Brief Communication and Review of the Literature

Anesthesia for Pediatric Lung Transplantation: Case Presentation and Review of the Literature

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Abstract

Pediatric lung transplantation is a relatively rare procedure offered to infants, children, and adolescents with end-stage lung disease. Compared to adult lung transplantation, the pre-operative condition of the patients, indications for transplantation, and the conduct of the surgery itself can be quite different. Through this case presentation of a 2-month-old undergoing bilateral lung transplantation, we discuss the unique anesthetic considerations in the management of the pediatric patient, and review the data on the recent era of pediatric lung transplantation. Other concerns relevant to the anesthesiologist such as the disease states leading to transplantation, the ages at which patients most commonly present, and causes of post-operative morbidity and mortality are also presented.

Keywords: Pediatric, Lung, Transplantation, Anesthesia

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Introduction

The first pediatric lung transplant was performed in 1987 at the University of Toronto in a 15-year-old with familial pulmonary fibrosis (1). Since that time, over 2000 children have received lung transplants worldwide, with an annual number ranging between 99 and 137 over the past decade (2).

While these numbers reflect the consistency in the need for this procedure, they also highlight its relative infrequency. Pediatric lung transplants have accounted for only 5.5% of all lung transplants since 1988 and represent an equally small percentage of all pediatric solid organ transplants (3). This lag has been attributed to the decreased incidence of end-stage lung disease in the pediatric population, a paucity of acceptable donors, and the modest late survival associated with transplantation. Nonetheless, pediatric lung transplantation has become a life-saving option for those with irreversible and progressive pulmonary parenchymal or vascular disease. For the anesthesiologist charged with managing these rare patients, an understanding of the indications that lead to transplantation, their pathophysiology, and the physiology of the transplanted lungs are critical.

To provide a context for the anesthetic management of the child undergoing lung transplantation, we discuss the case of a 2-month-old who underwent bilateral lung transplantation for intractable respiratory failure. Both the unique aspects of this case and pediatric lung transplantation, in general, are presented.

Case Report

A full-term infant who was the product of an uncomplicated gestation and an uneventful delivery presented to our institution at 10 weeks of age for bilateral lung transplant evaluation due to a pulmonary growth abnormality. Imaging on arrival demonstrated hyper-expansion of the right middle lobe causing both mediastinal shift to the left as well as compression of the right upper and lower lobes (Figure 1). This anatomy was reflected clinically with impaired ventilation and intermittent hypotension, presumably due to diminished venous return caused by the compressive effect of the right middle lobe on the right atrium.

Blood gases revealed a compensated respiratory acidosis with $PaCO_2$ levels chronically between 80-100 mmHg despite mechanical ventilation with paralysis and the use of inhaled nitric oxide (iNO, Table 1). Oxygenation, though also impaired, was acceptable with an increased FiO_2. Echocardiography revealed a patent foramen ovale, mild right ventricular hypertrophy, pulmonary hypertension, and normal biventricular function.

Medical management entailed aggressive diuresis and a strategy of differential lung ventilation to minimize the negative effects of the emphysematous right middle lobe. Through this process, the left lung was selectively ventilated via a cuffed oral endotracheal tube (ETT) placed in the left mainstem bronchus, while the right lung was ventilated via the tracheostomy (Figure 2). Using two ventilators, one for each lung, the right lung was ventilated more cautiously using a decreased rate and decreased inspiratory and positive end-expiratory pressures (Table 1). More ventilation that is effective was thereby achieved with less mediastinal shift. Given the infant's irreversible defect in lung growth, however, the patient was ultimately put forward for transplantation. Within 1 week of listing, a suitable organ became available.

