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Anesthesia for lung transplantation in children under 12 years of age: a single center experience of China

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Abstract

Purpose This study aims to provide a comprehensive overview of anesthesia management strategies employed in pediatric lung transplantation.

Methods A retrospective analysis was conducted on data from 14 pediatric patients who underwent lung transplantation at the Wuxi Center between September 2019 and November 2022. Patient demographics, surgical particulars, airway management, utilization of extracorporeal support, fluid administration, blood gas and electrolyte profiles, and postoperative outcomes were systematically documented and subsequently summarized.

Results Of the 14 patients, 7 received extracorporeal membrane oxygenation (ECMO) and 1 received cardiopulmonary bypass (CPB). The average operation time was 303 ± 53 min, with the median extubation time of 26 h. The entirety of pediatric lung transplant procedures was executed successfully, resulting in the discharge of thirteen patients postoperatively. Regrettably, one patient died due to infectious shock on the fourth postoperative day.

Conclusion The achievement of successful pediatric lung transplantation necessitates effective perioperative anesthesia management, with a focal emphasis on circulatory control. Real-time measurements serve as the cornerstone for decision-making. Proactive administration of vasoactive agents is integral to sustaining hemodynamic stability. The judicious assessment of ECMO necessity is paramount, favoring central ECMO during the surgical intervention.

Keywords Pediatric, Anesthesia management, Lung transplantation

1 Introduction

In terms of irreversible, progressive lung parenchymal or vascular disease, pediatric lung transplantation has emerged as a life-saving option. However, advances in this field remains limited due to the difficulty in finding matching donors, technical barriers related to surgery, and high perioperative complications. Pediatric lung transplants account for only 2.19% of all lung transplants [1–4]. In China, the implementation of pediatric lung transplantation has only just begun. Although many lung transplantation centers in China are increasingly performing pediatric lung transplantation, the total number of cases remains relatively small to date. For anesthesiologists responsible for the management of these rare cases, it is critical to understand the indications for transplantation, the related pathophysiology, and the physiology of

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the transplanted lung, particularly in younger children, who present a greater challenge in terms of anesthesia management.

The Affiliated Wuxi People's Hospital of Nanjing Medical University stands as a modern, Grade III Class A-rated comprehensive hospital, seamlessly integrating medical care, teaching, scientific research, and rehabilitation. Boasting a capacious infrastructure comprising over 2,000 beds and a dedicated workforce of nearly 3,000 personnel, the hospital maintains a robust annual surgical volume, exceeding 50,000 procedures. As reported by Yue et al. [5], Wuxi People's Hospital, as the largest lung transplantation center in China, had successfully performed 10 cases of pediatric lung transplantation from 2007 to 2019, with the youngest case being 11 years old. From 2019 to 2022, our center has carried out 14 lung transplants for children under the age of 12, the youngest of whom is only 2 years old.

The aim of this study was to describe our experiences at WuXi center related to anesthesia for pediatric lung transplantation in children under 12 years of age.

2 Patients and methods

A retrospective analysis of the medical records of patients who underwent lung transplantation at WuXi center was performed for the period from September 2019 to November 2022. This study referred to STROBE guidelines [6]. The Ethics Committee of Wuxi People's Hospital approved this study (approval no. 2023-KY23167, given on 1 December 2023) and waived the need for additional consent from individual patients due to the retrospective nature of the study.

Fourteen pediatric patients underwent double lung transplantation under general anesthesia. The surgical incisions were all clam incisions. After surgery, all the patients were admitted to the intensive care unit (ICU) with a single lumen endotracheal tube. We recorded the preoperative basic information, intraoperative and postoperative vital signs, intraoperative blood loss and fluid replacement volume, operation time, ICU stay time, survival rate up to the time of writing. Descriptive statistics were used to report the data.

3 Results

From September 2019 to November 2022, fourteen children under 12 years old have undergone bilateral sequential lung transplantation at our institution. The recipient distribution by age and diagnosis is depicted in Table 1, where ten children were diagnosed bronchiolitis obliterans syndrome (BOS), two with cystic pulmonary fibrosis (CF), one with idiopathic pulmonary arterial hypertension (IPAH) and another one with idiopathic pulmonary fibrosis (IPF). To date, the pediatric transplant patient with longest survival has undergone surgery 3 years ago when he was eight years old and the youngest patient at 2 years old (Figs. 1 and 2).

The external support and airway management of the pediatric patients are shown in Table 2. We chose the appropriate intubation mode and extracorporeal membrane oxygenation (ECMO) assistance according to patients' own condition (Fig. 3). The veno-venous extracorporeal membrane oxygenation (V-V ECMO) was

Table 1 General characteristics of pediatric patients

Case	Sex	Age (y)	Height (cm)	Weight (kg)	BMI (kg/m^2)	Diagnosis	discharge
1	F	8	110	18	14.9	BOS	Y
2	M	7	131	31	18.1	BOS	Y
3	M	2	88	12	15.5	BOS	Y
4	F	10	130	22	13.0	CF	Y
5	F	5	91	12	14.5	BOS	Y
6	F	4	84	10	14.2	BOS	Y
7	M	4	99	12	12.2	IPAH	Y
8	F	9	136	24	13.0	CF	Y
9	F	8	140	36	18.4	BOS	N
10	F	8	135	35	19.2	BOS	Y
11	M	10	130	15	8.9	IPF	Y
12	M	8	110	22	18.2	BOS	Y
13	M	11	147	25	11.6	BOS	Y
14	F	12	124	14	9.1	BOS	Y

BOS bronchiolitis obliterans syndrome, *CF* cystic pulmonary fibrosis, *IPAH* idiopathic pulmonary arterial hypertension, *IPF* idiopathic pulmonary fibrosis, *M* male, *F* female, *BMI* body mass index

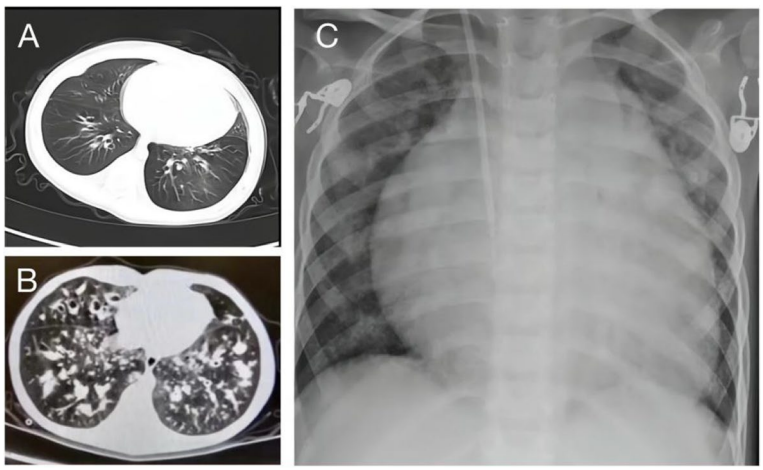

Fig. 1 Radiogical examinations of different pulmonary etiopathogensis. **A** A computerized tomography (CT) examination image of a child diagnosed with bronchiolitis obliterans syndrome (BOS); **B** A CT examination image of a cystic pulmonary fibrosis (CF) child; **C** A chest radiograph of a child patient with idiopathic pulmonary arterial hypertension (IPAH) which led to cardiac dilatation was taken before surgery

