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Oral Communication Abstract
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Time restricted feeding ameliorates fibrosis by restoring disrupted peripheral clock in adenine induced CKD model

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Objectives: Circadian disruption has recently been demonstrated to be closely associated with various metabolic diseases. Time restricted feeding (TRF) is a dietary strategy that limit the time of eating to a window of 4-12hr per day and has been shown to resynchronize peripheral clock. In this study, we aimed to investigate the relationship between circadian disruption and chronic kidney disease (CKD). We also tested whether TRF confer renoprotective effect via restoration of peripheral clock.

Methods: First, we compared the oscillation of peripheral clock genes as well as physiologic parameters in the control and adenine induced CKD mice. To determine the role of circadian disruption on CKD progression, renal function was compared between WT and Bmal1 knockout mice. In addition, adenine-induced CKD mice were given either a ad libitum diet or a TRF for 8 weeks and the effect of TRF on CKD progression as well as oscillation of peripheral clock genes were measured.

Results: Adenine induced CKD mice showed disrupted oscillation of peripheral clock genes and this was associated with loss of rhythmic oscillations of GFR, tubular functions and urine output. Meanwhile, more severe fibrosis and lower GFR were observed in Bmal1 knockout mice compared to WT mice, showing a bidirectional relationship between disturbed circadian rhythm and CKD progression. TRF in adenine induced CKD mice significantly suppressed interstitial inflammation as well as cell cycle arrest and ultimately ameliorated worsening of renal function and fibrosis. These changes were accompanied by partial restoration of disturbed oscillation of peripheral clock genes, suggesting that renoprotective effect of TRF is partially mediated by restoration of peripheral clock.

Conclusions: Our data demonstrated a unique bidirectional relationship between the circadian disruption and CKD and suggest that disruption of peripheral clock might contribute to CKD progression. The renoprotective effect of TRF might be mediated via resynchronizing disrupted peripheral clock in the kidney.