



Bariatric endoscopic antral myotomy: first-in-human proof of concept of a novel therapeutic method to delay gastric emptying and induce weight loss

Christopher C. Thompson, MD, MSc, Roberto Trasolini, MD, MSc, Pichamol Jirapinyo, MD, MPH

Boston, Massachusetts, USA

As knowledge regarding the pathophysiology of obesity and mechanisms of action for bariatric procedures has evolved, opportunities have been created to develop new interventions that more directly address these mechanisms. One potential target is gastric emptying. This is a critical step in digestion that has been found to be more rapid after prolonged exposure to a high-fat diet in both animal and human studies, with rapid emptying also being more common in young people with obesity in some studies.^{1,2} Medications, such as GLP-1 receptor agonists, and interventions, such as intragastric balloons (IGBs), have been shown to delay gastric emptying as part of their mechanism to treat obesity. This appears to be effective even in those with normal baseline emptying rates.

More recently, gastroplasty with endoscopic myotomy (GEM) has been shown to consistently delay gastric emptying without triggering symptoms of gastroparesis and to produce substantial weight loss.³ This procedure involves submucosal tunneling, similar to a typical gastric peroral endoscopic myotomy procedure; however, the tunnel is substantially longer and the myotomy only involves the antrum, leaving the pylorus intact. A modified endoscopic sleeve gastroplasty (ESG) is also performed proximal to the myotomy. Based on our experience with GEM, we hypothesized that a pylorus-sparing antral myotomy alone, referred to as bariatric endoscopic antral myotomy (BEAM), would produce a consistent delay in gastric emptying and lead to reproducible and durable weight loss independent of ESG.

METHODS

This is an initial case report from a single-arm, prospective, first-in-human pilot study undertaken to examine the effects of the BEAM procedure (clinical trial registration number: NCT05725967). Patients with body mass indices ≥ 30 kg/m² who were unable or unwilling to undergo bariatric surgery were recruited from a weight management clinic. Exclusion criteria were diabetes, gastroparesis, severe reflux, gastric surgery, and taking GLP-1 receptor agonists,

anticoagulants, or antiplatelet agents. Primary outcomes were technical feasibility and safety, and secondary outcomes were percentage of total weight loss (TWL), gastric emptying assessed using a gastric-emptying breath test (Cairn Diagnostics, Brentwood, Tenn, USA) reported as gastric-emptying half-time, and change in gastroparesis cardinal symptom index (GCSI) at 1, 3, and 6 months. The study was approved by the institutional review board (IRB protocol: 2022P001757).

BEAM procedure

With patients under general anesthesia, an endoscopic pylorus-sparing antral myotomy was performed. Specifically, a mucosal incision was performed using a T-type hybrid knife (Erbe, Tübingen, Germany) at the level of the incisura along the level of the greater curvature using a Carr-Locke needle (Steris, Mentor, Ohio, USA) and 6% hetastarch with diluted methylene blue without epinephrine. Submucosal tunneling was then performed using a T-type hybrid knife and a VIO 3 electrosurgical unit (Erbe, Tübingen, Germany, Endocut Q 2-2-2, PreciseSECT6.0, SoftCoag 6.0 settings). The tunnel was stopped immediately proximal to the pylorus. Two parallel lines of partial-thickness myotomy were then performed from the distal to proximal antrum using the same T-type hybrid knife (Endocut Q 2-2-2). The myotomy was stopped approximately 2 cm distal to the mucosotomy site. Subsequently, 2% lidocaine was sprayed in the tunnel before closure of the mucosotomy site using the Overstitch suturing device (Apollo Endosurgery, Austin, Tex, USA).

End-tidal carbon dioxide, abdominal fullness, and peak ventilation pressures were monitored throughout the procedure. Patients were monitored overnight for adverse events followed by an upper GI series before diet advancement. Patients undertook a liquid protein diet for 6 weeks postoperatively, followed by 2 weeks of a soft solid diet, and then advancing to a regular caloric-restricted diet. Follow-up was scheduled at 2 weeks and at 1, 3, 6, 9, and 12 months, with a repeat gastric-emptying study at 3 months.

