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# Rescue Therapy with Early Extracorporeal Membrane Oxygenation for Primary Graft Dysfunction after Bilateral Lung Transplantation

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## Introduction

Lung transplantation (LTX) is an established therapy for end-stage pulmonary disease worldwide.[1] Although primary graft dysfunction (PGD) is a type of acute lung injury that

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typically develops in the first 72 hours after LTX, it remains clinically important because it independently predicts for adverse outcomes in LTX both in the short- and long-term.[2–3] Consequently, the perioperative management of PGD is critical to optimize clinical outcomes and may require extracorporeal membrane oxygenation (ECMO) as a bridge to clinical recovery.[4–5] We present a case of severe PGD after bilateral LTX that was managed successfully with early ECMO. The case discussion has been presented in a multidisciplinary fashion to encompass perspectives from the entire perioperative management team for LTX.

## Case Report

A 62 year-old Caucasian female with end-stage chronic obstructive pulmonary disease presented for bilateral LTX via sternotomy on cardiopulmonary bypass (CPB). She required supplemental oxygen therapy at home and reported severe dyspnea with activities of daily living. Her past medical history included superventricular tachycardia, hyperlipidemia, and gastro-esophageal reflux. Her past surgical history included a variety of non-cardiothoracic procedures. She had undergone extensive multidisciplinary assessment for LTX. The patient had ceased smoking tobacco 12 years earlier.

On clinical assessment, the patient was 153 cm tall and weighed 62 kg. Her physical exam, laboratory tests, clinical imaging and pulmonary function tests were all consistent with her known lung disease. Transthoracic echocardiography revealed no septal defects, normal biventricular function, mild tricuspid regurgitation, and an estimated pulmonary artery systolic pressure of 27 mmHg. Cardiac catheterization revealed mild coronary disease.

The patient underwent balanced general endotracheal anesthesia with routine monitors, a right radial arterial line and an oximetric pulmonary artery catheter via the right internal jugular vein. Selective lung ventilation was obtained with left-sided double lumen endotracheal tube positioned under bronchoscopic guidance. After midline sternotomy, mediastinal dissection and systemic heparinization, cardiopulmonary bypass was initiated via aorto-atrial cannulation.

After bilateral pneumonectomy, the donor lungs were implanted sequentially in a standard fashion. The double-lumen endotracheal tube was changed to a single lumen endotracheal tube during CPB. The ischemic times were 250 minutes for the left lung and 330 minutes for the right lung. Total CPB time was 269 minutes. During CPB, packed red blood cells were transfused to maintain a hematocrit of at least 25%. Although the patient was weaned from CPB on low-dose epinephrine and room air, the $FiO_2$ had to be gradually increased over an hour to 1.0 to maintain systemic oxygen saturation above 90%. Diagnostic bronchoscopy revealed supracarinal position of the endotracheal tube, no mucous plugging and patent airways bilaterally. Positive end-expiratory pressure was titrated in an effort to optimize alveolar recruitment and oxygenation. Inhaled prostacyclin was administered to augment ventilation-perfusion matching. Additional packed red blood cell transfusion was added to maintain the hematocit at 30%. Transesophageal echocardiography (TEE) demonstrated normal biventricular function, no intracardaic shunts, normal valvular function, and laminar flow across all the pulmonary venous anastamoses.

Despite this aggressive management, the allografts became increasingly edematous. Arterial blood gas analysis demonstrated a pH of 7.23, $PCO_2$ of 47 mm Hg, a $PaO_2$ of 106 mmHg on a $FiO_2$ of 1.0, corresponding to a $PaO_2/FiO_2$ ratio of 106. The diagnosis of severe rapidly progressive PGD was made. At this juncture, abundant pink frothy fluid from both lungs was suctioned from the endotracheal tube. Given the rapid deterioration despite maximal management, venovenous ECMO was promptly instituted after systemic heparinzation via the right femoral and right internal jugular veins. The position of both venous cannulas was confirmed by TEE. This peripheral cannulation was chosen because at this point the sternal incision had been closed. After initiation of ECMO, systemic oxygen saturation rapidly recovered to 100% with ECMO flows of 2.8 liters per minute.

