

Early and Mid-Term Impacts of Cardiopulmonary Bypass on Coronary Artery Bypass Grafting in Patients With Poor Left Ventricular Dysfunction

— A Propensity Score Analysis —

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Background Cardiopulmonary bypass may exacerbate myocardial damage in compromised left ventricles. Early and mid-term outcomes of off-pump coronary artery bypass grafting (OPCAB) vs on-pump coronary artery bypass grafting (On-pump CABG) were compared in patients with poor left ventricular dysfunction, using an analysis of a propensity score matching.

Methods and Results Between December 2000 and November 2005, 1,473 patients underwent isolated coronary artery bypass grafting in our institute and 153 patients who had a left ventricular ejection fraction (LVEF) lower than 35% were enrolled. The OPCAB group contained 100 patients and the On-pump CABG group contained 53 patients. Preoperative risk factors were compared and 50 patients in each group were matched. The mean follow-up time was 35.5 ± 17.3 months. Three deaths (3.0%) occurred in the matched cohort, with no significant difference between 2 groups. The operation time, ventilation time, intensive care unit admission time and occurrence of respiratory failure were significantly lower in the OPCAB group. The mean LVEF of the 2 groups improved significantly. The overall 6-year actuarial survival rates of the OPCAB and On-pump CABG group were 88.2% and 72.4% ($p=0.2$), respectively, and there were no significant differences in 6-year rates of freedom from major adverse cardiac and cerebrovascular events ($p=0.97$).

Conclusions Coronary artery bypass grafting in patients with poor left ventricular dysfunction improved myocardial function. Postoperative respiratory failure was significantly related to the cardiopulmonary bypass for surgical myocardial revascularization. Off-pump and On-pump surgical revascularization resulted in equivalent mid-term outcomes. (Circ J 2007; 71: 1387–1394)

Key Words: Coronary artery bypass surgery; Heart failure; Off-pump; On-pump

Off-pump coronary artery bypass grafting (OPCAB) is an alternative to conventional cardiopulmonary bypass-supported myocardial revascularization and is becoming increasingly popular, as it allows complete myocardial revascularization with excellent surgical results in most patients.^{1,2}

Severe left ventricular dysfunction has been reported to be an independent predictor of operative mortality in patients undergoing coronary artery bypass grafting (CABG) and patients with impaired left ventricular function undergoing revascularization on cardiopulmonary bypass (CPB) have increased mortality and morbidity when compared with patients with normal left ventricular function.^{3–5} Left ventricular dysfunction also often leads to low cardiac output and a high postoperative morbidity, with many patients requiring inotropic or mechanical support, and vasopressors for hours to days after surgery.⁶

It has been speculated that extracorporeal circulation

may exacerbate myocardial damage in compromised left ventricles as a result of the activation of inflammatory mediators, the non-physiologic ventricular geometry of the empty heart impeding collateral flow to ischemic areas and worsened preservation of interventricular septal movement.^{7,8} It may seem advisable to avoid cardiopulmonary bypass in patients with severe left ventricular dysfunction; however, many surgeons still choose conventional CABG using a CPB machine (On-pump CABG) due to hemodynamic instability concerns such as ventricular arrhythmia, hypotension and cardiac arrest during OPCAB.

The present study evaluates the effects of cardiopulmonary bypass and the efficacy of OPCAB by comparing the short and mid term results of OPCAB and On-pump CABG in patients with severe left ventricular dysfunction with an analysis of a propensity score matching.

Methods

Patient Selection

From December 2000 through November 2005, 1,473 patients underwent isolated CABG without a concomitant operation—such as left ventricular volume reduction surgery, arrhythmia operation or valve surgery—at Yonsei Cardiovascular Center, Yonsei University College of Medicine. Preoperative and postoperative data were obtained using a

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retrospective review of the registry database, medical notes and charts. One hundred and fifty-five (10.5%) of these patients had a preoperative left ventricular ejection fraction (LVEF) of 35% or less, as calculated using echocardiography, ventriculography or nuclear imaging. Two patients in conversion from OPCAB to On-pump CABG were excluded to prevent a crossover between the 2 types of procedures and 153 patients were enrolled in the present study. These were divided into 2 groups: 100 patients who underwent OPCAB and 53 patients who underwent On-pump CABG. Patients were selected according to the surgical technique used, whether OPCAB or On-pump CABG, based on 3 individual surgeons' preferences. The present study was approved by the Institutional Review Board of Medical College of Yonsei University. Individual patient consent was waived.

Operative Techniques

All patients underwent general endotracheal anesthesia with continuous Swan-Ganz catheter monitoring, transesophageal echocardiography and arterial pressure monitoring. A thorough TEE evaluation was undertaken in each patient to assess wall motion abnormalities, the presence and degree of mitral regurgitation, severity of atherosclerotic disease of the aorta, and right and left ventricular function.