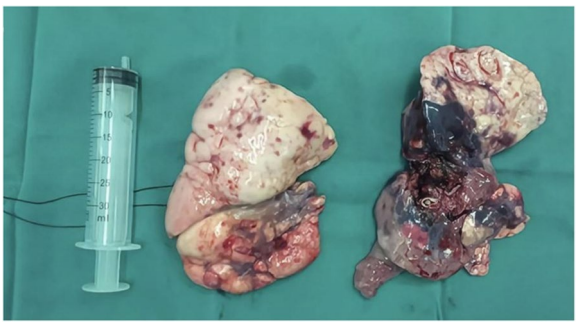

Fig.2 Resected specimens of diseased lung of BOS

applied in three patients to bridge for lung transplantation before surgery, and continued during and after surgery; Three patients adopted central veno-arterial extracorporeal membrane oxygenation (C-VA ECMO) during surgery and were withdrawn after surgery; One patient used cardiopulmonary bypass (CPB) during the operation. One patient underwent endotracheal intubation preoperatively, whereas another patient presented in a preoperative tracheostomy state. In ten patients, double-lumen bronchial intubation was adopted during the operation, with the remaining four younger patients

Table 2 Mechanical support and airway management strategies

Case	Mechanical support			Airway management		
	Preoperative	Interoperative	Postoperative	Preoperative	Interoperative	Postoperative
1	N	N	N	N	DLT	ETT
2	V-V ECMO	V-V ECMO	V-V ECMO	ETT	DLT	ETT
3	V-V ECMO	V-V ECMO	V-V ECMO	tracheotomy	ETT	tracheotomy
4	N	N	N	N	DLT	ETT
5	N	C-VA-ECMO	N	N	ETT	ETT
6	N	N	N	N	ETT	ETT
7	N	N	N	N	ETT	ETT
8	N	CPB	N	N	DLT	ETT
9	N	N	N	N	DLT	ETT
10	N	C-VA-ECMO	N	N	DLT	ETT
11	N	N	N	N	DLT	ETT
12	N	C-VA-ECMO	N	N	DLT	ETT
13	V-V ECMO	V-V ECMO	N	N	DLT	ETT
14	V-V ECMO	V-V ECMO	N	tracheotomy	DLT	tracheotomy

V-V ECMO veno-venous extracorporeal membrane oxygenation, *C-VA-ECMO* central veno-arterial extracorporeal membrane oxygenation, *CPB* cardiopulmonary bypass, *DLT* double-lumen tube, *ETT* tracheal catheter

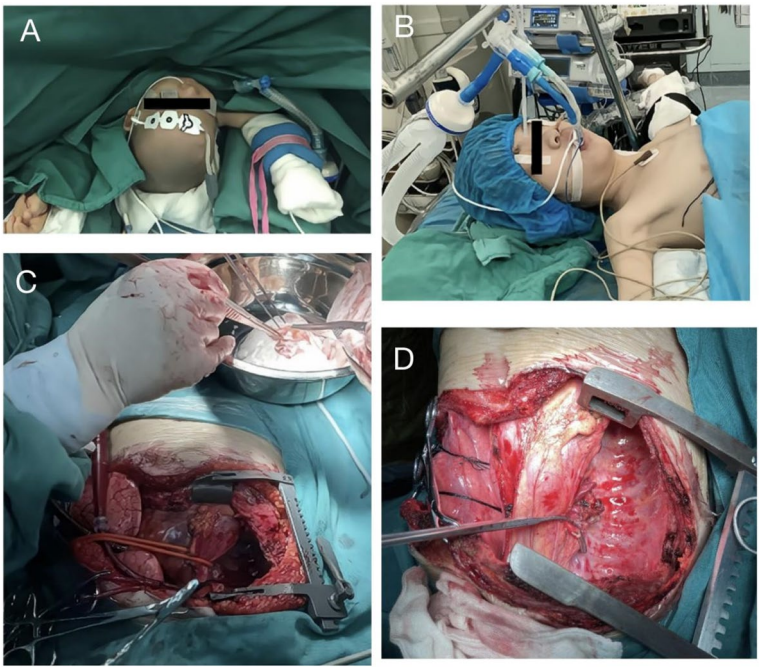

Fig.3 Selection of endotracheal catheter and different extracorporeal membrane oxygenation (ECMO) configurations. **A** A two-year-old child was intubated with a single-lumen tracheal catheter (ETT); **B** A senior child was intubated with a DLT (double-lumen tube); **C** Central veno-arterial extracorporeal membrane oxygenation (C-VA-ECMO) was appiled to the child intraoperatively; **D** No employment of ECMO

Table 3 Operative data and outcomes

Operation duration (min)	Cold ischemia time (min) Mean ± SD		Extubation time (h) Median (IQR)	ICU stay (d) median (IQR)	Survival (n)
	Left	Right			
303 ± 53	435 ± 91	426 ± 86	26 (19–187)	4 (4–6)	13

SD standard deviation, *IQR* interquartile range, *ICU* intensive care unit

(under 5 years old) inserted unilaterally by single-lumen tracheal intubation to achieve single-lung ventilation.

The average operation time was 303 ± 53 min, with the median extubation time of 26 h. Median post-operative ICU stay duration was 4 days (Table 3). The average cold ischemia time for the left lung was 435 ± 91 min and for the right lung was 426 ± 86 min.

Thirteen out of the 14 patients under consideration were successfully discharged, reflecting positive outcomes in the majority of cases. Unfortunately, one patient diagnosed with BOS did not survive, succumbing on the fourth day post-surgery. Notably, the surgical procedure involved the utilization of C-VA-ECMO, which was effectively removed after completion. Throughout the perioperative period, prophylactic antibiotics were systematically administered. Upon initial postoperative assessment on the first day, the patient exhibited stable vital signs, characterized by a P/F (PaO2/FiO2) of 437 mmHg and a lactate level of 3.3 mmol/L. Subsequent evaluations on the second day indicated improvement, with a P/F of 467 mmHg, a lactate level of 2.9 mmol/L, and a white blood cell count of 9.27×10^9. However, a concerning development emerged on the third day when the patient presented with a temperature of 39.4 °C. This was accompanied by a notable decline in the P/F to 107 mmHg and a reduction in the white blood cell count to 0.72×10^9. Despite the implementation of aggressive antimicrobial interventions, the infectious shock escalated on the fourth day, coinciding with diminished urine output. High-dose vasopressors were administered in an attempt to stabilize vital signs; however, these proved ineffective, ultimately leading to the regrettable pronouncement of the patient's demise.

