Ex Vivo Lung Perfusion

Clinical and experimental studies

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For patients who are suffering from end-stage lung disease, lung transplantation is a life-prolonging therapy. The number of donor lungs is limited and the majority of available donor lungs, in some regions up to 85%, are discarded due to known or presumed organ dysfunction. Lung donations after cardiac death (DCD) and increased utilization of lungs from donations after brain death (DBD) could increase the availability of donor organs. *Ex vivo* lung perfusion (EVLP) is a method that has been developed for the preservation and evaluation of donor lungs during continuous perfusion and ventilation. EVLP is applicable to lungs harvested from DCD, as well as to the lungs of DBD with suboptimal lung function.

Method: In Papers I and II, an uncontrolled DCD situation was simulated in a pig model. The currently suggested protocol for DCD lung procurement, involving post-mortem administration of heparin followed by chest compressions and intrapleural cooling of the lungs to 12**°C,** was compared to a simplified procurement method that does not use heparin and employs a less-invasive cooling technique. In Papers III–V, the methods and results for EVLP for the salvage of initially rejected human donor lungs were investigated. Rejected donor lungs with inferior function were retrieved and connected to the EVLP system. Assessments of lung function, with respect to circulatory and respiratory parameters, were performed. EVLP-treated lungs that were deemed to have normal function were transplanted into recipients from the conventional waiting list for transplantation. The short-term and long-term outcomes for the recipients of the EVLP-treated lungs were compared to a consecutive series of patients who received non- EVLP lungs prepared according to the standard protocol.

Results: In Papers I and II, the lung function assessed during EVLP and at post-EVLP analyses in terms of the water content of lung tissues and markers of lung injury, did not differ significantly between the treatment and control groups. In Papers III–V, 25 pairs of rejected donor lungs underwent EVLP. Eighteen double lungs and four single lungs were transplanted after EVLP, and the recipients (EVLP group; N=22) were compared with recipients of conventionally prepared lungs (Control group; N=115). The median time to extubation (p=0.26) and the median stay in the intensive care unit (p=0.06) did not differ significantly for the two groups. Primary graft dysfunction higher than grade 1 was noted for 14% of the recipients in the EVLP group and 11% of the Control group at 72 hours post-transplantation. The cumulative 1-year survival rates were 89% for the EVLP group and 82% for the Control group. The cumulative survival rates for up to three years of follow-up were comparable for these two groups (p=0.67).

Conclusion: Papers I and II provide support for the notion that a no-touch period of 1 hour after death in cases of uncontrolled DCD would not compromise donor lung function. This would allow the next-of-kin to spend time with the deceased and to facilitate the making of a well-founded decision about organ donation. Papers III–V demonstrate that EVLP of initially rejected lungs from DBD can be safely performed and contribute to the lung transplantation program without compromising the outcomes for recipients. With the implementation of a well-functioning EVLP program, up to 50% of lungs from DBD multi-organ donors could be transplanted.

Key Words: Lung transplantation; ex vivo lung perfusion; donation after cardiac death; donor lung procurement.

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I. **Wallinder A**, Steen S, Liden H, Hansson C, Hussein A, Sjöberg S, Dellgren G.
Heparin does not improve graft function in uncontrolled non-heart-beating lung donation: an experimental study in pigs.
European journal of cardio-thoracic surgery: 2013. 43(2): p. 413-9.

II. **Wallinder A**, Hansson C, Steen S, Hussein A, Sjöberg T, Dellgren G.
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J Heart Lung Transplant: 2014. 33(5):528–35

III. **Wallinder A**, Ricksten SE, Hansson C, Riise GC, Silverborn M, Liden H, Olausson M, Dellgren G.
Transplantation of initially rejected donor lungs after ex vivo lung perfusion.
The Journal of thoracic and cardiovascular surgery, 2012. 144(5): p. 1222-8.

IV. **Wallinder A**, Ricksten SE, Silverborn M, Hansson C, Riise GC, Liden H, Jeppsson A, Dellgren G.
Early results in transplantation of initially rejected donor lungs after ex vivo lung perfusion: a case-control study.
European journal of cardio-thoracic surgery: 2014. 45(1): p. 40-4; discussion 44-5.

V. **Wallinder A**, Riise GC, Ricksten SE, Silverborn M, Dellgren G.
Transplantation after Ex-Vivo Lung Perfusion: a follow-up
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