The patient was admitted to the surgical intensive care unit in stable condition on venovenous ECMO. The patient was maintained on a low-stretch lung-protective pressure-controlled ventilation (discussed later). Over the course of the next 5 days, the ECMO $FiO_2$ was gradually weaned to 0.21, signaling excellent recovery of the allografts and allowing discontinuation of ECMO the same day (refer to figure 1). The patient experienced ongoing steady clinical improvement and underwent successful tracheal extubation during postoperative day 9. She was discharged from the intensive care unit on postoperative day 12. After continued pulmonary rehabilitation, she was discharged from hospital on postoperative day 23 with systemic oxygen saturations of 96% on room air.

## Commentary: The Pulmonologist's Perspective (Dr Lee)

From a transplant pulmonologist's perspective, severe PGD is the most feared early post-transplant complication, as it is the leading cause of early mortality following lung transplantation.[2–3] As this case clearly illustrates, the early initiation of ECMO can be a powerful tool in the armamentarium of a coordinated multidisciplinary team dedicated to the support of lung transplant recipients. However, it remains a highly technical procedure that requires skill and experience to implement. Since the initiation of ECMO in critically ill and immunosuppressed LTX recipients has significant complications, it is imperative for the perioperative team to be certain that PGD is the diagnosis being addressed and to have a comprehensive understanding of clinically significant PGD.

In 2005, an International Society for Heart and Lung Transplantation working group was convened to standardize the definition of PGD, previously known by such terms as `primary graft failure' and `reperfusion edema'.[6–7] Their published guidelines established the currently standard definition and grading of PGD, based on the presence or absence of chest x-ray infiltrates and the $PaO_2/FiO_2$ ratio in the absence of other identifiable cause.[6] The severity of PGD is graded by the determined by the $PaO_2/FiO_2$ ratio, with values below <200 classified as Grade 3 PGD, as iin this presented case (refer to table 1).[6] Prior to this standardization, a variety of definitions of PGD caused drastically differing and inconsistent reporting of PGD, with less stringent definitions of PGD leading to reported incidences of up to 80% of all transplants.[7–8]

Furthermore, PGD is graded at the following time points after LTX: Time (T) = 0 (within six hours after graft reperfusion), T = 24 (24 hours after graft reperfusion), T = 48 (48 hours

after graft reperfusion), and T = 72 hours (72 hours after graft reperfusion). The temporal aspect of this definition allows for the differentiation between different forms of PGD such as `early-onset PGD', `late-onset PGD', `early resolving PGD', and `persistent PGD'. As more experience is gained with these phenotypes of PGD, the clinician will have a greater understanding of their clinical impact. While several groups have suggested refining the PGD grading system (adjusting for single versus bilateral lung transplantation; adding time points for grading), these have not yet been adopted.[9–10] The current definition has since been validated in large series and has been shown to have good discriminatory validity to predict outcomes based on PGD grade.[11–12]

With this definition in mind, when the clinician caring for a lung transplant recipient observes refractory hypoxemia, decreased lung compliance, and radiographic infiltrates without other identifiable cause during the first 72 hours after surgery, clinically significant PGD should be considered and taken very seriously. Ideally, the pre-transplant risk for developing severe PGD would be known *before* the actual lung transplant procedure, based on a combination of measureable biomarkers, as well as clinical and/or genetic risk factors identified from the recipient and donor. Such knowledge would then allow for the actual prediction of severe PGD based these factors, and potentially to allow for the matching of PGD high-risk donors to low-risk recipients, and vice versa, thereby expanding the effective donor pool. Numerous chemokine and cytokine biomarker profiles of severe PGD have been published, but are not yet at a point-of-care stage suitable for widespread use.[13] Similarly, genetic analysis and microarray work is underway to determine the genetic signature of patients most at risk for developing PGD, but this technology is not yet feasible for clinical application.[14]

