

Case 2-2022: An Adolescent Male in Cardiac Arrest 3 Days After Liver Transplantation for End-Stage Liver Disease

KEY WORDS: cardiac arrest; end-stage liver disease; extracorporeal membrane oxygenation; liver transplantation; pulmonary hypertension; right-sided heart failure

PRESENTATION

Dr. Melody Duvall (Critical Care)

A 19-year-old male with a history of Crohn's disease, primary sclerosing cholangitis, autoimmune hepatitis, and decompensated cirrhosis had progressed over 6 years to end-stage liver disease, manifested by thrombocytopenia, coagulopathy, portal hypertension with grade 2–3 esophageal varices, and refractory ascites. He was deemed a suitable liver transplant candidate and initially placed on deceased-donor waitlist at the age of 17 years with a Model for End-Stage Liver Disease score of 22. There were no identified absolute or relative contraindications to liver transplantation in this patient. His past medical history was remarkable for mild intermittent asthma and sickle cell trait. He developed clinical decompensation and disease progression with hypoalbuminemia, ascites, and edema, and his transplant-listing status was changed to active at 18 years old.

Eleven months following active transplant listing, the patient underwent deceased-donor, whole-organ orthotopic liver transplantation (OLT_x). Total liver allograft ischemia time was 7 hours and 20 minutes. There were no intraoperative surgical or anesthetic complications, and he was admitted to the non-cardiac PICU for post-transplant monitoring after endotracheal extubation in the operating room.

The patient's postoperative course in the PICU was remarkable for hyperglycemia, attributed to perioperative high-dose steroids, for which insulin was administered, and anemia and thrombocytopenia, for which packed RBCs and platelets were transfused in the first 24 hours after surgery. His prescribed immunosuppression regimen included basiliximab (20 mg on days 0 and 4), methylprednisolone (500 mg on day 0, tapered off over 4 wk), and tacrolimus (0.5 mg on day 0, titrated slowly to goal serum trough of 10–12 ng/mL). Routine, serial abdominal ultrasound (US) demonstrated patent hepatic and portal vessel anastomoses with preserved flow, normal hepatic echogenicity, prominent portal triads, splenic enlargement with normal echogenicity, and mild ascites on postoperative days 0 and 1. From a cardiorespiratory profile, he had a regular rate and rhythm, intermittent mild hypertension, central venous pressure less than or equal to 6 mm Hg, normal electrocardiogram tracings, and unlabored breathing with pulse oximetry oxyhemoglobin saturations (Sp_O₂) greater than or equal to 96% on 1 L/min of oxygen via nasal cannula. He

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was transferred to the transplant surgery ward on postoperative day 1 per routine.

Dr. Christopher Weldon (Surgical Critical Care)

Twenty-four hours after transfer to the ward (postoperative day 2), the patient developed persistent sinus tachycardia (rate, 110–130 beats/min) and hypoxia with escalation of his oxygen support to 4 L/min of oxygen via nasal cannula. He was afebrile and normotensive. Laboratory tests revealed stable anemia (hemoglobin, 7.9–8.4 g/dL), worsening thrombocytopenia (peak, 34,000 cells/ μ L; nadir, 6,000 cells/ μ L), improving mild transaminitis (aspartate aminotransferase, 78 units/L; alanine aminotransferase, 129 units/L), stable hyperbilirubinemia (total, 4.2 mg/dL; direct, 1.0 mg/dL), improved hyperglycemia (glucose, 106–172 mg/dL off insulin), and normal lactic acid (0.8 mmol/L) (**Table 1**). An anteroposterior chest radiograph demonstrated retrocardiac opacification, mild interstitial edema, and trace pleural effusions (**Fig. 1**). Despite diuresis and optimization of analgesia, he became progressively more tachycardic, tachypneic, and hypoxemic, requiring 5 L/min of nasal cannula oxygen to maintain $SpO_2 > 90\%$, and a hospital emergency call for PICU-team bedside assistance was activated on postoperative day 3.

Dr. Eleonore Valencia (Critical Care)

Upon arrival of the PICU team, the patient developed bradycardia, loss of consciousness, and pulselessness and was in pulseless electrical activity (PEA) arrest. Cardiopulmonary resuscitation (CPR) was initiated using the Pediatric Advanced Life Support algorithm (1). The patient was intubated with an endotracheal tube (ETT) and transferred to the PICU with ongoing CPR.

Return of spontaneous circulation was not achieved, so the extracorporeal membrane oxygenation (ECMO) team was emergently activated. Resuscitation was marked by pulmonary hemorrhage as well as several ventricular tachyarrhythmias (i.e., ventricular fibrillation, polymorphic ventricular tachycardia, and torsades de pointes) that required use of electrical defibrillation, lidocaine, and magnesium sulfate. End-tidal capnometry before pulmonary hemorrhage ranged from 15 to 40 mm Hg during CPR. A transthoracic echocardiogram (TTE) obtained prior to completion of ECMO cannulation demonstrated mildly depressed left ventricular (LV) function, severely depressed right

ventricular (RV) function, RV dilation, and RV hypertension (RV pressure 2/3 systemic; RV pressure ~55 mm Hg plus the right atrial v-wave, while noninvasive systolic blood pressure 80 mm Hg). There was no evidence of pericardial effusion, and there was no evidence of pulmonary embolism at the bifurcation of the main or proximal branch pulmonary arteries (**Fig. 2A**). After approximately 220 minutes of resuscitation, an adequate circulation was achieved via veno (right internal jugular vein)—veno (right common femoral vein)—arterial (left common femoral artery) (venovenous [VVA]) ECMO. A distal reperfusion cannula was also placed in the distal left common femoral artery.

