The feasibility of extubation in the operating room after bilateral lung transplantation in adult emphysema patients: an observational retrospective study

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Abstract

OBJECTIVES: We introduced an extubation strategy for emphysema patients after bilateral lung transplantation. Patients who met the extubation criteria were extubated in the operating room (OR) followed by non-invasive ventilation, and the other patients were extubated in the intensive care unit (ICU). The primary objective was to determine the extubation rate. The secondary outcomes were to determine the factors allowing for extubation in the OR and the postoperative course.

METHODS: This study is a single-centre retrospective database analysis of 96 patients. Anaesthesia was performed using automated titration of total intravenous anaesthesia combined with thoracic epidural analgesia. Extubation criteria included arterial partial pressure oxygen (PaO2)/fraction of inspired oxygen (FiO2) ratio, chest radiograph, oedema and haemodynamic stability. Data were compared using non-parametric tests and expressed as median (interquartile ranges) or number (%).

RESULTS: Fifty-three (55%) patients were extubated in the OR (the OR group) with 1 requiring reintubation and 43 (45%) patients were extubated in the ICU (the ICU group). Preoperative pulmonary hypertension, the requirement for intraoperative extracorporeal membrane oxygenation (ECMO), bleeding and ex vivo lung reconditioning donors were lower in the OR group. At the end of the procedure, the PaO2/FiO2 ratio was better (352 (289–437) vs 206 (144–357), P = 0.004), and the need for postoperative ECMO, mechanical ventilation duration, length of stay in the ICU [5 (4–7) vs 12 (8–20) days, P < 0.0001], Grade 3 primary graft dysfunction at 72 h [1 (2%) vs 10 (24%), P = 0.002] and 1-year mortality [5 (9%) vs 11 (26%) patients, P = 0.014] were lower in the OR group than in the ICU group.

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CONCLUSIONS: Half of patients were extubated in the OR, and this strategy does not require additional ICU resources.

Keywords: Bilateral lung transplantation · Emphysema · Extubation

INTRODUCTION

In the past decade, both the number of lung transplantsations and the survival rate thereafter have increased dramatically. The most common primary indication for lung transplantation worldwide is emphysema [1]. Lung transplantation is a complex procedure, and invasive mechanical ventilation is the usual practice in the postoperative period [2]. Specifically, after lung transplantation, prolonged mechanical ventilation may carry associated risks of bronchial anastomosis damage [3]. Invasive mechanical ventilation in immunocompromised patients and endotracheal intubation are predisposing factors for developing nosocomial infections [4]. Moreover, invasive mechanical ventilation requires the use of sedative agents that may inhibit gastrointestinal motility [5].

For emphysema patients undergoing lung transplantation, extubation in the operating room (OR) is considered feasible. Previous reports have described extubation in the OR especially after single-lung transplantation for emphysema patients [6-8], but extubation after bilateral lung transplantation (BLT) has rarely been reported [9]. Early extubation can reduce the length of stay in the intensive care unit (ICU) and improve ICU resource utilization [10].

Since 2006, we have developed OR extubation guidelines at our institution for emphysema patients undergoing BLT. Patients with correct graft function at the end of BLT were extubated in the OR followed by non-invasive ventilation (NIV) [3, 7]. The primary objective of this retrospective analysis of the database was to evaluate the extubation rate in the OR using this strategy. The secondary outcomes were the determination of patient or intraoperative factors allowing for extubation in the OR and the evaluation of the postoperative course. We mainly compared the survival rate and the ICU resource utilization between patients extubated in the OR and patients extubated in the ICU.

PATIENTS METHODS

This study is a retrospective analysis of the prospectively maintained institutional Anaesthesia Lung Transplant Database. The database has received approval from the Institutional Review Board of the French Learned Society of Pneumology (Société de Pneumologie de Langue Française, 24 February 2012). Patient consent was waived.

This cohort study was performed on emphysema patients undergoing BLT between May 2007 and September 2016 at a single centre (Foch Hospital, Suresnes, France). This centre maintains strict compliance with the ethics statement of the International Society for Heart and Lung Transplantation. Patients with single-lung transplantation, retransplantation, preoperative extracorporeal membrane oxygenation (ECMO) or multiorgan transplantation were excluded. BLT was performed using grafts from brain-dead donors with or without ex vivo lung reconditioning [11]. Donor characteristics were evaluated using the lung donor score [12]. Sequential BLT was performed using bilateral anterolateral thoracotomy. ECMO was placed during the procedure if required. Data were extracted from the medical records, including patient, donor and intraoperative and ICU characteristics. Before lung transplantation, we explained to patients who did not use NIV, how to use it and that the NIV will be used systematically after extubation.

