

Extracorporeal Membrane Oxygenation as Salvage Therapy for Acute Massive Pulmonary Embolism after Surgery for Tibiofibular Fractures

Xiao-Yan Wu^{1,2}, Zhi-Qing Zhuang³, Rui-Qiang Zheng¹, Song-Qiao Liu²

¹Department of Critical Care Medicine, Northern Jiangsu People's Hospital, Clinical Medical College of Yangzhou University, Yangzhou, Jiangsu 225001, China

²Department of Critical Care Medicine, Zhong-Da Hospital, Southeast University, Nanjing, Jiangsu 210009, China

³Department of Neurology, Affiliated Wutaishan Hospital, Clinical Medical College of Yangzhou University, Yangzhou, Jiangsu 225001, China

Xiao-Yan Wu and Zhi-Qing Zhuang contributed equally to this work.

To the Editor: Surgery for fractures is a major risk factor for pulmonary embolism (PE). Massive PE (MPE) remains an important clinical challenge with a high mortality rate. The potential for sudden and fatal hemodynamic deterioration highlights the need for prompt and appropriate interventions.^[1] The optimal treatment approaches for MPE are typically restricted to patients who are critically ill. Some case reports have demonstrated the use of extracorporeal membrane oxygenation (ECMO) as a potentially lifesaving therapeutic option that could provide clinical stability to allow definitive treatment. Here, we reported the successful use of ECMO alone without definitive therapy in a 52-year-old man who developed an MPE after surgery for tibiofibular fractures and presented with hemodynamic instability and severe hypoxemia. Because of the patient's unstable hemodynamic status and the high risk of bleeding, thrombolysis and embolectomy were not administered. ECMO alone was successfully used as salvage therapy for the MPE, and the patient experienced a good recovery.

A 52-year-old man was admitted to Zhong-Da Hospital with chest compression and shortness of breath for 5 h in October 2016 after having undergone a surgery of open reduction and internal fixation for tibiofibular fractures. The patient was a manual laborer and had no significant medical or family history. He underwent orotracheal intubation and ventilation because of refractory hypoxemia. His hemodynamic status was unstable, maintaining an average arterial blood pressure (BP) of 89/54 mmHg (1 mmHg = 0.133 kPa) with a noradrenaline dose of 20 µg/min and adrenaline dose of 0.04 µg·min⁻¹·kg⁻¹. Electrocardiogram showed SI, QIII, TIII, and right bundle branch block [Figure 1a]. Echocardiography revealed diffuse hypokinesis with severe right ventricular dilatation and pulmonary hypertension as well as a left ventricular ejection fraction of 15% [Figure 1b]. Pulmonary computed tomography angiography demonstrated a large thrombus in the bilateral pulmonary arteries [Figure 1c]. The patient's central venous pressure was 24 mmHg. Laboratory examinations revealed the following: total creatine phosphokinase (CPK), 136 U/L (reference range: 0–171 U/L); CPK-MB, 21.0 ng/ml

(reference range: 2.0–7.2 ng/ml); myoglobin, 488 ng/ml (reference range: 23–112 ng/ml); B-type natriuretic peptide, 4080 pg/ml (reference range: 300–900 pg/ml); and troponin I, 0.680 ng/ml (reference range: 0.010–0.023 ng/ml). Arterial blood gas analysis showed a pH of 7.17, PCO₂ of 42 mmHg, PaO₂ of 138 mmHg, and PaO₂/FiO₂ (P/F) of 171 mmHg.

The patient was diagnosed with an MPE. Due to the recent surgery and intravertebral anesthesia, we did not administer urokinase or recombinant tissue plasminogen activator for thrombolysis owing to the high risk of bleeding. Moreover, surgical pulmonary embolectomy was not performed because of the patient's unstable hemodynamic status. Instead, anticoagulation with unfractionated heparin at a dose of 10 U/min was performed. The patient's BP decreased to 40/20 mmHg, his heart rate dropped to 50 beats/min, and no peripheral oxygen saturation was detected 2 h after admission. Epinephrine (2 mg) was delivered intravenously in a timely manner; however, it was very difficult to maintain the BP at the level of 89/60 mmHg with a noradrenaline dose of 200 µg/min and epinephrine dose of 0.10 µg·min⁻¹·kg⁻¹. The patient's circulation and respiratory function deteriorated progressively, accompanied by an increase in lactic acid level up to 12.6 mmol/L, P/F as low as 100 mmHg, and oliguria.

