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Awake extracorporeal membrane oxygenation bridging for pulmonary retransplantation provides comparable results to elective retransplantation

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BACKGROUND: Lung retransplantation became an accepted treatment for bronchiolitis obliterans syndrome (BOS). However, the value of different bridging modalities for these patients is controversial.

METHODS: We analyzed outcomes of 39 patients listed for retransplantation between 2008 and 2012. Patients were divided in 3 groups: 23 patients without any bridge modality (elective, Group 1), 11 patients on ventilation and full sedation with or without extracorporeal membrane oxygenation (ECMO) support (sedated bridging, Group 2), and 5 patients awake on ECMO support (awake bridging, Group 3).

RESULTS: Waiting list mortality was 13% in Group 1, 39% in Group 2, and 0% in Group 3. Perioperative mortality was 20% in Group 1, 29% in Group 2, and 0% in Group 3. Significant differences between Groups 1 and 2 were calculated for time on post-operative ventilation (17.4 vs 27.3 days, $p = 0.022$), intensive care unit stay (22.0 vs 32.9 days, $p = 0.026$), and hospital stay (34.7 vs 54.1 days, $p = 0.013$). However, there were no significant differences between Groups 1 and 3 for post-operative ventilation time (17.4 vs 13.4 days, $p = 0.192$), for intensive care unit stay (22.0 vs 26.4 days, $p = 0.169$), or for hospital stay (34.7 vs 34.8 days, $p = 0.367$). Survival rates at 90 days, 1 year, and 2 years were 80%, 70%, and 53% in Group 1; 71%, 43%, and 29% in Group 2; and 100%, 60%, and 60% in Group 3, respectively.

CONCLUSION: Awake ECMO bridging for retransplantation provides comparable results to elective retransplantation.

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Bridging with extracorporeal membrane oxygenation (ECMO) to primary lung transplantation (LTx) has become an accepted treatment option for patients with advanced stages of respiratory failure. Several reports have demonstrated success rates of up to 80% and outcomes that are almost similar to those of elective LTx.[1–5] This has resulted in broader and earlier use of ECMO for bridging of terminal patients. More recently, the concept of "awake" ECMO bridging was introduced[6–8] in which ECMO is applied as an alternative to intubation/ventilation or in the intention to wean patients from both. This strategy has resulted in further improved outcomes and has led to a paradigm shift for the use of bridging devices.

In parallel to the achievements made in primary LTx, results for retransplantation (re-Tx) have improved as well, and re-Tx has become an established procedure. The 2013

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International Society for Heart and Lung Transplantation (ISHLT) Registry[9] reported 970 re-Tx cases between 1995 and 2012, with a constant increase in recent years. However, the general recommendation is to perform lung re-Tx only in elective patients, and the need for a bridging procedure to re-Tx is widely considered to be an exclusion criteria. Moreover, the overall experience of extracorporeal support techniques in the setting of re-Tx for bronchiolitis obliterans syndrome (BOS) is very limited.[10] We therefore have reviewed our institutional experience with ECMO bridging to lung re-Tx in general and with a special emphasis on the use of the "awake" bridging strategy to re-Tx in particular.

Methods

A retrospective analysis was performed of all patients listed for re-LTx for BOS between 2008 and 2012 at the Department of Thoracic Surgery of the Medical University of Vienna. The Institutional Ethic Board approved the study. Indications for listing for re-Tx were BOS 3, absence of other organ dysfunction, age younger than 60 years, and absence of pronounced, especially immune suppression–related comorbidity. Patients were divided into 3 groups:

Group1 (elective): Patients in stable condition undergoing re-LTx under elective conditions.

Group 2 (sedated bridging): Patients with further respiratory deterioration during the waiting period that necessitated intubation, sedation, and invasive mechanical ventilation (IMV), eventually supported with additional ECMO support.

Group 3 (awake bridging): Patients with deterioration who initially were intubated but received early ECMO support, followed by cessation of sedation, combined with full or partial weaning from IMV, thus allowing for mobilization, communication, and oral nutrition.

