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Recent data on off-pump coronary artery bypass grafting: the CORONARY and GOPCABE trials

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Background

Motivated by a desire to reduce the morbidity of a well-established and effective procedure for coronary artery disease, up to 30% of coronary bypass operations are being performed without the use of a heart-lung pump. Concerns remain about the quality of the coronary anastomoses and the completeness of revascularisation. Randomised trials have not revealed the significant reduction in morbidity or mortality that the early enthusiasts had hoped for. However, a number of non-randomised studies have shown clinical benefit from the avoidance of an extracorporeal circulation, but these have been criticised for potential bias in patient selection and management. A majority of surgeons have not yet adopted this technique and are waiting for the accumulation of more evidence.

In contrast to the small incision approaches, off-pump coronary artery surgery through a median sternotomy has gained clinical acceptance, and in many centres constitutes 20% to 30% of the total volume of coronary surgery. Creation of the distal anastomoses is facilitated by the use of stabilisers that reduce the motion of the heart in an area of approximately 2 cm^2. The argument in favour of this approach is to avoid the historical, well-documented adverse effects of cardiopulmonary bypass on end-organ function: coagulation, renal impairment, lung injury and, most important in an ageing population, avoidance of stroke, delirium and more subtle neurocognitive changes. The counter-argument is that potential suboptimal exposure and haemodynamic instability during off-pump procedures could produce inferior short- and long-term results.

Clinical outcome

The distinction between on-pump and off-pump coronary artery surgery is over-simplistic since both methods encompass a range of techniques. On-pump coronary surgery may be performed on the beating heart without the need for an aortic cross-clamp and at various temperatures. It can be carried out with miniaturised circuits without a venous reservoir and a very small priming volume[1,2]. Even when an aortic cross-clamp is employed, myocardial protection can be achieved by a wide variety of cardioplegic techniques or by non-cardioplegic methods. The use of composite arterial grafting can minimise aortic manipulation in on-pump surgery and eliminate it completely in the off-pump situation. Calafiore and colleagues[3] have shown that avoidance of aortic manipulation is at least as important as the avoidance of cardiopulmonary bypass in reducing the risk of brain injury.

The experience of setting up off-pump coronary surgery in a large private practice in Dallas is instructive. Michael Mack and colleagues[4] conducted a retrospective review of a five-year experience with 12,540 patients who underwent isolated coronary bypass grafting; 15% of these (n=1,915) underwent off-pump surgery. A gradual increase in the percentage of coronary operations performed off-pump was observed from 1.2% in 1995 to 34.1% in 2000. Individual surgeon adoption rates increased from 1% to 96% by the end of the study period and the mortality rate in off-pump surgery decreased to 3.2% compared with an overall observed mortality rate of 4.0% in the five years before the start of their off-pump experience. There was a significant difference in observed mortality between the off-pump and on-pump groups (1.9% vs. 3.5%, $p<0.001$), despite a higher mean predicted risk among the patients in the off-pump group (3.13% vs. 2.8%, $p<0.004$). Furthermore, there was less morbidity in the off-pump group as evidenced by a reduced need for blood products (28.5% vs. 54.7%, $p=0.0001$), prolonged ventilation (5.83% vs. 10.93%, $p=0.001$), and a shorter hospital stay (6 days vs. 7 days, $p=0.001$). One of the questions this study was designed to answer was whether off-pump surgery could be safely incorporated into a surgical practice and be performed by most surgeons. In the Dallas practice studied[4], there were 22 surgeons of whom six were enthusiastic early and persistent adopters of the off-pump approach and who carried out 73% of all off-pump procedures. Eight of the 22 surgeons did fewer than 10 off-pump operations per year. In the five-year period before the introduction

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of off-pump procedures, the composite mortality rate of coronary artery surgery for the three surgeons with the lowest off-pump adoption rate was 38% greater than the composite mortality rate of the three surgeons with the highest rate of off-pump surgery adoption (4.0% vs. 2.9%, p<0.001). Thus, off-pump surgery was being performed by the most accomplished surgeons. Although off-pump surgery can be safely incorporated into a large practice, it seems unlikely that it will be used on a regular basis by most surgeons. The use of off-pump coronary artery bypass surgery is not widespread in Western Europe (approximately 15-30%).