Procedure

In the operating room. The local anaesthesia protocol included a hot-air warming blanket and a thoracic epidural catheter (if there were no contraindications, a mixture of levobupivacaine and sufentanil was infused throughout the procedure). A right radial artery catheter, an oximetric pulmonary arterial catheter (Swan-Ganz continuous cardiac output or mixed venous oxygen saturation catheter; Edward Life Sciences Corp., Irvine, CA, USA), transoesophageal echocardiography (Vivid 7, GE healthcare, Fairfield, CT, USA) and a central venous catheter were inserted. To facilitate the drug administration during the procedure, we have developed a prototype allowing the automated titration of propofol and remifentanil using the bispectral index (Medtronic, Dublin, Ireland) to target a bispectral value between 40 and 60 during induction and maintenance of general anaesthesia [9, 13]. A low concentration of norepinephrine was infused systematically. An atracurium bolus was administered to facilitate tracheal intubation by a left double-lumen tube. The tube was controlled using a fiberoptic bronchoscopy. A tidal volume of 5–6 ml·kg⁻¹ or 3–4 ml·kg⁻¹ was used during double-lumen or single-lung ventilation, respectively, associated with a positive end-expiratory pressure of 5 cm H₂O. Tidal volumes were adjusted accordingly to arterial blood gas analysis, and inhaled nitric oxide was administered accordingly.

At the end of the procedure, the endobronchial double-lumen tube was changed to a single-lumen tube. A fiberoptic bronchoscopy was performed for bronchial toilette to check for bronchial anastomosis or oedema, and recruitment manoeuvres were also performed. The possibility of extubation in the OR was evaluated if the patient met the following criteria, including a fully awake and alert state after the stop of propofol and remifentanil infusion and antagonism of neuromuscular block, body temperature >36°C, controlled blood loss (<100 ml·h⁻¹) with an acceptable trend of haemodynamic stability, the absence of major pulmonary oedema evaluated using fiberoptic bronchoscopy, trend of blood gas analysis with arterial partial pressure oxygen (PaO₂)/fraction of inspired oxygen (FiO₂) ratio >200, lactataemia <3 mmol·l⁻¹ and the absence of radiographic infiltrates on chest radiograph performed systematically before the extubation attempt in the OR. Extubation was performed in the OR in a sitting position followed by immediate NIV via a face mask using the Respironics ventilator (Philips Healthcare, Netherlands). NIV parameters, such as FiO₂, positive end-expiratory pressure and pressure support, were adapted to obtain an acceptable tidal volume, end-tidal CO₂ and arterial saturation. We considered extubation to be a success if the patient under NIV was well-oriented, pain free, without clinical signs of acute respiratory distress with acceptable blood gas analysis (PaO₂/FiO₂ ratio >150 and arterial pressure carbondioxide (PaCO₂) <50 mmHg or one similar to preoperative PaCO₂). Patients were transferred to the ICU with NIV. In patients without a thoracic epidural catheter, pain control was performed using a multimodal approach with paracetamol, nortem, ketamine and intravenous morphine titration followed by patient-controlled analgesia of intravenous morphine. Paravertebral catheters were not used in this series.
In the intensive care unit. Patients extubated in the OR (the OR group) were placed on NIV in the ICU. NIV parameters were adjusted according to blood gas analysis, arterial saturation and clinical tolerance. Patients in the ICU group were extubated at the discretion of the attending intensive care physician. Primary graft dysfunction (PGD) was evaluated during the initial 72 h postoperatively. Grade 3 PGD at 72 h was defined as a PaO₂/FI O₂ ratio <200, and bilateral infiltrates on chest radiograph were recorded 72 h postoperatively. Grade 3 PGD was also defined by the need for postoperative ECMO or the use of inhaled nitric oxide for >48 h during mechanical ventilation. Patients having hyperacute rejection, venous anastomotic obstruction, cardiogenic pulmonary oedema or pneumonia were excluded from Grade 3 PGD [14]. Within 24 h, a fibreoptic bronchoscopy with video recording was performed systematically on patients.

