Letter to the Editor

Sarcopenia plays a crucial role in liver transplantation

Toshimi Kaido, Yuhei Hamaguchi, Shinji Uemoto

Division of Hepato-Biliary-Pancreatic and Transplant Surgery, Department of Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Correspondence to: Toshimi Kaido, MD. Division of Hepato-Biliary-Pancreatic and Transplant Surgery, Department of Surgery, Graduate School of Medicine, Kyoto University, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan. Email: kaido@kuhp.kyoto-u.ac.jp.

Provenance: This is an invited Letter to the Editor commissioned by Editor-in-Chief Yilei Mao (Department of Liver Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China).

Response to: Pagano D, Barbieri L, Seidita A, *et al*. Importance of sarcopenia parameter changes after living donor liver transplantation. Hepatobiliary Surg Nutr 2017;6:193-5.

Submitted Aug 09, 2017. Accepted for publication Aug 23, 2017.
doi: 10.21037/hbsn.2017.08.05
View this article at: http://dx.doi.org/10.21037/hbsn.2017.08.05

To the editor,

We are grateful to Pagano *et al.* for commenting on our recent studies regarding the role of sarcopenia on outcomes after liver transplantation (LT) (1-7), including our recent paper describing the effects of pretransplant sarcopenia and sequential changes in sarcopenic parameters after living donor liver transplantation (LDLT) (7).

Based on our previous findings regarding the impact of pretransplant nutritional status, including skeletal muscle mass, we have added a new criterion for LT since January 2013 to exclude patients with severe sarcopenia: inability to walk unaided. Surprisingly, the 1-year overall survival rate after LT significantly improved to 94% compared with the rate under the previous criteria after implementation of the new criteria (8). Interestingly, patient background, including MELD score and Child-Pugh classification, did not significantly differ between patients in this cohort and that of our previous retrospective cohort (7). In other words, the outcome has dramatically improved only by adding one criterion, to exclude patients who cannot walk unaided, although the severity of patient condition or underlying liver disease did not differ before and after revision of our criteria. This finding validates our new criteria for LDLT that incorporate one sarcopenic factor. Moreover, in the present study, we defined the presence of sarcopenia by measuring not only skeletal muscle mass but also grip strength before LT to correctly define sarcopenia according to the definition of sarcopenia proposed by the European Working Group on Sarcopenia (9) and the Asian Working Group for Sarcopenia (10), although the cut-off value for skeletal muscle mass used in the present study was different from cut-off values proposed by these working groups. Consequently, the prospective cohort study demonstrated that patients with preoperative sarcopenia had significantly worse survival compared with patients without sarcopenia.

We first clarified the postoperative change in skeletal muscle mass and muscle strength after LT. Skeletal muscle mass declined after LDLT and did not recover to preoperative levels until 12 months later, while grip strength sharply decreased at 1 month after LDLT and recovered to preoperative levels 5 months later. These findings suggest that not only perioperative intervention, but also mid- or long-term intervention by rehabilitation and nutritional therapy, is necessary and important for patients to increase their activities of daily living after LT.

The new exclusion criterion of inability to walk unaided is a simple criterion to exclude patients with severe sarcopenia without using any devices. However, the criterion is somewhat lacking in objectivity. We therefore tried to establish a more objective criterion to consider sarcopenia. We reported that both pretransplant skeletal muscle mass and low skeletal muscle quality (muscle steatosis), measured using computed tomography (CT), were independent risk factors for death after LDLT (5). We chose three variables related to sarcopenia and body composition: skeletal muscle mass, quality of skeletal muscle, and visceral adiposity. We evaluated these parameters by the skeletal muscle mass index (SMI), intramuscular adipose tissue content (IMAC), and the visceral to subcutaneous adipose tissue area ratio (VSR)

at the L3 level according to plain CT, respectively. We examined the impact of these 3 factors on overall survival after adult LDLT. Consequently, the overall survival rates after LDLT were observed to significantly decrease based on the increase in the number of prognostic body composition factors (low SMI, high IMAC, and high VSR) (11). One-year overall survival in patients with these 3 abnormal factors simultaneously was 41%. Based on the results, we proposed new criteria, to exclude patients with low skeletal muscle mass, low quality of skeletal muscle, and visceral adiposity from the LDLT waiting list instead of the single criterion of inability to walk unaided. We would like to validate the criteria when the number of adult LDLTs performed reaches 100 cases. In contrast, we do not apply the new criterion for deceased donor LT (DDLT), since the simultaneous presence of these 3 abnormal factors had no significant impact on survival after DDLT.

We recently proposed a new score, the Muscle Model for End-stage Liver Disease (Muscle-MELD) score, to predict post-LDLT mortality (6). The score includes pre-transplant muscularity, muscle quality as well as quantity, with the MELD score.

