Influence of skeletal muscle mass on graft regeneration after living-donor liver transplantation

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Body composition (BC) is defined as the relative proportion of fat, water, protein, and mineral components in the body and varies greatly among individuals. While skeletal muscle depletion is frequently seen in severely ill patients, sarcopenia, defined as a pathological reduction of skeletal muscle mass (SMM) and strength, is one of the most significant features of the metabolic imbalance related to end stage liver disease (ESLD). Accordingly, the assessment of BC was recently implemented in the European Association for the Study of the Liver (EASL) and American Association for the Study of Liver Diseases (AASLD) practice guidelines on nutrition in chronic liver disease. While sarcopenia was linked to clinical outcomes in a large variety of medical conditions, the prognostic value of muscle quality (muscle density or myosteatosis) over muscle quantity (SMM or sarcopenia) was recently identified by our group as a prognostic marker in deceased donor liver transplantation (LT) (1,2).

Over the last decades, the global prevalence of organ shortage and waiting list mortality has prompted physicians to transplant an increasing amount of extended criteria donor (ECD) allografts (3,4). An alternative strategy to address the problem of organ shortage is the implementation of living-donor liver transplantation (LDLT). In this scenario, ongoing liver graft regeneration represents a crucial process aiming at normalizing portal hypertension associated small-for-size syndrome and to meet metabolic and biosynthetic requirements of the recipient. As such, anabolic graft regeneration may also depend on the adequate availability of energy and metabolites (5).

In a recent article by Pravisani et al., the authors investigated the effects of loss of SMM as assessed preoperatively on computed tomography (CT) at L3 level on the graft regeneration rate (GRR) in 106 consecutive patients undergoing LDLT. While low SMM and sarcopenia are well known prognostic factors in patients undergoing whole-organ LT, little is known on BC-assessment and its impact on the GRR in the setting of LDLT. As such, the authors analyzed CT-images form 106 LDLT patients using the Synapse Vincent imaging processing software (Fujifilm, Tokyo, Japan). In brief, the third lumbar vertebra skeletal muscle index (L3-SMI) was expressed as cross-sectional muscle area/height, and the cut-off for a diagnosis of low muscle mass was L3-SMI <42 cm$^2$/m$^2$ for men and L3-SMI <38 cm$^2$/m$^2$ for women, according to recommendations of the Japanese Society of Hepatology. The study population showed a male-to-female ratio of 43:63 with a median BMI of 22.9 (20.8–26.5), and a mean pre-LT SMI of 47.2±9.1 and 39.1±7.1 for men and women respectively (P<0.001). While a low muscle mass was diagnosed in 45 patients (42.5%), the median graft volume-to-recipient standard liver volume percent (GV/SLV%) and graft-to-recipient weight ratio (GRWR) were 40% (36–47%) and 0.78 (0.66–0.92) respectively. Interestingly, pre-LT SMI showed a significant correlation with the postoperative GRR in man but not in women (P=0.04). Overall, a low GRR was significantly associated in patients with sarcopenia. When fitting a multivariable model with GV/SLV%, donor age, gender, pre-LT SMI, and SMIv%, pre-LT SMI remained
statistically associated with the GRR after LDLT. The authors conclude that during the anabolic process of liver regeneration, male recipients are rather affected from muscle loss while female patients experience fat depletion. Other factors, influencing GRR were the recipient's severity of illness preoperatively and the capability of the stress caused by the transplantation as a major surgical procedure, the immunosuppression and the impact of shear effect caused by perfusion after transplantation (5).

Sarcopenia and malnutrition in recipients before LT are well known predictors of morbidity and mortality (6). While the prognostic value of muscle quality (skeletal muscle density and myosteatosis) in comparison to muscle quantity (SMM, as the morphological aspect of sarcopenia) was recently investigated by our group in a cohort of whole-graft LT (1,2), its significance for LDLT remains to be determined. Myosteatosis describes pathological intramuscular adipose fat tissue deposition caused by metabolic dysregulation in patients with ESLD. The relevance of myosteatosis on graft regeneration may be linked to a muscle-to-liver-cross talking, with increased secretion of pro-inflammatory cytokines, adipocytokines and lowers the concentrations of myokines (7). This imbalance may in turn lead to systemic inflammation with an unfavorable immune response and restrained graft regeneration or even early allograft dysfunction (EAD) (2).

The assessment of the recipients BC- and nutritional status are not displayed in the current Model for End-Stage Liver Disease (MELD) LT-scoring system. Even though, the clinical estimation of BC and the assessment of their physical strength using conventional parameters (body weight, waist circumference, BMI, ability to walk or physical activity, and handgrip) is usually a difficult task to accomplish in these waiting-list patients, the present work from Pravisani et al. and others emphasize the relevance of BC-assessment in this LT context. Therefore, current and future clinical trials should also incorporate therapeutic interventions such as the monitoring of dietary intake, protein or branched-chain amino acid supplementation, prehabilitation, physical exercise, and/or pharmacotherapy.

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