ADVANTAGES AND PITFALLS OF OPCAB SURGERY

Ennker J (1,2), Ennker IC (1)
MediClin Heart Institute Lahr/Baden, Germany (1)
Institute of Cardiovascular Medicine, University Witten Herdecke, Germany (2)

Introduction
Coronary artery surgery will be influenced substantially by a variety of factors. Drivers of change will be the industry, the patient, the health service, the health service purchaser, the craft of coronary surgery itself, the residence, the media and the cardiologist and, especially the surgeon (Sergeant 2004). Of paramount importance in this regard are, of course, the surgeon and the surgical techniques he is using. Concerning technology, the debate whether off-pump coronary artery bypass grafting (OPCAB-surgery) is more beneficial for the patient than the traditional on-pump artery bypass grafting (CABG-surgery) is ongoing.

Off-pump CABG has remained at 15-20 % in Europe and the United States, while it plays an eminent role in evolving countries. In particular, the vision that off-pump surgery would lead to inferior revascularization due to reduction of peripheral anastomoses lead to a recent decline in the United States. In addition to this, no study was able to demonstrate any documented clinical advantage of the off-pump technique versus the traditional technique using cardiopulmonary bypass.

ROOBY TRIAL
In order to analyze off-pump CABG versus on-pump CABG, Shroyer and colleagues randomly assigned 2203 patients scheduled for urgent or elective CABG to either on-pump or off-pump procedures. They reported this from the Randomized On Versus Off Bypass trial (ROOBY). The primary short-term endpoint was a composite of death or complications before discharge or within 30 days after surgery. The primary long-term endpoint was a composite of death from any cause, a repeat revascularization procedure or a non-fatal myocardial infarction within one year after surgery. Secondary endpoints included the completeness of revascularization, graft patency at 1-year, neuropsychological outcomes and the use of major resources. The results showed that there was no significant difference between off-pump and on-pump CABG in the rate 30 day composite outcome (7.0 vs 5.6 respectively, p=0.19). The rate of 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 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 3371 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 of short use of major resources. The authors concluded that at 1-year of follow-up, patients in the off-pump group had worse composite outcomes and poorer graft patency than the patients in the on-pump group. Also no significant differences between the techniques were found in neuropsychological outcomes or use of major resources. (1)

Postoperative atrial fibrillation
The group of Almassi also analyzed the predictors and impact of postoperative atrial fibrillation (POAF) on patients’ outcomes. They reported this from data based on the ROOBY trial. They found that the strategy of revascularization did not affect the rate of postoperative atrial fibrillation. Age, race and hypertension were predictors of POAF which was independently associated with a higher short-term morbidity and a higher 1-year mortality rate. (2)
COPD
Almassi et al. analyzed the sub-segment of chronic obstructive pulmonary disease and the impact of the two surgical procedures. 220 patients were randomized to OPCAB and 238 patients to ONCAB within the ROOBY trial. For COPD patients, the baseline characteristics were similar between the two revascularization approaches. In these patients the intraoperative complication rate was higher with OPCAB than ONCAB (21.9 vs 10.1 %, respectively; p<0.001) but there were no significant differences in the 30-day (7.3 vs 7.6 %, p=1.00) or 1-year composite outcome rates (9.5 vs 7.1 %, p=0.39) between the groups. Comparing the COPD patients with propensity-matched non-COPD patients, there was no difference in 1-year major adverse cardiovascular events (including the 1-year composite major adverse cardiac events (MACE) outcome, as well as the individual MACE outcomes for all cause death, acute myocardial infarction, or repeat revascularization). (3)