The primary outcome was the incidence of patients extubated in the OR. Failure in the OR group was noted when the patient was reintubated in the OR or in the ICU within 48 h postoperatively. Patients extubated in the OR were allocated to the OR group, and patients extubated in the ICU were allocated to the ICU group. For the secondary outcomes, we evaluated the patient characteristics (demography, history and treatments), the donor characteristics, the intraoperative events (fluid loading, ECMO requirement and bleeding) and the postoperative course (the mechanical ventilation duration, the need for tracheostomy, the length of stay in the ICU and the Grade 3 PGD at 72 h). In particular, we analysed the survival rate to evaluate the safety of our strategy.

In this observational study, the analysis of the data was performed without the use of risk-adjustment methods to decrease the bias. Indeed, the sample size was too small.

Statistical analysis

The OR and ICU groups were compared using non-parametric tests. The Boschloo’s test was used for all categorical variables except 1-month survival and 1-year survival. The Boschloo’s test is an unconditional test, it has the advantage of preserving significance level and is more powerful than the Fisher’s exact test for moderate to small samples. The Mann–Whitney U-test was used for all continuous variables. Categorical variables are presented as number (%) or number and frequencies with 95% confidence interval (CI) calculated using the Wilson procedure with a correction for continuity. Differences in time to 1-year survival were reported using the Kaplan–Meier curve, and statistical significance was calculated using the log-rank test. Continuous variables are presented as medians (25th–75th percentiles). All comparisons were performed without correction for multiple testing. A bilateral P-value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 11.0 (SPSS Science Inc., Chicago, IL, USA) and R Core Team version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria) with the package Exact 2x2 version 1.5.2.

RESULTS

Between May 2007 and September 2016, 96 patients had sequential BLT using bilateral anterolateral thoracotomy (Fig. 1), and 53 patients (55%, CI 95% 45–65) were extubated in the OR and underwent NIV. One patient was reintubated: the patient had acute agitation and pain despite the use of thoracic epidural analgesia related to opioid-withdrawal syndrome. This patient was sedated, reintubated, mechanically ventilated within 12 h postoperatively and analysed in the OR group. Three patients among this group required tracheal intubation related to acute graft rejection, pneumonia or septic shock. The tracheal intubation was followed by a tracheotomy.

Forty-three patients (45%, CI 95% 35–55) remained intubated at the end of the procedure (the ICU group) and were transferred to the ICU under mechanical ventilation (Fig. 1). However, 7 patients were extubated within 24 h postoperatively, and the reasons for non-extubation in the OR were related to the intraoperative requirement for ECMO (n = 3), the absence of thoracic...
epidural analgesia (n = 2), hypothermia (n = 1) and other (n = 1); no patients were reintubated within 48 h. Hence, 60 patients (62%, C1OR = 51–72) were extubated within 24 h postoperatively.

Patient and donor characteristics were similar except for the number of ex vivo lung reconditioning and preoperative pulmonary hypertension (Table 1).

Thoracic epidural catheters were placed in 86% (C1OR = 95 77–92) of patients (Table 2). Three patients in the OR group had a contra-indication for epidural catheter insertion. For the ICU group, we had failure of epidural catheter insertion. For the ICU group, we had 1 failure of catheter insertion and 8 contraindications for epidural insertion (2 post-plasmapheresis coagulopathies and 6 preoperative anticoagulant therapies). For the 9 patients in the ICU group without thoracic epidural analgesia, the PaO2/FiO2 ratio at the end of the procedure was higher than 300 for 4 patients, and 2 patients were extubated within 24 h in the ICU.

The blood loss or total bleeding was higher in the ICU group compared to patients with PGD grade <3 (∗P = 0.001), fresh frozen plasma [8 (4–11) vs 6 (4–8), ∗P = 0.007] or colloid [3 (2–5) vs 2 (1–3) ml kg−1 h−1, ∗P = 0.005] was increased as compared to patients with PGD grade <3 (n = 84), whereas total bleeding [1500 (675–4250) vs 1000 (575–1525) ml, P = 0.16] and the rate of intraoperative ECMO [4 (36%) vs 18 (21%), P = 0.27] were similar in patients with Grade 3 and patients with Grade <3. In patients with Grade 3 PGD at 72 h, 1-year survival was 56% (C1OR = 26–83).