Six hours after admission, venoarterial (VA)-ECMO support was initiated to substitute for cardiopulmonary function. Two cannulas were surgically inserted into the femoral vessels using the semi-Seldinger technique with heparinized polyvinyl chloride tubing and a membrane oxygenator. The flow of the pump

Address for correspondence: Dr. Xiao-Yan Wu, Department of Critical Care Medicine, Northern Jiangsu People's Hospital, Clinical Medical College of Yangzhou University, Yangzhou, Jiangsu 225001, China
E-Mail: ntywxy@163.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

© 2018 Chinese Medical Journal | Produced by Wolters Kluwer - Medknow

Received: 20-06-2018 **Edited by:** Xin Chen

How to cite this article: Wu XY, Zhuang ZQ, Zheng RQ, Liu SQ. Extracorporeal Membrane Oxygenation as Salvage Therapy for Acute Massive Pulmonary Embolism after Surgery for Tibiofibular Fractures. Chin Med J 2018;131:2611-3.

Access this article online

Quick Response Code:



Website:
www.cmj.org

DOI:
10.4103/0366-6999.244102

(Jostra-Maquet, Germany) was initially set to 4–5 L/min. The venous cannula was positioned under echocardiographic control. The heparin infusion dose was 8–12 U/min, and the activated partial thromboplastin time goal was 40–60 s. When the ECMO started to work, the patient's peripheral oxygen saturation rose to 98%, and the epinephrine and noradrenaline doses could quickly be lowered within a few hours [Table 1]. Ultrasonography of the lower limbs indicated deep vein thrombosis in the right lower limb. The patient was successfully extubated from mechanical ventilation when his respiratory function recovered 3 days after admission. Five days after admission, he was decannulated of the ECMO as his circulation function recovered [Table 1].

Unfortunately, the patient developed renal failure, which was considered a complication of the MPE. Continuous renal replacement therapy for 6 days was initiated on day 3. One week after admission, the patient presented with chills and a fever (with

a body temperature up to 39°C–40°C). The results of multiple blood cultures showed *Enterococcus faecium*; thus, the central venous catheters were replaced, and a blood filter catheter and daptomycin (0.5 ivgtt qd) were administered.

On day 8 of heparin therapy, the patient's platelet count dropped (from $87 \times 10^9/L$ to $30 \times 10^9/L$) while on heparin infusion of 10 U/min. The calculated 4T's score at the time (3 of 8) indicated a high pretest probability of heparin-induced thrombocytopenia (HIT). Therefore, anticoagulation was changed to rivaroxaban, and 3 units of platelets were transfused. With the discontinuation of heparin, the patient's platelet count rose significantly (range: 100 – $120 \times 10^9/L$), and he did not require additional transfusion of platelets throughout the rest of his hospitalization.

The patient's clinical condition improved progressively, and serial echocardiography revealed a gradual recovery of heart contractility (with an increase in the left ventricular ejection fraction

