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CASE REPORT | LIVER

# Intragastric Balloons: An Emerging Therapy for Nonalcoholic Steatohepatitis and Fibrosis?

Pichamol Jirapinyo, MD, MPH[1,2], Odise Cenaj, MD[2,3], Marvin Ryou, MD[1,2], and Christopher C. Thompson, MD, MSc[1,2]

[1]*Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital, Boston, MA*
[2]*Harvard Medical School, Boston, MA*
[3]*Department of Pathology, Brigham and Women's Hospital, Boston, MA*

## ABSTRACT

Weight loss through lifestyle intervention remains the mainstay treatment for nonalcoholic steatohepatitis (NASH). Nevertheless, only a minority of patients undergoing lifestyle intervention are able to achieve the weight loss threshold that reverses NASH histologic features. This case report demonstrates a minimally invasive method of treating NASH using an intragastric balloon. With endoscopic ultrasound-guided liver biopsy at the time of intragastric balloon removal, we demonstrate a significant improvement in NASH histologic features including steatosis, ballooning, lobular inflammation, and fibrosis. This endoscopic method may offer an alternative solution to patients with NASH who fail lifestyle intervention.

## INTRODUCTION

Nonalcoholic fatty liver disease is the most common cause of chronic liver disease in the United States representing greater than 75% of chronic liver disease as of 2008.[1] It represents a spectrum of liver condition ranging from simple steatosis to nonalcoholic steatohepatitis (NASH) and finally to cirrhosis. In addition to a minimum of 5% of fat within hepatocytes, NASH is defined as the presence of inflammation and hepatocyte injury with or without fibrosis.[2] Unlike simple steatosis, NASH is more aggressive with a risk of approximately 10%–29% of progression to cirrhosis within 10 years.[3] To date, weight loss achieved through lifestyle intervention remains the mainstay of NASH treatment. We present a novel therapy for NASH in a patient who has failed lifestyle intervention.

## CASE REPORT

A 29-year-old woman with a history of Down's syndrome, hypothyroidism, surgical repair of atrial and ventricular septal defects, and NASH presented for evaluation of obesity and NASH. The patient had been dealing with obesity almost her entire life. She previously tried calorie-restricted diet and exercise with modest weight loss. Two years before presentation, she was found to have elevated transaminases at an outside hospital. Workup included liver biopsy, which showed grade 2 steatohepatitis with stage 1 fibrosis (Figure 1).

Medications included aspirin 81 mg daily and levothyroxine 125 mcg daily. She had previously tried vitamin E. Family history was notable for her sister, who recently underwent liver transplantation for NASH cirrhosis. Her vital signs were notable for blood pressure of 126/55 mm Hg, weight of 181 pounds, height of 4 feet and 10 inches, and body mass index (BMI) of 37.8 kg/m$^2$. Examination was notable for a conversant woman with upslanting palpebral fissures and a flat nasal bridge. Her abdominal examination was otherwise unremarkable. Laboratories were notable for normal chemistry, complete blood count, and liver function tests. Although her hemoglobin A1c was within a normal range (5.5%), her homeostatic model assessment of insulin resistance was elevated up to 19.4. The patient and her parents were interested in a minimally invasive treatment option for weight loss and NASH.

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**Correspondence:** Christopher C. Thompson, MD, MSc, Brigham and Women's Hospital, Brigham and Women's Hospital, Division of Gastroenterology, 75 Francis St, Boston, MA 02115 (cthompson@hms.harvard.edu).

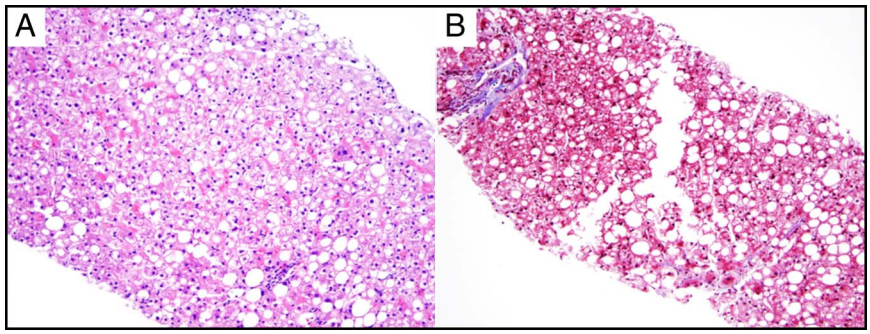


**Figure 1.** (A) Hematoxylin and eosin staining showing grade 2 steatohepatitis. Macrovascular steatosis with lobular inflammation, foci of neutrophilic satellitosis, and hepatocellular ballooning degeneration. (B) Trichrome staining showing stage 1 focal pericellular fibrosis.

