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Clinical and Angiographic Outcome of Coronary Surgery with and without Cardiopulmonary Bypass: A Prospective Randomized Trial

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ABSTRACT

Background: Off-pump coronary artery bypass surgery has emerged as an alternative technique to traditional on-pump surgery. The aim of this randomized study was to compare perioperative morbidity and mortality and intraoperative and short-term graft patency in off-pump and on-pump coronary artery bypass grafting.

Methods: One hundred twenty patients were randomized for coronary revascularization with or without cardiopulmonary bypass. In all patients grafts and anastomoses were monitored with transit time Doppler ultrasonography and angiography. Angiography was repeated 3 months after the procedure in 115 of the patients.

Results: Angiography 3 months postoperatively revealed that internal mammary artery patency was 98% in both groups. Vein graft patency was 83% in the off-pump group and 91% in the on-pump group, a difference that was not statistically significant. One perioperative death was recorded in each group. Two strokes were recorded in the on-pump group, none in the off-pump group.

Conclusion: In this prospective, controlled study, perioperative and short-term outcome of off-pump coronary surgery equaled that of on-pump surgery.

INTRODUCTION

Off-pump coronary artery bypass surgery has emerged as an alternative technique to traditional on-pump surgery in the care of an increasing number of patients [Mack 2002]. Because cardiopulmonary bypass is avoided, adverse effects of extracorporeal circulation can be eliminated [Roach 1996]. On the other hand, surgery on a beating heart is more demanding and requires training of surgeons, anesthesiologists, and other staff. Quality and extensiveness of revascularization and number of complications are major outcome variables that must be addressed when this method is introduced. Results of several nonrandomized trials conducted with patients undergoing off-pump operations have demonstrated morbidity and mortality lower than and patency comparable with those for on-pump operations [Boyd 1999, Cleveland 2001, Plomondon 2001, Puskas 2001]. The aim of this prospective, randomized study was to compare perioperative morbidity and mortality as well as intraoperative and short-term graft patency in off-pump and on-pump coronary artery bypass grafting.

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MATERIAL AND METHODS

Study Design and Patients

Patients with stable angina pectoris and moderate or good left ventricular function eligible for coronary artery bypass surgery were included if off-pump surgery was considered possible. The study protocol was approved by the Regional Ethics Committee, and the patients provided written consent. One hundred twenty patients were included between March 1999 and March 2002. The patients were randomized in blocks of 20. This system allowed minor changes in protocol during the study without bias of randomization. All operations were performed in an operation theater with integrated angiography equipment to allow intraoperative coronary angiography [Fosse 2000]. In the first 40 cases, patients with significant lesions of the circumflex artery were excluded from the study, because the table of the angiography system (Advantix; GE Medical Systems, Milwaukee, WI, USA) could not be tilted sideways to facilitate surgery on the posterior wall. In the last 80 cases, the operation was performed on a tiltable angiography table (Koordinat OR; Siemens, Erlangen, Germany) combined with Angiostar Plus operating room angiographic equipment (Siemens), and the anatomical location of the stenosis was no longer an exclusion criterion. Exclusion criteria were ejection fraction less than 30% and/or renal failure (serum creatinine concentration >200 mmol/L). Randomization was performed after induction of anesthesia, and no changes were made regarding surgeons or other staff after randomization. The same surgical team of 4 surgeons and 4 anesthesiologists performed the surgery in both groups.

Operative Technique

Surgery was performed with the patient in balanced anesthesia with opiates and barbiturates together with inhalation anesthesia and administration of propofol at the end of the operation. This method allowed early extubation.

A standard midline sternotomy incision was used to expose the heart after harvesting of the internal mammary artery (IMA). The pericardium was opened with an inverted T-shaped incision. In the off-pump group the right pleural space was opened if necessary to minimize hemodynamic compromise. Saphenous vein grafts were used as single or sequential grafts. In the on-pump group, Spiral Gold oxygenators and tubing sets, in which the entire blood-contact surface, including the filter, was coated with Duraflo II heparin surface (Bentley/Baxter, Uden, The Netherlands), were used with a roller pump and cardiotomy suction.

