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European Journal of Cardio-thoracic Surgery 40 (2011) 233—239
EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY
www.elsevier.com/locate/ejcts

Is off-pump superior to conventional coronary artery bypass grafting in diabetic patients with multivessel disease?☆

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Received 4 September 2010; received in revised form 27 October 2010; accepted 2 November 2010; Available online 16 December 2010

Abstract

Objective: Diabetic patients often present with diffuse coronary disease than nondiabetic patients posing a greater surgical challenge during off-pump revascularization. In this study, the safety, feasibility, and completeness of revascularization for this subset of patients was assessed. **Methods:** From 2002 to 2008, 1015 diabetic patients underwent myocardial revascularization. Patients received either off-pump coronary artery bypass (OPCAB; $n = 540$; 53%) or coronary artery bypass grafting (CABG; $n = 475$; 47%). Data collection was performed prospectively and data analysis was done by propensity-score (PS)-adjusted regression analysis. Primary endpoints were mortality, major adverse cardiac and cerebrovascular events (MACCEs), and a composite endpoint including major noncardiac adverse events (MNCAEs) such as respiratory failure, renal failure, and rethoracotomy for bleeding was applied. An index of complete revascularization (ICOR) was defined to assess complete revascularization by dividing the total number of distal anastomoses by the number of diseased vessels. Complete revascularization was assumed when ICOR was >1. **Results:** OPCAB patients had a significantly lower mortality-rate (1.1% vs 3.8%; propensity-adjusted odds ratio (PAOR) = 0.11; $p = 0.018$) and displayed less frequent MACCE (8.3% vs 17.9%; PAOR = 0.66; $p = 0.07$) including myocardial infarction (1.3% vs 3.2%; PAOR = 0.33; $p = 0.06$) and stroke (0.7% vs 2.3%; PAOR = 0.28; $p = 0.13$). Similarly, a significantly lower occurrence of the noncardiac composite endpoint (MNCAE) (PAOR = 0.46; confidence interval (CI) 95% 0.35—0.91; $p < 0.001$) was detected. In particular, lesser respiratory failure (0.9% vs 4.3%; PAOR = 0.24; $p = 0.63$) and pleural effusions (3.3% vs 7.5%; PAOR = 0.45; $p = 0.04$) occurred, so that fast extubation (≤12 h postoperative) was more frequently possible (58.3% vs 34.2%; PAOR = 1.64; $p = 0.007$). The number of arterial grafts was significantly higher among OPCAB patients (1.54 ± 0.89 vs 1.33 ± 0.81; $p = 0.006$) due to a more frequent use of the right-internal mammary artery (35.6% vs 22.9%; $p < 0.001$). ICOR was significantly higher among CABG patients (1.24 ± 0.34 vs 1.30 ± 0.28; $p = 0.001$). However, for similar proportions in both groups, an ICOR > 1 was achieved clearly indicating complete revascularization (94.3% vs 93.7%; $p = 0.24$). **Conclusions:** OPCAB offers a lower mortality and superior postoperative outcomes 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.

Keywords: Diabetes; Coronary artery disease; Off-pump; Coronary artery bypass grafting; Surgery; Myocardial revascularization

1. Introduction

Diabetes mellitus (DM) is a well-known risk factor for the development of coronary artery disease (CAD) [1]. Affected patients often present with advanced and more diffuse disease, involving multiple vessels and rapidly progressive CAD when compared to nondiabetic patients [2]. Therefore DM is a well-established predictor for adverse outcome of both surgical as well as percutaneous revascularization [3].

Particularly percutaneous coronary interventions (PCIs), including angioplasty and stent placement, have been reported to carry a higher risk for re-stenosis and recurrent symptoms. This has been confirmed by various randomized trials, suggesting that coronary artery bypass grafting (CABG) is the most appropriate therapy (according to the guidelines of the American College of Cardiology/American Heart Association) for diabetic patients with multivessel disease (MVD) than PCI [4—6].