As shown in Table 4, anesthetic induction was conducted with propofol in all cases and accompanied by midazolam in 78.6% of the cases. Maintenance of anesthesia was achieved with sevoflurane in all cases. Opioid agent used at the induction was sufentanil (92.9%) and fentanyl (21.4%), then maintained by sufentanil (100%) and remifentanil (85.7%). Cisatracurium was the most commonly used muscle relaxant (85.7%).

To maintain hemodynamic stability, the most commonly used vasoactive drug was norepinephrine (85.7%), followed by epinephrine (50.0%), dopamine (28.6%),

Table 4 Anesthetic agents and vasoactive mediations

	Numbers of patients
Induction drug	
Propofol	14 (100.0%)
Midazolam	11 (78.6%)
Analgesia drug	
Fentanyl	3 (21.4%)
Sufentanil	13(92.9%)
Remifentanil	12 (85.7%)
Muscle relaxation drug	
Cisatracurium	12 (85.7%)
Rocuronium	2 (14.3%)
Inhalational anesthetic	
Sevoflurane	14(100.0%)
Vasoactive drugs	
Epinephrine	7 (50.0%)
Norepinephrine	12 (85.7%)
Dopamine	4 (28.6%)
Dobutamine	2 (14.3%)
Cedilanid	3 (21.4%)
Nitroglycerin	2 (14.3%)

Table 5 Hemodynamic monitoring

Hemodynamic Monitoring	Numbers of patients
Standard hemodynamic monitoring	
Electrocardiography	14 (100.0%)
Invasive blood pressure	14 (100.0%)
Central venous pressure	14 (100.0%)
Pulse oximetry	14 (100.0%)
Depth of anaesthesia	14 (100.0%)
Body temperature	14 (100.0%)
Advanced hemodynamic monitoring	
PiCCO	8 (57.1%)
Vigilance	3 (21.4%)
EV1000	11 (78.6%)
Direct pulmonary arterial pressure	14 (100.0%)

PiCCO Pulse index continuous cardiac output, Vigilance: Edwards continuous cardiac output monitor, EV1000: Edwards Clinical Monitor

cedilanid (21.4%), and dobutamine (14.3%). Nitroglycerin was used in two patients (14.3%).

The standard and advanced hemodynamic monitoring devices used intraoperatively are shown in Table 5. During the operation, the heart rate, invasive blood pressure, and central venous pressure of the patients were continuously monitored, preoperatively, after occlusion of the first pulmonary artery (interoperative1) as well as after that of the second pulmonary artery (interoperative2), and on the 1st, 2nd, and 3rd days after the operation, and the values were recorded. In addition, the patients' basal pulmonary artery pressure (PAP) was measured after surgical pulmonary artery exposure was initiated, and again after occlusion of the first pulmonary artery. The intraoperative hemodynamic indexes of the children are listed in Table 6.

The median volume of blood loss during the operation was 30.5 ml/kg. The median urine volume was 27.3 ml/kg. The median intraoperative infusion volume involved 26.3 ml/kg of crystalloid, 1.19 g/kg of albumin, 20.3 ml/kg of red blood cells, and 22.2 ml/kg of plasma (Table 7).

The blood gas and electrolytes of the children during surgery and within 3 days after surgery are shown in Table 8. The pH value gradually returns to normal during and after the operation, with the acidosis corrected. P/F was also improved to some extent compared with that in preoperative stage. The partial pressure of carbon dioxide decreased significantly during and after surgery, where the lactate level gradually increased.

4 Discussion

While relatively mature norms and expert consensus on the peri-anesthesia management of adult lung transplantation have been established, similar guidelines do not exist for management of pediatric patients, particularly those younger than 12 years old. We attempted to provide some clinical reference for the anesthesia management of lung transplantation in young children through this retrospective analysis and summary of our experience of 14 such cases.

The primary diseases of children with lung transplantation differ from those of adults. In adults, the most common causes of lung transplantation are interstitial lung disease and chronic obstructive pulmonary disease, while in children under 10, the causes are most typically cystic fibrosis and pulmonary hypertension [7, 8]. In 2020, primary pulmonary arterial hypertension for the first time surpassed cystic fibrosis as the main indication for pediatric lung transplantation in the United States. In addition, there has also been an increase in the number of pediatric cases of interstitial lung disease, including surfactant protein deficiencies and disorders, bronchiolitis obliterans, lymphoid interstitial pneumonia, and idiopathic pulmonary fibrosis [9]. In this study, the most common primary disease among 14 children is BOS. The unique physiology, anatomical features, and differences in primary diseases in children indicate that the anesthetic management of lung transplantation in children should be different from adults.

4.1 Preoperative assessment

In the management of pediatric patients grappling with chronic end-stage lung disease, the consideration of

Table 6 Hemodynamic management

	Preoperative Median (IQR)	Interoperative1 Median (IQR)	Interoperative2 Median (IQR)	Postoperative Median (IQR)	Postoperative–1st day Median (IQR)	Postoperative–2nd day Median (IQR)	Postoperative–3rd day Median (IQR)
HR (beats/min)	115 (94–140)	108 (94–123)	123 (110–128)	117 (97–130)	121 (100–130)	107 (95–115)	100 (90–114)
MAP (mmHg)	77 (62–97)	67 (55–74)	76 (62–87)	86 (68–94)	90 (74–99)	87 (82–96)	82 (77–90)
PAP (mmHg)	36 (27–45)	45 (31–50)	33 (20–52)	22 (20–36)	–	–	–
CVP (cmH_2O)	16 (13–20)	16 (13–23)	17 (14–21)	7 (6–8)	–	–	–

Interoperative1, after occlusion of the first pulmonary artery; Interoperative2, after occlusion of the second pulmonary artery

HR heart rate, *MAP* mean arterial pressure, *PAP* pulmonary artery pressure, *CVP* central venous pressure

Table 7 Fluid management

Crystalloid (ml/kg) Median (IQR)	Albumin (ml/kg) Median(IQR)	RBC (ml/kg) Median (IQR)	Plasma (ml/kg) Median (IQR)	Urine (ml/kg) Median (IQR)	Bleeding (ml/kg) Median (IQR)	Drainage (ml/kg) Median (IQR)
26.3 (20.8–34.2)	1.19 (0.69–2)	20.3 (16.6–27.3)	22.2 (17.3–25.1)	27.3 (20.5–45.5)	30.5 (24.2–36.4)	8.1 (6.7–13.7)

