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Off-Pump Surgery Is Not a Contraindication for Patients with a Severely Decreased Ejection Fraction

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ABSTRACT

Background: A severely impaired left ventricular ejection fraction (EF) (30%) increases the risk of surgical myocardial revascularization. We evaluated the safety and feasibility of off-pump coronary artery bypass (OPCAB) surgery in patients with a severely decreased EF.

Methods: We compared 79 patients with an EF ≤30% (group A) with 863 patients with an EF >30% (group B) who underwent myocardial revascularization between 2003 and 2008. The relationship between EF and outcome after OPCAB was assessed by univariate and logistic regression analyses. A composite end point was constructed from 30-day mortality, renal failure, length of stay in the intensive care unit (ICU) >2 days, neurologic complications, and use of an intra-aortic balloon pump (IABP). Additionally, the completeness of revascularization was assessed.

Results: The mortality rates for groups A and B were comparable (1.3% and 2.0%, respectively; $P = .55$), and the 2 groups did not differ with regard to serious postoperative complications, such as stroke (2.5% versus 1.4% for groups A and B, respectively; $P = .42$), peripheral neurologic complications (2.5% versus 0.7%, $P = .14$), renal failure (0% versus 1.1%, $P = 1.00$), use of an IABP (1.3% versus 0.8%, $P = .50$), ICU length of stay >2 days (17.7% versus 19.6%, $P = .77$). Similarly, groups A and B did not differ with regard to ventilation time (11.2 ± 12.7 hours versus 12.4 ± 15.5 hours, $P = .82$), indicating similar postoperative courses for the 2 groups of patients. In contrast, the composite end point occurred significantly more frequently in group A (43.0% versus 29.7%, $P = .02$), a result driven by the increased rate of rethoracotomy for bleeding in that group (11.4% versus 2.9%, $P = .001$). The 2 groups were similar with respect to the total number of grafts used per patient (3.82 ± 0.89 versus 3.63 ± 1.01, $P = .10$) and the completeness of revascularization (94% versus 93%, $P = .49$).

Conclusion: A standardized OPCAB approach is safe for patients with a severely decreased EF, and its use does not come at the cost of less complete revascularization.

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INTRODUCTION

Although it remains a challenge, surgical myocardial revascularization for coronary artery disease is the treatment of choice for patients with a severely decreased left ventricular ejection fraction (EF) [Eagle 2004]. Current data indicate an increased perioperative mortality rate and high morbidity among these high-risk patients [O'Connor 1992]. This feature is also implemented in the EuroSCORE (http://www.euroscore.org). In this risk-stratification system, a severely decreased EF is an independent risk factor for a worse outcome after cardiac surgery.

Conventional coronary artery bypass grafting (CABG) is performed with cardiopulmonary bypass (CPB), which itself is associated with serious complications, such as stroke [Taylor 1998], renal dysfunction [Weerasinghe 2005], low cardiac output, postoperative bleeding, and systemic inflammatory response syndrome [Wan 2004]. The worse clinical outcome in these high-risk patients with a low EF may be partially related to the use of CPB, as well as to the effects of the use of cardioplegic solutions on the myocardium.

Various reports have suggested that off-pump coronary artery bypass (OPCAB) has a comparable risk-adjusted mortality rate [Cleveland 2001; Puskas 2003; Hannan 2007; Puskas 2008] and fewer associated major complications [Cleveland 2001; Plomondon 2001; Magee 2003; Puskas 2003; Hannan 2007; Puskas 2008] compared with conventional CABG. On the other hand, the report of a recent prospective trial [Shroyer 2009] proposed that conventional on-pump CABG is superior with respect to long-term outcome and graft patency. For this reason, OPCAB remains controversial and highly debated. Only a few reports are available [Moshkovitz 1997; Arom 2000; Chamberlain 2002; Shennib 2002], however, especially for high-risk patients with an impaired EF, and surgeons thus far have been cautious about subjecting these high-risk patients to these techniques. In this study, we evaluated the safety and feasibility of standardized OPCAB surgery for patients with a severely decreased EF (≤30%).