We are left with striving for a robust understanding of the clinical risk factors for the development of PGD. Numerous small studies using the aforementioned inconsistent definitions of PGD have been published, identifying several clinical risk factors such as extremes of donor age (<21 or >45 years old), ischemic times, and recipient female gender.[15] The risk factor most well described for the development of PGD is the presence of elevated pulmonary arterial pressures in the recipient at the time of transplant.[16] A recent multi-centered prospective cohort study in LTX (N = 1255: 10 centers from 2002 – 20100) has documented a 16.8% incidence of grade 3 PGD.[16] Multivariate analysis of this dataset demonstrated the following clinical risk factors for this outcome: donor smoking history (odds ratio 1.8; 95% confidence interval 1.2 – 2.6; P = 0.002); single LTX (odds ratio 2.0; 95% confidence interval 1.2 – 3.3; P = 0.008); recipient obesity (odds ratio 2.3; 95% confidence interval 1.3 – 3.9; P = 0.004); preoperative sarcoidosis (odds ratio 2.5; 95% confidence interval 1.1 – 5.6; P = 0.03); utilization of CPB bypass (odds ratio 3.4; 95% confidence interval 2.2 – 5.3; P < 0.001); and, pulmonary arterial hypertension (odds ratio 3.5; 95% confidence interval 1.6 – 7.7; P = 0.002).[16] This clinical trial also highlighted the aforementioned outcome importance of PGD by documenting that PGD was significantly associated with mortality at both 3 months (relative risk 4.8; P < 0.001) and at 1 year (relative risk 3.0; P < 0.001) after LTX.[16] A second registry multicenter trial (N = 6984: 1994–2002) showed that recipient female gender independently predicts for PGD after LTX.[17] In the case presented herein, the recipient risk factors that predisposed to PGD

included female gender and exposure to CPB. It is likely that further large trials will further clarify the clinical risk factors for PGD after LTX.

Regardless of the risk factors for PGD, the possibility of other etiologies for the lung edema must be entertained. As detailed in the case report, readily accessible information at the bedside can be obtained to help eliminate causes of acute perioperative hypoxemia. Bronchoscopy is essential to assess airway patency as well as the quantity and quality of secretions to rule out infectious concerns. Transesophageal echocardiography can determine if pulmonary venous thromboses are present in the setting of hypoxia, chest x-ray infiltrates, and hypotension. Surgical issues such as excessive bleeding from difficult native lung explanation and size mismatching would usually be apparent intra-operatively.

Hyperacute rejection is exceedingly rare and has only been described anecdotally as the rapid onset of profound clinical deterioration, minutes to hours after reperfusion.[18–19] It is felt to be the result of preformed recipient antibodies leading to complement deposition from ABO incompatibility or unrecognized significant antibodies to the donor. Clinically, the patient will exhibit frothy sputum, profound hypoxemia, and microscopic platelet thrombi formation.[18] In contrast to the rapid course of humoral rejection, acute cellular rejection is rarely seen any sooner than one week after transplant and therefore would be unlikely in this case.

With the diagnosis of severe PGD in hand, the clinician's attention turns to treatment. Pathologically, the diffuse alveolar damage observed in severe PGD resembles the histologic changes that accompany the acute respiratory distress syndrome (ARDS). The initial supportive management of severe PGD is modeled after ARDS with low-stretch mechanical ventilation and permissive hypercapnea. However, it is important to realize that no prospective randomized trials have definitively proven a benefit from applying such well-established strategies for ARDS in patients with severe PGD following LTX. Post-operative care remains center-specific and is often not protocol-driven.

In general, our approach at the University of Pennsylvania is to minimize fluid administration with concurrent vasopressor support to maintain perfusion to vital organs as necessary. Although inhaled pulmonary vasodilators have been studied in PGD after LTX, they have not been shown to prevent PGD when used prophylactically upon reperfusion.[20–23] When used as a treatment in established PGD, however, these selective pulmonary vasodilators can help improve oxygenation to stabilize the patient clinically which may allow optimization of other factors.[24] In this presented case, inhaled prostacyclin was utilized in the multimodal management of the severe PGD.