Conventional CABG is performed with cardio-pulmonary bypass (CBP), which is associated with serious complications such as stroke [7], renal dysfunction, and systemic inflammatory response syndrome (SIRS) [8]. Off-pump coronary artery bypass (OPCAB) surgery has been demonstrated to have a comparable risk-adjusted mortality and to be associated with less major complications [9,10]. Current

☆ Presented at the 24th Annual Meeting of the European Association for Cardio-thoracic Surgery, Geneva, Switzerland, September 11—15, 2010.

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1010-7940/$ — see front matter
doi:10.1016/j.ejcts.2010.11.003

data suggest that OPCAB may be superior for high-risk patients [11]. However, for diabetic patients with MVD only limited data are available [12,13].

In this study, we compare OPCAB to conventional CABG for diabetic patients with MVD with regard to mortality, postoperative morbidity, and completeness of revascularization.

2. Material and methods

From 2002 to 2008, 1015 diabetic patients with MVD underwent myocardial revascularization at our institution. Patients received either OPCAB ($n = 540$; 53%; group A) or CABG ($n = 475$; 47%; group B). Data collection was performed prospectively and was approved by our local institutional review board (IRB), including a waiver of informed consent. Surgery was performed as follows: elective (68.7% vs 64.4%; $p = 0.16$), urgent (24.6% vs 30.9%; $p = 0.029$), and emergent (6.7% vs 4.6%; $p = 0.18$), respectively. Mean preoperative risk stratification was performed by use of the European System for Cardiac Operative Risk Evaluation (Euroscore).

Tables 1 and 2 summarize demographics and preoperative variables for both the groups. In brief, OPCAB patients and CABG patients were well comparable with regard to mean EuroScore (3.9 ± 1.2 vs 4.1 ± 1.1), age, and gender distribution. OPCAB patients presented more significantly with left main disease (31.1% vs 23.8%; $p = 0.009$), whereas patients undergoing CABG more frequently suffered from triple vessel disease (76.7% vs 88.4%; $p = 0.001$) and presented more frequently for redo surgery (2.8% vs 9.1%; $p = 0.001$).

OPCAB patients appeared to suffer more significantly from peripheral artery disease (PAD) (21.0% vs 14.1%; $p = 0.005$) and had a more frequent history of previous cardiogenic shock (>90 days) (10.0% vs 5.1%; $p = 0.013$). By contrast, CABG patients presented with higher instable angina (11.7% vs 20.6%; $p = 0.001$) requiring preoperative implantation of an intra-aortic balloon pump (IABP; 11.5% vs 23.1%; $p = 0.0001$).

Table 1. Preoperative characteristics and demographics.

Parameter	OPCAB ($n = 540$)	CABG ($n = 475$)	p-Value
Age (years)	65 ± 10	64 ± 9	0.18
Male (%)	73	77	0.08
Female (%)	27	23	0.08
EuroScore	3.9 ± 1.2	4.1 ± 1.1	**0.01**
EF (%)	55 ± 14	56 ± 14	0.12
BMI (kg/m^2)	28 ± 4	28 ± 4	1.00
Elective (%)	68.7	64.4	0.16
Urgent (%)	24.6	30.9	**0.029**
Emergent (%)	6.7	4.6	0.18
Sinus rhythm (%)	97.3	96.2	0.54
Atrial fibrillation (%)	2.0	2.9	0.49
Pacemaker (%)	0.7	0.8	1.00
No of diseased vessels	2.75 ± 0.47	2.95 ± 0.25	**0.001**
1-vessel disease (%)	1.9	1.9	1.00
2-vessel disease (%)	21.5	9.7	**0.001**
3-vessel disease (%)	76.7	88.4	**0.001**
Left main disease (%)	31.1	23.8	**0.009**
CCS 1 (%)	5.4	5.7	0.89
CCS 2 (%)	34.7	29.3	0.09
CCS 3 (%)	45.6	46.9	0.69
CCS 4 (%)	14.3	18.1	0.13
NYHA 1 (%)	57.1	73.3	**<0.0001**
NYHA 2 (%)	28.6	16.2	**<0.0001**
NYHA 3 (%)	12.9	8.4	**0.029**
NYHA 4 (%)	1.4	2.1	0.47
Redo surgery (%)	2.8	9.1	**0.001**

EF: ejection fraction, BMI: body mass index, CCS: Canadian Cardiovascular Society Angina Classification, NYHA: New York Heart Association. All values which are significant ($p < 0.05$) are bold.