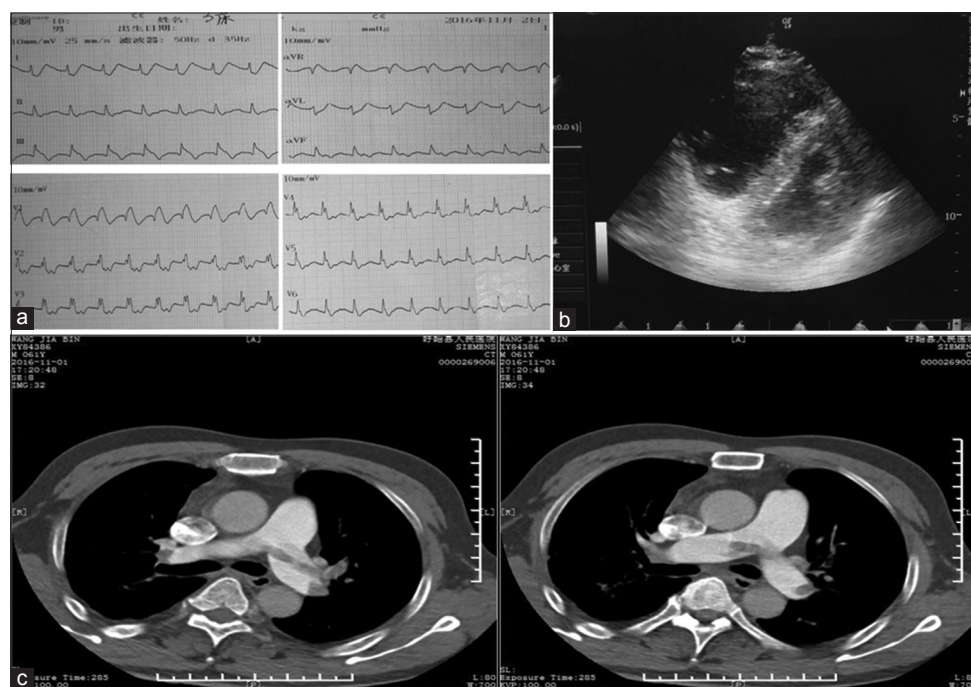


Figure 1: A 52-year-old man with massive pulmonary embolism. (a) The 12-lead electrocardiogram showing SI, QIII, TIII, and right bundle branch block. (b) Echocardiography indicating right ventricular dilatation and septum deviation shaped like a “D”. (c) Computed tomography angiography (axial image) showing a large thrombus in the bilateral pulmonary arteries.

Table 1: Hemodynamic status and respiratory function pre- and post-ECMO in the 52-year-old man with MPE

Items	Admission (day 1)	ECMO (day 2)	ECMO (day 3)	ECMO (day 4)	ECMO (day 5)	Off-ECMO (day 6)
HR (beats/min)	149	110	109	93	88	86
BP (mmHg)	95/62	132/80	135/85	145/92	142/88	145/89
CVP (mmHg)	24	14	14	12	10	12
Lactic acid (mmol/L)	12.6	5.2	1.8	1.6	1.5	1.5
Noradrenaline ($\mu\text{g}/\text{min}$)	200	30	8	4	No	No
Epinephrine ($\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$)	0.10	0.02	0.02	0.02	0.01	0.01
MV	Yes	Yes	Yes	No	No	No
P/F (mmHg)	171	233	238	267	336	324
Heparin (U/min)	10	8–14	16	14–16	12–14	9–12
Urea ($\mu\text{mol}/\text{L}$)	285 (7 h)	1150	730	695	630	280
CRRT	No	No	Yes	Yes	Yes	Yes

BP: Blood pressure; CRRT: Continuous renal replacement therapy; CVP: Central venous pressure; HR: Heart rate; MV: Mechanical ventilation; P/F: $\text{PaO}_2/\text{FiO}_2$; ECMO: Extracorporeal membrane oxygenation; MPE: Massive pulmonary embolism.

from 15% to 48% within 8 days). The patient was transferred to the emergency ward on day 16, and anticoagulation with warfarin was performed. However, he developed pulmonary and surgical site infections and required prolonged hospitalization. The patient was discharged on hospital day 42 with intact neurological and recovered renal function.

The present case demonstrated that ECMO might be an effective salvage therapy in patients with MPE in whom thrombolysis or embolectomy was strictly contraindicated. Fat embolism (FE) is most recognizable after orthopedic trauma, with the highest incidence for at-risk fractures (closed long-bone fractures of the lower extremities, particularly of the femur). The classic clinical sign of FE syndrome is cutaneous petechiae; the characteristic petechial rash is observed in areas such as the head, neck, axillae, subconjunctiva, and anterior thorax.^[2] In this case, the patient did not have cutaneous petechiae, and transesophageal echocardiography showed severe right ventricular dilatation and pulmonary hypertension; thus, he was diagnosed with PE, not FE.

In order to prevent deep venous thrombosis and even PE, it is essential that patients with long-term immobilization receive adequate anticoagulation drugs. In cases where patients with MPE are not eligible for thrombolysis or embolectomy therapy, they may be resuscitated and supported by ECMO until clot dissolution occurs or other interventions, such as an embolectomy, can be performed. VA-ECMO provides inherent advantages in the treatment of MPE because it requires anticoagulation and decompresses the acutely overloaded right atrium and ventricle, restoring the hemodynamic status of the patient and permitting adequate organ oxygenation and CO₂ removal.^[3,4]

Whether to use thrombolysis in a patient with PE requires a clinical assessment of the patient's hemodynamic status and potential bleeding risk.^[5] In this case, neither thrombolysis nor embolectomy was administered because of the high risk of bleeding and the patient's unstable hemodynamic status. Moreover, neither of the procedures was performed after the ECMO because of the patient's improved circulation and respiratory function. However, this did not mean that the therapy described here was appropriate. If the hemodynamic effects of thrombolysis far outweigh its potential bleeding risk when the patient does not receive ECMO support, thrombolysis should be performed. Embolectomy can be administered more safely under ECMO support, which may shorten the hospital stay.

