Upper-body extracorporeal membrane oxygenation as a strategy in decompensated pulmonary arterial hypertension

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ABSTRACT

Pulmonary arterial hypertension (PAH) is a disease with significant morbidity and mortality, particularly during an acute decompensation. We describe a single-center experience of three patients with severe Group 1 PAH, refractory to targeted medical therapy, in which an extubated, nonsedated, extracorporeal membrane oxygenation (ECMO) strategy with an upper-body configuration was used as a bridge to recovery or lung transplantation. All three patients were extubated within 24 hours of ECMO initiation. Two patients were successfully bridged to lung transplantation, and the other patient was optimized on targeted PAH therapy with subsequent recovery from an acute decompensation. The upper-body ECMO configuration allowed for daily physical therapy, including one patient, who would otherwise have been unsuitable for transplantation, ambulating over 850 meters daily. This series demonstrates the feasibility of using ECMO to bridge PAH patients to recovery or transplantation while avoiding the complications of immobility and invasive mechanical ventilation.

Key Words: ambulatory, extracorporeal membrane oxygenation, extubated, pulmonary arterial hypertension, upper-body

Pulmonary arterial hypertension (PAH) is a disease with high morbidity and mortality, particularly in the setting of an acute decompensation with rapidly progressive right ventricular failure, when there is either insufficient time to optimize targeted therapy or inadequate response to maximal medical therapy.¹ For medically-refractory PAH, lung transplantation represents the only viable long-term treatment option.² However, because of limited organ availability and high waitlist mortality, patients may not survive until transplantation.³⁴ Extracorporeal membrane oxygenation (ECMO) has been variably successful as a bridge to transplantation (BTT) for patients with PAH, including reports in which patients were awake and extubated.⁵⁻¹⁰ A recent report demonstrated improved post-transplant outcomes with an extubated, non-sedated ECMO strategy compared to historical controls receiving mechanical ventilation, despite relative immobility due to femoral cannulation.¹¹ We are unaware of any documented cases of this same strategy being used intentionally as bridge to recovery (BTR) from decompensated PAH. We report on our center’s experience with patients who have severe, Group 1 PAH in whom an extubated, non-sedated ECMO strategy with one of two upper-body configurations enabled ambulation while bridging to either lung transplantation or recovery from an acute decompensation.

CASE REPORTS

Case 1
A 23-year-old woman with PAH associated with an unrepaired 15-mm secundum atrial septal defect (ASD) with bidirectional shunting and WHO functional Class III symptoms on intravenous and oral PAH therapies presented...
with severe hypoxemia from decompensated PAH that was refractory to inhaled nitric oxide and inotropic agents (Table 1). ECMO was initiated as BTT. A bicaval dual-lumen cannula, designed to drain deoxygenated blood from the vena cavae and reinfuse oxygenated blood across the tricuspid valve, was inserted via the right internal jugular vein (RIJV; Table 2). [12,13] By directing reinfused blood across the ASD toward the left atrium, an oxygenated right-to-left shunt was created, effectively providing venoarterial ECMO with a single venous access site. [14] The patient was extubated in the operating room. Pulmonary vasodilators were down-titrated both to divert oxygenated reinfusion flow away from the pulmonary vasculature and through the ASD, and to avoid systemic vasodilation which may occur with shunting of pulmonary vasodilators into the systemic circulation. On ECMO Day 7, the patient underwent successful lung transplantation and ASD closure, and was discharged home 20 days post-transplant.  

**Case 2**

A 22-year-old woman with PAH following an arterial switch operation as a newborn for transposition of the great vessels, stenting for left pulmonary vein stenosis, and WHO functional Class III symptoms, who had been well-controlled on oral PAH therapy presented with hypoxemic respiratory failure due to pneumonia. Despite noninvasive ventilation, inotropes, diuretics, and antibiotics, she had progressive right heart, respiratory, and renal failure, with suprasystemic pulmonary artery pressures on echocardiogram. She was intubated and placed on venoarterial ECMO as BTR. A drainage cannula was inserted through the RIJV and a reinfusion cannula was grafted to the right subclavian artery. [15] She was started on intravenous epoprostenol and was extubated within 24 hours. She participated in physical therapy within 48 hours of extubation, ambulating 30 feet by ECMO Day 6. With up-titration of epoprostenol and volume removal with dialysis, ECMO was discontinued after eight days. Within two weeks, she was optimized on oral PAH therapy and iloprost, and epoprostenol was discontinued. She was discharged home 20 days post-ECMO, remaining off oxygen and on a stable PAH regimen.  

