

## JOURNAL CLUB CRITIQUE

# Using pump for bypass surgery – on-off-on again?

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### Expanded abstract

#### Citation

Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, Lucke JC, Baltz JH, Novitzky D for the Veterans Affairs Randomized On/Off Bypass (ROOBY) Study Group: On-pump versus off-pump coronary artery bypass surgery. *N Engl J Med* 2009, **361**:1827-37

#### Background

Coronary-artery bypass grafting (CABG) has traditionally been performed with the use of cardiopulmonary bypass (on-pump CABG). CABG without cardiopulmonary bypass (off-pump CABG) might reduce the number of complications related to the heart-lung machine.

#### Methods

**Objective:** To compare off-pump to on-pump CABG in terms of short- and long-term composite of complications and death from any cause, as well as completeness and durability of the procedure/grafting, neuropsychological outcomes, and use of major resources.

**Design:** Multi-center single-blind, randomized controlled trial.

**Setting:** 18 Veterans Affairs medical centers, 16 of which were teaching hospitals.

**Subjects:**

2203 patients who were scheduled for urgent or elective CABG-only procedures.

**Intervention:** Patients were randomized to either on- or off-pump CABG. They underwent neuropsychological testing at baseline and one year, as well as follow-up angiography.

**Outcomes:** 1) Primary short-term end-point: composite of death or major complications (reoperation, new mechanical support, cardiac arrest, coma, stroke or renal

failure requiring dialysis) at discharge or day 30. 2) Primary long-term composite end-point: death from any cause within 1 year, nonfatal myocardial infarction between 30 days and 1 year, or repeat revascularization between 30 days and 1 year. 3) Secondary outcomes: completeness of revascularization, graft patency at 1 year, scores on neuropsychological tests.

#### Results

There was no significant difference between off-pump and on-pump CABG in the rate of the 30-day composite outcome (7.0% and 5.6% respectively,  $P = 0.19$ ). The rate of the 1-year composite outcome was higher for off-pump than for on-pump CABG (9.9% vs 7.4%,  $P = 0.04$ ). The proportion of patients with fewer grafts completed than originally planned was higher with off-pump CABG than with on-pump CABG (17.8% vs 11.1%,  $P < 0.001$ ). Follow up angiograms in 1371 patients who underwent 4093 grafts revealed that the overall rate of graft patency was lower in the off-pump group than in the on-pump group (82.6% vs. 87.8%,  $P < 0.01$ ). There were no treatment-based differences in neuropsychological outcomes or short-term use of major resources..

#### Conclusions

At 1 year of follow-up, patients in the off-pump group had worse composite outcomes and poorer graft patency than did patients in the on-pump group. No significant differences between the techniques were found in the neuropsychological outcomes or use of major resources.

#### Commentary

Cardiopulmonary bypass (CPB) was developed in 1954 and revolutionized cardiac surgery [1]. Almost since its inception, there has been literature attributing neurocognitive dysfunction, as well as a post-operative systemic inflammatory response syndrome (SIRS)-like phenomenon associated with organ failure, to the CPB machine used in cardiac surgery [2,3]. In the 1990s, cardiac surgeons responded by developing “off-pump” coronary artery bypass grafting (CABG), and this new technique has grown in popularity among surgeons and patients, the latter often requesting the procedure to avoid “pump-head.”

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Numerous large observational studies and small randomized trials have been published in the past 15 years suggesting benefits from off-pump CABG. Among these benefits are a reduction in stroke, time on mechanical ventilation, need for reoperation, bleeding, wound infection, renal failure, post-operative length of stay [4] and decreased atrial fibrillation and inotrope requirement [5].

Enthusiasm was tempered by studies that showed that not only was the new technique perhaps inferior in achieving the goal of complete and durable revascularization [6], but also was associated with reduced survival and an increase in non-fatal cardiac-related events at 4 to 6 months [7]. A 2005 meta-analysis noted that randomized controlled trials did not find the statistically significant reductions in short-term morbidity and mortality demonstrated by observational studies [8]. Finally, a sub-analysis of a large randomized controlled trial concluded that the apparent benefits of off-pump CABG essentially disappeared when the morbidity and mortality of emergency intra-operative conversion to the on-pump procedure were taken into account [9,10].

