



## Case report

# Continuous veno-venous hemofiltration with oXiris hemofilters for the treatment of Fournier's gangrene: A case report series

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## A B S T R A C T

**Background:** Fournier's gangrene (FG) is a severe form of necrotizing fasciitis primarily caused by gram-negative bacteria. FG can rapidly progress to septic shock, resulting in high mortality rates. In the past, the management of the inflammatory response caused by gram-negative bacteria has been limited. Continuous Venous Hemofiltration with oXiris hemofilters (oXiris-CVVH) has shown promise in adsorbing inflammatory factors and endotoxins, making it an attractive approach for treating FG. This study aims to provide insights into the characteristics of patients with FG and septic shock who have been successfully treated using oXiris-CVVH, based on a series of patient cases.

**Results:** This study presents the management of 4 cases in the intensive care units of a tertiary hospital in southern China. The use of oXiris-CVVH in patients with septic shock and FG yielded valuable practical insights.

**Conclusion:** Based on the experience gained from these 4 cases, the utilization of oXiris-CVVH demonstrated potential in reducing the Sequential Organ Failure Assessment (SOFA) score, improving prognosis, and effectively lowering the levels of lactic acid and procalcitonin (PCT) in the blood. Additionally, it facilitated a reduction in the dosage of noradrenaline. Therefore, oXiris-CVVH should be considered as an adjunctive therapy in the treatment of patients with FG and septic shock.

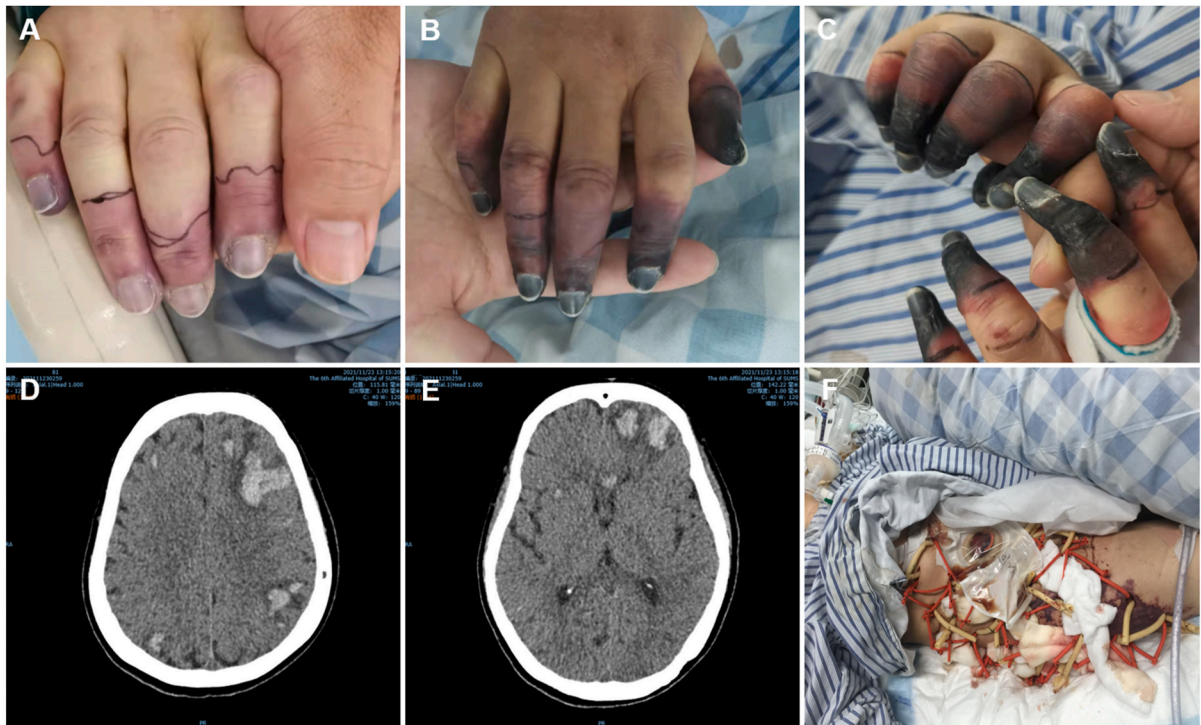
## 1. Introduction

Fournier's gangrene (FG), a type of necrotizing fasciitis (NF), is an uncommon, rapidly progressive, and life-threatening infection that affects the external genitalia and/or perineum [1,2]. The mortality rate associated with FG has been reported to be as high as 67% [2,3]. FG can rapidly lead to septic shock and subsequent death, accounting for up to 78% of mortalities [4-6]. The main causative pathogen of FG is Gram-negative bacillus [7,8], which produces significant amounts of lipopolysaccharides (LPS). LPS activates the innate immune system and triggers the excessive production of proinflammatory cytokines, leading to multiple organ failure and potentially fatal outcomes in patients. Therefore, the removal of LPS and cytokines holds promise as a treatment for sepsis in FG patients [9].