The extracorporeal circuit was primed with 1800 mL Ringer's acetate. Heparin, 3 mg/kg body weight, was administered intravenously to all patients before initiation of cardiopulmonary bypass. Minimum allowed activated coagulation time (ACT) was 480 seconds.

All operations were performed in moderate general hypothermia (28°C-32°C) with topical cooling with ice slush. Cold St. Thomas cardioplegic solution was given in the aortic root.

Cardiopulmonary bypass was instituted with a single right atrial 2-stage cannula and an ascending aorta perfusion cannula. Bypass management included membrane oxygenators, arterial line filters, nonpulsatile flow of 2.4 L/min per square meter, mean arterial pressure greater than 50 mm Hg, and moderate systemic hypothermia. After the distal coronary anastomoses were performed, the proximal anastomoses were performed during rewarming and partial aortic clamping. Protamine sulfate was given at the end of the procedure until ACT reached preoperative value.

In the beating-heart operations, heparin (1 mg/kg) was administered during IMA takedown, and ACT was maintained at greater than 250 seconds. The distal anastomoses were performed with the use of snares (3-0 Gore-Tex; W. L. Gore, Newark, DE, USA), Octopus I and II stabilizers (Medtronic, Minneapolis, MN, USA), a deep pericardial retraction suture, and eventually an apical suction device (Starfish; Medtronic). Coronary shunts were not routinely used, unless large or noncollateralized coronary arteries were grafted. A CO_2 blower (CardioVations, Somerville, NJ, USA) was used to obtain a bloodless field. The distal anastomoses were performed first and the proximal anastomoses successively thereafter with the aid of a partial aortic clamp. Protamine sulfate was given at the end of the procedure to achieve ACT of 150 to 200 seconds or if there was excessive bleeding.

Intraoperative Monitoring

In all patients, cardiac function and hemodynamic performance were monitored with Swan-Ganz catheters and transesophageal echocardiography. Graft blood flow was measured with transit time Doppler flow measurement (MediStim AS, Oslo, Norway). The graft was revised if indicated.

At the end of the operation, graft angiography was performed on table. The grafts were revised if angiography revealed occluded grafts or questionable quality of the anastomosis or the graft.

Postoperative Findings and Follow-up

The following postoperative outcomes were recorded: hours on ventilator, need for reintubation, postoperative bleeding, revision for bleeding, units of red cells and plasma given, new atrial fibrillation, renal failure defined as anuria or serum creatinine greater than 200 mmol/L, intraaortic balloon pumping, aspartate aminotransferase (AST) and creatine kinase MB (CK-MB) on the first postoperative day, stroke, mediastinitis, and early mortality (<30 days).

The patients were routinely transferred to local hospitals on the second or third postoperative day if the postoperative course was uneventful. Three months postoperatively, the patients were readmitted for clinical examination and coronary and graft angiography.

Statistics

The statistical comparison was based on intention to treat, and possible crossover between groups therefore was not taken into account. Accordingly, 7 patients in the off-pump group who were converted to on-pump surgery were kept in the off-pump group. Data are presented as mean ± SD. For numerical data, *t* test and Mann-Whitney test were used. For categorical data, χ^2 or Fisher exact test was used. $P < .05$ was considered statistically significant.

RESULTS

Preoperative patient characteristics are presented in Table 1. The groups did not differ significantly with respect to major risk factors. The distribution of 1-, 2- and 3-vessel disease was the same in the two groups (Table 2). One patient had undergone previous cardiac surgery.

The number of distal anastomoses did not differ between the groups; however, sequential vein grafting was performed in 15 patients in the on-pump group, compared with 6 patients in the off-pump group ($P = .03$). Maximum flow in the IMA grafts before closure did not differ between the groups. The operation time was significantly longer in the off-pump patients compared with the on-pump patients (Table 3).

