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For the first time in Japan, off-pump coronary artery bypass grafting (OPCAB) was compared with the conventional on-pump technique, retrospectively examining the morbidity associated with coronary artery bypass grafting (CABG) and assessing the efficacy of OPCAB. In 2000, 158 patients underwent CABG: 95 patients (60%) had OPCAB (Group I) and 63 patients (40%) had conventional CABG (Group II). The operating time, length of intensive care unit (ICU) stay, ventilation time, postoperative bleeding, transfusion, postoperative renal function, occurrence of stroke, and early graft patency were examined in both groups. There were no hospital deaths in either group. The operating time, ICU stay, and ventilation time were significantly ($p<0.0001$, $p=0.013$, and $p<0.0001$, respectively) shorter in Group I (351 ± 85 min, 3.0 ± 1.4 days, and 5.1 ± 2.8 h) than in Group II (449 ± 112 min, 3.6 ± 1.8 days, and 13.7 ± 18.0 h). The postoperative blood loss within 12 h and the transfusion volume were significantly ($p=0.0004$ and $p<0.0001$, respectively) smaller in Group I (480 ± 210 ml and 300 ± 490 ml) than in Group II (720 ± 430 ml and $1,230\pm 1,180$ ml). Peak serum blood urea nitrogen and creatinine concentrations (excluding patients with preoperative chronic renal failure, ie a preoperative serum creatinine >1.5 mg/dl) were significantly ($p<0.0001$ and $p<0.0001$, respectively) lower in Group I (16.2 ± 15.2 mg/dl and 0.81 ± 0.72 mg/dl) than in Group II (19.2 ± 7.6 mg/dl and 0.92 ± 0.28 mg/dl). There were no perioperative strokes in Group I, but 6.4% of Group II patients suffered a stroke. There was no significant difference in graft patency between the groups (95.6% vs 94.9%). OPCAB reduced the mortality and morbidity of coronary revascularization, with a shorter operating time and more rapid recovery from surgery. (Circ J 2002; 66: 795–799)

Key Words: Coronary artery bypass grafting; Minimally invasive cardiac surgery; Off-pump CABG

Off-pump coronary artery bypass grafting (OPCAB) has become the procedure of choice in patients with operative risk factors for standard cardiopulmonary bypass (CPB); its frequency has increased gradually over the past 5 years¹ and since May 2000 it has been the standard procedure at the National Cardiovascular Center for multivessel coronary revascularization. CPB induces a systemic inflammatory response that has various adverse consequences, but to date there has not been a comparison of OPCAB and the conventional on-pump technique in Japanese patients with multivessel coronary artery disease (CAD), so we retrospectively examined the morbidity associated with coronary artery bypass grafting (CABG) and assessed the efficacy of OPCAB.

Methods

In the calendar year 2000, 158 patients underwent CABG at the National Cardiovascular Center (Osaka, Japan): 95 patients (60%) had OPCAB (Group I) and 63 patients had CABG (Group II). Preoperative patient data are summarized

in Table 1. The mean age at operation was significantly younger in Group I than in Group II (64.6 ± 8.2 years vs 66.6 ± 7.7 years, $p=0.025$). The frequency of emergency or urgent operations was higher in Group I than in Group II (11.6% vs 3.2%, $p=0.059$). There were no differences in the severity of CAD or other preoperative risk factors. We received informed consent from all patients after explaining the advantages and disadvantages of OPCAB.

Surgical Technique

Conventional CABG was performed with CPB using an ascending aortic perfusion cannula and single or bicaval drainage cannulas. Myocardial protection was achieved with antegrade and retrograde tepid blood cardioplegic arrest under aortic cross-clamping.

OPCAB was performed through a median sternotomy. The pericardium was opened, and deep pericardial retraction sutures were placed. The target vessel was exposed and stabilized with an Octopus II+ or III stabilizer (Medtronic, Minneapolis, MN, USA). Only a temporary proximal tie was placed with Retract-O-tape (Quest Medical, Inc, Allen, TX, USA). After coronary arteriotomy, the surgical field was kept free from blood by a CO₂ blower and an intracoronary shunt (Visuflo and Anastaflo, Edwards Lifesciences LLC, Irvine, CA, USA). Partial clamping of the ascending aorta was done for the proximal anastomosis in 21 patients (22.1%). In 74 patients (77.9%), OPCAB was done by the aortic non-touch technique with a combination of in-situ and composite grafting.