As the patient was maintained on differential lung ventilation in the intensive care unit (ICU), a central consideration in our pre-operative evaluation was the safety and feasibility of maintaining this arrangement for transport and in the operating room. Due to concerns about this approach, we opted to trial

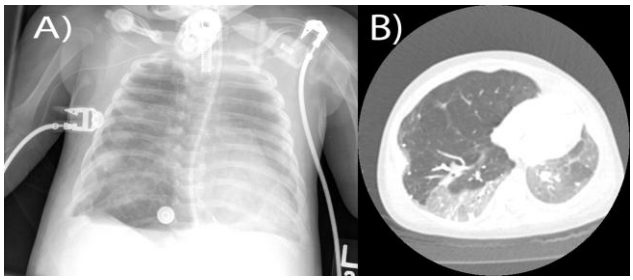

Figure 1. A Chest X Ray of the patient B CT demonstrating hyperexpansion of the right middle lobe, displacement of the mediastinum to the left, and compression of adjacent lung fields.

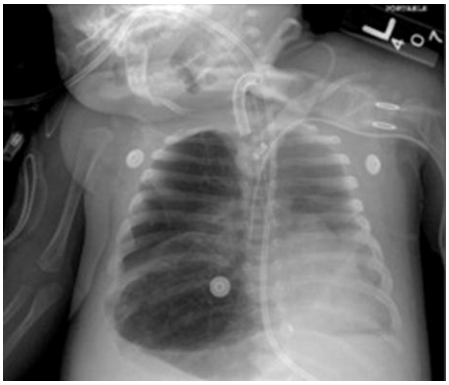

Figure 2. Differential lung ventilation. The left lung is ventilated via an oral ETT placed into the left mainstem bronchus while the right lung is ventilated via the tracheostomy.

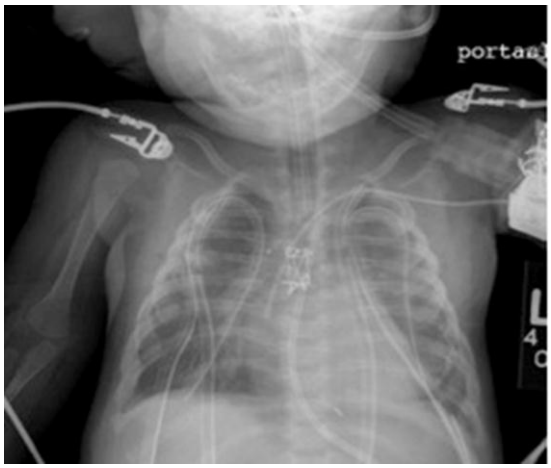

Figure 3. Chest x-ray on postoperative day 1.

the effect of stopping differential ventilation in the ICU in favor of ventilating both lungs through the tracheostomy at lower ventilatory settings. No significant change in hemodynamics or ventilation resulted, and so we proceeded with this traditional means of ventilation (Table 1).

Once in the operating room, the tracheostomy

Table 1: Ventilatory Settings and Blood Gases at Different Times in Management.

Time	*Conduit*	*Ventilator Mode*	*PIP[a] cmH$_2$O*	*Rate*	*PEEP[b] cm H$_2$O*	*FiO$_2$*	*iNO ppm*	*Blood Gas: pH/PCO2/PO2*
1	Tracheostomy	PCV[c]	38	40	5	0.7	20	7.23/121/146
2	*Right lung:* Tracheostomy	SIMV/PC[d]	30	28	5	0.6	5	
	Left lung: Bronchial cuffed oral ETT	SIMV/PC	38	28	8	0.6	5	7.35/89/41[e]
3	Cuffed nasal ETT	PCV	30-33	28	6	1.0	5	7.44/76/332
4	Cuffed nasal ETT	PCV	23	24	5	0.45	20	7.39/46/83

1: Arrival to our institution
2: Morning of transplantation
3: Initial operating room (OR) ventilatory settings
4: Following transplantation and liberation from cardiopulmonary bypass

a: Peak inspiratory pressure
b: Positive end-expiratory pressure
c: Pressure control ventilation
d: Synchronized intermittent mandatory ventilation/pressure control
e: Venous blood gas

Table 2: General goals for ventilation following transplantation (Texas Children's Protocol).