Extracorporeal blood purification (EBP) has been proposed as an additional therapeutic intervention for sepsis patients, aiming to remove LPS and inflammatory cytokines from the bloodstream [10]. However, various types of hemofilters, such as polymyxin-B hemoperfusion (PMX-HP) [11,12], CytoSorb filter [13], and high-cutoff membranes, have been found to be ineffective in reducing the overall mortality rate of sepsis patients. oXiris hemofilter is a polyacrylonitrile-based membrane hemofilter that not only provides renal support but also possesses the ability to remove endotoxins and adsorb inflammatory cytokines [14,15]. Consequently, it can help correct systemic hemodynamics and improve organ function in sepsis patients [16-18]. A few previous studies have focused on

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**Fig. 1.** Clinical characteristics and image data of patient in case 1. A&B&C refer to gangrene of finger tips on November 22, 27 and December 6, 2021, respectively. D and E show the cranial CT indicating cerebral hemorrhage on November 23, 2021. F exhibits FG drainage after surgery. CT, computerized tomography; FG, Fournier's gangrene.

the application of Continuous Venovenous Hemofiltration with oXiris hemofilters (oXiris-CVVH) on septic patients. However, to the best of our knowledge, only a limited number of studies have validated the effectiveness and safety of oXiris-CVVH in patients with FG and septic shock, where circulating inflammatory cytokines and LPS play a vital role in the development of the condition.

The objective of this study was to investigate the effectiveness and safety of oXiris-CVVH in managing septic shock among patients with FG. The study involved the analysis of 4 cases within an intensive care unit (ICU) at a university hospital. These findings aim to contribute to the clinical practice and future application of oXiris-CVVH in treating septic shock in FG patients.

## 2. Case descriptions

### 2.1. Case 1

A 58-year-old female with a one-month history of melaena was admitted to the hospital on November 10, 2021. She was diagnosed with transverse colon adenocarcinoma, with computerized tomography (CT) staging of T4aN1M0. Laparoscopic radical right hemicolectomy was performed on November 17, 2021. On the second postoperative day, she complained of severe abdominal pain, accompanied by redness, swelling, and warmth in the right upper abdomen and the perianal areas. This manifestation worsened with the development of septic shock. A significant drop in white blood cell count indicated a severe intra-abdominal infection in the patient. Hence, she underwent exploratory laparotomy and ileostomy on November 19, 2021. Anastomotic leakage and abdominal abscess were discovered during the surgery. After the procedure, she was transferred to ICU. The infusion rates of norepinephrine and adrenaline after the operation were 1.0  $\mu\text{g}/\text{kg}/\text{min}$  and 0.35  $\mu\text{g}/\text{kg}/\text{min}$ , respectively. Following the surgery, the patient experienced multiorgan dysfunction, including acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), and acute kidney injury (AKI). Additionally, the patient suffered a cerebral hemorrhage during treatment, fortunately without affecting her consciousness (Figure 1D, E). Results from the blood examination revealed a white blood cell count (WBC) of  $1.17 \times 10^9/\text{L}$ , platelet count of  $37 \times 10^9/\text{L}$ , procalcitonin (PCT) level above 100 ng/ml, and lactate level of 10.5 mmol/L, PaO<sub>2</sub>/FiO<sub>2</sub> was 86 mmHg, serum creatinine level was 94.06  $\mu\text{mol}/\text{L}$ , D-Dimer level was 5.32  $\mu\text{g}/\text{ml}$ , international normalized ratio (INR) was 2.17, activated partial thromboplastin time (APTT) was more than 120 seconds, and fibrinogen (FIB) was 2.7 g/L. The  $\beta$ -D-glucan test (G test) showed a level of 192.13 pg/ml, exceeding the normal range of 0–70 pg/ml. Consequently, the patient was administered a comprehensive antimicrobial regimen comprising intravenous meropenem (2.0 g every 8 hours), vancomycin (1.0 g every 12 hours), and caspofungin (50 mg daily), targeting a broad spectrum of pathogens. The positive blood culture results confirmed the presence of *extended-spectrum  $\beta$ -lactamase-producing Escherichia coli (ESBL- E. coli)* and *Bacteroides fragilis* three days later (Table 1).

