

World Journal of *Transplantation*

Quarterly Volume 14 Number 1 March 18, 2024



EDITORIAL

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ORIGINAL ARTICLE

Retrospective Cohort Study

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Observational Study

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CASE REPORT

Sánchez Pérez B, Pérez Reyes M, Aranda Narvaez J, Santoyo Villalba J, Perez Daga JA, Sanchez-Gonzalez C, Santoyo-Santoyo J. New therapeutic strategy with extracorporeal membrane oxygenation for refractory hepatopulmonary syndrome after liver transplant: A case report. *World J Transplant* 2024; 14(1): 89223 [DOI: [10.5500/wjt.v14.i1.89223](https://doi.org/10.5500/wjt.v14.i1.89223)]

ABOUT COVER

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The primary aim of *World Journal of Transplantation* (WJT, *World J Transplant*) is to provide scholars and readers from various fields of transplantation with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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INDEXING/ABSTRACTING

The WJT is now abstracted and indexed in PubMed, PubMed Central, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The WJT's CiteScore for 2022 is 2.8 and Scopus CiteScore rank 2022: Transplantation is 23/51.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Yan-Liang Zhang; Production Department Director: Xu Guo; Editorial Office Director: Jia-Ping Yan.

NAME OF JOURNAL

World Journal of Transplantation

ISSN

ISSN 2220-3230 (online)

LAUNCH DATE

December 24, 2011

FREQUENCY

Quarterly

EDITORS-IN-CHIEF

Maurizio Salvadori, Sami Akbulut, Vassilios Papalois, Atul C Mehta

EDITORIAL BOARD MEMBERS

<https://www.wjnet.com/2220-3230/editorialboard.htm>

PUBLICATION DATE

March 18, 2024

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<https://www.wjnet.com/bpg/GerInfo/288>

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<https://www.wjnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



New therapeutic strategy with extracorporeal membrane oxygenation for refractory hepatopulmonary syndrome after liver transplant: A case report

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Specialty type: Transplantation

Provenance and peer review:

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

P-Reviewer: Sunder T, India

Received: October 24, 2023

Peer-review started: October 24, 2023

First decision: November 21, 2023

Revised: November 24, 2023

Accepted: December 22, 2023

Article in press: December 22, 2023

Published online: March 18, 2024



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Abstract

BACKGROUND

Due to the lack of published literature about treatment of refractory hepatopulmonary syndrome (HPS) after liver transplant (LT), this case adds information and experience on this issue along with a treatment with positive outcomes. HPS is a complication of end-stage liver disease, with a 10%-30% incidence in cirrhotic patients. LT can reverse the physiopathology of this process and restore normal oxygenation. However, in some cases, refractory hypoxemia persists, and extracorporeal membrane oxygenation (ECMO) can be used as a rescue therapy with good results.

CASE SUMMARY

A 59-year-old patient with alcohol-related liver cirrhosis and portal hypertension was included in the LT waiting list for HPS. He had good liver function (Model for End-Stage Liver Disease score 12, Child-Pugh class B7). He had pulmonary fibrosis and a mild restrictive respiratory pattern with a basal oxygen saturation of 82%. The macroaggregated albumin test result was > 30. Spirometry demonstrated a forced expiratory volume in one second (FEV1) of 78%, forced vital capacity (FVC) of 74%, FEV1/FVC ratio of 81%, diffusion capacity for carbon monoxide of 42%, and carbon monoxide transfer coefficient of 57%. He required domiciliary oxygen at 2 L/min (16 h/d). The patient was admitted to the intensive care unit (ICU) and extubated in the first 24 h, needing high-flow therapy and non-invasive ventilation and inhaled nitric oxide afterwards. Reintubation was needed after 72 h. Due to the non-response to supportive therapies, installation of

ECMO was decided with progressive recovery after 9 d. Extubation was possible on the tenth day, maintaining a high-flow nasal cannula and de-escalating to conventional oxygen therapy after 48 h. He was discharged from ICU on postoperative day (POD) 20 with a 90%-92% oxygen saturation. Steroid recycling was needed twice for acute rejection. The patient was discharged from hospital on POD 27 with no symptoms, with an 89%-90% oxygen saturation.

CONCLUSION

Due to the favorable results observed, ECMO could become the central axis of treatment of HPS and refractory hypoxemia after LT.

Key Words: Liver transplantation; Hepatopulmonary syndrome; Refractory hypoxemia; Treatment; Extracorporeal membrane oxygenation; Case report

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Core Tip: Extracorporeal membrane oxygenation (ECMO) has been used as a rescue therapy in refractory hypoxemia after liver transplant (LT) in hepatopulmonary syndrome (HPS), with positive results. We present a patient with HPS who underwent LT and developed refractory hypoxemia requiring postoperative ECMO support. The literature demonstrates an 80% survival rate with an acceptable morbi-mortality. ECMO can become the central axis in the treatment of patients with HPS which present with refractory hypoxemia after LT.

