## Response

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## Hyperglycemia Is Associated with Impaired Muscle Quality in Older Men with Diabetes: The Korean Longitudinal Study on Health and Aging (*Diabetes Metab J* 2016;40:140-6)

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We thank Dr. Moon for his comments in response to our study, "Hyperglycemia is associated with impaired muscle quality in older men with diabetes: The Korean Longitudinal Study on Health and Aging" [1].

The definition of muscle quality is still incompletely established, with various definitions such as: muscle strength per unit muscle mass/cross sectional area (CSA) [2,3], the degree of intramuscular or intermuscular adipose tissue [4,5], muscle fiber type change [6], or histological changes (including myofibrosis and myosteatosis) [7]. Even though it has not reached a consensus yet, muscle strength per muscle mass/area has been widely used as a definition of functional muscle quality in previous studies [2,3,8,9]. As Dr. Moon mentioned, since intramuscular or intermuscular adipose tissue is associated with decreased muscle strength as well as insulin resistance [10-12], it is possible that the relationship between severe hyperglycemia and muscle quality impairment is not a cause and effect. Therefore, we performed further analyses in order to evaluate the relationships between muscular fat, insulin resistance, blood glucose level and muscle quality using data from 217 subjects who took a mid-thigh computed tomography scan. The mid-thigh fat (perimuscular subcutaneous fat+intermuscular fat) CSA, not intermuscular fat area or intramuscular fat, was the only measurement available. The mid-thigh muscle-to-fat CSA ratio showed a significant negative correlation with HOMA-IR (r=-0.169, P=0.013), but did not have a significant relationship with fasting blood glucose or glycosylated hemoglobin (HbA1c; r=0.066, P=0.332; r=-0.025, P=0.713, respectively). Moreover, there was no significant association between the mid-thigh muscle-fat ratio and muscle quality (r=0.004, P=0.954). With these results, it is less likely that intermuscular fat confounded the relationship between hyperglycemia and poor muscle quality in our study.

As pointed out by Dr. Moon, diabetic complications may contribute to the deterioration of muscle quality. Unfortunately, diabetic complications like peripheral artery disease and diabetic neuropathy were not evaluated in our study participants, and therefore the effects of these conditions could not be excluded. However, we investigated the history of angina pectoris and myocardial infarction, which could reflect the macrovascular complication status. Among the subjects with a history of myocardial infarction or angina pectoris, one (4.8%) was in HbA1c <6.5% group, three (9.7%) were in 6.5%  $\leq$  HbA1c <7.5% group, but no one was in 7.5%  $\leq$  HbA1c <8.5% or HbA1c

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≥8.5% group, in which the differences in prevalence were statistically insignificant. Subjects with a history of cerebrovascular disease were excluded from the analysis. Also, diabetic complications tend to increase with duration of the disease. According to an analysis of variance analysis, the duration of diabetes significantly differed among the groups with different glycemic control status; however, in the post-hoc analysis, the duration of diabetes mellitus in the subjects with HbA1c  $\geq$ 8.5% (mean  $\pm$  standard deviation, 110  $\pm$ 112 months) was not significantly different compared with that in the subjects with 6.5%≤HbA1c<7.5% (111±120 months) and 7.5%≤HbA1c< 8.5% (171 ± 199 months). Therefore, confounding by diabetic complication status is possible but may not be serious in our study.

Also, we hope a future study will demonstrate the clinical consequences of muscle quality impairment in the near future. We appreciate Dr. Moon for the valuable comments and suggestions.

## **CONFLICTS OF INTEREST**

No potential conflict of interest relevant to this article was reported.

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