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Impact of aging on kidney-gut crosstalk after acute kidney injury

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Objectives: The interactions between the kidneys and distant organs could significantly affect the outcome of AKI, however the impact of aging on the remote organ effects of AKI are still unknown. Here, we investigated the effects of aging on kidney and gut crosstalk in animal models.

Methods: In young and aged C57BL/6 mice, 25min bilateral ischemia reperfusion injury (IRI) was applied, and then colon inflammation, histological changes and intestinal barrier integrity were compared for 28 days post-IRI. To determine the role of the microbiome on kidney-gut crosstalk, we analyzed microbiome from feces in young and aged mice and examined the effects of probiotics supplementation.

Results: M1 predominant inflammation was observed in the kidneys of aged mice compared to young mice for 28 days after IRI. Interestingly, this intrarenal inflammatory milieu in aged mice was similarly observed in the colon on day3 post IRI. The increased inflammatory cytokines in the colon were accompanied by an increase in TUNEL-positive apoptotic colon epithelial cells, resulting in increased intestinal permeability in aged mice for 28 days. The AKI-induced "leaky gut" also showed a strong positive correlation with high TNF- α expression in mesenteric lymph nodes. Microbiome analysis revealed that microbial community of aged mice was clearly distinguished from young mice and a decrease in Lactobacillus is one of the major changes in microorganisms in aged mice at the genus level, suggesting that microbiota alteration in aged mice contributes to increased colon inflammation and permeability. However, Lactobacillus supplementation to aged mice did not show a positive effect on the increased AKI-induced leak gut.

Conclusions: AKI in aged mice results in a more M1-related inflammation and "leaky gut", which might be mediated by dysbiosis in aged mice. However further research is needed to clarify the role of aging-related microbiota alteration in kidney and gut crosstalk.