The postoperative courses differed between groups. The duration of invasive mechanical ventilation, the length of stay in the ICU, the need for tracheotomy or postoperative ECMO were lower in the OR group (Table 3). Moreover, as expected, the rate of Grade 3 PGD at 72 h was lower in the OR group. One-year mortality data were obtained for all patients and were lower in the OR group (Table 3 and Fig. 2). In the overall population, 1-month survival rate was 92% (C1OR = 84–96), and 1-year survival was 83% (C1OR = 74–90).

For the patients (n = 11) with Grade 3 PGD at 72 h, the intraoperative fluid administration of red blood cell [7 (4–10) vs 4 (4–11) units, P = 0.03], fresh frozen plasma [8 (4–11) vs 6 (4–8), P = 0.02] or colloid [3 (2–5) vs 2 (1–3) ml kg−1 h−1, P = 0.005] was increased as compared to patients with PGD grade <3 (n = 84), whereas total bleeding [1500 (675–4250) vs 1000 (575–1525) ml, P = 0.16] and the rate of intraoperative ECMO [4 (36%) vs 18 (21%), P = 0.27] were similar in patients with Grade 3 and patients with Grade <3. In patients with Grade 3 PGD at 72 h, 1-year survival was 56% (C1OR = 26–83).

The requirement for intraoperative ECMO was lower in the OR group (Table 2). The use of intraoperative ECMO (n = 22) increased bleeding [1800 (1100–3750) vs 900 (500–1400) ml, P = 0.001], the units of red blood cells [4 (4–11) vs 3 (2–5), P = 0.007] and the units of fresh frozen plasma [6 (4–11) vs 3 (2–4), P = 0.001].

As expected at the end of the procedure, the PaO2/FiO2 ratio was higher, and the lactic acidemia was lower in the OR group (Table 2).
In emphysema patients undergoing BLT, extubation in the OR followed by NIV was possible for half of the patients after combining thoracic epidural analgesia with total intravenous anaesthesia. Preoperative pulmonary hypertension, the grafts obtained after ex vivo lung conditioning, the requirement for intraoperative ECMO or major bleeding decreased the possibility of extubation in the OR. For patients extubated in the OR, the postoperative course or prognosis was not altered.

Extrathoracic patients following BLT are considered as a goal for some teams [6–8], but the feasibility of extubation for emphysema patients after BLT has rarely been reported. In an observational study, we have reported extubation in the OR for 3 of 5 emphysema patients after BLT, and none of the patients were reintubated [9]. Other studies have reported only the feasibility of extubation after single-lung transplantation in emphysema patients. In a series of 6 patients, 2 were extubated in the OR [7].

In 91 patients, 53% were extubated in the OR, but 21% of these patients were reintubated [6]. In a series of 57 patients, 21 (37%) patients were extubated in the OR, and 2 (10%) patients were reintubated [8]. After BLT, the rate of extubation in the OR has been reported mainly in cystic fibrosis patients. Recently, a study of 89 cystic fibrosis patients undergoing BLT reported that 45 patients were extubated in the OR, and 4 were reintubated [15]. The success rate of early extubation was probably related to the systematic use of NIV [3]. Indeed, NIV is effective in improving gas exchange of either PaO2 or PaCO2 without sedation [16] after BLT [3]. Finally, the strategy for extubation in the OR was feasible without an increase in procedure duration (Table 2). The anaesthetic approach allowing for early extubation includes effective analgesia, normothermia, the use of short-acting anaesthetic drugs [5, 6, 17] and a skilled anaesthesiologist to maintain cardiorespiratory homeostasis continuously. In the absence of contraindication, thoracic epidural analgesia is the standard for postoperative pain control after bilateral thoracotomy: thoracic epidural analgesia decreases the duration of mechanical ventilation, the length of stay in the ICU and the rate of respiratory complication [18]. In this study, 4 patients without thoracic epidural analgesia were not extubated at the end of the procedure although they had met the criteria for extubation in the OR. Indeed, pain control after bilateral thoracotomy without epidural analgesia with a multimodal approach can induce sedation and respiratory depression. Epidural haematoma has never been described during lung transplantation, but a very low risk of haematoma exists [19]. The use of short-acting anaesthetic drugs needs continuous control and vigilance by the anaesthesiologist to avoid drug overdosing, thereby reducing side effects such as vasoplegia and vasopressor use [20]. The maintenance of anaesthesia was performed in all patients using an automated controller of total intravenous anaesthesia, allowing for the continuous titration of propofol and remifentanil guided by the electrocortical activity [13]. The protocol of our department was to use the controller systematically to reduce the workload [21] during this long and complicated procedure [9]. Extubation in the OR involves continuous interdisciplinary communication and cooperation among all members of the team.

