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Potential conflict of interest: Nothing to report.

Reply:

We thank Pesta and Burtscher for their comments on our study. In this article, we have demonstrated, for the first time, that 4 months of resistance (RES) or aerobic (AER) training are equally effective in reducing hepatic fat content among sedentary type 2 diabetes subjects with nonalcoholic fatty liver disease (NAFLD).[1] This study was a subproject of the RAED2 Study, a randomized, controlled trial aimed at comparing the metabolic effects of RES and AER training in diabetic patients.[2]

Pesta and Burtscher hypothesized that in untrained overweight/obese subjects with little experience in exercise, RES training would be unable to induce the specific adaptations characteristic of this exercise modality, and that this, in turn, might explain why the results of AER and RES training were similar.

We agree that, in untrained subjects, there may be some overlap between the effects of AER and RES training, and that the full-blown effects of these different exercise modalities can be only appreciated when sustained high-intensity training is performed, as occurs in athletes. Nonetheless, the latter would not be an appropriate model for assessing the effects of these training modalities on hepatic fat accumulation of sedentary subjects with type 2 diabetes, which was the aim of our study.

Moreover, as reported previously,[2] in our study, peak oxygen uptake improved after training in both groups, but to a greater extent in the AER group, whereas increased strength was found only in the RES group. In addition, lean mass of the limbs significantly increased in the RES group, but not in the AER group. These findings clearly indicate that the stimulus was quite different between the two protocols.

These differences were guaranteed through a careful supervision of exercise sessions as well as a progressive increase of workload. In particular, as concerns the RES group, workload was gradually increased to 70%-80% 1-RM, with the weight being adjusted approximately every 2 weeks to match the progress of the subjects.

With regard to baseline data, there were not statistically significant differences between groups.

Overall, most type 2 diabetes patients are sedentary and have no experience with exercise programs. The clinical message that we were able to give is that exercise alone can provide benefit for NAFLD management in these patients, and that, after 4 months of training, RES exercise is as effective as AER exercise in reducing hepatic fat content in these subjects. Future research should address this important issue in the long term.

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Microsatellite Polymorphism in the Heme Oxygenase-1 Gene Promoter Is Not Associated With Alcoholic Liver Disease Severity

To the Editor:

Induction of heme oxygenase-1 (HO-1) was shown to prevent liver fibrosis[1] and ethanol-induced liver damage in mice.[2,3] A functional microsatellite $(GT)_n$ repeat variant in the HO-1 promoter region is tightly correlated with inducibility of HO-1 protein expression, i.e., short (<26) $(GT)_n$ repeat carriers present increased HO-1-expression-derived antiinflammatory and cytoprotective effects.[4] As opposed to cardiac or pulmonary disease, HO-1 gene polymorphisms in human liver disease have been largely unexplored.

We tested the genetic association between the HO-1 promoter $(GT)_n$ repeat variant and the presence and severity of alcoholic liver disease (ALD). To this end, we genotyped 487 biopsy-proven ALD Caucasian patients (383 with cirrhosis and 193 with alcoholic hepatitis [AH]; 69% male, median age 54.4 [range, 27-84] years) and 203 healthy Caucasian controls. Analysis of allelic frequency distribution disclosed two peaks at 23 and 30 $(GT)_n$ repeats in controls and in ALD patients. The distribution of homozygote long (>29) $(GT)_n$ profiles (LL) in controls was no different from that of cirrhosis patients or patients with AH (Table 1). The LL genotype proportion was not significantly higher in patients with alcoholic cirrhosis and AH than in those without AH. Moreover, the length of the (GT)n repeat variant was not correlated with Model for Endstage Liver Disease (MELD) or Child-Pugh scores, nor with the Maddrey score for patients with AH. Populations were in Hardy-Weinberg equilibrium and the size of the cohort corresponded to a power of 82.3%, in light of the 12% allelic frequency difference observed in other diseases.[5] Our cohort had been previously validated for another genetic polymorphism association