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Comparison of Coronary Artery Bypass Graft-First and Percutaneous Coronary Intervention-First Approaches for 2-Stage Hybrid Coronary Revascularization

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Background: Hybrid coronary revascularization (HCR) was developed to combine the advantages of coronary artery bypass graft (CABG) with percutaneous coronary intervention (PCI). However, it is still controversial whether it is more optimal to perform CABG or PCI first. The purpose of this study was to compare the clinical outcomes of these 2 approaches. **Methods:** Eighty patients who underwent HCR from May 2010 to December 2015 were enrolled in this retrospective analysis. The CABG-first group comprised 12 patients and the PCI-first group comprised 68 patients. Outcomes of interest included in-hospital perioperative factors, major adverse cardiac and cerebrovascular events (MACCEs), and the incidence of repeated revascularization, especially for the target vessel lesion. **Results:** No significant difference was found in the amount of postoperative bleeding (p=0.239). The incidence of MACCEs was similar between the CABG-first and PCI-first groups (1 of 12 [8.3%] vs. 5 of 68 [7.4%], p＞0.999). Repeated revascularization was performed on 3 patients (25%) in the CABG-first and 9 patients (13.2%) in the PCI-first group (p=0.376). **Conclusion:** There were no significant differences in postoperative and medium-term outcomes between the CABG-first and PCI-first groups. Based on these results, it can be inferred that it is safe to opt for either CABG or PCI as the primary procedure in 2-stage HCR.

Key words: 1. Coronary artery disease
2. Coronary artery bypass surgery
3. Percutaneous coronary intervention
4. Hybrid operation

Introduction

Hybrid coronary revascularization (HCR) was devised in the mid-1990s [1] to combine the advantages of left internal thoracic artery (LITA) to left anterior descending (LAD) coronary artery bypass graft (CABG) with percutaneous coronary intervention (PCI) on non-LAD lesions. This new strategy for controlling coronary artery disease provides greater durability without the trauma and prolonged recovery time of conventional CABG, and was therefore a major advance in cardiovascular medicine [2].

HCR can be performed either simultaneously or as a 2-stage procedure. The former approach implies concurrent CABG and PCI in a hybrid operating room, with CABG followed by PCI within minutes. However, this 1-stage procedure can be undertaken only in a single hybrid suite featuring surgical and interventional equipment in the same place. Conversely, a successful 2-stage approach requires a surgical bypass operation in a conventional operating room and percutaneous intervention in a pre-existing catheterization laboratory.

When surgeons and interventional cardiologists perform a 2-stage procedure, the sequence of PCI and CABG should be determined carefully in order to obtain better results with fewer complications. The CABG-first approach enables angiographic validation of the LITA–LAD graft, but poses the potential risk of ischemia of the non-LAD lesion. Although the PCI-first strategy overcomes this limitation, it presents the disadvantage of increased bleeding risk due to antiplatelet therapy after percutaneous intervention. Research that directly compares the 2 different procedure orders for HCR is lacking.

The purpose of this study is to compare the clinical outcomes of patients undergoing CABG-first HCR and PCI-first HCR. Postoperative data were assessed, as well as the medium-term outcomes of major adverse events and repeated revascularization.

Methods

A total of 411 patients underwent elective CABG at Seoul Saint Mary's Hospital from May 2010 to December 2015. A total of 80 patients underwent 2-stage HCR during this study period, and they were enrolled in the retrospective analysis. Patients were categorized into 2 groups: the CABG-first (CABGF) group, which comprised 12 patients, and the PCI-first (PCIF) group, which comprised 68 patients.

HCR was defined as a planned surgical revascularization of the LITA–LAD juncture combined with percutaneous revascularization of at least 1 non-LAD target within 2 weeks, whether during a single or multiple hospitalizations. Patients for whom PCI alone posed high risks, either with diffuse stenosis or severe calcification, were considered candidates for HCR. Relative contraindications for HCR included significant (stenosis ≥50%) left main disease, a non-

graftable LAD, hemodynamic instability, an emergency situation, and non-LAD disease for which treatment with PCI was not anticipated to be successful.

