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The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

ORIGINAL CLINICAL SCIENCE

# Transplantation after ex vivo lung perfusion: A midterm follow-up

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**KEYWORDS:**
lung transplantation;
ex vivo lung perfusion;
lung evaluation;
chronic lung allograft dysfunction;
primary graft dysfunction

**BACKGROUND:** A large proportion of donor lungs are discarded due to known or presumed organ dysfunction. Ex vivo lung perfusion (EVLP) has proven its value as a tool for discrimination between reversible and irreversible donor lung pathology. However, the long-term outcome after transplantation of lungs after EVLP is essentially unknown. We report short-term and midterm outcomes of recipients who received transplants of EVLP-evaluated lungs.

**METHODS:** Single-center results of recipients of lungs with prior EVLP were compared with consecutive recipients of non-EVLP lungs (controls) during the same period. Short-term follow-up included time to extubation, time in the intensive care unit, and the presence of primary graft dysfunction at 72 hours postoperatively. Mortality and incidence of chronic lung allograft dysfunction were monitored for up to 4 years after discharge.

**RESULTS:** During a 4-year period, 32 pairs of initially rejected donor lungs underwent EVLP. After EVLP, 22 double lungs and 5 single lungs were subsequently transplanted. During this period, 145 patients received transplants of conventional donor lungs that did not have EVLP and constituted the control group. Median time to extubation was 7 hours in the EVLP group and 6 hours in the non-EVLP control group ($p = 0.45$). Median intensive care unit stay was 4 days vs. 3 days, respectively ($p = 0.15$). Primary graft dysfunction grade $> 1$ was present in 14% in the EVLP group and in 12% in the non-EVLP group at 72 hours after transplant. Survival at 1 year was 92% in the EVLP group and 79% in the non-EVLP group. Cumulative survival and freedom from retransplantation or chronic rejection were also comparable between the 2 groups ($p = 0.43$) when monitored up to 4 years.

**CONCLUSIONS:** Selected donor lungs rejected for transplantation can be used after EVLP. This technique is effective for selection of transplantable donor lungs. Patients who received lungs evaluated under EVLP have short-term and midterm outcomes comparable to recipients of non-EVLP donor lungs.

J Heart Lung Transplant ▮▮▮▮;▮:▮▮▮–▮▮▮

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The use of lungs from multiorgan donors remains between 15% and 50%,[1,2] suggesting that up to 85% of donor lungs are discarded in some regions. Uncertainty about the donor lung quality is often the reason for rejection. The challenge facing the transplant team is to identify a reversible donor lung dysfunction from an irreversible one.

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http://dx.doi.org/10.1016/j.healun.2016.05.021

Fear of transplanting a non-functioning organ will often lead to the conservative approach of turning down a marginal donor lung that may have been an excellent organ long-term.

Suggestions were made even before the use of ex vivo lung perfusion (EVLP) that more than 40% of rejected donor lungs could be potentially usable for lung transplantation.[3] EVLP provides the means for a functional test of the donor lung under the control of the transplant team.[4] This method may also hold a potential for organ improvement through various treatments.[5] The EVLP method itself may also still be improved, as shown by several recent studies of modified circulation and tests of lung performance ex vivo.[6,7] An increasing number of centers have reported encouraging clinical experiences with EVLP, but data from longer-term follow-up are still sparse.[8–10]

EVLP was introduced in our clinical practice in 2011.[11] In this study, we reviewed results of up to 4 years of follow-up of transplant recipients of EVLP-evaluated lungs and compared them with contemporary recipients of non-EVLP lungs.

## Methods

The University of Gothenburg Ethics Committee approved this study. All patients were informed and consented upon listing for transplantation about the possibility of having EVLP-evaluated lungs, otherwise matched according to standard criteria.