Table 2. Risk factors and co-morbidities.

Parameter	OPCAB ($n = 540$)	CABG ($n = 475$)	p-Value
Hypercholesterinemia (%)	70.7	74.9	0.21
Hypertension (%)	58.5	75.4	**<0.0001**
Positive family history (%)	30.7	29.9	0.78
Smoking (%)	48.5	49.7	0.74
Adipositas (%)	58.7	52.0	**0.037**
PAD (%)	21.0	14.1	**0.005**
COPD (%)	7.2	7.4	1.00
Acute myocardial infarction (<90 days) (%)	17.2	21.3	0.11
Previous MI (>90 days) (%)	40.0	44.0	0.2
Preoperative cardiogenic shock (%)	1.7	1.5	1.00
Previous cardiogenic shock (>90 days) (%)	10.0	5.1	**0.013**
Cerebrovascular disease (%)	2.0	1.3	0.47
Previous syncope (%)	1.7	2.1	0.79
Renal disease (%)	5.7	3.6	0.2
Instable angina (%)	11.7	20.6	**0.001**
IABP preoperative (%)	11.5	23.1	**0.001**

PAD: peripheral artery disease, COPD: chronic obstructive pulmonary disease, MI: myocardial infarction, IABP: intra-aortic balloon pump.

2.1. Surgical technique

CABG was performed using standard CBP techniques and proximal anastomosis was done with complete clamping of the aorta. OPCAB procedures were performed as previously described [14]. In brief, heparin was administered to obtain active clotting time (ACT) in excess of 350 s and repeated if necessary. Epicardial temporary pacemaker wires were placed, before a stabilizer (Octopus®4 Tissue Stabilizer, Medtronic, Minneapolis, USA) was used to expose the target vessel. A shunt (ClearView® Intracoronary Shunt, Medtronic, Minneapolis, USA) was routinely inserted and a mister blower (Guidant, Indianapolis, USA) with CO_2 and water was used to clear the surgical field. If no T-graft was performed, proximal anastomosis was carried out in a clampless fashion ('no touch' technique for proximal anastomosis) using the heartstring device (Heartstring™ Proximal Seal System, Guidant, Indianapolis, USA). Routine ultrasound flow measurement (MediStim QuickFit®) was done in all cases. The strategy for the perioperative glycemic control was based on the Portland scheme described by Furnary et al. [15].

2.2. Strategy for revascularization

Surgical revascularization was mainly started by left internal mammary artery (LIMA) to left anterior descending (LAD) grafting. Following this, the right coronary system was approached, and finally the circumflex territory was revascularized. In patients with left main disease, LAD and circumflex arteries were always grafted, regardless of the degree of stenosis. All other vessels with significant lesions (>70%) were identified preoperatively in the angiogram and selected as target for revascularization.

2.3. Statistical analysis

Endpoints analyzed are mortality and major adverse cardiac events (MACCEs) including death, myocardial infarction, recurrent angina, and stroke. A composite endpoint including major noncardiac adverse events (MNCAEs) such as respiratory failure, renal failure, and rethoracotomy for bleeding was created. For converted patients, the 'intention-to-treat' methodology was applied.

An index of complete revascularization (ICOR) was calculated for each patient. The CRI was defined as the total number of distal grafts divided by the number of the affected coronary vessels reported on the preoperative coronary angiogram. Complete revascularization (CR) was assumed when the number of distal anastomoses was larger than that of diseased vessels [9].

Continuous data are presented as mean $\pm$ standard deviation and are compared using the Mann–Whitney test. Categorical data are presented as number and percentage and are compared using the Chi-square test or Fisher's exact test, where appropriate. Odds ratios with 95% confidence intervals are computed using univariate logistic regression. A propensity score (PS) was computed using logistic regression with 52 preoperative variables to balance characteristics between OPCAB and on-pump groups (*c*-statistic 0.87). In this computation, missing values in preoperative variables were replaced using regression methods. The PS then was divided into quintiles and analyzed as a categorical variable. PS-adjusted logistic regression analysis was performed to assess binary endpoints and two-way analysis of variance for continuous endpoints. All analyses were performed using SPSS 18 (SPSS Inc., Chicago, IL). *P*-values < 0.05 are assumed to be statistically significant.

