High HLA class II DR/DQ Epitope-Mismatch loads are associated with poor allograft kidney survival

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Background/Aims: HLA matching has been an essential role of the risk assessment for long term graft outcome in kidney transplantation recipients. Recent HLA epitope matching at HLA-DR and HLA-DQ loci between donor and recipient are better predictors for the development of de novo DSAs(donor specific antibody) and graft outcome. Purpose of this study is to evaluate clinical significance of HLA class II epitope mismatch for development of de novo DSA and graft outcome.

Methods: We examined 178 kidney transplant recipients for development of DSAs from June 2015 to June 2018. We excluded patients whose data on HLA-DQ matching were missing and HLA class II epitope matching was not available. A nadir FK trough level was collected over 6 months prior to the development of de novo DSA. We compared HLA-DR/DQ matching / HLA class II epitope matching and a nadir FK level over 6month prior to DSA occurrence for the development of de novo DSA and graft outcome.

Results: 25 of 178 stable KTRs (14.0%) had HLA class II DSAs (10DR-DSA/14DQ-DSA,1 combined DR-and DQ-DSA) on SAB, The median follow-up was a 90.0±5.9 month (range 0-215). Mean HLA mismatch numbers were 3.5±0.2. Six (3.4%) of 25 de novo HLA class II DSA had biopsy-proven CABMR (chronic antibody-mediated rejection). Three of 5DQ-DSA positive-patients and one of 1DR-DSA positive patient were lost graft function to CABMR. Not High DR epitope mismatch load(DR epitope mm≥10) but High DQ epitope mismatch loads(DQ epitope mm ≥17) and the lowest FK trough level (<6ng/ml) during the past 6month prior to de novo DSA occurrence were significantly associated with the development of de novo DQ-DSA. Independent predictors of graft failure on multivariate analysis were CABMR, development of de novo DQ DSA.

Conclusions: Our study showed that combined high DR /DQ epitope mismatch loads and less than 6ng/ml of FK trough levels over 6month prior to development of de novo DSAs are associated with the development of de novo DSAs which subsequently lead to CABMR and graft failure.