Recruitment maneuvers	< 30 cm H_2O
Ventilatory Mode	Pressure Control Ventilation
Peak inspiratory pressure (PIP)	< 25 cm H_2O
Positive end expiratory pressure (PEEP)	5
Tidal volumes	Donor-appropriate, < 10 cc/kg
FiO_2	0.4-0.5, goal SpO_2 > 90%

tube was exchanged for a nasal cuffed endotracheal tube (ETT) to allow a more exposed surgical field. A femoral arterial line was placed and central venous access was obtained. Bilateral cerebral near-infrared spectroscopy monitors (Somanetics INVOS, Troy, Michigan) were also placed to assess cerebral oxygenation. Anesthesia was maintained with isoflurane, fentanyl, and midazolam, and induction immunosuppressive therapy was administered as directed by the transplant service.

When the donor lungs were visualized and deemed acceptable, the recipient dissection was begun via a bilateral thoracosternotomy or "clamshell" incision. Due to the patient's size, tenuous respiratory status, and abnormal lung anatomy, the removal of the patient's lungs and placement of the donor lungs was performed on cardiopulmonary bypass. The transplantation was uneventful: three anastomoses were created in a posterior to anterior fashion with first the bronchi on each side, then the pulmonary veins, and finally the pulmonary arteries.

Prior to weaning from bypass, bronchoscopy was performed to evaluate the bronchial anastomoses and clear the airway of blood and secretions. Vasoactive agents to assist right ventricular function and minimize pulmonary vascular resistance were also initiated and included epinephrine 0.02

mcg/kg/min, milrinone 0.375 mcg/kg/min, prostaglandin E_1 0.025 mcg/kg/min, and inhaled nitric oxide (iNO) at 20 parts per million (PPM). Minimal peak inspiratory pressure, positive-end expiratory pressure, and inspired oxygen concentration were chosen to avoid further injury to the newly transplanted lungs (Tables 1 and 2). To augment ventilation, gentle recruitment maneuvers and suctioning were needed at regular intervals to combat atelectasis and prevent obstruction from bloody secretions.

The patient was successfully weaned on this regimen. Donor lung ischemic time was 6 hours and 47 minutes with a total CPB time of 6 hours and 5 minutes. The anticipated post-bypass coagulopathy was treated with platelets, cryoprecipitate, and recombinant activated factor VII. A total of 3 units of packed red blood cells, 3 units of fresh frozen plasma, 2 units of cryoprecipitate, and 1 unit of apheresis platelets were used during the bypass and post-bypass periods.

On arrival to the ICU, the patient's ABG was pH 7.46, $paCO_2$ 43, and paO_2 275. Chest x-ray demonstrated areas of atelectasis and pulmonary congestion, but symmetric lung fields and a normally positioned heart (Figure 3). In the days following transplantation, evidence of mild graft dysfunction appeared with a subsequent need for increased PIP and a slow wean of FiO_2. The allograft function remained acceptable, however, and progress was made in decreasing PIP and FiO_2 over time.

Discussion

What are the most common indications for pediatric lung transplantation?

The most common indications for pediatric lung transplantation include cystic fibrosis, pulmonary hypertension, interstitial lung disease, and obliterative bronchiolitis (2, 3). Of note, the indications largely correlate with age (Table 3). For those greater than 6 years, cystic fibrosis (CF) was the most common indication between 2000 and 2015 (2). In those who were less than 5 years, pulmonary hypertension, interstitial lung disease, congenital heart disease, and surfactant protein B deficiency led the indications for transplantation (2).

Contraindications to pediatric lung transplantation likely vary among institutions, but absolute contraindications may include systemic disease with major extra-pulmonary manifestations, severe multi-organ dysfunction, left ventricular failure, and severe scoliosis.

What are the characteristics of transplant recipients?

