Successful introduction of off-pump coronary artery bypass grafting in Southeastern Asian countries: A single center's experience in Thailand

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ABSTRACT

Background: Off-pump coronary artery bypass grafting has not been standardized in Southeastern Asian countries because it is technically demanding. However, this method could be suitable for economically disadvantaged institutions because it saves cost on the heart–lung machine. We summarized our results to assess the validity of our early introduction of this method.

Methods: We reviewed the data from 750 patients who underwent off-pump coronary artery bypass grafting at our institution. Before the introduction of off-pump coronary artery bypass grafting, experts from Japan were enlisted to teach our surgeons technicalities of the procedure. The primary outcome was in-hospital mortality, and secondary outcomes included any major adverse cardiac or cerebrovascular event.

Results: The in-hospital mortality rate was 1.5%. The rates of survival and freedom from major adverse cardiac or cerebrovascular event 3 years after the operation were 92.5% ± 1.8% and 90.7% ± 2.2%, respectively. In the multivariable analysis, the independent risk factors for major adverse cardiac or cerebrovascular event were chronic obstructive pulmonary disease (adjusted hazard ratio = 2.35, 95% confidence interval = 1.35–4.10, P = .003) and renal insufficiency (adjusted hazard ratio = 2.70, 95% confidence interval = 1.52–4.80, P = .001), whereas risk factors for in-hospital death were pump conversion (relative risk = 17.4, 95% confidence interval = 1.63–4.41, P < .001).

Conclusion: Successful introduction of off-pump coronary artery bypass grafting provided a favorable outcome almost equal to that in high-volume centers in developed countries.

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INTRODUCTION

Technical considerations required for off-pump coronary artery bypass grafting (OPCAB) have been established and applied for the past 20 years [1,2]. However, this method has not been standardized in Southeastern Asian countries, likely because it is still regarded as a technically demanding procedure. Opponents of OPCAB in Southeastern Asian countries regard OPCAB and on-pump arrested coronary artery bypass grafting (ONCAB) as equally invasive in terms of the requirement for a sternotomy incision. Another reason for the low use of OPCAB is speculative and might be related to the technical complexity of OPCAB, with concerns related to graft patency and complete revascularization with multiple arterial grafts [3], which are recommended for achieving long-term arterial patency.

However, one advantage of OPCAB is the absence of the heart–lung machine, which results in medical cost savings and is also physiologically less invasive. This aspect is quite crucial for economically disadvantaged countries. From this point of view, there could be great value in the introduction of the OPCAB technique in Southeastern Asian countries.

Our hospital is a regional hospital supported by the Thailand government, and the budget for medical service is relatively small. In 2011, during the commencement of service in the Department of Cardiothoracic Surgery, we spent several months learning the OPCAB method directly from several experts in Japan, where approximately 60% of cardiovascular
units adopt the OPCAB method [4]. Surgeons in our service also underwent repeated simulation through off-the-job training. Consequently, since the beginning of our service, OPCAB has been the first-choice method for almost all patients with coronary artery disease (CAD).

The aim of this study was to determine the feasibility of the early but safe introduction of this technique for patients with CAD in a provincial area in Thailand.

METHODS

Patient Characteristics. From April 2011 to November 2017, 812 people underwent CABG in our center. Among all patients, 750 (92.4%) underwent OPCAB and 62 (7.6%) who had multiple small, diffused target vessels and poor left ventricular function underwent ONCAB at Lampang Hospital, Lampang, Thailand. In this study, 19 patients (2.5%) had previous history of coronary intervention with cardiac stent who all had single- or double-vessel disease in the past. The indication of surgical interventions for the patients with CAD in our unit is (i) triple-vessel disease, (ii) double-vessel diseases with significant stenosis in the proximal portion of LAD, and (iii) relatively young patient who have significant stenosis in proximal LAD. We do not attack single or double target vessels in general if they exist in RCA and/or LCx, not in LAD. We defined low ejection fraction as <35% of ejection fraction and renal insufficiency as an estimated glomerular filtration rate [5] (GFR) < 60 mL·min⁻¹·1.73 m²⁻².