Following extracorporeal-cardiopulmonary resuscitation to VVA ECMO cannulation, the patient was supported with full ECMO flows (5 L/min), and postcardiac arrest neuroprotective measures were instituted. Neurologic examination revealed intact pupillary light reflex, spontaneous eye opening, and localization and withdrawal to painful stimuli. Electroencephalography demonstrated nonepileptiform slowing without seizure activity or asymmetry. Portable head CT obtained at 72 hours postcardiac arrest demonstrated preserved gray-white matter differentiation, no cerebral edema, and no intracranial hemorrhage. Abdominal US revealed patent hepatic vein, hepatic artery, and portal venous anastomoses and preserved flow waveforms.

REFRACTORY CPR DIAGNOSES

All Discussants

This 19-year-old adolescent male with a history of primary sclerosing cholangitis and autoimmune hepatitis sustained a PEA arrest requiring ECMO cannulation to regain circulation on postoperative day 3 following uneventful OLTx. In this context, the approach involves identifying reversible causes of cardiac arrest, the so-called four “Hs” and four “Ts” (i.e., hypoxia, hypokalemia/hyperkalemia, hypothermia/hyperthermia, hypovolemia, tension pneumothorax, tamponade, thrombosis, and toxins) (1). In our patient, attention was focused on the following causes.

Acute Pericardial Tamponade

Despite the patient's history of autoimmune disease, he did not have risk factors for pericardial disease, and TTE did not demonstrate a pericardial effusion.

TABLE 1.
Postoperative Trend of Laboratory Data

Variable	Reference Range ^a	POD 0	POD 1, Prior to Transfer to the Ward	POD 2, Prior to Cardiac Arrest
Hematology				
WBC count (k cells/ μ L)	5.78–10.33	7.62	7.21	8.75
Hemoglobin (g/dL)	11.9–13.5	9.3	7.1 ^b	7.9
Hematocrit (%)	33.0–43.4	26.4	20.3 ^b	22.4
Platelet (k cells/ μ L)	146–326	65	34 ^b	6
Mean corpuscular volume (fL)	83.5–90.2	95.0	93.5	92.6
Red cell distribution width corpuscular volume (%)	11.6–14.6	16.7	16.7	16.9
Nucleated RBC (%)	0	0.0	0.0	0.8
Reticulocyte (%)	0.80–2.20	-	-	5.08
Neutrophil/band (%)	39.0–75.0	90.7	93.0	76.7
Immature granulocytes (%)	0.0–0.6	0.7	1.5	1.6
Lymphocyte (%)	7.0–36.0	3.3	2.8	8.2
Monocyte (%)	4.0–8.0	5.2	2.6	11.1
Eosinophil (%)	2.0–4.0	0.0	0.0	2.2
Basophil (%)	0.0–1.0	0.1	0.1	0.2
Coagulation				
Prothrombin (s)	12.1–14.6	21.4	18.7	15.9
International Normalized Ratio	< 1.13	1.81	1.53	1.24
Partial thromboplastin time (s)	25.0–37.0	40.6	31.9	26.1
Chemistry and hepatology				
Sodium (mmol/L)	135–148	135	140	139
Potassium (mmol/L)	3.20–4.50	3.37	3.80	3.51
Chloride (mmol/L)	96–109	101	108	107
Carbon dioxide (mmol/L)	22–30	16	23	24
Anion gap (mmol/L)	7.0–14.0	18.0	9.0	8.0
Glucose (mg/dL)	70–199	340	132	133
Blood urea nitrogen (mg/dL)	7–18	8	9	13
Creatinine (mg/dL)	0.60–1.30	0.41	0.46	0.51
Lactic acid (mmol/L)	0.5–2.2	6.9	0.4	0.8
Calcium (mg/dL)	8.4–10.5	8.7	7.8	7.7
Phosphorus (mg/dL)	2.7–4.9	3.5	4.8	3.2
Magnesium (mg/dL)	1.6–2.6	1.4	1.4	1.6
Amylase (unit/L)	40–220	-	-	34
Aspartate aminotransferase (unit/L)	2–40	358	219	78
Alanine aminotransferase (unit/L)	3–30	218	162	129
Lactate dehydrogenase (unit/L)	100–210	-	-	510
Gamma glutamyl transferase (unit/L)	12–55	-	59	51
Alkaline phosphatase (unit/L)	30–120	89	74	63
Albumin (g/dL)	3.0–4.6	3.3	2.8	3.0
Total protein (g/dL)	5.5–8.2	5.7	5.1	5.3
Bilirubin, total (mg/dL)	0.3–1.2	4.6	4.8	4.2
Bilirubin, direct (mg/dL)	0.0–0.4	1.7	1.1	1.0

POD = postoperative day.

^aReference ranges are per the Boston Children's Hospital Department of Laboratory Medicine. They are adjusted according to age and sex, specifically for a 19-year-old male in this case.