The patient underwent intragastric balloon (IGB) placement, which was filled with 600 cc of normal saline and methylene blue (Figure 2). She tolerated the procedure well with mild nausea and abdominal spasm, which spontaneously resolved on post-procedural day 1. She was prescribed proton pump inhibitor 40 mg daily and was adherent to lifestyle intervention. At 6 months, her weight decreased to 110 pounds with a 39.2% total weight loss (TWL), and a BMI of 23 kg/m$^2$. The IGB was removed endoscopically at 6 months without complications. During the same endoscopy session, an endoscopic ultrasound-guided liver biopsy was performed using a 19-gauge SharkCore biopsy needle (Medtronic, Dublin, Ireland) (Figure 3). Pathology showed complete resolution of steatohepatitis and no significant fibrosis (Figure 4).

## DISCUSSION

Weight loss achieved through lifestyle intervention remains the mainstay treatment of NASH.[2] To reverse histologic features of NASH, a minimum of 10% TWL is recommended. Nevertheless, on average, less than 10% of patients undergoing lifestyle intervention are able to achieve 10% TWL.[4] On the other hand, bariatric surgery is effective at inducing greater than 10% TWL. However, patients must otherwise qualify for bariatric surgery based on BMI criteria as NASH alone is currently not an indication.[2]

Endoscopic bariatric and metabolic therapy (EBMT) is an emerging field for the treatment of obesity and its related comorbidities. To date, there are 3 types of EBMTs that are approved by the Food and Drug Administration including IGBs, endoscopic suturing or plication for gastroplasty, and aspiration therapy.[5] Despite robust data on the weight loss efficacy of EBMT, its effect on NASH remains unclear.[6]

In 2012, Lee et al randomized 18 patients with obesity and biopsy-proven NASH to undergo placement of the BioEnterics intragastric balloon, the predecessor of the current Orbera IGB (Apollo Endosurgery, Austin, TX), vs sham procedure. At 6 months, total nonalcoholic fatty liver disease activity score, which represents the sum of steatosis, ballooning, and lobular inflammation scores, was significantly lower in the BIB group. There was also a trend toward improvement in the steatosis scores in the BioEnterics intragastric balloon group. However, there was no change in the ballooning, lobular inflammation, or