In 2009 the University of Pittsburgh published their experience using ECMO in heart-lung and lung transplant recipients over a 15 year period.[4] Of 763 patients, 7.6% required ECMO instituted within the first 7 days after transplant. Of these 58 patients, 39 were successfully weaned off ECMO. Thirty day-, 1 year-, and 5 year-survival was 80%, 59%, and 33% respectively.[4] The recently published Duke University experience highlights that venovenous ECMO was the *routine* treatment for severe PGD, suggesting perhaps a lower threshold for ECMO initiation compared to previous studies.[25] Over a 9 year period of time,

28 of 498 (6.0%) patients required ECMO. Patients were weaned 96% of the time, and survival rates were better compared to previously published reports: 82%, 64%, and 49% at 30 day, 1 year and 5 years, respectively. While encouraging, the authors did notice worse allograft function in ECMO survivors after 3 years.[25]

These recent series illustrate that with evolving technology and importantly, with increased experience, ECMO may be successfully utilized in select cases of severe PGD following LTX. Importantly, it remains clearly shown that late institution of ECMO has led to nearly universal poor outcomes.[26–27] Because complications with ECMO even in experienced hands are not trivial (bleeding, renal failure, and vascular injury), it would be ideal if one was able to predict which lung transplant patients will require ECMO following lung transplantation. In such situations, one might even advocate for the prophylactic use of ECMO.

This case illustrates severe PGD developing after bilateral LTX that benefitted from the early institution of VV ECMO. From a pulmonologist's perspective, it is important to understand the definition of PGD, acknowledging that different patterns of onset of PGD may potentially represent different injury patterns. Before the widespread application of a biomarker panel or genetic microarray technologies for rapid analysis of recipient-donor pairings for assessment of PGD risk, clinical factors will likely increasingly help estimate risk for PGD development. In the setting of clearly severe PGD, increasing evidence points to good success rates with early initiation of ECMO in experienced hands.

## Commentary: The Surgeon's Perspective (Dr Cantu)

In-hospital mortality for lung transplantation is higher than for other solid organs.[28] Significant contributors to this early hazard are ischemia-reperfusion injury and infection.[29] PGD is the clinical manifestation of ischemia-reperfusion injury and is a common cause of perioperative mortality in LTX.[2–3; 16–17] PGD contributes to early mortality, increased length of stay, increased ICU care, and increased cost.[30–31] Consequently, improved perioperative support may lead to decreased PGD mortality and thus improve short-term outcomes. Description of extracorporeal membrane oxygenation (ECMO) as a supportive adjunct for patients with primary graft dysfunction after lung transplantation has been described since the late 1970s and its use has significantly reduced perioperative mortality from this problem.[32–35] However, there are several considerations which may impact the success of this adjunct which include timing and technique.

At the University of Pennsylvania, timing is decided by the individual surgeon but our preference is to initiate ECMO early (defined as within 24 hours of development of grade 3 PGD). This strategy has been used to minimize exacerbating lung injury related to barotrauma and concomitant high oxygen requirements.[36–37] We consider ECMO in PGD after LTX when peak inspiratory pressures exceed 30 cm $H_2O$ and the $FiO_2$ surpasses 0.80. TEE is used routinely to ensure there are no technical issues which explain hypoxia such as intracardiac shunts and pulmonary venous thrombosis. These criteria are similar to other previously published series.[4; 33]

Our preference is to use venovenous ECMO through access gained at the right femoral vein and internal jugular vein or through the right internal jugular vein exclusively using a specially designed dual-lumen catheter.[38] Peripheral venous cannulation allows the chest to be closed and the risk of infection to be minimized.[33] Percutaneous access via a Seldinger technique is confirmed using echocardiography and/or a chest radiograph. Though venovenous ECMO is preferred, it is not always possible. When significant hemodynamic instability occurs, we use a central cannulation strategy and veno-arterial ECMO.

Venovenous ECMO is preferred because the transplanted lungs are dependent on pulmonary artery blood flow unless the bronchial arteries are reimplanted. Additionally, pulmonary artery pulsatility may be difficult to achieve with veno-arterial ECMO without compromising systemic perfusion. A high flow of oxygenated blood through the PA actually reduces PA pressure and facilitates lung recovery.[33] Additionally, the new heparin coated circuits and high efficiency membranes allow for significantly lower systemic heparinization which reduces bleeding complications and secondary injury to the lung from transfusion-related lung injury. These reasons together with the decrease embolic load to the central nervous system, ease of peripheral cannulation allowing for chest closure and evidence that results are superior to veno-arterial ECMO explain our preference for this type of ECMO.

