□ CLINICAL RESEARCH □

https://doi.org/10.5090/kjtcs.2019.52.2.70

Outcomes of Coronary Artery Bypass Grafting after Extracorporeal Life Support in Patients with Cardiac Arrest or Cardiogenic Shock

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Background: Extracorporeal life support (ECLS) is used as a bridge to revascularization in high-risk patients with ischemic heart disease. We reviewed our experiences of coronary artery bypass grafting (CABG) after ECLS in patients with cardiac arrest or refractory cardiogenic shock. **Methods:** We retrospectively reviewed 4,616 patients who underwent CABG at our institution between May 2006 and February 2017. We identified patients who underwent CABG following ECLS for cardiogenic shock or cardiac arrest. Twenty-three patients (0.5% of all CABG cases) were enrolled in the analysis. Their median age was 65 years (Q1–Q3, 58–77 years). Nine patients (39.1%) were diagnosed with ST-elevation myocardial infarction. Mechanical complications after acute myocardial infarction, including acute mitral regurgitation, left ventricular rupture, and ventricular septal defect, occurred in 9 patients (39.1%). **Results:** The median time from cardiopulmonary resuscitation to ECLS initiation was 25 minutes (Q1–Q3, 18.5–28.5 minutes). Conventional CABG was performed in 10 patients (43.5%) who underwent concomitant intracardiac procedures. Postoperative ECLS was required in 16 patients (69.5%). The rate of successful ECLS weaning was 91.3% (n=21). There were 6 early mortalities (26.1%). **Conclusion:** CABG after ECLS was very rare in real-world circumstances. Although the early mortality rate was high, the risk of mortality may be acceptable under such devastating circumstances.

Key words: 1. Extracorporeal membrane oxygenation
2. Coronary artery bypass surgery

Introduction

Cardiogenic shock and cardiac arrest are the leading causes of death in patients with ischemic heart disease (IHD) [1,2]. In these patients, early revascularization is essential. Percutaneous coronary inter-vention (PCI) can be performed promptly and is relatively noninvasive; therefore, it is the preferred option [3]. However, coronary artery bypass grafting (CABG) is only considered a last resort by most clinicians, since the time to reperfusion is prolonged and there is a high likelihood of cardiac arrest or mul-

ti-organ failure before surgery. However, extracorporeal life support (ECLS) is widely used to stabilize patients before revascularization and even allows successful revascularization in high-risk patients. Several studies on ECLS-supported PCI have been reported [4,5]. The 30-day mortality rate was lower in patients undergoing extracorporeal membrane oxygenation (ECMO)-assisted primary PCI than in patients undergoing PCI without ECMO. However, few studies have investigated ECLS-supported CABG, even though CABG is a feasible option for IHD complicated by hemodynamic compromise [6-8]. Accordingly, we evaluated the outcome of CABG following veno-arterial (VA) ECLS in patients with IHD complicated by cardiogenic shock or cardiac arrest.

Methods

1) Patient population

We retrospectively reviewed 4,616 patients who underwent CABG between May 2006 and January 2017 at Samsung Medical Center. Of these, 29 underwent CABG following VA ECLS for IHD complicated by refractory cardiogenic shock or cardiac arrest. We excluded 3 patients with primary valvular heart disease who suffered from iatrogenic coronary dissection during preoperative coronary angiography because they were not originally indicated for CABG and were promptly cannulated in the intervention room, which could have affected their outcomes. In addition, we also excluded 3 cases in which ECLS was discontinued before CABG. Finally, 23 patients were enrolled in this study.

In addition, we compared the enrolled patients with 44 cases who underwent CABG with an intra-aortic balloon pump (IABP) to assess the impact of ECLS on CABG.

This retrospective study was approved by the Institutional Review Board of Sungkyunkwan University (IRB approval no., 2017-11-061-001). And patient consent was waived based on the nature of this study.

2) Extracorporeal life support application and management

VA ECLS was considered for cardiac arrest or refractory cardiogenic shock. Refractory cardiogenic shock was defined as the inability to maintain a sys-

tolic blood pressure above 90 mm Hg under maximum medical support, with concurrent signs of low cardiac output, such as decreased urine volume or elevated lactate levels. Cannulation was performed peripherally and percutaneously using the Seldinger technique in all patients. Distal perfusion was performed at the time of or after ECLS initiation. In the latter case, the ECLS team initiated distal perfusion in patients who showed a color change in the lower limbs or decreased blood flow on Doppler ultrasound.

