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Clinical Experiences of High-Risk Pulmonary Thromboembolism Receiving Extracorporeal Membrane Oxygenation in Single Institution

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Abstract

Background: The main cause of death in pulmonary embolism (PE) is right-heart failure due to acute pressure overload. In this sense, extracorporeal membrane oxygenation (ECMO) might be useful in maintaining hemodynamic stability and improving organ perfusion. Some previous studies have reported ECMO as a bridge to reperfusion therapy of PE. However, little is known about the patients that benefit from ECMO.
Methods: Patients who underwent ECMO due to pulmonary thromboembolism at a single university-affiliated hospital between January 2010 and December 2018 were retrospectively reviewed.
Results: During the study period, nine patients received ECMO in high-risk PE. The median age of the patients was 60 years (range, 22–76 years), and six (66.7%) were male. All nine patients had cardiac arrests, of which three occurred outside the hospital. All the patients received mechanical support with veno-arterial ECMO, and the median ECMO duration was 1.1 days (range, 0.2–14.0 days). ECMO with anticoagulation alone was performed in six (66.7%), and ECMO with reperfusion therapy was done in three (33.3%). The 30-day mortality rate was 77.8%. The median time taken from the first cardiac arrest to initiation of ECMO was 31 minutes (range, 30–32 minutes) in survivors (n=2) and 65 minutes (range, 33–482 minutes) in non-survivors (n=7).
Conclusion: High-risk PE with cardiac arrest has a high mortality rate despite aggressive management with ECMO and reperfusion therapy. Early decision to start ECMO and its rapid initiation might help save those with cardiac arrest in high-risk PE.

Keywords: Pulmonary Embolism; Extracorporeal Membrane Oxygenation; Cardiac Arrest

Introduction

Acute pulmonary embolism (PE) is a preventable and treatable condition with a wide range of clinical presentations and outcomes. The mortality rate for acute PE ranges from 2.3% for low-risk patients to 68.4% for high-risk patients with cardiac arrest[1,2]. High-risk PE accounts for a small proportion of PE, but immediate and vigorous treatment is required due to its high mortality. The primary cause of death in PE is right-heart failure due to acute pressure overload. In this sense, extracorporeal membrane oxygenation (ECMO) might be useful in high-risk PE patients by providing time for the recovery of pulmonary flow and maintaining the patient's hemodynamic stability[3,4]. Recently, there has been increasing attention to the utilization of ECMO for high-risk PE. However, little is known about the patients that benefit from ECMO. In this study, we report our clinical experiences of high-risk PE patients who received ECMO.

Materials and Methods

1. Study design and data collection

The data is collected from the thrombosis clinic database of Soonchunhyang University Seoul Hospital, a 720-bed university-affiliated hospital, in Seoul, Republic of Korea. Electronic medical records of the patients who were diagnosed with acute high-risk PE from January 2010 to December 2018 were reviewed. Data including the patient's demographics, body mass index, past medical history, PE risk factor, initial presenting symptom, vital signs, imaging, and biomarker results were collected. The time of the first recognition, cardiac arrest, anticoagulation administration, ECMO initiation, and duration of cardiopulmonary resuscitation (CPR) were also collected. The time of the first recognition refers to the time of in-hospital patients' first symptom identification or the time of arrival at the hospital in out-of-hospital patients.

Diagnosis of PE was confirmed by a multidetector computed tomography (CT). According to the European Society guidelines, acute high-risk PE is defined as acute PE with persistent hypotension (systolic blood pressure [BP] <90 mm Hg or a systolic BP drop ≥40 mm Hg for >15 minutes), or obstructive shock (systolic BP <90 mm Hg or vasopressors required to achieve a BP ≥90 mm Hg despite adequate hydration, in combination with end-organ hypoperfusion), or cardiac arrest. The Acute Physiology and Chronic Health Evaluation (APACHE II) score and the Survival after Veno-Arterial ECMO (SAVE) score were calculated based on the worst value within the initial 24 hours in the intensive care unit. The primary outcome was the 30-day mortality rate. The study protocol was approved by the Institutional Review Board of the Soonchunhyang University Seoul Hospital (SCHUH 2021-11-008), which waived the requirement for informed consent because of the retrospective nature of the analysis.

2. Statistical analysis

All the analyses were performed using IBM SPSS software version 22.0 (IBM Corp., Armonk, NY, USA). Data were described as median (range) for continuous variables and as a number (%) for categorical variables. Kaplan-Meier survival analysis curves were built to estimate the 30-day mortality rate using a log-rank test.