OPCAB Off-pump coronary artery bypass surgery was performed through a full sternotomy incision with harvesting of the left internal thoracic artery in a skeletonized fashion. The radial artery was harvested from the non-dominant forearm using a Harmonic scalpel (Ethicon Endosurgery Inc, Cincinnati, OH, USA). The right internal thoracic artery, saphenous vein or right gastroepiploic artery were also harvested if necessary. Heparin was given at a dose of 1 mg/kg to achieve a target activated clotting time of at least 350s before ligation of the distal internal thoracic artery. After the pericardium was opened, the extent of disease, epicardial anatomy, size of target vessels and size of the heart were assessed, and the strategy of grafts was decided. A single deep pericardial traction suture was placed in the posterior pericardium two-thirds of the way from the inferior vena cava to the left inferior pulmonary vein. Stabilization of the target arteries was accomplished using an Octopus tissue stabilizer (Medtronic, Minneapolis, MN, USA). When hemodynamic instability was expected, a Starfish heart positioner (Medtronic, Minneapolis, MN, USA) was used during anastomoses of arteries that were placed on the lateral and posterior wall of the heart. In most instances, anastomosis of the left internal thoracic artery to the left anterior descending artery was first performed using intracoronary shunts. A proximal silastic snare was used to anastomose other coronary arteries. A misted CO₂ blower and irrigation with warm saline were used to remove blood from the sites of arteriotomy.

On-Pump CABG On-pump coronary artery bypass surgery was performed through a full sternotomy incision and the graft harvesting techniques were the same as those of OPCAB procedure. Anticoagulation was achieved using 3 mg/kg of heparin. CPB was achieved using cannulation of the ascending aorta and right atrium. Cold blood cardioplegia was delivered intermittently in antegrade and retrograde fashion for myocardial protection of the arrested heart. All CPBs were performed with a centrifugal pump and membrane oxygenator under moderate hypothermia (32°C).

Clinical Data Collection and Follow-up

Data were collected prospectively and the degree of

stenosis of coronary artery disease was analyzed using coronary angiography, and the ejection fraction was calculated using echocardiography, left ventriculography or nuclear imaging studies.

One hundred and forty-one patients (92.2%) were re-evaluated with trans-thoracic echocardiography at postoperative day 5–7 before discharge from the hospital. Follow-up echocardiography occurred 1 year after the operation and every third year thereafter. One hundred and twenty-three (81 in the OPCAB group and 42 in the On-pump CABG group) among the 148 discharged survivors underwent follow-up echocardiography (83.1%). The mean duration from operation to follow-up echocardiography was 26.7±24.1 months (range, 4 to 64 months).

The blood pressure, sugar level and cholesterol level of the patient, which can affect the long-term efficacy of grafts, were strictly monitored and maintained at normal levels, with regular follow-up by cardiologists and the referred physician. Mid term follow-up was obtained for all patients using an outpatient clinic visit, telephone interview or mailed questionnaire. All patients were completed the follow up (100%). The mean follow-up was 35.5±17.3 (range, 4 to 72 months).

Definition of Terms

Perioperative myocardial infarction was diagnosed by finding at least 2 of the following 4 criteria: (1) Prolonged (>20 minutes) typical chest pain not relieved by rest and/or nitrates. (2) Enzyme level elevation: either creatine kinase (CK)-MB >5% of total CK, CK greater than 2-fold normal, LDH subtype 1 > LDH subtype 2; or troponin >0.2 µg/ml. (3) New wall motion abnormalities. (4) Serial ECG (at least 2) showing changes from baseline or serially in ST-T and/or Q waves that are 0.03 s in width and/or larger than one-third of the total QRS complex in 2 or more contiguous leads. Peripheral arterial obstructive disease is defined by stenosis of more than 50% of the diameter in arteries that are derived directly from the aorta. Complete revascularization was defined as the placement of at least 1 graft to each of the 3 major vascular regions that included stenosis of more than 50% of diameter (if 1 existed)^{9,10}. Postoperative respiratory failure was defined as prolonged ventilation for more than 72 h resulting from respiratory causes, newly developed pulmonary edema, adult respiratory distress syndrome, reintubation due to respiratory causes and tracheostomy. A major adverse cardiac and cerebral event (MACCE) was defined as death from all causes, non-fatal myocardial infarction, repeat revascularization using either percutaneous intervention or bypass surgery and stroke. A major adverse cardiac event (MACE) was defined as death from all causes, non-fatal myocardial infarction and repeat revascularization by either percutaneous intervention or bypass surgery. Other variables were defined according to the Society of Thoracic Surgeons Adult Cardiac Database Definition of Terms Version 2.52.1 (http://www.ctsnet.org/file/rptDataSpecifications252_1_ForVendorsPGS.pdf).

Statistical Analysis

Preoperative, intraoperative and postoperative variables were compared between the 2 groups, using univariate analysis (Fisher's exact test or chi-square test) and Student's t-test as appropriate. A repeated measures ANOVA test was adopted for comparing changes of ejection fraction and other echocardiographic parameters at follow-up between 2 groups.

