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Analysis of Risk Factors for Conversion from Off-Pump to On-Pump Coronary Artery Bypass Graft

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Background: Off-pump coronary artery bypass (OPCAB) is performed worldwide, but significant risks are associated with conversion to on-pump surgery. Therefore, we evaluated the composite outcomes between an OPCAB group and a conversion group. **Methods:** From January 2008 to December 2012, 100 consecutive patients underwent OPCAB at Hallym University Sacred Heart Hospital, of whom 84 underwent OPCAB without adverse events (OPCAB group), and 16 were converted to on-pump surgery (conversion group). Early morbidity, early and long-term mortality, and major adverse cardiac and cerebrovascular events (MACCEs) were the primary and long-term composite endpoints. **Results:** The mean follow-up period was 55±26 months, with 93% of the patients completing follow-up. The composite outcomes in the OPCAB and conversion groups were as follows: early morbidity, 2.3% versus 12.5%; early mortality, 4.7% versus 0%; long-term mortality, 14.3% versus 25.0%; and MACCEs, 14.3% versus 18.8%, respectively. No composite endpoints showed statistically significant differences. Preoperative acute myocardial infarction (AMI) was identified as an independent risk factor for conversion (p=0.025). **Conclusion:** The conversion group showed no statistically significant differences in early mortality and morbidity, MACCEs, or long-term mortality compared with the OPCAB group. The preoperative diagnosis of AMI was associated with an increased number of conversions to on-pump surgery.

Key words: 1. Coronary artery bypass
2. Conversion
3. Risk factors

Introduction

In 1967, Kolessov [1] reported 6 cases in which coronary artery bypass grafting (CABG) was performed without cardiopulmonary bypass (CPB); this was the first report of off-pump coronary artery bypass (OPCAB). After more than 2 decades, extensive efforts by Calafiore and Subramanian in the mid-1990s revived the concept of OPCAB [2,3]. Moreover, several technical and clinical advances have led some physicians to prefer OPCAB [4].

Despite the multiple benefits of OPCAB, its long-term outcomes associated with the patency of grafts have been controversial. Moreover, patients who undergo OPCAB occasionally require conversion to on-pump surgery with CPB. These conversions induce an eme-

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rgent situation, which significantly increases the risks of morbidity and mortality [5,6]. Nevertheless, few reports have evaluated the risks and outcomes associated with conversion during OPCAB.

In the present study, we compared the composite short-term and long-term outcomes between patients who underwent OPCAB without adverse events and those who required conversion to on-pump CABG (ONCAB), and analyzed the risk factors for conversion.

Methods

From January 2008 to December 2012, 101 consecutive patients underwent OPCAB at Hallym University Sacred Heart Hospital. One emergency case was excluded from the study. The institutional review board of our hospital approved this study with a waiver of informed consent (No. 2016-I004).

Eighty-four patients underwent OPCAB without adverse events (OPCAB group), while 16 were converted from OPCAB to ONCAB during the operation (conversion group). The mean follow-up period was 55±26 months, and 7 patients were lost to follow-up (follow-up completion rate, 93%). Among the 100 consecutive patients, 74 were men, the mean age at operation was 64.5±10.2 years, and the mean number of distal anastomoses was 3.1±0.7. The preoperative diagnosis was divided into 3 categories: stable angina (2 patients), unstable angina (75 patients), and acute myocardial infarction (AMI, 23 patients).

The diagnostic criterion for AMI was the detection of increased troponin I values by a fluoroimmunoassay (above the 99th percentile upper reference limit) with at least 1 of the following: symptoms of ischemia, new significant ST-T wave changes or new left bundle branch block, the development of pathological Q waves on electrocardiography, imaging evidence of new loss of viable myocardium or a new regional wall motion abnormality, or the identification of an intracoronary thrombus by angiography [7].

Unstable angina was defined as chest discomfort or pain, with at least 1 of the following 3 features: occurring at rest or with minimal exertion; lasting longer than 10 minutes; having a recent onset within the past 2 weeks; and/or having a crescendo pattern, without an increased biomarker of necrosis [8].