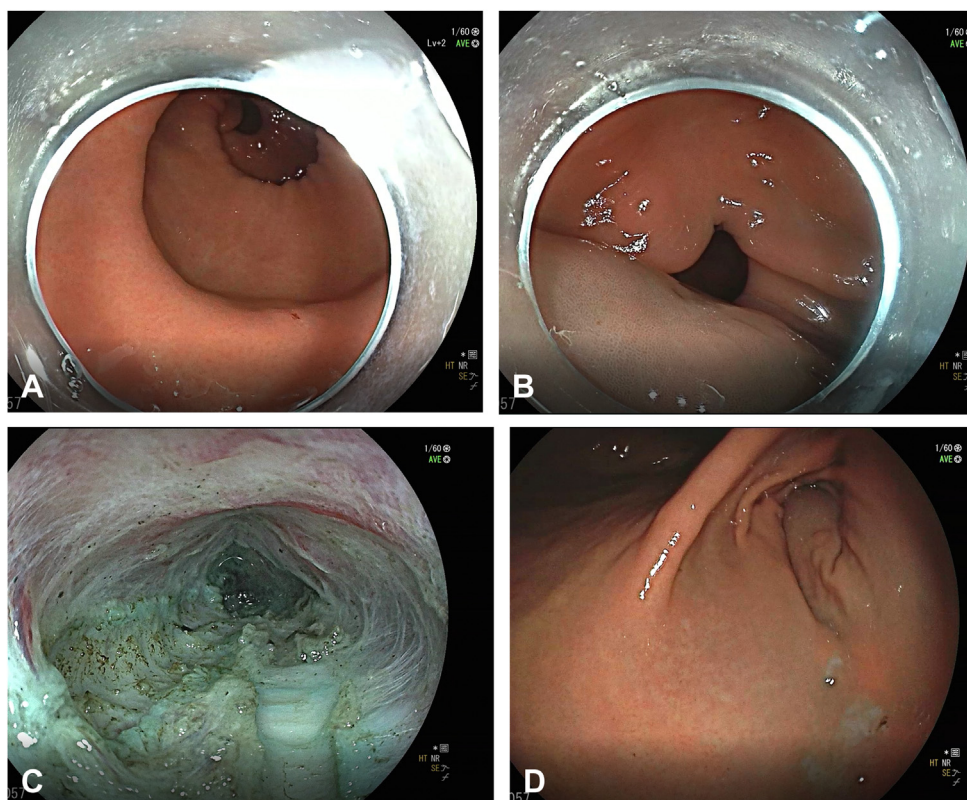


Figure 1. Bariatric endoscopic antral myotomy procedure. **A**, Rapid antral contractions before the procedure. **B**, Submucosal tunnel extending to the prepyloric region. **C**, Parallel partial-thickness pylorus-sparing antral myotomies. **D**, Postprocedure gastric deformation with gastric shortening and angulation.

RESULTS

Technical feasibility and safety

A 28-year-old woman with class III obesity (body mass index of 41.3 kg/m^2), polycystic ovary syndrome, and nonalcoholic fatty liver disease was recruited from the bariatric endoscopy clinic. She previously attempted lifestyle modification with hypocaloric diets, cardiovascular and resistance exercise, and phentermine and over-the-counter supplements but was unable to achieve clinically significant weight loss. After discussing benefits and risks, she was enrolled in the study and successfully underwent the BEAM procedure. Specifically, a 15-cm-long submucosal tunnel was created along the greater curvature extending from the incisura to the prepyloric region. Subsequently, 2 parallel partial-thickness myotomies were performed along the greater curvature from distal to proximal extending approximately 12 cm in length. The mucosotomy site was then closed using a running suture pattern with 6 stitches (Fig. 1). The total procedure time was 73 minutes.

There were no intra- or postprocedure adverse events or serious adverse events. Postprocedurally, the patient reported 2 out of 10 for abdominal pain on a Likert scale. She was admitted per protocol. An upper GI series performed on postoperative day 1 showed a smooth, bulging antrum

with delayed contrast entry into the duodenum, without contrast extravasation (Fig. 2). She was discharged home on postoperative day 1.