For HCR procedures, the order and timing of the surgical and percutaneous interventional procedures are determined by the patient's coronary anatomy or the location of the culprit lesion, which is a joint decision between the surgeon and the interventional cardiologist. Decisions in this study were made after a diagnostic angiogram and followed by PCI on non-LAD lesions immediately if HCR could be safely performed. Therefore the number of PCIF patients was greater than the number of CABGF patients. Second generation drug-eluting stents (XIENCE; Abbott Vascular, Santa Clara, CA, USA) were used for PCI in all patients. All of the operations were performed with off-pump CABG through a sternotomy, with a small skin incision. With PCIF, the antiplatelet regimen, including clopidogrel (75 mg daily), was continued during the course of HCR. With CABGF, clopidogrel (75 mg daily) was administered after the surgery, without an additional loading dose before PCI.

Outcomes of interest included in-hospital outcomes such as reoperation, the amount of bleeding during postoperative 24 hours, the duration of ventilation, and several complications such as atrial fibrillation and renal failure, as well as major adverse cardiac and cerebrovascular events (MACCEs, the composite of death, stroke, and myocardial infarction). In addition, the rates of repeated revascularization, especially for the target vessel lesion, were compared.

To test for differences between the CABGF and PCIF groups, the Student t-test for normally distributed variables and the Mann-Whitney rank sum test for variables with a non-normal distribution were used. The chi-square and Fisher exact tests were used for categorical variables. Time-to-event analyses (MACCE, target vessel revascularization) were conducted using the Kaplan-Meier product limit estimator. The differences were considered to be statistically significant for $p < 0.05$.

Results

All basal characteristics showed no significant differences between the CABGF and PCIF groups ($p > 0.05$) (Table 1). Two CABGF patients (8.3%) and 7 PCIF patients (2.9%, p=0.617) showed clinical pre-

Table 1. Patient demographics and baseline characteristics

Characteristic	Coronary artery bypass graft first (n=12)	Percutaneous coronary intervention first (n=68)	p-value
Age (yr)	65.7±10.6	66.5±9.7	0.787
Male sex	11 (91.7)	53 (77.9)	0.442
Diabetes mellitus	3 (25.0)	36 (52.9)	0.116
Chronic lung disease	2 (16.7)	8 (11.8)	0.641
Dyslipidemia	7 (58.3)	38 (55.9)	>0.999
Hypertension	8 (66.7)	51 (75.0)	0.723
Renal failure	1 (8.3)	7 (10.3)	>0.999
Prior myocardial infarction	1 (8.3)	2 (2.9)	0.390
Left ventricular ejection fraction (%)	59.18±7.5	59.08±6.7	0.963
European System for Cardiac Operative Risk Evaluation	4.33±2.5	4.24±2.3	0.892
No. of diseased vessels	2.83±0.4	2.74±0.4	0.476
Single-vessel	0	0	>0.999
Double-vessel	2 (16.7)	18 (26.5)	0.720
Triple-vessel	10 (83.3)	50 (73.5)	0.720
Location of diseased vessels			
Left anterior descending coronary artery	12 (100.0)	68 (100.0)	>0.999
Circumflex distribution	12 (100.0)	57 (83.8)	0.201
Right coronary artery distribution	10 (83.3)	61 (89.7)	0.617
Coronary artery disease presentation			
Stable angina	3 (25.0)	30 (44.1)	0.341
Unstable angina	7 (58.3)	31 (45.6)	0.535
Non-STEMI	2 (16.7)	6 (8.8)	0.344
STEMI	0	1 (1.3)	>0.999

Values are presented as mean±standard deviation or number (%).
STEMI, ST-elevation myocardial infarction.

Table 2. Procedural characteristics

Variable	Coronary artery bypass graft first (n=12)	Percutaneous coronary intervention first (n=68)	p-value
Interval between 2 procedures (day)	4.67±1.5	4.04±2.9	0.156
No. of revascularizations	2.17±0.4	2.31±0.5	0.319
No. of stented lesions	1.17±0.4	1.31±0.5	0.319
Operative outcomes			
Total operating time (min)	127.83±25.4	136.90±29.6	0.322
Cardiopulmonary bypass use	0	0	>0.999
Bypassed left internal thoracic artery–left anterior descending coronary artery	12 (100.0)	68 (100.0)	>0.999

Values are presented as mean±standard deviation or number (%).

sentations of myocardial infarction. More than 70% of the study patients had triple-vessel disease (83.3% for CABGF versus 73.5% for PCIF, p=0.720). The intervals between the 2 procedures were 4.67±1.5 days for CABGF and 4.04±2.9 days for PCIF (p=0.156). The numbers of revascularized vessels for CABGF and PCIF were 2.17±0.4 and 2.31±0.5, respectively (p= 0.319) (Table 2). All patients underwent off-pump CABG without cardiopulmonary bypass conversion.