For this study, we retrospectively reviewed the medical records of all patients who underwent OPCAB in our institution. We extracted patient characteristics, preoperative evaluation details, operative procedures, and postoperative outcomes. The primary outcome of this study was in-hospital mortality, and the secondary outcomes were overall mortality and any major adverse cardiac or cerebrovascular event (MACCE). MACCE included myocardial infarction, cardiac death, heart failure requiring hospitalization, repeat revascularization, and stroke [6]. The institutional review board of Lampang Hospital approved this retrospective study and waived the need for written patient consent.

Surgical Procedure. Before the commencement of OPCAB use in our center, several experienced OPCAB experts from Japan, where OPCAB has been widely popularized, taught our surgeons technicalities of the procedure. In addition, all members in the unit underwent repeated off-the-job training, including a wet lab or cadaver training and case studies on the web.

The operative procedures were as follows: A median sternotomy was performed, followed by harvesting of the internal thoracic artery in a full skeletonized fashion. The target vessel for each anastomosis was exposed appropriately using a tissue stabilizer (Octopus tissue stabilizer, Medtronic Inc, Minneapolis, MN, USA) with or without a deep pericardial stitch or heart positioner. Complete revascularization of the major coronary artery branches was achieved in every case. On-pump conversion was considered if the intraoperative transthoracal echocardiography (TEE) revealed aggravation of mitral regurgitation or a sustained ventricular arrhythmia accompanied by the loss of blood pressure in the early phase of the operation.

Follow-Up. Information on all causes of death and cardiac complications during the follow-up period was collected and entered into the Lampang Hospital databank. All patients in this study were directly followed up 2 weeks, 1 month, and 6 months after the operation at our outpatient clinic. In addition, the chief surgeon (NA) and outpatient clinic manager kept in touch with the patients or the patients’ family members through telephone calls every 6 months. All data were documented to ascertain the follow-up and end points. Loss of follow-up rate in this study at 1, 3, and 5 years was 0%, 0.7%, and 1.6%, respectively, and these patients were excluded in the analysis of survival and MACCE free in the mid or long term because the power of the number seems quite trivial. Postoperative follow-up coronary angiography was not routinely performed because of the lack of insurance reimbursement for this procedure in Thailand, but it was considered for patients who developed clinical symptoms indicative of suspected cardiac ischemia.

Statistical Analysis. Baseline patient characteristics, operative data, postoperative complications, and outcome rates were compared using Pearson’s chi-squared test or Fisher’s exact test for categorical variables or using Student’s t test or the Wilcoxon rank-sum test for continuous variables. For the time-to-event analysis, log-rank tests and the Kaplan–Meier method were used. To identify potential risk factors of hospital death and MACCE, each variable of the baseline characteristics and operative data was included in the univariable analysis and then used for multivariable risk regression analyses with the step-backward elimination method, which was presented as risk ratio (RR) with a 95% confidence interval (CI). To identify independent prognostic factors of MACCE, a univariable or multivariable Cox regression analysis was used, which was presented as the hazard ratio (HR) with 95% CI. Any risk factors or prognostic factors with a P value < .1 in the univariable analysis and other potential clinical confounders associated with in-hospital mortality or MACCE were included in the multivariable analysis. We tested for multicollinearity of independent factors before performing multivariable analysis. The Kaplan–Meier method was used to demonstrate overall survival and freedom from MACCE. Statistical analyses were performed using STATA version 15.1 (StataCorp LP, College Station, TX, USA).

RESULTS

This study included 750 patients. Preoperative patient characteristics are listed in Table 1. The patients consisted of 418 men and 332 women, with a mean age of 64.3 ± 8.5 years. The mean New York Heart Association (NYHA) classification was 2.7 ± 0.6. The mean Canadian