3. Results

3.1. Crude outcome data (Table 3)

OPCAB patients had a significantly lower mortality rate than CABG patients (1.1% vs 3.8%; odds ratio (OR) = 0.28; confidence interval (CI) 95% 0.11–0.72; $p = 0.008$) and suffered from significantly less major adverse cardiac events (MACCEs) (8.3% vs 17.9%; OR = 0.41; CI 95% 0.28–0.61; $p < 0.001$) and major noncardiac adverse events (MNCAE) (9.4% vs 18.5%; OR = 0.46; CI 95% 0.31–0.66; $p < 0.001$). In detail, OPCAB patients displayed a significant benefit with regard to stroke (0.7% vs 2.3%; OR = 0.31; CI 95% 0.10–0.99; $p = 0.043$), reoperation for bleeding (3.9% vs 6.7%; OR = 0.56; CI 95% 0.31–0.98; $p = 0.044$), need for postoperative IABP implantation (0.2% vs 2.5%; OR = 0.07; CI 95% 0.01–0.55; $p = 0.011$), as well as the occurrence of respiratory failure (0.9% vs 4.3%; OR = 0.21; CI 95% 0.05–0.91; $p = 0.038$). This was clearly reflected by the lower frequency of prolonged ventilation (7.3% vs 14.3%; OR = 0.46; CI 95% 0.29–0.73; $p = 0.01$), the lower rate of pleural effusions and/or pneumothorax (3.3% vs 7.5%; OR = 0.42; CI 95% 0.20–0.87; $p = 0.02$), as well as the overall shorter time to extubation (<12 h) (58.3% vs 34.2%; OR = 2.69; CI 95% 2.00–3.51; $p < 0.001$) clearly indicating a more straightforward postoperative course. Similarly, the frequency of myocardial infarction (1.3% vs 3.2%; OR = 0.41; CI 95% 0.13–1.26; $p = 0.12$), graft occlusion (1.4% vs 2.1%; OR = 0.65; CI 95% 0.17–2.40; $p = 0.52$), low cardiac output (1.4% vs 4.1%; OR = 0.33; CI 95% 0.09–1.15; $p = 0.08$), and renal failure (4.1% vs 6.3%; OR = 0.63; CI 95% 0.35–1.10; $p = 0.63$) was lower in the OPCAB group, but failed to achieve statistical significance.

Table 3. Crude outcome data.

Parameter	OPCAB ($n = 540$)	CABG ($n = 475$)	OR	CI 95%	*p*-Value
Mortality (%)	1.1	3.8	0.28	0.11–0.72	**0.008**
Neurological events (central) (%)	0.7	2.3	0.31	0.10–0.99	**0.043**
Neurological events (peripheral) (%)	0.7	0.6	1.17	0.26–5.27	0.83
Re-thoracotomy for bleeding (%)	3.9	6.7	0.56	0.31–0.98	**0.044**
Myocardial infarction (%)	1.3	3.2	0.41	0.13–1.26	0.12
Low cardiac output (%)	1.4	4.1	0.33	0.09–1.15	0.08
Graft occlusion (%)	1.4	2.1	0.65	0.17–2.40	0.52
Cardiac tamponade (%)	0.5	0.2	2.20	0.13–35.39	0.57
Arrythmia (%)	0.9	2.1	0.43	0.09–1.99	0.28
IABP postop (%)	0.2	2.5	0.07	0.01–0.55	**0.011**
Renal dysfunction (%)	4.1	6.3	0.63	0.35–1.10	0.10
Dialysis (%)	3.3	3.2	1.00	0.46–2.38	0.99
No ventilation (%)	2.8	1.7	1.66	0.67–4.10	0.27
Ventilation <12 h (%)	58.3	34.2	2.69	2.00–3.51	<**0.001**
Ventilation > 12 h (%)	31.9	49.8	0.47	0.36–0.62	<**0.001**
Prolonged ventilation > 24 h (%)	7.3	14.3	0.46	0.29–0.73	**0.01**
Respiratory failure (%)	0.9	4.3	0.21	0.05–0.91	**0.038**
Pleural effusions/pneumothorax (%)	3.3	7.5	0.42	0.20–0.87	**0.02**
Sinus rhythm (%)	94.3	94.7	0.92	0.49–1.74	0.80
Atrial fibrillation (%)	4.3	4.2	1.00	0.50–2.10	0.93
Need for pacemaker (%)	2.0	1.1	1.91	0.58–6.34	0.28
MACCE (%)	8.3	17.9	0.41	0.28–0.61	<**0.001**
MNCAE (%)	9.4	18.5	0.46	0.31–0.66	<**0.001**