Transplant recipients between 1988 and 2008 had a mean age of 12±5.6 years and a mean weight of 33.6±16.3 kg (3). Adolescents (age≥13) were the group most commonly transplanted (58%), followed by those between 2 to 12 years (31%), with infants (11%) being the group least commonly transplanted (3). On average, 3-5 infants are transplanted annually. When listed, infants tend to be in the ICU and either mechanically ventilated or on extracorporeal membrane oxygenation (ECMO). Some, like our patient, may even have a tracheostomy pre-transplant (Table 4). This is in contrast to older children, many of whom wait at home while listed and are able to oxygenate and ventilate without support.

Median overall waiting times once listed are 5 months with a range of 0-96 months; infants have a significantly shorter waiting time of 1 month, with a range of 0-7 months, perhaps reflecting the small number of infants who are listed as well as the severity of their disease state at the time of listing.

Pre-operative evaluation

Pre-operative assessment should focus on the patient's indication for transplantation, the disease process's current effect on oxygenation and ventilation, and any other end-organ dysfunction that may be present. Of particular concern, regarding co-morbidities are those patients with cystic fibrosis. Given that the mutated gene, the cystic fibrosis transmembrane regulator (CFTR), is expressed in multiple organs, such patients can also present with diverse manifestations including diabetes, pancreatic exocrine insufficiency, and hepatic dysfunction (Table 5). Moreover, patients with end-stage cystic fibrosis often have multi-drug resistant bacteria. If not otherwise stated in the patient's transplant plan, such a history should prompt a discussion regarding the intraoperative antibiotics to be administered during the transplant.

In reviewing previous surgeries, particular attention should be given to prior thoracic procedures.

Table 3: Most Common Indications for Pediatric Lung Transplantation by Age, 2000-2015.

Diagnosis	***Age < 1 year (%)***	***1-5 years (%)***	***6-10 years (%)***	***12-17 years (%)***
Cystic fibrosis	-	4%	50%	67.8%
Idiopathic pulmonary hypertension	12.3%	27.3%	10.2%	7.7%
Non-idiopathic pulmonary hypertension	24.6%	18.2%	3.7%	1.6%
Interstitial lung disease	19.3%	18.2%	12.9%	6.7%
Surfactant protein B deficiency	21.1%	4%	0.5%	-
ABCA3 transporter mutation	7%	4%	0.5%	0.1%
Bronchopulmonary dysplasia	7%	3%	1.4%	0.3%
Obliterative bronchiolitis (non-retransplant)	-	8.1%	12.5%	4.6%
Retransplant	-	7%	4.6%	6.7%

Adapted from the Registry of the International Society for Heart and Lung Transplantation: Nineteenth Pediatric Lung and Heart-Lung Transplantation Report

Table 4: Support status and location of patients prior to lung transplantation at Texas Children's Hospital 2002-2011.

Age	*Tracheostomy*	*Otherwise mechanically ventilated*	*ICU*	*Home*
< 1 year	5/7	1/7	6/7	1/7
1-5 years	5/16	2/16	7/16	9/16
6-11 years	3/21	1/21	4/21	17/21
12-17 years	3/59	2/59	5/59	54/59
Total	16/103 (16%)	6/103 (6%)	22/103 (21%)	81/103 (79%)

Their presence may suggest an increased risk of bleeding and/or a lengthy dissection period during the transplant due to adherent tissues.

Vascular access

It is our institution's preference to use femoral arterial access for lung transplants. This choice has its basis in the clinical observation that radial arterial lines often seem to fail in this population. This may, in part, be due to the clamshell incision that can lead to compression of the subclavian artery, or as is the case in patients with cystic fibrosis, the decrease in systemic vascular resistance that can occur due to dissection-induced bacteremia.

Central venous access is routinely obtained unless a patient has an indwelling peripherally-inserted central catheter. Given the potential for intraoperative bleeding, adequate peripheral access should also be obtained.

Not surprisingly, vascular access may be challenging, particularly in those who have required care in the ICU prior to their transplant. A thorough review of prior invasive lines and any history of major vessel occlusion may assist in planning which vessels to access.

Analgesia: is there a role for a thoracic epidural?