Cost
Wagner and co-workers had a look at the cost effectiveness of on-pump versus off-pump coronary artery bypass surgery again as part of the ROOBY trial. The adjusted cost of the indexed coronary artery bypass graft surgery hospitalization was $36.046 on-pump and $36.536 off-pump (p=0.16). At 1-year on-pump adjusted costs were $56.023 vs $59.623 off-pump. Off-pump to on-pump conversions after first distal anastomosis, 4.8 % had significantly higher 1-year costs. Excluding conversions there were no significant differences between treatments for indexed hospitalization or 1-year total costs.(4) Contrary to this report, Houllind and co-workers found the opposite. A randomized, controlled trial of 900 patients above 70 years of age subjected to coronary artery bypass surgery was performed. The mean costs were 148.940 D.Kr for an on-pump patient and 138.693 D.Kr for an off-pump patient. The ICER (incremental cost-effectiveness ratio) base-case point estimate was 6.829.999 D.Kr/QALY (Quality-Adjusted Life Years). The cost-effectiveness acceptability curve showed 89 % probability of off-pump being cost-effective at a threshold value of 169.400 D.Kr./QALY.(5)

CORONARY TRIAL
Lamys reports the effects of off-pump and on-pump coronary artery bypass grafting at 30 days in 2012 and after one year in 2013. This study, involving 4752 patients, is the largest prospective randomized trial investigating the relative efficacy of off-pump CABG. Patients were enrolled in 79 centres in 19 countries. Quality of life and cognitive function at discharge at 30 days and at 1-year and clinical outcomes at 1-year were assessed. At 1-year there was no significant difference in the rate of primary composite outcome between off-pump and on-pump CABG (12.1 and 13.1 respectively), hazard ratio with off-pump CABG 0.91; 95 % confidence interval 0.77 to 1.07, p=0.24). The rate of primary outcome was also similar in the two groups in the period between 30 days and 1-year (hazard ratio 0.79; 95 % confidence interval (CI) 0.55 to 1.13; p=0.19). The rate of repeat coronary revascularization at 1-year was 1.4 % in the off-pump group and 0.8 % in the on-pump group (hazard ratio 1.66; 95 % CI 0.95 to 2.89; p=0.07). There were no significant differences between the two groups at 1-year in measures of quality of life or neuro-cognitive function contrary to the ROOBY trial where significant differences between two surgical techniques were documented.(6)

Differences between the ROOBY and the CORONARY trial have to be noted. The ROOBY trial includes surgeons of varying degrees of experience; resident was frequently the primary surgeon. On the contrary, in the CORONARY, surgery was performed by surgeons with more extensive off-pump experience and, in addition to this, no trainees were permitted to act as primary surgeons. Further more, in the latter trial inclusion criteria for patients consisted of patients with higher risk, defined for different decades of age. The results of the CORONARY trial after a long period of time will define the role of OPCAB surgery and of specific patient
subgroups that may benefit from this procedure more precisely.

Reoperations
Sepehripour and others were using the off-pump coronary revascularization method also in patients who needed a re-operative coronary artery surgery. They identified 12 studies incorporating 3471 patients per systematic literature review. These were meta-analyzed using random-effects modelling. Primary endpoints were 30-day and mid-term mortality. Secondary endpoints were completeness of revascularization, mean number of grafts per patient and the effect of intra-operative conversion of mortality. The results showed a significantly lower rate of 30-day mortality in the OPCAB group (odds ratio (OR) 0.51, 95 % CI [0.35, 0.74]). However, no difference was demonstrated in mid-term mortality. Significantly less complete revascularization and mean number of grafts per patient were observed in the OPCAB group. Meta-regression revealed no change in 30-day mortality when the effect of conversion from the technique to the other was assessed. The authors concluded that off-pump techniques may reduce early mortality in selected patients undergoing re-operative CABG; however, this does not persist into mid-term follow-up. OPCAB may also lead to intraoperative conversion and, although this did not affect outcomes in this study, these results are constrained by the limited data available. Furthermore, OPCAB may increase target vessel revascularization and, consequently, incomplete revascularization which, whilst not reflected in the short-term outcomes, requires longer-term follow-up in order to be fully assessed.(7)