Subgroups of AMI according to non-ST-elevated or ST-elevated myocardial infarction (MI) and the period of MI were not considered.

Left ventricle (LV)-related indices such as LV dimensions, wall thickness, LV function, and mitral regurgitation (MR) were evaluated as risk factors for conversion.

Under routine anesthetic monitoring and techniques, all procedures were performed through a median sternotomy. One surgeon operated on all the patients. The left internal mammary artery (IMA) was used as a conduit for the left anterior descending artery (LAD) in all patients, except in 1 patient with poor IMA flow. The radial artery and great saphenous vein were used as additional conduits. The anesthesiologist actively managed hemodynamic instability resulting from displacement of the heart and occlusion of the target coronary arteries during OPCAB through a combination of positioning the operating table, administering intravenous fluids and blood products if needed, and providing pharmacologic therapies, including the continuous infusion of dopamine, dobutamine, and amrinone, and an intermittent bolus injection of phenylephrine. Deep pericardial sutures and stabilization devices, such as the Octopus Tissue Stabilizer (Medtronic Inc., Minneapolis, MN, USA) and the Guidant OPCAB System (Guidant Co., Santa Clara, CA, USA), were used to elevate and stabilize the heart when required. Apical retraction was achieved using cardiac suction devices such as the Starfish heart positioner (Medtronic Inc.). Coronary anastomoses were performed using a monofilament suture in the following order: the totally occluded coronary artery, the LAD, the right coronary artery (RCA), and the circumflex artery (Cx). If conversion was required during distal coronary anastomosis, the heart was repositioned to its normal position with an in situ intracoronary shunt, and CPB was performed as soon as possible.

Major postoperative morbidities included low cardiac output syndrome requiring an intra-aortic balloon pump (IABP) or extracorporeal membrane oxygenation, acute renal failure (ARF) requiring dialysis, cerebrovascular accidents (CVAs), reoperation for bleeding, prolonged ventilator care for over 48 hours, and infections such as pneumonia and mediastinitis. Early mortality and major morbidity were the composite endpoints for early outcomes. Late mortality and major adverse cardiac and cerebrovascular events (MACCEs) were the composite endpoints for long-term outcomes. MACCEs included CVAs, MIs, reintervention, and heart failure that required hospital admission.

Univariate and multivariate analyses were used to identify independent risk factors for conversion to ONCAB. The preoperative demographics and characteristics were compared between the OPCAB and conversion groups.

Table 1. Data related to conversion in our patient sample

Variable	Conversion (n=16)
Urgency of conversion	
Urgent or emergent conversion	13
Elective conversion	3
Cause of conversion	
Hemodynamic instability	12
Ventricular fibrillation	1
Anastomotic difficulty	3
Timing of conversion	
During anastomosis of the circumflex coronary artery	11
During anastomosis of the right coronary artery	4
During anastomosis of the left descending coronary artery	1

1) Statistical analysis

Numerical variables were compared in an unadjusted manner using the two-sample Student t-test, and categorical variables were compared across groups using the chi-square or Fisher exact test. Independent risk factors for conversion were identified through multivariable regression analysis. Logistic regression analysis was used for adjustments. The backward elimination method was used to model logistic re-

