

Non-alcoholic steatohepatitis and bariatric surgery

Abstract

Non-alcoholic steatohepatitis is a component of a wide spectrum of hepatic diseases that range from steatosis and non-alcoholic fatty liver disease, to cirrhosis and hepatocellular carcinoma. NASH has been identified in a significant amount of morbidly obese patients, and a lot of these patients have been undergoing bariatric surgery for weight loss management, as weight loss is the objective and most effective treatment. NASH by itself is a risk factor for the surgery and screening could be done for these patients, although risk/cost/benefits should be assessed. The desirable improvements in the metabolic components of the disease, as well as the procedure itself diminishes significantly hepatic disease, although there is still concern on increasing fibrosis in the long postoperative term. Surgery is still the best option for these patients, but controlled randomized studies are still needed.

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Abbreviations: BS, bariatric surgery; LRYGB, laparoscopic roux-en-y gastric bypass; LSG, laparoscopic sleeve gastrectomy; NASH, non-alcoholic steatohepatitis; NAFLD, non-alcoholic fatty liver disease

Introduction

Non-alcoholic steatohepatitis (NASH) is a component of a wide spectrum of diseases that go from non-alcoholic fatty liver disease (NAFLD) to cirrhosis, and hepatocellular carcinoma in 40-60% of patients with NASH-related cirrhosis in a 5-7 year follow-up.¹ NASH has become one of the leading causes of liver disease in the developed world. With NAFLD believed to have doubled in the past 20 years,² there is alerting evidence showing that these events are majorly secondary to the global epidemic of obesity.^{3,4}

The best way to combat this entity is by having patients lose weight, reportedly 3 to 5% to improve steatosis, 5-7% to decrease inflammation, and up to 10% to experience NAFLD/NASH remission and regression of fibrosis.⁵ Weight loss is aimed to be of 0.5 to 1 kg per week, as higher rates have been related to hepatic damage as evidenced by hepatic function tests.⁶ Medical treatment for this condition has not been approved as such, therefore pharmacological agents are focused on the pathophysiological mechanisms of the disease such as insulin resistance, oxidative stress, inflammation pathways, lipid metabolism and others.

In the past years, bariatric surgery (BS) has become a safe and efficient alternative treatment for morbid obesity. It has proven to revert some ailments associated to obesity that are related as well to NASH. The two most performed techniques are Laparoscopic Sleeve Gastrectomy (LSG) and Laparoscopic Roux-en-Y Gastric Bypass (LRYGB); the latter being the gold standard.⁷⁻⁹ As weight loss is the cornerstone in NASH approach, these procedures are often necessary to prevent the fatalities that can arise if not treated.¹⁰ This is related as well to the insulin resistance drop as well as the procedure per se.^{11,12}

Discussion

Nash as a risk factor in patients undergoing bariatric surgery

The presence of NAFLD and NASH is a common finding in

morbidly obese patients undergoing bariatric surgery.^{13,14} In a cohort of 212 patients studied by Ong et al, 93% presented NAFLD, similar to other studies,^{15,16} while 24% had NASH (although others studies mention up to 70%¹⁵), and 9% already presented advanced fibrosis.¹⁷ The discrepancy between NASH rates between studies can be explained as there is no standardized diagnostic criteria for NASH, therefore it is not simple to estimate its actual prevalence. Bedossa et al.,¹⁸ propose that patients should only be classified as NASH, when they present hepatocyte ballooning, obtaining a prevalence of NASH of 34% in a study of patients with morbid obesity.¹⁸

Various components are known to be associated with the development of NASH, such as hyperlipidemia, insulin resistance, type 2 diabetes, and hypertension.^{12,19,20} In recent studies, Losekann et al.,¹⁵ have observed that there is a linear correlation between age and the prevalence of fibrosis. Furthermore, it has been suggested that patients with morbid obesity, advanced age, elevated triglycerides and ALT may be at higher risk for hepatic disease.¹⁵ Despite of this, in a study published by Wolter et al.,¹⁴ they did not find a correlation between BMI and advanced liver disease.¹⁴