^bPosttransfusion of packed RBCs and platelets.

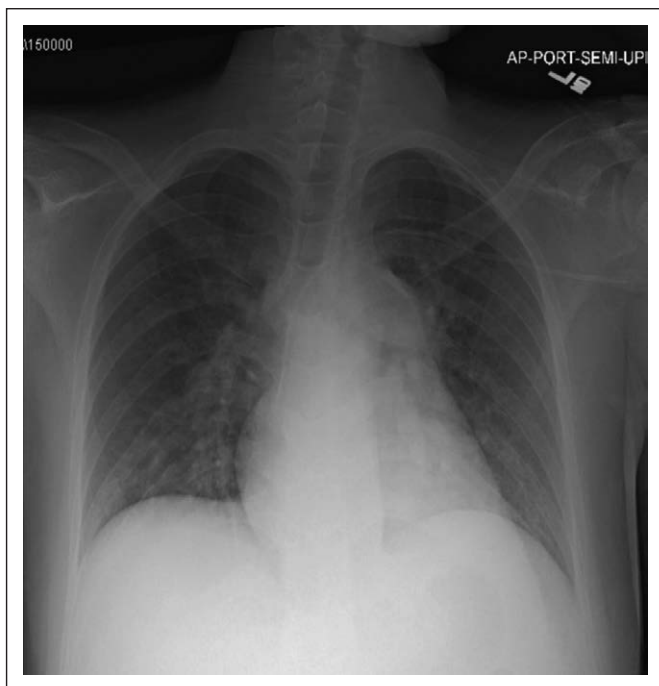


Figure 1. Precardiac arrest chest radiograph. Portable-anterior chest radiograph 12 hr prior to cardiac arrest. AP-PORT-SEMI-UP = anteroposterior-portable-semi-upright.

Acute Tension Pneumothorax

Even though the patient's demographics, including male sex and adolescent age, increased his risk for a spontaneous primary pneumothorax, the chest radiograph obtained after cardiorespiratory deterioration (Fig. 1) did not show pneumothorax. Bilateral breath sounds and symmetric chest rise were appreciated following ETT intubation at the beginning of CPR. Repeat chest radiograph during CPR did not show pneumothorax.

Acute Pulmonary Embolism

The patient had multiple risk factors for venous thromboembolism, including his postoperative status, immobility, hepatic venous anastomosis with known inferior vena cava-caudate dissection and manipulation, and inflammatory bowel disease (2). He also had refractory thrombocytopenia with a platelet count of 6,000 cells/ μ L immediately prior to the arrest, which may have been indicative of consumption secondary to thrombosis of the portal vein or other organs. However, his history of portal hypertension and hypersplenism were also plausible explanations for his thrombocytopenia.

Our patient was too unstable for transport to CT pulmonary angiography or ventilation perfusion

scanning, and we concluded that acute pulmonary embolism was unlikely. However, there was evidence of RV strain on TTE, but no pulmonary embolus was seen at the bifurcation or proximal aspect of the bilateral branch pulmonary arteries (Fig. 2A). In addition, abdominal US on the day of his cardiac arrest showed normal and patent vascular anastomoses with no thrombus.

Other “Hs” and “Ts” as Reversible Causes

The patient had acutely worsening hypoxia, leading up to and at the time of the cardiac arrest. However, this was likely secondary to another primary pathology, given that he did not have return of spontaneous circulation with bag mask ventilation or ETT intubation. A panel of metabolic tests before the cardiac arrest did not show elevated anion gap or deranged carbon dioxide (Table 1), which would have suggested significant acidosis or intravascular hypovolemia as inciting events. Controlled ventilation, sodium bicarbonate, and administration of IV fluid boluses did not reverse the event. He did not have hyperkalemia, hypoglycemia, or hypothermia before the arrest; and inpatient toxin exposure would have been unlikely.

REFRACTORY CPR DIAGNOSES IN LIVER DISEASE OR POST-OLTx

Dr. Ravi Thiagarajan (Cardiac Critical Care)

Patients with nonalcoholic fatty liver disease are at increased risk for coronary artery disease and acute coronary syndrome. The American Association for the Study of Liver Diseases and the American Society of Transplantation have a 1B recommendation for using screening stress echocardiography in adult (i.e., a person ≥ 18 yr) liver transplant candidates at the time of listing by the United Network for Sharing (3). In the absence of familial hypercholesterolemia or congenital heart disease, there are no recommendations for screening for coronary artery disease in pediatric (i.e., age < 18 yr) candidates for liver transplant at the time of listing (4). Hence, acute myocardial infarction as the primary etiology for decompensation and cardiac arrest, with refractory CPR, is unlikely in this patient. In addition, TTE during and after CPR showed antegrade perfusion of the right and left coronary arteries and no regional wall motion abnormality.

