Utilization of extracorporeal membrane oxygenation for a severe cardiocirculatory dysfunction recipient in liver transplantation
A case report

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Abstract
Rationale: Severe cardiac dysfunction or severe pulmonary hypertension is a contraindication of liver transplantation (LT). Extracorporeal membrane oxygenation (ECMO) is an advanced therapy for severe lung and/or cardiocirculatory dysfunction or failure. The application of ECMO to patients during the LT perioperative period may help recipients with severe cardiac disease to maintain the heart function and alleviate the reperfusion syndrome.

Patient concerns: A female liver recipient complained about weakness for 6 months.

Diagnoses: The patient was diagnosed as hepatitis B virus (HBV)-related hepatic cirrhosis (MELD 24, Child–Pugh C) with severe mitral regurgitation, severe tricuspid regurgitation, left atrium and left ventricle enlargement, cardiac insufficiency, pulmonary arterial hypertension, and hypoxemia.

Interventions: The patient underwent LT from a cardiac deceased donor. The surgery was completed by venoarterial ECMO. The femoral vessels cannulation was done after the dissection of the patient’s liver and before the venous blocking. Venous cannula reached to the position below renal vein, while arterial cannula reached to common iliac artery. We regulated the ECMO index according to the patient’s condition. The dosage of heparin was adjusted on the basis of the activated clotting time. Respiratory support, milrinone, furosemide, and mannitol were used to improve the circulation. The bleeding volume of surgery was 1200 mL. The cardiocirculatory function and other vital signs remained good in the perioperative period. In the first 24 hours after surgery, central venous pressure decreased from 17 to 7 cmH2O. Thirty hours after surgery, the ECMO was removed. Eighteen hours later, the recipient did not need respiratory support.

Outcomes: No complications of transplantation or ECMO were found.

Lessons: It is feasible to utilize ECMO as a cardiocirculatory function support in the LT. ECMO does not increase the risk of hemorrhage. ECMO can play an important role in ensuring the security of the liver recipients in the surgery and in the postoperative period.

Abbreviations: ACT = activated clotting time, CVP = central venous pressure, ECMO = extracorporeal membrane oxygenation, LAD = left atrial diameter, LT = liver transplantation, LVED = left ventricular end diastolic diameter, MRA = mitral regurgitation area, PG = pressure gradient, TRA = tricuspid regurgitation area, VA-ECMO = venoarterial extracorporeal membrane oxygenation.

Keywords: cardiac dysfunction, extracorporeal membrane oxygenation, liver transplantation

1. Introduction

Extracorporeal membrane oxygenation (ECMO) is an advanced therapy for severe lung and/or cardiocirculatory dysfunction or failure. Several reports have showed that ECMO was applied in the cases with acute lung and cardiocirculatory failure, severe pulmonary infection, or septicemia. The anticoagulant used in the ECMO was considered to intervene the coagulation function; therefore, all the applications of ECMO in liver recipients were only performed for the emergency complications during the operation, such as heart thrombus, reperfusion syndrome, and so on.[1–4] Here, we reported a liver recipient suffering from severe valvulopathy, which was considered as a great risk factor inducing acute heart failure in the operation, especially as the perfusion of inferior vena cava was recovered. The utilization of venoarterial ECMO (VA-ECMO) was accomplished before the blocking of inferior vena cava to prevent the acute heart failure. According to our knowledge, this is the first case report about prophylactic ECMO used in the liver transplantation (LT) for the recipient with a high risk of heart failure.

2. Case report

The study has been approved by the institutional review board of Jilin University. Informed written consent was obtained from the
patient for publication of this case report and accompanying images. We report a 44-year-old female liver recipient suffering from hepatitis B virus (HBV)-related hepatic cirrhosis (MELD 24, Child-Pugh C) with New York Heart Function Assessment Class III. Before the surgery, arterial blood gas showed oxygen partial pressure as 59 mmHg. Cardiac ultrasound revealed that left atrial diameter (LAD) was 47 mm, left ventricular end diastolic diameter (LVED) was 5.5 mm, mitral regurgitation area (MRA) was 10.2 cm², tricuspid regurgitation area (TRA) was 5.8 cm², max regurgitation velocity was 311 cm/s, and pressure gradient (PG) was 38 mmHg, which indicated the presence of severe mitral regurgitation, severe tricuspid regurgitation, left atrium and left ventricle enlargement, cardiac insufficiency, pulmonary arterial hypertension, and hypoxemia. VA-ECMO was taken into consideration seeing that the patient might not tolerate the large amount of fluid load during the perioperative period as well as to prevent the reperfusion syndrome.

Laboratory examination showed that activated partial thromboplastin time was 53 seconds, prothrombin time was 27 seconds, international normalized ratio was 2.29, and activated clotting time (ACT) was 255 seconds. With comprehensive consideration of the heart function and the bleeding risk in the LT, the time for femoral vessels cannulation (VA-ECMO) was decided to be after the dissection of the recipient’s liver and before the venous blocking. Before this time, the ACT was regulated at the level of 130 to 150 seconds through monitoring the thromboelastograph and ACT, as well as infusing associated coagulation components. The application of coagulation components did not cease until the dissection of the first porta hepatitis was done. The bleeding volume was about 800 mL before the venous blocking.