Pagano *et al.* stated the criticism that this study has several limitations including its retrospective design and an incorrect definition of sarcopenia. As for the former criticism, we are now investigating its validity. In terms of the latter criticism, we did not name the new score as the Sarcopenia-MELD score, but as the Muscle-MELD score. Therefore, the criticism is incorrect, since we combined only the quality and quantity of skeletal muscle with the MELD score. However, a new score that defines sarcopenia by decrease in muscle mass and muscle strength or physical activity with the MELD score would be beneficial. Furthermore, we are also examining the validity of the Muscle-MELD score in predicting mortality in patients with cirrhosis awaiting DDLT.

In addition to LT, we recently reported the significance of preoperative low quality as well as quantity of skeletal muscle in patients who underwent surgery for hepatocellular carcinoma, intrahepatic cholangiocarcinoma, biliary cancer, and pancreatic cancer (12-15). In these cancers, low skeletal muscle mass and muscle quality are closely involved with impaired outcomes. The negative impact of sarcopenia would be a common finding in various kinds of diseases and is widely known. Therefore, we should move on to next stage from analysis to intervention including nutritional therapy and rehabilitation. Moreover, the mechanism of sarcopenia should be elucidated.

In conclusion, recent studies have disclosed the significance of sarcopenia in the field of LT. Outcomes after LT have dramatically improved after implementation of new criteria considering sarcopenia. As Pagano *et al.* mentioned in their letter, establishment of pre- and post-LT appropriate nutritional support and rehabilitation programs for patients undergoing LDLT and DDLT is warranted to more significantly improve outcomes after LT.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Kaido T, Ogawa K, Fujimoto Y, et al. Impact of sarcopenia on survival in patients undergoing living donor liver transplantation. Am J Transplant 2013;13:1549-56.
2. Kaido T, Uemoto S. Direct segmental multi-frequency bioelectrical impedance analysis is useful to evaluate sarcopenia. Am J Transplant 2013;13:2506-7.
3. Kaido T, Mori A, Ogura Y, et al. Pre- and perioperative factors affecting infection after living donor liver transplantation. Nutrition 2012;28:1104-8.
4. Kaido T, Mori A, Ogura Y, et al. Impact of enteral nutrition using a new immune-modulating diet after liver transplantation. Hepatogastroenterology 2010;57:1522-5.
5. Hamaguchi Y, Kaido T, Okumura S, et al. Impact of quality as well as quantity of skeletal muscle on outcomes after liver transplantation. Liver Transpl 2014;20:1413-9.
6. Hamaguchi Y, Kaido T, Okumura S, et al. Proposal of Muscle-MELD score, including muscularity, for prediction of mortality after living donor liver transplantation. Transplantation 2016;100:2416-23.
7. Kaido T, Tamai Y, Hamaguchi Y, et al. Effects of pretransplant sarcopenia and sequential changes in sarcopenic parameters after living donor liver transplantation. Nutrition 2017;33:195-8.
8. Sato A, Kaido T, Iida T, et al. Bundled strategies against infection after liver transplantation: lessons from multidrug-resistant Pseudomonas aeruginosa. Liver Transpl 2016;22:436-45.
9. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia:

European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010;39:412-23.
10. Chen LK, Liu LK, Woo J, et al. Sarcopenia in Asia: consensus report of the asian working group for sarcopenia. J Am Med Dir Assoc 2014;15:95-101.
11. Hamaguchi Y, Kaido T, Okumura S, et al. Impact of skeletal muscle mass index, intramuscular adipose tissue content, and visceral to subcutaneous adipose tissue area ratio on early mortality of living donor liver transplantation. Transplantation 2017;101:565-74.
12. Hamaguchi Y, Kaido T, Okumura S, et al. Preoperative intramuscular adipose tissue content is a novel prognostic predictor after hepatectomy for hepatocellular carcinoma. J Hepatobiliary Pancreat Sci 2015;22:475-85.
13. Okumura S, Kaido T, Hamaguchi Y, et al. Impact of skeletal muscle mass, muscle quality, and visceral adiposity on outcomes following resection of intrahepatic cholangiocarcinoma. Ann Surg Oncol 2017;24;1037-45.
14. Okumura S, Kaido T, Hamaguchi Y, et al. Impact of the preoperative quantity and quality of skeletal muscle on outcomes after resection of extrahepatic biliary malignancies. Surgery 2016;159:821-33.
15. Okumura S, Kaido T, Hamaguchi Y, et al. Impact of preoperative quality as well as quantity of skeletal muscle on survival after resection of pancreatic cancer. Surgery 2015;157:1088-98.

Cite this article as: Kaido T, Hamaguchi Y, Uemoto S. Sarcopenia plays a crucial role in liver transplantation. HepatoBiliary Surg Nutr 2017;6(6):434-436. doi: 10.21037/hbsn.2017.08.05