MACE: major adverse cardiac events, MNACE: major noncardiac adverse events.

3.2. Propensity-adjusted outcome data (Table 4)

After PS adjustment, OPCAB patients still displayed a significantly lower mortality rate (propensity-adjusted odds ratio (PAOR) = 0.11; CI 95% 0.01–0.68; $p = 0.018$) as well as a significantly lower occurrence of the noncardiac composite endpoint (MNCAE) (PAOR = 0.46; CI 95% 0.35–0.91; $p < 0.001$). Next, still significantly more OPCAB was extubated within the first 12 h (PAOR = 1.64; CI 95% 1.14–2.36; $p = 0.007$) and presented with less pleural effusions or pneumothorax (PAOR = 0.45; CI 95% 0.21–0.96; $p = 0.04$) reflecting a faster postoperative course.

With regard to MACCE (PAOR = 0.66; CI 95% 0.42–1.04; $p = 0.07$) and major single complications such as stroke (PAOR = 0.28; CI 95% 0.05–1.42; $p = 0.12$), reoperation for bleeding (PAOR = 0.58; CI 95% 0.28–1.23; $p = 0.16$), postoperative IABP implantation (PAOR = 0.15; CI 95% 0.02–1.27; $p = 0.08$), and respiratory failure (PAOR = 0.23; CI 95% 0.05–1.07; $p = 0.06$), the protective benefit of OPCAB remained detectable, but failed to achieve statistical significance after PS adjustment.

Table 4. Propensity adjusted outcome data.

Parameter	OR	CI 95%	*p*-Value
Mortality (%)	0.11	0.01–0.68	**0.018**
Neurological events (central) (%)	0.28	0.05–1.42	0.12
Neurological events (peripheral) (%)	0.10	0.01–4.80	0.24
Re-thoracotomy for bleeding (%)	0.58	0.28–1.23	0.16
Myocardial Infarction (%)	0.33	0.10–1.07	0.06
Low cardiac output (%)	0.34	0.09–1.24	0.10
Graft occlusion (%)	0.39	0.09–1.59	0.18
Cardiac tamponade (%)	1.35	0.61–29.66	0.85
Arrythmia (%)	0.97	0.19–4.85	0.97
IABP postop (%)	0.15	0.02–1.27	0.08
Renal dysfunction (%)	0.57	0.25–1.27	0.17
Dialysis (%)	0.85	0.32–2.19	0.73
No ventilation (%)	2.32	0.65–8.34	0.20
Ventilation <12 h (%)	1.64	1.14–2.36	**0.007**
Ventilation > 12 h (%)	0.71	0.49–1.02	0.06
Prolonged ventilation > 24 h (%)	0.59	0.32–1.07	0.86
Respiratory failure (%)	0.23	0.05–1.07	0.06
Pleural effusions/pneumothorax (%)	0.45	0.21–0.96	**0.04**
Sinus rhythm (%)	0.59	0.28–1.24	0.17
Atrial fibrillation (%)	1.75	0.77–3.98	0.18
Need for pacemaker (%)	1.68	0.35–8.14	0.51
MACCE (%)	0.66	0.42–1.04	**0.07**
MNCAE (%)	0.57	0.35–0.91	**0.02**

MACE: major adverse cardiac events, MNACE: major noncardiac adverse events.

3.3. Intra-operative data and completeness of revascularization (Table 5)

The need for intra-operative implantation of an IABP was similar in both groups (3.5% vs 6.1%; $p = 0.80$) and conversion to CPB became necessary in 5.6% of all OPCAB patients. If converted, the operation was continued in a beating-heart fashion.

