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MECHANICAL VENTILATION FOR THE LUNG TRANSPLANT RECIPIENT

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Abstract

Mechanical ventilation (MV) is an important aspect in the intraoperative and early postoperative management of lung transplant (LTx)-recipients. There are no randomized-controlled trials of LTx-recipient MV strategies; however there are LTx center experiences and international survey studies reported. The main early complication of LTx is primary graft dysfunction (PGD), which is similar to the adult respiratory distress syndrome (ARDS). We aim to summarize information pertinent to LTx-MV, as well as PGD, ARDS, and intraoperative MV and to synthesize these available data into recommendations. Based on the available evidence, we recommend lung-protective MV with low-tidal-volumes (≤6 mL/kg predicted body weight [PBW]) and positive end-expiratory pressure for the LTx-recipient. In our opinion, the MV strategy should be based on donor characteristics (donor PBW as a parameter of actual allograft size), rather than based on recipient characteristics; however this donor-characteristics-based protective MV is based on indirect evidence and requires validation in prospective clinical studies.

Keywords

Lung transplantation; primary graft dysfunction; acute respiratory distress syndrome; mechanical ventilation; tidal volume; lung protective ventilation; ventilator induced lung injury

INTRODUCTION

Lung transplantation (LTx) is an important treatment option for select patients with end-stage pulmonary disease. Remarkable progress has been made since the modern LTx era began in 1983[1]. The field of LTx has grown rapidly over the last thirty years with improved

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surgical techniques and medical management strategies[2,3]. However there is little information on mechanical ventilation (MV) strategies after LTx, and no guidelines specific to this setting exist[4,5].

Primary graft dysfunction (PGD) represents one of the most common complications observed in the early period following LTx with incidence rates between 10% and 57%[6,7]. PGD is clinically and histologically analogous to the acute respiratory distress syndrome (ARDS)[7,8], and results from a variety of often simultaneously contributing insults. It is characterized by diffuse pulmonary infiltrates with an abnormal oxygen requirement occurring within 72 hours of transplantation[6,7]. Histologic examination in PGD shows diffuse alveolar damage[7]. Severe PGD represents both the main risk factor for early mortality after LTx as well as a risk factor for the development of bronchiolitis obliterans syndrome, which is the primary late complication limiting long-term survival of LTx patients[6,7,9]. Therefore, interventions that reduce the rates of PGD could improve both short-term and long-term outcomes for LTx recipients. Management of MV may present an opportunity for such an intervention. Evolving approaches to MV for patients at risk for ARDS and patients with ARDS have resulted in tangible improvements in outcomes[10–16]. Lung-protective MV strategies incorporating low tidal volumes (V_T) limit ventilator-induced lung injury (VILI), reduce morbidity in patients on MV and improve survival in patients with ARDS[8,11,17–19]. Guidelines embrace the use of lower V_T in patients with ARDS[17].

The benefits of a lung-protective MV strategy extend to patients at risk for ARDS[13,20–23]. Higher V_T were associated with the development of ARDS in patients who came to the intensive care unit without ARDS but had risk factors for it[22]. Furthermore, in patients with no prior lung injury who received MV during cardiac surgery in the operating room, higher V_T settings were associated with higher inflammatory mediator levels[24]. The IMPROVE study provided further evidence that even brief periods of intra-operative lung-protective ventilation result in lower rates of lung injury in surgical patients at intermediate to high risk of pulmonary complications[25]. While not specifically studied in the context of LTx, the tenets of lung-protective MV are likely generalizable to this conceptually similar setting, and in the absence of direct data, should inform MV strategies.

