

Elucidation of the pathogenesis of muscle sarcopenia caused by liver fibrosis

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In patients with liver fibrosis, muscle mass and muscle strength tend to decline, which affects their prognosis. In 2016, the *Sarcopenia Criteria for Liver Disease (First Edition)* was established. However, it is unclear why hepatic fibrosis leads to muscle weakness. We induced hepatic fibrosis by performing bile duct ligation (BDL) in mice and investigated the pathogenesis of muscle atrophy caused by hepatic fibrosis. In BDL mice, the weight and cross-sectional area of the tibialis anterior muscle decreased from the first week after surgery in the early stage of fibrosis. We performed forelimb grip tests to confirm a significant decrease in muscle strength. From these results, we considered that hepatic fibrosis-dependent muscle sarcopenia model had been established.

Using this model, we investigated the cause of hepatic fibrosis-dependent muscle atrophy. We applied BDL mouse serum to cultured myotube cells in vitro, and myotube atrophy was induced. This suggested the possibility of multi-organ linkage in which atrophy-inducing factor was transmitted via blood as a mechanism of muscle atrophy dependent on liver fibrosis. Currently, in order to search for atrophy-inducing factors present in the blood, we are analyzing several cytokines that have been reported to be involved in muscle atrophy.