**Table 1**  
Cases and treatment details.

|                   | Case 1  | Case 2  | Case 3  | Case 4   |
|-------------------|---|---|---|--|
| Case Descriptions |   |   |   |  |
| Age               | 58  | 50  | 32  | 67   |
| Gender            | Female  | Male  | Male  | Female   |
| Infection sites   | Right lumbar and perineum                               | Perianal, perineum and left leg                         | Perianal, perineum, scrotum, anterior pubic symphysis | Right lumbar and perineum                                    |
| Etiology          | <i>Escherichia coli</i> and <i>Bacteroides fragilis</i> | <i>Escherichia coli</i> and <i>Enterococcus faecium</i> | Negative culture                                      | <i>Enterobacter cloacae</i> and <i>Klebsiella pneumoniae</i> |
| AKI stages        | Stage II  | Stage II  | Stage I   | Stage I  |
| Operations        | Debridement and thread-drawing drainage after oXiris    | Incision and thread-drawing drainage before oXiris      | Incision and thread-drawing drainage before oXiris    | Incision and thread-drawing drainage before oXiris           |
| History           | Tumour  | Diabetes mellitus                                       | None  | Tumour   |

AKI, acute kidney injury; CVVH, continuous venovenous hemofiltration.

**Table 2**  
oXiris prescription details.

|                              | Case 1   | Case 2   | Case 3   | Case 4   |
|------------------------------|--|--|--|--|
| Start time                   | November 19, 2021  | March 22, 2020   | March 27, 2019   | March 15, 2019   |
| End time                     | November 27, 2021  | March 26, 2020   | March 30, 2019   | March 18, 2019   |
| Mode                         | CVVH   | CVVH   | CVVH   | CVVH   |
| Dose, mL/kg/h                | 35   | 35   | 30   | 35   |
| Blood flow, ml/min           | 150  | 200  | 180  | 200  |
| Predilution, ml/h            | 800  | 1200   | 1200   | 800  |
| Postdilution, ml/h           | 1450   | 1300   | 1300   | 1450   |
| Fluid balance, ml/h          | 800→-500   | 500→-300   | 300→-200   | 600→-300   |
| Additional anticoagulant     | Citrate  | Citrate  | Citrate  | Citrate→Heparin  |
| Replacement fluid            | Na <sup>+</sup> 136mmol/L,<br>K <sup>+</sup> 2mmol/L,<br>HCO <sub>3</sub> <sup>-</sup> 36mmol/L. | Na <sup>+</sup> 136mmol/L,<br>K <sup>+</sup> 4mmol/L,<br>HCO <sub>3</sub> <sup>-</sup> 35mmol/L. | Na <sup>+</sup> 136mmol/L,<br>K <sup>+</sup> 4mmol/L,<br>HCO <sub>3</sub> <sup>-</sup> 30mmol/L. | Na <sup>+</sup> 136mmol/L,<br>K <sup>+</sup> 2mmol/L,<br>HCO <sub>3</sub> <sup>-</sup> 36mmol/L. |
| Replacement fluid rate, ml/h | 2250   | 2500   | 2500   | 2250   |
| Mean duration per filter, h  | 15   | 24   | 18   | 24   |

CVVH, continuous venovenous hemofiltration.

oXiris-CVVH was performed 5 hours after admission to the ICU on the day of the surgery, and was anticoagulated with trisodium citrate (Table 2). 12 hours later, the infusion rate of norepinephrine was significantly reduced from 1.00 µg/kg/min to 0.55 µg/kg/min, the lactate level decreased to 5.6 mmol/L, and the urine output increased to 30–100 ml/h. The patient's recovery was slow over the next two days. The skin and soft tissue infection progressed to NF in the right waist and perineal areas, hence surgical debridement and incision-thread-drawing procedure were performed on the second day after the operation (Fig. 1F). After that, oXiris-CVVH continued to be utilized with multimodal treatments, which comprised infection source control, adequate antibiotic therapy, hemodynamic stability, and organ support care. A total of thirteen sets of oXiris hemofilters were employed for the treatment during the following 8 days (Table 3).

The hemodynamics were gradually stabilized with improvement in organ function. Three days after oXiris-CVVH treatment (November 22, 2021), low molecular weight heparin was administered once daily due to symmetrical peripheral gangrene caused by septic shock (Fig. 1A, B, and C). The oXiris-CVVH treatment was successfully discontinued on the ninth day (November 30, 2021) when the urine output returned to 1000 ml per day. The patient was transferred from the ICU to the ward on December 6, 2021. The amputation of gangrenous toes (ten toes) and gangrenous planectomy (ten fingers) were performed on January 20, 2022, and February 11, 2022, respectively. Finally, the patient was discharged on March 29, 2022.