The ACT was examined as 217 seconds after the dissection of the liver; therefore, heparin-free strategy of VA-ECMO was utilized. Venous cannula reached to the position below renal vein, while arterial cannula reached to common iliac artery. We regulated the ECMO index according to the patient’s condition. Respiratory support, milrinone, furosemide, mannitol, and a small amount of norepinephrine and dopamine were used to improve the circulation. The bleeding volume of surgery was 1200 mL. The cardiocirculatory function and other vital signs remained good during the operation. The surgery proceeded successfully.

The recipient was transferred to intensive care unit after the operation, and VA-ECMO was used continually. The coagulation function of the patient restored to normal gradually; therefore, heparin was administered to maintain the level of ACT at 160 to 195 seconds.

In the first 24 hours after surgery, central venous pressure (CVP) decreased from 17 to 7 cmH₂O. Thirty hours after the surgery, the cardiac ultrasound showed that the LAD was 42 mm, LVED was 60 mm, MRA was 12.2 cm², TRA was 7 cm², max regurgitating velocity was 348 cm/s, and PG was 48 mmHg. On the basis of the normal level of heart rate as well as blood pressure along with decreased support of ECMO, the ECMO was removed successfully. Eighteen hours later, the recipient did not need respiratory support. No complications of transplantation or ECMO were found.

3. Discussion
Cardiovascular complications are the key factor contributing to nongraft-related mortality early after LT.[1] On the one hand, underlying cardiac pathology in many LT recipients with end-stage liver disease is characterized by compromised inotropic and chronotropic responsiveness to stress, together with altered diastolic relaxation. On the other hand, it is rare for the liver recipients with severe lung and/or cardiocirculatory dysfunction or failure to receive LT because of the high surgical risk such as the weak coagulation function and the enormous bleeding volume, which would intervene the hemodynamics seriously.[16,17]

Therefore, it is reasonable to observe that about 50% of recipients with cirrhosis develop cardiac dysfunction within the first week after LT.[6] However, limited studies or guidelines on the cardiac assessment and clinical management of LT recipients have been performed. It is until this year that 1 article about consensus recommendations on cardiac and pulmonary vascular disease was published.[5]

Transthoracic echocardiogram shows that our patient is with severe valvular regurgitation, which indicates severe valvular heart disease. And on the basis of her elevated PG level, this patient may be with pulmonary hypertension, while right heart catheterization is necessary to make the definition. According to the consensus recommendations, severe irreversible valvular heart disease is one of the absolute contraindications to LT.[5] Meanwhile, Raval et al[7] support that patients with elevated pulmonary artery pressure (examined by transthoracic echocardiogram) should consider to postpone LT. In a word, this patient was at a high cardiac risk and not able to tolerate LT.[8] Severe liver dysfunction made it impossible to wait in the LT list until her cardiac function improved.

On the basis of published reports, no suggestions on the intraoperative transient support for cardiac function have been provided in guidelines or consensus recommendations. ECMO was an effective strategy to help patient to safely tolerate the hemodynamic fluctuating during the perioperative period. There are only a few articles covering less than 50 LT recipients undergoing ECMO perioperatively.[16-18] It is worth noting that in most of the cases mentioned above, ECMO was utilized as a salvage measure for complications (pneumonia, acute respiratory distress syndrome, or septic shock) after LT. In 3 pediatric liver recipients, they developed graft failure and pulmonary failure after the first LT, supported by ECMO for a few days, and got retransplantation.[12,14,15] Only 1 patient who suffered from acute respiratory distress syndrome clearly underwent ECMO before LT (13 days).[19] Our case is the first case using ECMO as a measure to prevent cardiocirculatory failure in LT.

In our case, the time for femoral vessels cannulation (VA-ECMO) was after the dissection of the recipient’s liver and before the venous blocking. The anticoagulation state required by ECMO can increase hemorrhage risk in surgery; therefore, it is better to decrease the duration of ECMO. Also, reperfusion in LT can intervene the hemodynamics more seriously.[7] Thus, with comprehensive consideration of heart function and bleeding risk in the LT, we chose the time. This is the first case of intraoperative cannulation and starting ECMO.

In most situations, the anticoagulation was indispensable for the ECMO to operate smoothly; however, anticoagulation in the surgery may contribute to bleeding. Therefore, the specific heparin-free strategy was designed for this LT, that is, femoral vessels cannulation for ECMO was accomplished just before the venous blocking; different coagulation function regulatory methods were adopted when with/without ECMO, and on the basis of ACT and surgical field bleeding volume, heparin-free strategy can also be suitable. Meanwhile, it is acceptable to maintain the ACT level around 180 seconds in the LT, because this level of coagulation function does not increase the bleeding.
volume. Therefore, it is also reasonable to use ECMO in other liver recipients with poor coagulation function (such as acute liver failure) as well as with more severe lung or cardiocirculatory dysfunction to accomplish the improvements in circulation before the surgery. In some other kinds of operations, ACT less than 150 seconds also seemed to be available. Until now, only Choi et al. reported that no anticoagulation agents were utilized in parts of LT recipients undergoing ECMO.