MATERIALS AND METHODS

From 2004 to 2009, 942 patients underwent isolated OPCAB for symptomatic multivessel disease at our institution. The

procedures were performed by 6 different surgeons. We prospectively collected the data and compared the results for patients with an EF ≤30% (group A, n = 79; 8.4%) with those for patients with an EF >30% (group B, n = 863; 91.6%). EF was documented by transthoracic echocardiography as well as by ventriculography during a coronary angiography evaluation before surgery and was confirmed intraoperatively via transesophageal echocardiography. Most of the patients were male (78.6%, n = 740; 21.4% female patients, n = 202) and the mean (±SD) age at the time of surgery was 65.5 ± 9.8 years. The indication for surgery was elective (69.6%, n = 656), urgent (19.4%, n = 183), or emergent (11.0%, n = 104). Tables 1, 2, and 3 summarize the demographic and preoperative data.

Surgical Technique

The OPCAB technique is performed in 95% of all coronary cases and is 100% standardized at our institution. In brief, complete arterial revascularization was planned for patients <65 years of age. Heparin (250 IU/kg body weight) administration was initiated to obtain an activated clotting time of >350 seconds, and it was reversed with protamine after the procedure. Temporary pacemaker wires were placed, and rolled-up surgical swabs were used for cardiac positioning. An Octopus 4 tissue stabilizer (Medtronic, Minneapolis, MN, USA) was used to properly expose the target vessel, and a blower/mister (Guidant Corporation, Indianapolis, IN, USA) was used to clear the operating field. A shunt (ClearView Intracoronary Shunt; Medtronic) was inserted whenever possible to maintain the blood supply during distal anastomoses. Proximal anastomoses were performed in a clampless fashion by using the HEARTSTRING device (HEARTSTRING Proximal Seal System; Guidant Corporation). Flow was measured with MediStim QuickFit ultrasound probes (MediStim, Oslo, Norway) in all cases.

Strategy for Revascularization

Surgical revascularization was standardly started by grafting the left anterior descending coronary artery to the left internal mammary artery. That was followed by grafting the right coronary system and finally the circumflex territory.

Hemodynamic Management

Measurement via a pulmonary artery catheter was used to assess hemodynamics, and optimization was attempted by efficient volume management, Trendelenburg positioning, atrial pacing, and inotrope administration. If these approaches were

Table 1. Preoperative Demographic Characteristics*

Parameter	Group A (EF ≤30%; n = 79)	Group B (EF >30%; n = 863)	P†
Age, y	65 ± 10	66 ± 10	.39
Male sex, n (%)	61 (77)	700 (81)	.40
Female sex, n (%)	18 (23)	163 (19)	.59
EuroSCORE	5.6 ± 3.0	5.1 ± 2.9	.41
EF, %	24 ± 6	59 ± 12	<.0001
BMI, kg/m^2	27 ± 4	27 ± 3	.75
History of smoking, n (%)	47 (59)	509 (59)	1.00
Diabetes, n (%)	38 (48)	190 (22)	<.0001
Hypertension, n (%)	19 (24)	211 (24)	.93
PAD, n (%)	7 (9)	103 (12)	.70
COPD, n (%)	0 (0)	26 (3)	.16
Positive family history, n (%)	31 (39)	319 (37)	.72
Myocardial infarction (<90 d), n (%)	29 (37)	337 (39)	.72
IABP preoperatively, n (%)	6 (8)	78 (9)	.84
Left main disease, n (%)	31 (39)	294 (34)	.39
Elective surgery, n (%)	58 (73)	596 (69)	.51
Urgent surgery, n (%)	16 (20)	190 (22)	.76
Emergent surgery, n (%)	5 (7)	77 (9)	.52
Redo surgery, n (%)	2 (3)	9 (1)	.23

*Data are presented as the mean ± SD where indicated. EF indicates ejection fraction; BMI, body mass index; PAD, peripheral artery disease; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump.

†A *P* value <.05 denotes a statistically significant difference.

Table 2. Preoperative Medications*

Parameter	Group A (EF ≤30%; n = 79)	Group B (EF >30%; n = 863)	P†
Heparin, n (%)	28 (35)	173 (20)	.002
Aggrastat, n (%)	14 (18)	155 (18)	1.00
Plavix, n (%)	6 (8)	69 (8)	1.00
Aspirin, n (%)	67 (85)	786 (91)	.06
ACE inhibitors, n (%)	19 (24)	130 (15)	.036
Beta-blocker, n (%)	31 (39)	250 (29)	.07

*EF indicates ejection fraction; ACE, angiotensin-converting enzyme.

†A *P* value <.05 denotes a statistically significant difference.

