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**Editorial: Out of Shape May Impact More Than Your Figure**

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Healthy eating and increased physical activity targeted toward weight loss remain first line therapy for nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH).<sup>1</sup> Despite a strong body of evidence supporting these lifestyle behaviors, a significant knowledge gap persists regarding the highest yield approach for dietary changes and physical activity regimens and predictors of likelihood to achieve improvements in steatosis and histologic components of NASH. Specifically, the pathophysiologic mechanism driving these histologic improvements and the role cardiorespiratory fitness plays in mediating or moderating this relationship requires further characterization.

In a recent issue, Argo et al investigate the association between aerobic fitness, anthropometrics, fat distribution on imaging, self-reported physical activity and histologic components of NASH.<sup>2</sup> In this cross-sectional analysis, 36 overweight or obese patients with biopsy proven NASH [ NAFLD activity score (NAS)  $\geq$  4, mean fibrosis score 1.7) completed exercise testing (VO<sub>2</sub> analysis) and were compared to 148 sedentary control subjects without known metabolic disease as well as age and gender-matched norms. Interestingly, among NASH patients, fitness was similar in obese and overweight individuals and was not correlated with visceral adiposity or histologic components of NASH. Notably, NASH patients were significantly more deconditioned than sedentary controls and the general population.

This study has several strengths including a detailed assessment of fitness using standardized measures and adjunctive MRI-based assessments of distribution of fat in a well characterized population of patients with biopsy proven NASH. Several limitations worth highlighting include the small sample size, concerns regarding generalizability of both the case and control populations, the cross-sectional nature of the study, and lack of nutritional assessment. Patients who had previously been selected to undergo liver biopsy as part of their general care likely represent a different cohort than the broader population of patients with underlying NASH. Also, subjects in this study had relatively minimal fibrosis (mean 1.7). It is also unclear if the control group, which consisted of individuals in the study lab, is representative of a true general population control.

Overall this study adds to the existing body of literature on the role of physical fitness in NASH and outlines areas of interest to explore further in future studies. Additional investigation into the relationship between fat distribution, histologic components of NASH, and other potential correlates

between physical fitness and NASH is warranted given the paucity of data on this topic and conflicting results to date.<sup>3-6</sup> In particular, further delineation about how visceral adiposity and stage and grade of NASH mediates or moderates cardiorespiratory fitness and the propensity to respond to lifestyle interventions is needed. It would also be relevant to focus specifically on characterization of sedentary behavior such as total sitting time as this is a separate but related behavior that likely impacts overall physical fitness and was not specifically evaluated in this study.<sup>7</sup> Most importantly, as highlighted by the authors, it would be of value to continue to evaluate the impact of change in physical fitness on liver disease burden, as lifestyle interventions remain first line therapy for this burgeoning disease.<sup>8,9</sup>

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