The main limitation of this case report is that it is a study of a single patient. But on the basis of the case, we suggest that it is feasible to utilize ECMO as a cardiocirculatory function support in LT to expand the surgical indications of LT. ECMO does not increase the risk of hemorrhage. ECMO can play an important role in ensuring the safety of the liver recipients in the surgery and in the postoperative period. Heparin-free strategy can also be suitable for some recipients.

Author contributions
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References
[1] Khan HH, Schroder L, Fitzpatrick MS, et al. Successful venoarterial extracorporeal membrane oxygenation for prolonged hepatopulmonary syndrome following pediatric liver transplantation: a case report and review of the literature. Pediatr Transpl 2017;21:e13036.
[2] Kim S, DeMaria Sjr, Cohen E, et al. Prolonged intraoperative cardiac resuscitation complicated by intracardiac thrombus in a patient undergoing orthotopic liver transplantation. Semin Cardiothorac Vasc Anesth 2016;20:246–51.
[3] Martucci G, Burgio G, Lullo F, et al. Veno-arterial extracorporeal membrane oxygenation as an intraoperative rescue option in case of portopulmonary hypertension recognized during liver transplantation. Minerva Anestesiol 2017;83:1336–7.
[4] Yoo CS, Shin YH, Ko JS, et al. Anesthetic management including extracorporeal membrane oxygenation therapy of liver transplant recipient with life-threatening hypoxemia: a case report. Korean J Anesthesiol 2013;65:151–7.
[5] VanWagner LB, Harinstein ME, Runo JR, et al. Multidisciplinary approach to cardiac and pulmonary vascular disease risk assessment in liver transplantation: an evaluation of the evidence and consensus recommendations. Am J Transplant 2018;18:30–42.
[6] Liu H, Jayakumar S, Traboulssi M, Lee SS. Cirrhotic cardiomyopathy: implications for liver transplantation. Liver Transpl 2017;23:826–35.
[7] Raval Z, Harinstein ME, Skaro AL, et al. Cardiovascular risk assessment of the liver transplant candidate. J Am Coll Cardiol 2011;58:223–31.
[8] Flesher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on periprocedural cardiovascular evaluation and care for noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Anesth Analg 2008;106:685–712.
[9] Biondi RS, Barzilai VS, Watanabe ALC, et al. Use of extracorporeal membrane oxygenation for treating acute cardiomyopathy after liver transplantation: a case report. Rev Brasil Terap Intensiv 2018;30:233–6.
[10] Lee KW, Cho CW, Lee N, et al. Extracorporeal membrane oxygenation support for refractory septic shock in liver transplantation recipients. Ann Surg Treat Res 2017;93:152–8.
[11] Phillips MR, Priest M, Beaty C, et al. Extracorporeal membrane oxygenation in a pediatric patient with hepatopulmonary syndrome and interrupted inferior vena cava after living related liver donation. ASAIO J 2018;Epub ahead of print.
[12] Scott JP, Hong JC, Thompson NE, et al. Central ECMO for circulatory failure following pediatric liver transplantation. Perfusion 2018;Epub ahead of print.
[13] Sharma NS, Wille KM, Diaz Guzman E. Extracorporeal membrane oxygenation after liver transplantation in a patient with hepatopulmonary syndrome and an atrial septal defect. Int J Artif Organs 2015;38:170–2.
[14] Fujita S, Hemming AW, Fujikawa T, et al. Expanded efficacy and indication of extracorporeal membrane oxygenation for preoperative pulmonary bleeding on pediatric cadaveric orthotopic liver transplantation. Transplantation 2005;79:1637.
[15] Landsman B, Karsanaic CJ. Case report: pediatric liver retransplantation on an extracorporeal membrane oxygenation-dependent child. Anesth Analg 2010;111:1275–8.
[16] Monsel A, Mal H, Brisson H, et al. Extracorporeal membrane oxygenation as a bridge to liver transplantation for acute respiratory distress syndrome-induced life-threatening hypoxaemia aggravated by hepatopulmonary syndrome. Crit Care (London, England) 2011;15:R234.
[17] Riley JB, Scheers GJ, Nuttall GA, et al. Coagulation parameter thresholds associated with non-bleeding in the eighth hour of adult cardiac surgical post-cardiomyotomy extracorporeal membrane oxygenation. J Extra Corp Technol 2016;48:71–8.
[18] Choi NK, Hwang S, Kim KW, et al. Intensive pulmonary support using extracorporeal membrane oxygenation in adult patients undergoing liver transplantation. Hepatogastroenterology 2012;59:1189–93.