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Conventional lung preservation

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Lung preservation is an essential procedure for a successful lung transplantation, encompassing all process from pre-procurement to transplant. The aim of this lecture is to explain the classical and conventional techniques for lung preservation.

1) Preservation solution

Lung preservation solutions are generally divided into extracellular (colloid solutions) and intracellular (high potassium, low sodium crystalloid type) fluids. Extracellular solutions include low-potassium dextran (LPD)-glucose solution (e.g., Perfadex® (XVIVO, Sweden)), Cambridge solution, Celsior, and Papworth (which contains Ringer's lactate, mannitol, albumin, and donor blood). Intracellular solutions include Euro-Collins and University of Wisconsin solution.

1) Perfadex®

Perfadex® is the most commonly used lung preservation solution in which Dextran-40 is the main component functioning as an oncotic agent. It helps maintain plasma in the blood vessels, reduces interstitial edema, decreases the aggregation of red blood cell and platelets, thus sustaining microcirculation and preventing cell activation. The solution has a low potassium concentration, avoiding an increase in pulmonary artery pressure. The glucose in the solution supports aerobic metabolism (Oxygen can be delivered to tissue due to intra-alveolar oxygen in inflated lung), and maintains the cell integrity during long ischemic period.

2) Prostaglandins E1 (PGE1, alprostadil) or I2 (PGI2, prostacyclin, iloprost (PGI2 analog))

The purpose of PGE1 injection is to induce vasodilation to prevent pulmonary vascular constriction due to the infusion of cold preservation solution into the lungs. This can make the preservation solution to be evenly distributed in the lung. Additionally, PGE1 mitigates ischemia-reperfusion injury by inhibiting the expression of proinflammatory cytokines. PGE-1 can be directly infused through the pulmonary artery or central vein.

3) Methylprednisolone

High dose of methylprednisolone is used for anti-inflammatory purposes. The dosage is 15 mg/kg, which can be administered to the donor before lung procurement and to

the transplant recipient just before reperfusion.

2) Temperature of preservation solution

Though there is disagreement, most institutes maintain a temperature of 4-8 ºC. Hypothermia is intended to inhibit metabolism, allowing cells to survive even in absent blood flow state (5% of the metabolic rate at 37ºC). Low-temperature storage is crucial in classical lung preservation technique.

3) Anterograde and retrograde flush

Anterograde flush is administered through the pulmonary artery and drained through the left atrium. Retrograde flush is injecting 250 mL each through the remaining pulmonary veins in the left atrial posterior wall after heart extraction and draining through the cut pulmonary artery. Lung preservation has been demonstrated to be superior when using retrograde flush compared to using anterograde flush alone. This effect is interpreted to result from the complete removal of remaining red blood cells in the capillaries, allowing for a more even distribution of the lung preservation solution. Additionally, retrograde flush plays a role in removing thrombi or clots remaining in the pulmonary vessels.

4) Infusion pressure of preservation solution

It is necessary to apply sufficient pressure to thoroughly flush the pulmonary vasculature, but excessively high pressure can cause damage to pulmonary vessels. Therefore, it is essential to infuse at an appropriate pressure. In the most institutes, infusion is done at around 10-15 mmHg, and caution is exercised not to exceed 22 mmHg (30 cm H2O), to avoid potential damage.

5) Temperature of lung preservation temperature

Although the optimal temperature for lung preservation is not definitive, preserving at 4-8ºC helps reduce cellular metabolism, aiding in preserving cellular function. Despite various advantages of low temperature preservation, it can cause ischemia-reperfusion injury, that is, increase extravascular fluid and induce pulmonary vascular constriction, leading to decreased oxygen exchange and increased pulmonary vascular resistance after reperfusion.

6) Ischemic time

The permissible maximum ischemic time is not well-established. However, as the ischemic time lengthens, the risk of reperfusion injury increases. Typically, an 8-hour cold ischemic time is widely accepted. There are reports suggesting an increase in primary graft dysfunction and 30-day mortality when the ischemic time exceeds 8 hours, although some cases with ischemic times of 10-12 hours have also been reported. Therefore, in cases where a prolonged ischemic time is anticipated, careful consideration, taking into account factors such as age, smoking history, clinical status, and the condition of the transplant recipient, is essential for making decisions.