Table 2. Comparison of preoperative data between the OPCAB and conversion groups

Variable	OPCAB (n=84)	Conversion (n=16)	p-value
Patient profile			
Age (yr)	64.5±10.4	64.5±9.2	0.986
Age >70 yr	26 (31.0)	7 (43.8)	0.318
Age >75 yr	11 (13.1)	0	0.204
Sex (female)	21 (25.0)	5 (31.3)	0.756
Acute myocardial infarction	15 (18.0)	8 (50.0)	0.009
Smoking	36 (43.4)	6 (37.5)	0.691
Body surface area (m^2)	1.713±0.164	1.776±0.210	0.178
Underlying disease			
Hypertension	61 (73.5)	13 (81.3)	0.552
Diabetes mellitus	39 (47.0)	9 (56.3)	0.471
Cerebrovascular accident	7 (8.43)	1 (6.3)	>0.999
Chronic renal failure	7 (8.43)	0	0.594
Asthma	0	1 (6.3)	0.160
Dyslipidemia	63 (75.0)	7 (43.8)	0.018
Chronic obstructive pulmonary disease	0	2 (12.5)	0.024
Preoperative atrial fibrillation	3 (3.6)	2 (12.5)	0.180
Preoperative data			
Aspirin	80 (96.4)	14 (87.5)	0.245
Clopidogrel	47 (56.6)	11 (68.8)	0.342
3-Vessel disease	68 (81.0)	15 (93.8)	0.294
Mean blood pressure (mm Hg)	88.1±10.5	84.5±12.0	0.220
Hemoglobin (g/dL)	12.7±1.9	13.0±1.6	0.610
Blood urea nitrogen (mg/dL)	19.1±11.9	20.0±10.6	0.774
Creatine (mg/dL)	1.3±1.5	1.1±1.1	0.646
Creatine kinase–myocardial band (ng/mL)	5.46±16.32	27.43±68.9	0.224
Troponin-I (ng/mL)	1.29±3.86	2.38±3.91	0.322

Values are presented as mean±standard deviation or number (%).
OPCAB, off-pump coronary artery bypass.

Table 3. Comparison of preoperative factors related to the left ventricle

Preoperative LV factors	Off-pump coronary artery bypass (n=84)	Conversion (n=16)	p-value
Mitral regurgitation	20 (23.8)	4 (25.0)	>0.999
LVEF (%)	50.5±13.5	45.2±13.5	0.154
LVEF <40%	21 (25.0)	6 (37.5)	0.359
LVEF <30%	5 (6.0)	1 (6.3)	>0.999
LV end-diastolic diameter (mm)	49.6±6.08	51.5±8.38	0.287
Interventricular septum dimension at diastole (mm)	9.9±2.21	10.3±2.93	0.675
LV posterior wall dimension at diastole (mm)	9.5±1.84	9.7±2.4	0.739

Values are presented as number (%) or mean±standard deviation.
LVEF, left ventricular ejection fraction; LV, left ventricular.

Table 4. Comparison of operative and postoperative data between the OPCAB and conversion groups

Postoperative outcomes	OPCAB (n=84)	Conversion (n=16)	p-value
Atrial fibrillation	20 (24.1)	2 (12.5)	0.512
Left ventricular ejection fraction (%)	52.3±14.2	50.1±13.9	0.566
Hemoglobin (g/dL)	11.1±1.2	11.5±1.4	0.228
Blood urea nitrogen (mg/dL)	17.7±10.5	18.5±7.3	0.774
Creatine (mg/dL)	1.2±1.4	1.1±1.1	0.838
Hospital stay (day)	12.0±10.9	13.3±8.9	0.678
Chest tube drainage (mL)	966.9±793.6	1,538.1±956.7	0.012
Ventilator duration (hr)	29.9±226.3	9.4±6.8	0.719
Creatine kinase-myocardial band (ng/mL)	2.52±2.79	18.7±18.55	0.269
TnI (immediately after operation, ng/mL)	1.7±1.67	3.81±2.31	0.011
TnI (6 hr after operation, ng/mL)	3.96±5.05	6.40±4.14	0.249
TnI (18 hr after operation, ng/mL)	5.20±10.62	4.44±3.20	0.856
TnI (maximum value after operation, ng/mL)	5.70±10.25	6.92±4.00	0.746
No. of grafts	3.1±0.7	3.3±0.4	0.519

Values are presented as number (%) or mean±standard deviation.
OPCAB, off-pump coronary artery bypass; TnI, troponin I.

gression analysis. Logistic regression analysis was used to analyze the associations between conversion and the postoperative outcomes. Finally, Kaplan-Meier analysis was used to analyze the estimated early and late survival associated with convertsion. This statistical estimation was performed using IBM SPSS ver. 23.0 (IBM Co., Armonk, NY, USA).