## 2.2. Case 2

On March 22, 2020, a man aged 50 with poorly controlled type 2 diabetes was admitted to the hospital due to painful swelling in the scrotum and perianal region (Table 1). Upon admission, he presented with a fever of 39.1 °C, tachycardia (heart rate of 150 bpm), and hypotension (blood pressure of 89/42 mmHg). He exhibited cyanosis and had a respiratory rate of 30–40 breaths per minute. The oxygen saturation level was 90%, with PaO<sub>2</sub>/FiO<sub>2</sub> of 146 mmHg. Necrotic tissue was observed in the scrotum and perineum. A pelvic CT scan identified subcutaneous emphysema in the scrotum and perianal fascia. The patient was promptly diagnosed with extensive FG and septic shock, and surgical debridement and transverse colostomy were performed. Following the surgery, the patient was transferred to ICU. Blood tests showed that the WBC count elevated to 16.68 × 10<sup>9</sup>/L, platelet count decreased to 84 × 10<sup>9</sup>/L, serum creatinine level was 67.71 µmol/L, lactic acid level was 6 mmol/L, PCT level was above 100 ng/ml, INR was 1.9, APTT was 68 seconds, and FIB level was 7.4 g/L (Table 3). Considering the patient's clinical status and diagnostic findings, we initiated a comprehensive antimicrobial treatment involving intravenous meropenem (1.0 g every 8 hours), linezolid (0.6 g every 12 hours), and caspofungin (50

