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On a knife-edge—weight-loss surgery for NAFLD in adolescents

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Abstract

A new position statement from Europe endorses expert-based recommendations to consider bariatric surgery as a treatment for severe NAFLD in severely obese adolescents. This article discusses the problem of severe paediatric obesity, its relationship with NAFLD, and the knowledge and needs regarding bariatric surgery in adolescents.

A new position statement from the Hepatology Committee of the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) provides an overview of adolescent bariatric surgery indications and outcomes, with a particular emphasis on adolescents with NAFLD.[1] In many countries, NAFLD is the most common form of chronic liver disease in children. NAFLD ranges from bland steatosis to NASH, which includes inflammation, hepatocellular injury and can progress to cirrhosis. The high prevalence of NAFLD among children raises concern that childhood-onset NASH will lead to high future rates of liver transplantation, given that no proven, safe and effective pharmacotherapy options exist for children with NAFLD or NASH.[2] Because many children with NAFLD are overweight or obese, lifestyle interventions, including weight loss, are often recommended as the first-line intervention.[2]

In the USA, one in three children are overweight or obese, while severe obesity prevalence has quadrupled to 5% of adolescents.[3] However, obesity and NAFLD should not be considered interchangeable. Not every overweight or obese child has NAFLD, and children with NAFLD have higher rates of dyslipidaemia, impaired glucose metabolism, and hypertension than their age, sex, and weight-matched peers.[4] We also routinely see children who are normal weight with NAFLD. Thus, although some children with NAFLD are severely obese, most children with NAFLD are younger and less obese than adolescents undergoing surgical treatment of obesity.

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Competing interests

The authors declare no competing interests.

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In children, improvement in health via weight loss typically requires participation in intensive comprehensive lifestyle interventions, which include frequent visits to work with multidisciplinary specialists.[5] Although these programs can reduce BMI by 1.9 to 3.3 units compared with conventional counselling, they are not widely available.[5] Further, sustained clinically significant weight loss is even more challenging for children with severe obesity. Only one comprehensive lifestyle study included a large proportion of severely obese adolescents and yielded only a -1.7 unit BMI decrease with a very high attrition rate of 53%.[6] Moreover, the presence of NAFLD might also make weight loss more difficult.

There is great interest in bariatric surgery as a potential treatment for severe NAFLD in adolescents because of a high prevalence of severe paediatric obesity, a dearth of effective pharmacotherapy options, and the reliance on weight loss as a primary therapy. Bariatric surgery can substantially reduce BMI in severely obese adolescents (Supplementary Box 1). Furthermore, bariatric surgery can yield favorable changes in glucose tolerance, dyslipidaemia and systemic inflammation, all of which might theoretically benefit NASH.[1]

As summarized in Table 1, clinical guidelines regarding adolescent bariatric surgery have evolved. The earliest guideline in 2004 was the most conservative, reflecting limited outcome and safety data in adolescents.[7] Subsequently, studies have shown that adolescent bariatric surgery can produce meaningful weight loss, improvements in cardiometabolic risk factors, and quality of life (Supplementary Box 1). Accordingly, the BMI threshold proposed for adolescent bariatric surgery was lowered to a BMI of ≥35 kg/m^2 with type 2 diabetes, obstructive sleep apnoea, pseudotumor cerebri or severe NAFLD.[8,9] The rationale for including these comorbidities as surgical criteria at a lower BMI is their potential to increase short-term morbidity. However, as the ESPGHAN statement notes, the data supporting improvements in diabetes and sleep apnoea are more robust in adults, with only a few small case series showing improvements in teenagers with these conditions.[1]

Notably, no comprehensive lifestyle or bariatric surgery studies have focused specifically on severely obese adolescents with NAFLD (Supplementary Box 1). Therefore, the safest and most effective approach to weight loss for the treatment of NASH in adolescents remains unknown and controversial, with divergent recommendations on whether NASH should be an indication for bariatric surgery. Although some adolescent bariatric surgery guidelines include NASH as an indication[8,9]—on the basis of preliminary data in adults—a practice guideline on NAFLD management from three major gastroenterology and hepatology professional societies did not recommend bariatric surgery as a specific treatment for NASH owing to a lack of controlled studies.[2] Similarly, a 2010 Cochrane meta-analysis of bariatric surgery for NASH concluded that, “the lack of scientifically sound evidence precludes any recommendation to support or reject bariatric surgery to treat patients with NAFLD”.[10] In addition, it is important to remember that bariatric surgery is not always appropriate for every adolescent even if they meet accepted criteria for surgery. It requires a high degree of commitment and psychosocial readiness on the part of the adolescent and their family to be maximally successful.

Critical knowledge gaps remain, including the following: one, does bariatric surgery result in significant improvement in more histologically severe NASH, in particular advanced

fibrosis; two, is bariatric surgery safe in patients with compensated NASH-related cirrhosis; three, does the hepatic outcome in response to bariatric surgery depend upon the response of specific comorbid conditions, such as type 2 diabetes and obstructive sleep apnoea; four, can NASH recur long-term, particularly if substantial weight regain occurs; five, does the type of surgery affect NASH outcome; and six, are there beneficial effects from surgery independent from weight loss? For example, bariatric surgical procedures have been shown to have varying actions on gastrointestinal hormone and bile acid pathways that might have a role in the pathogenesis of NAFLD and might also alter the gastrointestinal microbiome, which has been linked to NAFLD.