In smaller surgical units, unless there is a core of enthusiasm, it seems unlikely that many surgeons will adopt the technique. The exponential rise in the use of PCI with drug-eluting stents gives rise to a situation in which there is a dearth of low-risk patients requiring double or single bypass grafts and who might be considered for off-pump surgery early in a surgeon's experience. An alternative approach is to adopt the technique wholesale after a period of intense training or "re-engineering" as pursued by Sergeant and colleagues[5].

Non-randomised registry reports have continued to emerge since these early studies. The most recent from Kuss and co-workers[6] revealed significant reductions in mortality and morbidity in more than 120,000 propensity-matched operations. Less impressive were the results of the ROOBY trial reported by Shroyer and colleagues[7], which at one-year follow-up revealed worse composite outcomes for off-pump compared to on-pump (9.9% vs. 7.4%, p=0.04). This composite included death from any cause, a repeat revascularisation procedure, or a non-fatal myocardial infarction within the first year after operation. This paper which came from a large group of Veteran Administration hospitals in the USA, a system roughly analogous to the NHS, has been widely criticised by off-pump enthusiasts because of the finding that 12% of patients had to be converted from off to on-pump surgery. While this does reflect the relative lack of experience of some of the surgeons, many of whom were residents in training, it nevertheless reflects "real world" experience. Furthermore, there was no difference in primary short-term or one-year composite outcomes, regardless of the participating surgeon's experience (>50 or >100 previous off-pump cases) or whether the consultant or a trainee was the primary surgeon. These findings remained consistent in both the intention-to-treat analysis and after the exclusion of surgical conversions.

Even the most recent randomised studies do not suggest a superior outcome for off-pump surgery. In the MASS III trial 309 patients were randomised to on or off-pump coronary bypass surgery[8]. There was no significant difference in major in-hospital complications or at a mean of five years post operation. These complications included mortality, stroke, myocardial infarction and the need for repeat revascularisation. There was a trend to use fewer grafts in the off-pump group and thus a tendency towards incomplete revascularisation. In patients with three-vessel disease, the completeness of revascularisation is a significant determinant of the relief of symptoms over a five-year period[9]. A similar result was reported in a randomised trial[10] of 341 patients undergoing on or off-pump coronary bypass surgery described as high risk defined by a EuroSCORE >5. After a mean follow-up of 3.7 years there was no significant difference in the primary outcome of MACCE, and all-cause mortality but not cardiac mortality was higher in the off-pump group.

Recently, the 30-day results of the CORONARY study have been reported[11]. In the largest trial of off-pump coronary surgery so far, with 4,752 patients from 79 centres in 19 countries, no significant difference between off-pump and on-pump surgery was observed in the primary outcome of death, myocardial infarction, stroke or the need for renal support at 30 days (9.8% vs. 10.3%, p=0.59). However, there was a lower rate of transfusion and a higher rate of repeat revascularisation in the off-pump group. Two further reports of randomised trials were presented at the American College of Cardiology in March 2013 and appeared in the same month in the New England Journal of Medicine.

The CORONARY trial[12] has reported the one-year quality of life and neurocognitive outcomes and found no significant difference between off-pump and on-pump coronary surgery in the composite outcome of death, myocardial infarction, stroke or renal support at one year (12.1% vs. 13.3%, p=0.24). Repeat revascularisation remained more common in the off-pump group (1.4% vs. 0.8%, p=0.07), and quality of life and neurocognitive outcomes were similar in the two groups. The second study is the GOPCABE trial[13]. Working on the hypothesis that older patients will benefit from off-pump surgery, investigators randomly assigned 2,539 patients aged 75 years or older from 12 German centres to off-pump or on-pump coronary surgery. No significant difference between groups was observed in the primary outcome of death, myocardial infarction, stroke, repeat revascularisation or new renal support at 30 days (7.8% vs. 8.2%, p=0.74) or at one year (13.1% vs. 14.0%, p=0.48). As in previous studies, there were fewer transfusions and more repeat revascularisations in those undergoing off-pump operations. To avoid the criticism of the ROOBY trial, both of these recent trials required the surgeons to have similar and considerable experience in on-pump and off-pump surgery.

Completeness of revascularisation and graft patency

In observational studies published before 2000, the number of grafts performed off-pump tended to be less than on-pump[14,15]. In the recent era this situation has changed. Completeness of revascularisation has been reported in only five randomised trials. Czerny[16] and Hueb[8] have reported significantly reduced completeness of revascularisation for off-pump versus on-pump, whereas Khan, Puskas and van Dijk reported no difference[17-19]. The use of an index of completeness (number of grafts performed/number of grafts planned) was similar in the two groups.