There are important differences between the LTx recipient and a general intra-operative or post-operative critically ill patient[26,27]. LTx recipients have mechanical impairments including: 1) a fresh thoracotomy wound that creates thoracic cage abnormalities, 2) frequent phrenic nerve dysfunction, and 3) pleural dysfunction[28]. The bronchial anastomoses sites and the allograft airway mucosa are prone to ischemia, poor healing, infection and subsequent anastomotic airway complications[29]. Another important aspect unique to LTx is that the size of the transplanted lungs can differ significantly from the size of the recipient's thoracic cavity[30–36], figure 1. In a study of bilateral LTx recipients, V_T during MV were substantially higher if the allograft was undersized compared to oversized allografts, when V_T were indexed to donor predicted body weight (as an estimate of the actual size of the allograft)[37,38].

There are no randomized controlled trials (RCT) that address MV in the specific context of LTx. We will approach the review of MV of the LTx recipient by first providing a concise summary of potentially generalizable principles derived from key studies in critical care medicine and will then aim to synthesize these principles into strategies that incorporate the unique aspects of LTx[12,39].

General principles

In the past MV strategies with V_T of 10 to 15 mL/kg were commonly utilized both intraoperatively and in critically ill patients. V_T of that size were believed to be necessary to prevent hypoxemia and atelectasis. However, mounting evidence from experimental and clinical studies consistently demonstrates that the application of high V_T during MV may aggravate or cause lung injury[40]. MV using large V_T can result in over-distention of alveoli and lead to ventilator-induced lung injury (VILI), which can amplify the risk for lung injury[40,41]. Lung-protective MV refers to the use of low V_T and positive end-expiratory pressure (PEEP)[11,18,19]. The ARMA study (or tidal volume study), a RCT reported in 2000 by the NHLBI ARDS Network, provided landmark evidence to support a lung-protective MV strategy in the presence of ARDS[11]. Investigators in that trial examined an approach relating V_T to estimated lung sizes expressed as milliliters (mL) per kilogram (kg) predicted body weight (PBW) and compared lung-protective low V_T ventilation to conventional V_T strategies[11]. V_T targets of 6 mL/kg PBW and strategies limiting maximum allowable plateau pressure to 30 cm H2O were compared to V_T targets of 12 mL/kg PBW with a maximum allowable plateau pressure of 50 cm H2O. The low V_T strategy was associated with reduced 30-day mortality (31% versus 39.8%, p = 0.007)[11]. The timing of lung-protective ventilation is important for patients who already have ARDS[10]. ARDS patients who received lung-protective ventilation from the beginning of their lung injury had a lower mortality compared to patients who were initially given larger V_T and then were changed to a protective strategy later in their ARDS course[10]. Each increase of 1 mL/kg PBW in initial V_T was associated with a 23% increase in ICU mortality risk (adjusted hazard ratio 1.23, 95% confidence interval [CI] 1.06–1.44, p=0.008)[10].

Open questions remain regarding the importance of limiting plateau pressure to < 30 cm H2O, limiting V_T to 6 mLs/kg PBW, the optimal setting of PEEP and the role for recruitment maneuvers within the lung protective ventilation strategies for patients with ARDS[18,19,42–47]. However the benefits of a lung-protective MV strategy appear to extend even to patients without lung injury, but who are at risk for the development of ARDS[13,20–23]. Greater V_T were associated with the development of ARDS in patients who came to the intensive care unit without ARDS but had risk factors for it[20–22]. In the context of donor management for transplant, a RCT compared low V_T (6 mL/kg PBW) against a standard donor ventilation strategy (VT 10–12 mL/kg-PBW) and showed a significantly higher proportion of donor lungs from the low V_T group could be utilized for LTx (54% versus 27%, P = 0.004)[13]. Based on the above evidence lung protective ventilation strategies should remain the preferred method of MV for most critically ill patients (with or without the presence of ARDS)[17,22,23].