Table 3. Intraoperative Data*

Parameter	Group A (EF ≤30%; n = 79)	Group B (EF >30%; n = 863)	P†
No. of grafts per patient	3.82 ± 0.89	3.63 ± 1.01	.10
No. of diseased vessels	2.86 ± 0.35	2.76 ± 0.50	.03
Complete revascularization, n (%)	74 (94)	803 (93)	.49
CRI	1.36 ± 0.38	1.40 ± 0.66	.35
EC (300 mL/unit), units	2.6 ± 3.8	2.0 ± 3.5	.20
FFP (300 mL/unit), units	1.6 ± 2.9	1.1 ± 2.6	.11
TC (300 mL/unit), units	0.18 ± 0.48	0.21 ± 0.79	.70

*Data are presented as the mean ± SD unless otherwise indicated. EF indicates ejection fraction; CRI, completeness-of-revascularization index; EC, erythrocyte concentrates; FFP, fresh frozen plasma; TC, thrombocyte concentrates.

†A *P* value <.05 denotes a statistically significant difference.

insufficient, insertion of an intra-aortic balloon pump (IABP) was initiated intraoperatively (n = 8, 0.8%). If none of these approaches were successful, the patient was converted to CPB via classic central arterial/venous cannulation (n = 56, 5.9%). Prior to nonemergent conversion to CPB, transesophageal echocardiography and pulmonary artery catheter measurements were made to evaluate the degree of hemodynamic compromise. Emergent conversion to CPB was avoided, and a beating heart procedure was attempted whenever possible. Cardioplegic arrest was performed only in difficult cases (n = 15, 1.6%).

Statistical Analysis

Continuous data are presented as the mean ± SD and were evaluated statistically with the Mann-Whitney test. Categorical data are presented as a number (percent) and were compared with the chi-square test or the Fisher exact test, as appropriate. The completeness of revascularization was assessed for each patient and was defined as the total number of distal grafts divided by the number of the affected coronary vessels revealed in the preoperative coronary angiogram. A composite end point was constructed from 30-day mortality, postoperative renal failure, intensive care unit (ICU) length of stay >2 days, neurologic complications, and use of an IABP. Logistic regression was performed to analyze whether EF (≤30%) is an independent predictor of the composite end point. All analyses were performed with SPSS software (version 13; SPSS, Chicago, IL, USA). A 2-sided *P* value <.05 was considered statistically significant.

RESULTS

The patients in group A (EF ≤30%) and the patients in group B (EF >30%) were comparable in age, sex, laboratory parameters, and comorbidities, such as peripheral artery disease and chronic obstructive pulmonary disease. The mean EuroSCORE was 5.6 ± 3.0 for group A and 5.1 ± 2.9 for group B (*P* = .41). With regard to cardiovascular risk factors, it became apparent that the patients in group A had a significantly greater incidence of diabetes mellitus (48.1% versus 22.4%; *P* < .0001), whereas the groups were comparable with respect to all other cardiovascular risk factors. Recent myocardial infarction within the previous 90 days (36.7% versus 39.3% for groups A and B, respectively; *P* = .72) and preoperative implantation of an IABP (7.6% versus 9.4%, *P* = .84) were similarly frequent in the 2 groups. As expected, the patients in group A received more heart failure medication, such as angiotensin-converting enzyme inhibitors (24.1% versus 14.8%, *P* = .036) and beta-blockers (39.2% versus 29.1%, *P* = .07), and significantly more patients in

Table 4. Composite End Point and Postoperative Data*

Parameter	Group A (≤EF 30%; n = 79)	Group B (EF >30%; n = 863)	*P*†
Composite end point, n (%)	34 (43.0)	256 (29.7)	.02
Mortality, n (%)	1 (1.3)	17 (2.0)	.55
IABP intraoperatively, n (%)	1 (1.3)	7 (0.8)	.50
Neurologic events (central), n (%)	2 (2.5)	12 (1.4)	.33
Neurologic events (peripheral), n (%)	2 (2.5)	6 (0.7)	.14
Rethoracotomy, n (%)	9 (11.4)	25 (2.9)	.001
Renal failure, n (%)	0 (0.0)	9 (1.1)	1.00
LOS in ICU >2 d, n (%)	14 (17.7)	169 (19.6)	.77
Ventilation time, h	11.2 ± 12.7	12.4 ± 15.5	.82
LOS in ICU, d	2.0 ± 2.1	2.2 ± 3.7	.57
LOS in hospital, d	10.8 ± 5.4	10.0 ± 5.2	.12
Hb (day 1; 11.7-15.3 g/dL), g/dL‡	9.6 ± 1.5	10.0 ± 1.4	.06
Hk (day 1; 35%-46%), %‡	28.5 ± 4.5	29.2 ± 4.0	.18
Lc (day 1; 3.0-9.6 $\times 10^3/\mu L$), $10^3/\mu L$‡	10.1 ± 3.8	9.9 ± 4.7	.55
Tc (day 1; 143-400 $\times 10^3/\mu L$), $10^3/\mu L$‡	153 ± 107	168 ± 90	.23
CK (day 1; <167 U/L), U/L‡	427 ± 419	448 ± 493	.79
CK-MB (day 1; <24 U/L), U/L‡	28 ± 43	31 ± 41	.72
Trop T (day 1; <0.014 μg/L), μg/L‡	4.5 ± 11.3	5.5 ± 19.0	.35
Creatinine (day 1; 44-80 μmol/L), μmol/L‡	82 ± 21	89 ± 46	.19