Into this setting the current paper was published as the largest randomized, controlled, single-blinded trial to evaluate the issue [11]. The study was designed to detect a reduction in major morbidity and mortality at both 30 days and 1 year for the off-pump procedure compared to the on-pump procedure. It also compared rates of achieving the anatomical goal of the operation—complete and durable revascularization—and results of neuropsychological tests.

Of note, there is some inconsistency between the authors' written hypothesis and the statistical design and power of the trial. The hypothesis in the 2007 clinical trials design paper [12] and the final NEJM paper [11] reads "We hypothesized that there would be no difference between the on-pump and off-pump procedures for the 2 primary outcomes." This describes an equivalence/non-inferiority trial, whereas the study was powered to demonstrate superiority of off-pump CABG over on-pump CABG. This discrepancy is a recurrent and important theme in study design [13,14] and had the study failed to show superiority of one technique over the other, it would have been underpowered to address its stated null hypothesis.

The authors found no difference between the two procedures in post-operative complications and short-term death from any cause. However, at 1 year, patients who underwent off-pump CABG had a significantly higher rate of the composite endpoint of morbidity and mortality, and death from cardiac causes, while no differences were observed in all-cause mortality. With regards to secondary outcomes, they found that patients who underwent off-pump CABG had significantly less

complete (fewer grafts done than planned) and less durable (decreased patency at one year) revascularization. There was no difference in neuropsychological outcomes or resources used. In summary, this study found harm rather than benefit from undergoing an off-pump CABG, most likely secondary to incomplete and less durable revascularization.

This study was a large, rigorously designed and executed study that addressed important clinical questions. For the population studied, it provided a definitive answer: on-pump CABG is better than off-pump CABG. However, some questions remain.

#### **1) To what patient population are these results applicable?**

Among the patients excluded from the trial were 3282 patients who needed emergent operation or were considered too high risk. Study patients were generally male, and, some respondents to the paper have claimed, healthier and younger than the average CABG population [15]. Observational data have suggested that off-pump CABG is better for women, the elderly, and those with severe coexisting illnesses [16]. In addition, the off-pump procedure may reduce the risk of stroke in patients with atheromatous aortas [17]. Future studies may reveal the specific types of patients who will benefit from off-pump CABG.

#### **2) Was the technical experience of the surgeons and anesthesiologists in this study sufficient, and how much experience with off-pump CABG is enough to ensure proficiency?**

The 12.4% intraoperative conversion from off-pump to on-pump CABG (5 times the rate reported in the National Database of Thoracic Surgeons) has been touted as evidence of the study practitioners' inexperience [18]. The authors addressed the issue of surgeon experience by doing a sensitivity analysis based on high volume (>50 pre-study cases) versus low volume (< 50 pre-study cases) operators, and found no significant difference in outcomes. This suggests that the results could be generalized to surgeons with variable off-pump experience. In addition, they excluded cases that crossed over to on-pump CABG and found no difference in the results. Nevertheless, some will question whether even 50 cases are sufficient to be considered proficient [15], and the experience of the anesthesiologist was not addressed. Although residents were considered the primary surgeon in many of the cases, this did not appear to have a clinical effect. The rate of complication in the study was lower than that typically published for both on- and off-pump CABG, and the group that involved more resident-surgeons (on-pump CABG) had a better outcome than that of the group that had fewer resident-surgeons (off-pump CABG).

### 3) What happened to the neurocognitive injury long associated with CPB? Is this a case of disappearing morbidity?

Consistent with some previous studies, this study failed to show neurocognitive dysfunction associated with CPB [16]. It is possible that CPB has undergone such technical refinement that the cognitive effects seen earlier are no longer a risk, or perhaps now only occur in the subgroup of patients largely excluded from this trial (women, the elderly, and more severely ill). The primary risk for neurocognitive dysfunction may now lie with the surgery itself, not CPB.

### Recommendation

Patients who fit the trial's inclusion criteria (men at low-to-moderate risk of death at 30 days and peri-operative complications), which will include many of those at the VA and most cardiac surgical groups, should now be counseled to undergo on-pump CABG. Sub-groups such as women and high-risk men that may benefit from off-pump CABG will likely be the subject of further studies. Future advances in CPB and off-pump CABG could yet change the landscape of this debate.

### Competing interests

The authors declare that they have no competing interests.

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