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LETTER

Comment on 'Exercise training decreases pancreatic fat content and improves beta cell function regardless of baseline glucose tolerance: a randomised controlled trial'

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Abbreviation
PFC Pancreatic fat content

To the Editor: With interest, we read a recently published article in *Diabetologia* by Heiskanen et al, who investigated the effect of exercise training, using pancreatic fat content (PFC) as a primary outcome and beta cell function as a secondary outcome [1]. The authors stated that, with exercise training, there was a similar decrease in PFC in healthy men and in men with prediabetes (defined as impaired fasting glucose and/or impaired glucose tolerance) or type 2 diabetes.

Although both sexes were included in this study, PFC and beta cell function were analysed only in men. This begs the question: why were women included in this study when the main conclusions (and the title) were extracted only using the information from male participants?

The authors used an interesting model to analyse the data and, based on their results, the effect of 2 weeks of exercise training (either sprint interval training [SIT] or moderate-intensity continuous training [MICT]) on PFC was significant for time ($p = 0.036$) and was not significant for the interaction between time and type 2 diabetes ($p = 0.52$). However, since the interaction was not significant, the p value for time indicates the exercise-associated change in PFC only for the reference category [2, 3]. The reference group was not clarified in the article by Heiskanen and colleagues [1]. If the reference group was the healthy individuals, then the significance for time indicates that the change in PFC was only significant for the healthy group, not in both the healthy group and prediabetes/diabetes group. This is explained by the following equation (where $\propto$ is the estimated parameter corresponding to the covariates):

$$\mathrm{PFC} = \propto_0 + \propto_1 .\mathrm{group} + \propto_2 .\mathrm{time} + \propto_3 .\mathrm{time.group}$$

$$\mathrm{Group}: \begin{cases} 0 & \text{if healthy} \\ 1 & \text{if prediabetic or diabetic} \end{cases}$$

$$\text{Healthy} \rightarrow \mathrm{PFC} = \propto_0 + \propto_2 .\mathrm{time}$$

$$\text{Prediabetic or diabetic} \rightarrow \mathrm{PFC} = \propto_0 + \propto_1 + \propto_2 .\mathrm{time} + \propto_3 .\mathrm{time} = (\propto_0 + \propto_1) + (\propto_2 + \propto_3).\mathrm{time}$$

Therefore, the significance of time and insignificance of the time × diabetes interaction observed by Heiskanen and colleagues [1] does not support the statements by the authors that 'exercise training decreased pancreatic fat similarly in healthy and prediabetic or type 2 diabetic men' or that 'both training modes decreased [PFC] in those individuals with fatty pancreas at baseline'.

Moreover, HbA_{1c} analysis reflects mean blood glucose levels over the preceding 2–3 months [4]. The total duration of the study by Heiskanen et al was 2 weeks [1]. As Tahara and Shima have shown, it requires 27.0–41.7, 15.0–19.2 and 19.1–36.1 days to observe a 50% change in HbA_{1c}, glycated albumin and fructosamine, respectively [5]. Moreover, others have suggested that glycated albumin is more sensitive than HbA_{1c}, especially with regards to short-term variation of

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glycaemic control during intervention [6, 7]. Except for HbA_{1c}, none of variables relating to pancreatic metabolism or beta cell function differed significantly in the study by Heiskanen et al. This may be owing to the selection of HbA_{1c} instead of glycated albumin as the biomarker for monitoring blood glucose changes during the 2-week interventions [8].

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