We compared the operating time, length of the stay in intensive care unit (ICU), ventilation time, postoperative

(Received January 30, 2002; revised manuscript received May 22, 2002; accepted May 31, 2002)

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This work was supported by Medical Frontier Strategy Research grants from the Ministry of Health, Labour and Welfare of Japan (Nos. 0225008 and 0322009).

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Table 1 Preoperative Demographics

	Group I (n=95)	Group II (n=63)	p value
Age, mean (SD) (years)	64.6 (8.2)	66.6 (7.7)	0.025
Male, %	75.8	85.7	0.13
Coronary artery disease			
LMT, %	18.9	12.7	0.30
1-vessel disease, %	3.2	1.6	0.54
2-vessel disease, %	18.9	17.5	0.81
3-vessel disease, %	59.0	68.2	0.24
Emergency operation, %	11.6	3.2	0.059
Diabetes, %	34.9	40.0	0.52
Hypertension, %	27.0	35.8	0.25
Hyperlipidemia, %	6.3	13.7	0.15
Old cerebral infarction, %	4.8	11.6	0.14
Carotid artery disease, %	3.2	4.2	0.74
COPD, %	3.2	8.4	0.18
Gastric ulcer, %	1.6	3.2	0.55
Abdominal aortic aneurysm, %	6.3	5.3	0.77
Peripheral vascular disease, %	1.6	8.4	0.07
Hepatitis %	3.2	6.3	0.38
Chronic renal failure, %	3.2	8.4	0.18
Dialysis, %	2.1	1.5	0.82
Prior CABG, %	4.8	1.1	0.15

CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; LMT, left main trunk.

Table 2 Intraoperative Demographics

	Group I (n=95)	Group II (n=63)	p value
Operating time, mean (SD) (min)	351 (85)	449 (112)	<0.0001
Blood loss, mean (SD) (ml)	1,070 (560)	1,550 (880)	<0.0001
No. of distal anastomoses, mean (SD)	3.1 (0.9)	3.8 (1.3)	0.0001
Distal anastomosis, %			
1	3.2	0	
2	18.9	14.3	
3	52.6	27.0	
4	21.1	33.3	
>5	4.2	25.4	
ST change, %	16.8	6.3	0.047
New IABP, %	1.1	3.2	0.34
Vein grafts, mean (SD)	1.04 (0.19)	1.26 (0.44)	0.016
Arterial grafts, mean (SD)	2.24 (0.67)	1.98 (0.71)	0.025
Proximal anastomosis, %	21.0	79.4	<0.0001

IABP, intra-aortic balloon pumping.

blood loss, need for transfusion, postoperative renal function, occurrence of stroke, and early graft patency in both groups. Blood samples were collected for determination of aspartate aminotransferase (GOT), lactate dehydrogenase (LDH), creatine kinase (CK), and hematology values on admission to ICU and subsequently. Perioperative myocardial infarction was defined as elevation of CK-MB concentration to more than 50 (U/L) with ST-T changes on the electrocardiogram. Postoperative coronary angiography was performed in 93.7% of the patients from 1 to 3 weeks after surgery.

Statistical Analysis

Data are presented as the mean $\pm$ standard deviation. Continuous variables were compared by the Wilcoxon rank sum test and discrete variables were analyzed with Fisher's exact test. Differences were considered statistically significant at $p < 0.05$.

Results

There were no hospital deaths in either group. The operating time was significantly shorter in Group I than in Group II (351 $\pm$ 85 min vs 449 $\pm$ 112 min, $p < 0.0001$). The intraoperative blood loss was significantly smaller in Group I than in Group II (1,070 $\pm$ 560 ml vs 1,550 $\pm$ 880 ml, $p < 0.0001$). The number of distal anastomoses was significantly fewer in Group I than in Group II (3.1 $\pm$ 0.9 vs 3.8 $\pm$ 1.3, $p < 0.0001$). Intraoperative ST elevation or depression was more frequently observed in Group I than in Group II (16.8% vs 6.3%, $p = 0.047$) (Table 2).

