Effects of Intraoperative Support Strategies on Endothelial Injury and Clinical Lung Transplant Outcomes

Objective:
In lung transplantation, postoperative outcomes favor the intraoperative use of extracorporeal membrane oxygenation (ECMO) over cardio-pulmonary bypass (CPB). This is attributed to lower anticoagulation goals, artificial surface interactions and inflammatory responses. Nevertheless, the biological effects of these support strategies and their correlation to lung transplant outcomes continue to be poorly characterized. This study focused on intraoperative endothelial damage and glycocalyx shedding. Our goal was to investigate the effect of different intraoperative support strategies on endothelial damage and its association to posttransplant outcomes.

Methods:
We collected plasma samples before and after lung transplant to measure syndecan-1 (SYN-1). SYN-1 is the main glycoprotein composing endothelial glycocalyx. Endothelial glycocalyx plasma levels serve as early and sensitive biomarkers of endothelial injury. Plasma levels were measured with LUMINEX assay. We compared the SYN-1 levels between patients undergoing transplantation with 1) No-Support, 2) venoarterial (VA)-ECMO and 3) CPB. Also, we evaluated the association between SYN-1 levels and severe primary graft dysfunction at 72 hours (PGD3).

Results:
52 patients were evaluated. Donor and recipient characteristics were comparable among the groups, except the lung allocation score (LAS). The LAS in No-Support was significantly lower than that in the VA-ECMO and CPB groups (mean 47.9, 65.1 and 67.1 respectively, p=0.02). The rate of PGD3 at 72 hours post-transplant was 57.9% in the CPB, 38.1% in the VA-ECMO and 25.0% in the No-Support groups (p=0.01). No significant difference of SYN-1 plasma level was found in the pretransplant samples among groups. Interestingly, the plasma level of SYN-1 at arrival in the ICU (T0) was significantly higher in the CPB group compared to VA-ECMO and No-Support groups (p<0.01, Figure A). No difference was found between VA-ECMO and No-Support groups. In patients with PGD3 at 72 hours, the time evolution of SYN-1 plasma level was higher compared to no PGD3 (Figure B). Peak values were observed at T0. In addition, the peak levels of SYN-1 at arrival in ICU (T0) in patients with PGD3 at 72 hours were significantly higher for the CPB when compared to VA-ECMO and No-Support groups (p=0.04).

Conclusions:
Our data demonstrates that vascular injury during lung transplantation is associated with the mode of intraoperative support. In addition, intraoperative endothelial injury is associated with the development of severe primary graft dysfunction at 72 hours. Based on our data strategies aimed at modulating endothelial injury during lung transplantation will help improve lung transplantation outcomes.

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