Seven procedures were converted from off-pump to on-pump surgery, in 2 cases because of angiographic findings and in 5 cases because of hemodynamic instability during surgery. Ten patients, 2 in the on-pump group and 8 in the off-pump group ($P = .095$), underwent revision procedures because of unsatisfactory intraoperative angiographic findings. All patients with significant lesions of the left anterior descending coronary artery underwent revascularization with left

Table 1. Patient Characteristics*

Variable	Off Pump (n = 60)	On Pump (n = 60)	*P*†
Age, y	64 ± 8	65 ± 8	.68
Sex, male/female	51/9	43/17	.08
Diabetes mellitus	8	12	.61
Hypertension	25	26	.85
Chronic obstructive pulmonary disease	5	10	.20
Stroke or transient ischemic attack	5	4	1.0
Creatinine concentration, mmol/L	99 ± 16	96 ± 16	.39
Body mass index	27 ± 6	27 ± 3	.90
Atrial fibrillation	4	3	.57
No. of previous myocardial infarctions			
0	31	34	.90
1	22	22	
>1	7	3	

*Values are mean ± SD or number of patients.

†χ^2 or Fisher exact test for categorical data and 2-tailed *t*-test or Mann-Whitney test for continuous numerical data.

IMA (n = 118) or right IMA (n = 1). Left IMA was anastomosed to a stenotic diagonal branch in 1 patient without LAD stenosis (Table 3).

Postoperative Characteristics

Postoperative characteristics are summarized in Table 4. One death was recorded in each group. One patient in the on-pump group experienced perioperative stroke. Multiorgan failure developed, and the patient died 3 weeks postoperatively. One patient in the off-pump group, in whom the anastomoses were revised on pump after intraoperative angiography, had an uneventful initial postoperative course but died suddenly 11 days postoperatively. Another on-pump patient experienced stroke but recovered completely.

Maximum postoperative CK-MB and AST levels did not differ significantly between the groups.

On-table angiography was performed on 57 patients in the off-pump group and 59 patients in the on-pump group. Final on-table IMA and vein graft patency did not differ between the groups (Table 5).

Table 2. Cardiac Performance*

Variable	Off Pump (n = 60)	On Pump (n = 60)	*P*†
Significant coronary lesions			
1-vessel	6	7	.55
2-vessel	21	26	
3-vessel	33	27	
Left main stenosis	6	3	.49
Left ventricular ejection fraction, %	71 ± 11	72 ± 10	.72

*Values are mean ± SD or number of patients.

†χ^2 or Fisher exact test for categorical data and 2-tailed *t* test for continuous numerical data.

Table 3. Intraoperative Characteristics*

Variable	Off Pump (n = 60)	On Pump (n = 60)	*P*†
IMA to LAD	58	60	.90
IMA to diagonal	1	0	1.0
No. of vein grafts	1.4 ± 0.7	1.5 ± 0.7	.60
No. of distal anastomoses	2.6 ± 0.9	2.8 ± 1.0	.21
No. of jump grafts	6	15	.06
Flow IMA, mL/min	30 ± 18	30 ± 15	.74
Operation time, min	192 ± 56	162 ± 45	.001
Cardiopulmonary bypass time, min		63 ± 24	
Aortic cross-clamp time, min		36 ± 18	

*Values are mean ± SD or number. IMA indicates internal mammary artery; LAD, left anterior descending artery.

†χ^2 or Fisher exact test for categorical data and 2-tailed t-test or Mann-Whitney test for continuous numerical data.

3-Month Follow-up

Of the 120 patients, 117 were examined at 3 months; 2 had died and 1 was lost to follow-up. Of the patients examined, 115 underwent both coronary and graft angiography at follow-up. The 3-month patency of the IMA grafts was 98% in both the off-pump and the on-pump groups (Table 5). The 3-month patency of the vein grafts was 83% in the off-pump group and 91% in the on-pump group. The difference was not statistically significant (Table 5).

