**Can exercise training prevent and treat liver fibrosis in diabetes?**

Metabolic dysfunction–associated steatotic liver disease, progressing to steatohepatitis (MASH) with fibrosis, is a common complication in type 2 diabetes, with no proven exercise-based treatment or preventive strategies. This study **aimed** to investigate whether exercise regimens can prevent and treat MASH fibrosis in our mouse Fat and Diabetes (FAD) model.

**Methods:** C57BL/6J mice were fed a high-fat-diet then low-dose streptozotocin (STZ) was administered at Week-15 to induce diabetes. Mice were randomly allocated to no exercise training (FAD-NoEx), endurance (FAD-END) or high-intensity-interval-training (FAD-HIIT), starting one week after STZ for 10 weeks in the prevention-model and 10 weeks after STZ for 15 weeks in the treatment-model. Chow-fed mice were controls (Chow). Bodyweight and blood glucose level (BGL) were measured. After sacrifice, liver fibrosis was assessed using Picro-Sirius Red (PSR) staining. Liver pro-inflammatory and pro-fibrotic genes were quantified by RT-qPCR.

**Results:** All FAD groups had higher bodyweight at Week-15 (*p*<0.0001) and BGL at Week-25 (*p*<0.05) than Chow in both models, with BGL and bodyweight increases lessening over time. In the prevention-model, FAD-NoEx showed more liver fibrosis than Chow (2.94 (1.73-7.60)% vs (1.35 (0.52-1.94)%, *p*<0.05), with prominent statistically significant changes in the portal tract. Liver fibrosis was reduced in FAD-HIIT (1.00 (0.18-1.81)%, *p*<0.01), but not in FAD-END. Pro-fibrotic markers: Collagen I (5-fold), Collagen III (11-fold), CCN2 (1.8-fold), TIMP-1 (19-fold) and TIMP-2 (2.3-fold) and pro-inflammatory markers: MCP-1 (17-fold) and TNF-α (6-fold) were upregulated in FAD-NoEx compared to Chow. Collagen III induction was prevented in FAD-END (*p*<0.05). In the treatment-model, FAD-NoEx exhibited marked liver fibrosis in both the central vein and portal tract, however, exercise training did not reduce fibrosis or alter marker expression.

**Conclusion:** This novel model shows that exercise training, particularly HIIT, prevents MASH fibrosis development in diabetes, but exercise alone does not reverse established liver fibrosis.

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