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Intrapatient variability of tacrolimus and acute kidney injury may be associated with the development of chronic kidney disease after liver transplantation

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Introduction: In this study, we aimed to examine the long-term effects of acute kidney injury (AKI) and inpatient variability of immunosuppressants (ISs) on the development of chronic kidney disease (CKD) and end-stage renal disease (ESRD) following liver transplantation (LT).

Methods: We consecutively enrolled patients who underwent LT at Seoul St. Mary's hospital between 1993 and 2018 in our study. Baseline kidney function was defined at the time of LT. The diagnosis of CKD was established based on a persistent eGFR lower than 60ml/min/1.73m^2 over six months. Stage 5 CKD (ESRD) was defined as an eGFR<15 ml/min/1.73m^2. The intrapatient variability (IP) of IS was evaluated based on the coefficient of variant for each patient.

Results: Among 1113 eligible patients, 952 were included in our study, divided into a normal group with eGFR≥60 ml/min/1.73m2 (n=752) and an AKI group with eGFR<60 ml/min/1.73m2 (n=200). The development of CKD was significantly earlier (15 vs. 9 months; P<0.05; Figure A) and more frequent (P<0.001, Figure B) in the AKI group compared to the normal group. The development of ESRD was also more common (n=23 [3.1%], normal group; n=20 [10.0%], AKI group) and earlier in the AKI group compared to the normal group (47.4 vs. 97.4 months, P<0.001). Regarding IS with tacrolimus in the normal group, patients with CKD development showed significantly higher and more variable drug level and level/dose compared to patients without CKD (Figure C). Finally, both in the normal and AKI groups, patients with CKD development demonstrated higher IP in the drug dose and level compared to patients without CKD during follow-up (Figure D).

Conclusion: Our study reveals that AKI and high IP of tacrolimus could be associated with the risk of developing CKD after LT. Consequently, preventing AKI prior to LT and implementing a tailored management of IS are vital in preventing CKD after LT.