In this case, the patient experienced an MPE and systemic hypotension, leading to inadequate perfusion of the vital organs. Unfortunately, he later also developed renal failure; the timely use of continuous renal replacement therapy was proved to be beneficial. A future in-depth study should examine how to prevent and treat patients with MPE, hemodynamic deterioration, and inadequate perfusion of the vital organs resulting in organ failure.

In patients with HIT, heparin can lead to massive platelet activation and thromboembolism. The incidence of HIT in patients undergoing ECMO support has been estimated to be below 1%. Only a few cases of HIT in patients managed by ECMO who developed acute oxygenation failure from thrombosis have been reported in the literature.^[6] This condition required an alternative anticoagulation approach such as bivalirudin, argatroban, or rivaroxaban.^[7]

Some case reports have demonstrated a beneficial effect of VA-ECMO support in hemodynamically unstable patients experiencing an acute MPE.^[8,9] Despite these findings, the current guidelines for the management of acute PE do not consider ECMO as first-line therapy during catastrophic disease.^[10] Large-scale randomized controlled trials, although desirable, are difficult to perform. Thus, based on the increased number of case reports and the current practice in many centers, international guidelines should consider ECMO as first-line therapy in cases of MPE in which classical thrombolytic therapies are contraindicated.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galie N, *et al.* 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism. The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). *Eur Heart J* 2014;35:3033-80. doi: 10.1093/eurheartj/ehu283.
2. Georgopoulos D, Bouros D. Fat embolism syndrome: Clinical examination is still the preferable diagnostic method. *Chest* 2003;123:982-3. doi: 10.1378/chest.123.4.982.
3. Brodie D, Bacchetta M. Extracorporeal membrane oxygenation for ARDS in adults. *N Engl J Med* 2011;365:1905-14. doi: 10.1056/NEJMc1114604#SA2.
4. Yusuff HO, Zochios V, Vuylsteke A. Extracorporeal membrane oxygenation in acute massive pulmonary embolism: A systematic review. *Perfusion* 2015;30:611-6. doi: 10.1177/0267659115583377.
5. Meyer G, Planquette B, Sanchez O. Pulmonary embolism: Whom to discharge and whom to thrombolize? *J Thromb Haemost* 2015;13 Suppl 1:S252-8. doi: 10.1111/jth.12944.
6. Glick D, Dzierba AL, Abrams D, Muir J, Eisenberger A, Diuguid D, *et al.* Clinically suspected heparin-induced thrombocytopenia during extracorporeal membrane oxygenation. *J Crit Care* 2015;30:1190-4. doi: 10.1016/j.jcrc.2015.07.030.
7. Welp H, Ellger B, Scherer M, Lanckohr C, Martens S, Gottschalk A, *et al.* Heparin-induced thrombocytopenia during extracorporeal membrane oxygenation. *J Cardiothorac Vasc Anesth* 2014;28:342-4. doi: 10.1053/j.jvca.2012.10.014.
8. Ko CH, Forrest P, D'Souza R, Qasabian R. Successful use of extracorporeal membrane oxygenation in a patient with combined pulmonary and systemic embolisation. *Perfusion* 2013;28:138-40. doi: 10.1177/0267659112463163.
9. Pavlovic G, Banfi C, Tassaux D, Peter RE, Licker MJ, Bendjelid K, *et al.* Peri-operative massive pulmonary embolism management: Is veno-arterial ECMO a therapeutic option? *Acta Anaesthesiol Scand* 2014;58:1280-6. doi: 10.1111/aas.12411.
10. Paden ML, Conrad SA, Rycus PT, Thiagarajan RR, ELSO Registry. Extracorporeal life support organization registry report 2012. *ASAIO J* 2013;59:202-10. doi: 10.1097/MAT.0b013e3182904a52.