Citation: Sánchez Pérez B, Pérez Reyes M, Aranda Narvaez J, Santoyo Villalba J, Perez Daga JA, Sanchez-Gonzalez C, Santoyo-Santoyo J. New therapeutic strategy with extracorporeal membrane oxygenation for refractory hepatopulmonary syndrome after liver transplant: A case report. *World J Transplant* 2024; 14(1): 89223

URL: <https://www.wjgnet.com/2220-3230/full/v14/i1/89223.htm>

DOI: <https://dx.doi.org/10.5500/wjt.v14.i1.89223>

INTRODUCTION

In recent years, extracorporeal membrane oxygenation (ECMO) has become the gold-standard method for the treatment of severe pulmonary/cardiac dysfunction or insufficiency in the peritransplant period in liver recipients unresponsive to previous therapies[1,2]. Conditions that can be treated by ECMO include hepatopulmonary syndrome (HPS), portopulmonary hypertension, and pulmonary arterial hypertension[3].

HPS is characterized by the triad of liver disease, intrapulmonary vascular dilatation, and arterial hypoxemia. Although HPS is most frequently associated with liver cirrhosis, it may be related to any acute/chronic terminal liver disease, with or without associated portal hypertension[4]. Around 10%-30% of cirrhotic patients develop HPS[4]. Liver transplant (LT) may reverse the physiopathology of this process and restore normal oxygenation. However, in some cases, refractory hypoxemia persists despite support therapy. It is in this scenario where ECMO gives the necessary time to revert pulmonary arteriovenous shunts and reduce morbimortality.

This is a case report and literature review of adult liver recipients that received ECMO therapy for HPS during the peritransplant period.

CASE PRESENTATION

Chief complaints

We report the case of a 59-year-old male patient included in the LT waiting list for HPS in March 2022.

History of present illness

The patient had good liver function, with a Model for End-Stage Liver Disease score of 12 and a Child-Pugh class of B7. The patient had concomitant chronic respiratory failure, with a mild restrictive ventilatory defect and bronchial hyperreactivity (with a previous positive bronchodilator test). The patient also had HPS and slow progressive pulmonary fibrosis.

History of past illness

The patient had a history of alcohol-related liver cirrhosis and pulmonary hypertension.

Personal and family history

There was no familial history of interest.

Physical examination

The patient used home oxygen at 2 L/min for at least 16 h a day and a portable oxygen concentrator for walking. His baseline oxygen saturation (O₂Sat) was 82%.

Laboratory examinations

The macroaggregated albumin test result was > 30. Spirometry demonstrated a forced expiratory volume in one second (FEV₁) of 78%, forced vital capacity (FVC) of 74%, FEV₁/FVC ratio of 81%, diffusion capacity for carbon monoxide of 42%, and carbon monoxide transfer coefficient of 57%.

Imaging examinations

No imaging examinations relevant to this case.

FINAL DIAGNOSIS

Refractory hypoxemia.

TREATMENT

LT was performed with a matched cadaveric donor. A temporary porto-cava shunt and piggy-back technique were used. The patient was admitted to the intensive care unit (ICU). Extubation was performed within the first 24 post-transplant hours, and the patient immediately needed a high-flow nasal tube, which was escalated to noninvasive mechanical ventilation plus inhaled nitric oxide. At 72 h, reintubation was required due to severe hypoxemia. Protective mechanical ventilation with a high fraction of inspiration O₂ was initiated. Inhaled nitric oxide and support with inhaled iloprost were maintained to reach an O₂Sat of 88%-92%. As the patient was unresponsive to support therapies, veno-venous ECMO (VV ECMO) was initiated. Anticoagulation by continuous perfusion of heparin sodium was also started to reach an activated clotting time of 140 s.

OUTCOME AND FOLLOW-UP

ECMO was maintained for 9 d, with progressive improvement of right-to-left shunt lesions and hypoxemia. The patient was extubated after 10 d on high-flow ventilation. The clinical course was excellent, with successful de-escalation to a conventional nasal tube in 48 h. The patient was discharged from the ICU at postoperative day (POD) 20 with an O₂Sat of 90%-92%. In relation to liver function, the patient required steroid recycling two times, due to acute cellular rejection in the ICU. The patient was discharged at POD 27 without any respiratory symptoms, with a constant O₂Sat of 89%-90% and very good tolerance.

Respiratory symptoms have disappeared since transplantation, and the patient showed good liver graft function. Lung function has improved with respect to pre-transplant status, with a basal O₂Sat of 98%. The patient no longer needs home oxygen therapy.