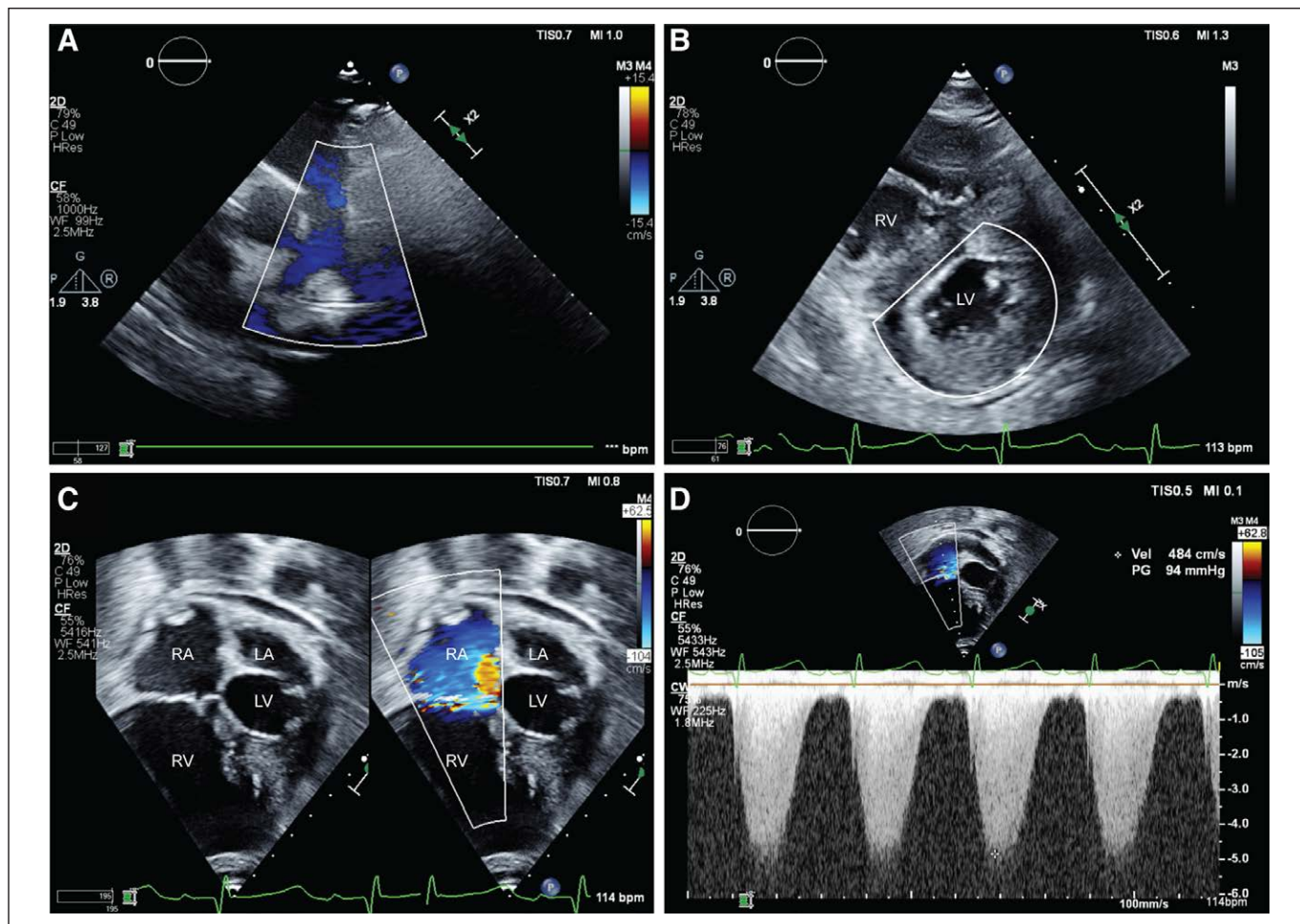


Figure 2. Transthoracic echocardiogram during and 48 hr following extracorporeal cardiopulmonary resuscitation. **A**, During resuscitation. Parasternal short axis. Antegrade blood flow via the pulmonary artery, bifurcation of the bilateral pulmonary arteries, and the proximal aspect of the bilateral branch pulmonary arteries during active chest compressions. No pulmonary embolus is visualized. **B–D**, 48 hr following resuscitation. **B**, Parasternal short-axis view. Septal flattening with a “D”-shaped left ventricle (LV) during end diastole is evidence of suprasystemic right ventricular pressure. **C**, Four-chamber view. *Left*: Right atrial and right ventricular dilations. *Right*: Tricuspid regurgitation during systole. **D**, Four-chamber view. The tricuspid regurgitation jet* ($v = 4.84$ m/s) plus the right atrial pressure estimate a right ventricular systolic pressure (pressure gradient = 94 mm Hg) that is equivalent to greater than the systemic pressure (arterial systolic blood pressure 92–100 mm Hg). *Derived from the modified Bernoulli equation (pressure gradient = $4v^2$). C = contrast, CF = color flow, CW = continuous wave, HRes = harmonics resolution, G = harmonics general, LA = left atrium, LV = left ventricle, MI = mechanical index, P = persist, PG = pressure gradient, R = harmonics resolution, RA = right atrium, RV = right ventricle, TIS = thermal index for soft tissue, WF = wave frequency.

Dr. Khashayar Vakili (Liver Transplant Surgery)

Patients with end-stage liver disease are at risk of developing pulmonary hypertensive crisis because of portopulmonary hypertension (PPHTN). In this adolescent, the precardiac arrest symptomatology 3 days after liver transplantation including tachycardia and hypoxia was consistent with early signs of a pulmonary hypertensive crisis, which subsequently led to acute RV failure and ultimately cardiac arrest. Although nonspecific, the TTE during resuscitation did show RV dilation, RV hypertension, and RV systolic dysfunction, a constellation of findings consistent with increased RV afterload.

