Measurement of Pyloric Pressures in Gastroparesis: Stiff Competition from EndoFLIP™

Aaron Shanker¹ · Mohammad Bashashati²

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Gastroparesis is a gastrointestinal motility disorder associated with delayed gastric emptying, manifested as dyspepsia variably combined with chronic and sometimes refractory nausea and vomiting, bloating, epigastric pain, and early satiety. Etiologies include diabetes complicated by neuropathy, gastric surgery, vagal nerve injury, or unknown. The precise pathogenesis of gastroparesis has not yet been clearly elucidated. Medical treatment options for gastroparesis include anti-emetics and prokinetic agents. Surgical and endoscopic options, usually considered in moderate–severe cases, consist of intrapyloric injection of botulinum toxin, endoscopic pyloromyotomy, pyloroplasty, or implantation of a gastric electrical stimulator (GES) in severe and refractory cases. In some cases, post-pyloric feeding through jejunostomy (J-tube) is necessary [1].

Normal pyloric functioning is essential for the success of gastric emptying. Pylorospasm, fibrosis, and vagal injury contribute to pyloric dysfunction in gastroparesis. The interstitial cells of Cajal (ICC) which are the pacemakers of gut motor function are depleted in the pylorus of gastroparesis patients, more prominently so than antral ICC [2].

Pyloroplasty has been reported as a successful treatment option in gastroparesis. Based on a recent study, there was 71% improvement in total symptom score of gastroparesis patients treated with pyloroplasty combined with GES. Remarkably, gastric emptying was normalized in 60% of the patients who were treated with GES plus pyloroplasty [3].

Despite the fact that pyloric interventions are important treatment options in gastroparesis, studying pyloric function

has not been routinely implemented into practice principally due to technical difficulties. Pyloric dysfunction in diabetic patients with gastroparesis features was first documented with manometric studies [4]. With the invention and utilization of the functional lumen imaging probe (EndoFLIP™ Medtronic, Minneapolis, MN, USA) in the pylorus, the evidence supporting pyloric dysfunction in gastroparesis is growing. Of note, EndoFLIP™ is a revolutionary impedance planimetry technique used in the assessment of gastrointestinal motility which as a “smart bougie” in the form of a balloon catheter simultaneously measures pressure and the dimensions in the gastrointestinal lumen [5]. By measuring the dimensions of the balloon, pressure/volume measurements are possible, in contrast to the simple pressures measured by conventional manometry balloons. The pressure/volume relationship is essential for the calculation of compliance or distensibility, in which a noncompliant or stiff structure dilates less at a given pressure. Though EndoFLIP™ is primarily utilized for the assessment of the esophageal motility disorders, there is growing evidence that this novel technique can also assess pyloric function.

Studies with EndoFLIP™ in gastroparesis are limited and still evolving. In an earlier study of 114 patients with nausea and vomiting with/without delayed gastric emptying, Snape et al. used sleeve manometry and EndoFLIP™ simultaneously in order to study pyloric function. The basal and peak pressures measured by sleeve manometry were comparable in patients with normal and delayed gastric emptying, whereas there was a significant decrease in distensibility of the pyloric sphincter in patients with increased gastric retention compared with patients with normal gastric retention. Increased EndoFLIP™ balloon pressure predicted a severe delay in gastric emptying [6]. These data all suggested that EndoFLIP™ was superior to sleeve manometry in documenting pyloric dysfunction in gastroparesis.

In this issue of *Digestive Diseases and Sciences*, Jehangir et al. study the utility of EndoFLIP™ in predicting the response to pyloric dilation for gastroparesis symptoms

✉ Mohammad Bashashati
Bashashati.md@gmail.com

¹ Department of Internal Medicine, Texas Tech University Health Sciences Center El Paso, El Paso, TX, USA

² Center for Neurogastroenterology and GI Motility, Division of Gastroenterology, Department of Medicine, Texas Tech University Health Sciences Center El Paso, 4800 Alberta Ave, El Paso, TX 79905, USA

refractory to pyloromyotomy/pyloroplasty. Briefly, in this single-center prospective study, the authors first sought to measure and characterize pyloric distensibility via EndoFLIP™ of subjects who had previously undergone surgical or endoscopic pyloric intervention prior to proceeding with through the scope (TTS) pyloric balloon dilation [7]. The clinical aspects and outcomes discussed in this paper are relevant and contemporary, given the considerable medical, mental, emotional, and socioeconomic toll uncontrolled gastroparesis can bring to bear on patients and healthcare systems.