The mean amount of chest tube drainage for 24 hours after the operation was numerically greater in the PCIF patients (723.0±283.8 mL) than in the CABGF patients (616.3±307.6 mL). However, the difference was not statistically significant (p=0.239).

Table 3. In-hospital outcomes

Variable	Total (n=80)	Coronary artery bypass graft first (n=12)	Percutaneous coronary intervention first (n=68)	p-value
Chest tube drainage (mL/24 hr)	707.0±288.0	616.3±307.6	723.0±283.8	0.239
Use of blood products	35 (43.8)	4 (33.3)	31 (45.6)	0.536
Reoperation	2 (2.5)	1 (8.3)	1 (1.5)	0.279
Duration of ventilator (hr)	5.29±3.8	4.11±1.9	5.50±4.0	0.245
Renal failure	1 (1.3)	0	1 (1.5)	>0.999
Atrial fibrillation	6 (7.5)	1 (8.3)	5 (7.4)	>0.999
Stroke	1 (1.3)	0	1 (1.5)	>0.999
Myocardial infarction	0	0	0	>0.999
Mortality	0	0	0	>0.999

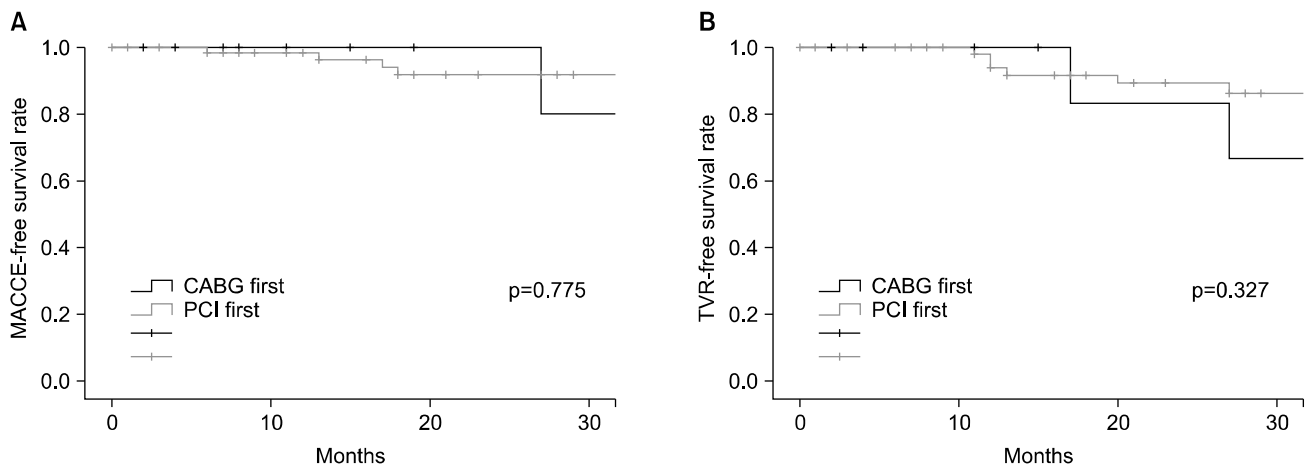Values are presented as mean±standard deviation or number (%).

Fig. 1. Kaplan-Meier curves show no statistically significant differences in MACCE (A) and TVR (B) rates between CABG-first and PCI-first group. MACCE, major adverse cardiac and cerebrovascular events; TVR, target vessel revascularization; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

There was 1 reoperation in each of the 2 groups due to postoperative bleeding (8.3% of CABGF versus 1.5% of PCIF, p=0.279). Postoperative mean duration of ventilation was 4.11±1.9 hours and 5.50±4.0 hours for CABGF and PCIF, respectively (p=0.245). There was no in-hospital mortality or myocardial infarction event after the hybrid procedure in either group. In 1 patient in PCIF, acute renal failure developed, requiring renal replacement therapy. The incidence of postoperative atrial fibrillation was similar for CABGF (n=1, 8.3%) and PCIF (n=5, 7.4%) (p>0.999). A neurovascular event occurred postoperatively in 1 PCIF patient (Table 3) who had a severe stenosis of the left internal carotid artery revealed by preoperative magnetic resonance angiography.