Our center formed a special team for ECLS management starting in 2013. This team is responsible for all patients supported by ECLS and assesses vital signs, inotrope and vasopressor requirements, mechanical problems, and complications such as hemolysis, limb ischemia, or heparin-induced thrombocytopenia.

3) Surgical indications and management

Although every referred patient was considered a surgical candidate, we carefully reviewed their general status, myocardial reversibility, and neurologic status. We evaluated the presence of myocardial thinning on echocardiography to assess reversibility and omitted quantitative testing considering the emergent situation. The neurologic evaluation included an examination of pupil size and determination of the Glasgow Coma Scale score. Brain imaging was not routinely performed unless the patient showed abnormal neurologic signs or the cause of cardiac arrest was unclear. We decided not to perform surgery if the duration of cardiopulmonary resuscitation (CPR) was over 30 minutes and the patient was in a coma or semi-coma. Additionally, we did not perform surgery if the target vessel size was less than 1 mm in diameter or if the patient's family refused surgery.

All patients underwent on-pump beating CABG except for cases that required concomitant intracardiac procedures. Since ECLS could not maintain adequate cardiopulmonary bypass flow, we inserted cannulas centrally through the ascending aorta and right atrium and maintained minimal ECLS flow. If cannulation of the ascending aorta was difficult due to calcification, we performed CABG relying on ECLS alone.

The left internal thoracic artery (LITA) was the preferred graft for the left anterior descending coronary artery. All internal thoracic arteries were prepared in a skeletonized fashion. Saphenous vein

grafts (SVGs) were generally used to bypass other target vessels. On completion of CABG, the surgeon and anesthesiologist decided whether to maintain ECLS, based on the patient's vital signs, ventricular function, arrhythmias, and postoperative bleeding risk.

4) Follow-up

Patients underwent regular follow-up at the outpatient clinic during a 3-month interval, and telephone and outpatient interviews were performed if a patient did not visit the clinic at the scheduled time. Follow-up was completed in all patients. The median follow-up duration was 35 months (Q1–Q3, 18.8–90.5 months).

5) Endpoints and definitions

The primary endpoint was early mortality, defined as death within 30 days after the operation. Secondary endpoints were rates of successful ECLS weaning and early morbidity. Lower limb ischemia was defined as present in patients who required surgical intervention, not just based on the requirement of distal hypoperfusion. Gastrointestinal bleeding was defined based on the need for surgical or endoscopic intervention. Hypoxic brain damage was defined as severe permanent neurologic damage with a cerebral performance score of 3–5.

6) Statistical analysis

Categorical variables are presented as number and percentage. Continuous variables are presented as median and interquartile range. Variables with p-values of <0.05 on univariate logistic regression (using the Firth penalized likelihood method for small or sparse binary events), along with variables considered clinically relevant, were entered into the multiple logistic regression model. We used multivariate logistic regression with the stepwise method to assess independent predictors for early mortality. All p-values <0.05 were considered to indicate statistical significance. The Statistical Package for R ver. 3.5.1 (https://www.r-project.org/) and IBM SPSS for Windows ver. 20.0 (IBM Corp., Armonk, NY, USA) were used for analysis.

Table 1. Baseline characteristics (N=23)	
Characteristic	Value
Age (yr)	68 (58–77)
Male	16 (69.6)
Hypertension	12 (52.2)
Diabetes	11 (47.8)
Previous percutaneous coronary intervention	9 (39.1)
History of coronary artery bypass grafting	1 (4.3)
Chronic kidney disease	5 (21.7)
Previous cerebrovascular accident	3 (13.0)
ST-elevation myocardial infarction	9 (39.1)
Non ST-elevation myocardial infarction	10 (43.5)
Ischemic cardiomyopathy	4 (17.4)
Left main disease	6 (26.1)
Three-vessel disease	18 (78.3)
Mechanical complication after acute myocardial infarction	9 (39.1)
Severe mitral regurgitation	6 (26.1)
Ventricular free wall rupture	2 (8.7)
Ventricular septal defect	1 (4.3)
Cardiac arrest	15 (65.2)
Preoperative intra-aortic balloon pump used	8 (34.8)
Cardiopulmonary resuscitation to ECLS initiation (min)	25 (18–35)
Time from ECLS initiation to surgery (hr)	5 (2–20)
Lactate level (mmol/L)	4.16 (1.15–7.50)
Total bilirubin level (mg/dL)	0.8 (0.6–1.1)

Values are presented as number of patients (%) or median (Q1–Q3). ECLS, extracorporeal life support.