**Table 3**  
Treatment outcomes details.

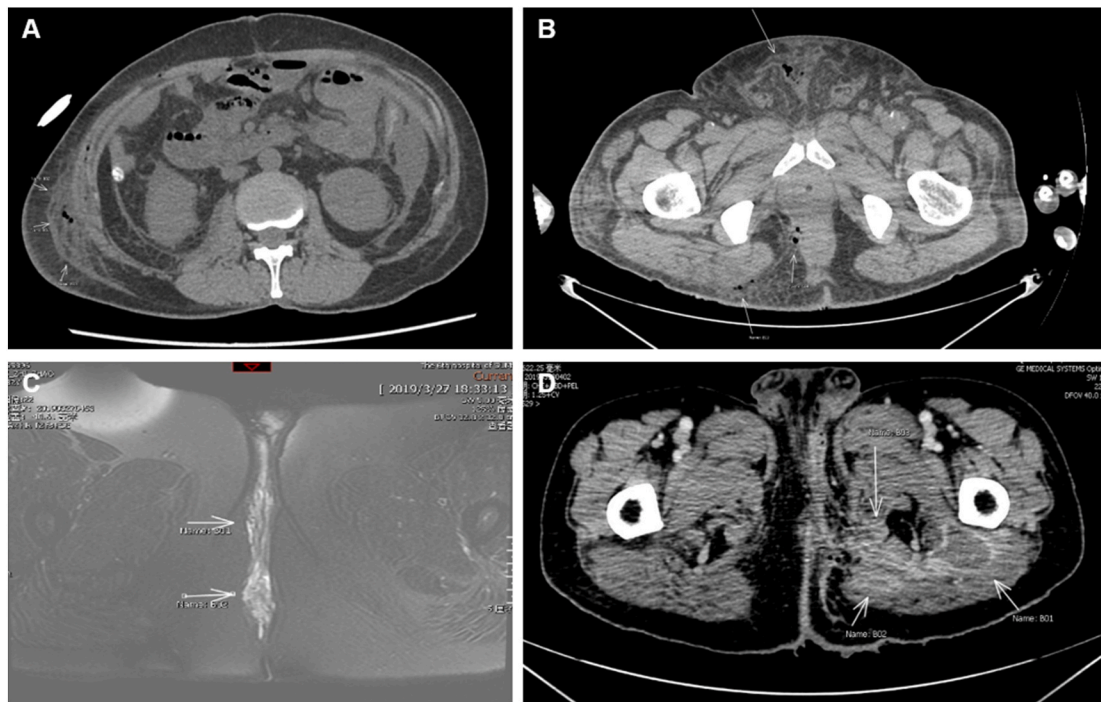
|  | Case 1 | Case 2 | Case 3 | Case 4 |
|--|--------|--------|--------|--------|
| APACHEII score                         |        |        |        |        |
| Before oXiris                          | 31     | 30     | 28     | 18     |
| After oXiris                           | 21     | 16     | 14     | 14     |
| Lactate, mmol/L                        |        |        |        |        |
| Day 0                                  | 10.5   | 6      | 1      | 12.5   |
| Day 1                                  | 5.5    | 3      | 1.7    | 15     |
| Day 2                                  | 6.5    | 2.5    | 1.4    | 12.4   |
| Day 3                                  | 9      | 1.9    | 1.3    | 4.4    |
| Day 4                                  | 10.1   | 1.5    | 0.8    | 5.9    |
| Day 5                                  | 10.3   | 0.9    | 0.6    | 3.7    |
| Day 6                                  | 6.3    | 1      | 0.7    | 3      |
| PCT, ng/ml                             |        |        |        |        |
| Day 0                                  | >100   | >100   | 7.9    | 97     |
| Day 1                                  | >100   | >100   | 9.6    | 46     |
| Day 2                                  | 61     | >100   | 3.5    | 42     |
| Day 3                                  | 40     | 60     | 1.3    | 22     |
| Day 4                                  | 22     | 32     | 0.66   | 19     |
| Day 5                                  | 18     | 21     | 0.47   | 11     |
| Day 6                                  | 15     | 11     | 0.43   | 6.9    |
| CRP,mg/L                               |        |        |        |        |
| Day 0                                  | 101.08 | >200   | 175.54 | 178.35 |
| Day 1                                  | >200   | >200   | 196.3  | 122.46 |
| Day 2                                  | >200   | >200   | 165.38 | >200   |
| Day 3                                  | >200   | 182.23 | 71.04  | >200   |
| Day 4                                  | >200   | 167.48 | 56.6   | >200   |
| Day 5                                  | >200   | 144.71 | 98.8   | 142    |
| Day 6                                  | 187.64 | 131.04 | 131.22 | 69.02  |
| SOFA score                             |        |        |        |        |
| Before oXiris                          | 11     | 11     | 10     | 12     |
| After oXiris                           | 8      | 8      | 8      | 7      |
| Creatinine, umol/L                     |        |        |        |        |
| Before oXiris                          | 91.7   | 190.05 | 98.99  | 103.10 |
| After oXiris                           | 60.71  | 39.25  | 52.51  | 78.74  |
| Urine output,ml/h                      |        |        |        |        |
| Before oXiris                          | 20     | 100    | 240    | 10     |
| After oXiris                           | 30     | 100    | 500    | 30     |
| Duration of ventilation, day           | 14     | 8      | 5      | 12     |
| Duration of vasoactive agent, day      | 12     | 6      | 5      | 13     |
| VDI                                    |        |        |        |        |
| Day 0                                  | 2.288  | 0.541  | 1.154  | 2.705  |
| Day 1                                  | 0.976  | 0.241  | 0.000  | 0.400  |
| Day 2                                  | 0.481  | 0.278  | 0.071  | 0.220  |
| Day 3                                  | 0.513  | 0.128  | 0.094  | 0.074  |
| Duration of CVVH, day                  | 10     | 4      | 3      | 7      |
| Duration of oXiris, day                | 8      | 4      | 3      | 3      |
| Lymphocyte count, × 10 <sup>9</sup> /L |        |        |        |        |
| Before oXiris                          | 0.11   | 0.45   | 1.01   | 0.23   |
| After oXiris                           | 0.51   | 0.62   | 1.20   | 0.78   |
| Fluid replacement, ml                  |        |        |        |        |
| Day 1                                  | 3020   | −379   | 6893   | 5980   |
| Day 2                                  | −1621  | 1284   | 526    | 200    |
| Day 3                                  | −535   | 602    | −237   | −1200  |
| Duration of ICU staying, day           | 17     | 10     | 10     | 12     |
| Pipeline coagulation, set              | 5      | 0      | 1      | 0      |

APACHEII, Acute Physiology And Chronic Health Evaluation II; PCT, procalcitonin; SOFA, Sequential (Sepsis-related) Organ Failure Assessment; VDI\*, Vasopressor Dependency Index; CVVH, continuous venovenous hemofiltration; ICU, Intensive Care Unit.

\*VDI = inotropic score/mean arterial pressure (MAP); inotropic score = (dopamine dose [ $\mu\text{g}/\text{kg}/\text{min}$ ] × 1 + (epinephrine dose [ $\mu\text{g}/\text{kg}/\text{min}$ ] × 100 + (norepinephrine dose [ $\mu\text{g}/\text{kg}/\text{min}$ ] × 100).

mg daily). Cultures from intraoperative specimens revealed the presence of *Escherichia coli* and *Enterococcus faecium* (Supplementary Table 1). The patient developed sepsis-induced acute kidney injury with oliguria lasting for more than 24 hours, and the infusion rate of norepinephrine was increased to 0.4  $\mu\text{g}/\text{kg}/\text{min}$ .

oXiris-CVVH was performed with trisodium citrate as anticoagulants 2 h after ICU admission (Table 2). Norepinephrine was reduced to 0.15  $\mu\text{g}/\text{kg}/\text{min}$ ; lactic acid decreased to 3.9 mmol/L after 12 hours of oXiris-CVVH. A total of five sets of oXiris hemofilters were used over four days (Table 3). The patient's condition was gradually improved with the use of broad-spectrum antibiotics, control of the infection source, and oXiris-CVVH. Norepinephrine was discontinued after March 29, 2020. He was successfully extubated on



**Fig. 2.** MRI of the patient in case 3. A&B&C&D revealed subcutaneous emphysema in the scrotum and perianal fascia and mesorectum. MRI, magnetic resonance imaging.