Results

We identified nine patients with acute high-risk PE with cardiac arrest who were treated with ECMO between January 2010 and December 2018. Baseline characteristics of the patients and risk factors of PE are shown in Table 1. The median age of the patients was 60 years (range, 22–76 years) and six patients (66.7%) were male. Most of the patients had no significant comorbidities. The risk factors of three provoked PE were surgery in two cases and trauma in one case. Among the other six patients with unprovoked PE, one patient had previous thromboembolism.

Table 2 summarizes the presentation of PE patients. The most common initial symptom was shortness of breath (n=6, 66.6%) followed by chest pain (n=2, 22.2%). Among the nine patients, six (66.7%) had a cardiac arrest in the hospital, and three (33.3%) had a cardiac arrest outside of the hospital. The median mean arterial pressure, heart rate, respiratory rate, and body temperature were 54 mm Hg (range, 0–119), 100 beats/min (range, 0–123), 22 breaths/min (range, 0–38),

Table 1. Baseline characteristics and risk factors of high-risk PE patients

Variable	Value (n=9)
Age, yr	60 (22–76)
Male sex	6 (66.7)
Smoking	3 (33.3)
BMI, kg/m^2	26.4 (20.8–36.3)
Comorbidity	
Prior myocardial infarction	0
Congestive heart failure	0
Cerebrovascular disease	1 (11.1)
Rheumatologic disease	0
Liver disease	0
Diabetes	2 (22.2)
Renal disease	1 (11.1)
Malignancy	0
PE risk factors	
Provoked	3 (33.3)
Unprovoked	6 (66.7)

Values are presented as median (range) or number (%).
PE: pulmonary embolism; BMI: body mass index.

Table 2. Initial presentation of high-risk pulmonary embolism patients

Variable	Value (n=9)
Initial presenting symptom	
Dyspnea	6 (66.7)
Chest pain	2 (22.2)
Dizziness	1 (11.1)
Syncope	1 (11.1)
Hemoptysis	0
Cardiac arrest	
In-hospital arrest	6 (66.7)
Out-hospital arrest	3 (33.3)
Initial vital sign	
MAP, mm Hg	54 (0 to 119)
SBP, mm Hg	62 (0 to 156)
DBP, mm Hg	50 (0 to 101)
Heart rate, beats/min	100 (0 to 123)
Respiratory rate, breaths/min	22 (0 to 38)
Body temperature, °C	36.0 (35.1 to 36.8)
APACHE II score	28 (14 to 41)
SAVE score	−11 (−18 to −2)
Diagnosis made on CT angiography	9 (100)
Bilateral pulmonary embolism	8 (88.9)
RV dilatation on CT (RV/LV ratio >1)	7 (77.8)

Values are presented as number (%) or median (range). MAP: mean arterial pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure; APACHE II score: Acute Physiology and Chronic Health Evaluation II score; SAVE score: Survival after Veno-Arterial extracorporeal membrane oxygenation score; CT: computed tomography; RV: right ventricle; LV: left ventricle.

and 36.0°C (range, 35.1–36.8), respectively. The median APACHE II score was 28 (range, 14–41) and the median SAVE score was −11 (range, −18 to −2). All the nine patients were diagnosed with a CT angiography, and eight (88.9%) had a bilateral pulmonary embolism. Right ventricular strain on CT was seen in seven patients (77.8%).

All the nine patients received mechanical support with veno-arterial ECMO and the median ECMO duration of 1.1 days (range, 0.2–14.0 days). ECMO was performed by a cardiothoracic surgeon. Arterial catheter size ranged from 16 to 18 FR, and venous catheter size ranged from 20 to 22 FR. Heparin was used as an anticoagulation agent to maintain ECMO. The target activated partial thromboplastin time was from 50 to 80 seconds.

The most common complication of ECMO was bleeding (n=7, 77.8%), none of which required transfusion. There were four ECMO catheter insertion-site oozing cases. The others included hemoptysis, hematuria, and gastrointestinal bleeding. In one case of the survivors, a pseudoaneurysm due to ECMO-related vascular injury developed and surgery was required for management.

The overall 30-day mortality rate was 77.8%. Therapeutic procedures performed for the treatment of PE and outcomes of the total population are shown in Table 3. All the nine patients had cardiac arrest before ECMO application, and reperfusion therapy was performed after ECMO application. Among the six patients who had in-hospital cardiac arrest, one patient was bridged to systemic thrombolysis with tissue plasminogen activator followed by surgical embolectomy. Another patient underwent catheter thrombectomy for reperfusion, and the other four received ECMO as a sole therapy with systemic anticoagulation. Among the three patients who had out-of-hospital cardiac arrest, one patient was bridged to reperfusion therapy using systemic thrombolytics. And the others received ECMO with anticoagulation. Two survivors experienced in-hospital cardiac arrest and were treated with ECMO alone. The cause of death was a multiorgan failure due to cardiac arrest in five patients, and refractory shock despite ECMO support in two patients. There were no deaths related to complications from ECMO or reperfusion therapy. The time taken from first cardiac arrest to initiation of ECMO was shorter in survivors (median, 31 minutes; range, 30–32 minutes) than in non-survivors (median, 65 minutes; range, 33–482 minutes). The duration of CPR was also shorter in survivors (median, 8 minutes; range, 3–13 minutes) than in non-survivors (median, 31 minutes; range, 15–87 minutes).