OPCAB patients presented with a lower mean number of the diseased coronary vessels (2.75 ± 0.47 vs 2.95 ± 0.25; $p = 0.001$) and also received a lower number of total distal grafts (3.37 ± 0.99 vs 3.83 ± 0.95; $p < 0.001$). In detail, the number of arterial grafts was significantly higher among these patients (1.54 ± 0.88 vs 1.33 ± 0.81; $p = 0.006$) following the more frequent use of the right internal mammary artery (RIMA) (35.6% vs 22.9%; $p < 0.001$) and the radial artery (13.5% vs 5.5%; $p = 0.001$). Furthermore, in OPCAB patients, significantly less proximal anastomoses (1.11 ± 0.59 vs 1.51 ± 0.63; $p < 0.001$) were performed and in 9.3% of these patients revascularization was done without necessity of any proximal anastomosis (9.4% vs 6.7%; $p = 0.013$). By contrast, OPCAB patients received less saphenous vein grafts (SVGs) when compared to the on-CABG group (78.7% vs 90.7%; $p < 0.001$).

The ICOR appeared to be significantly higher among CABG patients (1.24 ± 0.34 vs 1.30 ± 0.28; $p = 0.001$). However, for similar proportions in both the groups (94.3% vs 93.7%; $p = 0.24$), a CRI > 1 was achieved clearly indicating CR.

4. Discussion

OPCAB is a safe and feasible option for diabetic patients with MVD. The data presented here show a significant benefit with regard to mortality, MNCAEs, and the time to extubation

Table 5. Intra-operative data.

Parameter	OPCAB ($n = 540$)	CABG ($n = 475$)	*p*-Value
CPB conversion (%)	5.6	–	–
CPB time (min)	–	109 ± 40	–
Aortic X-clamp time (min)	–	53 ± 28	–
Arterial grafts per patient	1.54 ± 0.88	1.33 ± 0.81	**0.006**
LIMA (%)	94.6	92.8	0.68
RIMA (%)	35.6	22.9	**<0.001**
Radial artery (%)	13.5	5.5	**0.001**
SVG per patient	1.83 ± 1.24	2.50 ± 1.15	**<0.001**
Use of SVG (%)	78.7	90.7	**<0.001**
Total number of proximal anastomoses	1.11 ± 0.59	1.51 ± 0.63	**<0.001**
No proximal anastomosis/T-Graft (%)	9.4	6.7	**0.013**
Total number of grafts per patient	3.37 ± 0.99	3.83 ± 0.85	**<0.001**
Number of diseased vessels	2.75 ± 0.47	2.95 ± 0.25	**0.001**
Completeness of revascularization (%)	94.3	93.7	0.24
Index of complete revascularization (ICOR)	1.24 ± 0.34	1.30 ± 0.28	**0.001**
IABP intra-operative (%)	3.5	6.1	0.80

CPB: cardio-pulmonary bypass, LIMA: left internal mammary artery, RIMA: right internal mammary artery, SVG: saphenous vein graft, IABP: intra-aortic balloon pump.

for these patients. There was a clear trend to less MACCE and major complications such as stroke, rethoracotomy for bleeding, and postoperative IABP implantation, confirming the overall beneficial effect of OPCAB in this subset of patients.

Although various reports have suggested OPCAB to be superior for high-risk patients [11,16], only a few reports comparing OPCAB versus CABG in diabetic patients with MVD are available [12,13]. Magee et al. compared 2891 patients with diabetes, who underwent either OPCAB (n = 346) or classical on-pump surgery (n = 2545). Even though the authors did not find a survival advantage, they found OPCAB to be associated with a significantly decreased incidence of postoperative complications including prolonged ventilation and renal failure requiring dialysis [12]. Srinivasan et al. also recently analyzed 951 consecutive diabetic patients who underwent isolated CABG. Of these patients, 186 (19.6%) had off-pump coronary procedures. After risk adjusting with propensity scoring, off-pump patients had a significantly lower incidence of stroke and renal failure, whereas no in-hospital survival difference could be demonstrated [13]. Taken together, these reports indicate a benefit for diabetic patients with regard to postoperative morbidity, which is generally in line with our findings. In the context of the previous results, it is to mention that the study of Magee et al. involved 22 surgeons of various institutions with different selection criteria and a PS adjustment was not performed. The report of Srinivasan, although similar in size, showed a certain imbalance of patient group distribution.

