Response to "Relationship between soluble transferrin receptor and type 2 diabetes mellitus: A meta-analysis"

We thank Fernández-Cao[1] for the interest and constructive criticisms of our recent article published in the *Journal of Diabetes Investigation*[2].

First, in most of the studies included in the meta-analysis in our recent article in the *Journal of Diabetes Investigation*[2], the subjects were obese or non-obese. However, indicators related to obesity such as waist circumference or body mass index were adjusted for in the regression analysis, and we extracted the adjusted OR values in all these studies. Therefore, to analyze the association between soluble transferrin receptor (sTfR) and type 2 diabetes, we only extracted the OR values and 95% CIs corresponding to the non-obese group in Fernández-Cao *et al.*'s study[3]. Undoubtedly, as described by Fernandez-Cao[1], the results may be more reasonable based on subgroup analysis of the non-obese and obese groups for the relationship between sTfR and type 2 diabetes. However, to date, there has been only one clinical controlled study on the relationship between sTfR and type 2 diabetes in obese and non-obese individuals. If subgroup analysis is conducted, then there is only one study involving the non-obese group, which may introduce biased results.

Second, in a meta-analysis of the association between ferritin and type 2 diabetes, sensitivity and subgroup analyses were performed[2], and Rajpathak *et al.*'s[4] study did not identify a source of heterogeneity. To further clarify the impact of this study on the results, in the present study, the meta-analysis was carried out after excluding this study. The results showed that the serum median and high ferritin concentration groups remained significantly associated with the risk of type 2 diabetes [odds ratio (OR) 1.16, 95% confidence interval (CI) 1.04–1.29 and OR 1.43, 95% CI 1.28–1.59, respectively] (Figure 1a).

Third, in the present study, the reference groups of sTfR or sTfR-to-ferritin ratio in Arija *et al.*'s[5] study were adjusted as the low-concentration or low-ratio groups, respectively. Microsoft excel macros with VBA software were used to calculate the OR values and 95% CIs in the other three groups. The meta-analysis indicated that no significant association was observed between serum sTfR and type 2 diabetes (Figure 1b), whereas the sTfR-to-ferritin ratio was significantly inversely related to the risk of type 2 diabetes in the low, median, and high ratio subgroups (OR 0.69, 95% CI 0.50–0.95; OR 0.65, 95% CI 0.47–0.91; and OR 0.53, 95% CI 0.36–0.77, respectively) (Figure 1c). However, there are relatively few studies on the relationships between sTfR or sTfR-to-ferritin ratio and type 2 diabetes, and there are different serum sTfR or ferritin levels among various studies, which may lead to bias in the results. Further studies are needed to confirm the relationships between sTfR or the sTfR-to-ferritin ratio and the risk of type 2 diabetes.

DISCLOSURE

The author declares no conflict of interest.

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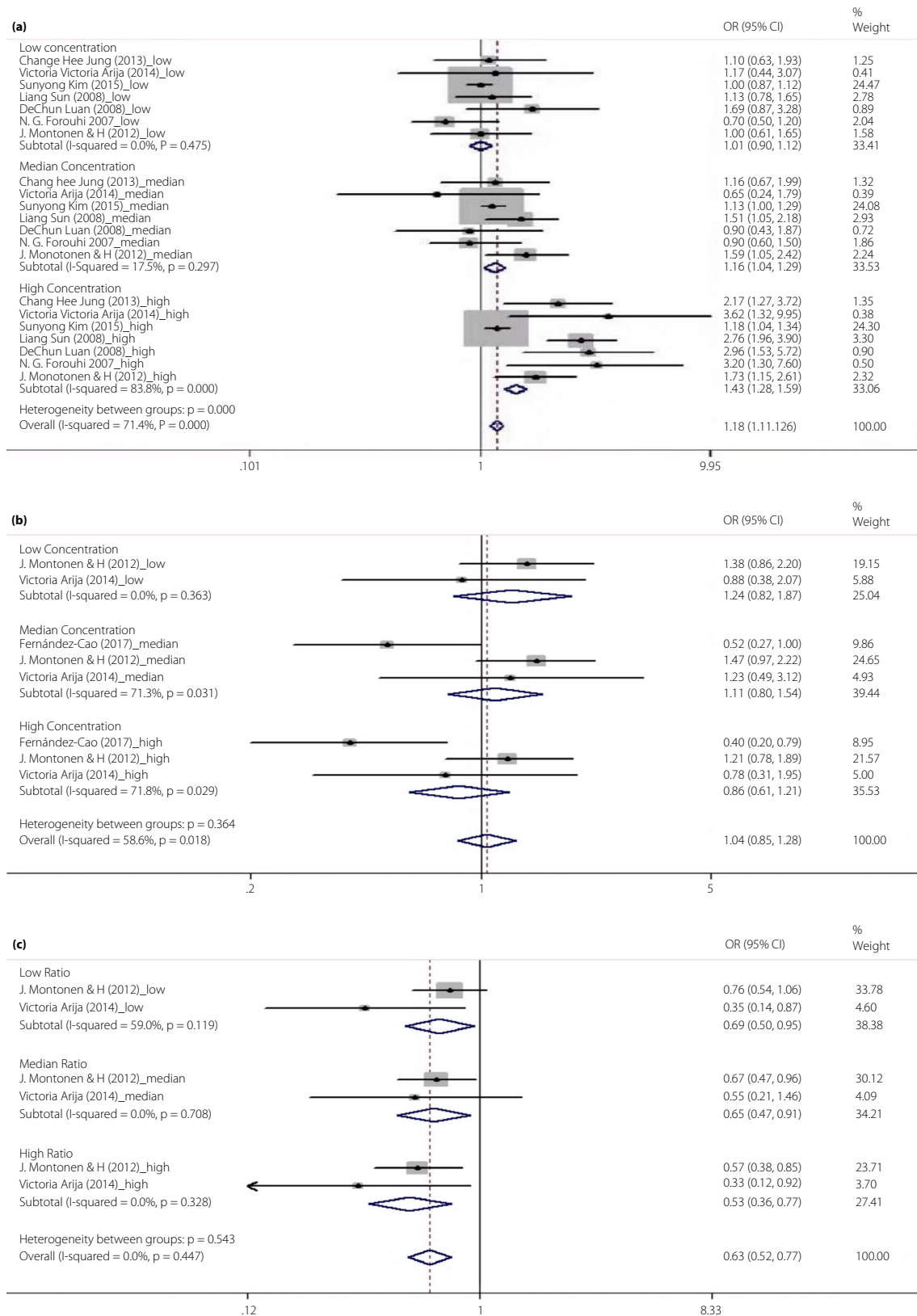E-mail address: ljf824168@126.com

Figure 1 | The associations between serum ferritin, sTfR or sTfR to ferritin ratio and type 2 diabetes. (a) ferritin; (b) sTfR; (c) sTfR to ferritin ratio. CI, confidence interval; OR, odds ratio.