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Significant regression in fibrosis in paired liver biopsies following a 12-week aerobic exercise intervention in individuals with non-alcoholic fatty liver disease

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Background and aims: Non-Alcoholic Fatty Liver Disease (NAFLD) is a rapidly growing health epidemic. Individuals with NAFLD often present with multiple comorbidities including; obesity, type 2 diabetes, metabolic syndrome and cardiovascular disease. In the absence of approved pharmacological treatments, lifestyle modifications are the first line of treatment. This study examined the benefits of a 12-week, aerobic exercise intervention (EI) on hepatic and extrahepatic outcomes in individuals with NAFLD and the sustainability of the benefits 12 weeks after completion.

Method: Individuals with biopsy proven NAFLD consented to take part in the EI. Pre-exercise assessments included review of liver biopsies by a single pathologist, baseline pre-exercise CAP and liver stiffness scores (Fibroscan, FS), cardiovascular fitness (VO_{2max}), physical activity levels (PAL), anthropometry, blood profile and frailty measures. These measures were recorded before the EI (T0), immediately after the EI (T1) and three months after T1 (T2). The EI consisted of two supervised and three unsupervised aerobic exercise sessions per week with increasing intensity (45-75% heart rate reserve) and duration (24-45 minutes) for 12-weeks. Control participants completed only three physical assessments. A repeated measures ANOVA and Wilcoxon signed rank test were used to examine for significant differences in parametric and non-parametric measures, respectively.

Results: 25 individuals (16 exercise, 9 controls) completed the EI with 96% mean adherence. At T1, there was a significant regression of fibrosis ($p = 0.025$) in the exercise group which corresponded to a significant reduction in CAP ($p = 0.015$) and stiffness scores ($p = 0.025$) via FS. Additionally, there was a significant increase in VO_{2max} ($p = 0.034$), PAL ($p = 0.022$) and the number of individuals achieving WHO PAL guidelines ($p = 0.046$) at T1. There were significant reductions in BMI ($p = 0.01$), fat mass ($p = 0.001$), waist circumference (WC, $p < 0.0001$), HbA1c ($p = 0.047$) and in self-reported ($p = 0.034$) and test based ($p = 0.025$) frailty measures. At T2, CAP score ($p = 0.005$), BMI ($p = 0.04$) and WC ($p = 0.001$) remained significantly improved from T0. The remaining improvements at T1 were not sustained at T2.

Conclusion: This study demonstrates a significant regression in hepatic fibrosis in response to exercise therapy as assessed by paired liver biopsy and FS, with additional improvements in VO_{2max} , anthropometry and frailty measures. That the benefits were not maintained at T2 indicates a need for strategies to integrate exercise and physical activity into a community-based setting to promote long term adherence to the therapy.