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Impact of Individual Eplets to Acute Rejection in Kidney Transplant Recipients: Machine Learning Analysis of Korean Organ Transplantation Registry

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Introduction: Epitope matching has been shown to predict allograft survival and development of de novo donor-specific antibodies. However, superiority of eplet mismatch to predict rejection outcome than that of HLA genotype mismatch were not thoroughly investigated.

Methods: Patients included in the Korean Organ Transplantation Registry(KOTRY) were used. Kidney transplant recipients who received transplants from 2014 to 2021 were enrolled. HLA four-digit genotypes were imputed by matching to the four-digit haplotype distribution as our previous method. The primary outcome measurement was acute rejection, biopsy-proven acute rejection (BPAR), T-cell mediated rejection (TCMR) and B-cell mediated rejection (BCMR) within 1 year. Ten-fold cross-validated Extreme Gradient Boost (XGBoost) model and logistic regression were used as statistical method and cross-validated receiver operating characteristics (ROC) curves were compared.

Results: Among 9,150 donor-recipient pairs, four digits HLA estimation were successful in 7,607 pairs. Exact 1:1 matching of HLA haplotype were successful in 1,980 pairs (call 4 digits group). Mean class I and class II eplet mismatches were 10.6 ± 7.1 and 17.8 ± 12.4 respectively. As depicted in Table, area under curve (AUC) of individual eplets are not better than HLA mismatch numbers in total population (0.549 vs. 0.576 by XGBoost and 0.562 vs 0.568 by logistic regression). In call 4 digits group, individual eplets using XGBoost better predict acute rejection (0.585 vs 0.575), BPAR (0.536 vs 0.500), TCMR (0.535 vs 0.500) than HLA mismatch numbers. Sum of eplet mismatch by logistic regression did not show any better predictability to rejection episode than HLA mismatch numbers.

Conclusion: In this Korean population study, individual eplet mismatches predicted acute rejection better than HLA mismatches in the subpopulation who had accurate 4 digits matched subpopulation. Sum of eplet mismatch number did not show better predictability than HLA mismatch numbers.