Combined Lung and Liver Transplantation With Extracorporeal Membrane Oxygenation Instead of Cardiopulmonary Bypass

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COMBINED BILATERAL lung and liver transplantation (CLLT) may be a treatment option for patients with end-stage lung disease and impaired liver function when they are not expected to survive with either transplantation alone.[1,2] Cystic fibrosis (CF), as well as alpha-1 antitrypsin deficiency or portopulmonary hypertension, which can affect both lung and liver, may be possible indications for CLLT.[3,4] Because of the absence of randomized controlled trials on CLLT and the overall paucity of clinical data regarding this particular intervention, no recommendations for the anesthetic management during CLLT and, more specifically, for the use of mechanical circulatory support have been published to date. In fact, most cases are reported by cardiac/thoracic surgeons, and transplantation centers presumably act according to self-established protocols. Cardiopulmonary bypass (CPB) during CLLT often is used[1,4–7] but is not mandatory.[3,8,9] The use of CPB during CLLT also has been reported inconsistently.[2,10]

To the best of the authors' knowledge, extracorporeal membrane oxygenation (ECMO) has not been reported during CLLT. Consequently, this case report showed for the first time, that CLLT could be performed successfully with intraoperative ECMO. Moreover, an overview of the published data on CLLT with regard to mechanical circulatory support is provided and whether ECMO may be an alternative to implementation of CPB with full heparinization for this intervention is discussed.

Written informed consent was obtained from the patient before submission and publication of this case.

CASE REPORT

A 24-year-old Caucasian man (height, 177 cm; weight 51 kg; body mass index: 16.3 kg/m^2; lung allocation score: 52), American Society of Anesthesiologists physical status IV, with CF was scheduled for CLLT. His past medical history included severe end-stage obstructive lung disease (forced expired volume in 1 second: 0.79 L; pulmonary vital capacity: 20% of predicted) and mild pulmonary hypertension (mean pulmonary artery blood pressure [mPAP]: 32 mmHg). The patient also presented with liver cirrhosis Child A and portal hypertension, esophageal varices III°, and hypersplenism with thrombocytopenia (model for end-stage liver disease score 9). Other comorbidities included insulin-dependent diabetes mellitus and osteopenia. The preoperative assessment is recorded in Table 1. In an interdisciplinary approach with thoracic, cardiac, and visceral surgeons as well as anesthesiologists it was agreed to begin with the lung transplantation followed by the liver transplantation. Moreover, veno-arterial (va)-ECMO, rather than CPB, was to be instituted, but only in case of surgical difficulties, primary graft dysfunction (PGD), hypoxia, or right heart failure with pulmonary hypertension. This case report is divided into 6 distinct phases, as follows.

PHASE I: ANESTHESIA INDUCTION

Induction of anesthesia was performed according to the standard operating procedure for lung transplantation at the authors' institution. Under local anesthesia, a 20G arterial cannula was placed in the left radial artery. After sufficient preoxygenation, general anesthesia was induced with 40 μg of sufentanil, 150 mg of propofol, and 5 mg of midazolam via intravenous (IV) access on the left forearm. After neuromuscular blockade with 50 mg of rocuronium, a left-sided double-lumen endotracheal tube was placed (39 Charrière, Cormack/Lehane °I). Total IV anesthesia was maintained with sufentanil (1 μg/kg/h) and propofol (6-8 mg/kg/h). Inspiratory oxygen fraction (FIO_2) was kept at 1.0. Maximum inspiratory pressure, positive endexpiratory pressure (PEEP), and respiratory rate were adjusted according to arterial blood gas analyses to avoid excessive acidosis. Hemodynamic management included continuous infusions of norepinephrine (maximum 0.23 μg/kg/min) and epinephrine (maximum 0.1 μg/kg/min) aimed at maintaining mean arterial blood pressure (MAP) above 60 mmHg. Neuromuscular blockade with rocuronium (1 mg/kg) was repeated when needed. Two 12G dialysis catheters were inserted into the right internal jugular vein and the right femoral vein, respectively. A 7F pulmonary artery catheter (PAC) was placed via an 8F introducer into the right internal jugular vein. Hemodynamic monitoring including measurement of cardiac output was performed via CCOmbo-PAC (CI-Vigilance, Edwards Lifesciences Corporation, Unterschleissheim, Germany) after in vivo calibration using the commercially available Vigilance II monitor (Edwards Lifesciences Corporation, Unterschleissheim, Germany). Finally, a 12G gastric tube and a 14G bladder catheter were inserted. Antibacterial coverage was provided by repetitive doses of meropenem (in total 2 g). Antifibrinolysis was established with a single dose

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Table 1. Preoperative Anesthesiology Assessment