Table 1 Preoperative Characteristics Unadjusted and Adjusted for the Propensity Score Matching

	OPCAB	On-pump CABG	p value	OPCAB*	On-pump CABG*	p value after adjustment*
	(n=100)	(n=53)		(n=50)	(n=50)	
	n (%)	n (%)		n (%)	n (%)	
Age, mean±SD	62.9±8.8	62.0±9.2	0.54	61.0±9.4	62.4±9.3	0.48
Age ≥65	49 (49.0)	20 (37.7)	0.17	22 (44)	20 (40)	0.69
Female	27 (27.0)	15 (21.9)	0.79	17 (34)	14 (28)	0.52
Smoking history	50 (50.0)	20 (37.7)	0.13	22 (44)	19 (38)	0.54
BMI, mean±SD	24.2±2.9	24.0±3.1	0.72	24.4±2.6	23.9±3.2	0.40
BMI ≥30 kg/m ²	3 (3.0)	2 (3.8)	1.00	1 (2)	2 (4)	1.00
BSA <1.6 m ²	28 (28.0)	18 (34.0)	0.47	16 (32)	17 (34)	0.83
Diabetes mellitus	56 (56.0)	26 (49.1)	0.38	24 (48)	23 (46)	0.84
Hypercholesterolemia	46 (46.0)	22 (41.5)	0.56	21 (42)	23 (46)	0.69
Renal failure	14 (14.0)	7 (13.2)	0.87	7 (14)	7 (14)	1.00
Hypertension	60 (60.0)	26 (49.1)	0.17	27 (54)	26 (52)	0.84
History of CVA or TIA	12 (12.0)	4 (7.5)	0.58	4 (8)	4 (8)	1.00
Chronic lung disease	3 (3.0)	3 (5.7)	0.42	3 (6)	3 (6)	1.00
Peripheral vascular disease	21 (21.0)	6 (11.3)	0.13	9 (18)	7 (14)	0.59
Redo surgery	2 (2.0)	4 (7.5)	0.18	2 (4)	2 (4)	1.00
S/p PTCA	19 (19.0)	7 (13.2)	0.35	10 (20)	6 (12)	0.28
Priority						
Elective operation	84 (84.0)	40 (75.5)	0.21	43 (86)	39 (78)	0.30
Urgent operation	10 (10.0)	7 (13.2)	0.56	4 (8)	6 (12)	0.74
Emergency operation	6 (6.0)	6 (11.3)	0.25	3 (6)	5 (10)	0.72
Recent MI (within 1 month)	59 (59.0)	27 (50.9)	0.31	24 (48)	25 (50)	0.84
Unstable angina	47 (47.0)	30 (56.6)	0.28	28 (56)	28 (56)	1.00
Cardiogenic shock	8 (8.0)	6 (11.3)	0.59	6 (12)	4 (8)	0.74
CCS angina class, mean±SD	2.7±0.9	3.0±0.7	0.07	2.6±0.8	2.9±0.7	0.06
CCS angina class III/IV	61 (61.0)	38 (71.7)	0.21	32 (64)	35 (70)	0.52
NYHA functional class, mean±SD	2.5±0.9	2.8±0.9	0.10	2.5±0.8	2.7±0.9	0.13
NYHA functional class III/IV	47 (47.0)	33 (62.3)	0.08	22 (44)	31 (62)	0.07
LVEF, mean±SD	28.1±5.9	27.9±7.0	0.82	28.8±5.1	28.1±7.1	0.56
30–35%	44 (44.0)	25 (47.2)	0.66	26 (52)	24 (48)	0.69
20–30%	50 (50.0)	24 (45.3)	0.54	22 (44)	22 (44)	1.00
<20%	6 (6.0)	4 (7.5)	0.74	2 (4)	4 (8)	0.68
Three-vessel disease	85 (85.0)	46 (86.8)	0.87	42 (84)	44 (88)	0.56
Left main disease	29 (29.0)	16 (30.2)	0.91	14 (28)	14 (28)	1.00
Preoperative IABP	4 (4.0)	6 (11.3)	0.10	0 (0)	3 (6)	0.24
Additive EuroSCORE, mean±SD	7.0±3.9	7.0±2.8	1.00	6.9±3.7	6.8±2.7	0.92
Additive EuroSCORE ≥6	60 (60.0)	35 (66.0)	0.47	31 (62)	33 (66)	0.73
Logistic EuroSCORE, mean±SD	12.0±15.2	10.5±11.2	0.58	11.2±15.7	10.1±10.5	0.75

*Analysis adjusted for propensity score matching.

OPCAB, off pump coronary artery bypass grafting; On-pump CABG, on pump coronary artery bypass grafting; SD, standard deviation; BMI, body mass index; BSA, body surface area; CVA, cerebrovascular attack; TIA, transient ischemic attack; PTCA, percutaneous transluminal coronary angioplasty; MI, myocardial infarction; CCS, Canadian cardiovascular society; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; IABP, intra-aortic balloon pump; EuroSCORE, European system for cardiac operative risk evaluation.