Implementing this strategy requires significant support.[38–39] At the University of Pennsylvania, ECMO is managed by our ICU team with input from the perfusionists. A protocol-driven care plan is followed in our LTX transplant patients. The target flows, sedation, anticoagulation, cardiac output, saturation parameters, ventilator settings and resuscitative parameters are supervised by the attending intensivist in collaboration with the attending surgeon and transplant pulmonologist.

A stepped algorithm is followed. The first 24 hours are typically characterized by an inflammatory state (from both ECMO and PGD) requiring moderate resuscitation which we allow. During this period, hemodynamic stability is achieved with adequate oxygenation on lung-protective ventilator settings (PEEP 7–12 cm $H_2O$; tidal volume of 6 cc/kg; plateau airway pressure < 30 cm $H_2O$; and, $FiO_2$ < 0.40), inhaled prostacyclin and deep sedation without paralysis. The chest radiograph is expected to become more opacified over this time period. Anticoagulation is monitored by partial thromboplastin time which is maintained at 50–60 seconds for the first 24 hours, and thereafter at 60–70 seconds, if there is no evidence of hemorrhage.

Once stability has been achieved, gentle diuresis is begun and the oxygen concentration is gradually reduced on the ECMO circuit until 21% is achieved. Weaning is monitored by frequent arterial blood gas analysis to ensure adequate oxygenation. During this period, increasing lung compliance and slight improvement in the chest radiograph can be expected. After 21% is achieved on the blender, the sweep flow is incrementally decreased to 500 mL/min with frequent $CO_2$ monitoring. Once this is achieved, the lung has sufficiently recovered for ECMO decannulation which is performed at the bedside for peripherally cannulated patients. Heparinization is typically discontinued 1 hour prior to ECMO decannulation. Thereafter, gradual weaning of sedation and frequent bronchoscopy for

pulmonary toilette facilitate a smooth transition to tracheal extubation. ECMO support varies between patients but is usually required for 3–5 days in our experience.

Despite the significant resource utilization that ECMO after LTX requires, there is adequate recovery of function and mortality is significantly improved compared to those who do not have access to this type of therapy.[4; 25] We suggest that ECMO is strongly indicated in severe PGD where ongoing ventilator injury is a concern: it should be initiated early and managed in a protocol-driven multidisciplinary fashion to optimize survival.

## Commentary: The Perioperative Echocardiographer's Perspective (Dr Gordon)

There have been to date more than 25 000 lung transplants performed worldwide.[40] The indications for transesophageal echocardiography (TEE) in the setting of lung transplantation have varied from near routine at certain centers to reserved for complications such as refractory hypotension and unexplained hypoxia.[41] Although TEE does not directly diagnose PGD after LTX, it assists in the diagnosis and management of cardiopulmonary causes of hypoxia.[42] A comprehensive TEE exam allows detailed examination of the heart including valves, atrial septum, pulmonary veins, pulmonary arteries, and biventricular function.[43]

When the cardiac anesthesiologist is presented with progressive severe hypoxia shortly after LTX, there is a wide differential diagnosis that must be considered. Although PGD is a leading cause of hypoxia after LTX in the perioperative period, it remains a diagnosis of exclusion. A major role of TEE in this urgent setting is to rule out cardiopulmonary etiologies associated with hypoxia such as new right-to-left intracardiac shunt (e.g. patent foramen ovale), left ventricular failure with pulmonary edema, and pulmonary vein obstruction (PVO).[44–45]

The clinical presentation of PVO after LTX is often indicated by development of progressive edema in the affected lung. The TEE will typically exhibit turbulent flow on color Doppler imaging across the involved pulmonary venous anastomosis with a narrowed orifice on 2D-imaging and increased velocities on Doppler imaging.[46] If the pulmonary venous obstruction is severe, significant pulmonary edema and severe hypoxia may develop with consequent pulmonary hypertension and right ventricular failure.[43–46] It is also important to remember that PVO may present in a delayed fashion in the postoperative period with unexplained stroke, progressive deterioration in oxygenation and/or unilateral lung opacification on radiographic examination.[43] These delayed presentations are all indications for a evaluation of the pulmonary veins with TEE.[43] The mortality risk associated with PVO after LTX is not trivial and is higher in women and single LTX.[43–44]