Results

Conversion was emergently performed in 12 patients due to hypotension (systolic blood pressure <70 mm Hg without recovery after ceasing cardiac manipulation), and in 1 patient due to ventricular fibrillation. Three patients were electively converted to ONCAB due to anastomotic difficulties. The coronary anastomoses that prompted conversion involved the Cx in 11 cases, the RCA in 4 cases, and the LAD in 1 case (Table 1). Cardioplegia was used in 10 patients (62.5%) in the conversion group. The on-pump beating-heart technique was used in the other 6 patients according to the surgeon's preference.

The patients' demographic and preoperative characteristics are compared in Table 2. AMI, chronic obstructive pulmonary disease, and dyslipidemia were statistically significant risk factors for conversion to ONCAB (p=0.009, p=0.024, and p=0.018, respectively). Thus, these 3 variables were included in the adjusted multivariable model. After adjustment, only the preoperative diagnosis of AMI was identified as an independent risk factor for conversion to ONCAB (adjusted odds ratio, 4.238; 95% confidence interval, 1.2 to 19.2; p=0.025). Regarding LV-related risk factors for conversion, a comparison of the LV dimensions, wall

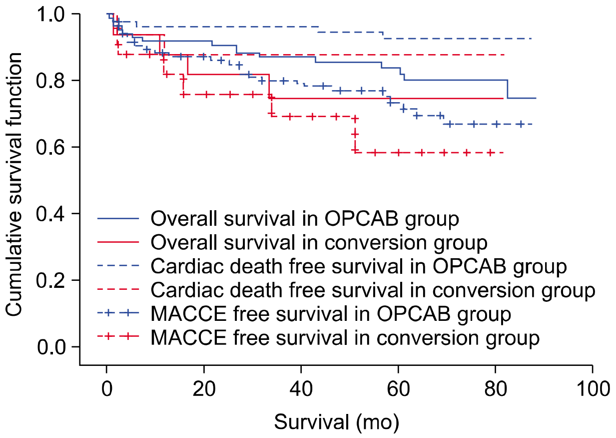

Fig. 1. Kaplan-Meier survival graph. OPCAB, off-pump coronary artery bypass; MACCE, major adverse cardiac and cerebrovascular event.

thickness, LV function, and MR between the two groups is presented in Table 3. No LV-related indices showed statistically significant differences.

The operative and postoperative variables are summarized in Table 4. The amount of chest tube drainage (CTD) between the 2 groups was the only statistically significant difference (p=0.012).

Early mortality occurred in 4 patients (4.7%) in the OPCAB group and 0 (0%) in the conversion group. The causes of early mortality in the OPCAB group were low cardiac output syndrome in 2 cases (2.3%) and pneumonia in the other 2 (2.3%), following early morbidity. Early mortality did not show a statistically significant difference between the groups. Two cases of early morbidity occurred in the OPCAB group (2.3%): 1 patient had an intracranial hemorrhage due to a CVA and the other patient underwent prolonged ventilator care. Both patients died of pneumonia, on the 58th and 33rd day postoperatively, respectively. In the conversion group, 2 patients (12.5%) underwent reoperations for bleeding. They were discharged home without complications. The amount of CTD was significantly greater in the conversion group than in the OPCAB group (p=0.012).

According to the results of the univariate analysis, reoperation for bleeding was significantly more frequent in the conversion group than in the OPCAB group (p=0.024). However, the results of the multivariate analysis did not show statistically significant differences (p=0.999).