The principles of lung-protective low V_T MV have recently been extended to even brief periods of MV, as required for general anesthesia during surgical procedures. Increasing evidence shows that in anesthetized patients without ARDS, lung-protective MV can lower the risk of pulmonary complications and ARDS[24,25,48]. The IMPROVE study, a RCT of lung-protective intra-operative MV, provided compelling evidence that lung-protective ventilation benefits surgical patients at intermediate to high risk of pulmonary complications[25]. The study demonstrated lower rates of pulmonary and extrapulmonary complications in the 7 days following surgery (27.5% versus 10.5%, p=0.001), when individuals received lung protective ventilation (V_T = 6–8 mL/kg predicted body weight [PBW], PEEP = 6–8 cm H2O, and 30-second recruitment maneuvers of 30 cm H2O every 30 minutes) intraoperatively rather than conventional ventilation (V_T = 10–12 mL/kg PBW, no PEEP, and no recruitment maneuvers)[25]. A recent meta-analysis of RCTs evaluated the effect of intraoperative lung-protective ventilation with lower V_T on clinical outcomes in patients undergoing surgery[48]. This meta-analysis of 19 RCTs showed that anesthetized patients who received ventilation with lower V_T during surgery had lower risks of lung injury and pulmonary infection than those who received conventional ventilation with higher V_T[48].

Lung transplant specific issues in mechanical ventilation of the recipient

Intraoperative considerations

There are several unique aspects regarding the intra-operative period during LTx[49–53]. Adult LTx can be performed with or without the use of cardiopulmonary bypass in the absence of severe pulmonary hypertension. An off bypass procedure is the preferred approach in many programs when feasible. Cardiopulmonary bypass is an independent predictor for the development of severe PGD in several studies[6,38]. To reduce the likelihood of requiring cardiopulmonary bypass, the least functional lung, as determined by preoperative quantitative ventilation and perfusion imaging, is usually resected and replaced first during a bilateral sequential LTx. Occasionally, patients with cystic fibrosis will have such voluminous purulent secretions that single lung ventilation, as required for an off-bypass LTx, can be difficult. Careful bronchoscopic airway clearance should be routinely done in the operating room before the start of the LTx in such patients with significant airway secretions. For a single LTx a lateral/anterior thoracotomy is performed. For a bilateral sequential LTx a clamshall incision or bilateral anterior thoracotomies are commonly used[54]. Alternatively, a median sternotomy can also be performed for bilateral lung transplantation on cardiopulmonary bypass. After implantation of the allograft it can be important to control the rate of reperfusion of the allograft by gradually releasing the clamp from the pulmonary artery to minimize reperfusion injury. During the period of single lung ventilation the entire cardiac output passes through the first implanted allograft, while the pulmonary artery on the contralateral side is clamped. Increased pulmonary blood flow results in greater sensitivity to develop VILI[55]. Consequently, careful attention to size of the V_T can be especially important during this vulnerable period. We recommend V_T of 6 mLs/kg-donor-PBW. The V_T should be further adjusted for single lung ventilation by reducing V_T approximately 50%. PEEP of +5 cm H2O should be used and in case of difficulties with oxygenation PEEP of up to +10 cm H2O can be considered. After

rewarming of the allograft and following deflation episodes careful recruitment maneuvers to allow complete initial inflation are used by manual bag-inflation, while trying to avoid peak inspiratory pressure above 30 cm H2O. Since the lungs are visible in the operating field the anesthesiologist should be in close communication with the LTx-surgeon to assure that all atelectatic lungs areas are visibly seen as recruited. An association between increased FiO2 at reperfusion and a higher risk of severe PGD has been reported in several studies[6,38]. This suggests that using the lowest FiO2 to maintain appropriate partial pressure of oxygen in the arterial blood [(PaO2) > 70 mmHg] and hemoglobin oxygen saturations [(SpO2) > 92%] should be used. Many LTx recipients have significant pre-transplant chronic hypercarbia from their end-stage lung disease. Intraoperative permissive hypercapnia with pCO2 in pre-transplant range can be helpful to allow for optimal cerebral perfusion and to facilitate the use of low V_T. However the allograft vasculature is often sensitive to elevated pCO2, which can cause vasoconstriction and elevated pulmonary arterial pressure and these factors need to be considered in the setting of permissive hypercapnia. Inhaled nitric oxide (iNO) or inhaled prostacyclin can be considered in case of pulmonary hypertension or to facilitate protective MV settings in case of significant PGD by improving oxygenation. However the routine use of iNO has no beneficial impact on outcomes[56–58].

