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Optimal Tacrolimus Trough Levels and Allograft Outcomes in Kidney Transplant Recipients: Insights from a Multicenter Real-World Study in South Korea

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Introduction: The optimal tacrolimus trough levels after kidney transplantation (KT) and its impact on allograft outcomes remains uncertain. Evidence regarding the association with long-term outcomes is limited. Our study aimed to evaluate the relationship between time-varying periodic mean tacrolimus trough levels and composite allograft outcomes in KT recipients across five transplant centers in South Korea.

Methods: Data from 10,329 patients who underwent KT during 2005-2020 was retrieved from the institutional clinical data warehouse (CDW). Two-month periodic mean was derived from outpatient tacrolimus trough levels for 2-12 months post-transplant and categorized into seven ranges. The inverse probability of treatment weighting (IPTW) method with stabilized weights was utilized to assess the relationship between time-varying tacrolimus levels and the 1-year composite outcome (biopsy-proven acute rejection, renal dysfunction, de novo donor-specific antibodies, and death-censored graft failure). We also analyzed the association between the 1-year periodic mean from 2-6 years post-transplant and the 6-year outcomes.

Results: The overall incidence of the composite allograft outcome at 2-12 months and 2-6 years post-transplant was 11.2% and 23.1%. With 8ng/ml as reference, tacrolimus levels below 3ng/mL and 3-3.9ng/mL were associated with a higher likelihood of developing the 1-year composite allograft outcome, while 4-4.9ng/mL showed higher hazards of dnDSA development and graft failure. Conversely, 5-5.9ng/mL, 6-6.9ng/mL, and 7-7.9ng/mL groups had lower risks of developing the composite allograft outcome (See Table). For the 2-6 year outcome, trough levels 5-5.9ng/mL and 6-

6.9ng/mL showed benefit over 8ng/ml (aHR 0.68, 95%CI 0.53-0.87, p=0.0024 and HR 0.65, 95% CI 0.50-0.85, p=0.0012)

Conclusion: This real-world multicenter study in South Korea provides important insights into the association between tacrolimus trough levels and allograft outcomes in KT recipients. The findings suggest that maintaining a target trough level of 5-7.9ng/mL during 2-12 months post-transplant, and 5-6.9ng/mL during 2-6 years post-transplant, is associated with better allograft outcomes.