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Indoxyl sulfate is more important predictor for sarcopenia than myostatin in patients with chronic kidney disease: post-hoc analysis from RECOVERY study

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Objectives: Serum myostatin levels are increased according to renal function decline and myostatin may be main mediator of chronic kidney disease(CKD)-related sarcopenia. In CKD animal model, indoxyl sulfate (IS) has increased myostatin expression, potentially leading to skeletal muscle atrophy. However, there is no data about relation between myostatin and IS in CKD patients. The aim of this study was to assess the association between serum myostatin and IS levels and muscle mass in CKD patients. We performed a post-hoc analysis of data extracted from a RECOVERY study.

Methods: A total of 150 CKD patients were enrolled in the multi-center randomized controlled study. Skeletal muscle mass index (SMI) was calculated for muscle mass and low muscle mass was defined as an SMI <7.0 kg/m² and <5.7 kg/m² in women. Sarcopenia was assessed using the AWGS 2019. We classified patients into two groups according to the median value of myostatin: patients with high myostatin levels (≥4.5 ng/mL) and those with low myostatin levels (<4.5 ng/mL). In addition, IS levels were divided into high (≥0.365 pg/mL) and low (<0.365 pg/mL) groups.

Results: The proportion of sarcopenia and low muscle mass was higher in patients with low myostatin levels or high IS levels than in those with high myostatin levels or low IS levels. Myostatin levels were negatively associated with IS levels. Myostatin levels had a positive association with SMI, while IS levels had a negative association with SMI. Myostatin levels were not associated with creatinine, but IS levels and myostatin/SMI reflecting muscle mass were associated with creatinine. Sarcopenia were independently associated with older age and higher IS levels after adjustment for gender, DM, creatinine, and myostatin/SMI. Myostatin levels were not predictor for sarcopenia in CKD patients.

Conclusions: These data suggest that IS has the potential to decreased muscle mass resulting in suppressing myostatin expression in CKD patients.