Several situations frequently necessitate the use of cardiopulmonary bypass during LTx. Patients with severe pulmonary hypertension, for example, are most safely transplanted on bypass. After allograft implantation while on bypass, protective resting ventilator settings should be used with V_T 4–6 mLs/kg-donor-PBW (further reduced for single lung ventilation) and PEEP of +5 cm H2O. Before coming off cardiopulmonary bypass it can be helpful to bronchoscopically remove blood clots and secretions from the allograft airways to maximize allograft function and facilitate successful weaning from bypass[59]. More recently, veno-arterial extracorporeal membrane oxygenation (ECMO) has emerged as a valid alternative method of support and was associated with decreased rates of pulmonary and renal complications, as compared with cardiopulmonary bypass[60]. Occasionally the chest remains open following the LTx[61]. If pressure-assist-control MV modes are used in that setting, the pressure control should be carefully adjusted to assure lung protective low V_T, as increased respiratory system compliance with an open chest is possible. Table 1 summarizes recommendations for the intraoperative MV of the LTX recipient.

Postoperative considerations

The goals of controlled MV immediately following LTx are to protect the allografts from injury while improving function and facilitating early weaning and extubation.

Bilateral Lung Transplant

A bilateral LTx is the most common LTx in the modern era[3]. There are limited data on MV after a LTx, however, a murine model of LTx demonstrated that the mode of mechanical ventilation applied during the early phase of reperfusion influenced the severity of PGD[62]. A protective ventilatory strategy that minimized pulmonary mechanical stress by low V_T was associated with less PGD and improved lung function after LTx. The study concluded that VILI might be an under-recognized phenomenon that contributes significantly to PGD after LTx and that protective ventilatory strategies with low V_T could potentially lead to

improved outcomes after LTx[62]. In a single-center observational cohort study, the implementation of a management guideline for respiratory and hemodynamic status within the first 72 hours after LTx resulted in less severe PGD[63]. The respiratory portion of the protocol was based on a lung-protective low V_T ventilation strategy[63]. The study also gave parameters for hemodynamic support that emphasized the use of vasoactive drugs over fluid administration to maintain a lower central venous pressure[63,64].

In an international survey of the LTx community, the majority of respondents indicated a preference for using lung-protective approaches to mechanical ventilation after LTx[4]. Low V_T based on recipient characteristics were frequently chosen[4]. Donor characteristics often were not considered and frequently were not known by the team managing mechanical ventilation after LTx[4]. In a single-center study, the relationship between donor-recipient lung size mismatch and postoperative MV V_T in a cohort of bilateral LTx patients was evaluated, figure 1. V_T settings were expressed as absolute values (in mL) and also as fractions of recipient and donor PBW[37]. Postoperative absolute V_T settings were comparable between subsets of patients with undersized, matched, and oversized allografts, and V_T settings according to recipient PBW was also similar. V_T settings according to donor PBW, however, revealed significant differences between undersized, matched, and oversized subsets (11.4 ± 3.1 versus 9.4 ± 1.2 versus 8.1 ± 2.1, respectively; $P < 0.05$)[37]. Thus, during mechanical ventilation after bilateral LTx, patients with undersized allografts received relatively greater V_T compared to those with oversized allografts when VT was related to donor PBW (as an estimate of the actual allograft size). Postoperatively, a single-center report linked hyperinflation of undersized allografts (i.e., donor lungs smaller than recipient thorax) to an increased risk of early allograft failure[65]. The results of other studies have demonstrated that patients with undersized allografts had worse outcomes, specifically increased rates of PGD, tracheostomy and resource utilization[30,38]. In an ancillary study to the LTx outcomes group, an undersized allograft was associated with a significantly increased risk of ISHLT grade 3 PGD after bilateral LTx[38]. Furthermore, a series of studies revealed an association between undersized allografts and risk of first-year mortality[30–36,38,66–69]. The mechanisms associating an undersized allograft with a higher risk of PGD and a higher risk of first-year mortality are unclear. Hyperinflation of significantly undersized allografts by V_T set according to recipient characteristics could increase the risk of VILI. A hypothesis generated from these investigations of lung size mismatch and clinical outcomes after LTx is that a lung-protective mechanical ventilation strategy based on estimates of the allograft size (i.e., donor PBW) could be protective for patients with undersized allografts. A clinical trial of allograft protective mechanical ventilation with V_T settings of 6 mL/kg donor PBW compared with routine mechanical ventilation after LTx could test this hypothesis[70]. Although a majority of respondents to a survey did not consider donor characteristics they indicated that they might modify MV settings if they knew the donor characteristics[4]; thus we recommend that donor characteristics should be communicated to and known by the team managing the MV[4,30,38,66]. This could be especially important in case of size reduced and lobar transplants[71,72].

