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Response: Sarcopenia Is Significantly Associated with Presence and Severity of Nonalcoholic Fatty Liver Disease (J Obes Metab Syndr 2019;28:129–38)

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Insulin resistance is considered to be an important factor in developing sarcopenia as well as nonalcoholic fatty liver disease (NAFLD).[1-3] Indeed, our study showed that insulin resistance-related metabolic factors such as diabetes, hypertension, and lipid profile have significant associations with both sarcopenia and NAFLD.[4] In this context, it is very important to properly adjust for these confounding factors when looking for the independent effects of sarcopenia on the risk of NAFLD.

Considering that, adjustment for confounders in our stratification analysis might have been insufficient. We had this discussion with reviewers during the review process. In the stratification analysis in our study, some subgroups were small in number. In addition, some variables that were applied in the main analysis had missing data, so there was concern that statistical power would not be robust when all these variables were applied to the stratification analysis. For this reason, we first analyzed all the variables and then selected the variables that seemed to have more confounding effects. As shown in Table 1, attenuation of the odds ratio for the risk of NAFLD was noticeable after correction for abdominal visceral fat area. However, further adjustment for diabetes, hypertension, total cholesterol, low-density lipoprotein cholesterol, smoking, triglyceride and high-density lipoprotein cholesterol didn't make much difference (Table 1). Due to these results, we believe that the results of stratification analysis would still be valid even if we consider additional confounders such as hypertension, diabetes, lipid profile, and smoking.

It is well-known that physical activity has a protective role against sarcopenia development.[5] Physical activity is also important in the pathophysiology and management of NAFLD and an exercise intervention showed beneficial effects on hepatic lipid reduction.[6] Given these associations with sarcopenia and NAFLD, physical activity can be an important confounder in analyzing the effects of sarcopenia on the risk of NAFLD. It would have been better if confounders, such as physical activity, had been further adjusted in our study. We look forward to further research to overcome this weakness in the future.

Insulin resistance is a possible link between sarcopenia and NAFLD.[1-3] In our study, we could not adjust insulin resistance in our analysis because of many missing values. However, abdominal obesity is associated with insulin resistance,[7] and we adjusted vis-

Table 1. NAFLD risk due to muscle mass reduction by subgroup

Variable	Odds ratio (95% CI)				
	Model 1	Model 2	Model 3	Model 4	Model 5
Age group (yr)					
T1 (19–49)	2.14 (1.94–2.36)	1.46 (1.30–1.64)	1.46 (1.30–1.64)	1.45 (1.29–1.63)	1.41 (1.25–1.59)
T2 (50–57)	1.87 (1.71–2.05)	1.31 (1.18–1.46)	1.30 (1.16–1.45)	1.30 (1.16–1.47)	1.28 (1.14–1.43)
T3 (58–87)	1.76 (1.60–1.94)	1.22 (1.09–1.36)	1.22 (1.09–1.37)	1.22 (1.09–1.37)	1.25 (1.11–1.41)
Sex					
Male	1.97 (1.84–2.11)	1.40 (1.30–1.52)	1.32 (1.22–1.44)	1.41 (1.30–1.52)	1.37 (1.27–1.49)
Female	1.78 (1.62–1.96)	1.17 (1.04–1.31)	1.13 (1.00–1.27)	1.14 (1.02–1.28)	1.16 (1.03–1.31)
Obesity					
No	1.64 (1.53–1.76)	1.22 (1.12–1.32)	1.22 (1.12–1.32)	1.22 (1.12–1.32)	1.21 (1.11–1.32)
Yes	1.52 (1.35–1.71)	1.27 (1.12–1.45)	1.27 (1.12–1.45)	1.27 (1.11–1.44)	1.26 (1.11–1.44)
Abdominal obesity					
No	1.63 (1.46–1.82)	1.27 (1.12–1.43)	1.26 (1.11–1.42)	1.25 (1.11–1.42)	1.25 (1.10–1.42)
Yes	1.52 (1.42–1.64)	1.29 (1.20–1.40)	1.29 (1.20–1.40)	1.29 (1.20–1.40)	1.28 (1.18–1.39)
DM					
No	1.92 (1.82–2.04)	1.33 (1.25–1.42)	1.32 (1.23–1.41)	1.32 (1.23–1.41)	1.30 (1.21–1.39)
Yes	1.97 (1.54–2.52)	1.35 (1.02–1.80)	1.39 (1.03–1.88)	1.39 (1.03–1.87)	1.36 (0.99–1.86)

Model 1, adjusted for age and sex; Model 2, model 1+visceral fat area; Model 3, model 2+DM, hypertension, total cholesterol, and low-density lipoprotein cholesterol; Model 4, model 3+smoking; Model 5, model 4+triglyceride and high-density lipoprotein cholesterol. ASM% quartile was used as an independent variable. ASM% quartile was treated as continuous variable, and odds ratio implies a degree of increased risk that NAFLD will accompany each ASM% quartile reduction.
NAFLD, nonalcoholic fatty liver disease; CI, confidence interval; DM, diabetes mellitus; ASM, appendicular skeletal muscle mass.

ceral fat area (in the form of a continuous variable) as a surrogate marker of insulin resistance. In the stratified analysis, we used abdominal obesity instead of visceral fat area, because abdominal obesity defined by waist circumference cutoff criteria has been widely used in many studies. The presence of abdominal obesity did not significantly modify the relationship between sarcopenia and NAFLD in our study.

We are grateful to have the opportunity to clarify our work by sharing the details of our analyses. We look forward to further comprehensive research with a larger sample size and more sophisticated evaluation tools that can robustly reveal the association between sarcopenia and NAFLD.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Study concept and design: all authors; acquisition of data: all authors; analysis and interpretation of data: all authors; drafting of the manuscript: JWY; critical revision of the manuscript: GEC; statistical analysis: all authors.

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