Renal impairment
Fuster et al. analyzed the impact of increasing degrees of renal impairment on outcomes of coronary artery bypass grafting. A total of 1769 patients undergoing primary CABG had complete data on glomerular filtration rate. 930 patients had Stage 2 renal insufficiency, 330 Stage 3, 27 Stage 4 and 465 normal function (Stage 1). The OPCAB technique was selectively used in 350 high-risk patients. Preoperative variables and postoperative outcomes were compared among eGFR subgroups and between matched and unmatched OPCAB versus ONCAB groups. Stages 3-4 patients were older (p<0.0001), with higher prevalence of diabetes (36.8, 35.0, 39.7 and 74.1 %, p<0.01, 1-4 eGFR groups) peripheral arteriopathy (6.0, 9.0, 15.8 and 29.6 %, p<0.0001) and lower left ventricular ejection fraction (LVEF) (GFR-LVEF correlation: Pearson: 0.12, p<0.0001). On-pump GFR groups had increasingly higher in-hospital mortality (1.0, 1.2, 3.5 and 15.4 %, p<0.0001), but no differences were observed in OPCAB (5.5, 4.8, 5.4, and 7.1 %, p=0.97). Similar trends on in-hospital morbidity were observed in ONCAB versus OPCAB groups: low cardiac output (p<0.01), pneumonia (p<0.01) and stroke (p<0.05). GFR only predicted mortality in ONCAB patients (odds ratio: 0.96, 95 % CI: 0.94-0.98; p<0.01). Patients with higher eGFR stages had statistically more reduced long-term survival, and this pattern was similar in the three treatment groups, also including the OPCAB group, who had the lowest survival in patients with eGFR stage 4. The authors concluded that patients with low GFR (Stages 3-4) undergoing ONCAB were at increased risk of early mortality. In contrast, there were no significant differences in operative morbimortality among eGFR groups in OPCAB patients. This ‘off-pump advantage’ on early outcomes was not observed at the long-term follow-up.(8)

On-vs off pump in patients with low ejection fraction
In addition to these two major trials several detailed questions in this matter were answered by various authors. Keeling and co-workers analyzed the effect of off-pump versus on-pump coronary revascularization in patients with low ejection fraction. Between January 1, 2008 and June 30, 2011 data of 25667 patients with an EF of less than 0.3 according to the Society of Thoracic Surgeons National Data Base, who underwent primary non-emergent coronary artery bypass grafting were analyzed. 20509 had an ONCAB procedure and 5158 an OPCAB
procedure. Propensity scores were estimated using 32 covariates and multivariate logistic regression was used to compare risk-adjusted outcomes between groups. The results showed that patients undergoing planned OPCAB were older, more frequently female and had a lower body mass index than those who underwent ONCAB. Unplanned conversion to CPB occurred in 270 (5.2 % of the 5158 patients). OPCAB was associated with a significant lower adjusted risk of death (odds ratio 0.82, stroke 0.67 and major adverse cardiac events (OR 0.75) and prolonged intubation (OR 0.78), post operative transfusion rates were significantly lower in the OPCAB group (54.8 % vs 51.6 %, p<0.001). There were no adverse outcomes that occurred more commonly in OPCAB patients. The advantages associated with OPCAB were found in the entire Society of Thoracic Surgeons National Database and among high-volume and low-volume OPCAB centres.(9)

**Diabetic patients**

Emmert and colleagues analyzed if off-pump surgery is superior to conventional artery bypass grafting in diabetic patients with multivessel disease and found that OPCAB offers a lower mortality and superior postoperative outcome in diabetic patients with multivessel disease. Arterial grafts are used more frequently that may contribute to better long-term outcomes and the OPCAB approach does not come at the cost of less complete revascularization.(10)

**Gastrointestinal ischemia**

Emmiler analyzed consequences of the off-pump versus on-pump coronary artery bypass grafting with respect to gastrointestinal ischemia related mortality. They retrospectively evaluated 2625 patients who underwent isolated coronary artery surgery during a 6-year period; OPCAB (658 patients) and ONCAB (1967) patients. Gastrointestinal ischemia developed in 0.4 % (7 of 1967) patients in the ONCAB group and in 0.2 % (1 of 658) patients in the OPCAB group (p=0.28). Mortality rates due to gastrointestinal ischemia were 0.2 % (4 of 1967) in the ONCAB group and no deaths occurred in the OPCAB group (p<0.4). Postoperative atrial fibrillation incidence with GII was 100 % (7 of 7) in ONCAB group and 0 % (0 of 1) in the OPCAB group (p<0.01).(11)