The postoperative outcome is summarized in Table 3. The length of ICU stay and the ventilation time were significantly ($p = 0.013$ and $p < 0.0001$, respectively) shorter in Group I (3.0 $\pm$ 1.4 days and 5.1 $\pm$ 2.8 h) than in Group II (3.6 $\pm$ 1.8 days and 13.7 $\pm$ 18.0 h). The postoperative blood loss within 12 h of admission to ICU and the transfusion volume were significantly ($p = 0.0004$ and $p < 0.0001$, respectively) smaller in Group I (480 $\pm$ 210 ml and 300 $\pm$ 490 ml) than in

Table 3 Postoperative Demographics

	Group I (n=95)	Group II (n=63)	p value
Length of ICU, mean (SD) (days)	3.0 (1.4)	3.6 (1.8)	0.013
Ventilation time, mean (SD) (h)	5.1 (2.8)	13.7 (18.0)	<0.0001
Blood loss for 12 h, mean (SD) (ml)	480 (210)	720 (430)	0.0004
Transfusion volume, mean (SD) (ml)	300 (490)	1,230 (1,180)	<0.0001
Transfusion incidence, %	35.8	74.6	<0.0001
GOT, mean (SD) (U/L)	33 (43)	42 (44)	0.21
LDH, mean (SD) (U/L)	250 (131)	338 (107)	<0.0001
CK, mean (SD) (U/L)	246 (202)	470 (490)	<0.0001
CK-MB, mean (SD) (U/L)	15 (14)	29 (42)	<0.0001
BUN, mean (SD) (mg/dl)*	13.0 (13.6)	13.2 (4.1)	0.037
max (SD) (mg/dl)*	16.2 (15.2)	19.2 (7.6)	<0.0001
Creatinine, mean (SD) (mg/dl)*	0.62 (0.75)	0.65 (0.16)	0.0005
max (SD) (mg/dl)*	0.81 (0.72)	0.92 (0.28)	<0.0001
WBC, mean (SD) ($\times 10^3/\mu\text{L}$)	9.1 (3.3)	7.6 (3.8)	0.009
Platelets, mean (SD) ($\times 10^3/\mu\text{L}$)	119 (43)	98 (55)	0.012
Low output syndrome, %	2.1	4.8	0.35
Atrial fibrillation, %	20.0	17.5	0.69
Central nervous system morbidity, %	0	6.4	0.013
Perioperative myocardial infarction**, %	0	6.4	0.013
Graft patency, %	95.6	94.9	0.62

*Except for preoperative chronic renal failure patients (serum creatinine >1.5 mg/dl); **ST change on ECG and max CK-MB >50 U/L.

Group II (720 $\pm$ 430 ml and 1,230 $\pm$ 1,180 ml). The incidence of transfusion was also significantly lower in Group I than in Group II (35.8% vs 74.6%, $p<0.0001$). None of the patients in Group I required re-exploration for bleeding.

There was no significant difference in the GOT concentration between the 2 groups. LDH, CK, and CK-MB concentrations were significantly (all $p<0.0001$) lower in Group I (250 $\pm$ 131 U/L, 246 $\pm$ 202 U/L, and 15 $\pm$ 14 U/L) than in Group II (338 $\pm$ 107 U/L, 470 $\pm$ 490 U/L, and 29 $\pm$ 42 U/L). In contrast, the white blood cell and platelet counts were significantly ($p=0.009$ and $p=0.012$, respectively) higher in Group I (9.1 $\pm$ 3.3 $\times 10^3/\mu\text{L}$ and 119 $\pm$ 43 $\times 10^3/\mu\text{L}$) than in Group II (7.6 $\pm$ 3.8 $\times 10^3/\mu\text{L}$ and 98 $\pm$ 55 $\times 10^3/\mu\text{L}$). Excluding patients with preoperative chronic renal failure (defined as a preoperative serum creatinine >1.5 mg/dl), the blood urea nitrogen was significantly ($p<0.0001$, respectively) lower in Group I (16.2 $\pm$ 15.2 mg/dl) than in Group II (19.2 $\pm$ 7.6 mg/dl). Serum creatinine on the first postoperative day and its peak value were also significantly ($p=0.0005$ and $p<0.0001$, respectively) lower in Group I (0.62 $\pm$ 0.75 and 0.81 $\pm$ 0.72 mg/dl) than in Group II (0.65 $\pm$ 0.16 and 0.92 $\pm$ 0.28 mg/dl). In patients with a preoperative serum creatinine >1.5 mg/dl, the maximum increase was 38 $\pm$ 26% in Group I and 62 $\pm$ 6% in Group II.