The comprehensive assessment of pulmonary venous patency has also been a major theme not only after LTX but in patients undergoing transcatheter ablation for atrial fibrillation.[43; 47] In these settings as well as LTX, computed tomography, magnetic resonance imaging and angiography besides TEE can all be utilized to evaluate for PVO, whether partial or complete.[43–44] Although angiography is a gold standard for the diagnosis

and quantification of PVO, its clinical disadvantages include its invasiveness, current inability to perform in an operating room, contrast nephropathy, and the transport of critically ill patients to and from the radiology suite. and our inability to do it in the operating room. The hazardous transport of hemodynamically unstable patients for diagnosis of PVO after LTX is also a perioperative limitation with .computed tomography and magnetic resonance imaging

In contrast, TEE is portable and rapidly available at the bedside or in the operating room. A recent systematic review of the diagnostic performance of TEE in the detection of PVO (N = 1344: 7 studies) found that TEE, when compared to pulmonary vein angiography, had a sensitivity of (82 –100)% and a specificity of (98 – 100) %.[47] Compared to computed tomography, TEE had a sensitivity of (86 – 100)% and a specificity of 95%. Compared to magnetic resonance imaging, TEE had a sensitivity of 100% with a specificity of (98 –99) %. Although the quality of the reviewed studies was limited by their retrospective design, the investigators concluded that TEE has a high sensitivity and specificity for detection of PVO and that combined with its wide availability and favorable side-effect profile, TEE has high clinical utility in this setting.[47] It is important to note that this systematic review was limited to cases of PVO after catheter ablation for atrial fibrillation.

A focused review of TEE for PVO after LTX also concluded that TEE has diagnostic advantages, but that echocardiogrpahic diagnostic criteria for PVO after LTX were not clearly defined.[43–44] This review identified the following clinical criteria that were suggestive of this complication: pulmonary venous diameter < 0.5 cm; peak systolic flow velocity > I meter per second; pulmonary vein-left atrial pressure gradient ≥ 10–12 mmHg; absence of flow through the pulmonary stenosis, and the presence of thrombus.[44] Given the diagnostic value of TEE in this setting, these investigators suggested that TEE for interrogation of pulmonary venous anastomoses be routine in LTX.[44]

For these reasons, it is essential for the perioperative echocardiographer to be familiar with the diagnostic approach with TEE for the detection of PVO after LTX.[43–44] However, while TEE is convenient and accurate for interrogation of pulmonary veins after LTX, it also requires significant operator skill. It is also vital for the perioperative echocardiographer to realize that the peak systolic flow velocity depends on multiple factors such as mechanical ventilation settings, cardiac output, cardiac rhythm, intravascular volume status, and the pulmonary distribution of blood flow. Furthermore, there is a lack of reference values in the lung transplant recipients.

The pulmonary venous – left atrial pressure gradient can be measured with high-fidelity transducers placed through a small incision in the pulmonary vein and then positioned with TEE guidance to measure pressures in the pulmonary vein of interest and the left atrium. This gradient will depend not only on the diameter of the pulmonary vein but also on the amount of blood flow across it. A measured gradient in excess of (10–12) mmHg suggests PVO.[44]

A recent comparison of intraoperative TEE and direct contact ultrasound for assessment of pulmonary vessels in bilateral LTX highlighted certain limitations with TEE.[52] The left

superior (P = 0.04) and left inferior (P = 0.02) pulmonary veins were significantly more often viewed with contact ultrasound (`epivenous technique'). Although both methods yielded similar pulmonary venous diameters, TEE significantly underestimated the diameter of the left superior pulmonary vein (P = 0.002). Furthermore, the left inferior pulmonary venous velocity was significantly higher by TEE than by contact ultrasound (P < 0.001).[52] Although the investigators concluded that caution is required in the TEE assessment of pulmonary veins in LTX, it is also important to remember the added utility of hand-held imaging in this scenario, as in the case with TEE and epiaortic imaging.