Logistic regression was used to determine a model to calculate the propensity score (the probability to be selected for On-pump CABG given a set of preoperative risk factors listed in Appendix). The effectiveness of the model was evaluated using the Hosmer and Lemeshow goodness-of-fit statistic and residual analysis. Each On-pump CABG patient was matched with the OPCAB patient with the closest propensity score.

Kaplan-Meier curves were generated, and a log-rank test was used for comparison between the 2 groups. Multivariable Cox proportional hazards regression models were used to calculate hazard ratios while adjustment was made for preoperative and intraoperative (including CPB) factors associated with mid-term mortality. The model selection was performed with a backward stepwise method, starting from all variables with $p \leq 0.05$ in univariate analyses. The model was then confirmed using a forward stepwise selection. All analyses were performed using SPSS 12.0 (SPSS, Chicago, IL, USA). Data were shown as the incidence (%) or the mean±the standard deviation. P values equal to or less than 0.05 indicated a significant difference,

and all p values were 2-tailed.

Results

Out of 153 patients with an LVEF $\leq 35\%$ (100 OPCAB and 53 On-pump CABG), we were able to match 50 patients in each group successfully. Demographics and preoperative characteristics unadjusted and adjusted for the propensity score analysis are listed in Table 1. In the matched analysis, the mean age of patients was 61.7 ± 9.3 years (61.0 ± 9.4 in the OPCAB group and 62.4 ± 9.3 in the On-pump CABG group, $p=0.48$). There were 69 men (69%) and 31 women (31%). Forty-four patients (44%) had LVEF between 20% and 30%, and 6 patients (6%) had LVEF $<20\%$. The mean LVEF was $28.4 \pm 6.2\%$ and there was no difference in LVEF between the groups ($p=0.56$). Also there were no differences between patients characteristics with respect to smoking history, BMI, diabetes mellitus, hypercholesterolemia, renal failure, hypertension, history of CVA or TIA, chronic lung disease, peripheral vascular disease, repeat surgery, history of PTCA, emer-

Table 2 Operative and Postoperative Data Adjusted for the Propensity Score Matching

	OPCAB (n=50) (%)	On-pump CABG (n=50) (%)	p value
Operation time (h), mean±SD	266.1±56.8	317.1±69.0	0.001
CPB time (min)	–	114.5±37.3	
ACC time (min)	–	89.4±27.4	
Number of distal anastomoses, mean±SD	3.2±0.7	3.4±0.9	0.27
Usage of left internal thoracic artery	49 (98)	48 (96)	1.0
Total arterial bypass grafting, n (%)	30 (60)	24 (48)	0.23
Number of arterial grafts, mean±SD	2.4±0.7	1.7±0.7	<0.001
Complete revascularization, n (%)	42 (84)	47 (94)	0.20
Vascular Territory*, distribution of anastomoses, n (%)			
Anterior territory	50 (100)	48 (96)	0.50
Lateral territory	38 (76)	39 (78)	0.81
Posterior territory	36 (72)	43 (86)	0.09
CK-MB (POD#0; mg/dl), mean±SD	8.4±11.5	35.1±51.3	0.001
CK-MB (POD#1; mg/dl), mean±SD	18.3±39.0	22.7±28.0	0.55
Inotrope usage (>8 h)	7 (14)	39 (78)	<0.001
Postoperative blood loss (ml, first 24 h), mean±SD	672.3±423.9	738.0±312.9	0.44
Ventilation time (h), mean±SD	14.6±7.3	19.4±12.5	0.04
ICU stay time (days), mean±SD	2.4±0.7	3.7±3.3	0.01
Hospital stay (days), mean±SD	14.4±10.6	15.6±10.3	0.57

*Anterior territory includes left anterior descending and diagonal arteries, lateral territory includes circumflex and marginal arteries, and posterior territory includes posterior descending and right coronary arteries.

CK-MB, creatine kinase-MB; POD, postoperative day; ICU, intensive care unit. Other abbreviations see in Table 1.

Table 3 Postoperative Outcomes Unadjusted and Adjusted for the Propensity Score Matching