PPHTN, a group 1 subtype of pulmonary arterial hypertension (PAH), is a well-described, severe complication among adults with end-stage liver disease. The prevalence of PPHTN in adults is at least 5% in those undergoing evaluation for liver transplantation, and the mortality rate may be at least 60% (5–7). Our pediatric cardiology experience of PPHTN is limited to case reports and series, which show variable but similarly high mortality rates up to 60%. Importantly, pediatric cases of PPHTN have been late diagnoses following the onset of symptoms and progression of disease, as children are not routinely screened for this entity (8–11). However, the International Liver Transplant Society

(ILTS) have provided a grade 1B recommendation for screening echocardiography for adult and pediatric liver transplant candidates with portal hypertension and a grade 1C recommendation for severe PPHTN to be considered an absolute contraindication to liver transplantation (12). In the adult population, many centers perform intraoperative screening via placement of a pulmonary artery (PA) catheter and abort the transplant if the mean PA pressure (mPAP) is greater than 35 mm Hg. The Pediatric Pulmonary Hypertension Guidelines from the American Heart Association and American Thoracic Society released a class I, level B recommendation for screening echocardiography in pediatric patients prior to liver transplant listing (13). The American Association for the Study of Liver Diseases issued a grade 2B recommendation for screening echocardiography at the time of pediatric liver transplant evaluation (4). Given the rare frequency of PPHTN in patients less than 18 years, children do not routinely undergo screening echocardiography (including our present patient, who was 17 years at the time of initial liver transplant listing) unless they have preexisting risk factors such as prematurity.

CLINICAL DIAGNOSIS

Refractory CPR due to previously unappreciated PPHTN.

ECHOCARDIOGRAM AND CARDIAC CATHETERIZATION DIAGNOSIS

Dr. Mary Mullen (Pulmonary Hypertension)

The initial postarrest echocardiograms at ECMO flow rates of 3.5–5 L/min revealed severe RV systolic dysfunction, LV systolic dysfunction, and severe RV hypertension (10–15 mm Hg suprasystemic by tricuspid regurgitation jet velocity) (**Fig. 2**). Cardiac catheterization showed severely elevated right- and left-sided filling pressures and PAH (**Supplemental Table 1**, <http://links.lww.com/PCC/C108>). Pulmonary angiography demonstrated tortuous proximal pulmonary arteries with distal pruning, suggestive of long-standing PAH, and no evidence of thrombus (**Fig. 3**). Additional medical history, taken in retrospect, found that an echocardiogram performed at another hospital 1 year before transplantation showed RV pressure $> \frac{1}{2}$ systemic, normal biventricular size and systolic function, and normal valvular function.

PPHTN is defined by mPAP greater than 20 mm Hg, pulmonary artery occlusion pressure less than 15 mm Hg, and pulmonary vascular resistance (PVR) greater than or equal to 3 Wood units, in the context of portal hypertension (14–17). PPHTN is further stratified as being mild (mPAP, <35 mm Hg), moderate (mPAP, 35–44 mm Hg), or severe (mPAP, >45 mm Hg) (12). The pathophysiology underlying PPHTN is considered multifactorial. Specifically, a disruption to the homeostasis of endogenous pulmonary vasoactive substances, as a result of portosystemic shunts that bypass hepatic metabolism, is implicated in the pathophysiology of PPHTN. An imbalance in pulmonary vasodilators such as nitric oxide and prostacyclin relative to vasoconstrictors including endothelin-1 and thromboxane-2 results in overall pulmonary vasoconstriction. Furthermore, the high cardiac output state associated with portal hypertension leads to increased pulmonary blood flow resulting in endothelial injury by way of shear stress and subsequent smooth muscle proliferation and platelet aggregation. The net effect is increased PVR, RV hypertension, and eventually RV failure (18).

Therefore, given the patient's long-standing RV hypertension, as evidenced by the historical TTE; pulmonary vascular remodeling and PAH as demonstrated by angiography and right heart hemodynamics; and history of portal hypertension, PPHTN complicated by an acute pulmonary hypertensive crisis resulting in severe RV failure, cardiogenic shock, and cardiac arrest is the most likely diagnostic sequence for the deterioration that occurred on day 3 post-OLTx.

DISCUSSION OF MANAGEMENT

All Discussants

Our management of PAH involved use of known empiric therapies. In our patient, we started with milrinone and IV sildenafil (phosphodiesterase-5 inhibitor). Sildenafil was titrated to 10 mg every 8 hours without adverse effect by day 3 of ECMO. Enteral pulmonary vasodilatory therapy was not used because the patient had ileus and intermittent gastrointestinal bleeding. His subsequent clinical course was complicated. On day 5 of ECMO, he had renal failure with anuria and fluid overload, for which he required hemodialysis. On day 9 of ECMO, he had pulmonary hemorrhage with complete opacification of the right hemithorax,

for which he required serial bronchoscopies for thrombus evacuation. On day 12 of ECMO, after 72 hours without any bleeding, he was given IV epoprostenol (prostacyclin analog), which was titrated to 6 ng/kg/min. Unfortunately, he had recurrent pulmonary hemorrhage 54 hours later, despite an adequate platelet count ($\geq 100,000$ cells/ μL), a partial thromboplastin time within range for his prescribed anticoagulation, and an otherwise normal coagulation profile. On day 15 of ECMO, epoprostenol was discontinued.