RBC red blood cells

Table 8 Blood gas and electrolyte management

	Preoperative Median (IQR)	Interoperative1 Median (IQR)	Interoperative2 Median (IQR)	Postoperative Median (IQR)	Postoperative-1st day Median (IQR)	Postoperative-2nd day Median (IQR)	Postoperative-3rd day Median (IQR)
PH	7.19 (7.14–7.35)	7.16 (7.05–7.46)	7.35 (7.23–7.48)	7.41 (7.27–7.49)	7.44 (7.38–7.51)	7.45 (7.40–7.54)	7.43 (7.39–7.46)
P/F (mmHg)	210 (123–307)	143 (77–374)	363 (210–456)	324 (200–484)	330 (258–431)	375 (204–442)	297 (238–426)
$PaCO_2$ b(mmHg)	64 (49–79)	73 (31–92)	50 (39–54)	46 (36–65)	41 (30–47)	39 (36–46)	45 (37–57)
BE	1.3 (-3.9–9.1)	3.8 (0.2–8.3)	5 (2.0–8.3)	4.4 (2.2–6.2)	3.6 (1.1–5.0)	4.3 (-0.2–6.8)	3.4 (-3.2–8.9)
K^+ (mmol/L)	3.8 (3.3–4.2)	4.2 (3.7–4.6)	4.1 (3.2–4.6)	3.6 (3.4–3.7)	3.7 (3.2–4.2)	3.5 (3.1–4.4)	3.8 (3.6–4.5)
Hb (g/L)	106 (89–114)	95 (83–109)	99 (73–107)	95 (86–101)	109 (88–127)	87 (83–112)	90 (80–93)
Lac (mmol/L)	0.7 (0.3–2.3)	0.6 (0.3–1.3)	2.1 (0.7–2.6)	1.6 (1.3–3.2)	4.0 (1.6–5.1)	2.5 (1.0–3.3)	2.0 (1.8–3.2)
Glu (mmol/L)	6.0 (4.9–6.5)	6.9 (6.1–8.3)	9.7 (7.2–11.1)	8.9 (7.0–10.5)	6.5 (6.1–7.2)	6.1 (5.2–8.5)	6.3 (4.2–8.1)

Interoperative1, after occlusion of the first pulmonary artery, Interoperative2, after occlusion of the second pulmonary artery

PH potential of hydrogen, *P/F PaO2/FiO2*, *PaCO2* arterial partial pressure of carbon dioxide, *BE* base excess, *Hb* hemoglobin, *Lac* lactic acid, *Glu* glucose

lung transplantation becomes imperative. This should be done when despite receiving optimal and judicious therapeutic interventions, there persists a relentless progression of declining lung function, coupled with a discernible absence of viable medical or surgical alternatives. It is crucial to recognize that certain conditions, such as irreparable dysfunction of vital organs like the heart, liver, and kidneys, as well as an unstable physiological status encompassing instances of sepsis, acute myocardial infarction, and acute liver failure, stand as contraindications for the pursuit of lung transplantation.

Comprehensive preoperative assessment can effectively reduce the risk of anesthesia. As the various physiological functions in children are not yet as fully developed as those in adults, and as they generally exhibit more severe systemic conditions if they develop end-stage lung disease, a careful preoperative evaluation is particularly critical in the management of pediatric lung transplantation.

Preoperative evaluation in children is similar to that in adults. Airway evaluation should be considered a top priority. The anatomy of the pediatric airway has some particular features. The pediatric airway anatomy is highly variable, with the diameter of the left bronchial opening being smaller than that of the right. Thus, intubation fitting the right bronchus may not fit the left bronchus. The opening of the right upper lobe, through which the right bronchial cannula is more likely to pass, is generally less than 1 cm from the carina. In addition, concomitant

diseases also have a greater impact on the airway of children. BOS is characterized by inflammation and fibrosis of the terminal and respiratory bronchioles leading to narrowing and/or complete obliteration of the airway lumen following an injury to the lower respiratory tract [10]. Pediatric patients with BOS present with obstructive pulmonary ventilation disorder, which is generally accompanied by repeated infections, bronchial mucosal congestion and edema, and blockage by inflammatory substances. Pediatric patients with cystic fibrosis have severe infections. In their lungs, mucous plugging from dehydrated thick secretions results in inflammation, chronic infection, progressive small airways obstruction and the development of bronchiectasis, which leads to decreased ability to clear secretions, causing increased rates of infections [11]. IPF is a chronic interstitial lung disease characterized by fibrosis, inflammation, and destruction of lung architecture. Such patients' pulmonary function testing shows a restrictive pattern measured as reduced forced vital capacity, reduced forced expiratory volume in 1 second, and reduced efficiency of lung gas transfer estimated with measurement of the diffusion capacity of carbon monoxide [12]. Thus, the airway anatomy and pulmonary function should be fully examined. which requires computed tomography (CT) images or CT 3D reconstruction technology if necessary, in order to measure the length and inner diameter of the child's trachea, the inner diameter of the left and right bronchus, and the distance from the carina to the left upper lung opening, to obtain comprehensive insight into the child's anatomy. This facilitates evaluation of difficult ventilation/intubation and allows adequate preparation.

Preoperative evaluation of pediatric patients with pulmonary hypertension requires particular attention. Accurate preoperative assessment of PAP in children is rather difficult, and the application of direct right ventricular catheterization or echocardiography to estimate PAP in children is insufficient, as their New York Heart Association cardiac function status is typically also poor, with the possibility of developing right ventricular failure at various stages of the perioperative period. Planned prophylactic ECMO is increasingly employed as a management strategy to minimize cardiopulmonary decompensation during anesthesia and to attenuate the risk of primary graft dysfunction in high-risk pulmonary hypertension patients [13].

4.2 Intraoperative management

4.2.1 Monitoring

Similar to adult lung transplantation (LTx), developing monitoring methods for pediatric LTx patients is essential, including basic cardio-respiratory and metabolic monitoring (electrocardiogram, SpO_2, end-tidal carbon dioxide, temperature, invasive arterial blood pressure, and central venous pressure). Additional data on cardiac output, stroke volume variation, pulse pressure variation, pulse contour cardiac index, and systemic vascular resistance index are also helpful. As some hemodynamic monitoring techniques, such as vigilance, EV1000 and pulse index continuous cardiac output may produce largely biased monitoring hemodynamic results [14, 15], they are not suggested in younger children (less than 6 years old) theoretically. In the process of utilizing these devices, we primarily observe the dynamic trends of various measurement indicators rather than their absolute values. Thus, some directly measured data, such as mean arterial pressure (MAP), heart rate (HR) and central venous pressure (CVP), should be the focus in hemodynamic monitoring during pediatric lung transplantation. Owing to the limitation of the equipment, the Swan-Ganz catheter cannot be applied in pediatric lung transplantation. Instead, PAP was measured by puncturing the pulmonary artery with a 24-G indwelling needle directly after thoracotomy.

