polymerization promoting protein family 3 and dicarbonyl and L-xylulose reductase ($p<0.05$).

Conclusion: Proteins released into the perfusate during early, EVHP are promising for use as biomarkers to evaluate graft quality/ damage. Improved protocols for cardiac graft evaluation may not only aid in the safe expansion of DCD heart transplantation, but may also provide better clinical outcomes by helping to identify grafts at risk for primary dysfunction. The use of EVHP holds potential for developing more precise and reliable evaluation techniques for cardiac graft evaluation.

(246)

Transcriptomic Profiling of Acute Cellular Rejection after Heart Transplantation

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Purpose: Whole genome transcriptomics can be used to understand the pathogenesis of acute cardiac cellular rejection by using a systems based agnostic approach which in turn can facilitate non-invasive diagnosis and potentially identify therapeutic targets.

Methods: A case-control study was performed with 18 patients with acute cellular rejection identified by biopsy and a control group of 12 without rejection (matched for age, sex and time from transplant). RNA sequencing was performed using whole blood samples collected pre and during rejection and compared to controls. Differentially expressed genes (DEGs), statistically significant at false discovery rate of 5%, were examined for pathway analysis. To identify transcripts associated with progression to rejection a multivariable classifier in a logistic regression model with a relaxed ElasticNet penalty (80% L1, 20% L2) was created. Five-fold cross validation was used to identify the best possible set of variables for classification and bootstrapping was used to estimate predictive performance.

Results: There were 248 DEGs identified during rejection as compared to baseline while only 63 DEGs were identified in controls at similar time points. Excluding 13 overlapping DEGs between the 2 groups, 235 rejection-specific genes were identified. The most significantly DEGs were *IFI27* (cytokine signaling) and *SERPING1* (complement cascade), which were upregulated 2.1 and 1.9 fold respectively during rejection. Significant rejection-specific pathways included the immune system pathway involving lymphocytes (*CD19, CD200 BLNK*), interferons (*IFI27, IFI35*), a class I MHC antigen processing and presentation gene (*DYNLL1*); the interleukin-2 signaling pathway (*CR2, CXCR5*) and the erythrocyte oxygen/carbon dioxide exchange (*CA2, HBB, HBA1*) pathway. Finally, variable selection resulted in the identification of one rejection predictive gene *DYNLL1* (OR 2.26; 95%CI (1.24, 4.43); p-value 0.028) and another gene *SERF2* (protein aggregation and toxicity) which were used in the logistic regression model resulting in a cross-validated receiver operating characteristic of 0.63.

Conclusion: RNA sequencing of whole blood during acute cellular cardiac rejection identified significant perturbation of the immune system as compared to controls with the differential expression of the *DYNLL1* gene being the most predictive of rejection.

(247)

The Varied Rna Transcript Isoform Landscape During Human Donor Heart Preservation

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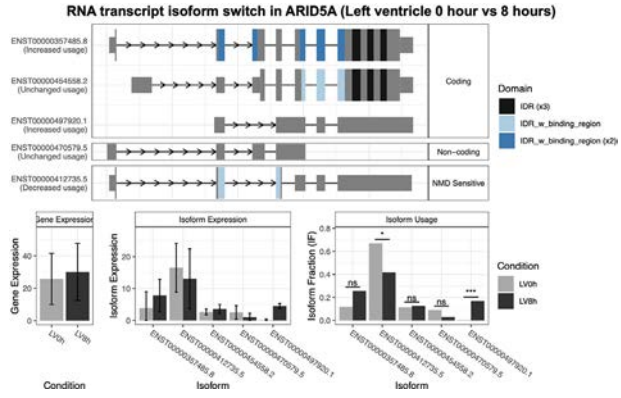
Purpose: Alternative ribonucleic acid (RNA) transcript splicing produces multiple RNA isoforms from the same gene which are associated with many heart diseases. However, little is known about alternative splicing events in donor hearts during cold preservation.

Methods: We examined the transcriptomic profile of the left ventricle of human donor hearts comparing 0 and 8 hours of cold preservation in histidine-tryptophan-ketoglutarate solution. Differential transcript usage (DTU) analysis was performed to examine for transcript isoform changes.

Results: Cold preservation of donor hearts induced a large variety of RNA transcript isoforms. We identified 190 genes showing differential transcript splicing with increasing duration of cold preservation. RNA Isoform switching in 130 genes can be predicted to result in important structural changes in its respective translated proteins. These include altered expression of key protein domains such as intrinsic disorder regions (IDR), and zinc finger domains. Interestingly, cardiac preservation was associated with RNA transcript intron retention or production of a noncoding transcript with no protein product. We identified that ARID5A (figure), a nuclei acid binding protein, had increased expression of a short length variant which results in the loss of IDR regions. ARID5A has important regulatory roles in modulating immune responses at the transcript level.