DISCUSSION

In several nonrandomized trials investigators compared off-pump and on-pump coronary surgery, but so far results of only a few randomized trials have been published [Angelini

Table 4. Postoperative Characteristics*

Variable	Off Pump (n = 60)	On Pump (n = 60)	*P*†
Time on ventilator, h	6.1 ± 0.5	5.0 ± 0.3	.83
Reintubation	1	2	1.0
Postoperative bleeding, mL	871 ± 412	698 ± 267	.001
Reoperation for bleeding	0	1	1.0
Units of erythrocytes	1.0 ± 1.9	0.6 ± 2.1	.37
Units of plasma	1.1 ± 5.2	0.4 ± 1.3	.29
New atrial fibrillation	18	20	.70
Intraaortic balloon pumping	2	0	.50
Aspartate aminotransferase, first day	104 ± 123	78 ± 42	.72
Creatine kinase MB, first day	65 ± 61	50 ± 24	.29
Stroke	0	2	.50
Mediastinitis	0	1	1.0
Early mortality (<30 d)	1	1	1.0
Total mortality at 3 months	1	1	1.0

*Values are mean ± SD or number of patients.

†χ^2 or Fisher exact test for categorical data and 2-tailed *t* test or Mann-Whitney test for continuous numerical data.

Table 5. Angiographic Patency*

Variable	Off Pump (n = 60)	On Pump (n = 60)	P†
IMA intraoperatively	57/57	57/58	1.0
IMA at 3 months	53/54	58/59	1.0
Vein graft intraoperatively	88/91	100/102	.67
Vein graft at 3 months	71/86	95/104	.11

*Values are number of patent grafts in relation to number of examined grafts. IMA indicates internal mammary artery.

†χ^2 or Fisher exact test.

2002, Nathoe 2003, Puskas 2003]. The present study on coronary artery bypass surgery performed on- or off-pump was the first single-center study with both intraoperative and follow-up angiographic control.

Graft Patency

There was no significant difference in graft patency as demonstrated angiographically on table and 3 months after surgery. Beating-heart surgery can thus be performed with the same intermediate graft patency as on-pump surgery. However, there were more graft revisions during surgery in the off-pump group after intraoperative angiographic control (8 versus 2). This finding may indicate that off-pump surgery is technically more demanding. If intraoperative angiography had not been performed on all patients, the 3-month results could have been different. We previously demonstrated limited predictive value of intraoperative angiography for long-term patency [Hol 2002]; however, it is likely that most of the grafts revised because of angiographic findings of surgery-related failure or poor runoff would have occluded before the end of the 3-month follow-up period. Zehr and coworkers [2000] found 90.2% graft patency immediately postoperatively in off-pump patients and postulated that the low patency was partly due to reversal of heparin. In our study, the revisions after angiography were performed because of anastomotic technical failure. After revision the patency was excellent, and the groups did not differ significantly at 3-month follow-up evaluation. This finding indicated that any reduced graft patency in beating-heart surgery may be due to technical difficulties and not due to hypercoagulability. In a recent multicenter study, Nathoe and coworkers [2003] conducted 1-year angiographic follow-up of 28 patients who underwent off-pump operations and 42 patients who underwent on-pump procedures. The investigators found the same patency rates in the 2 groups (93% and 91%). These values are in accordance with our findings.

Number of Grafts

Because of limitations of the combined operation and angiography table, we were unable to perform surgery on the posterior wall in the first 20 patients in each group. Because of block randomization of the patients, the change of operation table and surgical strategy did not bias the results. Thus an average of 2.6 distal anastomoses were performed in the off-pump group versus 2.8 in the on-pump group. This figure is less than that reported by Puskas et al [2003], who performed 3.4 grafts in beating-heart patients versus 3.4 grafts in patients undergoing on-pump operations, but marginally more than that reported by Nathoe et al [2003]. In both the study by Puskas et al [2003] and our study, the number of grafts did not differ between groups, indicating that beating-heart surgery does not limit the number of grafts.