	Unadjusted				Adjusted			
	OPCAB (n=100) (%)	On-pump CABG (n=53) (%)	OR (95%CI)	p value	OPCAB (n=50) (%)	On-pump CABG (n=50) (%)	OR (95%CI)	p value
Surgical mortality	3 (3.0)	2 (3.8)	1.25 (0.20–7.69)	0.81	2 (4)	1 (2)	2.00 (0.18–25.0)	1.00
Paroxysmal atrial fibrillation	14 (14.0)	12 (22.6)	1.96 (0.69–5.56)	0.18	7 (14)	12 (24)	2.00 (0.55–7.14)	0.29
Ventilation >24 h	9 (9.0)	12 (22.5)	2.70 (0.96–7.69)	0.05	4 (8)	9 (18)	2.86 (0.68–12.5)	0.15
Respiratory failure	2 (2)	7 (13.2)	7.38 (1.47–36.9)	0.01	0	6 (12)	–	0.03
Renal failure	3 (3)	4 (7.5)	2.61 (0.56–12.1)	0.21	0	3 (6)	–	0.24
IABP insertion	3 (3)	1 (1.9)	0.62 (0.06–5.88)	1.00	–	–	–	–
Perioperative MI	5 (5)	2 (3.8)	0.75 (0.14–4.00)	1.00	3 (6)	2 (4)	0.65 (0.01–4.00)	0.65
Ventricular arrhythmia	1 (1)	3 (5.7)	5.88 (0.59–58.0)	0.12	0	3 (6)	–	0.24
GI complication	3 (3)	2 (3.8)	1.28 (0.20–7.69)	1.00	1 (2)	1 (2)	1.0 (0.06–1.67)	1
Postoperative stroke	1 (1)	2 (3.8)	3.85 (0.34–50.0)	0.28	0	2 (4)	–	0.50
Re-exploration for bleeding	0	2 (3.8)	0	0.12	0	2 (4)	–	0.50

OR, odd ratio; CI, confidence interval; GI, gastrointestinal. Other abbreviations see in Table 1.

gent operation, recent MI within 1 month, unstable angina, cardiogenic shock, Canadian Cardiovascular Society (CCS) angina score, New York Heart Association (NYHA) functional class, three-vessel disease, left main disease, preoperative IABP and European System for Cardiac Operative Risk Evaluation value (EuroSCORE). Patient receiving On-pump CABG tended to have higher mean NYHA functional classes and mean CCS angina scores. The mean additive EuroSCORE was 6.9±3.2 (6.9±3.7 in the OPCAB group and 6.8±2.7 in the On-pump CABG group, p=0.92) and the mean logistic EuroSCORE was 10.6±13.2% (11.2±15.7 in the OPCAB group and 10.1±10.5 in the On-pump CABG group, p=0.75).

After adjustment for the propensity score, fewer differences in baseline characteristics between 2 groups were found (Table 1), indicating that the propensity model had successfully served to remove the imbalance in distribution of a number of prognostic factors.

The operation time was significantly longer in the On-pump CABG group. There was no significant difference in the number of grafts and use of left internal thoracic artery between both groups. Total arterial bypass grafting tended to be performed more in the OPCAB group and more arter-

ial grafts were anastomosed in the OPCAB group. The patients with On-pump CABG group tended to have more grafts. But there was no significant difference in the number of the distal anastomoses and complete revascularization between the groups. The distribution of distal anastomoses to the various vascular territories of the heart was not significantly different between the 2 groups and is presented in Table 2.

Serum CK-MB isoenzyme immediately after operation, need for inotropic support, ventilation time and intensive care unit stay duration were significantly lower in the OPCAB group. There was no significant difference in postoperative blood loss during the first 24h or hospital stay duration between the 2 groups.

Postoperative morbidity and mortality are reported in Table 3. Three (3.0%) patients died in the OPCAB group and 2 (3.8%) patients died in the On-pump CABG group (p=0.81). The 3 OPCAB deaths resulted from low cardiac output syndrome and consequent multi-organ failure. The 2 On-pump CABG deaths included 1 stroke and 1 low cardiac output syndrome. Paroxysmal atrial fibrillation, ventricular arrhythmia and re-exploration for bleeding occurred more frequently in the On-pump CABG group,