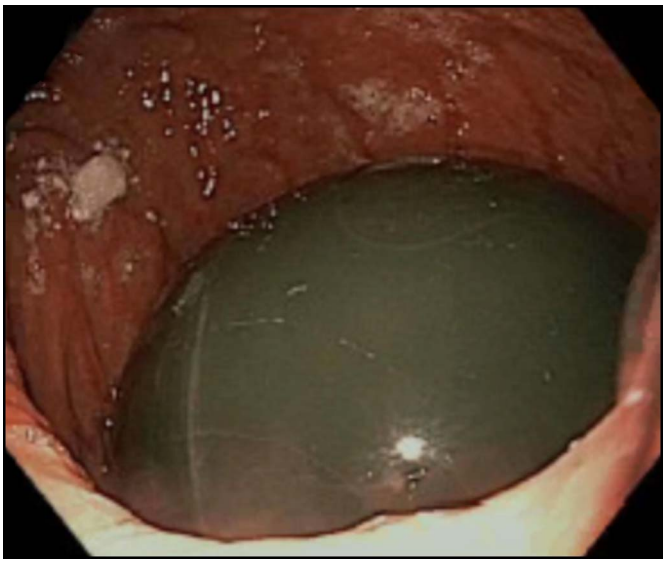

**Figure 2.** Intragastric balloon.

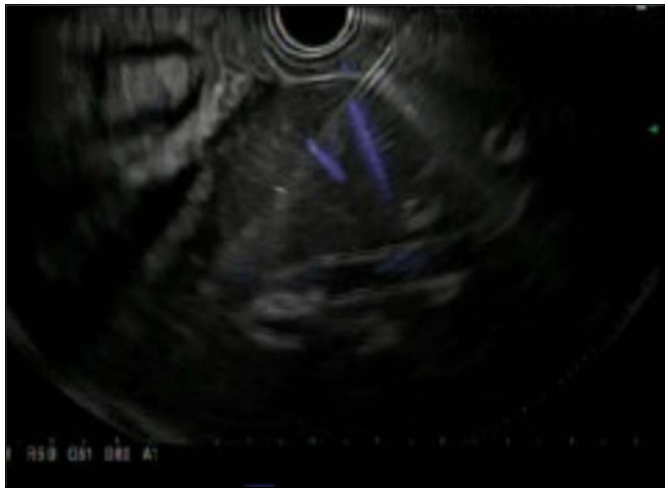

**Figure 3.** Endoscopic ultrasound-guided liver biopsy.

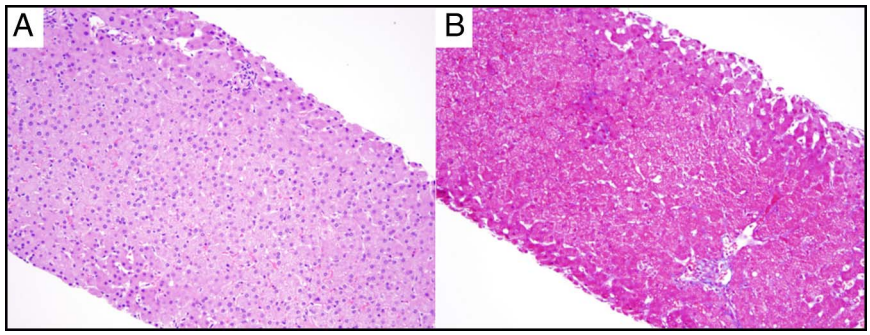


**Figure 4.** (A) Pathology revealing normal liver parenchyma with complete resolution of steatohepatitis. (B) Trichrome stain showing absence of fibrosis.

fibrosis scores in either group. Authors suggested that the study may have been underpowered.[7] A recent meta-analysis was conducted to assess the effect of IGB on obesity-related comorbidities. The study demonstrated a significant decrease in alanine aminotransferase and aspartate aminotransferase. However, there were not enough studies to pool the effect of IGB on changes in NASH histologic features.[8]

As far as we know, this is the first report demonstrating improvement in all histologic features of NASH, including the amount of fibrosis, with IGB therapy. The patient's significant weight loss and early stage of fibrosis at the time of IGB treatment likely had an impact on these results. Specifically, our patient experienced approximately 40% TWL, which was significantly higher than the average 10% TWL seen in most patients with IGB. This potentially could be due to the fact that placement of IGB prompted an increase in satiation and ultimately jumpstarted her weight loss by creating a positive feedback loop, where an initial decrease in BMI prompted an increase in activity and lifestyle modification (which she was initially unable to adhere to), which led to a further decrease in BMI. This is occasionally seen after other primary bariatric procedures, where patients find themselves to be more motivated and adherent to lifestyle modification after interventions. Additionally, it is unclear whether the patient's history of Down's syndrome may have played a role in the amount of weight loss following IGB. Patients with Down's syndrome have been shown to have a higher leptin level suggestive of leptin resistance. It is unclear whether the more dramatic weight loss seen in this patient may be due to alternative mechanisms in response to IGB placement. Future studies to formally establish the effect of IGB on NASH and to determine predictors of response are warranted. Given this unique history and the significant amount of weight loss experienced in this patient, generalizability of our results remains unclear.

## DISCLOSURES

Author contributions: P. Jirapinyo performed the procedure, collected data, and wrote the manuscript. O. Cenaj collected and interpreted the data. M. Ryou performed the procedure. CC Thompson performed the procedure, revised the manuscript, and is the article guarantor.

Financial disclosure: P. Jirapinyo and O. Cenaj have no conflict of interest. M. Ryou is the founder of, has equity interest in, and is a consultant for GI Windows, and is a consultant for Medtronic/Covidien. CC Thompson has contracted research for Aspire Bariatrics, USGI Medical, Spatz, Apollo Endosurery, has served as a consultant for Boston Scientific, Covidien, USGI Medical, Olympus, Fractyl, GI Dynamics, and holds stock and royalties for GI Windows and Endosim.

Informed consent was obtained for this case report.

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## REFERENCES

1. Younossi ZM, Stepanova M, Afendy M, et al. Changes in the prevalence of the most common causes of chronic liver diseases in the United States from 1988 to 2008. *Clin Gastroenterol Hepatol.* 2011;9(6):524–30.e1.
2. Chalasani N, Younossi Z. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology.* 2018;67(1):328–57.
3. Argo CK, Caldwell SH. Epidemiology and natural history of non-alcoholic steatohepatitis. *Clin Liver Dis.* 2009;13(4):511–31.
4. Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, et al. Weight loss through lifestyle modification significantly reduces features of nonalcoholic steatohepatitis. *Gastroenterology.* 2015;149:367–78.
5. Jirapinyo P, Thompson CC. Endoscopic bariatric and metabolic therapies: Surgical analogues and mechanisms of action. *Clin Gastroenterol Hepatol.* 2017;15(5):619–30.
6. Abu Dayyeh BK, Abu Dayyeh BK, Kumar N, et al. ASGE Bariatric Endoscopy Task Force systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting endoscopic bariatric therapies. *Gastrointest Endosc.* 2015;82:425–38.e5.
7. Lee YM, Low HC, Lim LG, et al. Intragastric balloon significantly improves nonalcoholic fatty liver disease activity score in obese patients with non-alcoholic steatohepatitis: A pilot study. *Gastrointest Endosc.* 2012;76(4):756–60.
8. Popov VB, Ou A, Schulman AR, Thompson CC. The impact of intragastric balloons on obesity-related co-morbidities: A systematic review and meta-analysis. *Am J Gastroenterol.* 2017;112:429–39.