While a thoracic epidural would offer the potential advantages of improved analgesia, earlier mobilization, and earlier extubation, unique risks are present in the setting of lung transplantation that warrant discussion. Because most cases of pediatric lung transplantation are performed using cardiopulmonary bypass (CPB), and thus involve systemic heparinization, the possibility of an associated neuraxial hematoma is theoretically

Table 5: Potential End-Organ Manifestations of Cystic Fibrosis.

Upper airway	• Chronic sinusitis • Nasal polyps
Pulmonary	• Productive cough • Wheezing and/or bronchospasm • Hemoptysis • Pneumothorax • Pulmonary hypertension
Cardiovascular	• Right ventricular dysfunction (cor pulmonale)
Gastrointestinal	• Gastroesophageal reflux • Meconium ileus in the neonate • Distal intestinal obstruction in adults • Intussusception • Fibrosing colonopathy
Hepatobiliary	• Gallstones • Cirrhotic liver disease • Hepatic steatosis
Exocrine pancreas	• Malnutrition • Steatorrhea • Fat-soluble vitamin deficiency
Endocrine pancreas	• CF-related diabetes mellitus
Bone and joints	• Fractures • Arthritis • Osteopenia • Osteoporosis

increased. Moreover, delaying the surgery in the event of a bloody insertion would be detrimental to the donor lungs by prolonging their ischemic time[6].

The age of the patient at the time of transplantation and the presence of other co-morbidities may also influence the decision on whether or not to place an epidural. On average, infants require 24±19 days of postoperative mechanical ventilation because of their accompanying medical issues[4], which would make epidural placement less advantageous; older patients with cystic fibrosis, on the other hand, are commonly weaned from mechanical ventilation within 1-3 days (5).

Consideration, then, needs to be given to the risks and benefits of an epidural as well as to the timing of placement should it be part of institutional practice. At our institution, we do not enough place epidurals due to the potential risk of a bloody tap and the observation that times to extubation and respiratory function do not appear compromised when using intravenous analgesics alone.

The role and impact of cardiopulmonary bypass in pediatric transplantation

In contrast to adult lung transplantation, the use of CPB in pediatric lung transplantation is commonplace. Often times the patient's airway size makes one-lung-ventilation with sequential single lung transplantation impractical; other times the patient's clinical status mandates the use of CPB to ensure a hemodynamically stable dissection and implantation. Disadvantages to CPB include an increased risk of coagulopathy and need for transfusion, and activation of the systemic inflammatory response with potential for allograft injury on reperfusion[8]. Our patient required both CPB and a brief period of aortic cross-clamping for closure of the patent foramen ovale (PFO).

Hemodynamics and fluid management

Assisting right ventricular function is a key

Table 6: Physiologic changes affecting lung function following transplantation.

Anticipated changes influencing lung function	***End-results of these changes***
Vagal denervation and loss of afferent stimuli	• Resting bronchodilation • Less effective cough • Decreased clearance of secretions • Decreased response to hypercapnea • Poor coordination between thoracic and abdominal musculature
Absence of lymphatic drainage	• Decreased lung compliance • Potential for worsening pulmonary edema with volume administration

Table 7: Common Causes of Death in Pediatric Lung Transplant Recipients by Age at Transplantation, 1990-2015.

Cause of death	***0-30 days*** **(n = 151)** **No. (%)**	***31 days – 1 year*** **(n = 212)** **No. (%)**	***>1-3 years*** **(n = 266)** **No. (%)**	***>3-5 years*** **(n = 128)** **No. (%)**	***>5 years*** **(n = 140)** **No. (%)**
Bronchiolitis Obliterans	0	24 (11.3)	96 (36.1)	49 (38.3)	65 (46.4)
Infection	23 (15.2)	72 (33.9)	43 (16.2)	22 (17.2)	10 (7.1)
Graft Failure	44 (29.1)	41 (19.3)	70 (26.3)	29 (22.7)	31 (22.1)
Acute rejection	3 (2)	5 (2.4)	6 (2.3)	3 (2.3)	1 (0.7)
Malignancy	0	12 (6.6)	8 (3.0)	4 (3.1)	12 (8.6)
Multiple Organ Failure	16 (10.6)	25 (11.8)	14 (5.3)	5 (3.9)	9 (6.4)
Cardiovascular	22 (14.6)	9 (4.2)	4 (1.5)	1 (0.8)	1 (0.7)
Technical	22 (14.6)	5 (2.4)	6 (2.3)	3 (2.3)	2 (1.4)