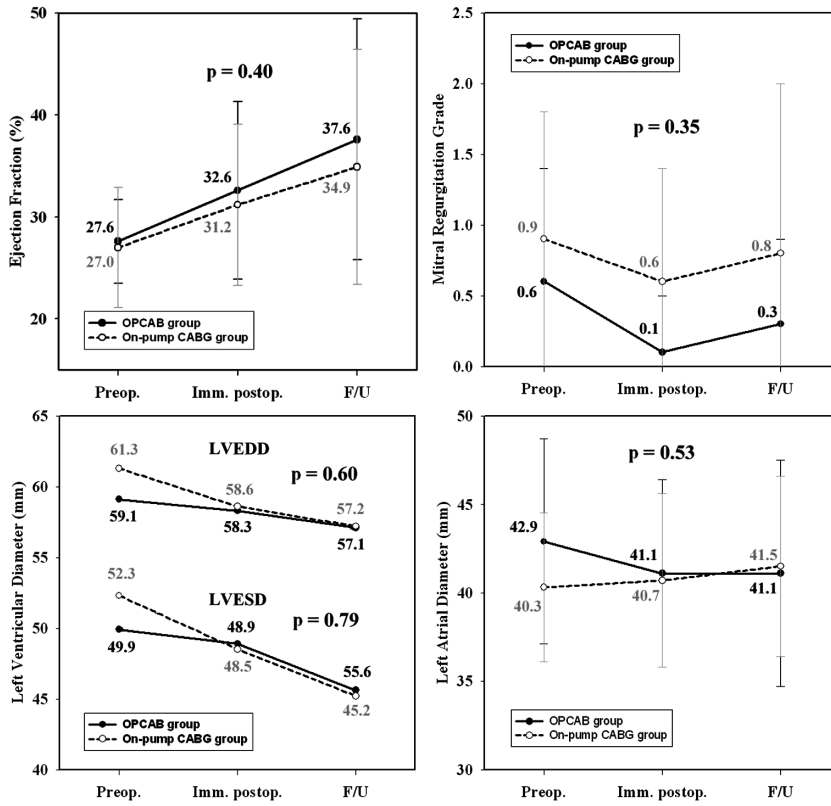


Fig 1. Changes of Echocardiographic results in the propensity-matched patients. Solid line and black-colored measures: off-pump coronary artery bypass grafting (OPCAB) group; dashed line and gray-colored measures: on-pump coronary artery bypass grafting (On-pump CABG) group. The p values are the results from repeated measures ANOVA that analyzed the effect of the use of cardiopulmonary bypass. Preop., preoperative evaluation; Imm.postop., immediate postoperative evaluation; F/U, follow-up evaluation; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension.

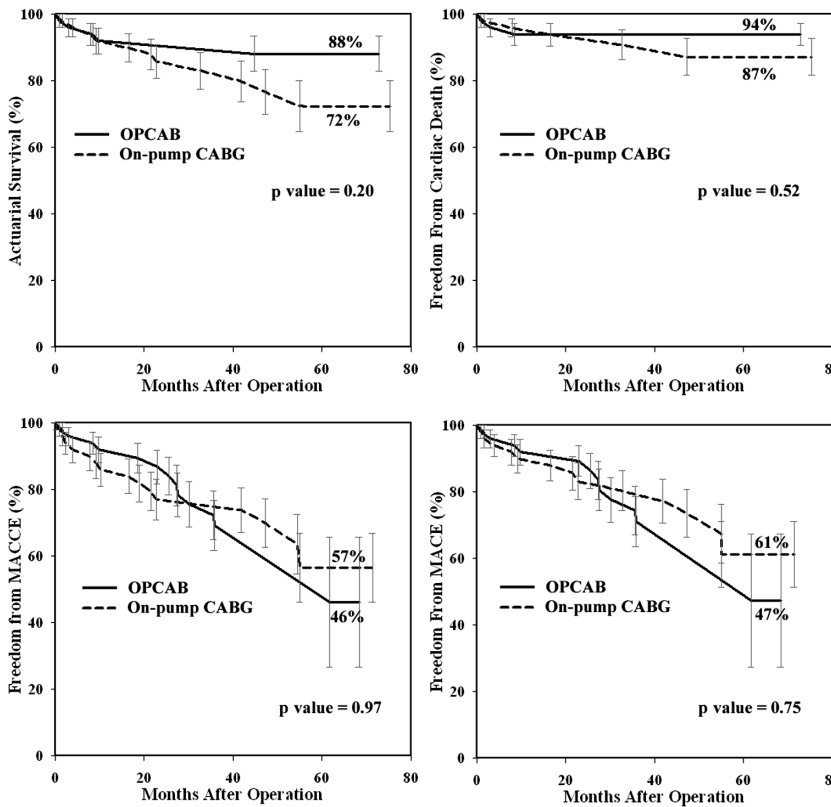


Fig 2. Mid-term outcomes after operation in the propensity-matched patients. Solid line, off-pump coronary artery bypass grafting (OPCAB) group; dashed line, on-pump coronary artery bypass grafting (On-pump CABG) group. MACCE, major adverse cardiac and cerebrovascular events; MACE, major adverse cardiac events.

Table 4 Independent Predictors for Mid-Term Mortality in Propensity-Matched Patients With Poor Left Ventricular Dysfunction (Multivariate Cox Regression Analysis)

	Coefficient	Standard error	p value	ORs	95%CI
Age ≥ 65	1.52	0.63	0.016	4.57	1.33–15.76
Peripheral vascular disease	2.20	0.68	0.001	8.99	2.35–34.36
NYHA ≥ 3	1.23	0.65	0.047	3.42	1.15–12.17

Abbreviations see in Tables 1,3.

but not significantly. There were no statistical differences in the postoperative occurrence of renal failure, intraaortic balloon pump insertion, perioperative myocardial infarction, gastrointestinal complications and stroke. The off-pump group was associated with a lower incidence of the need for ventilation more than 24 h and/or respiratory failure. After adjustment for the propensity score, the only postoperative morbidity to show a statistically significant difference was respiratory failure.

Multivariate logistic regression analysis, using the variables listed in Appendix, revealed that the independent factors for in-hospital mortality were ejection fraction (EF) less than 20% (odds ratio (OR) 11.4, 95% confidence interval (CI) 1.3–99.8, $p=0.03$), body surface area less than 1.6 m² (OR 10.7, 95%CI 1.1–109.0, $p=0.04$) and emergency operation (OR 14.1, 95%CI 1.9–103.2, $p=0.009$).