Led by Dr John Puskas at Emory University[20], the SMART trial randomised 200 patients with multivessel coronary artery disease to either off-pump CABG or on-pump CABG. At a mean follow-up of 7.5 years involving 87 patients who agreed to be re-investigated, graft patency was similar in the two groups (off-pump CABG: 76.0%, on-pump CABG: 83.5%; p=0.44). Recurrent angina was,

however, more frequent with off-pump CABG, although not significantly so (25.6% vs. 11.4%; p=0.09). The rate of repeat revascularisation by percutaneous coronary intervention was the same in both groups (2.3%). No patient underwent repeat CABG. The number of grafts per patient (off-pump CABG: 3.39, on-pump CABG: 3.40) and the completeness of revascularisation were similar in both groups. In a previous observational study at Emory University[18] involving 12,812 patients who underwent isolated CABG over a ten-year period, the risk-adjusted survival at ten years was similar in patients who had off-pump CABG and on-pump CABG (HR for death for off-pump CABG: 1.09, CI: 0.95-1.25; p=0.23).

This is clearly an excellent series, but as a single-surgeon experience it may not be applicable to all surgical practices. Procoagulant activity may be increased after off-pump surgery[21]. This may explain the few isolated reports of reduced graft patency after off-pump operations[22]. Current practice in experienced centres is to use full-dose heparinisation (300 mg/Kg) supplemented throughout the operation, and to use aspirin during and after the operation. Because of the hypercoagulable state after off-pump surgery, many surgeons use postoperative clopidogrel for the first three postoperative months[23].

Risk of cerebral injury

Three randomised trials have not firmly established a significant difference in neurological outcomes between off-pump and on-pump coronary artery surgery[24-26]. These patients were not stratified according to high-risk aortic disease, so the relative value of off-pump surgery in such patients is not known. However, in patients with significant ascending aortic atheromatous disease, it would seem wise to consider an "off-pump" and "no-touch aortic" technique.

Sergeant and colleagues[5] analysed a consecutive series of 3,333 patients undergoing coronary artery surgery (1,593 on-pump and 1,740 off-pump). They found a trend towards a 60% reduction of stroke which, after risk adjustment, fell below the level of significance for the total population, but the benefit persisted for patients with severe stenosis of the internal carotid artery. In a meta-analysis of nine observational studies[27], off-pump coronary surgery was associated with a lower incidence of stroke in patients over 70 years of age as compared to the on-pump technique (1% vs. 3%), with an odds ratio of 0.38 (95% CI: 0.22-0.65). The incidence of atrial fibrillation was examined in another meta-analysis[28] of eight non-randomised studies, which included 3,017 patients (764 off-pump and 2,253 on-pump). The incidence of atrial fibrillation was significantly less in the off-pump group compared to on-pump (OR=0.70; 95% CI: 0.56-0.89) in an elderly population over the age of 70 years.

Off-pump surgery in high-risk patients

There are few reports from randomised trials in selected high-risk patients, but evidence from Sellke and colleagues on behalf of the American Heart Association[29] suggested that the length of stay, mortality rate, and long-term neurological function and cardiac outcome appeared to be similar in OPCAB and standard coronary artery surgery.

In high-risk coronary patients, the left ventricle is often dilated. Retraction of large beating hearts, necessary for the off-pump technique, is often poorly tolerated and may require inotropic drugs. An alternative approach is to do these procedures on-pump but without a period of global ischaemia or cardioplegia. By decompressing the heart with some form of left ventricular vent and using the stabilisation devices, excellent exposure is obtained and both mitral regurgitation and subendocardial ischaemia are minimised.

Conclusion

The intense interest in the modern development of beating heart surgery for coronary artery disease has been fuelled by the expectation that morbidity compared to cardiopulmonary bypass would be dramatically lower. That this has not been apparent from several randomised trials has surprised many, but may reflect all the small, subtle improvements in anaesthetic and surgical techniques and equipment, such as the design of pumps, oxygenators and cannulae, that have taken place over the last 15 years. It is apparent that off-pump surgery is an exacting technique that takes time to perfect, but which can produce an outcome equivalent to that obtained on-pump. Although there is a consistent finding of fewer transfusions and more repeat revascularisations with off-pump surgery, it is unknown whether this translates into adverse outcomes that are important to patients.

Conflict of interest statement

The author has no conflicts of interest to declare.

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