When there is severe PGD, mechanical ventilation may not be able to safely meet the LTx recipients' needs in terms of oxygenation and minute ventilation, and the ventilator settings

needed may be harmful to the allograft. Many LTx centers use veno-venous ECMO as rescue strategy for severe PGD[73–75]. The advantages of using VV-ECMO are that it allows using protective ventilator settings and minimizing sedation[73–75]. Ventilator rest settings on VV-ECMO commonly use very low V_T of approximately 4 mL/kg (donor PBW) with PEEP 5–8 cm H_2O[76,77]. There is a prospective trial in progress testing whether ultra-protective ventilation using a tidal volume of 3 mL/kg combined with extracorporeal carbon dioxide removal will improve outcomes in severe ARDS compared with conventional low-V_T ventilation[78]. Furthermore, if a single dual-lumen bicaval cannula can be utilized for VV-ECMO, physical therapy and mobilization can occasionally be resumed.

Some patients fail extubation or have complications that require longer duration of mechanical ventilation or VV-ECMO. In these cases early tracheostomy is often performed[79–81]. This allows for safe weaning trials that lessen the risk of airway complications from repeated intubations and constant high pressure on the bronchial anastomoses[79–81]. Patients also have better comfort, oral hygiene, clearance of pulmonary secretions and a lower risk of vocal cord injury.

Single Lung Transplants

Single LTx represent a minority of procedures done in the modern era[3]. When managing these patients, it is important to consider that the native lung has end-stage disease from different etiologies and should not be relied upon to share the volumes and pressures during mechanical ventilation equally with the allograft. In idiopathic pulmonary fibrosis (IPF) the native lung is less compliant than the allograft, and most of the V_T will likely go to the more compliant allograft. Lung-protective ventilator V_T should be reduced, and we prefer an initial V_T of 4–6 mL/kg of the donor's PBW. Liberalization of V_T may be necessary to minimize patient sedation and to allow for early extubation. Recipients of a single LTx for IPF can also have an IPF flare in the native lung triggered by the LTx surgery. This can lead to more severe hypoxemia from shunt physiology through a very non-compliant IPF lung. Recipients of a single LTx for COPD on the other hand have a very compliant native lung, which has severe expiratory airflow obstruction. This can lead to over-distention of the recipient's native lung from dynamic hyperinflation and auto-PEEP. Here an approach to mechanical ventilation that maximizes expiratory time, by using a short inspiratory time, a low respiratory rate and a V_T that allows for full expiration are important. If these difficulties cannot be managed with conventional mechanical ventilation, patients may require independent lung ventilation with a double-lumen endotracheal tube and different ventilator settings for each lung[5]. However independent lung ventilation generally requires heavy sedation and a preferable approach can be to utilize VV-ECMO, or extracorporeal CO2 elimination as a rescue strategy, as discussed above.