*Data are presented as the mean ± SD where indicated. EF indicates ejection fraction; IABP, intra-aortic balloon pump; LOS, length of stay; ICU, intensive care unit; Hb, hemoglobin; Hk, hematocrit; Lc, leukocytes; Tc, thrombocytes; CK, creatine kinase; CK-MB, CK isoenzyme MB; Trop T, troponin T.

†A *P* value <.05 denotes a statistically significant difference.

‡Reference interval is indicated in parentheses.

group A were on heparin before their operations (35% versus 20%, $P = .002$; Tables 1 and 2).

Group A had significantly higher numbers of diseased vessels per patient (2.86 ± 0.35 versus 2.76 ± 0.50, $P = .03$), whereas the 2 groups were similar with respect to the total number of grafts per patient (3.82 ± 0.89 versus 3.63 ± 1.01, $P = .10$). Complete revascularization was achieved in 94% of the patients in group A and in 93% of the patients in group B (P = .49, Table 3).

Groups A and B had comparable mortality rates (1.3% versus 2.0%, respectively; $P = .55$). Except for an increased rate of rethoracotomy for bleeding in group A (11.4% versus 2.9%, $P = .001$), the 2 groups did not differ significantly with regard to serious complications, such as stroke (2.5% versus 1.4%, $P = .42$; total stroke rate for entire series, 1.5%; n = 14), peripheral neurologic complications (2.5% versus 0.7%, $P = .14$), renal failure (0% versus 1.1%, $P = 1.00$), perioperative IABP use (1.3% versus 0.8%, $P = .50$), length of stay in the ICU >2 days (17.7% versus 19.6%, $P = .77$), and length of hospital stay (10.8 ± 5.4 days versus 10.0 ± 5.2 days, $P = .12$). Furthermore, the 2 groups did not differ with regard to ventilation times in the ICU (11.2 ± 12.7 hours versus 12.4 ± 15.5 hours; $P = .82$), indicating similar postoperative courses for the 2 groups of patients.

A decrease in platelets in group A became apparent on the first postoperative day (153 ± 107 × 10^3/μL versus 168 ± 90 10^3/μL; $P = .28$), and the patients in group A required more units of erythrocyte concentrates (2.6 ± 3.8 units versus 2.0 ± 3.5 units, $P = .20$) and fresh frozen plasma (1.6 ± 2.9 units versus 1.1 ± 2.6 units, $P = .11$) (Tables 3 and 4).

The increased rethoracotomy rate among the patients in group A was responsible for the significant increase in the occurrence of the composite end point in these patients (43.0% versus 29.7%, $P = .02$) (odds ratio, 1.79; 95% confidence interval, 1.21-2.87; $P = .015$). When we excluded the factor of rethoracotomy for bleeding from the composite analysis, the difference in the composite end point failed to achieve statistical significance (Table 4).

DISCUSSION

In our experience, a standardized OPCAB approach is safe and feasible for high-risk patients with a severely decreased EF, as is reflected by the comparable rates of mortality and major complications, such as stroke, renal failure, need for an IABP, and extended stay in the ICU. In addition, the 2 groups did not differ with regard to ventilation time, indicating similarly straightforward postoperative courses for the 2 groups.