Late mortality and MACCEs were estimated as long-term composite endpoints. MACCEs occurred in 12 patients (14.3%) in the OPCAB group and 3 patients (18.8%) in the conversion group. The rate of MACCEs was not significantly different between the 2 groups. In the OPCAB group, 7 patients were diagnosed as having a new MI. Three of them underwent percutaneous coronary intervention, and the others recovered without reintervention. Another 3 patients were admitted for heart failure management, and 1 case each of cerebral hemorrhage and cerebral infarction occurred. In the conversion group, 1 patient each had MI, cerebral infarction, and heart failure that required hospital admission. Late mortality occurred in 12 patients (14.3%) in the OPCAB group and 4 (25.0%) in the conversion group. The causes of late mortality in the OPCAB group were sepsis in 2 cases (2.3%); sudden cardiac death in 2 cases (2.3%); and dementia, CVA, MI, brain cancer, trauma, and pneumonia in 1 case (1.2%) each. Two cases (2.3%) had unknown causes of death. The causes of late mortality in the conversion group were aplastic anemia in 1 case (6.3%), pancreatic cancer in 1 case (6.3%), and sudden cardiac death in 2 cases (12.5%). The 5-year survival rate was 83.5% in the OPCAB group and 73.9% in the conversion group. Additionally, the MACCE-free 5-year survival rate was 72.4% in the OPCAB group and 56.8% in the conversion group. The cardiac death-free 5-year survival rate was 92.7% in the OPCAB group and 87.5% in the conversion group. None of the survival indices differed between the groups to a statistically significant extent (Fig. 1).

Discussion

Since the introduction of OPCAB, controversy has emerged regarding its superiority to ONCAB. Early recovery after OPCAB due to avoiding CPB is the most important benefit. The adverse effects of CPB involve entire systems of the human body, including the brain, heart, kidneys, and lungs. Furthermore, systemic inflammation due to CPB disturbs immunologic and hematologic systems. Therefore, CPB increases operative risks such as CVA, myocardial injuries, ARF, pulmonary edema, bleeding, and infection. Chowdhury et al. [9] reported favorable outcomes in patients with OPCAB, especially in those with high-risk factors such as old age, female sex, LV dysfunction, and a history of previous stroke or sternotomy. Nevertheless, physicians opposed to OPCAB have insisted that its technical difficulty hinders complete revascularization, predisposes grafts to precocious occlusion, causes more MACCEs, and results in less favorable long-term outcomes. Furthermore, OPCAB operations may nonetheless require CPB for various reasons, including the patient being in an unstable condition, difficult dissection and anastomosis of the target coronary arteries, and revision due to inadequate graft flow.

Acute conversion from OPCAB to ONCAB requires emergent CPB, which increases the risk of morbidity and mortality. Nevertheless, few studies have investigated conversion, especially in association with long-term outcomes. In the literature, the conversion rate has been reported to range from 1.1% to 22.0%, with hemodynamic instability identified as the most common cause of conversion [10]. Conversion rates have been regarded as being dependent on the surgeon's experience. Our policy is the routine use of OPCAB in all patients with CABG, irrespective of their condition, and our threshold for conversion is relatively low. Additionally, the present study included cases of OPCAB within the learning curve of our institution. Therefore, the conversion rate of 16% in our study was high.

Hattler et al. [11] reported that the patency of grafts to the Cx and posterior descending coronary artery was significantly poorer in the OPCAB group than in the ONCAB group, although no statistically significant differences were found in the patency rates of grafts in the LAD or RCA between the two groups. The posterior areas of the LV are regarded as the most challenging for OPCAB. In this study, conversion to ONCAB was performed in 11 cases (68.75%) in which we operated on the Cx, 4 cases (25.0%) involving the RCA, and 1 case (6.25%) involving the LAD. The authors agree that manipulation of the posterior heart is the most difficult step of OPCAB, and suggest that cardiac positioners may be helpful to prevent conversion. Air embolism into the RCA caused ventricular fibrillation in 1 case during saline testing for anastomotic leakage.

Li et al. [12] reported that left main coronary artery disease, heart failure, 3-vessel coronary disease, and MI were associated with conversion [13]. The current study also found that the diagnosis of AMI was an independent risk factor for conversion. Regarding AMI, a severely depressed, dilated, thinned, or thickened LV has been considered to be a risk factor for conversion. The increased MR due to a distorted heart has also been considered to prevent successful OPCAB [14]. However, the present study did not demonstrate that poor LV indices and MR significantly increased the conversion rate. Further studies are needed to clarify the significance of the association of AMI with increased conversion rates.

Mukherjee et al. [15] reported that morbidities such as stroke, MI, renal failure, deep sternal wound infection, bleeding requiring reoperation, IABP, transfusion, and respiratory and gastrointestinal complications were more frequently associated with conversion.

