Sarcopenia: Multiple factors need to be considered in cirrhosis

Do Seon Song¹, U Im Chang¹, Jin Mo Yang¹

¹Department of Internal Medicine, St. Vincent’s Hospital, The Catholic university of Korea

Running title: Sarcopenia multifactorial disease in cirrhosis

Corresponding author: Jin Mo Yang, M.D., Ph.D.

Professor

Department of Internal Medicine, St. Vincent’s Hospital, College of Medicine, The Catholic University of Korea, 93 Jungbu-daero, Paldal-gu, Suwon, Gyeonggi-do, 16247, Korea

Tel: +82 31 881 8650, Fax: +82 31 254 8898

E-mail: jmyangdr@catholic.ac.kr

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Dear Editor,

Sarcopenia refers to progressive decline in skeletal muscle, function, and strength with advancing age. Sarcopenia is also highly prevalent in patients with cirrhosis, and the development of sarcopenia in cirrhosis is considered to be associated with systemic inflammation. In addition, sarcopenia has been reported to be associated with adverse clinical outcomes, such as cirrhotic complications, waitlist mortality, and post-transplantation mortality. For these reasons, the importance of assessment of sarcopenia in patients with cirrhosis is being emphasized. However, there are few studies on the association between changes in sarcopenia and the prognosis of cirrhosis. Thus, we read with great interest the article of Kim et al. that described that change of muscle mass was a good predictor of the development of cirrhotic complications independent of liver function. However, it is necessary that some issues not mentioned by Kim et al. have to be considered.

Firstly, sarcopenia has sex-specific difference. Sex-specific cutoff values are used to define sarcopenia, and the prevalence of sarcopenia is higher in male than female in patients with cirrhosis. In addition, some studies reported that the impact of sarcopenia on clinical outcomes could differ between male and female. The sex-specific difference of sarcopenia might be caused by sex hormone, such as testosterone. The rate of muscle mass reduction and the impacts of muscle mass reduction on the prognosis could vary by gender. Kim et al. described that the male patients had higher prevalence of sarcopenia than female patients, and the changes of muscle mass significantly predicted the development of complication of cirrhosis in both sex groups. However, it should be considered that changes in muscle mass may not be an independent prognostic factor after adjusting Child-Pugh and Model for End-stage Liver Disease (MELD) score if stratified by sex.

Secondly, the lifestyle of cirrhotic patients should be considered. In the study of Kim et al., alcohol-related liver disease accounts for 21.0% of all patients and is the second most etiology. In addition, alcohol-related liver disease was independent risk factor of development of complication. However, there was no description of alcohol use after enrollment. In alcohol-related liver disease, alcohol directly or its metabolite as well as hepatocellular dysfunction can cause skeletal muscle loss. Ongoing alcohol use after enrollment might be directly associated with development of cirrhotic complications. The other lifestyles to consider are nutrition and physical activity. Malnutrition is frequent in patients with cirrhosis by multifactorial etiologies, such as inadequate dietary intake, ascites, gastroparesis, hormonal change, and altered...
metabolism. In addition, reduced exercise capacity and impaired physical performance are commonly observed in patients with cirrhosis. Physical inactivity might lead to sarcopenia in cirrhotic patients because physical activity and exercise are anabolic stimuli that can improve the muscle protein balance, reducing the protein loss and increasing the muscle mass and contractile function. Therefore, it is necessary to consider the alcohol abuse, diets, and physical activity of enrolled patients during follow-up period.

Thirdly, quality of muscle is important as well as muscle mass. Muscle quality is associated with myosteatosis, which means ectopic fat infiltration in muscle. Myosteatosis is defined by lower mean skeletal muscle radiodensity on computed tomography (CT), and it is common in cirrhotic patients with prevalence of 16-82%. Myosteatosis is independently associated with mortality and complications in patients with cirrhosis. Since the CT was used for muscle mass evaluation, assessing the myosteatosis would also be possible in the patients enrolled in the study of Kim et al. Additional analysis of myosteatosis would provide more prognostic information in cirrhotic patients.

In conclusion, we genuinely appreciate the valuable work of Kim et al. which showed the change of muscle mass is independent prognostic factor in predicting the development of cirrhotic complications. However, consideration of other issues that can affect muscle mass and quality in cirrhotic patients will be more helpful in discriminating patients with a poor prognosis.
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