4.2.2 Realization of single-lung ventilation and protective pulmonary ventilation strategies.

In lung transplantation anesthesia, the double-lumen bronchial intubation is routinely used to achieve one-lung ventilation, which has the advantages of easy positioning and good lung isolation. However, the smallest double-lumen tube available in China is 26F and is only suitable for children over 8 years old. Children with end-stage lung disease generally also have stunted growth and a small body size, creating a challenge for the management of intraoperative one-lung ventilation. For younger children, the commonly used single-lung ventilation techniques include the use of single-lumen bronchial intubation and bronchial occluders. In our clinical experience, we have observed that an anatomical short distance from the tracheal prominence to the anastomosis in pediatric patients. This unique anatomical consideration has led us to encounter challenges with the use of bronchial occluders, as their cuffs may interfere with the bronchial anastomosis procedure, posing difficulties in suctioning secretions.To address these challenges, we predominantly opt for the single-lumen bronchial intubation technique. Careful attention is given to the positioning of the single-lumen tube to mitigate the risk of excessive length that could impede the surgical procedure. As a preventive measure, we insert only half of the single-lumen tube cuff into the bronchus, positioning the remaining half above the tracheal prominence. This modification ensures optimal placement and facilitates a smoother surgical process for pediatric patients undergoing lung transplantation (Fig .4). The positioning of the

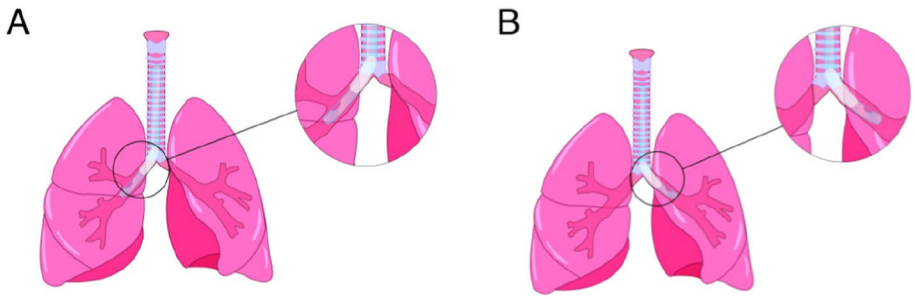

Fig.4 Position of the endotracheal for left and right mainstem endobronchial intubation. **A** Left mainstem endobronchial intubation; **B** Right mainstem endobronchial intubation

endotracheal tube is another challenge. Fiberoptic bronchoscopic guidance is limited by the diameter of the tracheal tube. The fiberoptic bronchoscope we currently use is 2.8 mm in diameter, which is difficult to pass through a tracheal tube with an inner diameter of less than 4 mm. For these patients, manually controlled breathing resistance combined with auscultation positioning is a better approach, which depends on the operator's clinical experience and proficiency. In addition, the position of the endotracheal tube can be adjusted under direct vision from the surgeon after opening the chest.

Achieving the balance between adequate gas exchange and minimizing damage to the pulmonary system in children is difficult, particularly when the pulmonary artery is opened, which causes pulmonary circulation pressure to drop rapidly, coupled with ischemia–reperfusion injury, which predisposes to pulmonary edema. We adopted a small tidal volume (3–4 ml/kg), low inspired oxygen concentration ($FiO_2 \leq 0.5$), and positive end-expiratory pressure (8–10 mmHg) mechanical ventilation to minimize lung damage. This approach also partially avoids the incidence of postoperative primary graft dysfunction.

4.2.3 Hemodynamic management

In pediatric lung transplantation, our goals for managing hemodynamics are to achieve adequate perfusion, maintain vascular resistance, and minimize PAP.

Severe hemodynamic fluctuations are likely to occur during anesthesia induction. During this process, we must administer anesthetics slowly and incrementally and apply vasoactive drugs appropriately with the goal of maintaining hemodynamic stability. For children with pulmonary hypertension, one should be on high alert for the occurrence of hypotension.

The primary goal of anesthesia maintenance is to ensure the stability of hemodynamics. In the context of pediatric patients, where cardiac output is predominantly reliant on heart rate. Maintaining a fast heart rate is beneficial to withstand the influence of surgical procedures such as pulmonary artery occlusion and left atrial clamp. So, a deliberate effort is made to sustain a relatively elevated heart rate throughout the procedure. This becomes especially pertinent during left lung transplantation, where heightened vigilance is warranted due to the potential risk of bradycardia and hypotension induced by surgical manipulations and traction. Proactive measures are implemented to mitigate these risks and uphold hemodynamic equilibrium during critical phases of the procedure.

Special attention should be paid when the pulmonary artery is clamped. Normally, PAP and pulmonary ventilation resistance increase sharply once the pulmonary artery is clamped, leading to a significant elevation of right ventricular afterload and a decrease in left ventricular preload, resulting in a marked reduction in cardiac output. At this point, non-operative lung blood flow increases, and the ventilation/perfusion mismatch is alleviated, leading to some improvement in oxygenation. However, when the pulmonary circulation pressure of the patient reaches or exceeds systemic circulation pressure, blood shunting from the right to the left occurs through intracardiac or extracardiac abnormal pathways, causing a significant decrease in PaO_2. A prolonged trial occlusion time is required before pulmonary artery occlusion. The surgical team initiates the occlusion of the pulmonary artery in a gradual and incremental manner. Throughout this process, vigilant monitoring ensues, focusing on the escalation of PAP, the decline in MAP, and comprehensive assessments of the child's oxygen saturation and overall physiological condition. This observation persists until the complete occlusion of the pulmonary artery is achieved, at which point a designated period of scrutiny is undertaken. Should the patient manifest signs of hemodynamic instability or a noteworthy reduction in peripheral oxygen saturation (SpO_2), prompt measures are taken to

reopen the pulmonary artery, ensuring the swift resolution of any adverse physiological responses.

Pre-administration of vasoactive drugs before occlusion can reduce the incidence of cardiovascular injuries. The preferred vasoactive drug in our institution is norepinephrine, followed by epinephrine, and for patients with poor heart function, inotropic agents are also administered.

4.2.4 Fluid management

The general principle of fluid management is to restrict the infusion based on blood pressure and CVP while maintaining hemoglobin above 100 g/L [16].

Excessive fluid infusion has the potential to induce lung injury and increase the susceptibility to primary graft dysfunction (PGD) [17]. Conversely, inadequate volume may result in insufficient perfusion of organs and tissues. The dynamic nature of hemodynamic fluctuations during lung transplantation underscores the importance of administering an appropriate volume load to maintain a relatively stable mean arterial pressure. To achieve this, we meticulously controlled the variation range of the MAP between −15% and 15% of baseline. In the context of pediatric lung transplantation, where hemodynamic stability is paramount, the control of infusion volume and the selection of infusion types assume heightened significance. Intravenous infusion therapy predominantly comprises crystals, with a lesser amount of macromolecular colloids, primarily albumin. The determination of fluid infusion volume is guided by various indicators such as urine volume, blood loss, and insensible fluid loss. Parameters like central venous pressure, extravascular lung water, stroke volume variation, and pulse pressure variation further inform the decision-making process.