Discussion

The prognosis of high-risk PE has improved due to advances in diagnosis and management, but it is still a fatal disease, and optimal management is unclear[3,5,6]. In this case series, we reported data on nine patients who underwent ECMO due to pulmonary thromboembolism. Among the nine patients, one underwent systemic thrombolysis, one underwent catheter thrombectomy, one underwent systemic thrombolysis followed by surgical embolectomy, and six others received ECMO as a sole therapy with systemic anticoagulation. All the patients had cardiac arrest before ECMO application, and the overall 30-day mortality rate was 77.8%.

Considering the rarity of the disease and the difficulty in studying critically ill patients, the clinical outcomes of high-risk PE requiring ECMO are elusive. Recently, Stadlbauer et al.[7] reported the long-term outcome of

Table 3. Individualized management and outcomes in patients with high-risk pulmonary embolism

Patient No.	Age (yr)	Sex	Location of cardiac arrest	The time interval between recognition and diagnosis of PE* (min)	The time interval between hospital arrival and cardiac arrest (min)	The time taken from the first cardiac arrest to the initiation of ECMO (min)	The time taken from the first cardiac arrest to the initiation of anticoagulation (min)	Duration of CPR (min)	Outcome	Reperfusion therapy
1	76	M	Out-of-hospital	90	-	85	88	85	Died	No
2	60	F	In-hospital	321	249	52	62	18	Died	No
3	46	M	In-hospital	118	11	32	55	13	Survived	No
4	65	F	Out-of-hospital	104	-	65	57	35	Died	Systemic thrombolysis
5	22	M	Out-of-hospital	133	-	82	237	22	Died	No
6	68	M	In-hospital	85	15	30	117	3	Survived	No
7	59	M	In-hospital	180	6,547	49	229	31	Died	No
8	63	F	In-hospital	94	1	33	33	15	Died	Catheter thrombectomy
9	25	M	In-hospital	55	191	482	–33	87	Died	Systemic thrombolysis+ surgical embolectomy

*Time interval between recognition and diagnosis of PE: The time interval between identification of the first symptom to diagnosis using computed tomography angiography for patients who were already admitted to the hospital for other reasons. For patients visiting the emergency department, the time interval between the hospital arrival to computed tomography diagnosis.
PE: pulmonary embolism; ECMO: extracorporeal membrane oxygenation; CPR: cardiopulmonary resuscitation.

119 patients who received ECMO for high-risk PE with an acceptable quality of life, and the overall survival to hospital discharge was 45.4%, this is the largest single-center study. But survival rate varies from 47% to 95% in smaller case series (Table 4)[8-13]. On the other hand, our report shows a lower survival rate (22.2%) despite the low prevalence of underlying comorbidities.

Cardiac arrest is a major prognostic factor in high-risk PE patients, and the mortality rate rises to 70% if it occurs[14]. Recent case series studies also showed that the prognosis of high-risk PE patients tends was poorer when the cardiac arrest occurred before or during ECMO application (Table 4). In our report, all the patients received ECMO only after cardiac arrest, which explains the low survival rate.

In high-risk PE patients, maintaining hemodynamic stability and preventing cardiac arrest through early ECMO application may have a greater impact on survival than choosing the optimal reperfusion therapy. As previously known, in the recent case series, the choice of reperfusion therapy does not seem to be related to survival (Table 4)[3]. Although there may be selection bias, even ECMO alone strategy has repeatedly shown non-inferior results in various studies[4,10,12,13]. On the other hand, cardiac arrest, low blood pressure, and high lactate level before ECMO application were related to mortality[4,7,8,13]. In our case series, the most notable difference between the survivors and non-survivors was the interval between cardiac arrest and ECMO initiation. The time taken from first cardiac arrest to initiation of ECMO was shorter in survivors (median, 31 minutes; range, 30–32 minutes) than in non-survivors (median, 65 minutes; range, 33–482 minutes). Because right-heart failure and death occur in the early stage of acute PE, immediate ECMO application may be crucial for survival[15,16]. The two survivors in our study also used the ECMO alone strategy, and reperfusion therapy was not performed because hemodynamic stability

