Sixth International Joint Meeting on THORACIC SURGERY

Barcelona - 20th, 21st and 22nd November 2024
Auditorio Foment del Treball Nacional. Barcelona (Spain)

11th International Meeting on General Thoracic Surgery
Clínic Barcelona | Universitat de Barcelona | Hospital Universitari Sagrat Cor

5th Meeting of the Thoracic Oncology, Thoracic Surgery, Techniques & Transplant, Respiratory Nursing and Respiratory Physiotherapy Areas of the Spanish Society of Pneumology and Thoracic Surgery (SEPAR)
Sociedad Española de Neumología y Cirugía Torácica (SEPAR)

10th International Workshop on Surgical Exploration of the Mediastinum and Systematic Nodal Dissection
Hospital Universitari Mútua Terrassa | Universitat de Barcelona

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3rd Joint Meeting of the Spanish Society of Thoracic Surgery (SECT)
SECT Sociedad Española de Cirugía Torácica

30th Congress of the "Asociación Iberoamericana de Cirugía Torácica" AIACT

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LUNG TRASPLANTATION: THE NEWEST THERAPIES OF EXVIVO LUNG PERFUSION, ARE WE IN THE FUTURE?

Irene Bello
Thoracic Surgery Department, Hospital Clínic

Lung transplantation is considered the final therapeutic option for select patients with end-stage lung disease. Since the first lung transplant, the procedure has become more common worldwide. However, a persistent shortage of donor lungs limits its broader application. Innovations have been introduced to increase the availability of donor lungs, including the use of cardiac death donors, optimization of donor management in intensive care, expanded donor criteria, and ex vivo lung perfusion (EVLP) systems.

1. Definition

EVLP has emerged as a clinical method for evaluating, preserving, and potentially reconditioning donor lungs before transplantation. This technique involves isolated lung perfusion under normothermic conditions, utilizing a machine to recirculate preservation solution through the pulmonary vasculature, supplemented by mechanical ventilation. EVLP facilitates graft evaluation, transportation, and potential reconditioning before transplantation.

2. Assessment

Originally developed for assessing donor lungs before transplantation, EVLP has shown success in clinical settings and has been associated with increased transplant rates, particularly from donation after circulatory death (DCD) and extended-criteria donors.

The European Society for Organ Transplantation (ESOT) consensus on cardiothoracic machine perfusion strongly recommends EVLP for extending donor lung utilization, though the recommendation for its use in compromised grafts is weaker.

The use of EVLP in controlled circulatory death donors (cDCD) is debated; in some countries, cDCD lungs must undergo EVLP assessment by law. French studies report that 76% of cDCD lungs transplanted after normothermic regional perfusion (aNRP) and EVLP had comparable outcomes to brain-death donors (DBD). Conversely, Mora et al. found that 90.6% of cDCD lungs were successfully transplanted without EVLP, showing similar outcomes to DBD donors.

The fact that uncontrolled cardiac death donors (uDCD) should be assessed via EVLP before use in transplantation is accepted.

3. Improvement

EVLP holds potential as a dynamic lung preservation and reconditioning platform. It enables active metabolic support, potentially aiding in lung resuscitation and repair.

a. Machine Learning

While existing physiological parameters in EVLP are validated for graft acceptance, single-parameter decisions are not feasible. The Toronto group has developed predictive models using combined donor and EVLP parameters to enhance transplant success predictions.

b. Genetic Modification

EVLP enables genetic interventions; for instance, the Toronto group engineered mesenchymal stromal cells to produce IL-10, an anti-inflammatory cytokine, reducing apoptosis and macrophage activation in animal models. This approach could optimize lung function and improve outcomes. Recently, researchers also demonstrated ABO blood type conversion, potentially expanding transplant compatibility and fairness.

c. Mitochondrial Therapy

Addressing mitochondrial dysfunction during ischemia could mitigate lung injury. Studies by Cloer and Dr. Lindstedt's team showed that mitochondrial transplantation might reduce injury and enhance lung function during EVLP.

d. Lung Microbiome

The lung microbiome influences immune responses, with specific microbial compositions associated with primary graft dysfunction (PGD) risk post-transplantation. Studies by Grando et al. are exploring how EVLP-modified lung microbiomes may decrease PGD incidence.

4. Lung Repair Centers

Centralized EVLP centers in the US and Europe now assess and repair donor lungs. These centers improve transplant logistics and outcomes, with studies (e.g., by Chen et al.) showing that lungs treated in centralized EVLP facilities perform comparably to those processed at individual transplant centers.