Results

1) Baseline characteristics

Baseline characteristics are shown in Table 1. There were more male patients (69.6%) than female. Their median age was 68 years (Q1–Q3, 58–77 years). Most patients (82.6%) were diagnosed with acute coronary syndrome. Nine (39.1%) were diagnosed with ST-elevation myocardial infarction. Eighteen (78.3%) had 3-vessel disease and 6 (26.1%) had left main disease. Cardiac arrest occurred in 15 patients (65.2%) preoperatively. The median time from CPR to initiation of ECLS was 25 minutes (Q1–Q3, 18–35 minutes). Nineteen patients (82.6%) were diagnosed with IHD that needed PCI or CABG before ECLS initiation. Four patients were diagnosed with IHD after ECLS initiation. The median time from ECLS initiation to surgery was 4.0 hours (Q1–Q3, 1.5–12.0 hours) in the former group and 20.5 hours (Q1–

Table 2. Intraoperative details (N=23)	
Variable	Value
CABG type	
On-pump beating CABG	13 (56.5)
Conventional CABG	10 (43.5)
Graft	
Left internal thoracic artery	14 (60.9)
Right internal thoracic artery	4 (17.4)
Saphenous vein graft	20 (87.0)
Concomitant procedure	
Mitral valve replacement	6 (26.1)
Aortic valve replacement	1 (4.3)
Tricuspid annuloplasty	1 (4.3)
Repair of left ventricular free wall rupture	2 (8.7)
Repair of ventricular septal defect	1 (4.3)
Intraoperative extracorporeal life support weaning	7 (30.4)
Cardiopulmonary bypass time (min)	172 (105–231)
Aortic cross-clamp time (min)	131 (67–175)

Values are presented as number of patients (%) or median (Q1–Q3). CABG, coronary artery bypass grafting.

Table 3. Early postoperative outcomes	
Variable	No. of patients (%)
Early mortality	6 (26.1)
Early morbidity	
Atrial fibrillation	10 (43.5)
Respiratory complication	4 (17.4)
Low cardiac output syndrome	2 (8.7)
Stroke	7 (30.4)
Acute kidney injury requiring dialysis	10 (43.5)
Reoperation for postoperative bleeding	3 (13.0)
Gastrointestinal bleeding	1 (4.3)
Limb ischemia	1 (4.3)

Q3, 6.3–101.5 hours) in the latter. Before CABG, 6 patients successfully underwent PCI of the culprit lesion. The median time from ECLS to surgery was 5 hours (Q1–Q3, 2.0–20.0 hours).

2) Intraoperative data

Operative data are shown in Table 2. On-pump beating CABG was performed in 13 patients (56.5%), of whom 4 underwent surgery on ECLS. The median operative time was 322 minutes (Q1–Q3, 254–460 minutes) and the median cardiopulmonary bypass time was 172 minutes (Q1–Q3, 105–231 minutes). The LITA was used in 60.9% of patients and a SVG was used in 87.0%. The median number of distal anastomoses was 4 (Q1–Q3, 2–5). Concomitant procedures were performed in 10 patients. Severe mitral regurgitation (MR) was present in 7 patients, including 2 with functional MR. Of these, 6 underwent mitral valve replacement (MVR) concomitantly.

3) Outcomes

Postoperative ECLS was required in 16 patients (69.5%). The rate of successful ECLS weaning was 91.3% (n=21). The median postoperative ECLS duration was 2 days (Q1–Q3, 0–4 days). The median stay in the intensive care unit was 15 days (Q1–Q3, 9–21 days). Table 3 shows immediate postoperative com-

plications. The early mortality rate was 26.1% (n=6). Causes of death included persistent low cardiac output due to myocardial infarction in 3 cases, septic shock in 2 cases, and brain death in 1 case. Most survivors (94.1%) were discharged without major neurologic deficits. Early death occurred in 3 patients who were successfully weaned off ECLS but failed to survive. These 3 patients were older than 70 years and had MR above the moderate grade. Case 1 showed severe hypoxic brain damage and could not sustain adequate blood pressure. Cases 2 and 3 died of severe sepsis and multi-organ failure. Three of the 5 patients (60%) who developed hypoxic brain damage postoperatively died within 30 days postoperatively. However, those who survived to discharge did not have major neurologic deficits at the last follow-up.

After discharge from the hospital, 2 patients died, 1 of septic shock and 1 of unknown causes. One patient underwent heart transplantation due to progression of ischemic cardiomyopathy.

To investigate the risk factors for early mortality after CABG, we performed univariate and multivariate analyses. The univariate analysis found that the variables associated with early post-CABG mortality with a p-value <0.05 were female sex, age, operation time, MVR, postoperative stroke, and postoperative acute kidney injury requiring continuous renal replacement. On multivariate analysis, age was the only significant risk factor (Table 4).