**Octogenarians**

Sarin et al. compared on- and off-pump coronary artery bypass grafting and the effect on short- and long-term outcomes in octogenarian patients. A propensity adjusted retrospective review of patients older than 80 years who underwent primary CABG from 01/1996 until 09/2008 was performed. OPCAB (n=540), ONCAB (n=397). A propensity score was calculated based on 29 pre-operative risk factors to adjust for the selection bias when comparing the groups for differences in death, stroke, myocardial infarction incidence and their composite. The authors found that the mean age (OPCAB 82.9±2.8 years vs ONCAB 82.3±2.4, p=0.003) and male sex (OPCAB 292/540, 54.1 % vs ONCAB 220/397, 55.4 %, p=0.68) were clinically similar between groups. Although the ejection fraction (OPCAB 52.1±12.5 vs ONCAB 50.7±13.1, p= 0.1) was similar between groups, the mean number of distal anastomoses (OPCAB 2.7 vs ONCAB 3.4 were less in the OPCAB group. The median postoperative length of stay was 7 days for OPCAB group and 6 days for ONCAB group. The Society of Thoracic Surgery predicted risk of in-hospital mortality was similar for OPCAB (5.4 %) and ONCAB (5.3%) patients (p=0.81). However, observed in-hospital mortality was improved for patients in the OPCAB group (OPCAB 15/540, 2.8 % vs ONCAB 37/397, 9.3 %, p=0.007). Ten-year survival was similar between groups (OPCAB: 28.8 % vs ONCAB 26.3 %, p=0.22). The authors concluded that in this series, OPCAB reduced the incidence of in-hospital mortality compared with ONCAB.(12)
**OPCAB trend over time**

Bakaeen et al. analyzed the trends over time in the relative use in associated mortality of on-pump and off-pump coronary artery bypass grafting in the Veterans Affairs Systems. They performed a retrospective analysis of data from the Veterans Affairs Surgical Quality Improvement Program (VASQIP). Data were collected from 42 Veterans Affairs Cardiac Surgery Centres, in total 65,097 patients who underwent isolated primary CABG from October 1997 to April 2011 were analyzed. Patients underwent either on-pump or off-pump CABG. As a function of time, the percentages of on- versus off-CABG cases were analyzed. In addition to this, trends over time in rates of conversion from off- to on-CABG, perioperative mortality (30-day or in-hospital mortality) and VASQIP predicted risk of mortality. The authors could define that the relative use of OPCAB peaked at 24 % in 2003 followed by a slow and mostly consistent decline to stabilize at about 19 %. The conversion rate decreased with time has stayed less than 3.5 % since 2007 (p<0.01), perioperative mortality rate decreased over time for both, off- and on-CABG (p<0.001) and has stayed less than 2 % for the entire cohort since 2006. The mortality associated with converted cases was high, regardless of the surgery year and exceeded the VASQIP predicted risk of mortality. Bakaeen and co-authors concluded that there has been a decline in the relative use of OPCAB in the Veterans Affairs Systems since 2003 and that this trend may affect the training of future generations of off-pump surgery and influence conversion rates and outcomes.(13)