The indication for intubation and IMV was progressive hypoxia and hypercapnia during the waiting period. Indication for ECMO implantation was further deterioration on IMV, despite of maximal ventilatory support.

Different types of ECMO systems were used according to the clinical need of each patient and to the availability of novel systems during the interval investigated. Initially a conventional pump-driven ECMO support (Medtronic Bio-Console 560, Medtronic Inc, Minneapolis, MN) combined with a hollow-fiber oxygenator (Medtronic CPMPCB Affinity BPX-80 or Affinity NT; Medtronic Inc, Minneapolis, MN) or a Quadrox poly-methyl-pentene membrane oxygenator (Jostra, Hirrlingen, Germany) were used in venovenous (VV) or venoarterial (VA) mode. A Bio-Medicus Cannula 15–17F was used for cannulation of the artery and a Bio-Medicus Cannula 17–19F was used for venous access (all from Medtronic Inc). The single Avalon Elite Bi-Caval double-lumen cannula (DLC; Avalon Laboratories, LLC, Rancho Dominguez, CA) was used later in the study interval for VV support.

For isolated dysfunction of CO_2 elimination in hemodynamically otherwise stable patients, a pumpless ECMO support with the iLA system (Novalung GmbH, Hechingen, Germany) was preferred, which allows for an AV pulsatile blood flow driven by the patient's own cardiac output. This device leads to a significant reduction of partial pressure of CO_2 but has no or only a very limited effect on oxygenation. In combination with a miniaturized pump, however, oxygenation can also be improved significantly. This combination, called iLA-activve, was used recently for VV approach combined with the Novaport Twin, a single-port 22–24F DLC (Novalung).

Results among the 3 groups were compared for survival at <90 days (early) and at 1 and 2 years, peri-operative and post-operative complications, intensive care unit (ICU) length of stay after Tx, and in-hospital length of stay. Continuous variables are shown as mean $\pm$ standard deviation or as median (range). Categoric variables are expressed as frequencies and proportions in parenthesis (% within each study group). In non-parametric distributed continuous data, the Mann-Whitney U test was used to detect significant differences between 2 groups and the Kruskal-Wallis test among 3 groups. Survival was estimated according to the Kaplan-Meier method, and the log-rank test was used to detect significant survival differences between the corresponding groups. For categoric data, the association of the groups with clinical characteristics was assessed by the two-sided Pearson chi-square test or Fisher's exact test between 2 groups and the likelihood ratio among 3 groups. Two-sided p-values were calculated and considered statistically significant at <0.05. All statistical analyses were performed using SPSS 22 software (IBM Corp, Armonk, NY).

Results

Demographics

A total of 39 patients with the diagnosis of BOS 3 were listed for re-LTx during the study interval (Table 1). Of these, 23 patients who underwent re-LTx under elective conditions were assigned to Group 1. During the waiting period, 16 patients deteriorated and needed IMV with full sedation. Four of these patients underwent LTx from the respirator, and 12 needed additional extracorporeal support

Table 1 Patient Demographics

Variables[a]	Result
	(N = 39)
Age, years	34.2 ± 15.3
Median (range)	31.5 (6.3–64.4)
Male sex	23 (59)
Diagnosis at first Tx	
COPD, emphysema, A1AD	10 (26)
Pulmonary fibrosis	8 (21)
PPH, CTEPH	9 (23)
Cystic fibrosis, bronchiectasis	12 (31)
Comorbidities	
Diabetes	5 (16)
Hypertension	5 (16)
Hyperlipidemia	6 (19)
Osteoporosis	6 (19)
Renal failure	1 (3)
First Tx procedure	
Double-lung	32 (82)
Single-lung	7 (18)
Waiting list mortality	7 (18)
Re-Tx procedure	
Double-lung Tx	31 (97)
Single-lung Tx	1 (3)

A1AD, α1-anti-trypsin deficiency; COPD, chronic obstructive pulmonary disease; CTEPH, chronic thromboembolic pulmonary hypertension; PPH, primary pulmonary hypertension; Tx, transplantation.

[a]Categoric data are shown as number (%) and continuous data as mean ± standard deviation or as indicated.