

Relationship between HLA sensitization and heart transplant outcome <u>Hyun-Ji Lee¹, Soo Yong Lee², Kyung-Hwa Shin³, Yun Ji Hong⁴ Shinae Yu⁵</u> ¹ Department of laboratory medicine, Pusan National University Yangsan Hospital ² Division of Cardiology, department of internal medicine, Pusan National University Yangsan Hospital 3 Department of laboratory medicine, Pusan National University Hospital 4 Department of laboratory medicine, Seoul National University Bundang Hospital 5 Department of laboratory medicine, Haeundae back Hospital Inje University College of Medicine,

INTRODUCTION

•Alloimmunization is triggered by left ventricular assist device (LVAD) surgery, and the number of highly sensitized patients with chronic heart disease is increasing. Historically, transplantation is not recommended if Human Antigen (HLA) crossmatching is positive. However, with Leukocyte advancements in medicine, desensitization therapy is used in a variety of ways, and transplantation is increasingly being performed, even in patients at a high risk of transplant rejection. This study examined the association between pre-transplant HLA antibody test results, HLA crossmatching and heart transplantation outcomes.

Material and Method

• In total, 121 heart transplant (HT) recipients between June 2014 and November 2023 were included in this study. Patients on the HT waitlist were screened for Penal Reactive Antibody (PRA) as part of a pre-transplant workup. The patient was tested for HLA-Donor-specific antibodies if the results were positive. When the heart was available for transplantation, the crossmatch test was performed. The B and T lymphocyte flow cytometry crossmatch (FCXM) assays were performed. Antibody-mediated reaction (AMR) and T-cell-mediated rejection (TCMR) were diagnosed according to the 2017 Banff classification.

Result

• The average age of the patients was 55.22±11.78 years. Of the 121 HT patients, 62 (51.2%) had a TCMR episode, and 9 (7.4%) had an AMR episode. The intensity of de novo HLA-DSAs ranged from 1,018 to 23,083, with a median of 2,283. Of the de novo HLA-DSAs, HLA classes I and II were present in 28 and 36 patients, respectively. HLA class I or II antibodies were present in 19 patients.

Table 1. Baseline characteristics of 121 heart transplant recipients

| Variables | Data |
|---------------|-------------|
| Sex (F/M) | 43/78 |
| Age | 55.22±11.78 |
| cPRA I | 19.40±30.65 |
| cPRA II | 27.26±35.25 |
| Preformed DSA | 20 |
| De novo DSA | 46 |
| CDC | 3 |
| FCXM-T | 8 |
| FCXM-B | 7 |
| Rejection | 53 |
| TCMR | 58 |
| AMR | 9 |
| Mortality | 22 |



Figure 1 Kaplan–Meier curves for (a) acute antibody–mediated rejection and (b) T cell-mediated rejection according to the sensitization status.

- Table 2 shows the relationships between cPRA values and mortality, FCXM, AMR, TCMR, de novo DSA, and preexisting DSA. Patients with cPRA values > 50 were associated with AMR occurrence and positivity for T-FCXM and B-FCXM compared to patients with cPRA values < 50.
- The incidence of rejection reactions was calculated using the Kaplan-Meier curve analysis based on the sensitization level The AMR hazard ratio in patients with HLA crossmatch positive relative to patients with cPRA 1-49 was 34.76 (95% CI = 1.92 - 626.71; P < 0.001).

Table 2. Association of cPRA with preexisting DSA, FCXM, and acute rejection using different cPRA cut-off values

| | cPRA(I) | | | | | | | | |
|-------------------|------------|---------------|-------|-------------|------------|-------|-------------|----------|-------|
| Variables | 35< (N=93) | ≥35 (N=28) | Ρ | 50< (N=104) | ≥50 (N=17) | Ρ | 90< (N=112) | ≥90(N=9) | Ρ |
| pDSA(N/Y) | 85/8 | 16/12 | 0.000 | 93/11 | 8/9 | 0.000 | 97/15 | 4/5 | 0.001 |
| De novo DSA (N/Y) | 64/29 | 11/17 | 0.005 | 68/36 | 7/10 | 0.057 | 71/41 | 4/5 | 0.260 |
| FCXM-T(N/P) | 92/1 | 21/7 | 0.000 | 102/2 | 11/6 | 0.000 | 107/5 | 6/3 | 0.001 |
| FCXM-B(N/P) | 92/1 | 22/6 | 0.000 | 101/3 | 13/4 | 0.001 | 107/5 | 7/2 | 0.028 |

| AMR(N/Y) | 91/2 | 21/7 | 0.000 | 102/2 | 10/7 | 0.000 | 107/5 | 5/4 | 0.000 |
|----------------|-------|-------|-------|-------|------|-------|-------|-----|-------|
| TCMR(N/Y) | 43/50 | 16/12 | 0.311 | 47/57 | 12/5 | 0.052 | 52/60 | 7/2 | 0.070 |
| Mortality(L/D) | 75/18 | 24/4 | 0.542 | 85/19 | 14/3 | 0.951 | 91/21 | 8/1 | 0.568 |



• It was observed that AMR incidence increased with patient sensitization level. Compared to patients with a cPRA \leq 50, patients with a cPRA \geq 50 were linked to

AMR development and FCXM positivity.