Edgerton et al. [16] classified conversion patients into elective, urgent, and emergent conditions according to the level of urgency of CPB and into the early and late phases of operation according to the timing of conversion; they found higher mortality rates in the urgent/emergent and late conversion groups. The urgency of conversion from OPCAB to ONCAB can predispose patients to ischemic injuries of major organs, which can lead to CVA, MI, ARF, or death. In the present study, no patient in the conversion group exhibited postoperative complications or mortality associated with ischemia of the major organs. Concerning myocardial insults, no statistically significant difference was found in the release of troponin I postoperatively in the conversion and OPCAB groups. In the present study, a period of 5–10 minutes was required to prepare and perform CPB. This timing did not cause CVA, MI, or fatal ischemia of the vital organs. Additionally, our small sample size may have led to a statistically insignificant result.

Many studies regarding OPCAB have reported worse outcomes for the conversion group than for the non-conversion group. Novitzky et al. [17] reported that converted patients had significantly more 30-day complications and deaths than unconverted patients and patients undergoing ONCAB (17.5% vs. 5.7% vs. 5.5%, respectively; $p < 0.001$). They also reported that converted patients had a higher 1-year composite adverse event rate (21.1%) than the other patients [17]. Reeves et al. [5] reported that converted OPCAB was associated with 12-fold and 8-fold higher hospital mortality than ONCAB or OPCAB without conversion, respectively; additionally, converted patients had a 6-fold increased risk of stroke and other serious postoperative complications in comparison to unconverted patients. They also reported that converted patients had an approximately 3-fold increased risk of death for 3 years after surgery than unconverted patients or patients who underwent ONCAB [5].

In contrast with previous reports, the early mortality rate and composite adverse outcomes in the present study were not significantly different between the OPCAB and conversion groups (4.7% vs. 0%, $p > 0.999$ and 2.3% vs. 12.5%, p=0.119, respectively). Moreover, no statistically significant differences were found between these groups in terms of MACCEs (14% vs. 19%, respectively; p=0.704) or the 5-year overall survival rate (83.5% vs. 73.9%, respectively; p=0.281). As previously mentioned, the small number of cases and low threshold for conversion at our institution may be the reasons for this finding. High risks of conversion are mainly due to the emergent situations requiring CPB rather than conversion itself. Most situations that require CPB support can be predicted when preparing and positioning the heart, or dissecting target coronary arteries for distal anastomoses. Therefore, prompt decision-making and the early implementation of CPB are essential to prevent further deterioration during conversion due to ischemia of the coronary artery and other vital organs.

The long-term adverse effects of conversion are controversial. Physicians who favor ONCAB think that patients who undergo conventional CABG have better long-term patency rates than those who undergo OPCAB with or without conversion. These issues must be studied further to reach a definitive conclusion.

Preventing conversion to ONCAB is also important, in addition to the prompt use of CPB. To avoid emergent conversion to ONCAB during OPCAB, physicians use several maneuvers such as grafting the LAD or collateralized vessels first, using epicardial pacing or intracoronary shunts, performing preconditioning trials before arteriotomy, using pharmacologic support or IABP prophylactically, and minimizing compression and retraction of the heart with the use of various cardiac positioners [14]. Kim et al. [18] reported that IABP can maintain a stable condition in patients with OPCAB. IABP would be a good option for facilitating OPCAB. Nevertheless, it causes vascular complications and requires more resources. Starfish or Urchin heart positioners (Medtronic Inc.) can help maintain a stable condition during OPCAB, but they may cause hematoma in the myocardium or bleeding.

The present study has other limitations in addition to a small sample size. It was a non-randomized, retrospective, observational study based on electronic medical records. It also lacked long-term patency data. These limitations affect the statistical power and implications of the findings of our study.

In conclusion, the preoperative diagnosis of AMI was associated with an increased risk of conversion to ONCAB. No statistically significant differences were found in early morbidity and mortality, MACCEs, or long-term mortality between the OPCAB and conversion groups.

Conflict of interest

No potential conflicts of interest relevant to this article are reported.

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