Impact of HLA Molecular Mismatch Load on Immune-Mediated outcomes in Heart Transplant Recipients Bridged with Temporary Mechanical Circulatory Support

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Introduction

Molecular HLA matching is an emerging approach for assessing donor-recipient compatibility and improving immunologic risk stratification after heart transplantation. We evaluated whether HLA molecular mismatch load is associated with post-transplant outcomes in heart transplant recipients bridged with temporary mechanical circulatory support (tMCS).

Objective

To determine the association between HLA molecular mismatch load, measured by PIRCHE-T2 and PIRCHE-B scores, and immune-mediated post-transplant outcomes in heart transplant recipients bridged with temporary mechanical circulatory support (tMCS), and to assess its potential utility for clinical risk stratification.

Methods

We retrospectively evaluated 50 heart transplant recipients (HTRs) bridged with temporary mechanical circulatory support (tMCS) at Mayo Clinic between 2020 and 2023, with up to 3 years of follow-up. HLA molecular mismatch load was assessed using donor HLA-derived indirectly recognizable T-cell epitopes (PIRCHE-T2) and surface-accessible HLA amino acid mismatches (PIRCHE-B). We determined the incidence of donor-specific antibodies (DSA), acute cellular rejection (ACR), cardiac allograft vasculopathy (CAV), antibody-mediated rejection (AMR) and C4d-associated acute cellular rejection.

Figure 1

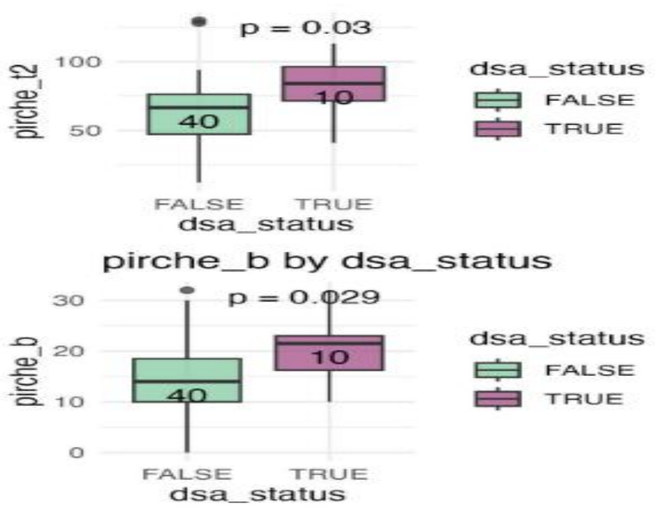


Figure 1. Higher PIRCHE-T2 and PIRCHE-B scores were associated with the development of donor-specific antibodies (DSA) (p=0.03 and p=0.029, respectively).

Figure 2

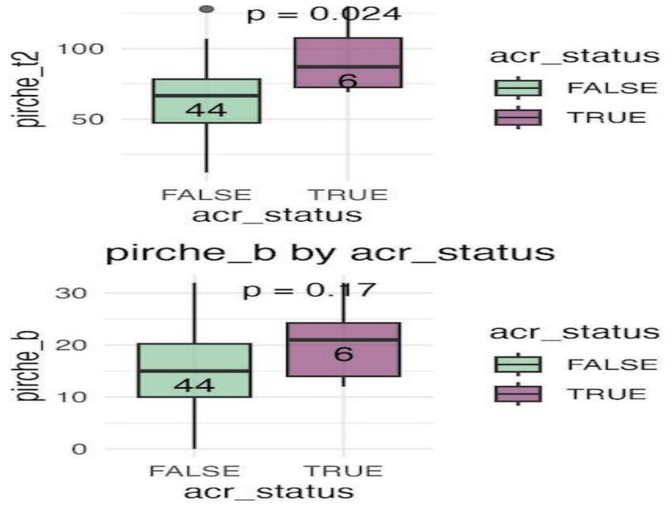


Figure 2. Higher PIRCHE-T2, but not PIRCHE-B, scores were observed in recipients with acute cellular rejection (ACR) (p=0.024 and p=0.17, respectively).

Figure 3

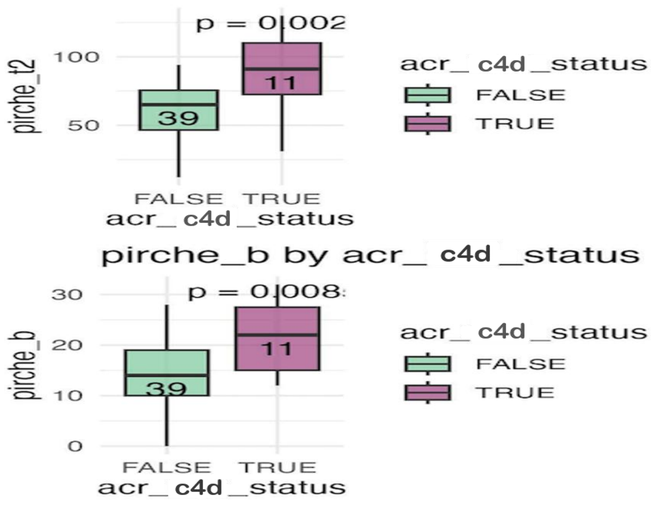


Figure 3. Higher PIRCHE-T2 and PIRCHE-B scores were associated with C4d-associated acute cellular rejection (p=0.002 and p=0.008, respectively).

Results

- Higher PIRCHE-T2 and PIRCHE-B scores were significantly associated with the development of HLA donor-specific antibodies (DSA) (p=0.03 and p=0.029, respectively).
- Higher PIRCHE-T2 and PIRCHE-B scores were also significantly associated with C4d-associated acute cellular rejection (p=0.002 and p=0.008, respectively).
- PIRCHE-T2, but not PIRCHE-B, was associated with an increased burden of de novo donor-specific antibodies (dnDSA).
- PIRCHE-T2 was significantly associated with a composite endpoint of acute cellular rejection (ACR), CAV, and C4d-associated rejection, reflecting cumulative alloimmune injury.

Conclusions

- Molecular HLA mismatch assessment using PIRCHE-T2 identifies heart transplant recipients bridged with tMCS who are at increased risk for immune-mediated post-transplant complications.
- Larger multicenter prospective studies are needed to validate these findings and further define the role of PIRCHE-based molecular matching in heart transplantation.

References

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