Table 4. Recent studies on the use of extracorporeal oxygenation in high-risk pulmonary embolism

Reference	Inclusion years (mo)	No. of patients	CA before or during ECMO, n (%)	Duration of ECMO, median (day)	Outcome (%)	Reperfusion therapy (%)
George et al.[8]	2012–2015 (48)	32	15 (47)	4 in survivors 2 in non-survivors	Survived index hospitalization (53.1) Mortality in CA before ECMO (73.3)	Systemic thrombolysis (16) Catheter thrombolysis (47) Surgical embolectomy (6) Catheter thrombectomy (13)
Al-Bawardy et al.[9]	2012 (12)	13	13 (100)	5.5	30-Day mortality (31)	Systemic thrombolysis (62) Catheter thrombolysis (23) Surgical embolectomy (31) ECMO alone (8)
Oh et al.[10]	2014–2018 (60)	16	12 (75) (10 in-hospital, 2 out-of-hospital)	1.5	30-Day mortality (43.8)	Systemic thrombolysis (25) Surgical embolectomy (56) ECMO alone (19)
Corsi et al.[11]	2006–2015 (109)	17	15 (88) (10 in-hospital, 5 out-of-hospital)	4	90-Day mortality (53)	Systemic thrombolysis (47) Surgical embolectomy (12) Catheter thrombectomy (6)
Pasrija et al.[12]	2014–2016 (32)	20	5 (25)	5.1	90-Day survival (95)	Catheter thrombolysis (5) Surgical embolectomy (55) ECMO alone (40)
Guliani et al.[13]	2017–2019 (29)	17	10 (59)	3.6 in survivors	Overall survival (76)	Catheter thrombolysis +thrombectomy (23) ECMO alone (77) (among 13 survivors)

CA: cardiac arrest; ECMO: extracorporeal membrane oxygenation.

was well maintained.

It is also important to identify PE quickly to maintain the patient's hemodynamic stability through ECMO. Although we did not analyze the clinical pretest probability for PE in this study, we can assume that most of the patients would have been in the moderate or high-risk group, considering the patients' risk factors, initial vital signs, and deep vein thrombosis prevalence (n=5, 55.6%). Earlier suspicion of PE would have made the diagnosis faster. Among the six patients who had in-hospital cardiac arrest, only one had clinical suspicion of PE before cardiac arrest. In two other patients, the time from admission to cardiac arrest was 249 minutes and 191 minutes, which might have been long enough to suspect pulmonary embolism. However, their symptom was underestimated, leading to a fatal result (Table 3). Accordingly, ECMO and other reperfusion therapy were done as a salvage intervention, with poor outcomes. The introduction of a multidisciplinary pulmonary embolism response team (PERT) is necessary to prevent delayed detection and diagnosis of PE.

The PERT has been tried for better management of moderate to severe PE[17,18]. It is generally composed of experts from different specialties, including pulmonology/critical care, cardiology, emergency medicine, and cardiac surgery interested in PE. The PERT can be activated in patients with confirmed or highly suspected PE and offers a real-time multidisciplinary discussion, decision-making, and plan execution. The PERT approach has not yet shown better outcomes, but it may bring positive results if the appropriate treatment strategy is applied[18-20]. Pasrija et al.[12] and Guliani et al.[13] adopted a strategy including aggressive, protocol-driven utilization of ECMO in patients with high-risk PE and reported good results with the survival of 95% and 76%, respectively. Based on these promising results, we may expect PERT to play a great role in responding to high-risk PE.

Since the introduction of PERT stems from the need for optimal application of newly developed promising therapeutic tools, it generally focuses on therapeutic approaches. Based on our experience, PERT composition with enhanced educational and diagnostic function to prevent delay in diagnosis may help to improve the PE survival rate by preventing delayed diagnosis.

The main limitation of this study is that it is difficult to generalize because the sample size was small. In addition, this study was conducted retrospectively in a single institution and might have a selection bias.

In conclusion, high-risk PE with cardiac arrest has a high mortality rate despite aggressive management with ECMO and reperfusion therapy. We report our clinical experiences of ECMO as hemodynamic support for cardiac arrest in patients with high-risk PE.

Authors' Contributions

Conceptualization: Kim YK, Lee BY. Formal analysis: Jang J, Kim YK, Lee BY. Data curation: Jang J, Kim YK, Lee BY, Koo SM, Kim KU, Uh ST, Jang GE, Chang W. Validation: Kim YK, Lee BY. Investigation: Jang J, Kim YK, Lee BY. Writing – original draft preparation: Jang J. Writing – review and editing: Jang J, Lee BY. Approval of final manuscript: all authors.

Conflicts of Interest

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

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