Adapted from the Registry of the International Society for Heart and Lung Transplantation: Nineteenth Pediatric Lung and Heart-Lung Transplantation Report

goal in patients undergoing lung transplantation, especially in the pre-bypass period when lung function is marginal. While it would ideal to minimize pulmonary vascular resistance through manipulating oxygenation, ventilation, and pH, this can be challenging due to the intrinsic lung abnormality. As such, one should have inotropes and pressors available to assist contractility as needed and to maintain an adequate coronary perfusion pressure to avoid right ventricular ischemia. Post-bypass, right ventricular function may be hyperdynamic assuming adequate graft function due to normalization in right ventricular afterload compared to the pre-transplant state. Vasoactive agents that can assist right ventricular function post-transplant include epinephrine, milrinone, prostaglandin E_1, and iNO.

Because transplanted lungs lack an intact lymphatic system, caution must be used with the administration of blood products and crystalloid in the immediate post-transplant period to avoid pulmonary congestion and subsequently impaired oxygenation and ventilation (6). This goal is often at direct odds, however, with the need to achieve hemostasis. As evidenced in the patient described, bypass times can often be several hours, leading to deficiencies in platelets, fibrinogen, and clotting factors that require replacement. Given that the transfusion of blood products is, at times, inevitable, one should look carefully for any change in ventilatory compliance and oxygenation that may indicate the onset of pulmonary edema. Such a change may prompt a new strategy towards the use of recombinant factor 7a or

another low-volume pro-coagulant like the prothrombin complex concentrates should coagulopathy remain an issue.

Ventilating and oxygenating the newly transplanted lungs

To avoid further injury to the donor lungs, our ventilatory strategy seeks to minimize the peak inspiratory pressures, positive-end expiratory pressures, and FiO_2 necessary to achieve adequate ventilation and oxygenation (Table 2). Common etiologies that may cause an acute increase in airway pressures include obstruction of the airways or ETT with blood or secretions, or airway compression due to surgical manipulation. Frequent suctioning either by suction catheter or with a bronchoscope is often necessary. When deciding what tidal volume is most appropriate with which to ventilate, one should consider the size of the donor patient (as this individual may have been smaller or larger than the recipient), and whether any lobes of the donor lung were surgically resected (as may be the case in significant size-mismatch).

Physiology of the newly transplanted lungs

Transplantation interrupts not only the donor lung's lymphatic drainage, but also its vagal innervation (Table 6). Vagal denervation manifests as resting bronchodilation, decreased ventilatory response to hypercapnea, diminished cough, and reduced mucociliary clearance. Proximal to the anastomosis, however, airway reflexes and mucociliary clearance are retained. Thus, if the upper airway or trachea is to be instrumented as in bronchoscopy, care should be taken to topicalize the airway with local anesthetic as one would in any other patient. Of note, hypoxic pulmonary vasoconstriction and the response to inhaled beta-agonists are preserved in the donor lung.

What are the concerns in the post-operative period following lung transplantation?

Post-transplant complications can be categorized into 3 phases: the immediate phase, representing the first week after transplantation; the early phase, including the first 3 months; and the late phase, entailing the time beyond 3 months.

Immediate and early phase complications

Primary graft dysfunction and ischemia-reperfusion Injury

These represent the most common graft complications following transplantation, occurring in 20-30% (9), and are the leading causes of death within the first 30 days posttransplant (2). The two conditions are inter-related in that primary graft dysfunction is the product of multiple insults of which ischemia-reperfusion injury is a major contributor (8). The clinical spectrum can range from mild hypoxemia with few infiltrates on chest x-ray to severe respiratory distress syndrome (8, 9).