Other medical therapies included use of low-dose epinephrine and macitentan (endothelin receptor antagonist), at an enteral dose of 5 mg daily. The patient also received ongoing ultrafiltration to optimize the elevated intracardiac pressures identified on catheterization.

At the time, we also considered the possibility of vitamin C deficiency as an associated causal factor in the

development of severe PAH, since vitamin C deficiency is a complication of Crohn's disease, even in patients with disease remission (19–22). We did prescribe vitamin C in this patient: we used high dosing via parenteral nutrition and eventually enterally. The blood level of vitamin C was measured 7 weeks after the cardiac arrest event, and it was severely low ($< 5 \mu\text{mol/L}$). There were also signs of deficiency, including hair loss. Our conclusion is that vitamin C deficiency may have contributed to our patient's acute decompensation or it may have been a consequence of extracorporeal clearance via ECMO and prolonged critical illness.

Dr. Francis Fynn-Thompson (Cardiac Surgery)

On day 17 of ECMO (day 20 post-OLTx), TTE showed persistent severe RV hypertension (≥ 35 -mm Hg suprasystemic), moderate-to-severe RV systolic dysfunction,

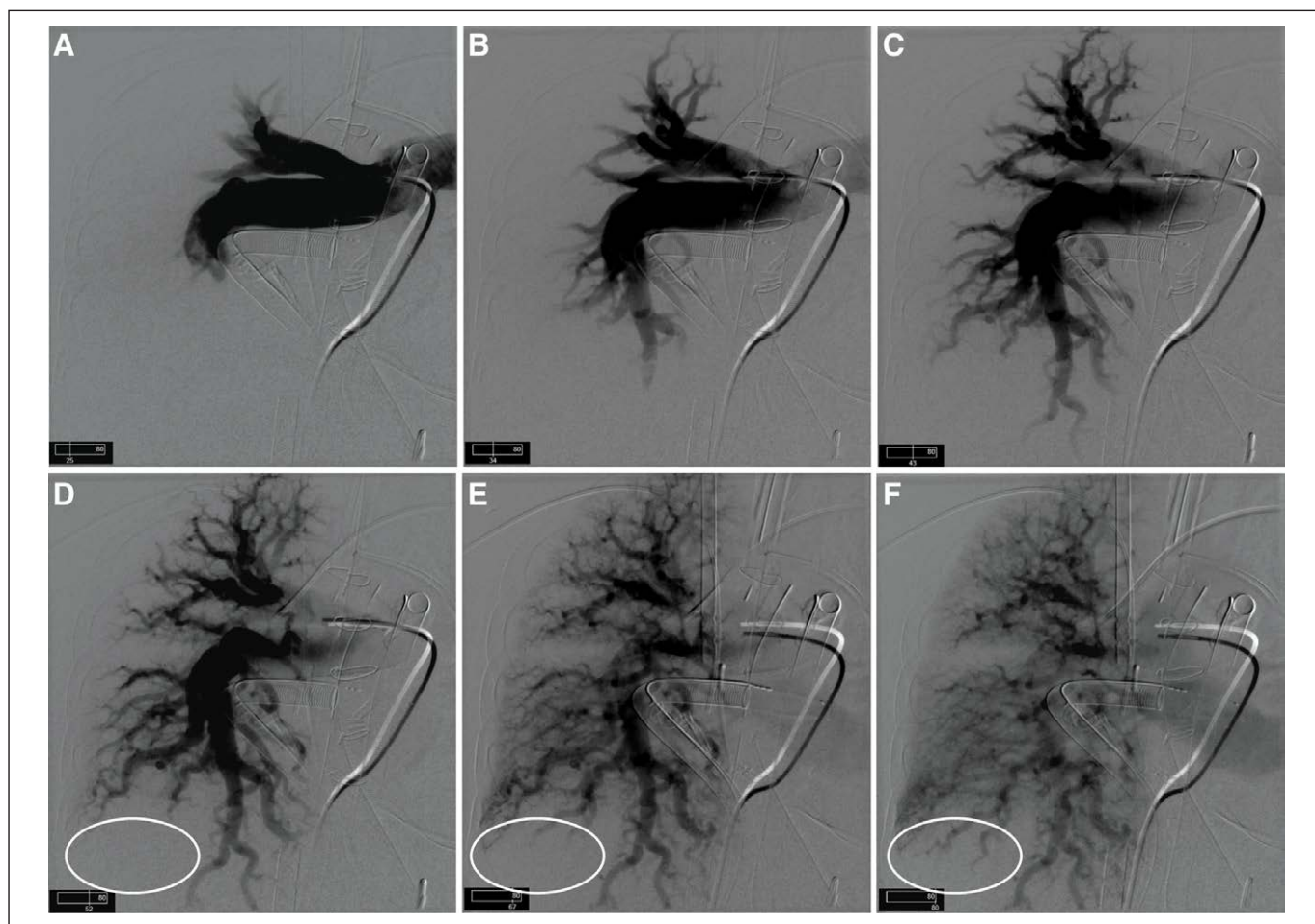


Figure 3. Postcardiac arrest pulmonary angiography. Serial angiograms of the right pulmonary arterial tree demonstrating dilation of the right main pulmonary and interlobar arteries (**A–C**) and pruning of the distal arterial vasculature and deficient right lower lobe perfusion (*white oval*) (**D–F**). Images were obtained 18 d after cardiac arrest while supported on peripheral extracorporeal membrane oxygenation.