DISCUSSION

In the last decades, HPS has gone from being a contraindication to becoming an indication for transplant. This has been made possible by our better understanding of the physiopathology of the disease, in addition to constant improvements in support therapies. However, in liver recipients with severe oxygenation deficit [severe hypoxemia: Arterial partial pressure of oxygen (PaO₂) < 50 mmHg], post-transplant mortality remains high, with a higher occurrence in the immediate postoperative period[5]. VV ECMO removes non-oxygenated blood, transfers it through devices that add oxygen to the blood, and returns it to the venous system. By this technique, arterial oxygen is controlled to ensure optimal oxygenation and support tissue metabolism[6] in the presence of standard cardiac output. This technique provides the time necessary to reverse lung disease.

VV ECMO had never been used before in our hospital to treat HPS, since LT had always been effective. However, as this patient developed refractory hypoxemia, the multidisciplinary team decided to use VV ECMO, despite the little scientific evidence available on the use of this support therapy in HPS. Ten cases have been reported (ours included) in the literature on adult liver recipients who received VV ECMO during the peritransplant period as a treatment for HPS (Table 1). In 80% of cases, ECMO was used to treat post-transplant refractory hypoxemia[5,7-10], intraoperatively in 20% [3,8,11], and as bridge-to-transplant therapy in 10%[12]. In all cases, the indication for ECMO was hypoxemia refractory to mechanical ventilation combined with conventional measures. Measured pretransplant PaO₂ was 48.12 mmHg (range:

Table 1 Review of extracorporeal membrane oxygenation in hepatopulmonary syndrome

Ref.	Age	Gender	MELD score	Etiology of liver disease	Pre-LT PaO ₂ (mmHg)	ECMO initiation	ECMO duration	ICU stay (d)	Days to discharge	State
Monzel <i>et al</i> [12]	51	M	N/D	OH	51	- 5	5	36	48	Alive
Auzinger <i>et al</i> [10]	44	N/D	N/D	OH	35	13	21	27	N/D	Alive
Sharma <i>et al</i> [5]	60	F	22	NASH	50	11	13	N/D	N/D	Alive
Braun <i>et al</i> [9]	50	M	25	OH	No	12	49	61	61	Dead
Braun <i>et al</i> [9]	28	M	31	Non-cirrhotic PH	No	5	10	58	58	Dead
Goussous <i>et al</i> [8]	52	F	26	HCV	No	1	10	N/D	N/D	Alive
Herden <i>et al</i> [7]	62	F	12	Idiopathic	No	7	6	N/D	N/D	Alive
Hogen <i>et al</i> [11]	42	F	N/D	N/D	52	Intraoperative	12	N/D	N/D	Alive
Laici <i>et al</i> [3]	45	F	31	OH	50	Intraoperative	36 h	N/D	42	Alive
This report	59	M	12	OH	57	3	9	N/D	28	Alive

M: Male; F: Female; MELD: Model for End-Stage Liver Disease; OH: Enolic; PH: Portal hypertension; N/D: Not described; LT: Liver transplant; PaO₂: Arterial partial pressure of oxygen; ECMO: Extracorporeal membrane oxygenation; ICU: Intensive care unit; NASH: Nonalcoholic steatohepatitis; HCV: Hepatitis C virus.

35–57 mmHg). Mortality in these patients is high, with 60% of the series having required kidney replacement therapy, and 70% a tracheostomy. Complications included hepatic infarction/hematoma secondary to migration of the cannula [7] and hemothorax that required reintervention [8].

Despite the use of anticoagulation in this setting, no hemorrhages or hematomas were reported, as described previously [7,8], which we explain by good graft function at that moment (international normalized ratio: 1.31; coagulation factor V: 98%; prothrombin time: 68%). In total, 80% of our patients were discharged. Two patients (20%) died; one patient had multiorgan failure, and the other had hepatic infarction followed by a biliary fistula and sepsis with multiorgan failure, which occurred after withdrawal of ECMO therapy. The mean time to initiation and mean duration of ECMO therapy were 7 d and 13.7 d, respectively. Early initiation of ECMO has been reported to reduce therapy duration, thereby decreasing the occurrence of associated complications and increasing survival [13].

CONCLUSION

ECMO therapy emerges as a cornerstone of perioperative support that improves survival in patients with HPS undergoing LT. In the light of the growing evidence available and good outcomes reported, ECMO will certainly become the gold standard treatment for severe pulmonary dysfunction/insufficiency in liver recipients during the peritransplant period.

FOOTNOTES

Author contributions: Sánchez Pérez B wrote the manuscript; Santoyo-Santoyo J, Perez Reyes M, and Santoyo Villalba J performed the research; Aranda Narvaez J and Sánchez Pérez B performed the surgery; Perez Daga JA analyzed the data; Sanchez-Gonzalez C translated and submitted the manuscript.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: The authors declare that they have no conflict of interest to disclose.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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S-Editor: Qu XL

L-Editor: Wang TQ

P-Editor: Qu XL

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