**Importance of training and surgical expertise**

Sergeant’s group from Leuven documented the quantification of operational learning in off-pump coronary artery bypass. They stated that the use of off-pump coronary artery bypass grafting (OPCAB) has been associated with similar or even worse results versus on-pump coronary bypass grafting (CABG). Different production processes demand re-engineering, operational learning and quality loops to study and reduce negative learning curves. They re-engineered CABG towards OPCAB in October 1999. A consecutive cohort of 3054 patients, representing 92.3 % (ranging from 90 % in 2000 to 99 % in 2001 and later) of all primary and redo isolated CABG from that same period, was divided into three consecutive cohorts of 1018 patients. An anniversary follow-up at 3 month was complete for 100 % of the patients. The 1- and 3-months survival are studied using saturated propensity score matching and stratification for cohort variability (area under the curve = 0.82). Despite a progressively worsening risk profile (history of vascular disease, stroke and diabetes, main stem stenosis, left ventricular dysfunction), a survival improvement was shown between the consecutive cohorts. This improvement remained valid after the propensity stratification and propensity matching at 1 (97.6 vs 99.3%, p<0.001) and at 3 months (96.7 vs 98.8 %, p<0.001). The authors underlined that OPCAB re-engineering, followed by operational learning, improved the early survival even in the presence of a worsening risk profile.(14)

**Discussion:**

A very recent publication advocated that off-pump coronary artery bypass grafting should be abandoned. The author summarized that retrospective non-randomized, prospective randomized and meta analyses trials did not state relevant improvements in short-term mortality with OPCAB techniques. (15)

However, the paper by Sergeant demonstrates the significance of re-engineering for quality improvement if a new surgical technique is introduced. This refers also to the OPCAB technique. Currently, superior results using the OPCAB technique are primarily generated by specialised groups completely devoted to off-pump procedure. To reach this level of expertise it is mandatory to initiate a complete reengineering as described by Sergeant. The approach to use the off-pump technology only in selected patients will not enable to master the learning curve.
To reach the best result for our patients, the aim is that coronary revascularization should not be exercised to use a suspected technical superiority but to reach optimal, complete revascularization for the patient with a perfect anastomosis in all situations. Relevant for the patients benefit is not a single surgical methodology raised to a dogma level, as to use the OPCAB technique, but also total arterial revascularization, subsequent flow measurement and the so-called aortic no-touch technique, where Y-grafts are used to avoid clamping of the aorta for proximal anastomosis (16). Table 1 shows our own policy. Using these surgical methods we have been able to secure a below 1% mortality for all patients for many years. In the patients in whom the no-touch technique was employed, the incidence of neurological complications was also below one percent. As neither the extracorporeal circulation nor the clamping of the aorta was employed, neurological sequelae of the revascularization procedure were not caused by surgical action but rather by intermittent atrial fibrillation and subsequent embolisation or intracranial pathology. In this regard: In his paper entitled: “Off-pump vs On-pump CABG: are we any closer to a resolution?” Taggart underlined, that registry data are consistently reporting relevant clinical benefits in term of reduction of mortality and major complications for higher risk patients, in particular the reduction of stroke. (17)

The OPCAB technique will continue to be beneficial for the patient with the concomitant pathology of atherosclerotic plaques or the situation of a porcelain aorta. Other patient cohorts are those with further contraindications for the use of extracorporeal circulation as those with liver cirrhosis or evolving failure.

There is no doubt, that the OPCAB technique will play its special role in the future. Long-term results by those groups who are using the latter in the majority of their patients, should clarify the current question, whether the OPCAB technology is detrimental to our patients or an enrichment of the surgical armamentarium.
Table 1: Current decision making in our institution in coronary artery surgery (16)

<table>
<thead>
<tr>
<th>Decision making factors</th>
<th>Applied technique</th>
<th>Short description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Procedure of first choice</strong></td>
<td>Clamp-less OPCAB with double IMAs as T-graft or in situ configuration</td>
<td>OPCAB &amp; No-touch-technique &amp; TAR.</td>
</tr>
<tr>
<td><strong>2. Octogenarians, insulin-dependent diabetes, severe COPD, short RIMA</strong></td>
<td>Clamp-less OPCAB with LIMA and radial artery / vein as T-graft</td>
<td>OPCAB &amp; No-touch-technique</td>
</tr>
<tr>
<td><strong>3. Short or small RIMA</strong></td>
<td>Tangential clamping of the aorta for proximal vein anastomoses</td>
<td>OPCAB</td>
</tr>
<tr>
<td><strong>4. Conversions due to hemodynamic instability, ischemia, intraseptal LAD</strong></td>
<td>On-pump CABG, Single Clamp</td>
<td>OPCAB conversion</td>
</tr>
<tr>
<td><strong>5. Instable hemodynamics, EF &lt; 25</strong></td>
<td>On-pump CABG with LIMA &amp; vein graft or TAR</td>
<td>CABG (poss.: TAR)</td>
</tr>
</tbody>
</table>