While intraoperative hemorrhage is an inevitable aspect, maintaining sufficient hemoglobin levels is crucial for ensuring optimal oxygen delivery to tissues. However, it is noteworthy that recent studies indicate that excessive blood transfusion poses an independent risk factor for the development of PGD. Consequently, a judicious approach to fluid and blood product management is imperative to mitigate the risk of complications and optimize outcomes in pediatric lung transplantation patients.

A study of lung transplants in adults established that red cell transfusion exceeding 1 L is an independent risk factor for PGD, and recommended thromboelastography as a guide for transfusion [18]. Therefore, it is necessary to weigh the amount of bleeding, hemoglobin content, etc., carefully, to minimize the need for intraoperative blood products.

4.2.5 Blood gas and electrolyte management.

Intraoperative blood gas and electrolyte changes and management also demand attention. First, it is necessary to monitor acid-base status of the child during surgery, after the first pulmonary artery is blocked, after the first pulmonary artery is opened, after the second pulmonary artery is blocked, and after ventilation of the new lungs on both sides. Based on the results of blood gas analysis, the imbalance of water and electrolytes should be actively corrected, the ventilator parameters should be adjusted according to PaO_2, and it should be evaluated whether external mechanical support is required.

It is worth noting that children with cystic fibrosis are generally already accustomed to chronic hypercapnia. Their blood pH, rather than arterial carbon dioxide tension, requires more attention. For children with pulmonary hypertension, the occurrence of hypoxia, hypercapnia, and acidosis should be strictly avoided to prevent further aggravation of pulmonary vasoconstriction. Such patients can be appropriately hyperventilated during surgery to maintain arterial carbon dioxide partial pressure at 30–35 mmHg.

The level and dynamic change trend of lactate are also key points requiring attention during the perioperative period. Numerous studies have demonstrated a positive correlation of blood lactate with both short- and long-term patient morbidity and mortality [19]. In a clinical study of adult double-lung transplantation, blood lactate level was found to increase during surgery and reach a maximum after the second lung implantation, and a value below the threshold of 2.6 mmol/L at the end of surgery yielded a high negative-predictive value for the occurrence of PGD at postoperative day 3 [20]. In our 14 pediatric lung transplantation cases, a gradual increase in lactate levels was observed. Insufficient tissue perfusion caused by reduced cardiac output, tissue hypoxia caused by microcirculatory dysfunction, and the release of catecholamines and other inflammatory mediators can all lead to increased perioperative lactate levels [21]. When it is found that the level of blood lactate increases, the first step is to improve circulation and find the cause. Then, the symptoms should be treated and the effect observed. Early detection of the cause of increased lactate and corresponding treatment, and aggressive improvement of tissue perfusion may be beneficial to the prognosis of such children.

4.2.6 Use of intraoperative mechanical support

In studies on adult LTx, the application of ECMO as a bridge strategy is reportedly superior to mechanical ventilation (MV) bridging [22]. According to some recently published studies, the use of ECMO as a bridge to

pediatric LTx has become increasingly effective, reliable, and durable [23]. Patients receiving V-V ECMO may have a reduced need for sedation and paralytics compared with patients receiving MV [24]. In our study, the V-V ECMO bridging strategy was prioritized for patients with refractory hypercapnia or hypoxemia.

For children who received ECMO preoperatively, ECMO was continuously applied intraoperatively. For patients without preoperative ECMO, the indications for ECMO were evaluated intraoperatively at the following four time points, because of the bleeding and vascular complications of ECMO.

1) The cardiac function of patients were evaluated before surgery. Consider preoperative ECMO for patients with a cardiac index less than 2.0 L/min/m^2 or PAP higher than 60 mmHg. For the patients who were predicted to have respiratory failure during one-lung ventilation or patients with cardiac dysfunction, ECMO was also applied before surgery.
2) After induction, one-lung ventilation was attempted and toleration of respiratory function was assessed. If SpO_2 was < 90%, or $PaCO_2$ is higher than 20% of the preoperative level, or hemodynamic disturbance occurred, ECMO was initiated immediately.
3) When the pulmonary artery was clamped, if SpO_2 fell below 90%, hemodynamic disturbance occurred, or pulmonary pressure surpassed systemic pressure, ECMO was initiated immediately.
4) When the secondary pulmonary artery is clamped during the secondary lung implantation, the new donor-lung accommodates all cardiac output. Special attention should be paid at this point, and ECMO initiated if necessary.

The use of central ECMO during surgery is preferable for the following reasons:

1) The carotid artery in young children is thinner, creating challenges in performing the operation.
2) Either peripheral V-VECMO or peripheral veno-arterial extracorporeal membrane oxygenation may cause differential hypoxemia to varying degrees, which can be effectively prevented with central ECMO [25, 26].
3) When there is an emergency need to activate extracorporeal circulation during surgery, the transformation from central ECMO to extracorporeal circulation is more convenient.

Although some clinical studies showed that the use of CPB should be discontinued during LTx [27], we chose to use CPB during surgery for patients with severe cardio-pulmonary insufficiency to provide complete hemodynamic and oxygenation support during LTx.The use of CPB is essential in some cases, particularly in pulmonary hypertension and in hemo-dynamically unstable patients. In the Toronto Program only 44% of transplants are operated on CPB, contrast to the pediatric age group (< 18 years)in which most are executed on CPB [28, 29].

4.2.7 Postoperative management

The physiological characteristics of children, transplantation conditions, and the difficulty of intraoperative management bring challenges to postoperative management. Studies have shown that children younger than 12 years of age have no significant difference in peritransplant complications and long-term survival as compared with adolescents, while they require longer mechanical ventilation and ICU stay [30]. Individualized and refined management of children is needed after surgery to avoid the occurrence of postoperative complications, to shorten their ICU stay time, and to speed up their recovery.

4.2.8 Extubation time

Studies have demonstrated the safety of early extubation (< 24 h) after lung transplantation in children. This is associated with a shorter length of stay and decreased hospital costs and may prevent complications related to mechanical ventilation [31]. However, various factors require careful consideration before extubation, including the patient's condition, surgical and donor lung factors, and postoperative complications. For pediatric patients with stable vital signs and good transplanted lung function, early extubation can be considered. However, for patients with hemodynamic instability who require vasoactive drugs and patients with postoperative neurological complications, preoperative invasive MV, CPB/ECMO support, prolonged extubation time, and respiratory support are required. In our study, the median extubation time was 26 h, and the shortest time to extubation was 10 h after surgery in one patient, and 6 children were extubated within 24 h after surgery.

