the two techniques but that OPCABG resulted in fewer distal anastomoses with a mean reduction of 0.28 grafts ($p < 0.001$). There are, however, two important limitations to these meta-analyses. The first is the question of how generalizable the results are to the whole population of CABG patients as most trials were conducted in predominantly low risk patients. The second, the question of the surgical experience of the operating surgeons, crucial to the greater technical complexity of OPCABG, was often not defined.

Recently, two of the largest randomised trials of OPCABG, the Coronary Trial (the CABG Off or On Pump Revascularization Study)[2,3] and the GOPCABE trial (German Off-Pump CABG Trial in Elderly Patients)[4] have been reported. These trials respectively randomised 4,752 and 2,539 patients with basic patient characteristics summarised in Table 1. In comparison to the previous individual largest randomised trial (the ROOBY Trial with 2,203 patients)[7] patients in the Coronary and GOPCABE Trials were older with a far greater proportion of female patients. In all three trials approximately 60–70% of patients had three-vessel disease. The predicted thirty-day mortality risk was 1.9% in the ROOBY Trial, 3.8% in the GOPCABE Trial and around 80% of patients in the Coronary Trial had a EuroSCORE <0,5 (i.e. a predicted mortality of around 2%).

Both the thirty-day outcomes and the one-year outcomes for the three trials are individually summarized in Tables 2 and 3. For the 3 trials there was no significant difference in the thirty-day composite primary endpoint between OPCABG and ONCABG or in the individual incidence of death MI,

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**Table 1. Baseline demographics.**

| | ROOBY | CORONARY | GOPCABE |
|---|---|---|---|
| Screened | 9663 | | 4355 |
| Randomized | 2203 | 4752 | 2539 |
| Mean Age | 63 | 68 | 78 |
| Female (%) | 0.5 | 19 | 31 |
| Diabetes (%) | 43 | 47 | 14 (IDD) |
| 3-Vessel Disease (%) | 67 | 58 | 61 |
| Mortality Risk at 30 days | 1.9 | Euroscore | 3.8% |

stroke or need for new renal dialysis. Both the Coronary and GOPCABE trials reported an increased risk of repeat revascularisation within thirty days for OPCABG with respective figures of 0.7% versus 0.2% and 1.3% versus 0.4%.

In terms of one-year outcomes, there was an increased incidence of the primary composite endpoint in the ROOBY Trial (9.9% versus 7.4%; $p = 0.04$). In contrast, the primary composite endpoint was lower for OPCABG in both the Coronary and GOPCABE trials, although this did not reach statistical significance. There was no significant difference in overall death, MI, stroke, new renal dialysis or repeat revascularisation in any of the trials.

Why should there be an apparent difference in one-year outcomes between the ROOBY trial suggesting inferior results with OPCABG and Coronary and GOPCABE which show off pump surgery to be at least as safe as on pump? The most likely explanation for this difference is the relative experience of the operating surgeons. As shown in Table 4 the OPCBAG experience of the operating surgeons in the three trials was substantial: it was 50 cases for ROOBY (with a minimum requirement of 20), 100 cases for the Coronary Trial and over 500 cases for GOPCABE. It is also noteworthy that in the ROOBY Trial over 12% of patients were converted from OPCABG to ONCABG. Mukherjee and colleagues have reported that conversion from OPCABG to ONCABG surgery, particularly when done in emergency situations, increases the odds ratio of mortality by a factor of almost seven.[8]

However, a major strength of the ROOBY Trial in contrast to Coronary and GOPCABE was follow-up angiography in over 60% of the patients one year after surgery.[9] This demonstrated that fewer OPCABG patients received effective revascularisation (50% versus 64%; $p < 0.001$) and that the overall quality of both saphenous vein and arterial grafts, as defined by perfect patency, was lower for OPCABG (85.8% vs. 91.4% for ONCABG; $p = 0.003$). Furthermore ineffective revascularisation resulted in poorer clinical outcomes with a one-year adverse cardiac event rate of 16.4% versus 5.9% in patients with effective revascularisation ($p < 0.001$). On the other hand, and as shown in Table 4, while the mean number of OPCABG grafts was statistically significantly lower in all trials by a mean of 0.1 to 0.2 grafts, this is unlikely to be clinically important.