| Variable | Number (%) or mean ± SD |
|----------|-------------------------|
| Age, y   | 64.3 ± 8.5               |
| Male:female | 418 (55.7):332 (44.3)     |
| BMI, kg·m⁻² | 23.3 ± 3.8               |
| NYHA class | 2.7 ± 0.6                |
| Canadian Cardiovascular Society class | 3.2 ± 0.5 |
| Taking β-blocker | 741 (98.8) |
| Taking ARB/ACE-I | 662 (88.3) |
| Taking statin | 727 (96.9)               |
| Smoking history | 277 (36.9)               |
| Comorbid diseases |                       |
| Diabetes mellitus | 329 (44.0)               |
| Oral medication | 254 (33.9)               |
| Insulin use | 75 (10.1)                |
| Previous stroke or TIA | 36 (4.8)               |
| Peripheral vascular disease | 94 (12.5)             |
| Chronic obstructive pulmonary disease | 81 (11.0)              |
| GFR, [mg/dL]median (IQR) | 1.0 (0.9–1.4)          |
| Renal insufficiency | 138 (18.4)              |
| On hemodialysis | 16 (2.1)                |
| LVEF, % | 51.4 ± 15.5              |
| Low EF (EF < 35%), % | 138 (18.4)              |
| Preoperative PCI history | 19 (2.5)               |
| Recent MI | 481 (64.1)               |
| STEMI | 105 (14.0)               |
| Preoperative IABP support | 140 (18.7)            |
| Euro score II, median (IQR) | 2.1 (1.2–3.8)          |
| Diagnosis |                       |
| Single-vessel disease | 22 (3.0)                |
| Double-vessel disease | 92 (12.3)               |
| Triple-vessel disease | 632 (84.7)              |

BMI, body mass index; NYHA, New York Heart Association; ARB, angiotensin II receptor blocker; ACE-I, angiotensin-converting enzyme inhibitor; TIA, transient ischemic attack; IQR, interquartile range; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; MI, myocardial infarction; STEMI, ST-segment elevation MI; and IABP, intraoperative balloon pump.
Cardiovascular Society Classification was 3.2 ± 0.5. The median EuroSCORE II was 2.1 (interquartile range [IQR] = 1.3–3.8). The number of patients with a low ejection fraction was 138 (18.4%) and that with renal insufficiency was 138 (18.4%). One hundred forty patients (18.7%) required preoperative intra-aortic balloon pump (IABP) support.

Intraoperative results, postoperative results, and long-term outcomes are presented in Table 2. The mean number of anastomoses per procedure was 3.4 ± 0.9. The conduits used in this series were the left internal thoracic artery (697 cases), right internal thoracic artery (177 cases), gastroepiploic artery (54 cases), radial artery (172 cases), and saphenous vein (590 cases). Revascularization using multiple arterial grafts was performed in more than one-third of the patients (290 cases, 38.7%). Total arterial revascularization was performed in 152 cases (20.3%).

In-hospital mortality occurred in 11 cases (1.5%) in the early perioperative period. Of all, 4 patients died in the hospital. Reasons for the intraoperative pump conversion were aggravation of ischemic mitral regurgitation (1 case), perioperative myocardial infarction (1 case), and hemodynamic collapse with or without sustained ventricular arrhythmia (11 cases) Of all, 4 patients died in the hospital. In addition, we compared pump conversion, mortality, and perioperative MACCE free rate in the first and second periods (N = 375, respectively) and found that the pump conversion and mortality were significantly higher in the early period compared to the late period (pump conversion, 1.6% vs 0.4%, P = .03; mortality, 1.9% vs 0.8%, P = .04), whereas there was no significant difference in perioperative MACCE free rate between these 2 periods (perioperative MACCE free rate, 98.7% ± 1.1% vs 98.2% ± 1.2%, P = .87).

Table 3 presents the univariable and multivariable risk regression analyses performed to identify risk factors for in-hospital mortality. The univariable analysis revealed that the risk factors for in-hospital mortality were older age, chronic obstructive pulmonary disease (COPD), higher NYHA classification, preoperative IABP, GFR, preoperative renal insufficiency, and pump conversion. However, the multivariable analysis revealed that pump conversion was a significant and strong negative factor for in-hospital mortality (pump conversion, RR = 17.4, CI: 1.63–4.41, P < .001, Table 3). For long-term follow-up, the median follow-up
dialysis for renal failure, and 8 cases (1.1%) experienced postoperative stroke with clinical symptoms (Table 2).