The need for ECMO was related to cardiopulmonary instability during the procedure and was associated with an increase in intraoperative bleeding (Table 2). Intraoperative instability as expected decreased the possibility of early extubation. For the anaesthesiologist, when the patient had an ECMO, the weaning from an assist device was prioritized over tracheal extubation. Intraoperative ECMO requirement and major bleeding have previously been reported to reduce the probability of early extubation in cystic fibrosis patients [15].

Ex vivo lung reconditioning [11] was used for rejected donor lungs with a low PaO2/FiO2 ratio and decreased extubation rate in the OR. While ischaemic graft duration is increased by the ex vivo procedure, there are no increase in the rate of Grade 3 PGD or one-year mortality as compared to conventional donors. This survival rate after the use of grafts provided by ex vivo lung reconditioning was similar to our experience [22].

As expected, postoperative ECMO requirement or the Grade 3 PGD [14] at 72 h were less frequent in the OR group. The criteria (PaO2/FiO2 ratio, chest radiograph or oedema) for extubation or for the evaluation of PGD are similar. These criteria at the end of the surgery in the OR were an early predictive marker of graft function, and the survival rate (Fig. 2) demonstrates that extubation in the OR seems to have no safety concerns. As also expected, extubation in the OR decreased mechanical ventilation

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The results are expressed as median (25th–75th percentiles) or number (%). All comparisons were performed without correction for multiple testing.

P-value was calculated using the log-rank test.

ECMO: extracorporeal membrane oxygenation; Grade 3 primary graft dysfunction at 72 h: PaO2/FiO2 ratio <200 and bilateral infiltrates on chest X-ray at 72 h; the use of ECMO or inhaled pulmonary vasodilator >48 h; ICU group: extubation in the intensive care unit; OR group: extubation in the operating room.
duration, the length of stay in the ICU and the need for tracheotomy (Table 3). This association does not imply causality, but it was related to patient selection in the OR group. Finally, this strategy does not require additional ICU resources. Indeed, the need for critical care has dramatically increased due to the increase in candidates having ECMO before or after lung transplantation [23], and ICU resources are sometimes limited.

The patients with Grade 3 PGD at 72 h (n = 11) received more packed red blood cells, fresh frozen plasma and collod during the intraoperative period, while the rate of total intraoperative bleeding was similar. The increase in the intraoperative fluid administration has been reported as a factor associated with an increased rate of Grade 3 PGD [24].

Limitations

This study is a retrospective analysis of a database from a single centre. It did not demonstrate that outcomes were different when the extubation was performed in the OR versus a few hours later in the ICU, when the patients had met the extubation criteria. Currently, the rate of emphysema patients extubated in the OR or within 24 h postoperatively after BLT has never been reported and remains unknown.

The use of risk-adjustment methods (stratification, multivariate analysis, propensity score and so on) was not performed in this study. Indeed, the sample size was too small to perform a robust and accurate analysis.

Over a 10-year period in a single institution, more than half of the adult emphysema patients could be extubated in the OR after BLT. This strategy involves a dynamic optimization of patient care, a rigorous selection of patients or grafts by skilled physicians and also close cooperation among all staff managing the candidates for lung transplantation. Extubation in the OR appears safe without the need for additional ICU resources in the postoperative period.

ACKNOWLEDGEMENTS

The authors thank Desmond McGlade, MBBS, FANZCA, lung transplantation. Extubation in the OR appears safe without the total rate of intraoperative bleeding was similar. The increase in the intraoperative fluid administration has been reported as a factor associated with an increased rate of Grade 3 PGD [24].

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