

# EDITORIAL COMMENT



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## On pump vs. off-pump surgery: still no definitive answers

The debate on which technique, on-pump or off-pump CABG, offers better outcome, is still going strong.

We may never know which one is the best, even though there is abundant evidence.

On-pump CABG is the most widely studied surgical procedure in the history of medicine, and has proven to be very effective and very safe in most cases, utilized worldwide by most centers and preferred by most surgeons. It theoretically offers more extensive revascularization, with better target vessel exposition and greater hemodynamically stability. Its known drawbacks are more aortic manipulation, myocardial ischemia during cardioplegia, more heparin and blood loss, and a higher frequency of post-operative atrial fibrillation.

On the other hand, off-pump surgery has been popularized in the late 80s/early 90s, and has exploded all over the world in the late 90's. Nevertheless, several publications have raised concerns about its ability to offer the same results as on-pump surgery while avoiding cardiopulmonary bypass, its higher heparin need, and its more frequent atrial fibrillation, acute renal failure and stroke rates of the pump approach. Concurrently, the fear of less complete revascularization and less than perfect anastomoses may compromise long term survival and freedom from repeat revascularization (RR).

This debate has been going on, and still this month new publications have come to light. Ever since this debate appeared, most publications seem to have favored the on-pump approach in most patients. Some subgroups of patients, like diabetics, with ventricular dysfunction, old age, high-risk, and redo CABG, have been favored by the off-pump approach in some studies.

The ROOBY trial<sup>1</sup>, from 2009, randomized 2200

patients for both arms. At 30 days, most outcomes were similar but with less grafts in off-pump, more failed grafts in off-pump, and worse results at one year.

The CORONARY trial<sup>2</sup>, which published its 5 years results in 2016, was a multicenter randomized with a median follow-up of 4.8 years, and showed similar outcomes, quality of life, and cost per patient. A few other smaller on-pump vs. off pump randomized studies were performed, and some meta-analyses are available.

Thakur et al<sup>3</sup> have looked at RCTs with more than 4 years follow-up, analysing death, stroke, Myocardia Infarction, or RR, and in a pool of 13.234 patients found that off-pump performs worst at 5 years in all cause mortality, being similar in stroke and MI; incomplete revascularization is more frequent in off-pump surgery, and these patients have higher degrees of RR at 1 and 5 years.

A similar paper by Smart et al<sup>4</sup> using the larger RCTs with 5 year results, encompassing 8145 patients, shows higher 5 year mortality with off pump (13.9% vs. 12.3 %) and same 5 years RR, myocardial infarction (MI) or angina, but does not mention effects of incomplete revascularization or total arterial revascularization.

A larger meta-analysis by Takagi et al<sup>5</sup>, published in 2017, aggregates 82316 patients from 16 smaller studies, and shows a higher all cause mortality at 10 years for off pump surgery (Hazard ratio 1.07, p=0.0008).

Let's then look at smaller studies. In the CABG subgroup of patients enrolled in the STITCH Trial<sup>6</sup>, 152 patients underwent off-pump surgery. These off-pump patients had a higher total arterial revascularization percentage (17% vs. 8% in the on-pump group), a higher incomplete revascularization

(34% vs. 17%), but a similar 30 day, 5 and 10 year mortality. It was hypothesized that arterial revascularization may counterbalance the attrition caused by incomplete revascularization.

A South Korean national cohort study by Kim et al<sup>7</sup> enrolling all CABG patients operated for 4 years, (4692 off pump vs. 2,999 on pump), shows better 3 year survival, and less dialysis for off-pump patients.

Another registry, this time a regional registry from Italy<sup>8</sup>, recorded 8488 on-pump patients and 894 off pump patients. After creating 560 pairs of patients, the two groups were analysed. Off pump patients were higher risk, and results show a better performance for on-pump patients regarding all cause mortality, later PCI, and cardiac death.

A similar mandatory registry from the state of New Jersey<sup>9</sup> paired 3895 pairs of off pump vs. on pump patients, through propensity score matching, and found higher incomplete revascularization, more RR and higher 10 year mortality for off pump patients. This registry had twice more patients in the on-pump group, 100 off-pump surgeries was the number considered necessary for proficiency in this type of operation, and off pump was chosen for selected patients, with the propensity score match (PSM) done retrospectively.