**Case 3**

A 34-year-old woman listed for lung transplantation with idiopathic PAH, status post-atrial septostomy, receiving sildenafil and intravenous treprostinil, with WHO functional Class III symptoms, presented with severe deconditioning, worsening right heart failure, and acute renal failure despite inotropes and diuresis, making her an inappropriate transplant candidate. Venoarterial ECMO was initiated to optimize her for transplantation, with the same configuration as in Case 2. The patient was 

### Table 1: Baseline demographics, duration of ECMO therapy, and outcomes

| Pt | Diagnosis | 6MWD (m) | Baseline PH interventions | Pre-ECMO HD | Therapeutic endpoint | Duration of ECMO (d) | Outcome | Post-ECMO HD | Follow-up PH medications |
|----|-----------|----------|--------------------------|-------------|---------------------|---------------------|---------|--------------|-------------------------|
| 1  | IPAH, ASD | 223      | Intravenous epoprostenol, ambrisentan, sildenafil | RAP 14, PAP: 113/60/81, PVR 23 WU, PA Sat 75%, CI 2.5 L/min/m² | BLTx | 7 | Discharged, alive, follow-up 31 months after BLTx | * | None |
| 2  | IPAH, repaired TGV, LPV stent | 526 | Ambrisentan, sildenafil, nifedipine | RAP 9, PAP: 57/25/39, PCWP 13, PVR 14 WU, PA Sat 66% | Recovery | 8 | Discharged, alive, follow-up 21 months | RAP 8, PAP 91/55/69 | Intravenous epoprostenol -> inhaled iloprost, ambrisentan, sildenafil, nifedipine |
| 3  | IPAH | 143 | Intravenous treprostinil, sildenafil, atrial septostomy | RAP 21, PAP 66/32/46, PA Sat 33%, PVR 21 WU, CI 2 L/min/m² | BLTx | 19 | Discharged, alive, follow-up 14 months after BLTx | * | None |

6MWD: six-minute walk distance; ECMO: extracorporeal membrane oxygenation; HD: hemodynamic; PH: pulmonary hypertension; IPAH: idiopathic pulmonary arterial hypertension; ASD: atrial septal defect; RAP: right atrial pressure; PAP: pulmonary arterial pressure; PVR: pulmonary vascular resistance; WU: wood units (mmHg×m/min/liter); CI: cardiac output; PCWP: pulmonary capillary wedge pressure; LVEDP: left ventricular end-diastolic pressure; LVEDP: left ventricular end-diastolic pressure; BLTx: bilateral lung transplantation; TGV: transposition of the great vessels; LPV: left pulmonary vein; PA: saturation pulmonary arterial oxygen saturation; *Data not available

### Table 2: ECMO configurations and settings

| Patient | ECMO Configuration | ECMO blood flow rate (L/min) | ECMO sweep gas flow rate (L/min) | ECMO FDO² |
|---------|-------------------|-------------------------------|-------------------------------|-----------|
| 1       | VV, RIJV 23Fr dual-lumen Avalon Elite⁴ | 2.2-2.7 | 1.5-3.3 | 100 |
| 2       | VA, RIJV 23Fr Bio-Medicus⁴, RSA 18Fr EOPA | 3.8-4.0 | 0.5-3.8 | 100 |
| 3       | VA, RIJV 23Fr Bio-Medicus⁴, RSA 24Fr EOPA | 2.7-3.4 | 2.0-2.5 | 100 |

ECMO: extracorporeal membrane oxygenation; F⁰₂O₂: fraction of delivered oxygen; VV: venovenous; VA: venoarterial; Fr: French; EOPA: elongated one-piece arterial cannula; RIJV: right internal jugular vein; RSA: right subclavian artery; LPV: left femoral vein; LFA: left femoral artery; Maquet Cardiovascular, Wayne, NJ, USA, Medtronic Inc., Minneapolis, MN, USA.
extubated in the operating room, and all intravenous PAH therapies were discontinued within 24 hours. Her renal failure and anasarca resolved within 48 hours, enabling her to ambulate over 850 m daily. Low-grade bleeding from an arterial cannula defect, which caused a hematoma and brachial plexopathy, was repaired at the bedside. On ECMO Day 19, she underwent lung transplantation and septostomy closure. She was discharged home one month after transplantation and has been living independently.

**DISCUSSION**

This series demonstrates the feasibility of venoarterial ECMO as a treatment modality for decompensated PAH, leading to significant improvement in hemodynamics, gas exchange, and end-organ perfusion (Table 3). Patients were maintained awake and extubated after cannulation.

