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O16 Toward a combined DR + DQ HLA molecular mismatch score for risk stratification of pediatric heart transplant patients

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Aim: Human leukocyte antigen (HLA) molecular mismatch (HLAMM) is considered a biomarker of rejection. Few studies have explored its use in assessing rejection risk in pediatric heart transplant (PHTx) recipients. We have determined HLAMM cutoffs for donor specific antibody (DSA) and antibody mediated rejection (ABMR) risk in this PHTx cohort using combinations of HLA molecular mismatch algorithms. Here we work towards the development of a single risk score to generate concise results for clinical reporting.

Methods: Our cohort consisted of 100 recipient/donor pairs enrolled in the Clinical Trials in Organ Transplantation in Children. High resolution HLA typing was performed via NGS sequencing and detailed clinical data on DSA and ABMR outcomes were collected including only post-transplant DSA. Using our previously defined combined algorithm scoring system we placed patients in high, intermediate, and low risk categories for HLA-DR and HLA-DQ for DSA and ABMR. Scores were assigned to each risk category (high = 2, intermediate = 1, low = 0) for each antigen (DR/DQ) and summed to arrive at a final risk score, which was used in a Cox proportional hazard models to generate survival curves.

Results: EPLET + PIRCHE (Fig. 1A and 1D), EMMA + PIRCHE (1B and 1E), and EPLET + EMMA + PIRCHE (1C and 1F) methods were all able to risk stratify patients with a score of 0 having the lowest risk of DSA and ABMR and with a score of 4 having the highest risk. The combination of all three algorithms resulted in statistically significant differences in freedom from DSA and ABMR. The combination of two or three HLAMM algorithms with DR and DQ scoring may simplify immunological risk stratification.

Conclusion: Our combined DR + DQ risk score may better stratify PHTx patients for risk of developing DSA and ABMR. This new tool may someday facilitate individualized immunosuppression and post-transplant surveillance.

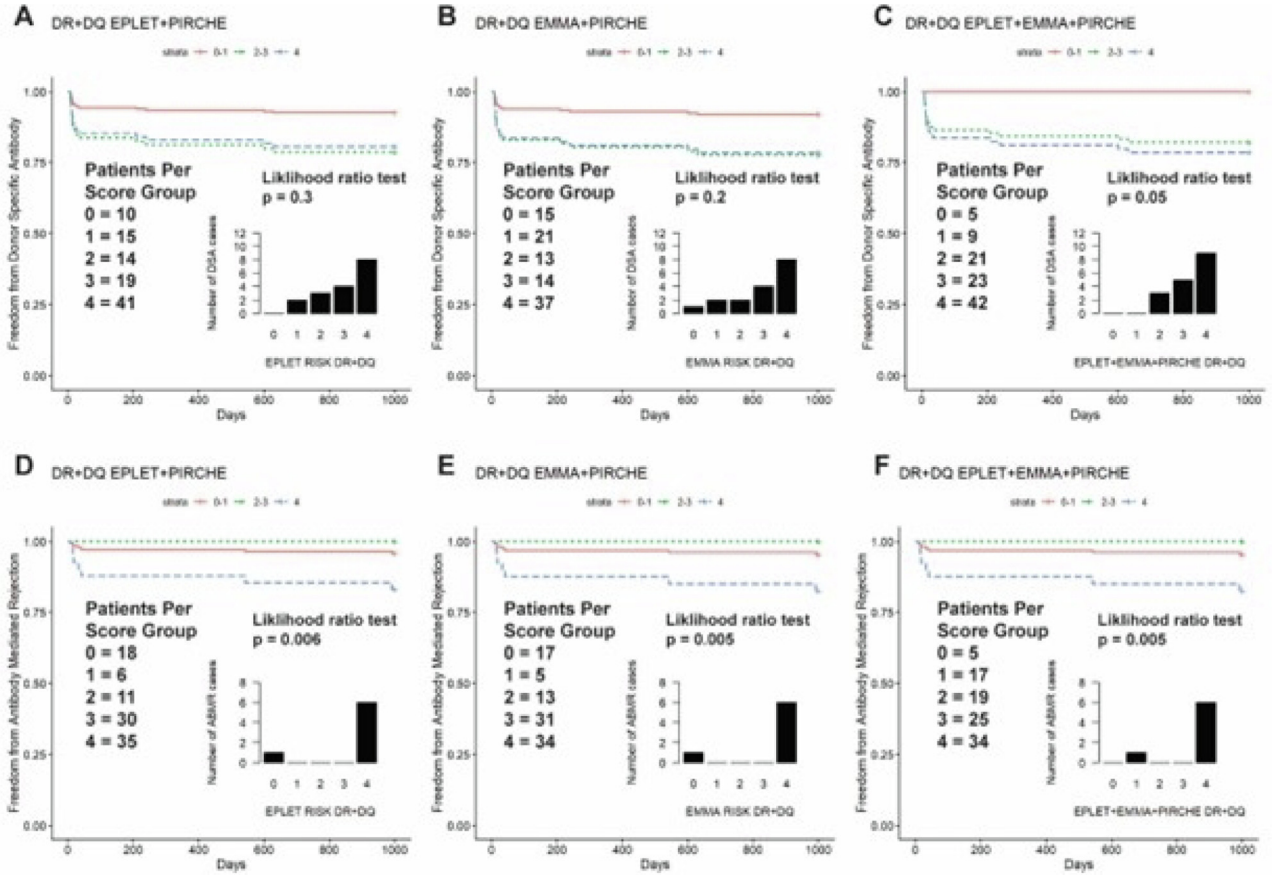

Fig. 1. Data from a Cox proportional hazard model for Freedom from Donor specific antibodies (A-C) and Freedom from Antibody mediated rejection (D-F). Scores are calculated as follows: for DR or DQ if a patient is considered high risk by the combined algorithm scoring method they receive two points, intermediate risk receives 1 point and low risk receives 0 points. Then scores for DR and DQ are summed for each patient to arrive at the score presented in this figure. Three HLA molecular mismatch algorithms were used: HLAMatchmaker (EPLET), HLA-EMMA (EMMA) and PIRCHE-II (PIRCHE). Combined scores were generated for EPLET + PIRCHE (A and D), EMMA + PIRCHE (B and E), and EPLET + EMMA + PIRCHE (C and F). Black bar graphs show the number of patients with the outcome of interest at each score level for the combined method being assessed.

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