Bronchial Anastomoses

A key aspect unique to LTx is the presence of the bronchial anastomoses. Anastomotic airway complications occur in approximately 10–20% of LTx recipients and often present both acute and long-term problems[29,82–87]. Anastomotic airway complications include infection, stenosis and dehiscence[29,82–87]. In general, the bronchial circulation is not restored during transplant, and ischemia of the transplanted airway and airway mucosa

frequently occur after LTx[29,88]. Thus the bronchial anastomoses sites are prone to poor healing, infection and anastomotic airway complications. There may be collateral flow from the pulmonary circulation, but the pulmonary circulation has relatively low vascular pressure and thus the magnitude of collateral flow is probably small. Therefore, positive pressure mechanical ventilation could potentially impair perfusion to transplanted airways, especially when high inflation pressures are required. In addition any allograft parenchymal pathology such as PGD, infection or rejection will reduce the pulmonary flow to the major bronchi and thereby impair anastomotic healing. Alternatively, it is possible that PEEP may increase perfusion through microscopic collateral vessels by redistributing blood flow from the pulmonary vessels which in this setting could be acting as a vascular capacitance bed. This theory is supported by a dog model of LTx without restoration of the bronchial arterial circulation, where increasing the PEEP from 5 to 10 cm H2O was associated with increased retrograde bronchial mucosal blood flow to the bronchial anastomoses[89]. However positive pressure ventilation can also contribute to bronchial wall and anastomotic stress. High airway pressures and prolonged ventilation times have been linked to the risk for anastomotic airway complications in some studies, however not in others[82,85,90]. The concern regarding high airway pressures and anastomotic airway complications are likely reflected in the responses on approaches to peak inspiratory pressure (PIP) and PEEP during MV after LTx in an international survey[4]. Almost all respondents (91%) reported routinely assessing airway pressures and most had a peak inspiratory pressure (PIP) limit[4]. The median limit was 30 cm H2O (IQR 30–35 cm H2O). The PIP limit differed significantly between volume assist/control (VAC) users and pressure assist/control (PAC) users (median 35 [IQR 35–40] versus median 30 [IQR 20–35], $p = 0.002$). In that survey the maximum acceptable PEEP level after LTx averaged 11 cm H2O (IQR 10–12.5 cmH2O)[4]. However, there is little evidence guiding optimal setting of PEEP and PIP for the LTx recipient and regarding how much pressure is too much for the anastomoses.

Modes of ventilation

Immediately after surgery there are many different providers and support staff involved in the management of the MV of the LTx recipient. An international survey indicated that the ventilator settings were determined by intensivists in 50% of centers, pulmonologists in 42%, surgeons in 28%, anesthesiologists in 26%, and respiratory therapists in several instances (multiple answers were allowed)[4]. Approximately equal percentages of respondents reported using pressure assist/control (PAC) ventilation (37%) and volume assist/control (VAC) ventilation (35%)[4]. This requires careful attention to the ventilator inputs and outputs as different providers have different preferences and levels of experience with specific ventilator modes. VAC modes are most likely to have consistent tidal volumes but require attention to peak and plateau airway pressures. PAC modes can avoid high peak but not transpulmonary pressures, sometimes providing larger V_T than intended. We emphasize that limiting peak inspiratory pressures does not assure that transpulmonary pressure remains in a lung protective range, except during general anesthesia or deep sedation. Therefore, we prefer the VAC or pressure regulated volume control (PRVC) modes, rather than PAC, during the period of controlled mechanical ventilation in the ICU. Management guidelines have been successfully implemented at individual LTx centers and can help to facilitate a consistent approach to mechanical ventilation of the LTx

recipient[4,63]. Table 2 summarizes recommendations for the postoperative MV of the LTX-recipient.