4.2.9 Pain management

Children may exhibit different pain behaviors than adults, and their ability to communicate or express their pain may be limited, especially in younger age groups. Thus, attention should be given to postoperative analgesia in this patient population. We are currently applying patient-controlled intravenous analgesia, providing opioid analgesics. The dependence on nonsteroidal anti-inflammatory drugs should be reduced to prevent damage to renal function in children. Additionally, gabapentinoids can also be considered as a choice for postoperative analgesics, which was proven

to be acceptable for certain pediatric populations [32]. A multi-modal approach to analgesia (use of intravenous analgesics, nerve blocks, thoracic epidural blocks) has been adopted in adult lung transplantation, and may also be the future direction of postoperative analgesia in pediatric lung transplantation.

4.2.10 Prevention and treatment of PGD

The main early complications after lung transplantation include PGD, hemorrhage, shock, and acute renal insufficiency. Among these complications, PGD has the highest incidence, occurring before 24 h in approximately 30% of cases and at 48–72 h in 15%–20% [33]. PGD is also the major cause of early morbidity and mortality [34]. Therefore, the focus of prevention and treatment of early complications after lung transplantation is on PGD. The known risk factors for PGD include preoperative pulmonary hypertension, massive intraoperative blood loss, massive transfusion, massive allogeneic blood transfusion, ischemia–reperfusion injury of the transplanted lung, use of intraoperative CPB. Thus, these factors should be avoided in the intraoperative management of these patients. PGD is characterized by radiographic findings of non-specific pulmonary infiltrates and hypoxaemia. Ischemic-reperfusion injury is thought to be a major contributor to the pathophysiology [35]. In 2016, an updated International Society for Heart and Lung Transplantation statement specified a 'start' time for the PGD clock beginning after the removal of the PA cross-clamp of the second lung [35]. This means that once the pulmonary artery is opened, one must closely monitor for the development of PGD. Pottecher et al. found that extravascular lung water indexed for ideal body weight, PaO_2/FiO_2 ratio, and soluble receptor for advanced glycation end products (an acute lung injury biologic marker) measured at the time of reperfusion were associated with the later development of PGD [34]. A decline in P/F levels or symptoms of pulmonary edema may be indicative of the development of PGD.

Once PGD occurs, ventilation may be adjusted to a mode that utilizes high-frequency, low tidal volume, and optimal positive end-expiratory pressure. The patient may require prolonged postoperative ventilation. In addition, a net negative fluid balance should be maintained, and inhaled nitric oxide and pulmonary vasodilators such as alprostadil may be administered. For patients with relevantly severe PGD, ECMO should be initiated immediately.

5 Conclusion

In conclusion, the lack of experience, the unique primary disease and physiological characteristics of children under the age of 12 have brought great challenges to the perioperative anesthesia management of lung transplantation. In pediatric lung transplantation, the intricacies of circulatory management often surpass those associated with respiratory considerations. Our key approach is a reliance on directly measured indicators, including HR, MAP, and CVP, for meticulous patient management. Sustaining a heart rate in the upper limit of normal for age is deemed critical, and vasoactive drugs are judiciously administered to maintain hemodynamic stability. The perioperative period demands a discerning evaluation to ascertain the necessity of employing ECMO. In instances where ECMO proves essential, our preference leans toward central ECMO during surgical interventions. While transesophageal echocardiogram stands as a valuable monitoring tool in pediatric lung transplantation anesthesia management, current equipment limitations have hindered its implementation in our practice. Additionally, acknowledging the distinctive pain management needs of pediatric patients, we advocate for a multimodal approach postoperatively to optimize care and facilitate recovery. Recognizing the evolving nature of this field, there exists a call for the continuous accumulation of experiential knowledge and collaborative efforts among interdisciplinary teams for the holistic advancement of pediatric lung transplantation.

Abbreviations

BE	Base excess
BMI	Bodi mass index
BOS	Bronchiolitis obliterans syndrome
C-VA-ECMO	Central veno-arterial extracorporeal membrane oxygenation
CF	Cystic pulmonary fibrosis
CPB	Cardiopulmonary bypass
CT	Computed tomography
CVP	Central venous pressure
DLT	Double-lumen tube
ECMO	Extracorporeal membrane oxygenation
ETT	Tracheal catheter
F	Female
Glu	Glucose
Hb	Hemoglobin
HR	Heart rate
ICU	Intensive care unit
IPAH	Idiopathic pulmonary arterial hypertension
IPF	Idiopathic pulmonary fibrosis
Lac	Lactic acid
LTx	Lung transplantation
M	Male
MAP	Mean arterial pressure
MV	Mechanical ventilation
P/F	PaO2/FiO2
$PaCO_2$	Arterial partial pressure of carbon dioxide
PAP	Pulmonary artery pressure
PGD	Primary graft dysfunction
PH	Potential of hydrogen
PiCCO	Pulse index continuous cardiac output
RBC	Red blood cells
SpO2	Peripheral oxygen saturation
V-V ECMO	Veno-venous extracorporeal membrane oxygenation

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Authors' contributions
XZ and GW conceived and designed the experiments, SY, YZ and XZ analyzed the data; SY, YZ, XZ, JC and GW analyzed and interpreted the data; XZ and GW wrote the paper. All authors contributed to the article and approved the submitted version.

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Availability of data and materials
All data related to this case report are contained within the manuscript.

Declarations

Ethics approval and consent to participate
This study has been approved by the ethics committee of Wuxi People's Hospital (2023-KY23167). Additional informed consent was waived due to the retrospective nature of the study.

Consent for publication
All authors gave their content for publication.

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The authors have no relevant financial or non-financial interests to disclose.

