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## **Gut microbiome and acute rejection after kidney transplantation**

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**Objectives:** Acute rejection (AR) is a common complication in kidney transplantation (KT) and associated with reduced patient-graft survival. Recent studies have shown that the gut microbiota modulates the host immune system and is related to complications in transplant recipients. Here, we aimed to evaluate the impact of the gut microbiota on AR after KT.

**Methods:** We prospectively enrolled renal transplant recipients and collected serial stool specimens before and at 3 and 12 months after transplantation in two tertiary centers. Metagenomic DNA was isolated from feces, sequenced using by Illumina MiSeq system, and analyzed for microbial composition. We investigated the association between fecal microbiomic composition of the three sample time points and biopsy-proven AR within a year after KT.

**Results:** A total of eighty-six recipients were included in the final analysis. The mean age was 49.1 ± 12.2 years and 45 (58.1%) were men. Among them, 35 (40.7%) experienced AR by either protocol or indication graft biopsies. In longitudinal microbiota analysis, over time, the Shannon diversity index as makers of microbial diversity showed a significant drop only in no AR group (p=0.000). Principal coordinate analysis was used to visualize sample relationships based on phylogenetic distance. Clear clustering of the samples was observed based on sampling time points only in no AR group (p=0.005). Microbiota compositions between before KT and 12 month after KT was more similar in AR group than in no AR group. Fecal *Bifidobacterium* abundance was positively correlated with eGFR at 3 month (R=0.33, P=0.001) and fecal *Christensenella*, *Eisenbergiella*, *Prevotella* abundance was negatively correlated with eGFR at 3 month (R=-0.33, P=0.002; R=-0.41, P=0.001; R=-0.38, P=0.002). The change patterns of these bacterial abundances showed no differences between two groups.

**Conclusions:** Our findings suggest that longitudinal changes in gut microbiota have the potential to be indicative of rejection.