Eighty-two patients (42 in the OPCAB group and 40 in the On-pump CABG group) in the 100 matched patients underwent follow-up echocardiography. The mean duration from operation to follow-up echocardiography in the matched cohort was 28.8 \pm 23.5 months (range, 6 to 64 months). The changes in echocardiographic parameters of each group are shown in Fig 1. LVEF increased significantly during follow-up in both groups, and there was no significant difference between the 2 groups in the degree of increase of LVEF ($p=0.4$). The mitral regurgitation grade significantly decreased in the postoperative period, but increased later so that ultimately there was no difference between preoperative and follow-up measurements. The left ventricular end-diastolic dimension and the left ventricular end-systolic dimension decreased significantly during follow-up in both groups, but there were no differences between the 2 groups in the degree of changes of parameters. In terms of left atrial dimension, there were no significant changes during follow-up (Fig 1).

In the matched cohort, there were 13 late deaths in total; 4 (8.3% among the 48 survivors) in the OPCAB group and 9 (18.4% among 49 survivors) in the On-pump CABG group. The overall 6-year actuarial survival was 78.3 \pm 5.5% and was higher in the OPCAB group (88.2 \pm 5.3% in the OPCAB group and 72.4 \pm 7.6% in the On-pump CABG group, respectively), but the difference between the 2 groups was not significant ($p=0.20$). There were 5 late cardiac-related deaths; 3 in the OPCAB group and 2 in the On-pump CABG group. The 6-year freedom from cardiac related death was 94.0 \pm 3.4% in the OPCAB group and 87.2 \pm 5.6% in the On-pump CABG group ($p=0.52$; Fig 2). No patients received surgical coronary revascularization and 11 patients needed percutaneous coronary intervention during follow-up (7 in OPCAB group and 4 in On-pump CABG group, respectively). The overall 6-year freedom from MACCEs was 52.3 \pm 9.4% and there was no significant difference between the 2 groups (46.2 \pm 19.5% in the OPCAB group and 56.5 \pm 10.4% in the On-pump CABG group, $p=0.97$). The overall 6-year freedom from MACEs

was 56.2 \pm 9.7% and there was no significant difference between the 2 groups (47.5 \pm 20.0% in the OPCAB group and 61.4 \pm 9.9% in the On-pump CABG group, $p=0.75$; Fig 2).

Multivariate Cox proportional hazard model revealed that independent variables for mid-term deaths were: age more than 65 years, peripheral vascular disease and a NYHA functional class of 3 or more (Table 4).

Discussion

There is an increasing incidence of moderate to severe left ventricular dysfunction in patients referred for CABG due to widespread use of thrombolysis, increased surgery in patients with recent acute myocardial infarction and angioplasty, which delays surgical intervention until coronary arteriosclerosis is more extensive and left ventricular dysfunction more severe, placing patients at much higher surgical risk.¹¹

While OPCAB produces local or regional ischemia, CBP with cross-clamping produces global ischemia, which proves to be detrimental in patients with left ventricular dysfunction who have minimal cardiac reserve. Indeed, left ventricular segmental wall motion has been found to be better in patients who underwent beating heart operations than with CPB.¹² It has been reported that OPCAB in patients with low LVEF has good surgical results and is an alternative to conventional On-pump CABG, but there are few reports of mid-term and long-term results of OPCAB in these patients.^{13–15} The present study evaluates the efficacy and surgical results, and the mid-term clinical results of OPCAB in low LVEF patients compared with conventional On-pump CABG.

Among the 12 patients who underwent emergency operations, IABP had been inserted preoperatively in 8 patients (66.7%). We tend to use IABP rapidly in patients who require high doses of inotropic agents and also frequently in the preoperative period for patients when maximal medical therapy has failed or for patients who had a failed attempt of angioplasty. A number of published studies have expanded the potential clinical applications of IABP, to include high risk patients who undergo CABG.^{16,17} Dietl et al undertook a 5-year retrospective analysis of 163 consecutive CABG patients with severe ventricular dysfunction (EF <25%).¹⁸ Thirty-seven patients had received IABP support preoperatively, while 126 did not. The 30-day mortality rate was 2.7% among patients receiving preoperative IABP vs 11.9% in the non-preoperative IABP group ($p<0.005$). This increased survival when using preoperative counterpulsation support was particularly evident among patients undergoing repeat operations, patients in NYHA functional class III or IV and in those who had experienced a recent myocardial infarction or with left main coronary artery stenosis.

The European System for Cardiac Operative Risk

Evaluation (EuroSCORE) is used as a preoperative risk index.¹⁸ EuroSCORE is the most efficient index for predicting the risk of cardiac operation, even in Japan.¹⁹ Despite an increase in the risk category of patients for CABG, mortality has tended to decline due to the use of OPCAB for high-risk patients and improvements in surgical techniques.²⁰ The cohort of the present study was a high-risk group according to EuroSCORE, and achieved better results than predicted in both OPCAB and On-pump CABG.