Venoarterial ECMO may be used for patients with severe, irreversible PAH as BTT when medical therapy alone is insufficient to prevent cardiopulmonary failure. By delivering oxygenated blood directly into the systemic circulation, venoarterial ECMO improves end-organ function, which is critical in maintaining transplant eligibility. With modern ECMO technology and lower anticoagulation targets (aPTT 40-60 s), we have experienced lower complication rates than previously reported, including less bleeding and hemolysis, infrequent equipment failure, and low rates of thrombosis.[16,17] Because modern circuits have significantly lower resistance than the pulmonary vascular bed in PAH even after prolonged usage, blood flow shunts away from the lungs and through the circuit, accounting for a significant percentage of the cardiac output. To magnify this effect, we discontinue pulmonary vasodilators in patients with end-stage PAH on venoarterial ECMO who are awaiting transplantation. ECMO can support patients for prolonged periods of time while awaiting transplantation,[16,18] and a nonsedated, extubated, ambulatory strategy can prevent the complications of invasive mechanical ventilation and immobility in this setting that may preclude transplantation. However, risks of cannula malpositioning and dislodgement or tenuous hemodynamic or respiratory status may limit the duration of this strategy. The timing of ECMO as a BTT requires collaboration between ECMO, transplant, intensive care, and PAH specialists.

For nontransplant candidates who are not maximized on targeted therapy at the time of an acute decompensation, ECMO can be used as BTR, ameliorating the physiological derangements of decompensated PAH while reversible processes are treated and PAH therapies are optimized. In our case of BTR, prostanoid therapy was initiated, allowing for successful ECMO decannulation and recovery. In acutely decompensated PAH, we consider ECMO as soon as it becomes apparent that cardiopulmonary failure is progressing despite maximal medical therapy. Because endotracheal intubation and mechanical ventilation carry significant risk in PAH, the decision to initiate ECMO ideally is made before intubation is necessary. All three cases were intubated during ECMO initiation; however, they were successfully extubated within 24 hours and none required reintubation.

Venoarterial ECMO traditionally involves femoral cannulation, which has major limitations. Antegrade aortic blood flow may impede reinfusion, compromising the delivery of oxygenated blood to the aortic arch and upper body. A second reinfusion cannula can be branched off the femoral arterial cannula into the RIJV, providing oxygenated blood to the right ventricle, which passes through the heart and into the ascending aorta. This configuration, venoarterial-venous (VAV) ECMO, improves oxygen delivery to the upper body; however, it relies on adequate cardiac function, which is problematic in decompensated PAH. Another major limitation is that femoral cannulae do not permit safe ambulation routinely due to a high risk of dislodgement. A third concern is limb ischemia associated with the femoral artery cannula, which may require insertion of an antegrade cannula to the distal extremity.

We use an alternative configuration consisting of drainage from the RIJV and reinfusion through a cannula grafted to the right subclavian artery. Oxygenated blood travels retrograde through the subclavian and innominate arteries, into the aortic arch, without relying on the patient’s native circulation.[15] Direct cannulation of the subclavian artery is avoided to prevent limb ischemia to the upper extremity. Upper extremity mobility is not restricted; however,

**Table 3: Laboratory analysis and oxygen requirements**

|       | Pt1     |        | Pt2     |        | Pt3     |        |
|-------|---------|--------|---------|--------|---------|--------|
|       | Pre-ECMO | 48 hrs on ECMO | Pre-ECMO | 48 hrs on ECMO | Pre-ECMO | 48 hrs on ECMO |
| Cr (mg/dL) | 0.7 | * | 9.1 | * | 2.3 | * |
| BNP (pg/mL) | * | 0.8 | * | 1.5* | 1560 | 445 |
| O₂ supply | NRM 12 L/min | NRM 12 L/min | Bilevel 18/12, FiO₂ 1.0 | NC 6 L/min | NC 2 L/min | Room air |
| SpO₂ (%) | 70-80 | >95 | 90-95 | >95 | >95 | >95 |

HFNC: high flow nasal cannula; Cr: creatinine; BNP: B-type natriuretic peptide; Plts: platelets; NRM: non-rebreather mask; HFNC: high-flow nasal cannula; FiO₂: fraction of inspired oxygen; ECMO: extracorporeal membrane oxygenation; SpO₂: oxygen saturation by pulse oximetry; *On continuous venovenous hemodialysis; *Data not available
brachial plexopathy occurred in one case. The upper-body configuration is ideal for ambulation and maintaining a patient’s conditioning despite critical illness. An ASD allowed us to use venovenous ECMO with a single access site to accomplish the same result (Case 1).

Patient mobilization was maximized due to our ability to maintain patients nonsedated and extubated on ECMO. Case 3 was so debilitated on presentation that she was deemed ineligible for transplantation. With the combination of ECMO and aggressive physical therapy she improved dramatically in both conditioning and transplant candidacy.

Complications included brachial plexopathy in one patient. There were no incidents of limb ischemia, significant hemolysis, embolic events, or infectious complications attributable to ECMO.

This single-center experience demonstrates the feasibility of an extubated, nonsedated ECMO strategy with an upper-body configuration as a novel and emerging approach to bridge PAH patients to recovery or lung transplantation when medical therapy alone is insufficient. This strategy facilitates physical therapy, thereby optimizing transplant candidacy.

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