Can Ex-Vivo Lung Perfusion expand the donor pool for lung transplants?

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Abstract

Lung transplant remains the gold standard for patients with end stage lung disease as a result of conditions such as COPD, cystic fibrosis and pulmonary fibrosis. Due to the low supply of donor lungs and high recipient demand, there is a shortfall leading to long waiting lists where the mortality is approximately 20% of patients. This is complicated by the fact that currently only 15% of donor lungs are viable for transplant.

Ex Vivo Lung Perfusion (EVLP) is an innovative and pioneering technology which aims to convert lungs considered marginal to viable options for transplantation. The aim of this poster is to review the development of EVLP and whether it has the capacity to expand the donor pool. The protocols and techniques involved are also discussed as well as the impact that EVLP has had in its short history.

Introduction

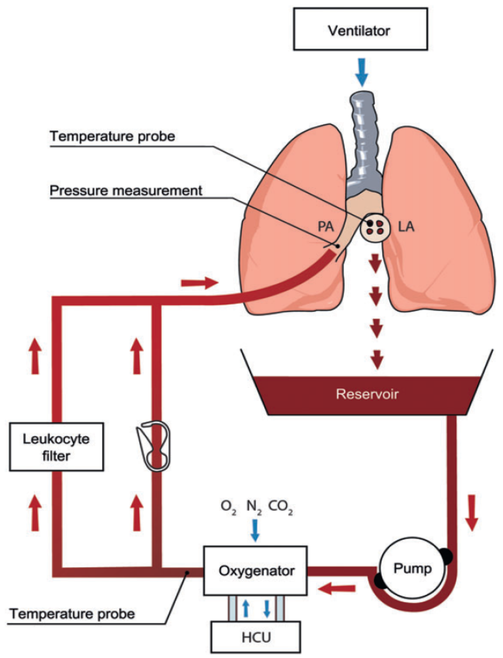
Due to the low supply of lung donors available, 21% of patients in the UK die whilst on the lung transplant waiting lists [1]: lung transplants are not very common in the UK with only 212 transplants carried out from April 2017 to April 2018 despite a waiting list of 356 patients at the end of the same period [2] and typical waiting times of up to 18 months.

The process of EVLP helps alleviate the stress on 'demand versus supply' through increasing the availability of viable lung donors and thus increasing the donor pool; currently only 20% of donor lungs are actually used in transplantation [2]. Common reasons for lungs rejected for transplantation include poor organ function, findings on biopsy and donor medical and social history. Below shows the criteria for determining which lung donors are suitable for transplantation.

Indicator	'Ideal' Donor	'Unusable Donor'
Age (years)	20-45	>65
PO_2/FiO_2	>350	200
Smoking History	Never	Upper limit
Chest X-Ray	Clear	Persistent Collapse
Microbiology	Culture Negative	Pan resistant organism
Bronchoscopy	Clear	Tumour

Methods

EVLP involves placing the donor lungs through a dome of ventilators, pumps and cannulas known as a perfusion rig where the lungs are primed as shown in the figure below. The lungs are treated with oxygen and antibiotics to clear any previous infections which helps 'renew' lungs that weren't working well previously but cannot reverse permanent lung damage. This involves a 4-6 hour process whereby the lungs are placed in a dome connected to a ventilator, pumps and filters. [3] The lungs are maintained at body temperature and treated with STEEN solution which consists of albumin and dextran which provides an optimal osmotic pressure and also protect the endothelium from leukocyte interaction. [3]



This system can be categorised into two main elements: the system which circulates and deoxygenates the fluid that flows through the lung vasculature, and the system which facilitates and ventilates oxygen to the lungs via the bronchus.

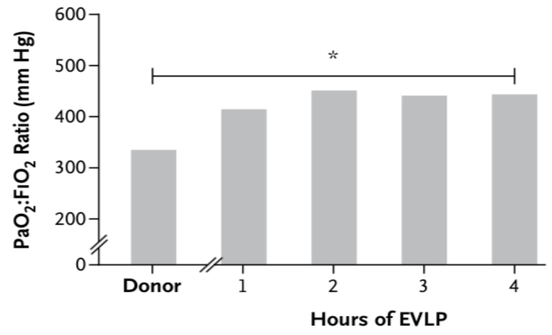
The blood drains into the reservoir from the remnant of the left atrium (LA). The oxygenator is used primarily for deoxygenation once body temperature has been achieved. The functionality of the lung and how it oxygenates and removes CO2 is now analysed through blood gases. Some centres perform this cycle multiple times over several hours whilst others are proceed to transplant once lung function is established.

Results

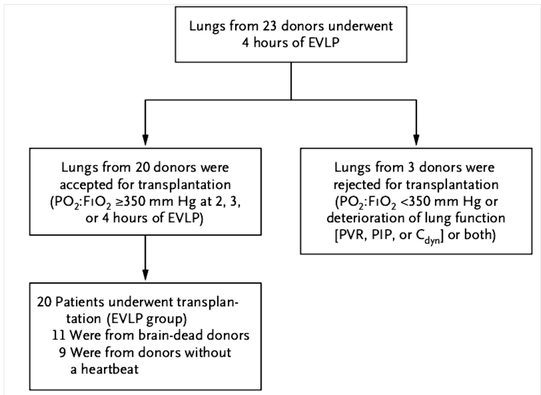
A study by Cypel et al in 2011,[4] examined the feasibility of transplanting marginal to high risk donor lungs that had been taken through the EVLP process.

In a prospective and non-randomised trial, the marginal donor lungs (PO_2/FiO_2 of less than 300) underwent EVLP for 4 hours. The control group were the lungs that had not undergone the EVLP in the same time period. The number of transplants with primary graft dysfunction after 72 hours was the main outcome being measured.

During this period 136 transplants were observed, 23 being eligible for EVLP and the remaining 116 lungs acting as the control group. Of those 23, 20 lung function remained stable during the process and the median PO_2/FiO_2 improvement over the 4 hour period as shown below (P<0.001). The remaining 3 lungs eligible for EVLP did not achieve the desired PO_2/FiO_2 of over 350 mm Hg.



The main outcome being measured was the primary graft dysfunction rate in the first 72 hours with 15% of the EVLP group being rejected compared to 30% of the control (P=0.11)



Discussion

Primary graft dysfunction (PGD) is a type of reperfusion injury commonly seen in transplant surgery. The tissue damage is due to the organ being subjected to a prolonged time period in a hypoxic state; this happens in between waiting for transplantation before blood supply is returned. PGD is the main cause of early death after a lung transplant with incidence rates of 15-25%

The study conducted by Cypel et al, showed that those lungs deemed marginal that were treated using EVLP had lower PGD rates than those lungs that were deemed suitable for conventional lung transplantation.

Conclusion

Through this research it has become apparent that the lung donor pool must expand to meet the rising lung transplant demand. Using the EVLP process and we can improve the quality of marginal lungs making them suitable for lung transplantation; hence addressing 59% of lungs rejected due to poor organ function.[4] Studies have shown an increase from 20% to 90% of lungs available for trans- plant post-EVLP.[2] It has also shown that this therapy cost-effectively improves quality of life for patients. Despite numerous studies, further research needs to be done in this relatively new field.

Despite ex vivo lung perfusion still being a relatively new technique, the trials that have been carried out have all showed a significant improvement in increasing the number of lungs that meet the transplant criteria and give lungs that were deemed unsuitable a new 'lease of life'; hence increasing the number of lungs available to recipients and reducing waiting times. Ex vivo lung perfusion is poised to change the face of transplantation over the next decade as more studies are carried out and hope to rectify the everlasting issue of organ rejection.

References

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