Conclusion: Alternative splicing events occur prominently in human donor hearts during preservation. Genes without overall changes in expression level may have nuanced transcript isoform changes that leads to impaired cardiac preservation quality. Expression of a shortened ARID5A isoform is likely to contribute to immune activation in donor hearts and may affect occurrence of primary graft dysfunction.



(248)

Early Graft Function by Hemodynamics is Similar Between Brain Death (DBD) and Circulatory Death Donors (DCD)

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Purpose: Heart transplants (HT) from donors after circulatory death (DCD) have been slowly adopted in the United States. Differences in procurement of DCD organs could increase risk of graft dysfunction due to prolonged ischemia after withdrawal of life-support and agonal time. Two methods exist for DCD heart procurement: an ex vivo perfusion system (TransMedics Organ Care System [OCS]) and normothermic regional perfusion (NRP) with extracorporeal membrane oxygenation. The differences of each procurement method could be responsible for abnormal hemodynamic indices. We sought to compare hemodynamic parameters in HT from donor after brain death (DBD) vs DCS and OCS vs NRP donors.

Methods: Single-center, retrospective study of all HT performed at our institution beginning the year of our first DCD HT. We divided our cohort by DBD and DCD transplants. In addition, we compared the two methods of DCD procurement, OCS and NRP. Measurements from protocolized,

routine right heart catheterizations (RHC) at 10 to 14 days post-transplant were used for this analysis.

Results: A total of 226 HT from 01/2020 to 9/2022 were included, 154 (68.1%) DBD and 72 (31.9%) DCD HT. Within the DCD cohort, 16 (22%) were procured by OCS and 56 (78%) by NRP. The RHC was performed at a mean of 10.8 days (SD 2.3). When comparing DBD to DCD, the only significant difference was mean pulmonary artery pressure. (Table 1) No statistically significant differences in hemodynamics were observed between the two methods of DCD procurement (Table 2).

Conclusion: Hemodynamic indices were similar between DCD and DBD HT recipients when measured around day 10 post-transplant. In particular, there were no differences in the parameters of RV dysfunction. Similarly, no differences were observed when comparing types of DCD procurement, OCS and NRP. These findings suggest that graft quality should be considered equal regardless of the type of donor or method of procurement.

Table 1. Comparison between brain death and circulatory death donors

	DBD (n=154, 68.1%)	DCD (n=72, 31.9%)	p-value
Mean right atrial pressure (mmHg)	8.4 (4.4)	7.5 (3.8)	0.15
Pulmonary artery pressure (mmHg)			
Systolic	33.3 (8.7)	30.8 (8.7)	0.06
Diastolic	14.7 (5.3)	13.7 (5.4)	0.22
Mean	22.1 (5.7)	20.3 (6.1)	**0.04**
Mean pulmonary capillary wedge pressure (mmHg)	13.5 (5.3)	12.8 (5.6)	0.39
Cardiac index (liters/meter/m²)	3.3 (0.7)	3.3 (0.7)	0.77
RA/PCWP	0.6 (0.2)	0.6 (0.2)	0.53
Pulmonary artery pulsatility index	2.25 [1.6-3.2]	2.30 [1.7-3.2]	0.76
RA/PCWP > 0.7	52 (36.4%)	14 (21.9%)	0.05
PAPI <2	56 (40%)	23 (35.9%)	0.64

PAPI: pulmonary artery pulsatility index, PCWP: pulmonary capillary wedge pressure, RA: right atrium

Table 2. Comparison between OCS and NRP donors

	OCS (n=16, 22%)	NRP (n=56, 78%)	p-value
Mean right atrial pressure (mmHg)	6.9 (3.3)	7.7 (3.9)	0.49
Pulmonary artery pressure(mmHg)			
Systolic	28.9 (4.3)	31.4 (9.6)	0.29
Diastolic	12.4 (4.2)	14.1 (5.6)	0.15
Mean	18.6 (3.5)	20.8 (6.7)	0.30
Mean pulmonary capillary wedge pressure (mmHg)	12.7 (3)	12.9 (6.2)	0.91
Cardiac index (liters/meter/m²)	3.5 (0.9)	3.2 (0.7)	0.22
RA/PCWP	0.5 (0.2)	0.6 (0.2)	0.26
Pulmonary artery pulsatility index	3.1 [1.9-4]	2.2 [1.7-3.1]	0.30
RA/PCWP > 0.7	53 (33.5%)	13 (26.5%)	0.39
PAPI < 2	4 (26.7%)	19 (38.8%)	0.54