OPCAB showed better results than On-pump CABG in terms of operation time, post-operative cardiac enzyme elevation, ventilator care period and intensive care unit stay. In a study that compared 132 On-pump CABG patients and 45 off-pump CABG patients with an ejection fraction less than 30%, Arom et al showed that patients who received OPCAB had better results in post-operative bleeding, operation time and peak cardiac enzyme level, but no difference in mortality and complications.²⁰ Similar results were seen in the present study, except for the incidence rate of prolonged ventilation and respiratory failure.

The results of follow-up echocardiography showed the significant increase on LVEF. Elefteriades et al also reported that solitary CABG had benefits in patients with left heart failure.²¹ In their study, mean LVEF increased substantially from 23.3% preoperatively to 33.2% on mid-term follow-up and this change represented a 43% increase above the initial baseline value. Furthermore, CABG had many benefits for patients with heart failure, such as symptomatic improvement, reverse remodeling of left ventricular dilatation and better long-term survival compared to medical treatment.

Although much has been published on the hospital results of patients undergoing OPCAB, little has been reported on the late outcomes in patients with poor left ventricular dysfunction. Loop et al reported a similar study involving 250 patients with ejection fractions of less than 30% who received either On-pump CABG or OPCAB, the 1 year and 3 year survival was 90% and 84% respectively, and the long-term results of OPCAB were comparable to On-pump CABG.²² The present study showed that the 1-, 3- and 6-year survival of the matched cohort was 92%, 87% and 75%. One-, 3- and 6-year survival rates of the OPCAB group was 92%, 92% and 88% respectively, compared to 92%, 83% and 72% for the on pump CABG group. However, there was no significant difference between 2 groups in actuarial survival. Sabik et al reported that OPCAB and On-pump CABG resulted in equivalent mid-term survival, myocardial infarction and all coronary intervention, which is similar to the present study.²³ In most series of comparisons between OPCAB and On-pump CABG in high-risk patients, there was a significant difference in the mean number of distal anastomoses.^{13–15} In the present study, no difference was found in the number of distal anastomosis and completeness of revascularization, and it may remove the bias of late effect of incomplete revascularization.

The use of arterial grafts in coronary artery bypass graft surgery is an important factor regarding the long term results, especially in patients with a low cardiac function and high risks.^{24–27} In the present study, there was a significant difference in the rates of total arterial revascularization and the number of arterial grafts. Although there may be several reasons why the total arterial revascularization did not affect late outcomes in the present study, we believe 2 are likely possibilities. The first may be that we use the left

internal thoracic artery in 97% of patients. Most studies emphasized that the left internal thoracic artery is the most important factor for late results. Second, the detrimental effects of non-total arterial revascularization increase with time, and patients in this study may not have been followed long enough for differences to emerge.

Study Limitations

The present study has several limitations. First, the present study was a clinical review of patients who underwent OPCAB and On-pump CABG. Patients were not randomly assigned to either group, but instead the choice of procedure was made by the surgeon at the time of operation. Therefore, selection bias may affect our findings. To reduce the effect of selection bias on outcomes, we used propensity matching to identify well-matched off-pump and on-pump patients for comparison. Second, the size of the cohort is somewhat small for comparison, but the statistical power () of the analysis of operative outcomes, which was performed to determine whether there was enough power in this model, was 0.81. Third, we compared the changes of the echocardiographic parameters between 2 groups, but the follow-up echocardiography was performed at different time points. To reveal the exact results and fair statistical analysis, regular and serial follow-up would be needed. Despite the limitations of this retrospective, non-randomized study and the small patient numbers, the results suggest that a prospective, randomized and long-term investigation is warranted.

Conclusion

The results of our series showed relatively low in-hospital mortality and morbidity rates associated with either OPCAB or On-pump CABG in patients with severe left ventricular dysfunction. OPCAB gave better results in terms of operation time, ventilation time, intensive care unit stay and incidence of respiratory failure compared to On-pump CABG. Both surgical strategies improved myocardial function and mid-term outcomes in patients with severe left ventricular dysfunction. OPCAB and On-pump CABG show equivalent mid-term outcomes.

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Appendix

Variables included in multivariate analysis of risk factors for early and mid-term mortality

Demography

Age

Sex

Preoperative risk factors

Body mass index

Body surface area

Smoking History

Diabetes mellitus

Hypercholesterolemia

Renal failure

Hypertension

History of cerebrovascular accident

Chronic lung disease

Peripheral vascular disease

Previous interventions

Redo surgery

History of percutaneous transluminal coronary angioplasty

Preoperative cardiac status

Unstable angina

Myocardial infarction (<30days)

Ejection fraction

Left ventricular end-diastolic/end-systolic dimension

Cardiogenic shock

Intra-aortic balloon pump insertion

Canadian cardiovascular society score

New York Heart Association functional class

Extent of coronary artery occlusive disease

Three vessel disease

Left main disease

Operative data

Urgent operation

Emergent operation

Total arterial grafting

Use of cardiopulmonary bypass

Use of left internal thoracic artery

Use of greater saphenous vein

Complete revascularization