Clinical decision-making in this setting must take into account not only the TEE findings but also the graft function. For example, even if PVO is correctly identified after LTX, no intervention may be required if there is no associated graft dysfunction.[53] In one trial, PVO had an incidence of 27%, but only case required surgical intervention.[53] Multiple studies indicate that intervention is required in the setting of seevre stenosis and/or thrombus due to excessive mortality risk.[43–44; 53–55]

The outcome importance of pulmonary venous thrombosis was highlighted in a prospective study of 87 LTX recipients.[55] This TEE study documented a 15% incidence of this complication, with a mortality rate of 38% at 90 days. Although this complication was more frequent in unilateral LTX, the incidence decreased significantly with surgical experience, highlighting the importance of technical factors in the development of PVO after LTX.[55]

Based upon the literature, TEE is a useful diagnostic tool in the perioperative management of LTX. It can enable one to quickly evaluate biventricular function, intracardiac shunts and the vascular anastomoses. Probable PVO after LTX is suggested by echocardiographic demonstration of a narrow venous diameter and flow acceleration across the identified stenosis.[43] While the diagnosis of PVO depends on the skill of the echocardiographer, TEE has high clinical utility in the armamentarium of the cardiothoracic anesthesiologist in the setting of hypoxia, hypotension, pulmonary edema and other frequently encountered problems associated with lung transplantation.

## Conclusion

This case conference has highlighted the successful, integrated and multidisciplinary management of PGD after bilateral LTX. The contemporary definition and classification of PGD provide a framework for its perioperative recognition and management. The early institution and protocol-driven management of ECMO for severe PGD after LTX at an experienced center can be life-saving. The role of comprehensive TEE in this clinical setting is essential.

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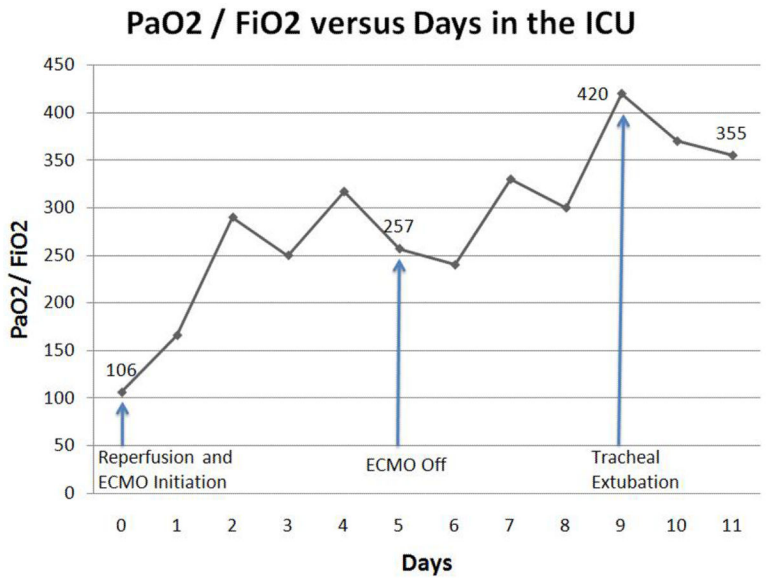


**Figure 1. $PaO_2$ / $FiO_2$ Ratio versus Time after Bilateral Donor Lung Reperfusion**

Day 0 begins the first hour after transplant graft reperfusion. The steady recovery of the $PaO_2$ / $FiO_2$ ratio is consistent with gradual resolution of the primary graft dysfunction which allowed withdrawal of ECMO and mechanical ventilation. ($PaO_2$ = arterial blood oxygen tension in mmHg; $FiO_2$ = fractional concentration of inspired oxygen; ECMO = extracorporeal membrane oxygenation; ICU = intensive care unit)

## Table 1

Grading Scheme of the International Society for Heart and Lung Transplantation (ISHLT) for Primary Graft Dysfunction after Lung Transplantation

| ISHLT Primary Graft Dyfunction Grading | | |
|---|---|---|
| **Grade** | **PaO2/ FiO2 Ratio** | **Radiographic Infiltrates Consistent with Pulmonary Edema** |
| **0** | >300 | Absent |
| **1** | >300 | Present |
| **2** | 200–300 | Present |
| **3** | <200 | Present |

**Adapted from** Christie J, Carby M, Bag R, et al. Report of the ISHLT Working Group on Primary Lung Dysfunction part II: definition. A consensus statement of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant 24:1454– 1459, 2005 (reference 6)