PAPI: pulmonary artery pulsatility index, PCWP: pulmonary capillary wedge pressure, RA: right atrium

(249)

Cumulative Incidence and Risk Factors for Early Post-Transplant Lymphoproliferative Disorder in Adult Heart Transplant Recipients: Single-Centre Experience

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Purpose: Post-transplant lymphoproliferative disorder (PTLD) arising within two years post-transplant is often EBV-associated and management includes minimisation of immunosuppression. The utility of routine EBV serostatus testing of donor and recipient at time of heart transplantation is uncertain and does not guide practice in our institution.

Methods: We conducted a retrospective cohort study of patients transplanted in our institution from April 2010 to January 2021 with at least 18 months follow-up and EBV serostatus determined for both donor and recipient to assess the contribution of the putative risk factors EBV serostatus, use of rabbit antithymocyte globulin (RATG) induction therapy, and any treated rejection in the first two years, for the outcome of early EBV-related PTLD.

Results: 179 patients met inclusion criteria. Median (inter-quartile range) age at transplant was 46 (33, 56) years and median follow-up 70 (52, 101) months. 5 (2.8%) patients developed early PTLD at a median 8 (8, 10) months post-transplant. Overall, the distribution of EBV serostatus (donor, D, recipient, R) was D+R+ 85.5%, D+R- 5.0%, D-R+ 9.5%, D-R- 0%; 162 (90.5%) received RATG induction; 52 (29.1%) had at least one treated rejection episode. Amongst those with early PTLD, all were EBV D+R-; all had received RATG induction; one had been treated for rejection. Amongst those without early PTLD, the distribution of EBV serostatus was D+R+ 87.9%, D+R- 2.3%, D-R+ 9.8%; 90.2% received RATG induction; 29.3% had been treated for rejection. On testing for equality of proportions, only D+R- serostatus was significantly over-represented in the early PTLD group ($chi^2 = 97$, df=2, $p = 8 \times 10^{-22}$).

Conclusion: In this cohort, all patients with early PTLD were EBV D+R- and received RATG induction, raising the question whether RATG induction should be avoided in mismatch recipients to reduce PTLD risk. However, there is currently insufficient evidence to reduce our standard induction regime. This could be revisited as the cohort expands.

(250)

Clinical and Histopathological Cardiomyopathy Diagnosis Discrepancies in Heart Transplant

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Purpose: Heart failure is a clinical syndrome with many underlying aetiologies, determined by clinical assessment and diagnostic tools. Correct identification affects patient care and in a genetic age, may also affect their families. Prior explant studies show clinical diagnosis is inaccurate in 6-23% of orthotopic heart transplants (OHT). A recent study showed no misdiagnosis when both cardiac magnetic resonance imaging (CMR) and endomyocardial biopsy were done. The aim was to identify the prevalence of clinical and histopathological discrepancy in OHT and assess the impact of CMR.

Methods: We retrospectively reviewed all OHT at our quaternary centre from December 2010 to January 2021. Unavailable explants were excluded. We compared the pre-transplant clinical diagnosis, determined by heart failure/transplant cardiologists and post-transplant pathological diagnosis, determined by cardiac pathologist.

Results: Over a decade 376 patients underwent OHT; mean age was 52 years, 73% (273) male. A clinical and histopathological discrepancy occurred in 54 (14%) cases. This improved from 7 of 23 patients (29%) in 2011 to 7 of 70 patients (10%) in 2020. When CMR was added to pre-transplant assessment diagnostic agreement rose from 85% to 91%. The most frequent misdiagnosis was dilated CM clinically (n=24), when histopathological diagnosis revealed ischaemic CM, myocarditis, hypertrophic CM or other (Table 1). Myocarditis and sarcoidosis were the most missed diagnosis with 77% and 57% respectively diagnosed on explant. In this group, only 1 patient had CMR but it had been performed 7 years prior to OHT.

Conclusion: In patients undergoing OHT 1 in 7 are misdiagnosed clinically, although this is improving with time and the utility of CMR. DCM is the most common misdiagnosis, whilst myocarditis and cardiac sarcoidosis remain the most common missed diagnoses. Precision in cardiac imaging techniques may allow for ongoing improvements in the diagnostic rates, improving targeted therapy and appropriate genetic screening.