Abstract Type : Poster exhibition
Abstract Submission No.: A-0645
Abstract Topic : Transplantation

Long-Term Tacrolimus Intra-Patient Variability Patterns and Their Prognostic Impact on Kidney Transplant Outcomes

Kyungho Lee[1], Sungjoo Lee[2], Junseok Jeon[1], Kyo Won Lee[3], Hye Ryoun Jang[1], Jung Eun Lee[1], Jae Berm Park[3], Kyunga Kim[2], Wooseong Huh[1]
[1]Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Korea, Republic of
[2]Department of Data Convergence & Future Medicine, Sungkyunkwan University School of Medicine, Korea, Republic of
[3]Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Korea, Republic of

Objectives : Tacrolimus intra-patient variability(TacIPV) is known as a marker of nonadherence and is associated with poor kidney transplant(KT) outcomes. While previous studies have focused on short-term TacIPV, long-term patterns of TacIPV and their clinical impact remain less understood. We aimed to classify TacIPV trajectories beyond one-year post-transplant using machine learning and evaluated their association with long-term KT outcomes.
Methods : We identified living donor KT recipients maintained on tacrolimus without changes between 2001 and 2016 at Samsung Medical Center. TacIPV was assessed in each of five post-transplant periods(6–12, 13–24, 25–36, 37–48, and 49–60 months) using variation independent of mean. Patients were clustered based on time-dependent TacIPV patterns using unsupervised machine learning. Primary outcome was a composite endpoint of late biopsy-proven acute rejection, doubling of serum creatinine, and death-censored graft failure. Cox regression models were used to determine association between TacIPV patterns and outcomes.
Results : Among 496 patients, the following four distinct TacIPV trajectory clusters were identified: Cluster 1(57%) exhibited persistently low TacIPV, while Cluster 2(22%) showed high TacIPV in early post-transplant period followed by a decrease. Cluster 3(16%) had initially low TacIPV, followed by a transient rise at one-year, before returning to low level thereafter. Cluster 4(5%) maintained consistently high TacIPV over time. Patients in Clusters 2, 3, and 4 had higher incidence rates of composite outcome compared to Cluster 1, with rates of 7.18(P=0.064), 9.61(P=0.001), and 8.91(P=0.059), respectively, versus 5.29/100 person-years in Cluster 1. Risk of composite outcome was significantly higher in Clusters 2, 3, and 4 compared to Cluster 1, with adjusted hazard ratios of 1.45(95%CI, 1.04–2.02), 1.77(1.23–2.55), and 1.79(1.03–3.12), respectively.
Conclusions : Transient fluctuations of TacIPV beyond one-year post-KT are associated with worse graft outcomes as persistently high TacIPV, highlighting critical importance of consistent medication adherence. Sustained adherence interventions with continuous TacIPV monitoring through a multidisciplinary approach may improve long-term graft outcomes.