Flow in Mammary Artery Graft

D'Ancona et al [2000] previously demonstrated that transit time flow measurements may be an important indicator for graft revision. In this study we performed transit time flow measurement in all patients with similar mean IMA flow, 30 mL/minute in both groups, indicating equivalent graft quality. However, we previously demonstrated poor correlation between transit time flow measurements and graft patency as demonstrated by angiography [Hol 2001].

Neurological Outcome

Two (3.3%) of the patients in the on-pump group and none in the off-pump group had strokes. The stroke rate in the on-pump group corresponded to the findings by Roach et al [1996]. However, the number of strokes was too small to be of significance. The total stroke rate in the two groups was 1.6%. In a previously described cohort of 52 of the patients included in this study, the number of cerebral high-intensity transient signals was recorded with transcranial Doppler ultrasonography. These patients also were followed up with preoperative and postoperative psychomotoric testing for evaluation of more sensitive parameters. Transcranial Doppler evaluation revealed an average of 90.0 (range, 15-274) microemboli in the middle cerebral artery during surgery in the on-pump group and 16.3 (range, 0-131) microemboli in the off-pump group ($P < .0001$). However, the groups did not differ significantly in results of psychomotoric tests performed 3 months postoperatively [Lund 2003]. In one randomized trial [Nathoe 2003] and 2 nonrandomized trials [Hernandez 2001, Sabik 2002], investigators found no significant difference in neurological outcome between on-pump and off-pump surgery. Our findings confirmed these observations. However, the large difference in microembolization between the groups indicated increased neurological challenge during on-pump coronary surgery, but the clinical implication is uncertain.

Bleeding

Several randomized and nonrandomized studies have demonstrated reduced shed mediastinal blood loss in beating-heart surgery [Ascione 2001, van Dijk 2001, Angelini 2002]. We did not reproduce this finding in the present study. However, overall bleeding was low in both groups (871 versus 698 mL). To avoid graft thrombosis, heparinization was rarely reversed in the off-pump patients. This factor may explain the increased bleeding in the off-pump group. Another explanation may be that 7 off-pump procedures were converted to on-pump surgery, but the patients remained in the off-pump group because of the intention to treat principle. All 7 of these patients had increased shed mediastinal blood owing to extended operating time.

The number of red blood cell transfusions was low and did not differ between the groups. We did not find the reduction in blood transfusion in off-pump surgery demonstrated by Angelini et al. However, the overall transfusion requirement was much lower in our study than was demonstrated by Angelini et al (21% of the patients in the off-pump group and only 16% in the on-pump group needed red blood cell transfusion). One patient in the on-pump group underwent surgery for tamponade after 4 days; this patient also developed mediastinitis. No revisions for bleeding or mediastinal infection were recorded in the off-pump group.

Operation Time

Average operation time was influenced by several ongoing perioperative studies performed on the patients. We found a significantly higher average operation time in the off-pump group (192 minutes versus 162 minutes). This figure included time for possible anastomosis revision and conversion to on-pump surgery if necessary.

Atrial Fibrillation

Angelini et al [2002] demonstrated reduction in atrial fibrillation in off-pump surgery. In the present study, 30% of the patients in both groups had postoperative atrial fibrillation. Avoiding cardiopulmonary bypass did not reduce atrial fibrillation rate.

Myocardial Infarction

The definition of myocardial infarction varies, thus information on perioperative myocardial infarction may be difficult to interpret. In a randomized trial comparing on- and off-pump surgery, Nathoe and coworkers [2003] did not find any difference in myocardial infarction rate between patients undergoing on-pump and those undergoing off-pump operations. In this study, we compared levels of the enzymes specific for myocardial injury. The 2 groups did not differ with respect to average first day CK-MB or ASAT, confirmation of the findings of Nahoe and coworkers.

CONCLUSION

In this prospective, randomized study, perioperative and short-term outcome in off-pump coronary surgery equaled that of on-pump surgery.