March 30, 2020, transferred from ICU to the ward on April 4, 2020, and discharged on April 29, 2020.

### 2.3. Case 3

A 32-year-old male patient presented with perianal swelling, pain, and pus discharge for 5 days. He was admitted to the hospital on March 27, 2019. Upon admission, his body temperature rose to 39.5 °C. He exhibited dyspnea with a respiratory rate of 30–40 breaths/minute, and a heart rate of 160 beats/minute. His blood pressure at admission was 159/113 mmHg, which subsequently dropped to 60/30 mmHg. Magnetic resonance imaging (MRI) revealed subcutaneous emphysema in the scrotum, perianal fascia, and mesorectum (Fig. 2A, B, 2C, 2D). Immediate surgical debridement was performed after admission to prevent infection progression, after which the patient was transferred to the ICU for further treatment. Septic shock persisted despite the surgical procedure, and the infusion rate of norepinephrine was 0.75 µg/kg/min upon ICU admission. The patient developed AKI with a urine output of less than 0.5 ml/kg per hour for 6 hours. The blood test showed an increase in WBC count to  $31.2 \times 10^9/L$ , platelet count was  $231 \times 10^9/L$ , serum creatinine was 98.99 µmol/L, PCT was 7.9 ng/ml, lactic acid was 1.0 mmol/L (Table 3), and glycated hemoglobin (HbA1c) was 7.8%. The patient initially received a regimen of intravenous antimicrobial therapy, consisting of meropenem (1.0 g every 8 hours), vancomycin (1.0 g every 12 hours), and caspofungin (50 mg daily). Despite this treatment, subsequent etiological tests yielded negative results.

oXiris-CVVH was started 2 hours after ICU admission due to sepsis-induced acute renal insufficiency. During the oXiris-CVVH treatment, the patient experienced hypotension, prompting adjustments in pressor dosage and an increase in the rate of positive fluid balance to manage the condition. Urine output returned to 30–50 ml/h 12 hours later, and the dose of norepinephrine decreased to 0.1 µg/kg/min. A total of 4 sets of oXiris hemofilters were used for 3 days (Table 3). After undergoing surgical debridement and receiving broad-spectrum antibiotics, the patient's condition gradually improved. The administration of noradrenaline was ceased on March 29, 2019. The patient was successfully extubated on April 2, 2019 and transferred from the ICU to the general ward on April 6, 2019. Finally, the patient was discharged on April 11, 2019.

### 2.4. Case 4

The 67-year-old female patient was diagnosed with rectal adenocarcinoma and hospitalized on February 27, 2019. She had a history of endometrial carcinoma one year ago and underwent surgical treatment for it (Table 1). On March 12, 2019, she underwent radical surgery for rectal cancer, intestinal adhesiolysis, and had an ileostomy performed. She developed septic shock and was admitted to the ICU three days later. Swelling, tenderness, and black necrosis appeared on the right abdominal wall near the ileostomy site and anal perineum. A CT scan confirmed the diagnosis of NF on March 15, 2019. Her blood pressure was 73/32 mm Hg, and her heart rate was 124 bpm. Blood tests showed that the WBC decreased to  $2.11 \times 10^9/L$ , PCT increased to 97 ng/L, and lactate levels increased to 12.5 mmol/L (Table 3). The patient was initially treated with intravenous meropenem (1.0 g every 8 h), linezolid (0.6 g/

12 h) and caspofungin (50 mg once daily). Abdominal drainage fluid culture revealed the presence of *Enterobacter cloacae*, and on March 18, 2019, a positive blood culture for *Klebsiella pneumoniae bacteremia* was reported. The norepinephrine infusion rate at ICU admission was 1.2 µg/kg/min and adrenaline were 0.45 µg/kg/min.

oXiris-CVVH was initiated upon the patient's admission to the ICU. The dosage of norepinephrine was reduced from 1.2 µg/kg/min to 0.5 µg/kg/min, and adrenaline administration was discontinued 8 hours afterwards. Exploratory laparotomy and debridement were conducted on March 16, 2019. The patient received three sets of oXiris hemofilter treatment for a duration of three days (Table 3). The infusion rates of vasopressors used to maintain hemodynamic stability were gradually decreased and ultimately discontinued on March 25, 2019. The patient was extubated on March 27, 2019, and discharged from the ICU on March 30, 2019. During the oXiris-CVVH treatments, the patient experienced clotting in the deaeration chamber. Consequently, we transitioned from citric to heparin anticoagulation for subsequent sessions to address this issue.