Summary

Lung transplantation is a very specialized field with unique surgical and medical aspects. The principles of lung protective ventilation have a strong evidence base in patients at risk for or with ARDS. Much of the recommendations presented in this review of lung transplant recipient mechanical ventilation are extrapolated from data in the general patient populations, because of the close relationship between PGD and ARDS, as well as the general influence of anesthesia on the respiratory system. All LTx recipients are at risk for PGD, which is similar to ARDS, and should receive mechanical ventilation according to the principles of lung-protective ventilation with low tidal volumes. In our opinion the low tidal volume strategy should be based on donor characteristics (i.e. donor predicted body weight as a parameter reflecting the actual allograft size), rather than based on LTx recipient characteristics.

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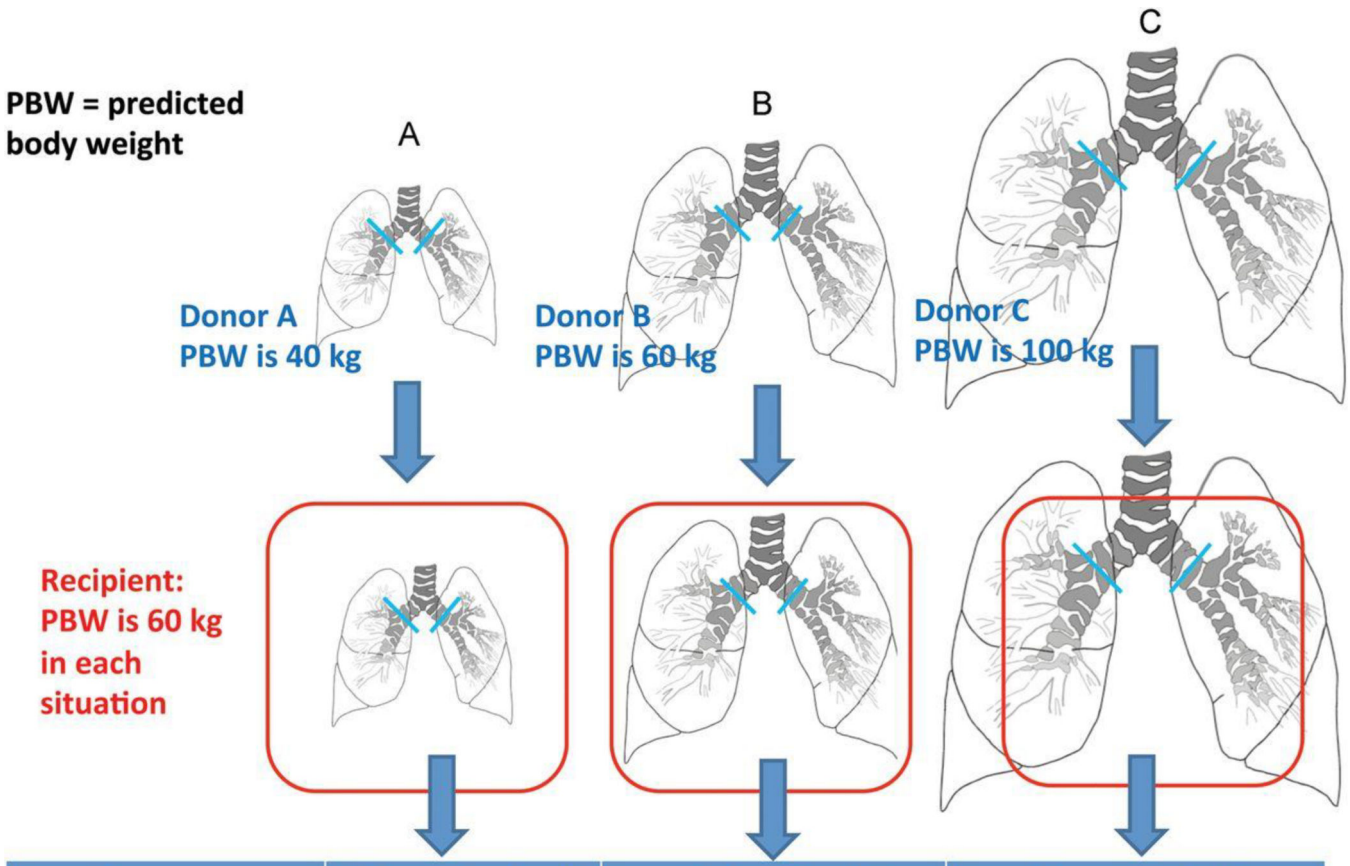