Rejection

Hyperacute rejection is rare as it represents a previous exposure to foreign tissue antigens that are generally screened for. Acute rejection, however, is more common and occurs at a rate comparable to that in adults. The majority of episodes of acute rejection occur in the first 6 months after transplant (10). Infants appear to have a much lower incidence compared to other pediatric age groups, perhaps because of their relatively immature immune systems (11).

Infection

Infection, always a concern following any transplantation, is of greater risk in the lung transplant recipient. Not only is there direct contact of the graft with the external environment, but there is also donor colonization of the airways and a diminished ability to cough due to vagal denervation and potential phrenic nerve injury. Of all age groups, infants are particularly susceptible to severe and fatal viral infections.

Surgical complications

Anastomotic complications, although rare, can involve bronchial dehiscence or pulmonary vascular stenosis. Bronchial stenosis occurs in approximately 10%, and can be treated effectively with serial dilation or angioplasty (10). Issues with the vascular anastomoses can be studied with perfusion lung scans or cardiac catheterization, often performed within the first 24 hours of transplant as a screening tool.

Late phase complications

Issues plaguing the late phases following transplantation include bronchiolitis obliterans (OB), malignancy, and immunosuppressant-related side effects.

Bronchiolitis obliterans

OB is a histiologic diagnosis with a clinical surrogate of decreased forced expiratory volume in 1 second (FEV_1). It is a major cause of death and the

need for retransplantation in those who survive 1 year following transplantation, and occurs in nearly 50% of long-term survivors (12).

Malignancy

The overall incidence of malignancy is 5-10%, and is mainly attributable to post-transplant lymphoproliferative disease (PTLD) (10). Primary Epstein-Barr virus (EBV) is a risk factor for PTLD (13). Children may be more susceptible to this complication because they are often seronegative for EBV at the time of transplantation, and can thus acquire a primary EBV infection thereafter.

Immunosuppresant-related side effects

Some of the most common causes of morbidity following pediatric lung transplantation are related to immunosuppressive therapy. Most patients are on a regimen of triple immunosuppression entailing an antimetabolite (azathioprine or mycophenolate mofetil), a calcineurin inhibitor (cyclosporine or tacrolimus), and systemic steroids as maintenance (8). Side effects that are particularly relevant to the anesthesiologist can include hypertension, diabetes, renal dysfunction, and seizures. Within 1 year, the prevalence of hypertension is 42%, renal dysfunction 10%, diabetes 21%, and hyperlipidemia 5% (2). At 5 years, the prevalence increases to 69%, 30%, 31%, and 18%, respectively (2).

What is the survival following transplantation?

Survival has increased over the years due to advances in surgical technique, immunosuppressive regimens, patient selection, and post-transplant care. However, as noted in a recent review of the preceding 2 decades of pediatric lung transplantation, the improved survival is attributable only to an increased 1-year survival (3). Beyond the first year, survival has remained unchanged, and remains low compared to heart and other solid organ transplantations.

The 5-year survival of pediatric lung transplant recipients between January 1990 and June 2014 was 51%, a number comparable to that observed in the adult population during the same period of time (2). Among the different ages of pediatric patients, no significant difference in survival was noted in pair-wise comparisons (3). Survival in the first year post-transplant, however, was lowest in infants, perhaps reflecting the effects of infection on their naïve and suppressed immune systems. Beyond one year, infant survival was comparable to that of other age groups.

The functional status of pediatric lung transplant recipients has been reported to be very good. 86% of those surviving 5 years after transplantation have no activity limitations (2).

What are the major causes of death?

The leading causes of death following pediatric lung transplantation include graft failure, infection, and bronchiolitis obliterans (2) (Table 7). In the first year after transplantation, infection and graft failure account for the majority of deaths, whereas bronchiolitis obliterans is the major cause after the first year. Malignancy and multi-organ system failure are also significant contributors.