The investigators examined 13 patients with severe gastroparesis who were refractory to pyloromyotomy/pyloroplasty and underwent EndoFLIP™ pyloric assessment followed by TTS balloon dilation. Outcomes were derived from two questionnaires administered to all the patients at regularly scheduled post-dilation follow-up encounters: the Gastroparesis Cardinal Symptom Index (used by patients to rate the severity of their symptoms, also administered one time before any evaluation or intervention to provide a baseline) and the Clinical Patient Grading Assessment Scale (used by patients to document the evolution—or lack thereof—of their symptoms after the intervention described in this study). Approximately one-third of their subjects demonstrated symptomatic improvement, associated with lower pre-dilation pyloric distensibility measurements suggesting a stiffer pylorus pre-distention in the subset of patients exhibiting improvement of their symptoms [7].

The incorporation of pyloric distensibility calculations to forecast outcomes in refractory gastroparesis patients after intervention was reported in other studies as well. Desprez et al. [8] studied botulinum toxin injections, reporting that lower pre-procedural pyloric distensibility values portended greater symptomatic improvement following the intervention. In the same vein, Vosoughi et al. utilized EndoFLIP™ to compute the pyloric cross-sectional area and distensibility index in an effort to determine whether a relationship existed between the aforementioned values and clinical outcomes in refractory gastroparesis patients undergoing gastric peroral endoscopic myotomy (G-POEM). In this latter study, EndoFLIP™ measurements were taken both before and after the G-POEM. The authors established that the post-G-POEM, EndoFLIP™ cross-sectional area (CSA), and the distensibility index (DI) of the pylorus at both 40 ml and 50 ml volume distention “were significantly higher in the clinical success group” [9].

Jehangir et al. found lower pre-dilation pyloric distensibility at 30 ml, 40 ml, and 50 ml in patients with symptom improvement [7]. In an earlier study from the same group, pyloric sphincter contour was best visualized at 40 ml balloon distension [10]. In another study again from the same group located at the Temple University School of Medicine [11], pyloric distensibility at 40 ml ($29.1 \pm 93.9 \text{ mm}^2/\text{mmHg}$)

was quantitatively higher with more variability compared with Jehangir et al. ($11.4 \pm 1.6 \text{ mm}^2/\text{mmHg}$) [7]. While this possibly might be due to a more severe spectrum of the disease in the latter study [7], future research should consider standardization of the technique in order to find the normal and abnormal values as well as the optimal volume of the EndoFLIP™ balloon.

The study at the focus of this editorial hypothesizes that the decreased pre-TTS balloon dilation EndoFLIP™ values seen in their cohort may be attributed to “incomplete myotomy, pyloric muscle regeneration, or pyloric stricture after pyloromyotomy/pyloroplasty decreasing the pyloric distensibility” [7]. Importantly, the investigators acknowledge that since some patients did not symptomatically improve after pyloric intervention, this finding reinforces the concept that pyloric dysfunction is not the sole factor in the etiopathogenesis of gastroparesis. Other mechanisms of action that may affect gastroparesis symptoms include “impaired gastric accommodation, hypersensitivity, and extragastric transit abnormalities” [12].

Ultimately, this paper highlights the potential of integrating pyloric distensibility data from EndoFLIP™ measurements in order to inform risk stratification of refractory gastroparesis patients and to prognosticate outcomes in said patients undergoing possible therapeutic interventions. This would mark a significant shift in the management of some of the most challenging patients in the realm of gastrointestinal motility.

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