

Oral Presentation

Molecular and proteomic signatures associated with preservation related graft injury: insight from human liver normothermic achine perfusion (NMP)

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Background

Continuous liver NMP is a novel technology associated with safe extension of organ preservation time, increased organ utilisation and reduced early graft injury¹. Increasingly, it is utilised as a 'back to base' application with cold storage for organ transport and NMP initiated at the implanting centre prior to transplantation². We aimed to evaluate the impact of additional cold ischaemia time (CIT) on the proteomic and molecular signature of NMP livers.

Methods

Liver tissue samples (N= 57) from a prospective clinical trial of 'back to base' NMP were analysed. Collection occurred at the end of cold storage (LT1), end of NMP/total preservation (LT2) and after organ reperfusion (LT3). Unbiased, label-free-quantitative (LFQ) proteomic analysis was conducted using liquid chromatography with tandem mass spectrometry and trapped ion mobility spectrometry (TIMS) to time-of-flight (TOF) mass analysis (LC-MS/MS TIMS-TOF). Differential expression and Gene Ontology/Pathway analysis were performed.

Results

LT2 samples with prolonged CIT (>6hr) prior to NMP had significant differential expression

of proteins associated with liver-specific oxidative stress, cellular haemostasis and removal of damaged or misfolded proteins (e.g. CYP3A5, PSMB1). LT3 samples, similarly, had reduced proteins involved in autophagy and cell-cycle regulation (e.g. STBD1, CD2AP, GADD45GIP1,) and increased expression of proteins involved in neutrophil chemotaxis, adhesion and aggregation (e.g. S100A9).

Discussion

The molecular signature of grafts at LT2 and LT3 varies depending on the length of CIT prior to NMP. Further exploration of the molecular signatures associated with preservation related graft injury is required to determine how best to apply this novel technology clinically.

References

1. Nasralla, D. et al. A randomized trial of normothermic preservation in liver transplantation. *Nature* 557, 50–56 (2018).
2. Ceresa, C. D. L. et al. Transient Cold Storage Prior to Normothermic Liver Perfusion May Facilitate Adoption of a Novel Technology. *Liver Transplant.* lt.25584 (2019). doi:10.1002/lt.25584