and mild LV systolic dysfunction despite an ECMO flow rate of 4L/min. The underlying pathophysiology of our patient's RV failure was elevated PVR leading to increased PA pressures and increased ventricular wall stress (i.e., afterload). In order to offload the RV and allow pulmonary vasodilator therapies to take effect, we devised a strategy to bypass the pulmonary circulation via a pumpless paracorporeal circuit draining blood from the main PA through a membrane oxygenator and returning blood to the left atrium. Our rationale with this strategy was to allow the RV to eject blood through the lower resistance paracorporeal

circuit until the resistance in the native pulmonary circulation decreased to more normalized levels.

As described above, our patient underwent cannulation of the PA and the left atrium with externalization to a paracorporeal circuit containing a Quadrox-iD Adult membrane oxygenator (Getinge, Gothenborg, Sweden) with delayed sternal closure (Fig. 4). Over the next 10 days, the ECMO flow rate was weaned from 4 to 1L/min with an evidence of adequate patient native cardiac output. Concurrently, the flow rate via the paracorporeal circuit decreased from 2 to 0.8L/min, suggesting that the native PVR had decreased to a point that blood

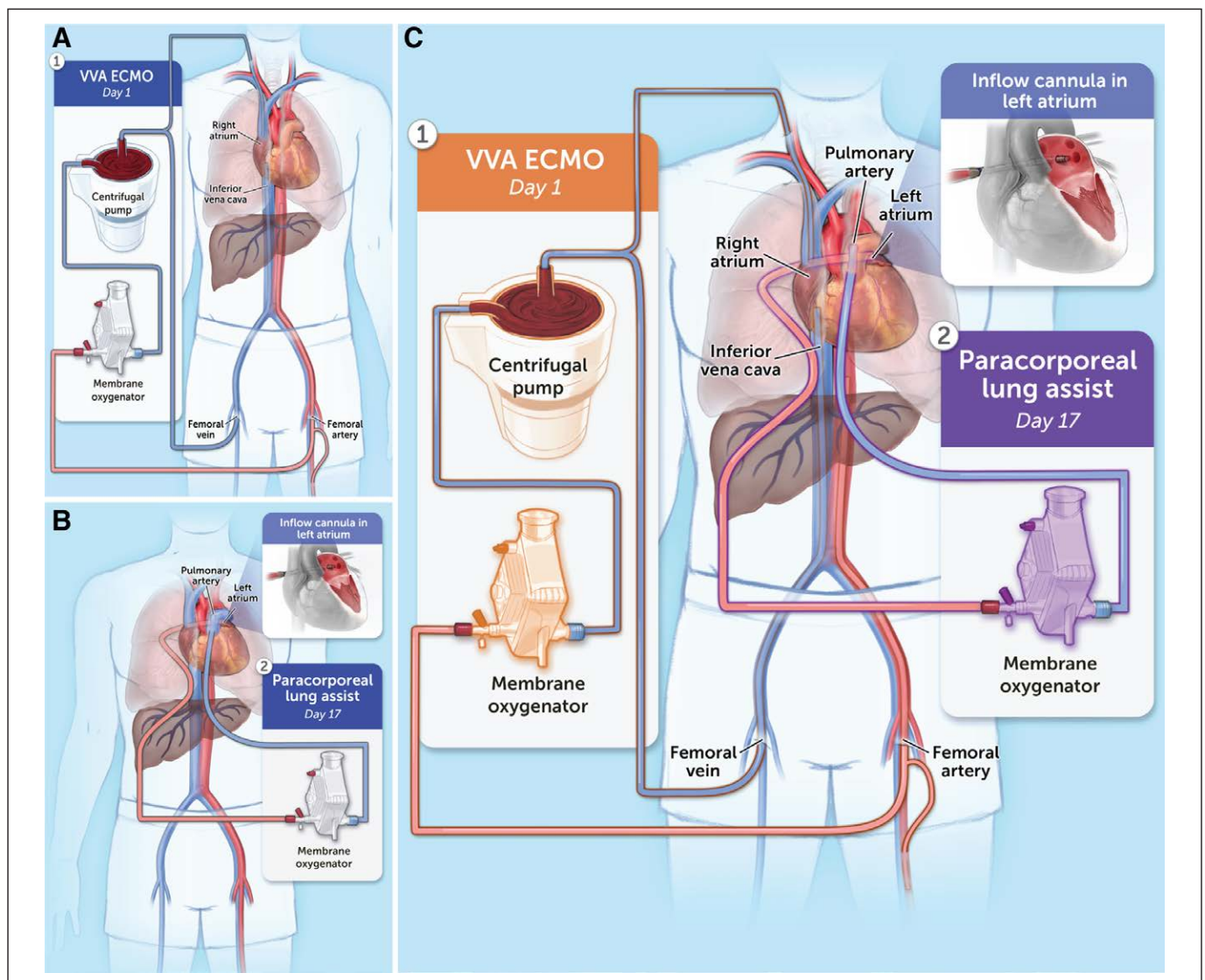


Figure 4. Venovenous extracorporeal membrane oxygenation (VVA ECMO) and paracorporeal lung-assist device configurations. **A**, VVA ECMO circuit with venous cannulas in the right internal jugular vein (blue) and the right common femoral vein (blue), an arterial cannula in the left common femoral artery (red), and an arterial reperfusion cannula in the distal left femoral artery (red). **B**, Paracorporeal pumpless lung-assist device with cannulas in the main pulmonary artery and the left atrium. **C**, VVA ECMO (1) and in line paracorporeal pumpless lung assist device (2) with previously described cannula positioning.

flow from the RV was preferentially ejected into the pulmonary circulation as opposed to the paracorporeal circuit. TTE 48 hours later showed mild-to-moderate RV systolic dysfunction and normal LV systolic function.

The patient underwent ECMO decannulation after 29 days and was solely supported by the paracorporeal lung-assist device. It should be noted that prior to removing the patient from ECMO, aggressive, serial bronchoscopies were required to ensure patent airways for gas exchange. Additionally, a PA catheter was placed for evaluation of readiness for decannulation from the paracorporeal lung-assist device. PA pressures ranged from 35/25 to 45/30 mm Hg (mPAP, 30–35 mm Hg) ($< \frac{1}{2}$ systemic). He was decannulated from the paracorporeal lung-assist device after 15 days (3-d post-ECMO decannulation). TTE thereafter demonstrated mild RV hypertension ($< \frac{1}{2}$ systemic) and normal biventricular systolic function.

FOLLOW-UP

All Discussants

There are no standard guidelines for the medical management of PPHTN in pediatric patients. The literature in adults suggests that PPHTN should be treated similar to PAH with pulmonary vasodilator therapy according to hemodynamic findings and disease severity (13). Liver transplantation has been shown to ultimately improve survival in PPHTN (23). The ILTS has made a grade 1C recommendation for pretransplantation PAH therapy in those with moderate and severe PPHTN. If there is subsequent improvement to mild disease, patients may be considered for liver transplantation (12).