The mean duration of follow-up after the revascularization procedure was 26.53±19.2 months. Six MACCEs were reported in the total population during the follow-up period. There was no significant difference in the time-related incidence of MACCEs between the 2 groups (Fig. 1A). Two patients in PCIF died of pneumonia after 6 months and 4 years, respectively. There was no cardiac-related death in either group, but a myocardial infarction occurred in 1 patient in each of the 2 groups (Table 4). A CABGF patient who had undergone a LITA–LAD bypass followed by PCI on the left circumflex artery complained of chest pain 3 years after the hybrid procedure and was diagnosed with a non-ST-elevation myocardial infarction. Angiographic examination of the patient revealed stenosis of the left main to proximal left circumflex artery, which was revascularized by

Table 4. Incidence of major adverse cardiac and cerebrovascular events

Variable	Total (n=80)	Coronary artery bypass graft first (n=12)	Percutaneous coronary intervention first (n=68)	p-value
Death	2 (2.5)	0	2 (2.9)	>0.999
Cardiac-related death	0	0	0	>0.999
Myocardial infarction	2 (2.5)	1 (8.3)	1 (1.5)	0.279
Stroke	2 (2.5)	0	2 (2.9)	>0.999
Any major adverse cardiac and cerebrovascular events	6 (7.5)	1 (8.3)	5 (7.4)	>0.999

Values are presented as number (%).

Table 5. Details of repeated revascularization events

Variable	Coronary artery bypass graft first (n=12)	Percutaneous coronary intervention first (n=68)	p-value
Follow-up duration (mo)	25.08±20.6	26.78±19.1	0.780
Angiographic follow-up	5 (41.7)	23 (33.8)	0.744
All repeated revascularization	3 (25.0)	9 (13.2)	0.376
Cause of revascularization			
Progression of native disease	3 (25.0)	5 (7.4)	0.094
Lesion in LITA or LITA–left anterior descending coronary artery	0	1 (1.5)	>0.999
In-stent restenosis	0	3 (4.4)	>0.999
Target vessel revascularization	2 (16.7)	6 (8.8)	0.344

Values are presented as mean±standard deviation or number (%).
LITA, left internal mammary artery.

percutaneous intervention. Another PCIF patient underwent CABG after PCI on the proximal left circumflex artery. When the patient was admitted to the institution for myocardial infarction 1 year after the HCR procedure, in-stent restenosis was found on coronary angiography and PCI for repeated revascularization was undertaken successfully.

Angiographic follow-up was performed on 5 CABGF patients (41.7%) and 23 PCIF patients (33.8%, p= 0.744). Incidence of repeated revascularization was not significantly different (p=0.376) between the CABGF (n=3, 25.0%) and PCIF (n=9, 13.2%) groups. All repeated revascularizations were performed by interventional cardiologists. There were no significant differences in the cause of revascularization. Compared with CABGF, PCIF patients had a slightly lower incidence of progression of native diseases (25.0% for CABGF versus 7.4% for PCIF), but the difference was not statistically significant (p=0.094) (Table 5). One LITA occlusion (1.5%) and 3 in-stent restenosis procedures (4.4%) occurred in the PCIF group, and repeated revascularization was applied. Except for 1 patient with in-stent restenosis, the 3 patients men-

tioned above reported no symptoms, but when annual angiographic follow-ups were performed, failures of revascularization were found. The rates of target vessel revascularization in CABGF (n=2, 16.7%) and PCIF (n=6, 8.8%) were not significantly different (p= 0.344). The survival rates for patients who did not undergo target vessel revascularization were also similar between the 2 groups (Fig. 1B).

Discussion

The latest revascularization guidelines have recognized HCR as a feasible alternative to conventional CABG in selected patients [3,4]. Moreover, Puskas et al. [2] recently reported no significant difference in major adverse events rates between patients treated with HCR or multi-vessel PCI. Kang et al. [5] and Hwang et al. [6] also reported satisfactory short-term outcomes for HCR in selected Korean patients. The rationale for HCR lies in the well-established survival benefits of LITA-to-LAD bypass [7-9], which has been demonstrated to have excellent long-term durability [10], and in the use of newer drug-eluting stent plat-

forms [11] featuring lower stent restenosis and thrombosis rates compared with venous graft stenosis and occlusion rates, respectively [12]. The major advantages of HCR when compared with conventional CABG are thought to be the avoidance of aortic clamping and cardiopulmonary bypass, as well as the minimal invasiveness of the surgical technique [13]. However, the current evidence for HCR is still limited to nonrandomized, single-institution or multicenter experiences that used various clinical criteria and definitions as well as techniques [14].

