Predictability of eplet mismatch to acute rejection in low level HLA mismatched kidney transplantation: validation analysis of Korean Organ Transplantation Registry (KOTRY) data

Jong Cheol Jeong¹, Hyeong Eun Son¹, Yeon Ho Park², Inwhee Park³, Jae Berm Park⁴, Dong Wan Chae⁵, Jaeseok Yang⁶, Yun Ji Hong⁷, Borae G. Park⁸

¹Division of Nephrology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

²Department of Surgery, Gachon University Gil Medical Center, Incheon, Korea

³Division of Nephrology, Department of Internal Medicine, Ajou University School of Medicine, Suwon, Korea

⁴Department of Surgery, Sungkyunkwan University School of Medicine, Suwon, Korea

⁵Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea

⁶Department of Surgery, Seoul National University Hospital, Seoul, Korea

⁷Department of Laboratory Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

⁸Department of Laboratory Medicine, Korea University Guro Hospital, Seoul, Korea

Background: Epitope matching has been shown to better predict allograft survival and development of de novo donor-specific antibodies. There was no large scale Korean study for epitope matching and kidney transplantation outcomes.

Methods: Patients included in the Korean Organ Transplantation Registry (KOTRY) were used. Kidney transplant recipients who received transplants from 2014 to 2017 were enrolled. As an external validation cohort, retrospective KOTRY data (kidney transplant pairs from 2009 to 2012) were used. Human leucocyte antigen (HLA) four-digit genotypes were imputed by matching to the four-digit haplotype distribution in the Korean bone marrow donor program. DQ genotyping was imputed by linkage-disequilibrium association. The primary outcome measurement was biopsy-proven acute rejection.

Results: Among 5,872 donor-recipient pairs, four-digit haplotype pairs were successfully imputed. Mean numbers of mismatched class I and class II eplets were 10.5 ± 6.8 (range, 0–35) and 24.1 ± 17.4 (range, 0–85), respectively. Mean eplet mismatch numbers were increased according to the number of HLA antigen mismatches (beta, 9.340; 95% confidence interval [CI], 9.145–9.534; $P < 0.001$). Eplet mismatch was associated with acute rejection in the unadjusted models (class I: 1.022, 95% CI, 1.011–1.033; $P < 0.001$; class II: 1.011, 95% CI, 1.007–1.015; $P < 0.001$). When controlled with clinical covariates and HLA mismatch numbers, eplet mismatch numbers did not show additional predictability for acute rejection (AUC comparison: eplet model vs. HLA serotype model, 0.615 [95% CI, 0.594–0.636] vs. 0.619 [95% CI, 0.598–0.640]; $P = 0.491$). However, eplet class II mismatches over 60 were shown to be significant risk predictors in low HLA serotype mismatches (one or two mismatches) in a non-linear model.

Conclusions: In this external validation study, eplet mismatches in class II MHC were found to be significant risk factors for acute rejection with a low number of HLA mismatches (one or two mismatches).

Corresponding author: Jong Cheol Jeong

E-mail: jcyj0425@empal.com

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