To address these questions, it is critical that adolescents with NAFLD undergoing bariatric surgery be evaluated and managed in bariatric surgery centres with appropriate paediatric multidisciplinary expertise and a commitment to rigorously phenotype NAFLD histology at baseline and to follow outcomes prospectively as long as possible. These procedures can be particularly challenging in adolescents, who are prone to relocate in adulthood and thus might not return for follow-up. High quality prospective multicentre studies with low attrition rates, such as the Teen Longitudinal Assessment of Bariatric Surgery (USA) and the Adolescent Morbid Obesity Study (Sweden) have begun to provide short to intermediate term (1–2 year) outcomes after adolescent bariatric surgery, but do not include prospectively collected data on histological liver outcomes to support evidence-based recommendations regarding NASH as a specific indication for bariatric surgery. However, given the benefits that are emerging for type 2 diabetes and sleep apnoea, (which are comorbid conditions often associated with NASH), we concur with previously published expert guidelines that conclude that bariatric surgery is not contraindicated in a non-cirrhotic patient with NAFLD who otherwise meets appropriate medical and psychosocial criteria for bariatric surgery.[2] The adolescent and family should, however, be counselled that a positive outcome with respect to NAFLD is, as yet, not a foregone conclusion.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Nobili, V., et al. Indications and limitations of bariatric intervention in severely obese children and adolescents with and without non-alcoholic steatohepatitis: the ESPGHAN Hepatology Committee Position Statement. J Pediatr Gastroenterol Nutr. http://dx.doi.org/doi:10.1097/MPG.0000000000000715

2. Chalasani N, et al. The diagnosis and management of non-alcoholic fatty liver disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology. 2012; 55:2005–2023. [PubMed: 22488764]

3. Kelly AS, et al. Severe obesity in children and adolescents: identification, associated health risks, and treatment approaches: a scientific statement from the American Heart Association. Circulation. 2013; 128:1689–1712. [PubMed: 24016455]
4. Schwimmer JB, et al. Cardiovascular risk factors and the metabolic syndrome in pediatric nonalcoholic fatty liver disease. Circulation. 2008; 118:277–283. [PubMed: 18591439]
5. Whitlock EP, et al. Effectiveness of weight management interventions in children: a targeted systematic review for the USPSTF. Pediatrics. 2010; 125:396–418.
6. Savoye M, et al. Effects of a weight management program on body composition and metabolic parameters in overweight children: a randomized controlled trial. JAMA. 2007; 297:2697–2704. [PubMed: 17595270]
7. Inge TH, et al. Bariatric surgery for severely overweight adolescents: concerns and recommendations. Pediatrics. 2004; 114:217–223. [PubMed: 15231931]
8. Michalsky M, et al. ASMBS pediatric committee best practice guidelines. Surg Obes Relat Dis. 2012; 8:1–7. [PubMed: 22030146]
9. Pratt JS, et al. Best practice updates for pediatric/adolescent weight loss surgery. Obesity (Silver Spring). 2009; 17:901–910. [PubMed: 19396070]
10. Chavez-Tapia, NC., et al. Bariatric surgery for non-alcoholic steatohepatitis in obese patients. Cochrane Database of Systematic Reviews. Art. No.: CD007340. http://dx.doi.org/10.1002/14651858.CD007340.pub2

Table 1

Overview of published recommendations for adolescent bariatric surgery criteria

Reference	Lower BMI criteria:	Higher BMI criteria:
Inge *et al.* (2004)[7]	BMI ≥ 40 kg/m^2 with: Type 2 diabetes Obstructive sleep apnoea Pseudotumor cerebri	BMI ≥ 50 kg/m^2 with: Hypertension Dyslipidaemias NASH Venous stasis disease Quality of life impairment
Pratt *et al.* (2009)[9]	BMI ≥ 35 kg/m^2 with comorbidities associated with greater short-term morbidity: Type 2 diabetes Severe steatohepatitis Pseudotumor cerebri Moderate-to-severe obstructive sleep apnoea	BMI ≥ 40 kg/m^2 with comorbidities associated with long-term morbidity (not specified)
Michalsky *et al.* (2012)[8]	BMI ≥ 35 kg/m^2 with major comorbidities: Type 2 diabetes Severe steatohepatitis Pseudotumor cerebri Moderate-to-severe obstructive sleep apnoea (apnoea-hypopnea index ≥ 15)	BMI ≥ 40 kg/m^2 and other comorbidities: Hypertension Insulin resistance Glucose intolerance Impaired quality of life Dyslipidaemia
Nobili *et al.* (2015)[1*]	BMI >97% percentile (or >40 kg/m^2) with major comorbidities: Type 2 diabetes mellitus Moderate to severe sleep apnoea Pseudotumor cerebri NASH with significant fibrosis (Ishak score ≥1)	BMI >97% percentile (or >50 kg/m^2) with other mild comorbidities: Hypertension Insulin resistance Glucose intolerance Substantially impaired quality of life Dyslipidaemia Milder sleep apnoea

* Please note, the BMI values are taken from Table 1 in the published ahead-of-print version of the article.