HCR consists of 2 independent procedures that can be performed at once in a hybrid operating room within minutes of each other, or within hours, days, or even weeks of each other by using a conventional operating room and catheterization facility. Discussion of the advantages and disadvantages of each strategy remains only theoretical due to a lack of reported clinical experience. The proposed advantages of HCR include a shorter recovery time and the possibility of direct conversion to CABG when PCI fails for a non-LAD lesion. Conversely, HCR presents the possible disadvantages of a higher risk of bleeding due to the use of dual antiplatelet therapy and a risk of stent thrombosis due to the inflammatory response to surgery [15], and its application is limited to large collaborating spaces, referred to as hybrid operating rooms.

The majority of HCR procedures were performed in stages rather than simultaneously. In general, the sequence of CABG and PCI is decided by clinical presentation and coronary anatomy through discussion between cardiac surgeons and interventional cardiologists. The American College of Cardiology Foundation/American Heart Association guidelines favor performing CABG first [16]. This approach offers the chance to examine the patency of the LITA graft before stenting non-LAD targets, enabling the surgery to be performed without dual antiplatelet therapy, and providing myocardial protection of LAD territory during PCI on high-risk non-LAD lesions [17]. Conversely, the disadvantages of the CABGF approach include the risk of ischemia of non-LAD territories during the LITA–LAD grafting and the possibility of surgical reintervention following unsuccessful PCI. A PCIF approach is suitable for acute coronary syndrome patients who have a non-LAD culprit lesion and need to be treated by PCI followed by CABG of the LAD. However, a PCIF approach poses disadvantages, including increased bleeding risk due to platelet inhibition and a risk of lability caused by LAD stenosis before CABG. Moreover, the PCIF approach does not allow angiographic confirmation of LITA–LAD patency. Although these expected outcomes should be considered when deciding the order of the hybrid procedure, there are few studies comparing the results of the 2 inverse approaches. Repossini et al. [18], in their subset of a study verifying the safety and feasibility of HCR, compared the outcomes of bleeding, early reintervention, and intensive care unit length of stay between CABGF and PCIF groups and found no differences.

This study is the first and the largest to compare the short- and medium-term outcomes of HCR between CABGF and PCIF groups. It was found that immediate postoperative results such as blood utilization and duration of ventilation were similar between the 2 groups. Additionally, there were no significant differences in the short-term mortality and morbidity or in longer-term outcomes between the CABGF and PCIF approaches. The difference in repeated revascularization events between CABGF and PCIF was not statistically significant. Although the incidence of revascularization for progression of native coronary artery disease was somewhat higher in CABGF than PCIF (25.0% versus 7.4%), this difference was not statistically significant (p=0.094). The prevalence of total repeated revascularization events was 15%, and one-third of the 15% was represented by target vessel revascularization. Other studies comparing hybrid revascularization with conventional CABG or PCI also reported somewhat higher incidences (10%–18%) of repeated coronary revascularizations [2,19], which is similar to the repeated revascularization rates for PCI alone. A potential contributing factor is that angiogram follow-up is conducted more routinely after PCI than after CABG. Nevertheless, these results suggest that careful patient selection for HCR is important for optimal long-term outcomes.

The study had several limitations. First, this study is of a retrospective nature, and thus patient selection bias may have existed. Second, the sample size was small, especially for the CABGF group. Further study with a larger population sample would allow a better understanding of the difference be-

tween the 2 groups. Third, follow-up coronary angio-grams were performed only in selected patients and therefore angiographic data were collected from less than half of the total population.

In summary, the outcomes of CABGF and PCIF HCR showed no differences in in-hospital outcomes, postoperative mortality and morbidity, MACCEs, or repeated revascularization events. Based on our results, it can be inferred that either CABG or PCI can be safely applied as a primary procedure in 2-stage HCR. Further investigation with a randomized controlled study would be necessary to provide a stronger empirical basis for decision-making.

Conflict of interest

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

Acknowledgments

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