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### Role of NRF2 in Adenine-induced CKD Model with Sarcopenia

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**Objectives :** Chronic kidney disease (CKD) that causes accelerated cardiovascular disease and the risk of death in the majority of patients, and loss of muscle mass is a common complication in patients with CKD. Moreover, sarcopenia in CKD strongly affected to mortality of CKD patients. However, the fundamental mechanism of sarcopenia in CKD remains unclear and its diagnostic biomarkers are uncertain.

**Methods :** To establish a CKD mice model, AIN93G-casein and AIN93G-0.15% adenine feed were prepared and fed to mice. Casein control diet was provided for 1 week to adapt. After the adaptation period, mice in the control group were provided with a casein control diet, and mice in the CKD-induced group were provided with a 0.15% adenine supplemented diet for 8 weeks. Renal function was measured by estimating serum creatinine and serum BUN. Skeletal muscle was determined in gastrocnemius tissue by staining H&E, M-T, and Sirius red.

**Results :** In adenine induced CKD mice, kidney was clearly reduced and kidney damage was observed compared to the control group. NRF2 knockout mice were given an adenine diet in order to examine the role of NRF2 in sarcopenia in the CKD. It was verified using H&E staining that the muscle fibers in the adenine diet group were smaller than those in the control group. M-T stain showed that CKD mice exhibited increased muscle fibrosis and exacerbated the severity of fibrosis in NRF2 deletion. Furthermore, CKD group had severe collagen deposition than control group, and it was worsened in NRF2 knockout mice.

**Conclusions :** In this study, we established CKD and demonstrated underlying association with sarcopenia through the adenine dietary model. Fibrosis and collagen deposition brought on by NRF2 deficiency aggravate sarcopenia in CKD. We propose a potential therapeutic approach for NRF2 activation in CKD-related sarcopenia, supporting significant association between NRF2 expression in sarcopenia of CKD.