There were 13 patients (1.7%) who required on-pump conversion. Reasons for the intraoperative pump conversion were aggravation of ischemic mitral regurgitation (1 case), perioperative myocardial infarction (1 case), and hemodynamic collapse with or without sustained ventricular arrhythmia (11 cases) Of all, 4 patients died in the hospital.
time was 25.7 months (IQR: 14.5–42.8). The overall survival rate at 1, 3, and 5 years was 96.8% ± 2.1%, 92.5% ± 1.8%, and 82.4% ± 2.6%, respectively (Fig 1).

The univariable analysis indicated that the risk factors for MACCE included COPD, NYHA class, recent myocardial infarction, low EF, GFR, and renal insufficiency. In addition, the multivariable analysis revealed that COPD and renal insufficiency were independent risk factors for MACCE (COPD, HR = 2.35, 95% CI: 1.35–4.10, P = .003; renal insufficiency, HR = 2.70, 95% CI: 1.52–4.80, P = .001; Table 4). In addition, patients who underwent OPCAB with the use of multiple arterial grafts were significantly less likely to have MACCE (HR = 0.49, 95% CI: 0.26–0.90, P = .022; Table 4). Freedom from MACCE at 1, 3, and 5 years was 95.9% ± 1.7%, 90.7% ± 2.2%, and 83.2% ± 1.9%, respectively (Fig 2). And the breakdown of the type of the MACCE such as myocardial infarction (MI), cardiac death, heart failure requiring hospitalization, repeat revascularization, and stroke in the follow-up periods was shown in Figure 3. Freedom from MI, cardiac death, heart failure requiring hospitalization, repeat revascularization, and stroke rates at 5 years were 97.6% ± 1.3%, 97.2% ± 1.1%, 94.0% ± 2.2%, 94.7% ± 2.1%, and 96.0% ± 1.2%, respectively (Fig 3, A–E).

**DISCUSSION**

The aim of this study was to determine the safety of initiating early introduction of a technically demanding operative method in a surgical unit startup. Similar research on whether OPCAB can be safely taught to OPCAB flyers was previously conducted [7], which concluded convincingly that OPCAB can indeed be taught without adverse effects under supervision and backup from experts. The operative outcome in this study revealed that in-hospital mortality was 1.5%, the survival rate at 3 years was 92.5%, and the freedom from MACCE at 3 years was 90.7%; thus, the introduction of the OPCAB technique in our unit appears to have been successful, as these outcomes were almost equal to those from leading OPCAB centers [8–10].

It was quite surprising that all the staff surgeon in Lampang had a very small number of conventional ONCAB training (around 10 cases) and on-pump beating CABG training (a several cases) prior to the commencement of OPCAB training in Lampang. Besides, in the introduction

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**Table 4**

Univariable and multivariable analyses for factors associated with MACCE

| Variable | Univariable analysis | Multivariable analysis |
|----------|----------------------|------------------------|
|          | HR 95% CI  P value    | HR 95% CI  P value    |
| Age      | 1.00 0.97–1.03 .818   |                        |
| Female versus male | 0.76 0.45–1.28 .299   |                        |
| COPD     | 2.09 1.11–3.94 .023   | 2.35 1.35–4.10 .003*   |
| NYHA class| 1.96 1.31–2.93 .001   | 1.36 0.89–2.09 .158   |
| Recent myocardial infarction | 2.65 1.38–5.11 .003   | 1.87 0.97–3.60 .080   |
| Preoperative IABP | 1.63 0.93–2.86 .088   |                        |
| Low EF (<35%) | 2.37 1.37–4.08 .002   | 1.60 0.92–2.81 .090   |
| GFR      | 1.00 0.98–0.99 .008   | 1.00 0.99–1.01 .894   |
| Renal insufficiency | 3.31 1.98–5.53 <.001   | 2.70 1.52–4.80 .001*   |

HR, hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association; IABP, intra-aortic balloon pump; and EF, ejection fraction.

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![Fig 2. Freedom from MACCE. The freedom from MACCE at 1, 3, and 5 years was 95.9% ± 1.7%, 90.7% ± 2.2%, and 83.2% ± 1.9%, respectively.](image)

![Fig 3. Breakdown of the type of the MACCE.](image)
period, several OPCAB expert surgeons came to Thailand and instructed how to perform OPCAB in the workshops and all staff surgeons had both wet lab and simulator-based skill training. However, all 750 cases in the current study were performed by the staff surgeon in Lampang hospital. The novel finding of this study is that the scale or area of the hospital is not always a hurdle to bringing new surgical technology into the unit if technical support is surely gained in an established manner. In addition to hands-on training in real practice, recent advances in off-the-job training, including simulator-based skill training, case studies on the web, and teamwork simulations using simulated operation scenarios, have contributed to the skill acquisition of the flyers [11].

