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Conflicts of interest
The authors disclose no conflicts.

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Weight Loss for a Healthy Liver

See "Weight loss through lifestyle modification significantly reduces features of nonalcoholic steatohepatitis," by Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, et al on page 367; and "Bariatric surgery reduces features of nonalcoholic steatohepatitis in morbidly obese patients," by Lassailly G, Caiazzo R, Buob D, et al on page 379.

Overweight and obesity undoubtedly drive the prevalence of nonalcoholic fatty liver disease (NAFLD) in the population, promoting liver fat accumulation. There is also evidence that obesity may increase disease progression to nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis and eventually to hepatocellular carcinoma. Hence, weight loss is considered essential in overweight/obese patients with NAFLD to reduce the burden of the disease[1]; even a limited amount of weight loss is associated with decreased hepatic triglyceride content, measured by proton magnetic resonance spectroscopy, and remission of ultrasound-assessed steatosis, in a dose-dependent manner. The possibility to reduce hepatic necroinflammation and fibrosis is less proven, although evidence is rapidly accumulating.

A small randomized, controlled trial (RCT),[2] carried out along the principles of cognitive-behavioral therapy,[3] showed that the adoption of healthy lifestyles was accompanied by a significant improvement of necroinflammation and resolution of NASH, compared to a control population (Table 1). Notably, the improvement was driven by weight loss of >7%, irrespective of treatment arm, not by participation in the experimental lifestyle treatment group. Similarly, studies in morbidly obese subjects undergoing bariatric (metabolic) surgery reported histological improvement during follow-up.[4] In summary, there is evidence from the literature that no matter how you lose weight, weight loss improves liver health.

In this issue of *Gastroenterology*, 2 large prospective cohort studies strengthen this evidence.[5,6] In 293 NASH patients enrolled into a 12-month lifestyle modification program in Havana, Cuba, Vilar-Moreno et al[5] reported a 25% resolution of NASH, a 47% reduction by ≥2 of the NAFLD Activity Score (NAS) without fibrosis worsening (primary outcome), and a 19% regression of fibrosis.[5] Improvement occurred more frequently in subjects who lost ≥5% of their body weight, and NASH resolution was only observed in subjects who achieved at least a modest 3% weight loss target. In the other study consisting of 109 morbidly obese subjects with NASH at bariatric surgery

Table 1. Treatment of Nonalcoholic Steatohepatitis: Comparison Between Behavioral and Surgical Weight Loss Studies and Recently Completed Phase IIb Drug Trials

Class Treatment/Drug	Mechanism of action	Study duration sample	Primary outcome	Results
[a]CBT program[2]	Healthy diet, physical activity weight loss	12 months 31 overweight/obese NASH	NAS improvement $\geq$3 points Post-treatment NAS $\leq$ 2 points	Change in NAS score $\geq$3, 61% vs 21% in C; $P = .04$ Posttreatment NAS $\leq$2, 67% vs 20% in C; $P = .02$
[b]Behavior treatment[5]	Healthy diet, physical activity weight loss	1 year 293 NASH	NASH remission, no worsening of fibrosis	NASH remission, 25% Change in NAS score $\geq$ 2, 25%
[b]Bariatric surgery (mainly LAGB or GBP)[6]	Weight loss	1 year 109 morbidly obese NASH	NASH remission	NASH remission, 85% fibrosis improvement in 34%
[a]FXR agonists obeticholic acid (FLINT trial)[14]	Insulin sensitizing and antiinflammatory properties	72 weeks 283 noncirrhotic NASH (interim analysis on 219 cases)	NAS improvement $\geq$ 2 points), no worsening of fibrosis	Change in NAS score $\geq$ 2, 45% vs 21% in PL; $P < .001$ NASH remission, 22% vs 13% in PL; $P = .08$
[a]GLP-1R agonists liraglutide (LEAN program)[15]	Incretin and insulin sensitizing activity, effects on appetite and gastrointestinal motility	48 weeks 52 NASH patients (45 available at follow-up)	NASH remission, no worsening of fibrosis	NASH remission (39% vs 9% in PL; $P = .035$)
[a]Dual PPAR-α/δ agonists GENFIT505 (GOLDEN trial)[17]	Insulin sensitizing and antiinflammatory properties	12 months 270 NASH patients (234 available at follow-up)	NASH resolution, no worsening of fibrosis	NASH resolution GFT505 vs PL; $P = .016$, RR = 2.03) Patients without an end of treatment biopsy considered as nonresponders

C, controls; CBT, cognitive-behavior therapy; FXR, farnesoid X receptor; GBP, gastric by-pass; GLP-1R, glucagon-like peptide-1 receptor; LAGB, laparoscopic adjustable gastric banding; NAS, NASH activity score; NASH, nonalcoholic steatohepatitis; PPAR, peroxisome proliferator-activated receptor; PL, placebo.
[a]Randomized, controlled study.
[b]Cohort study.