4) Comparison with patients supported by intra-aortic balloon pump

During the same period, 44 patients underwent CABG under IABP support. Their median age was

Table 4. Predictors of early mortality

Variable	Univariate analysis	
	Odds ratio (95% confidence interval)	p-value
Preoperative details		
Male sex	0.107 (0.013–0.880)	0.038
Age (yr)	1.167 (1.019–1.337)	0.025
Hypertension	0.889 (0.138–5.723)	0.901
Diabetes mellitus	0.444 (0.063–3.112)	0.414
Chronic kidney disease	0.650 (0.058–7.324)	0.727
Prior percutaneous coronary intervention history	1.833 (0.279–12.066)	0.528
ST-elevation myocardial infarction	0.714 (0.101–5.036)	0.736
Three-vessel disease	5.719 (0.207–157.761)	0.303[a]
Left main disease	0.480 (0.044–5.233)	0.547
Severe mitral regurgitation	37.500 (2.771–507.475)	0.006
Cardiac arrest	1.091 (0.153–7.802)	0.931
Preoperative intra-aortic balloon pump used	0.917 (0.128–6.556)	0.931
Time to surgery (hr)	1.004 (0.979–1.031)	0.740
Lactate level (mmol/L)	1.220 (0.905–1.645)	0.193
Intraoperative details		
Conventional coronary artery bypass grafting	3.667 (0.513–26.224)	0.196
Cardiopulmonary bypass time (min)	1.090 (0.934–1.273)	0.274
Length of operation (min)	1.009 (1.000–1.019)	0.039
Concomitant mitral valve replacement	15.000 (1.583–142.176)	0.018
Postoperative details		
Stroke	3.250 (0.461–22.928)	0.237
Acute kidney injury requiring dialysis	12.000 (1.103–130.586)	0.041
Atrial fibrillation	1.429 (0.220–9.262)	0.708
Respiratory complication	3.750 (0.396–35.544)	0.249

[a]Firth penalized likelihood method for small or sparse binary events.

74.5 years and 65.9% were male. The preoperative clinical characteristics were not significantly different between the 2 groups except for the proportion of cardiac arrest, which was much higher in the ECLS group than in the IABP group (65.2% versus 11.4%, p<0.001). Off-pump CABG was performed in 31.8% of patients and the LITA was used in 86.4%. The rate of postoperative stroke was significantly higher in the ECLS group than in the IABP group (30.4% vs. 4.5%, p=0.006). However, there was no statistically significant difference in early mortality between the 2 groups (IABP, 11.4%; ECLS, 26.1%; p=0.167). The overall survival is shown in Fig. 1.

Discussion

This study investigated the outcomes of ECLS-assisted CABG in patients with IHD complicated by cardiac arrest or cardiogenic shock and found that
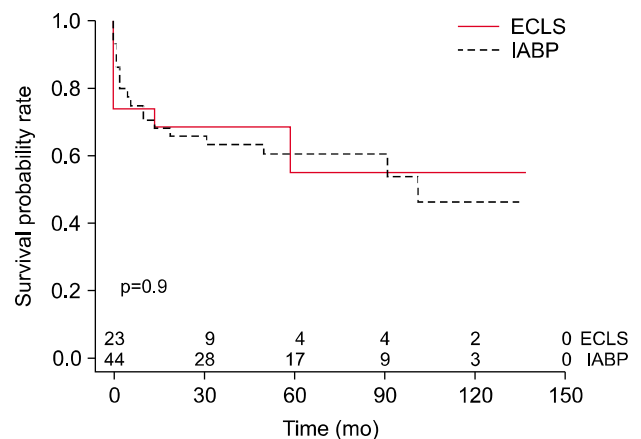
Fig. 1. Kaplan-Meier curve showing the survival of patients undergoing coronary artery bypass grafting after receiving ECLS or IABP support. ECLS, extracorporeal life support; IABP, intra-aortic balloon pump.

CABG was a feasible option. IHD complicated by hemodynamic compromise is known to show a poor prognosis with high mortality [9,10]. The importance of early revascularization was established in the 'Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK)' trial [3].

In the current American College of Cardiology Guidelines, CABG is a reasonable option for revascularization in shock, particularly for diffuse and multi-vessel disease, lesions not amenable to PCI, failed PCI, and mechanical complications after acute myocardial infarction. The best treatment modality is still a matter of debate for the large majority of patients with multi-vessel disease and no mechanical complications [11]. However, many clinicians are reluctant to perform CABG. In the IABP-SHOCK II trial, only 3.5% of the enrolled patients underwent immediate CABG or initial PCI with subsequent bypass surgery [12]. PCI may be preferred to CABG in acute myocardial infarction with cardiogenic shock because CABG has a longer time to reperfusion and higher surgical risk. In our center, 161 IHD patients, complicated by cardiac arrest or refractory cardiogenic shock, underwent PCI, whereas 29 underwent CABG in the same period after VA ECLS.