The historical and social background in Thailand has driven domestic surgeons to attempt to master the OPCAB technique in earnest. First, the number of active cardiac surgeons in Thailand is as small as 100, whereas the annual number of cardiac surgeries in the leading hospital in Thailand is more than 1,000. This situation provides each surgeon with a repeated chance to be exposed to cardiac surgeries as an operator, which can increase the sophistication of surgical skills over a short period. A recent report assessing OPCAB reported no significant difference between an OPCAB trainee and consultant outcomes in institutions with high case volumes [12].

Second, the budget for medical service is not always sufficient in Thailand. For example, in the government hospital, the charge for patients for any medical service, including admission and the entire surgical treatment, is only 1 to 2 dollars on average [13] despite the fact that the actual expense of providing any medical service is considerable. Under such a situation, cost-effective medical treatment is quite important. For this reason, OPCAB, which avoids the use of a costly heart–lung machine, is a reasonable method for CAD patients, especially in economically disadvantaged countries. Previous studies have compared costs of surgery and intensive care unit stay for OPCAB and those for conventional on-pump arrested CABG, with some concluding that OPCAB could reduce the cost more than conventional CABG with [14,15] or without [16] statistical significance, although the cost in the perioperative period is in fact multifactorial.

In this study, postoperative renal failure and COPD were found to be independent risk factors for MACCE. In Thailand, as in other low- and middle-income countries, renal replacement therapy by hemodialysis for postoperative renal failure is not standard [17], possibly because of economic reasons. Therefore, insurance reimbursement for postoperative hemodialysis for new renal failure is generally not approved. Moreover, there is a high rate of COPD because smoking is still very prevalent in Thailand [18,19]. Because of these economic and social backgrounds, OPCAB, which protects organ function from possible damage caused by on-pump heart arrest and lowers surgical costs, has been regarded as a better method for CAD patients in this country.

We experienced 13 cases (1.7%) of on-pump conversion in this study. With regard to the intraoperative risk management for OPCAB, it is essential to determine the optimal time for commencing IABP support [20] or on-pump conversion [21,22]. In our unit, prophylactic IABP support is established routinely for patients with significant left ventricular dysfunction to maintain hemodynamics throughout the operation. Another clinical hallmark of hemodynamic crash is a significant change in the color of the right atrium, right ventricle, and left ventricle. If the color of these areas becomes much darker and more congestive, it is a sign that the condition of the heart has deteriorated severely, and prompt assessment for cardiac contraction or a change in the severity of mitral regurgitation by TEE is required.

The limitations of this study include its retrospective nature and the low number of in-hospital deaths, which caused an overestimate of the risk ratio with a wide 95% CI. In addition, this study did not compare the outcome of OPCAB and ONCAB over the same period because the number of patients undergoing ONCAB so far in our hospital has been quite small, potentially making it difficult to properly perform a statistical analysis between these 2 groups. Thus, the present study cannot determine the superiority of OPCAB over ONCAB. Moreover, the number of perioperative and postoperative clinical parameters in this study was not very large, and the median follow-up period was relatively short (25.7 months).

In conclusion, under the technical support from experts in Japan combined with several kinds of off-the-job training, the introduction of OPCAB can be achieved safely and satisfactorily. Clinical outcomes in the short and medium terms in this study were almost equal to those in high-volume centers in developed countries.

Author Contribution

TS contributed to the design, analyzed the data, and wrote the manuscript. AT performed the statistical calculations. TS, NA, and HK conceived the study and were in charge of overall direction and planning. AC, BS, and JC carried out the implementation.

Conflict of Interest

All authors have no conflicts of interest or financial ties to disclose.

Funding Source

This research was conducted without financial support.

Ethic Approval

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. The institutional review board of Lampang Hospital approved this retrospective study and waived the need for written patient consent.

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