Recently, NASH has been proposed not only as a predictor for advanced hepatic disease, but as a predictor of mortality in severely obese patients who are candidates for bariatric surgery. A retrospective study of patients who had a gastric bypass performed between 1997 and 2004 was done in Switzerland, were peri-operative liver biopsies were obtained and analyzed.²¹ This study, which is the first one to follow long term outcomes after BS, concludes that despite of the significant weight loss and amelioration of comorbidities, there is increased mortality and overall survival may not improve. They have reported that the presence of NASH is correlated to increased risk of death in patients that undergo BS, compared to those that do not present it. Interestingly, they found an association of mortality from sepsis after BS, suggesting that NASH could be a predictor of non-hepatic mortality, while fibrosis a predictor of liver-related mortality.²¹

In patients that have undergone BS, impairment of BMI reduction is evident between patients with NASH and patients that do not show histologically characterized NASH; this is only partly explainable by the presence of diabetes.⁹ Goossens & collaborators²¹ have also suggested that more studies are required to verify if persistence of diabetes in association with NASH are involved in long-term mortality.²¹

As it has been commented previously, NASH represents higher risks for mortality and advanced disease in morbidly obese patients who plan to undergo BS¹⁵ as well as reports of worsening of fibrosis in the postoperative period.¹² Due to the previous observations a screening and surveillance system must be developed to determine the status in patients in whom liver disease is suspected and to prevent progression of hepatic disease.¹⁴ Praveenraj & collaborators²² determined in a morbidly obese South Indian population that hepatic biopsy is safe in these patients and would be beneficial for diagnosing NAFLD. This same group investigated whether shear wave velocity (SWV) was potentially diagnostic for NAFLD in morbidly obese patients, but their results did not correlate with liver biopsies,²² leaving hepatic biopsy still as the best source for diagnosis of fatty liver disease and fibrosis. Given the circumstances of the patients, an intra operative biopsy could possibly be enough to correlate the severity of disease and manage post operatively, as the surgery still remains the best course of action, and the prior circumstances are only worsening for the most part.

Nash after bariatric surgery

There is no evidence on controlled randomized studies, although retrospective and cohort studies have proven bariatric surgery to be effective in ameliorating steatosis, inflammation and some degree of fibrosis in obese patients.²³ Some studies have mentioned that it benefits up to 83% of patients with NAFLD and reverts NASH in up to 60%, resolving fibrosis in around 50%.²⁴ Despite of this, there are conflicting studies relating RYGB and increased liver fibrosis in up to 40% of the patients.²⁵

The direct impact of BS surgery on NAFLD has been studied by Bower and colleagues²⁶ through a systematic review that included 29 studies in a meta- analysis, assessing liver histology, previous and postoperative presence of steatosis, steatohepatitis, portal inflammation, lobular inflammation and hepatocyte ballooning, as well as liver fibrosis, biochemistry, and liver biomarkers. They present strong evidence that both pathological and histological features of NAFLD, as well as liver enzymes, are reduced in a beneficial pattern in patients after BS.²⁶

Some of the studies where increased fibrosis in the long run has been observed, are concerning (12). Increased fibrosis has been found, but over 95% of patients maintained a fibrosis score \leq F1, with NAFLD and NASH decreasing significantly. The fact that several other groups have shown severity of fibrosis reduction in up to 50%,²⁴ and in some cases even cirrhosis,^{27,28} as well as the conclusions of the severity of the fibrosis increase in the Mathurin article, opens a question towards if this is still concerning. This might be an outdated idea that remained in physicians minds after groups reported steatohepatitis and even liver failure as complications after jejunio-ileal bypass (which is no longer used).^{29,30}

Conclusion

NAFLD and NASH are risk factors on their own for surgery as they are intimately related. Nowadays, weight loss still remains as the best way to reduce liver fat infiltration, inflammation and fibrosis. Patients should initially undergo lifestyle modifications; unfortunately healthy eating habits and exercise will not resolve every patient's individual case. We believe that the best option for treatment of patients that present with both these entities is BS, with benefits diminishing the risks and providing the best course of action. Staging the severity of NAFLD/NASH in patients previous to surgery will aid assessing the risks, although options at this point are limited and percentages are

not sufficient proof to submit every bariatric patient to a liver biopsy previous to BS. We believe that surgeons should be able to perform a risk assessment during surgery to identify potential problematic patients and complications during the postoperative period. Close follow-up is necessary in order to better manage the patients that could progress into fibrosis, although this is not of huge concern as studies show. Further studies as large, prospective, randomized controlled trials are still necessary to be able to understand remaining unclear information about the benefits of bariatric surgery in morbidly obese patients that present with NASH.

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Conflicts of interest

Author declares there are no conflicts of interest.

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