Short-term weight loss

At 1 and 3 months, the patient experienced 6.8% TWL and 20.5% TWL, respectively. Her body mass index decreased from 41.3 kg/m^2 preprocedurally to 38.5 kg/m^2 and 32.9 kg/m^2 at 1 and 3 months, respectively. The patient began resistance training at 6 weeks after the procedure. No antiobesity medication was prescribed.

Physiologic changes

Gastric-emptying half-life increased from 47.9 minutes to 70.3 minutes at 3 months, representing a 68% delay from baseline (Fig. 3). The GCSI score increased from 0 to 1.67 and .83 at 1 and 3 months, respectively (Fig. 4). Specifically, the GCSI subscores at 1 month were 0 for nausea/vomiting, 4 for postprandial fullness and early satiety, and 1 for bloating. The GCSI subscores at 3 months were 0 for nausea/vomiting, 2.75 for postprandial fullness and early satiety, and 0 for bloating. Clinically, the patient reported no negative gastroparesis symptoms with no postprandial abdominal pain, discomfort, or vomiting.

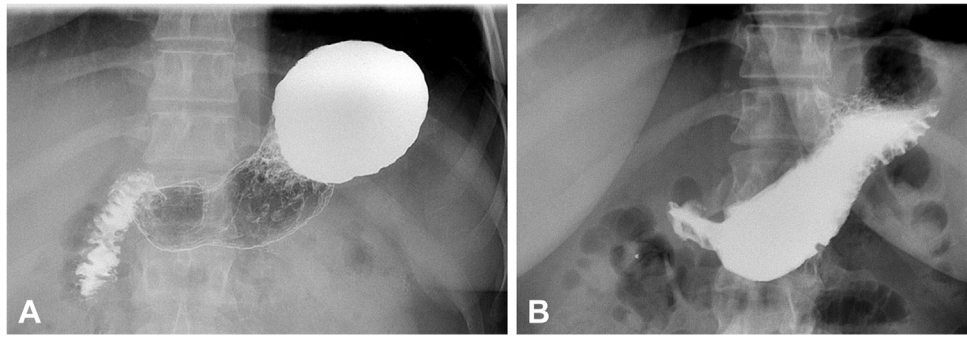


Figure 2. Upper GI series (A) at baseline and (B) 1 day after bariatric endoscopic antral myotomy. Note the smooth, bulging antrum with delayed contrast entry into the duodenum.

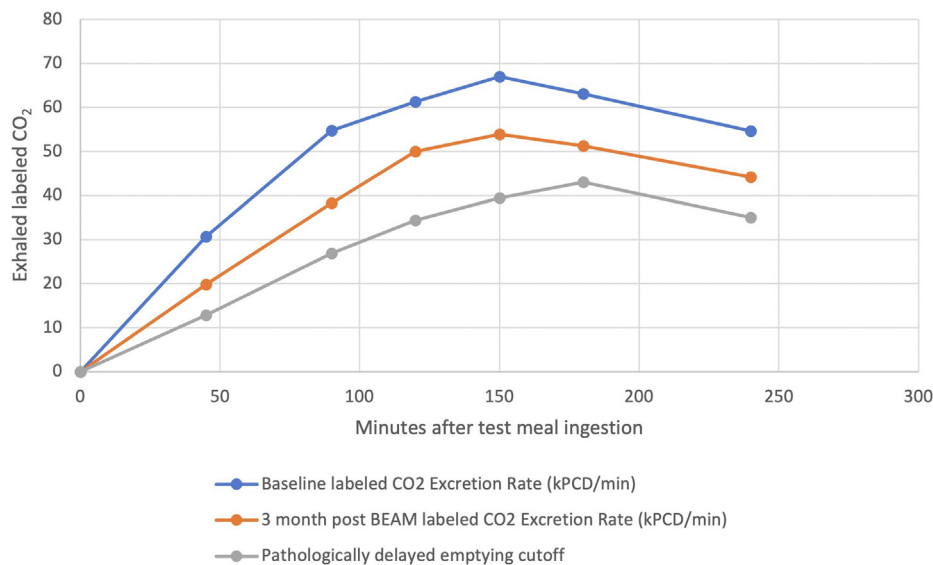


Figure 3. Delay in gastric-emptying rate after the bariatric endoscopic antral myotomy (BEAM) procedure measured with the gastric-emptying breath test. Baseline (blue, half-life of 47 minutes), 3 months after BEAM (orange, half-life of 71 minutes), and pathologic half-life cutoff (gray).