CPB has been demonstrated to be an independent risk factor for neurological events [7]. Various studies have proven embolic showers during cannulation, clamping or declamping maneuvers and especially with the release of the aortic cross-clamp [17]. Therefore, recent data proposed the protective effect of OPCAB despite requiring side bite clamping of the aorta for performing proximal anastomosis [18]. Thus, we avoided further reducing the risk of neurological events to 0.7% in the OPCAB patients by applying no-touch technique using the Heartstring (Guidant, Indianapolis, USA) device. The occurrence of stroke can be minimized with this technique; it is particularly helpful in patients presenting with a rapidly progressive CAD or advanced atherosclerosis [7] and yields similar results as with all arterial grafting using no-touch technique.

When comparing these results to studies in which patients underwent total arterial grafting strategies, that is, using bilateral internal thoracic arteries and T-grafts [19], our data demonstrate that our applied no-touch technique could minimize neurological complications to the level of the current gold standard, that is, the 'total arterial grafting technique'.

This is an important message, particularly when taking various randomized trials into account comparing the outcomes of PCI and CABG in diabetic patients with MVD. Recent studies [5,20,21] including the SYNTAX trial [5] and the ARTS-II tria [20] reported a higher incidence of stroke in the CABG group and created a major concern for surgical revascularization. The low stroke rate associated with a standardized OPCAB no-touch strategy can potentially minimize this problem. This finding is supported by a recent trial of Briguori et al. who did not detect a higher incidence for stroke when comparing outcomes after drug-eluting stent (DES) implantation versus OPCAB in patients with type 2 DM and MVD [4].

However, even with a technique in a standardized fashion, the risk of intra-operative stroke cannot be completely eliminated. This also applies to all arterial grafting [19] as well as interventional approaches [4–6,20] and is most probably linked to the underlying risk profile defined by the general health condition of a patient [22].

The standardized OPCAB approach comes not at the cost of less CR. This is an important finding, since CR has been reported to be a crucial predictor for the long-term outcome [9,10] and is one of the main arguments commonly used against OPCAB [23,24]. In this study, CR was achieved in similar levels for both the groups what is in line with the recent data of Puskas et al. who demonstrated feasibility of complete revascularization in OPCAB [10].

5. Limitations

Due to its retrospective nature and nonrandomized design, all established disadvantages apply. PSs are valuable and helpful tools, but the allocation of a patient to either off- or on-pump surgery is based on criteria that may be buried at the time of the decision and then impossible to be retrospectively recovered. Therefore, even after careful application of PSs, distinguishing between surgeon and treatment differences remains difficult. Although balancing scores constitute the most rigorous methods available for apples-to-apples investigation of causal effects on outcome in the retrospective, nonrandomized setting, they are not equal to randomized clinical trials and they cannot account for unknown variables affecting outcome that are not correlated strongly with measured variables [25]. In addition, our results lack the force of numbers and certainly a higher level of significance may have been achieved, had we had a larger patient cohort to analyze. Although the EuroScore and the total number of diseased vessels were included in the propensity adjustment, a certain bias may apply, since OPCAB patients had a significantly lower EuroScore and had less MVD. Finally, the study period was quite long with most CABG patients being from the early part of the study, whereas the major part of OPCAB patients was from the later part of the study period.

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Appendix A. Conference discussion

Mr G. Cooper (*Sheffield, United Kingdom*): I'd just like to ask you a little bit about the methodology, because, as you rightly pointed out in your last slide, in a cohort study such as this, a difference in outcome can be due to selection bias rather than to the treatment modality. And I wonder if you could just expand a bit on your method of selecting patients for off- or on-pump surgery.

Dr Emmert: Of course, this was basically explained by the time we performed this surgery. We introduced OPCAB in Zurich about 8 years ago, and it was fully established in 2004. By then certainly, the numbers of OPCAB increased and the numbers of on-pump decreased. Now we are performing and we are planning (and this is very important) almost every patient in the OPCAB fashion. So this was actually the methodology.