OPCAB = Off-pump coronary artery bypass; IMA = internal mammary artery; COPD = chronic obstructive pulmonary disease; RIMA = right internal mammary artery; LIMA = left internal mammary artery; LAD = left anterior descending; CABG = coronary artery bypass; TAR = total arterial revascularization; EF = ejection fraction.

References

1. SHROYER L, GROVER FL; HATTLER B, et al.
   On-Pump versus Off-Pump Coronary Artery Bypass Surgery

2. ALMASSI GH, PECSI SA, COLLINS JF, et al.
   Predictors and Impact of Postoperative Atrial fibrillation on Patients’ Outcomes: A Report from the Randomized On Versus Off Bypass Trial
   J Thorac Cardiovasc Surg 2012 Jan; 143(1)93-102

3. ALMASSI GH, SHROYER AL, COLLINS JF; et al.
   Chronic Obstructive Pulmonary Disease Impact Upon Outcomes: The Veterans Affairs Randomized On/Off Bypass Trial.
   Ann Thorac Surg; July 31, 2013 [Epub ahead of print]

   On-Pump Versus Off-Pump Coronary Artery Bypass Surgery: Cost-Effectiveness Analysis Alongside a Multisite Trial
5. HOULIND K, KIELDSEN BJ; MADSEN SN, et al. 
   OPCAB Surgery is Cost-Effective for Elderly Patients 

   Effects of Off-Pump and On-Pump Coronary Artery Bypass Grafting at 1 Year 

   Does Off-pump Coronary Revascularization Reduce Mortality in Re-operative Coronary 
   Artery Surgery? A Meta-Analysis of Observational Studies 

8. FUSTER GR, PAREDES F, PELAEZ GA, et al. 
   Impact of Increasing Degrees of Renal Impairment on Outcomes of Coronary Artery 
   Bypass Grafting: The Off-pump Advantage 

   Off-Pump and On-Pump Coronary Revascularization in Patients with Low Ejection 
   Fraction: A Report from the Society of Thoracic Surgeons National Database 
   Ann Thorac Surg; 2013 July; Vol 96:1; 83-89

10. EMMERT MY, SALZBERG SP, SEIFERT B, et al. 
    Is Off-pump Superior to Conventional Coronary Artery Bypass Grafting in Diabetic 
    Patients with Multivessel Disease? 

    Gastrointestinal Ischemia Related Mortality in Patients Undergoing Off- or On-pump 
    Coronary Artery Bypass Grafting 

12. SARIN EL, KAYATTA MO, KILGO P, et al. 
    Short- and Long-Term Outcomes in Octogenarian Patients Undergoing Off-pump 
    Coronary Artery Bypass Grafting Compared with On-pump Coronary Artery Bypass 
    Grafting 
    Innovations (Phila) 2011 Mar;6(2): 110-5

13. BAKAEEN FG, KELLY RF, CHU D, et al. 
    Trends Over Time in the Relative Use and Associated Mortality of On-Pump and Off- 
    Pump Coronary Artery Bypass Grafting in the Veterans Affairs System 

14. PETTINARI M, SERGEANT P, MEURIS B 
    Quantification of Operational Learning in Off-Pump Coronary Bypass 
    Eur J Cardiothorac Surg 2013 Apr; 43(4):709-14

15. LAZAR HL 
    Should Off-pump Coronary Artery Bypass Grafting be Abandoned 
16. ENNKER JC, ENNKER IC
   Coronary Artery Surgery: Now and in the Next Decade

17. TAGGART DP, ALTMAN D
   Off-pump vs On-Pump CABG: Are we any closer to a resolution?
   Eur Heart J 2012 (33): 1181-1183