DISCUSSION

This first-in-human case report of the BEAM procedure, using parallel pylorus-sparing antral myotomies along the greater curvature of the stomach, was technically feasible and well tolerated. This myotomy alone produced a delay in gastric emptying and subsequent weight loss that was on the high end of that typically seen with endoscopic bariatric and metabolic therapies. Of note, the BEAM procedure was well tolerated, and our patient did not develop any symptoms characteristic of gastroparesis. There was no significant increase in the GCSI subscales for nausea and vomiting or bloating. This suggests that the clinical manifestations of gastroparesis are likely because of neuropathy or other mechanisms and not the delay in emptying alone. The only subscale increase seen was for fullness and early satiety, which was the intended consequence of the procedure.

Many endoscopic bariatric and metabolic therapies have focused on gastric physiology and digestion to induce

weight loss. The original primary obesity surgery endoluminal procedure addressed the first phase of gastric digestion by placing plications in the gastric fundus to limit fundal accommodation. This resulted in only a 5% TWL in a controlled trial, and the pattern has been subsequently modified to focus on the gastric body.^{4,5} IGBs and ESG concentrate more on the second phase of digestion, limiting the breakdown and mixing of food into chyme. These deliver more weight loss, ranging from 10% to 18% TWL.^{6,7} The transpyloric shuttle is a temporary implant similar to the IGB. It consists of a balloon that resides in the antrum connected to a smaller bulb that sits in the duodenum and is believed to delay gastric emptying by causing intermittent pyloric obstruction. This delivered a 9.5% TWL and a safety profile similar to IGBs.^{8,9} The BEAM procedure aims to more directly and permanently inhibit the antral pump by creating longitudinal partial-thickness antral myotomies and leaving the pylorus intact. Based on the results of the GEM procedure and the

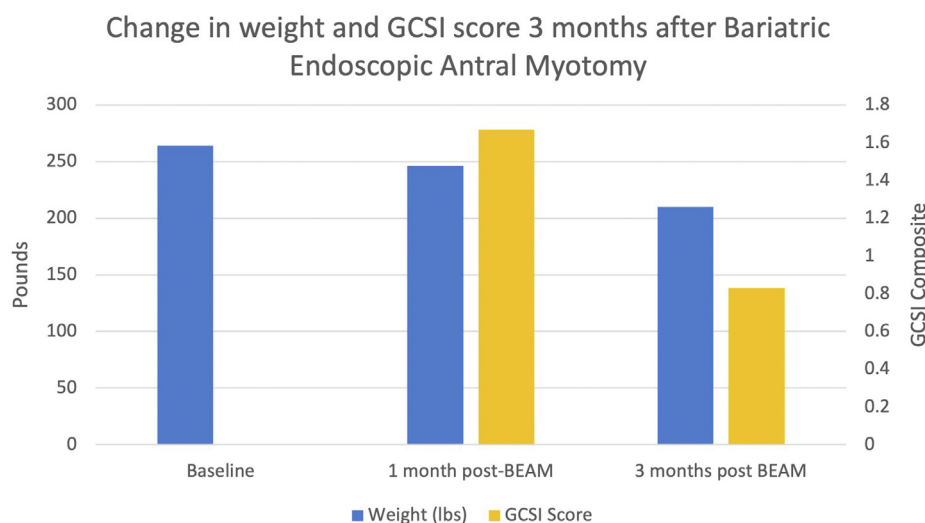


Figure 4. Weight loss and GCSI change after BEAM. GCSI, Gastroparesis cardinal symptom index; BEAM, bariatric endoscopic antral myotomy.

transpyloric shuttle, it was hypothesized that BEAM without ESG could produce a significant delay in gastric emptying with significant weight loss.