REFERENCES

Angelini GD, Taylor FC, Reeves BC, et al. 2002. Early and midterm outcome after off-pump and on-pump surgery in beating heart against cardioplegic arrest studies (BHACAS 1 and 2): a pooled analysis of two randomised controlled trials. Lancet 359:1194-9.

Ascione R, Williams S, Lloyd CT, et al. 2001. Reduced postoperative blood loss and transfusion requirement after beating-heart coronary operations: a prospective randomized study. J Thorac Cardiovasc Surg 121:689-96.

Boyd WD, Desai ND, Del Rizzo DF, et al. 1999. Off-pump surgery decreases postoperative complications and resource utilization in the elderly. Ann Thorac Surg 68:1490-3.

Cleveland JC, Shroyer LW, Chen AY, et al. 2001. Off-pump coronary artery bypass grafting decreases risk-adjusted mortality and morbidity. Ann Thorac Surg 72:1282-9.

D'Ancona G, Karamanoukian HL, Ricci M, et al. 2000. Graft revision after transit time flow measurement in off pump coronary artery bypass grafting. Eur J Cardiothorac Surg 17:287-93.

Fosse E, Hol PK, Samset E, et al. 2000. Integrating image-guidance into the cardiac operating room. Minim Invasive Ther Allied Technol 9:403-9.

Hernandez F, Cohn WE, Baribeau YR, et al. 2001. In hospital outcomes of off-pump versus on-pump coronary artery bypass procedures: a multicenter experience. Ann Thorac Surg 72:1528-34.

Hol PK, Fosse E, Lundblad R, et al. 2002. The importance of intraoperative angiographic findings for predicting long term patency in coronary artery bypass operations. Ann Thorac Surg 73:813-8.

Hol PK, Fosse E, Mørk BE, et al. 2001. Graft control by transit time flow measurement and intraoperative angiography in coronary artery bypass surgery. Heart Surg Forum 4:254-8.

Lund C, Hol PK, Lundblad R, et al. 2003. A comparison of cerebral embolization during off-pump and on-pump coronary artery bypass surgery. Ann Thorac Surg 76:765-70.

Mack M, Duhaylongsod FG. 2002. Through the open door! Where has the ride taken us? J Thorac Cardiovasc Surg 124:655-9.

Nathoe HM, van Dijk D, Janssen EWL, et al. 2003. A comparison of on-pump and off-pump coronary bypass surgery in low risk patients. N Engl J Med 348:394-402.

Plomondon ME, Cleveland JC, Ludwig ST, et al. 2001. Off-pump coronary artery bypass is associated with improved risk adjusted outcomes. Ann Thorac Surg 72:114-9.

Puskas JD, Thourani VH, Marshall JJ, et al. 2001. Clinical outcomes, angiographic patency, and resource utilization in 200 consecutive off-pump coronary bypass patients. Ann Thorac Surg 71:1477-84.

Puskas JD, Williams WH, Duke PG, et al. 2003. Off-pump coronary artery bypass grafting provides complete revascularization with reduced myocardial injury, transfusion requirements and length of stay: a prospective randomized comparison of 200 unselected patients undergoing off-pump versus conventional coronary artery bypass grafting. J Thorac Cardiovasc Surg 125:797-808.

Roach GW, Kanchuger M, Mangano CM, et al. 1996. Adverse cerebral outcomes after coronary bypass surgery. N Engl J Med 335:1857-63.

Sabik JF, Gillinov AM, Blackstone EH, et al. 2002. Does off-pump coronary surgery reduce morbidity and mortality? J Thorac Cardiovasc Surg 124:698-707.

Van Dijk D, Nierich AP, Jansen EWL, et al. 2001. Early outcome after off-pump versus on-pump coronary surgery: results from a randomized study. Circulation 104:1761-6.

Zehr KJ, Handa N, Bonilla LF, et al. 2000. Pitfalls and results of immediate angiography after off-pump coronary artery bypass grafting. Heart Surg Forum 3:293-9.