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References

1. Boucek MM, Edwards LB, Keck BM, Trulock EP, Taylor DO, Mohacsi PJ, et al. The registry of the international society for heart and lung transplantation: fifth official pediatric report-2001 to 2002. J Heart Lung Transplant. 2002;21(8):827–40.
2. Hertz MI, Taylor DO, Trulock EP, Boucek MM, Mohacsi PJ, Edwards LB, et al. The registry of the international society for heart and lung transplantation: nineteenth official report-2002. J Heart Lung Transplant. 2002;21(9):950–70.
3. Chambers DC, Perch M, Zuckermann A, Cherikh WS, Harhay MO, Hayes D Jr, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-eighth adult lung transplantation report - 2021; Focus on recipient characteristics. J Heart Lung Transplant. 2021;40(10):1060–72.
4. Hayes D Jr, Harhay MO, Cherikh WS, Chambers DC, Khush KK, Hsich E, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Twenty-third pediatric lung transplantation report - 2020; focus on deceased donor characteristics. J Heart Lung Transplant. 2020;39(10):1038–49.
5. Yue B, Wu B, Zhang J, Xu H, Wei D, Hu C, et al. Pediatric lung transplantation in the largest lung transplantation center of China: embarking on a long road. Sci Rep. 2020;10(1):12471.
6. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg. 2014;12(12):1495–9.
7. Chambers DC, Cherikh WS, Goldfarb SB, Hayes D Jr, Kucheryavaya AY, Toll AE, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-fifth adult lung and heart-lung transplant report-2018; Focus theme: Multiorgan Transplantation. J Heart Lung Transplant. 2018;37(10):1169–83.
8. Jhang WK, Park SJ, Le E, Yang SI, Hong SJ, Seo JH, et al. The first successful heart & lung transplant in a Korean child with humidifier disinfectant-associated interstitial lung disease. J Korean Med Sci. 2016;31(5):817–21.
9. Avdimiretz N, Benden C. The changing landscape of pediatric lung transplantation. Clin Transplant. 2022;36(4): e14634.
10. Kavaliunaite E, Aurora P. Diagnosing and managing bronchiolitis obliterans in children. Expert Rev Respir Med. 2019;13(5):481–8.
11. Dickinson KM, Collaco JM. Cystic Fibrosis. Pediatr Rev. 2021;42(2):55–67.
12. Glass DS, Grossfeld D, Renna HA, Agarwala P, Spiegler P, DeLeon J, et al. Idiopathic pulmonary fibrosis: Current and future treatment. Clin Respir J. 2022;16(2):84–96.
13. Marczin N, de Waal EEC, Hopkins PMA, Mulligan MS, Simon A, Shaw AD, et al. International consensus recommendations for anesthetic and intensive care management of lung transplantation. An EACTAIC, SCA, ISHLT, ESOT, ESTS, and AST approved document. J Heart Lung Transplant. 2021;40(11):1327–48.
14. Tribuddharat S, Sathitkarnmanee T, Ngamsaengsirisup K, Sornpirom S. Efficacy of early goal-directed therapy using FloTrac/EV1000 to improve postoperative outcomes in patients undergoing off-pump coronary artery bypass surgery: a randomized controlled trial. J Cardiothorac Surg. 2022;17(1):196.
15. Yang HL, Jung CW, Yang SM, Kim MS, Shim S, Lee KH, et al. Development and validation of an arterial pressure-based cardiac output algorithm using a convolutional neural network: Retrospective study based on prospective registry data. JMIR Med Inform. 2021;9(8):e24762.
16. Brzezinski M, Mladinov D, Neyrinck A. Anesthetic management during lung transplantation - What's new in 2021? Thorac Surg Clin. 2022;32(2):175–84.
17. Martin AK, Yalamuri SM, Wilkey BJ, Kolarczyk L, Fritz AV, Jayaraman A, et al. The impact of anesthetic management on perioperative outcomes in lung transplantation. J Cardiothorac Vasc Anesth. 2020;34(6):1669–80.
18. Diamond JM, Lee JC, Kawut SM, Shah RJ, Localio AR, Bellamy SL, et al. Clinical risk factors for primary graft dysfunction after lung transplantation. Am J Respir Crit Care Med. 2013;187(5):527–34.
19. Pino RM, Singh J. Appropriate clinical use of lactate measurements. Anesthesiology. 2021;134(4):637–44.
20. Fessler J, Vallée A, Guirimand A, Sage E, Glorion M, Roux A, et al. Blood lactate during double-lung transplantation: A predictor of grade-3 primary graft dysfunction. J Cardiothorac Vasc Anesth. 2022;36(3):794–804.
21. Attanà P, Lazzeri C, Picariello C, Dini CS, Gensini GF, Valente S. Lactate and lactate clearance in acute cardiac care patients Eur Heart J Acute Cardiovasc Care. 2012;1(2):115–21.
22. Fuehner T, Kuehn C, Hadem J, Wiesner O, Gottlieb J, Tudorache I, et al. Extracorporeal membrane oxygenation in awake patients as bridge to lung transplantation. Am J Respir Crit Care Med. 2012;185(7):763–8.
23. Olsen MC, Anderson MJ, Fehr JJ, Christensen JL, Shepard MP, Poe JB. ECMO for Pediatric Lung Transplantation. ASAIO Journal. 2017;63(6):e77–e80
24. Chiel LE, Winthrop ZA, Fynn-Thompson F, Midyat L. Extracorporeal membrane oxygenation and paracorporeal lung assist devices as a bridge to pediatric lung transplantation. Pediatr Transplant. 2022;26(5):e14289.
25. Falk L, Sallisalmi M, Lindholm JA, Lindfors M, Frenckner B, Broomé M, et al. Differential hypoxemia during venoarterial extracorporeal membrane oxygenation. Perfusion. 2019;34(1_suppl):22–9.
26. Cakici M, Gumus F, Ozcinar E, Baran C, Bermede O, Inan MB, et al. Controlled flow diversion in hybrid venoarterial-venous extracorporeal membrane oxygenation. Interact Cardiovasc Thorac Surg. 2018;26(1):112–8.
27. Ruszel N, Kiełbowski K, Piotrowska M, Kubisa M, Grodzki T, Wójcik J, et al. Central, peripheral ECMO or CPB? Comparsion between circulatory support methods used during lung transplantation. J Cardiothorac Surg. 2021;16(1):341.
28. Solomon M, Grasemann H, Keshavjee S. Pediatric lung transplantation. Pediatr Clin North Am. 2010;57(2):375–91.
29. Werner R, Benden C. Pediatric lung transplantation as standard of care. Clin Transplant. 2021;35(1):e14126.
30. Iablonskii P, Carlens J, Mueller C, Aburahma K, Niehaus A, Boethig D, et al. Indications and outcome after lung transplantation in children under 12 years of age: A 16-year single center experience. J Heart Lung Transplant. 2022;41(2):226–36.

31. Labarinas S, Coss-Bu JA, Onyearugbulem C, Heinle JS, Mallory GB, Gazzaneo MC. Influence of early extubation on post-operative outcomes after pediatric lung transplantation. Pediatr Transplant. 2021;25(2):e13776.
32. Burjek NE, Hafeman M, Guthrie D, Desai A, Jin Z, Brockel M, et al. Perioperative use of gabapentinoids in pediatric patients. Anesthesiol Perioper Sci. 2023;1(3):21.
33. Diamond JM, Arcasoy S, Kennedy CC, Eberlein M, Singer JP, Patterson GM, et al. Report of the International Society for Heart and Lung Transplantation Working Group on Primary Lung Graft Dysfunction, part II: Epidemiology, risk factors, and outcomes-A 2016 Consensus Group statement of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. 2017;36(10):1104–13.
34. Shah RJ, Diamond JM. Primary graft dysfunction (PGD) following lung transplantation. Semin Respir Crit Care Med. 2018;39(2):148–54.
35. Avtaar Singh SS, Das De S, Al-Adhami A, Singh R, Hopkins PM, Curry PA. Primary graft dysfunction following lung transplantation: From pathogenesis to future frontiers. World J Transplant. 2023;13(3):58–85.

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