### 3. Discussion

#### 3.1. Overview

We report on 4 cases of oXiris-CVVH therapy for patients with septic shock caused by FG in the ICU of a university hospital in China. This series of four cases aims to provide a comprehensive understanding of the oXiris-CVVH treatment modality for FG patients. Detailed clinical profiles of these cases are outlined below.

#### 3.2. Early initiation of oXiris-CVVH treatment

FG is a rapidly progressive NF affecting the perineum and external genitalia with a potential to lead to septic shock. The bacteria present in the affected tissue release toxins, causing severe systemic toxicity and triggering the release of inflammatory mediators [8]. Hence, it is crucial to mitigate the inflammatory response at an early stage of FG. The oXiris hemofilter has demonstrated its ability to adsorb LPS and a broad range of immune response mediators. It can effectively remove approximately 100% of interleukin-10 and around 90% of interleukin-6, high-mobility group box 1 protein, and tumor necrosis factor-α [16,19]. Previous clinical studies have demonstrated that the use of the oXiris hemofilter is effective in maintaining stable hemodynamic parameters and reducing the need for vasoactive drugs [17,18,20]. While the majority of studies have not shown a significant improvement in mortality among septic shock patients after cytokine removal via Continuous Veno-Venous Hemofiltration (CVVH), our report highlights the cases of case 1 and case 4 where surgical debridement was carried out by surgeons only after observing improved hemodynamics with oXiris-CVVH. It is believed that achieving earlier hemodynamic stabilization can significantly minimize surgical risks and enhance safety considerations.

#### 3.3. Anticoagulant for oXiris-CVVH treatment

Septic shock is frequently accompanied by coagulation dysfunction, specifically sepsis-induced coagulopathy (SIC) [21,22]. The prevalence of SIC in the septic ICU population has been reported to be as high as 50.9% [23]. The formation of immunothrombosis often leads to the occlusion of the EBP pipeline or hemofilter, while coagulation factors contribute to a state of hypocoagulation [24]. Although the oXiris membrane is coated with heparin to reduce the risk of coagulation, clinical studies have shown that the risk of coagulation may still persist even when patients exhibit hypocoagulation [25]. Following the recommendations of the Kidney Disease Improving Global Outcomes (KIDGO) guidelines [26], all our patients received regional citrate. In cases 1 and 3, blood clotting occurred in the extracorporeal bypass pipeline or hemofilter, possibly due to individual differences. It is important to highlight that case 1 not only experienced gangrene at the end of the limbs but also suffered from intracranial hemorrhage.

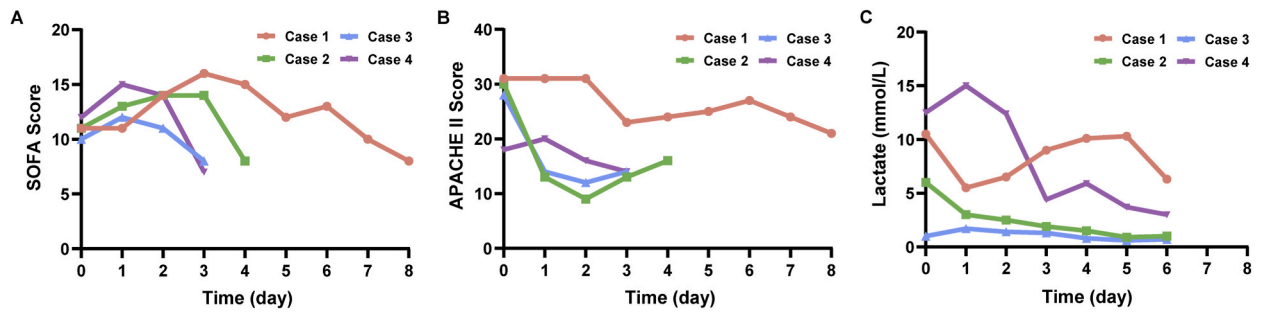
Moreover, platelet consumption can occur during CVVH, which might further exacerbate the coagulation dysfunction. Local anticoagulation has proven to be effective in relieving this phenomenon.