BEAM could also be thought of as a member of the POEM family and may be referred to as Bariatric POEM (B-POEM). However, it is important to note that all POEM procedures to date have been performed for exactly the opposite reason of making esophageal or gastric transit more rapid in patients who are struggling to eat and maintain their weight. This could be confusing for patients, and even physicians, who are researching the procedure. Additionally, we feel that POEM terminology is somewhat less descriptive and may ultimately be less helpful in understanding the procedure. BEAM is the opposite of a typical gastric peroral endoscopic myotomy, which involves transection of the pyloric ring and leaves the antrum intact in an effort to increase the rate of gastric emptying. Development and refinement of endoscopic submucosal tunneling and closure techniques have allowed for safe and reproducible interventions on submucosal lesions and the muscularis propria. To date, submucosal tunneling-based procedures have been used to remove subepithelial tumors¹⁰ and release muscular sphincters of the oropharynx, esophagus, pylorus, and rectum¹¹⁻¹⁴ as well as to treat refractory sleeve stenosis.¹⁵ Submucosal tunneling and myotomy of the antral pump to delay gastric emptying are novel concepts first used by our group in combination with a sutured gastropasty for the treatment of obesity in the GEM procedure. This procedure produced a significant delay in gastric emptying and substantial weight loss.³ However, ESG may delay gastric emptying independently of myotomy,¹⁶ and this is the first report to evaluate the impact of an isolated antral myotomy. Antral myotomy alone, without the need for gastric suturing or plication, would have several potential benefits if there was good weight loss efficacy.

Compared with suturing and plication-based endobariatric approaches, BEAM may allow for a shorter procedure time, improved reproducibility with less variability of technique, minimal perioperative discomfort, and increased durability. Compared with IGBs, BEAM is more permanent and does not require use of a temporary implant. It also appears to be better tolerated than most IGBs. The technique may also be cost-saving because of the need for only a needle-knife and injection solution, compared with other procedures that rely on more sophisticated and expensive equipment.

This procedure is important as a proof of concept and may ultimately be a valuable addition to the endoscopic management of obesity if efficacy and safety are confirmed in the ongoing study and subsequent controlled trials with longer-term follow-up. Furthermore, pylorus-sparing antral myotomy, by decreasing the gastric-emptying rate, may have potential in the treatment of pathologically rapid gastric emptying, such as that seen in idiopathic dumping syndrome. These observations provide a potential new therapeutic target for endoscopic myotomy and deepen our understanding of gastric physiology. Because BEAM has such a clear mechanism of action, it may also allow a more personalized and targeted approach to the management of patients with obesity.

In conclusion, BEAM appears to be technically feasible and induces a delay in gastric emptying that is associated with significant weight loss and no symptoms of gastroparesis. Long-term study is underway to better understand these results.

DISCLOSURE

The following authors disclosed financial relationships:
C. C. Thompson: Consultant for Apollo Endosurgery,

Boston Scientific, Medtronic, Enterasense Ltd, EnVision Endoscopy, Fractyl, Fujifilm, GI Dynamics, GI Windows, Lumendi, Olympus, USGI Medical, Xenter, and EndoQuest Robotics; research support from Apollo Endosurgery, Boston Scientific, Erbe, Fujifilm, GI Dynamics, Lumendi, Olympus, and USGI Medical; advisory board member for Fractyl, Fujifilm, USGI Medical, Xenter, and EndoQuest Robotics; founder of, board member for, and ownership interest in Enterasense Ltd, EnVision Endoscopy, and GI Windows; speaker for Boston Scientific, Fujifilm, and Olympus; royalties from GI Windows, EndoSim, and Enterasense Ltd. R. Trasolini: Consultant for Fractyl. P. Jirapinyo: Research support from Apollo Endosurgery, Boston Scientific, Fractyl, GI Dynamics, and USGI Medical; consultant for Apollo Endosurgery, Erbe, GI Dynamics, and Spatz Medical; royalties from Endosim.

Abbreviations: BEAM, bariatric endoscopic antral myotomy; ESG, endoscopic sleeve gastropasty; GCSI, gastroparesis cardinal symptom index; GEM, gastropasty with endoscopic myotomy; IGB, intragastric balloon; TWL, total weight loss.