Risk factors for increased early and overall mortality **include** preoperative chronic steroid use, pre-transplant ventilatory dependence, and re-transplantation.

An update on our patient

Our patient's postoperative recovery was initially hindered by infectious pulmonary complications, including a CMV pneumonitis and bacterial pneumonia. She was able to overcome these issues, though, and was weaned off the ventilator. Her tracheostomy was decannulated shortly thereafter and she was subsequently discharged home, approximately 3 months after transplantation.

Conclusion

Pediatric lung transplantation has become an accepted therapy for selected patients with otherwise untreatable pulmonary parenchymal or vascular disease, and represents a growing field in medicine. Unique challenges include the limited availability of suitable donor organs, the prevalence of bronchiolitis obliterans, infection, and graft failure following transplantation, and the related effort to maximize survival, growth, and quality of life in these patients.

Anesthesiologists can contribute greatly to the care of these patients in their intraoperative management during the transplantation itself or in the post-transplant period when the patient returns for biopsies, bronchoscopies, or procedures otherwise common to the pediatric population. Care during the transplantation should focus on careful ventilation, oxygenation, and fluid management to optimize graft function. Post-transplant anesthetics, beyond an

assessment of graft function, should direct attention to the immunosuppressant-induced and primary disease-related comorbidities present.

Acknowledgment

None

Conflicts of Interest

The authors declare that there are no conflicts of interest.

References

1. Grossman RF, Frost A, Zamel N, et al. Results of single-lung transplantation for bilateral pulmonary fibrosis. N Engl J Med. 1990;322:727-33.
2. Goldfarb SB, Levvey BJ et al. The Registry of the International Society for Heart and Lung Transplantation: Nineteenth Pediatric Lung and Heart-Lung Transplantation Report—2016. J Heart and Lung Transplant. 2016;1196-205.
3. Zafar F, Heinle JS, Schecter MG, et al. Two decades of pediatric lung transplant in the United States: Have we improved? J Thorac Cardiovasc Surg. 2011;141:828-32.
4. Huddleston CB, Sweet SC, Mallory GB, et al. Lung transplant in very young infants. J Thorac Cardiovasc Surg. 1999;118:796–804.
5. Meneloff EN, Huddleston CB, Mallory GB, et al. Pediatric and adult lung transplantation for cystic fibrosis. J Thorac Cardiovasc Surg. 1998;115:404–13.
6. Williams GD, Ramamoorthy C. Anesthesia Considerations for Pediatric Thoracic Solid Organ Transplant. Anesthesiology Clin N Am. 2005;23:709-31.
7. Patterson GA. Bilateral lung transplantation: indications and techniques. Semin Thorac Cardiovasc Surg. 1992;4(2):95-100.
8. Solomon M, Grasemann H, Keshavjee S. Pediatric Lung Transplantation. Pediatr Clin N Am. 2010;57:375-91.
9. King RC, Binns OAR, Rodriguz F, et al.: Reperfusion injury significantly impacts clinical outcome after pulmonary transplantation. Ann Thorac Surg. 2000;69:1681–5.
10. Huddleston CB. Pediatric Lung Transplantation. Current Treatment Options in Cardiovascular Medicine. 2011;13:68-78.
11. Huddleston CB, Sweet SC, Cohen AH, Mendeloff EN, Mallory GB: Bronchiolitis obliterans after pediatric lung transplantation. J Heart Lung Transplant. 1998;17:65.
12. Sundaresan S, Trulock EP, Mohanakumar T, Cooper JD, Patterson GA: Prevalence and outcome of bronchiolitis syndrome after lung transplantation. Ann Thorac Surg. 1995;60:1341–6.
13. Walker RC, Paya CV, Marshall WF, et al.: Pretrans- plantation sero-negative Epstein–Barr virus status is the primary risk factor for post-transplantation lymphoproliferative disease in adult heart, lung and other solid organ transplantation. J Heart Lung Transplant. 1995;14:214–21.
14 Sweet SC. Pediatric Lung Transplantation. Proc Am Thorac Soc. 2009;6:122-7.