Parameter	Value	Comment
Pulmonary vital capacity (L)	1.09	20% of predicted
Forced expiratory volume in 1 sec (L)	0.79	Tiffeneau index 72%
Mixed venous oxygen saturation (%)	66	
Cardiac output (L/min)	8.5	
Cardiac ejection fraction (%)	72%	Transthoracic ultrasound
Pulmonary arterial pressure (mmHg)	44/32/20	Systolic/mean/diastolic
Pulmonary vascular resistance (Wood units)	2.4	
Pulmonary capillary wedge pressure (mmHg)	12	
Ventilation/perfusion scintigraphy	No mismatch	Shift toward the left side and the basal areas of both lungs
Bilirubin (mg/dL)	0.5	Serum
Creatinine (mg/dL)	0.7	Serum
Urea (mg/dL)	22	Serum
Alanine aminotransferase (U/L)	11	Serum
C-reactive protein (mg/dL)	4.4	Serum
Quick (%)	70	Citrate
Hemoglobin (g/dL)	11.0	EDTA
Platelets (G/L)	104	EDTA

Abbreviation: EDTA, ethylenediaminetetraacetic acid.

of tranexamic acid (2.5 g). A 17F cannula for venovenous bypass during liver transplantation were placed into the left femoral vein by the liver surgeons.

PHASE II: TRANSPLANTATION OF THE RIGHT LUNG

Lung transplantation was performed via clamshell incision starting with the right lung. Because of recurrent pulmonary infections, explantation of the lungs and reimplantation of the donor lungs was extremely difficult. Hemodynamic stability (MAP higher than 60 mmHg) was maintained throughout transplantation of the right lung by norepinephrine and epinephrine. In this phase of the intervention, the lowest cardiac output recorded was 2.1 L/min with concomitant ejection fraction of 15% (Table 2). As mPAP increased to 46 mmHg after clamping of the right pulmonary artery, therapy with inhaled nitric oxide (NO, 5 parts per million) was initiated. Activated clotting time (ACT) was 113 seconds (Table 3). Clamping time of the right pulmonary artery was 90 minutes and cold ischemic time of the right lung was 5 hours and 35 minutes. Toward the end of the transplantation of the right lung, 20 µg of inhaled iloprost were given once to combat mPAP rising to 42 mmHg. With decreasing mPAP, NO was discontinued. Because of persisting anuria, continuous renal replacement therapy (hemodiafiltration; Multifiltrate, Fresenius Medical Care, Bad Homburg, Germany) was initiated via the right femoral vein.

PHASE III: TRANSPLANTATION OF THE LEFT LUNG

Transplantation of the left lung was carried out shortly after declamping of the right pulmonary artery. Administration of norepinephrine and epinephrine was continued to maintain hemodynamic stability. When mPAP increased to 49 mmHg about 10 minutes after clamping of the left pulmonary artery, continuous administration of milrinone was started at 0.33 µg/kg/min. When the need for vasopressors increased considerably (norepinephrine, 0.5 µg/kg/min, epinephrine, 0.16 µg/kg/min), vasopressin was started at 0.02 U/kg/h and milrinone infusion rate reduced to 0.06 µg/kg/min. In this phase of the intervention, the lowest cardiac output recorded was 5.6 L/min with concomitant ejection fraction of 27% (Table 2). ACT was 115 seconds (Table 3). Multiplate (Roche Diagnostics, Mannheim, Germany) testing showed regular platelet function. Clamping time of the left pulmonary artery was 87 minutes and cold ischemic time of the left lung was 7 hours and 16 minutes. After reperfusion of the left

Table 2. Hemodynamic Parameters and Cardiovascular Medication in Phases I to IV (Before ECMO)

	I Induction	II Right Lung Tx	III Left Lung Tx	IV (Before ECMO)	Comment
MAP (mmHg)	59/129	53/122	42/78	43/106	min/max
Heart rate (beats/min)	46/101	55/117	91/112	93/110	min/max
Cardiac output (L/min)	4.7/5.0	2.1/7.0	5.6/7.0	4.5/7.0	min/max
mPAP (mmHg)	23/50	31/46	29/49	25/37	min/max
PaO_2 (mmHg)	88.7	61.6/305.0	46.1/61.0	73.2	min/max
$PaCO_2$ (mmHg)	64.6	66.6/111	82.0/108.3	79.5	min/max
pH	7.37	7.25/7.28	7.15/7.24	7.25	min/max
Norepinephrine (µg/kg/min)	0.23	0.23	0.5	0.45	max
Epinephrine (µg/kg/min)	0.1	0.1	0.16	0.16	max
Vasopressin (U/kg/h)	NA	NA	0.02	0.05	max
Milrinone (µg/kg/min)	NA	NA	0.33	0.06	max

Abbreviations: ECMO, extracorporeal membrane oxygenation; MAP, mean arterial blood pressure; mPAP, mean pulmonary artery pressure; min/max, minimum/maximum; NA, not applicable Tx, transplantation.