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Editorial: sarcopenia in liver transplantation – our weakest patients may need the strongest push

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Sarcopenia was identified nearly 60 years ago as a common manifestation of advanced cirrhosis. Although risk prediction in advanced liver disease has been focused on laboratory-derived criteria such as the MELD score, sarcopenia has garnered recent attention due to its association with adverse outcomes independent of MELD[1].

Bhanji *et al* reported the findings of a retrospective study of 293 adults who underwent liver transplantation between 2002 and 2006[2]. They characterized body composition using CT scans performed during routine clinical care and reported a progressive decrease in skeletal muscle index (SMI) with a concomitant increase in myosteatosis both leading up to transplantation with continuation post-operatively. After a year post transplant, only five patients resolved their pre-transplant sarcopenia and an additional 25 developed sarcopenia *de novo*. A limitation (not unique to this study) is the acquisition of sarcopenia measures from non-protocol-driven imaging resulting in high rates of missing follow-up imaging. Data extrapolated in this manner can also be heavily influenced by selection bias as patients who undergo imaging usually have some concern for complication or are being monitored for cancer, both of which are associated with sarcopenia[3]. While limited by its retrospective nature, this study broadens our understanding of the time course of sarcopenia post-transplant and its recovery—or lack thereof.

Sarcopenia in cirrhosis is thought to be multifactorial with metabolic, endocrine, and mechanical causes (Figure 1). The primary drivers of sarcopenia may be related to scavenging of skeletal muscle in order to obtain amino acids for gluconeogenesis in the absence of adequate hepatic function, ammonia-related myostatin activity, and low levels of anabolic hormones[4]. Although early satiety from ascites can be a contributing factor, portosystemic shunting induces skeletal muscle loss even in the absence of cirrhosis or ascites in rat models[5]. Furthermore, post-transplant recovery may be hampered by immunosuppression with corticosteroids and other anti-rejection therapy. In fact, muscle cell regeneration is thought to be mediated by a calcineurin-driven process[6].

Myosteatosis, denoted by hypoattenuation on CT, is the infiltration of fat into muscle and is associated with poor outcomes. The FrAILT study, among others, found that myosteatosis on CT but not SMI was more tightly correlated with waitlist mortality even after adjustment for grip strength, MELD, and Short Physical Performance Battery[1,7].

Despite its rising importance, no treatments definitively improve sarcopenia. Small uncontrolled studies in humans suggest a reversal of sarcopenia with Transjugular

Intrahepatic Porosystemic Shunt placement, increased muscle mass with testosterone replacement, and mitigated skeletal muscle loss with branch chain amino acid supplementation.[8–10] Despite several studies showing increased muscle mass, quality of life, and exercise capacity after short intensive physical activity programs, there is no existing evidence suggesting that these interventions alter waitlist or post-transplant outcomes[11]. Given the strong associations found in the literature with poor patient outcomes as well as the concerning signals noted in the study by Bhanji *et al*, a controlled, prospective study is warranted to track outcomes and body composition changes, and test the efficacy of interventions for this important problem.

Statements of Interests

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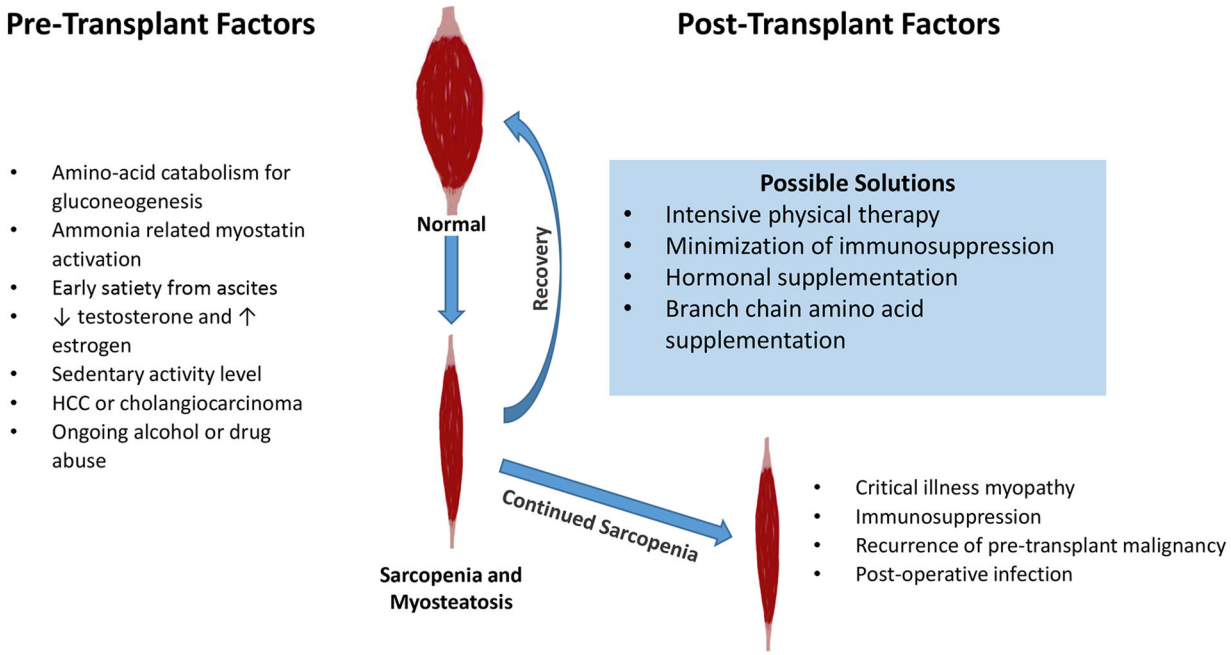

Figure 1.
Sarcopenia pathways and possible solutions.