Although this is a single-arm study that investigated the outcomes of CABG supported by ECLS, we compared the outcomes of ECLS patients to those of IABP patients. Since the severity of patients who underwent ECLS-supported CABG was much higher than that of those who underwent IABP-supported CABG, the outcomes of this study were not disappointing. The early mortality rate was 26%. Kagawa et al. [13] reported that rapid-response ECMO plus intra-arrest PCI was feasible because the 30-day survival was 29%, with favorable neurological outcomes in 24%. Chung et al. [4] reported an early mortality rate of 53% in patients with ST-elevation myocardial infarction complicated by profound shock after ECMO-assisted PCI. However, we believe that selection of surgical candidates among these critically ill patients is essential to achieve satisfactory outcomes. Therefore, our center did not perform CABG if the anastomosis seemed difficult because the target vessel diameter was less than 1 mm, the duration of CPR was over 30 minutes and the patient was in a coma or semi-coma, or the patient's family refused surgery.

There is often a dilemma regarding whether to proceed with CABG without neurologic evaluation. However, we performed CABG without neurologic imaging in most cases because the patients were very unstable on ECLS and needed revascularization as soon as possible. Hosmane et al. [14] reported that resuscitated patients with ST-elevation myocardial infarction in the emergency department should be seriously considered for emergent angiography and revascularization, regardless of the neurologic status. In their study, 92% of the patients experienced full neurologic recovery. In the present study, 94.1% of survivors were discharged without major neurologic deficits. It may be possible to perform CABG in an emergent situation where it is difficult to perform brain imaging owing to unstable vital signs or requirements for bulky equipment.

During the study period, there was no change in the surgical strategy. If a concomitant intracardiac procedure was not required, on-pump beating CABG was performed. When left anterior descending artery territory needed revascularization, the LITA (60.9%) was used as an *in situ* graft. Otherwise, the SVG (87%) was used in other territories and the right internal thoracic artery (17.4%) was used in young patients without comorbidities. Mitral valve surgery (MVS) was only indicated in patients with severe MR, although there is still debate about concomitant MVS in patients with less than severe MR [15]. Six of the 7 patients with severe MR underwent MVS. MVS was not performed in 1 patient due to a very high surgical risk of redo CABG. Although it remains unclear which method is better in IHD patients with severe functional MR, we chose MVR for MVS in all patients because replacement generally shows predictable results and is more rapid than repair in high-risk patients [16,17].

Several studies support the use of CABG based on long-term outcomes. Gaudino et al. [7] reported that more than 60% of the patients discharged from the hospital were alive, ischemia-free, and had good functional status and quality of life almost 11 years after CABG. These results might reflect the use of the LITA. In this study, the LITA was used in 14 patients (60.9%) and late death occurred in 2 patients. Although harvesting the LITA is time-consuming, doing so can be worthwhile if we consider the long-term outcomes of revascularization. However, it

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is also important to take other factors such as age, level of emergency, and the location of the culprit lesion into account.

It is necessary to keep in mind that there was a change in the use of mechanical circulatory support (MCS) devices during the study period. Since the IABP-SHOCK II trial, IABP has been selectively applied to postinfarct ventricular septal defect, and its use is decreasing in our center [18]. In contrast, the application of ECLS is gradually increasing. MCS equipment such as TandemHeart or Impella has been introduced in Europe and other countries, but not in Korea.

The present study has several potential limitations. First, this study had a retrospective design with some bias in the analysis. Second, we did not compare the results of CABG with those of PCI. As a result, our findings are not sufficient to support CABG over PCI in emergency revascularization. However, since no research has yet been conducted on CABG in patients on ECLS, our findings are nonetheless meaningful. If sufficient data on CABG after ECLS are gathered, it will be possible to conduct a comparison with the PCI results. Finally, this study included a small number of patients, and as a result definite risk factors for early mortality in patients undergoing CABG could not be determined. Therefore, further studies should be conducted to support our results and to obtain more generalizable results about CABG in patients on ECLS.

In conclusion, CABG after ECLS was very rare in real-world circumstances. Although the early mortality rate was high, the risk may be acceptable under such devastating circumstances. Careful patient selection is important before proceeding to surgery.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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