At the time when the patients arrived at the ICU, the cardiac index determined by the thermodilution method was similar in both groups (3.6 $\pm$ 1.0 L $\cdot$ min $^{-1}\cdot$ m $^{-2}$ in Group I and 3.4 $\pm$ 1.0 L $\cdot$ min $^{-1}\cdot$ m $^{-2}$ in Group II, $p=0.15$). There was also no significant difference in the incidence of low output syndrome between the 2 groups (2.1% in Group I and 4.8% in Group II, $p=0.35$).

Furthermore, the incidence of postoperative atrial fibrillation (AF) was not different between the 2 groups (20.0% in Group I and 17.5% in Group II, $p=0.69$). Stroke or delayed recovery of consciousness were significantly less common in Group I than in Group II (0% vs 6.4%, $p=0.013$). However, the occurrence of perioperative myocardial infarction was not different between the groups (14.7% in Group I and 11.1% in Group II, $p=0.51$). Graft

patency also showed no significant difference between the groups (95.6% in Group I and 94.9% in Group II, $p=0.62$).

Discussion

We hypothesized that OPCAB would reduce the mortality and morbidity of coronary revascularization without the expense of CABG. In the present study, OPCAB did decrease the ICU stay, operating time, ventilation time, bleeding, transfusion, renal failure, and neurological complications, but the incidence of low output syndrome, AF, and perioperative myocardial infarction did not change significantly. Similar results have been described in the elderly, the patients requiring a subsequent noncardiac operation like concomitant malignant disorders, and after repeat CABG²⁻⁵. An adverse consequence of OPCAB in previous reports has been the decreased number of distal graft anastomoses; however, Arom et al reported better early clinical results: after adjustment with the STS database model, they found that outcomes were better in the OPCAB group than in the conventional CABG group if the predicted risk was high⁶.

The shorter operating time in the OPCAB group is probably because of the shorter time required for hemostasis, which is also related to the other results such as less intraoperative and postoperative blood loss, a lower incidence of re-exploration for bleeding, a smaller transfusion volume, and a lower incidence of transfusion. CPB induces platelet dysfunction and coagulation abnormalities⁷ and also activates the complement system and promotes fibrinolysis. Previous studies of OPCAB have unanimously reported a decrease in bleeding^{6,8-10}. Blood transfusion impairs the function of the lungs and other organs, and may also cause ominous postoperative infections, such as HIV, hepatitis, and adult T cell leukemia. The shortening of the procedure time with OPCAB is also related to the smaller number of grafts, no time spent on cannulation, the incidence of cardiac arrest, and rewarming from the hypothermia during CPB.

The shorter ICU stay and ventilation time in the OPCAB group may be related to lack of the pulmonary dysfunction that occurs after CPB. Postoperative pulmonary shunting and an alveolar-arterial oxygen gradient are features of postperfusion lung dysfunction,^{1,12} and many authors contend they are the result of an inflammatory response.^{13,14} Pulmonary sequestration of neutrophils with release of elastase during CPB leads to parenchymal and endothelial injury, and several studies have shown that the inflammation can be inhibited by a heparin-coated CPB circuit,¹⁵ leukocyte depletion,^{16,17} corticosteroids^{16,18} and aprotinin.^{13,16} However, all these methods are only partially effective in decreasing CPB-mediated inflammatory changes. Ascione et al showed that the levels of elastase, interleukin-8, C3a, C5a, and the white blood cell, neutrophil, and monocyte counts were significantly lower after OPCAB than after conventional on-pump CABG.¹⁹