Another important clinical consideration is the conflicting evidence over whether OPCABG surgery reduces the overall incidence of stroke as reported by Afilalo and colleagues[5] but disputed by Moller and colleagues.[6] OPCABG will only reach its full potential to reduce the risk of neurological injury if a true no-touch aortic technique is used. While avoidance of cannulation and cross-clamping of the aorta by itself reduces aortic manipulation and the risk of embolic debris the placement of vein grafts to the ascending aorta increases the risk. In a meta-analysis of 11,398 patients from eight studies, Misfield and colleagues reported that the relative risk of neurological injury was 0.46 (95% confidence intervals 0.29–0.72; $p = 0.0008$) when there was complete avoidance of any aortic manipulation.[10]

How consistent are the findings in the most recent randomised trials with those of large propensity matched registries? Puskas and colleagues[11] analysed the STS database of 42,471 patients matched for

**Table 2. 30 day outcomes.**

| 30 DAY: OFF vs ON | ROOBY | CORONARY | GOPCABE |
|---|---|---|---|
| Composite % | 7.0 vs 5.6 (0.19) | 9.8 vs 10.3 (0.59) | 7.8 vs 8.2 (0.74) |
| Death % | 1.6 vs 1.2 (0.47) | 2.5 vs 2.5 | 2.6 vs 2.8 (0.75) |
| MI % | – | 6.7 vs 7.2 | 1.5 vs 1.7 (0.79) |
| Stroke % | 1.3 vs 0.7 (0.28) | 1.0 vs 1.1 | 2.2 vs 2.7 (0.47) |
| Renal Dialysis % | 0.8 vs 0.9 (0.82) | 2.0 vs 2.6 | 2.4 vs 3.1 (0.36) |
| Repeat Revasc % | – | 0.7 vs 0.2 (0.01) | 1.3 vs 0.4 (0.04) |

**Table 3. 1-year outcomes.**

| 1 YEAR: OFF vs ON | ROOBY | CORONARY | GOPCABE |
|---|---|---|---|
| Composite % | 9.9 vs 7.4 (0.04) | 12.1 vs 13.3 (0.24) | 13.1 vs 14 (0..48) |
| Death % | 4.1 vs 2.9 (0.15) | 5.1 vs 5.0 | 7 .0 vs 8.0 (0.38) |
| MI % | 2.0 vs 2.2 (0.76) | 6.8 vs 7.5 | 2.1 vs 2.4 (0.70) |
| Stroke % | – | 1.5 vs 1.7 | 3.5 vs 4.4 (0.26) |
| Renal Dialysis % | – | 1.3 vs 1.3 | 2.9 vs 3.5 (0.37) |
| Repeat Revasc % | 4.6 vs 3.4 (0.18) | 1.4 vs 0.8 (0.07) | 3.1 vs 2.0 (0.11) |

**Table 4. Surgical experience.**

| | ROOBY | CORONARY | GOPCABE |
|---|---|---|---|
| Median number of OPCABG Cases | 50 | 100 | 322 |
| Mean number of grafts OFF vs ON | 2.9 vs 3.0 (0.002) | 3.0 vs 3.2 (<0.001) | 2.7 vs 2.8 ($p < 0.001$) |
| Cross Over (OFF to ON) 12.4% | 7.9% | 9.7% | |
| Cross Over (ON to OFF) | 3.6% | 6.4% | 5.1% |

32 clinical risks and reported that OPCABG resulted in significant reductions in the risk of death, stroke, MI and major adverse cardiovascular events. Likewise, Kuss and colleagues analysed 38 propensity matched studies of 123,137 patients and again reported highly significant reductions in the risk of mortality, stroke, renal failure, prolonged ventilation and other aspects of morbidity with off pump surgery.[12] One possible explanation for the apparent differences between the randomised trials and the registries is the suggestion that the major benefits of OPCABG surgery appear when the predicted mortality for CABG exceeds 5%. Very few such patients were included in the randomized trials and even in GOPCABE the predicted mortality risk was 3.8%.

In summary, the best available evidence now clearly demonstrates that for most patients OPCABG can be performed at least as safely in terms of mortality and major morbidity as ONCABG when undertaken by surgeons appropriately trained and experienced in the technique. On the other hand, there is accumulating evidence that both the number and quality of grafts is inferior with OPCABG and whether this simply reflects the greater technical expertise necessary for OPCABG or loss of the antiplatelet effect of cardiopulmonary bypass (and consequently the need for dual antiplatelet therapy in OPCABG patients) is unresolved. If inferior graft patency is confirmed then there will be a diminishing role for routine performance of OPCABG with the possible exception of the no-touch aortic technique to reduce neurological complications in patients with diseased ascending aortas.

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