REFERENCES

1. Pajot G, Camilleri M, Calderon G, et al. Association between gastrointestinal phenotypes and weight gain in younger adults: a prospective 4-year cohort study. *Int J Obes* 2020;44:2472-8.
2. Little TJ, Horowitz M, Feinle-Bisset C. Modulation by high-fat diets of gastrointestinal function and hormones associated with the regulation of energy intake: implications for the pathophysiology of obesity. *Am J Clin Nutr* 2007;86:531-41.
3. Thompson CC, Jirapinyo P, Shah R, et al. Gastropasty with endoscopic myotomy (GEM) for the treatment of obesity: preliminary efficacy and physiologic results. *Gastroenterology* 2022;163:1173-5.
4. Sullivan S, Swain JM, Woodman G, et al. Randomized sham-controlled trial evaluating efficacy and safety of endoscopic gastric plication for primary obesity: the ESSENTIAL trial. *Obesity* 2017;25:294-301.
5. Jirapinyo P, Thompson CC. Endoscopic gastric body plication for the treatment of obesity: technical success and safety of a novel technique (with video). *Gastrointest Endosc* 2020;91:1388-94.
6. Abu Dayyeh BK, Bazerbachi F, Vargas EJ, et al. Endoscopic sleeve gastropasty for treatment of class 1 and 2 obesity (MERIT): a prospective, multicentre, randomised trial. *Lancet* 2022;400:441-51.
7. Shah R, Davitkov P, Abu Dayyeh BK, et al. AGA technical review on intragastric balloons in the management of obesity. *Gastroenterology* 2021;160:1811-30.
8. Puri S, Chevalier JJ, Rothstein RI. Long-term weight loss outcomes of endoscopic treatment with the BAROnova transpyloric shuttle: a prospective observational cohort study. *Am J Gastroenterol* 2021;116:S489-90.
9. Rothstein RI, Woodman G, Swain J, et al. Transpyloric shuttle treatment improves cardiometabolic risk factors and quality of life in patients with obesity: results from a randomized, double-blind, sham-controlled trial. *Gastroenterology* 2019;156:S237.
10. Xu MD, Cai MY, Zhou PH, et al. Submucosal tunneling endoscopic resection: a new technique for treating upper GI submucosal tumors originating from the muscularis propria layer (with videos). *Gastrointest Endosc* 2012;75:195-9.
11. Kedia P, Fukami N, Kumta NA, et al. A novel method to perform endoscopic myotomy for Zenker's diverticulum using submucosal dissection techniques. *Endoscopy* 2014;46:1119-21.
12. Werner YB, Hakanson B, Martinek J, et al. Endoscopic or surgical myotomy in patients with idiopathic achalasia. *N Engl J Med* 2019;381:2219-29.
13. Vosoughi K, Ichkhanian Y, Benias P, et al. Gastric per-oral endoscopic myotomy (G-POEM) for refractory gastroparesis: results from an international prospective trial. *Gut* 2022;71:25-33.
14. Bapaye A, Waghlikar G, Jog S, et al. Per rectal endoscopic myotomy for the treatment of adult Hirschsprung's disease: first human case (with video). *Dig Endosc* 2016;28:680-4.
15. de Moura DTH, Jirapinyo P, Aihara H, et al. Endoscopic tunneled stricturotomy in the treatment of stenosis after sleeve gastrectomy. *Video-GIE* 2019;4:68-71.
16. Vargas EJ, Rizk M, Gomez-Villa J, et al. Effect of endoscopic sleeve gastropasty on gastric emptying, motility and hormones: a comparative prospective study. *Gut* 2023;72:1073-80.

© 2023 Published by Elsevier Inc. on behalf of American Society for Gastrointestinal Endoscopy. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.igie.2023.04.010>

Received April 5, 2023. Accepted April 17, 2023.

Current affiliation: Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA.

Reprint requests: Christopher C. Thompson MD, MSc, AGAF, FACP, FASGE, FJGES, Brigham and Women's Hospital, Division of Gastroenterology, Hepatology and Endoscopy, 75 Francis St, Boston, MA 02115.

How to cite iGIE articles: Johnson R, Webber C, Thompson TJ, et al. Article title. *IGIE* 2023;2:10-26.