Mr Cooper: So if my understanding is correct, most of the on-pump surgery was done before 2004 and the off-pump surgery was done from 2004 onwards?

Dr Emmert: Not at all. Because, as I mentioned, we introduced it in 2004 and then we increased year by year, of course.

Dr Cooper: But the selection is then by time?

Dr Emmert: By time, yes.

Dr Cooper: In the UK, between 2001 and 2008, we saw a 25% reduction in mortality for coronary bypass surgery over that period. Do you think your results could be explained by a similar trend in mortality reduction in Switzerland?

Dr Emmert: Actually, that's a good question, and you see that I'm still very young, but I try to comment. What I found when I queried our database was that the off-pump cases increased by time. In this study, I'm just presenting 1000 patients; however, I evaluated over 6000 patients and indeed detected similar trends to less mortality as you just mentioned.

Dr D. Taggart (*Oxford, United Kingdom*): If you look at your two groups of patients, you see that there was a far higher use of bilateral IMAs in the off-pump group. Now you could argue that people doing off-pump surgery may be technically better? Certainly the use of internal mammary arteries again requires a different degree of technical expertise. So do you not think that, perhaps, the real difference in mortality that you saw in these patients was that you had two groups of surgeons with different operating skills?

Dr Emmert: That's correct. I agree with you because, of course, we all know the better outcome when performing total arterial grafting. On the other hand, here in Zurich all surgeons perform OPCAB and are experienced with this technique. However, this is a retrospective study with all the disadvantages that apply and I don't want to claim anything. Zurich is a very experienced OPCAB center now, we can just show our data and try to give an idea to all the surgeons attending this Congress about the clinical routine. So you're certainly right that there may be a selection bias, and the best trial would be, as shown by the ROOBY trial, a prospective trial, but otherwise I also think we can provide a high number of patients in our experience and this might be of help for the audience.

Dr J. Ennker (*Lahr, Germany*): Our experience in OPCAB dates back to September 1997, and my question to you is: Why are you using the Heartstring procedure so often? Because it has been proven and shown in the literature that you can put a vein graft into the LIMA and you can do Y grafting, so there is only very rarely an indication to place a proximal anastomosis. I can't see your point for that.

Dr Emmert: That's a good question. As I mentioned, for technical aspects I would refer this question to one of my coauthors in the audience to comment.

Dr Salzberg: In regard to the usage of Heartstring versus composite graft, we tend to do composite grafts in arterials, so we're using two mammaries, but no veno-arterial composite grafts. And therefore, vein grafts or radials are implanted into the aorta with the Heartstring.

We actually saw in a subgroup analysis that we decrease the stroke rate to 0.9% for all-comers with a proximal anastomosis. I think it's 1.9% compared to partial clamping and over 3% for on-pump. So there is a significant decrease there. And we're going to publish 1500 proximal anastomoses.

Dr Ennker: That's very fine, but it's unnecessary. It has been shown by Calafiore in thousands of cases and in my own experience since 1997. But this is your way.

Dr S. Attaran (*Liverpool, United Kingdom*): I have two questions for you.

Firstly, what patient characteristics did you use to match the groups? Clearly, they are very different. But did you go for EuroSCORE or any other preoperative modality?

And my second question is that with your findings, has it actually changed your practice, or are you planning to do your diabetic patients all off-pump from now on?

Dr Emmert: First, of course, I took advice from a specialist in statistics and in this study we introduced 52 variables for the preoperative adjustment, as for example, cardiovascular risk profiles, emergent or urgent or elective cases, prior myocardial infarction, the number of diseased vessels and others. So we tried to do our best to eliminate the disadvantages of a retrospective design we clearly know about.

Your second question is a very good question. When I joined this clinic in 2008, the OPCAB strategy was fully in place. However, there might be one aspect to be addressed. Some surgeons still perform partial clamping for the proximal anastomosis. And in presenting my results, I have tried to highlight that whenever the aorta is clamped, whether partial or even cross-clamped, there is no difference in reduction for stroke. And that's why I think when a proximal anastomosis is needed, the Heartstring device might be helpful.