#### 3.4. Duration time for oXiris-CVVH treatment

For patients with sepsis-induced AKI, the recovery of renal function is considered the primary indication for discontinuing CVVH treatment [27]. However, determining the ideal timing for discontinuation remains a challenge in clinical practice, and it should be personalized based on the patient's condition and initial treatment goals. Potential indicators for discontinuation in our cases include a decrease in vasopressor dosage, a reduction in serum levels of lactic acid and PCT, and an increase in urine output.

#### 3.5. Survival benefit potential of oXiris-CVVH treatment

The four cases described above, which were treated with the oXiris filter, effectively recovered from septic shock caused by FG. Within one day of oXiris-CVVH treatment, the dosage of vasopressors was gradually reduced or even discontinued. PCT, blood lactic acid levels and vasopressor dependency index (VDI), all decreased within three days of oXiris-CVVH treatment. Additionally, we observed reductions in SOFA score, APACHE II score and lactate in patients across all four cases after undergoing oXiris-CVVH treatment (Fig. 3A&B&C). These findings are in line with other reported cases [17,18,20]. Recent meta-analysis shows oXiris reduces sepsis 28-day mortality, ICU days, improves SOFA scores, lowers norepinephrine, IL-6, and lactate [28,29]. This aligns with our



**Fig. 3.** The daily changes of SOFA score, APACHE II score, and lactate. A: The daily change of SOFA score. B: The daily change of APACHE II score. C: The daily change of lactate. SOFA, Sequential Organ Failure Assessment; APACHE II, Acute Physiology And Chronic Health Evaluation II.

study findings. Theoretical considerations and clinical evidence have both demonstrated that early implementation of oXiris-CVVH in FG patients can yield numerous benefits.

$VDI = \text{inotropic score} / \text{mean arterial pressure (MAP)}$

$\text{inotropic score} = (\text{dopamine dose } [\mu\text{g} / \text{kg} / \text{min}]) \times 1 + (\text{epinephrine dose } [\mu\text{g} / \text{kg} / \text{min}]) \times 100 + (\text{norepinephrine dose } [\mu\text{g} / \text{kg} / \text{min}]) \times 100.$

### 3.6. Applications of oXiris-CVVH treatment in other critical illnesses

oXiris is widely used not only in severe infection or sepsis, but also in other critical diseases. Early small-size case series collectively found that a reduced level of overexpressed proinflammatory cytokine levels, stabilization of hemodynamic status, and staged improvement of organ function during the treatment with Oxiris filter in critically ill COVID-19 patients [30–32]. In contrast, Kang et al. reported CRRT with oXiris filter may not effectively alleviate cytokine release syndrome in non-AKI patients with severe and critical COVID-19, which might be attributed to the relatively lower concentration of IL-6 in COVID-19 patients than in patients with septic shock [33]. Additionally, a study has applied the oXiris filter in cardiopulmonary bypass surgery to decrease related inflammation [34].

### 3.7. Limitations

There are some limitations in our study. Firstly, as a case series, it involves a small patient cohort, offering a limited view of oXiris-CVVH therapy outcomes. Secondly, the absence of a randomized control group reduces the strength of our conclusions. Furthermore, the 2021 Surviving Sepsis Campaign highlighted a lack of evidence supporting alternative blood purification techniques [35]. A recent meta-analysis emphasized the necessity for more randomized trials to pinpoint patient groups that might benefit from extracorporeal blood purification [36]. Consequently, further research is essential to validate the effectiveness and accuracy of oXiris-CVVH therapy.

## 4. Conclusions

Based on the four cases reported above, it can be inferred that the use of oXiris-CVVH may effectively reduce the SOFA score, improve patient prognosis, and effectively decrease blood levels of lactic acid and PCT, as well as reduce the dosage of noradrenaline in patients. Therefore, it is recommended that oXiris-CVVH be considered as an adjuvant therapy for patients with FG and septic shock. It is important to initiate oXiris-CVVH early in the treatment process for septic shock in FG patients.

### Data availability statement

The data presented in this study might be available depending on the type of demand and use. A request must be sent to the corresponding author with the permission of all authors.

### Ethical statement

Informed consent was obtained from all participants/patients (or their proxies/legal guardians) for the publication of all their data and/or images.

### CRedit authorship contribution statement

**Yang Yang:** Writing – review & editing, Writing – original draft, Investigation, Data curation, Formal analysis, Methodology, Software. **Enhe Liu:** Visualization, Validation, Data curation, Investigation, Writing – original draft. **Xijian Zhang:** Writing – review & editing, Validation, Software, Data curation. **Lichun Wang:** Visualization. **Lei Chen:** Supervision, Conceptualization, Investigation,

Resources, Validation, Writing – review & editing.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2024.e30463>.

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