Sarcopenia: multiple factors to be considered in cirrhosis—author’s reply

Tae Hyung Kim, Young Kul Jung, and Hyung Joon Yim

Department of Internal Medicine, Korea University Ansan Hospital, Gyeonggi-do, Republic of Korea.

Correspondence:

Young Kul Jung, MD, PhD
Division of Gastroenterology and Hepatology, Department of Internal Medicine, Korea University Ansan Hospital
123 Jeokgeum-ro, Danwon-gu, Ansan-si, Gyeonggi-do 15355, Republic of Korea
E-mail: 93cool@hanmail.net
Phone: +82-31-412-7670
Fax: +82-31-412-5582
ORCID: 0000-0002-6566-1382

Running Title: Factors related to sarcopenia in LC
Dear Editor,

We sincerely appreciate the letter from Dr. Song, Chang, and Yang for contemplating our recent paper on the prognostic impact of muscle mass change in outpatients with cirrhosis, published in *Clinical and Molecular Hepatology.*

We agree that sex and lifestyle influence muscle mass and that myosteatosis is an important prognostic marker in patients with cirrhosis.

Many diagnostic criteria for sarcopenia have been established based on sex-specific differences, and this study was conducted by adopting one of them. However, the change in muscle mass may differ from the muscle mass itself. In our study, $\Delta SMI/yr\%$, which represented the change in muscle mass, was not an absolute value but a rate value divided by the muscle mass at inclusion. Thus, regardless of sex, the impact of $\Delta SMI/yr\%$ could be consistent.

The analysis of subgroup according to sex, which was not presented in the original paper, revealed that $\Delta SMI/yr\%$ continued to be an independent predictor for the development of cirrhosis complications in men even after adjusting for the model for end-stage liver disease score. In the case of women, the correlation marginally significant (Table 1), which might be attributed to the fact that women in our cohort are fewer and have a lower incidence of cirrhosis complications than men. In addition, every 1-point increase in $\Delta SMI/yr\%$ was associated with a 5.4% and 4.0% reduction in the risk of cirrhosis complications in men and women, respectively.

Of course, there were other results suggesting sex-specific differences such as cut-offs for the development of cirrhosis complications within 6 months (-5.74 and -2.62 in men and women, respectively).

Continuous alcohol consumption is an obvious aggravating factor for muscle loss, decompensation, and mortality in patients with alcohol-related liver disease. In addition, abstinence is a fundamental treatment with long-term benefits, including a 10–30% reduction in mortality. Thus, drinking behavior after inclusion could be an important factor in the prognosis of patients with cirrhosis, as mentioned by Song et al. However, drinking behavior is highly variable, and there is no standardized method for measuring it, making it difficult to incorporate into research. Malnutrition and insufficient physical activity are well-known risk factors for sarcopenia and the prognosis of patients with cirrhosis. Conversely, a well-controlled diet and regular exercise could improve sarcopenia even in patients with cirrhosis.

Several pioneering studies have shown that myosteatosis is significantly associated with decompensation, hepatocellular carcinoma development, and mortality in patients with chronic liver disease. Even in these studies, it was unclear whether myosteatosis was a better prognostic predictor than sarcopenia. However, it appeared to be a prognostic predictor acting independently of sarcopenia.

Myosteatosis and lifestyle, including drinking behavior, nutrition, and physical activity, are now considered essential in sarcopenia-related studies. However, as mentioned in the limitations of
the original paper, the protocol in our cohort did not include measurements for these factors. Therefore, further studies are required to address these factors.

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References

1. Song DS, Chang UI, Yang JM. Sarcopenia: multiple factors need to be considered in cirrhosis. Clin Mol Hepatol 2023;29:0-0.
additive value of sarcopenia, myosteatosis and hepatic encephalopathy in the predictivity of model for end-stage liver disease. Dig Liver Dis 2019;51:1508-1512.
Table 1. Multivariable Cox-regression analyses for the development of LC complication after 1-year CT according to sex

<table>
<thead>
<tr>
<th>ΔSMI/yr%</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (n=381)</td>
<td>0.946</td>
<td>0.917–0.976</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Women (n=214)</td>
<td>0.960</td>
<td>0.921–1.001</td>
<td>0.055</td>
</tr>
</tbody>
</table>

Results were derived after adjusting for age and MELD score.

CT, computed tomography; LC, liver cirrhosis; MELD, model for end-stage liver disease; ΔSMI, Change in muscle mass; CI, confidence interval.