Limited pediatric case series and several adult studies have reported benefits of pulmonary vasodilator therapy for PPHTN with prostacyclin analogs, phosphodiesterase-5 inhibitors, and endothelin receptor antagonists. Hemodynamic response to combination therapy, including decreased PVR and mPAP, and increased cardiac index on evaluation by catheterization, has been documented as early as 3 months following initiation (9, 10, 23).

Extracorporeal life support, including the paracorporeal lung-assist device, has been used as a bridge to lung transplantation and clinical recovery in patients with RV failure secondary to non-PPHTN pulmonary hypertension (24, 25). There is a case report of a 43-year-old man with alcoholic cirrhosis, diagnosed with PPHTN

while undergoing OLTx, complicated by acute decompensation on postoperative day 3, who was bridged with ECMO while pulmonary vasodilator therapy was titrated to effect (26). Otherwise, the use of ECMO in conjunction with a paracorporeal lung-assist device has not been described as a salvage therapy for severe acute PPHTN in the pediatric or adult populations. In our post-OLTx 19-year-old patient with severe PPHTN identified after cardiac arrest, we have used ECMO and then in-line paracorporeal pumpless lung-assist device as a bridge to native recovery in conjunction with dual combination pulmonary vasodilator therapy.

Our patient was discharged to an inpatient rehabilitation center for 6 weeks following decannulation from the paracorporeal lung-assist device with preserved hepatic graft function and return of end organ function, including no further dependence on mechanical ventilation or hemodialysis. Brain MRI showed multiple foci of susceptibility effect in the deep hemispheric white matter, corpus callosum, deep gray nuclei, brain stem, and cerebellum, consistent with microhemorrhages. The patient did not have any focal neurologic deficit or apparent gross cognitive impairment 21 months after his transplant. At discharge, his pulmonary vasodilator therapy included enteral sildenafil and enteral macitentan. He was weaned from sildenafil 5 months later and from macitentan 12 months later. Follow-up echocardiogram at 21-month post-transplant demonstrated low RV pressure and qualitatively normal RV function. His follow-up vitamin C level at the time of pulmonary hypertension resolution had normalized (49 $\mu\text{mol/L}$ [reference range, 23–114 $\mu\text{mol/L}$]). He also underwent tracheostomy decannulation 6 weeks following his initial discharge. He has since returned to college without neurocognitive or physical limitations.

FINAL DIAGNOSIS

Acute RV failure secondary to undiagnosed severe PPHTN.

ACKNOWLEDGMENTS

In memoriam of Dr. Thomas Kulik, a world expert in pediatric pulmonary hypertension, whose expertise and dedication saved the life of the patient described in this case and innumerable others. This case was presented and discussed at the Boston Children's Hospital, Division of Critical Care Medicine's recurring case

conference series. The patient and family provided consent for publication.

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This case occurred at Boston Children's Hospital.

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