On the other hand, patients with a low EF appeared to have a higher frequency of the composite end point, which was mainly driven by the increased rate of rethoracotomy for bleeding in group A. We believe that a major reason for this higher rate of bleeding complications may be related more to the significantly increased preoperative use of heparin in patients with a low EF (35% versus 20%, $P = .002$) than to the risk factor of a low EF itself. When we excluded bleeding complications from the composite end point, the 2 groups showed no detectable differences with regard to any other major complications, and the difference in the composite end point failed to achieve statistical significance. Furthermore, the 30-day mortality rate was not affected or compromised.

With regard to the general safety and feasibility of OPCAB in high-risk patients, our data are supported by Stamou and associates [2005], who recently reviewed 513 high-risk patients. They found OPCAB to have a lower mortality rate and comparable event-free survival. Furthermore, they suggested that OPCAB could even be the better operative strategy in this subset of patients [Stamou 2005]. Similarly, Al-Ruzzeh et al [2003] found that OPCAB patients had significantly fewer major postoperative complications and lower mortality. In addition, Puskas and colleagues compared 14,766 patients and found OPCAB in high-risk patients to be associated with a lower operative mortality rate and a disproportionately higher benefit [Puskas 2009].

We and others [Al-Ruzzeh 2003; Stamou 2005; Puskas 2009; Thomas 2009; Emmert 2010] believe that the worse outcomes among patients who undergo the classic on-pump approach may be related to the damaging effects of CPB on the myocardium. These effects include the activation of various inflammatory mediators that significantly hinder the functionality of the already compromised myocardium, especially after prolonged CPB times [Moshkovitz 1997].

The OPCAB technique seems to be safe and feasible for patients with a low EF, and although a recent prospective randomized trial identified OPCAB to have no advantage for low-risk patients [Shroyer 2009], it appears to be the superior method of revascularization for high-risk patients [Al-Ruzzeh 2003; Stamou 2005; Puskas 2009]. With regard to the size of the series, the sizes of the cohorts in the studies of Stamou et al [2005] and Al-Ruzzeh et al [2003] are comparable to the size of our study. On the other hand, these authors focused on the comparison of on-pump and off-pump surgeries, whereas our study analyzed the outcomes of high-risk patients within an off-pump cohort. Furthermore, these studies did not focus specifically on the outcomes of patients with a low EF, but rather on patients with a general high-risk profile, including such factors as renal failure, recent myocardial infarction, cerebrovascular disease, and advanced age.

More similarly to our study, Arom and colleagues focused in their recent report on patients with EFs of ≤30%. The authors suggested that multivessel bypass grafting via the OPCAB approach in patients with a depressed left ventricular function is appropriate and applicable, but at a cost of less complete revascularization [Arom 2000]. These data were confirmed by Shennib and colleagues, who found OPCAB to be effectively applicable in high-risk patients with an impaired EF, but they also found it to be associated with fewer distal grafts per patient [Shennib 2002]. These findings are in line with our overall findings and support our thesis that OPCAB is safe and reasonable for high-risk patients with a decreased EF.

Our data demonstrate that a standardized OPCAB approach in these patients does not come at a cost to the completeness of revascularization. This finding is important, because this aspect has been reported to be a crucial predictor of long-term outcome [Puskas 2003; Lattouf 2008], but it has also been described as a general problem associated with

the OPCAB approach [Yeatman 2001; Chamberlain 2002; Thomas 2009]. Our results highlight that the total numbers of grafts per patient were similar and that complete revascularization was achieved in both groups. This finding is in line with the results of Puskas et al [2003], who recently demonstrated the feasibility of complete revascularization with OPCAB. Our data indicate that complete revascularization is possible even in high-risk patients with a severely impaired EF. We believe that this important finding might be explained by our standardized OPCAB approach, as well as by our clear strategy for revascularization.

In summary, our data confirm that a standardized OPCAB approach is safely applicable to high-risk patients with a severely decreased EF and produces reasonable clinical outcomes. Furthermore, OPCAB is not associated with less complete revascularization, and such considerations therefore should no longer deter a surgeon from performing this technique in this subset of patients.

Limitations

There are several limitations in this study. First, because of its retrospective nature and nonrandomized design, all established disadvantages of this design apply. Second, our results lack the force of numbers, and a higher level of significance certainly might have been achieved had we had a larger patient cohort to analyze. Finally, we did not perform follow-ups for our patients. That might have increased the significance of our data. Nevertheless, we have shown that OPCAB is safe and feasible for patients with a low EF, with short-term outcomes comparable to conventional CABG. That was one of the major aims of this study, and we believe that these results might be very useful for surgeons for preoperative decision-making in the clinical routine.

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