Neurological dysfunction did not occur after OPCAB in the present study. Stroke or impaired cognitive function is one of the most severe complications of conventional CABG and the reduction of cerebrovascular accidents by OPCAB has been emphasized.^{20–22} However, the risk of neurological complications and stroke still remains because partial aortic cross-clamping may cause atheromatous emboli, particularly in patients older than 70 years.⁹ Murkin et al examined the extradural pressure via an intracranial catheter and associated cerebral embolization by transcranial Doppler during CPB and reported that fewer cerebral emboli, less cerebral venous hypertension, and better maintenance of the arterial pressure during OPCAB contributed to the lower incidence of neurologic complications.²¹ Although maintaining the mean arterial pressure during OPCAB may reduce the incidence of neurologic complications, watershed infarction because of low blood pressure during manipulation of the heart is thought to be uncommon. Chavanon et al reported an increased incidence of acute dissection of the ascending aorta in OPCAB patients,²³ probably caused by the higher blood pressure and the increased pulsation during aortic clamping.⁷ If the ascending aorta did not have severe calcification, we carefully partially clamped it for proximal graft anastomosis, although partial aortic clamping has been recently abandoned in favor of the 'aorta no touch' technique. Avoiding partial aortic clamping for proximal graft anastomosis probably played an important role in the marked decrease of stroke that was noted in the present study.

The incidence of renal dysfunction was also lower in the OPCAB group and Ascione et al reported similar results in a randomized study of CABG.²⁴ They found that creatinine clearance and the urinary microalbumin to creatinine ratio were significantly worse in the conventional CABG group, so the glomerular filtration rate and renal tubular function are better protected by OPCAB than by conventional CABG.

Atrial fibrillation remains frequent after CABG and increases the risk of stroke. Although initial reports emphasized a favorable effect,^{20,25,26} OPCAB has not actually reduced the occurrence of postoperative AF and in the present study, its incidence was not influenced by the use of CPB or the occurrence of myocardial ischemia during cardioplegic arrest. The incidence of AF was almost identical with that reported by van Dijk et al.¹⁰ Stamou et al examined the risk factors for AF after OPCAB and found that patients were more likely to be older, to have insulin-dependent diabetes, an ejection fraction <34%, multivessel

disease, or previous stroke.²⁷ Postoperative pulmonary complications (pulmonary edema and pleural effusion), an older age at operation, the severity of coronary lesions, the number of bypasses, and postoperative medical treatment (prophylactic use of β -blockers) were also related to the occurrence of AF.

Van Dijk et al reported that omitting CPB led to less extensive cardiac enzyme release,¹⁰ and the lower postoperative CK-MB release in the present OPCAB group suggests that avoiding CPB reduces the extent of myocardial damage. Parameters of myocardial injury, such as CK-MB and troponin I concentrations, were significantly lower in another study of OPCAB patients⁸ and in the present study, the OPCAB group usually had a smaller elevation of CK-MB, although the incidence of CK-MB >50 U/L was the same as after conventional CABG.

As for graft patency, the mid-term and long-term results of OPCAB are comparable to those of conventional on-pump CABG. Ömeroglu et al compared graft patency between OPCAB and conventional CABG at 24–61 months after surgery and found comparable rates for both techniques, and that especially high patency rates when the internal mammary arteries were used.²⁸ Early graft patency was also satisfactory in the present OPCAB. In our experience, postoperative angiography on the day after diagnosis of perioperative myocardial infarction will reveal a clot-like filling defect in the graft or coronary artery. Repeat coronary angiography before discharge showed that none of the present patients had graft stenosis or occlusion, probably because of early restoration of normal coagulation resulting from intact platelet function. Therefore, we currently administer heparin at 100 U·kg⁻¹·h⁻¹ for several hours postoperatively and aspirin (162 mg/day) from the next morning after OPCAB.

The number of distal anastomoses was significantly smaller in the OPCAB group and other reports have indicated a similar result.^{6,8,9} The patients who needed many bypass grafts were assigned to conventional CABG in the present study. Because OPCAB is technically demanding, smaller or unimportant coronary branches are generally not grafted. Arom et al reported that OPCAB patients have more frequent angina attacks and require more re-intervention procedures up to 1 year after surgery.⁶ However, such trends may have only occurred during the learning period of OPCAB because more advanced cardiac stabilization methods have already solved those problems.

Study Limitations

Patients were not randomly assigned to the 2 groups and this was a retrospective study of patients operated on in the year 2000. Although most patients in the OPCAB group after May 2000 had similar preoperative and postoperative management to those in the other group, some patients were assigned for conventional on-pump CABG because of small coronary arteries and poor left ventricular function. In order to remove these biases, a randomized prospective study of OPCAB is necessary to confirm our preliminary results. However, the present early results of OPCAB are encouraging, although the objective of CABG is to achieve improved long-term survival, so follow-up for more than 5 years is required. Prospective and randomized studies will clarify the exact indications for OPCAB in the future.

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