Parameter	"Very undersized"	"Perfect Match"	"Very oversized"
Absolute TV	**500**	**500**	**500**
TV in ml/kg **PBW-Recip**	(= 500 / 60) = **8.3**	(= 500 / 60) = **8.3**	(= 500 / 60) = **8.3**
TV in ml/kg **PBW-Don**	**(= 500 / 40) = 12.5**	(= 500 / 60) = **8.3**	**(= 500 / 100) = 5.0**

Figure 1.

Conceptual graphic on the possible effect of lung-size mismatch on mechanical ventilation tidal volumes expressed as mL/kg-predicted body weights of the donor. Reproduced with permission from Dezube et al[37]. Recip = Recipient; Don = Donor.

Table 1

Recommendations for intraoperative mechanical ventilation

Off CPB transplant	**On CPB**
- Lung protective allograft ventilation with 6 mL/kg donor predicted body weight, adjusted for single lung ventilation and/or lobar transplant. - PEEP of 5 cm H2O. - Careful recruitment maneuvers, as needed. - Lowest FiO2 possible to maintain appropriate PaO2 > 70 mmHg] and hemoglobin oxygen saturations (SpO2) ≥ 92%. - Consider keeping P_aCO2 in range of pre-transplant. - Bronchoscopic airway clearance.	- During bypass support and after implantation, allograft rest ventilation with 4–6 mL/kg donor predicted body weight, adjusted also for single lung ventilation. - Otherwise same recommendations as off CPB.

CPB: Cardiopulmonary bypass; PEEP: Positive end expiratory pressure; FiO2: Fraction of inspired oxygen; P_aO2: partial pressure of oxygen in the blood; P_aCO2: Partial pressure of carbon dioxide in the blood

Table 2

Recommendations for post-operative mechanical ventilation

No PGD	PGD
- Protective allograft ventilation with V_T 6 mL/kg donor predicted body weight, adjusted for single lung ventilation and/or lobar transplant. - Volume assist control or PRVC mode preferred. - PEEP of 5 cm H_2O. - Plateau pressure ≤ 30 cm H_2O. - Lowest FiO2 possible to maintain P_aO2 > 70 mm Hg and hemoglobin oxygen saturations (SpO2) ≥ 92%. - Bronchoscopic airway clearance if clinically indicated. - Early extubation if possible.	In addition to “no PGD” recommendations: - Consider inhaled Nitric Oxide to facilitate protective ventilation. - PEEP increased to maximal level of 10 cm H2O. - Early initiation of VV-ECMO, preferably upper body cannulation to facilitate mobility. - On ECMO protective allograft ventilation with V_T 4 mL/kg (donor PBW) and PEEP 5–8 cm H_2O. - Early tracheostomy if prolonged intubation is expected.

PGD: Primary graft dysfunction; PEEP: Positive end expiratory Pressure; FiO2: Fraction of inspired oxygen; P_aO2: partial pressure of oxygen in the blood; P_aCO2: Partial pressure of carbon dioxide in the blood; VV ECMO: venovenous extracorporeal membrane oxygenation; PBW: Predicted body weight. PRVC: pressure regulated volume controlled