Another retrospective single center studies by Deutsch et al<sup>10</sup>, with almost 1900 pairs of patients, showed slightly less grafting in off-pump patients (2.74 vs 2.88 grafts), less stroke and mortality at 1 year in the off-pump group, and similar 10 year mortality, and a similar study by Kirmani et al<sup>11</sup> also a PSM, showed better short and long term results of off pump surgery.

In patients with LV depression, Marin-Cuartas et al<sup>12</sup> performed a PSM which showed in 430 pairs of patients, similar 30 day mortality, but shorter hospital admission, less transfusion and similar 5 year mortality.

A paper<sup>13</sup> with data from Japanese National Registry of CABG patients with LV ejection fraction <30% used a PSM to create 918 pairs of patients, and off-pump patients had lower 30 day mortality, operating mortality, mediastinitis, reoperation for bleeding and prolonged ventilation than on pump patients. Other studies showed similar results<sup>14</sup>.

In old patients, Li et al<sup>15</sup> showed better results in the short term (except completeness of revascularization) but worse results at long term, including increased hospital readmissions, MACCE and stroke rate for off pump patients, probably reflecting a higher cardiovascular burden.

The GOPCABE trial<sup>16</sup>, which involved about 1200 patients in each group above 75 years old, showed similar 5 years result, with incomplete revascularization associated with less survival regardless of the type of surgery.

In high risk patients, the BEST BYPASS trial, published in 2015<sup>17</sup>, included patients with EUROSCORE 1 above 5%, and excluded patients with severe ejection fraction. At 3 years, mortality was higher in off-pump patients, and there was a tendency for increased MI.

In the setting of redo CABG, off pump had less ICU and total hospital admission times, in a small study by Rufa et al<sup>18</sup>. A study originating from the Japanese national Registry,

by Doi et al<sup>19</sup>, also showed better short term results in off pump patients, with lower mortality, ICU stay, ventilation and transfusion.

The BARI 2D trial<sup>20</sup>, in diabetic patients, showed similar short term results, but higher RR, stroke, MI and death associated with the off pump surgery. Other smaller single center studies<sup>21,22</sup>, showed better short term results but similar or worse results in off pump patients.

In an obese patients PSM study, with 2890 pairs of patients, on pump was associated with higher intra-hospital mortality but similar long term mortality<sup>23</sup>.

A post-hoc analysis of the EXCEL trial<sup>24</sup>, in which left main patients were treated with both types of surgery, showed less grafting for the right coronary and lateral with off pump, but with more frequent bilateral artery mammary grafting. At 3 years mortality was higher with off-pump.

More recently, an analysis of the long term follow up the ROOBY trial patients<sup>25</sup> showed that at 10 years both surgeries were equivalent in mortality, with a slightly shorter time for a composite endpoint of death, repeat CABG, PCI for off-pump patients (4.3 months earlier than on pump patients on average).

In all this abundance of heterogeneous evidence, we may find some light. First, older studies, and the ones with longer follow-up, reflect older practices, and the quality of both techniques as performed in the early 2000 's has surely changed. Second, studies from centers or countries with high off pump utilization show at least equivalent, and frequently superior outcomes in the short and long term for off-pump technique. On the other hand, RCT (considered the gold standard of modern medicine), frequently with a few patients enrolled per center, show far better results for on-pump in the long term. Third, incomplete revascularization may be a clear driver for worse outcomes in the long term, while more arterial revascularization may offer better long term results. Fourth, the teams experience probably influences significantly short and long term results.

Off pump surgery is at least as safe as on pump surgery in all subgroups of patients in the short term, and probably preferable in low ejection fraction, more fragile or older patients, and in calcified aortas. As the scientific evidence stands, there is no reason for teams to change their practice overnight, or to believe they are doing the right thing and users of the contrary technique the wrong one, and it will probably stay that way for many years. Any technique seems to be very effective and safe for most patients as long as teams measure their results and try to improve their chosen technique.

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