### Study design

Data were prospectively collected and retrospectively analyzed for 4 years. Donor lungs rejected for transplantation were evaluated as possible candidates for EVLP. Lungs that during EVLP proved to have good function, defined as (1) partial pressure of arterial oxygen/fraction of inspired oxygen (P/F) ratio >40 kPa, (2) pulmonary vascular resistance and pulmonary compliance deemed as normal, and (3) macroscopic appearance and manual palpation without major pathology, were transplanted. Short-term and long-term results for patients who received lungs with (EVLP group) or without prior EVLP were compared.

### Recipients

All recipients on the regular lung transplant waiting list, including urgent patients and patients with ventilator support or on extracorporeal membrane oxygenation (ECMO), were eligible for lung transplant, with or without prior EVLP. Recipients were routinely matched for compatible blood group, size, and urgency, and were admitted to the transplantation center during the organ retrieval procedure. Recipient characteristics are presented in Table 1.

### Donor selection and characteristics

The initial inclusion criteria for evaluation of rejected donor lungs using EVLP included a P/F ratio < 40 kPa and/or X-ray findings consistent with pulmonary edema. The inclusion criteria were later expanded to also include donor lungs (1) where function was impossible to evaluate (i.e., a donor on ECMO); (2) with suspected injury not possible to evaluate in the donor (i.e., pulmonary embolism or severe trauma as causes of death) or (3) anamnestic, radiologic, or macroscopic findings suggestive of severely impaired lung function preventing the use of the lungs. The decision to proceed to EVLP when a donor lung was rejected for direct use was taken after discussion between at least 2 transplant surgeons. All lungs were from donors after brain death, because the Swedish authorities have not yet approved donation after cardiac death.

**Table 1** Donor and Recipient Characteristics

| Variables | EVLP | Non-EVLP | *p*-value |
|---|---|---|---|
| Donors | | | |
| No | 27 | 145 | |
| Age, mean ± SD, years | 47 ± 18 | 50 ± 17 | 0.37 |
| P/F ratio,[a] mean ± SD, kPa | 29.0 ± 11.4 | 56.8 ± 11.0 | <0.001 |
| Recipients | | | |
| Age, mean years | 55 ± 13 | 52 ± 14 | |
| Diagnosis, % | | | |
| IPF | 22 | 24 | |
| PAH | ... | 8 | |
| COPD | 33 | 24 | |
| α1-anti-trypsin deficiency | 7 | 13 | |
| Repeat transplantation | 4 | 9 | |
| Cystic fibrosis | 19 | 7 | |
| Other | 15 | 15 | |
| Preoperative bridge, No. (%) | | | |
| Ventilator | 1 (4.5) | 7 (4.8) | |
| ECMO | 0 | 10 (6.9) | |

COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; EVLP, ex vivo lung perfusion; IPF, idiopathic pulmonary fibrosis; PAH, pulmonary artery hypertension; P/F, partial pressure of arterial oxygen/fraction of inspired oxygen; SD, standard deviation.

[a]One donor was supported with ECMO and therefore excluded from the mean value of this parameter.

The procurement of the donor lungs was performed according to our standard protocol. An antegrade Perfadex flush (XVIVO AB, Gothenburg, Sweden) of 4 liters before lung harvest and a complementary retrograde flush of Perfadex provided before implantation of the lungs was administered. The lungs were stored cold in Perfadex during transport and kept on ice. EVLP was performed at the recipient hospital.

### EVLP strategy

The EVLP strategy has been previously described.[4,11] Briefly, the perfusion was performed with the semiautomated Vivoline LS1 device (Vivoline Medical AB, Lund, Sweden) and Steen Solution (XVIVO AB) mixed with red blood cells to a hematocrit of 10% to 15%. Lung perfusion was restricted to 70 ml/min/kg ideal donor weight. The allowed pulmonary artery pressure was gradually increased to reach a maximum of 20 mm Hg during the evaluation of lung function.

Mechanical volume-controlled ventilation with a positive end-expiratory pressure level of 5 cm $H_2O$ and a tidal volume of 6 to 8 ml/kg ideal donor weight were applied after bronchoscopy at 32ºC. An incremental positive end-expiratory pressure trial was performed at 36ºC. Repeated blood samples for gas analysis were

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