Pyloric dilation with the esophageal functional lumen imaging probe in gastroparesis improves gastric emptying, pyloric distensibility, and symptoms CME

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Background and Aims: The role of decreased pyloric distensibility in gastroparesis as measured by the endoluminal functional luminal imaging probe (EndoFLIP) has been receiving increasing attention. In this study, we present clinical outcomes to pyloric dilation with the esophageal FLIP (EsoFLIP) in regard to gastric emptying, symptom evolution, and FLIP metrics.

Methods: Patients evaluated for gastroparesis (gastric emptying studies of $t_{1/2} \geq 180$ minutes during ^{13}C-octanoic acid breath test and/or gastric remnants during gastroscopy after a sufficient fasting period) were scheduled for EsoFLIP controlled pyloric dilation. Pre- and postprocedural gastric emptying studies, questionnaires (Patient Assessment of Upper GI Symptoms Severity Index [PAGI-SYM; including the Gastroparesis Cardinal Symptom Index] and Patient Assessment of Quality of Life Index [PAGI-QOL]), and FLIP metrics were documented. Dilation was conducted according to a self-developed algorithm.

Results: Forty-six patients were analyzed (72% women; median age, 39 years [range, 18-88]). Etiologies of gastroparesis were diabetic in 10 patients (22%), idiopathic in 33 (72%), and postoperative in 3 (6%). Postprocedural gastric emptying time decreased from a median of 211 minutes to 179 minutes ($P = .001$). In accordance, pyloric distensibility, PAGI-SYM, PAGI-QOL, and Gastroparesis Cardinal Symptom Index values improved significantly. After a median follow-up of 3.9 months, 57% of all treated patients with returned questionnaires reported improved symptoms.

Conclusions: Pyloric EsoFLIP controlled dilation shows value in the treatment of gastroparesis, both subjectively and objectively. Long-term follow-up to assess efficacy and comparative trials are warranted. (Gastrointest Endosc 2021;94:486-94.)

Gastroparesis is a debilitating condition, associated with a significant increase in healthcare costs and a reduction in annual income for affected patients.[1] Although its pathophysiology is complex and not fully understood, pharmacologic treatment options are limited by side effects, questionable efficacy, and/or off-label status.[2]

Abbreviations: CPGAS, Clinical Patient Grading Assessment Score; CSA, cross-sectional area; DI, distensibility; EndoFLIP, endolumenal functional luminal imaging probe; EsoFLIP, esophageal functional luminal imaging probe; FLIP, functional luminal imaging probe; GCSI, Gastroparesis Cardinal Symptom Index; G-POEM, gastric peroral endoscopic myotomy; PAGI-QOL, Patient Assessment of Quality of Life Index; PAGI-SYM, Patient Assessment of Upper GI Symptoms Severity Index.

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Pyloric dysfunction is increasingly recognized as an important factor in gastroparesis. Data have emerged that demonstrate a link between decreased pyloric distensibility (DI) and gastric emptying, as measured with the functional lumin imaging probe (FLIP; Medtronic, Minneapolis, Minn, USA).[3-5] Impedance planimetry enables FLIP to calculate GI sphincter DI by measuring pressure and cross-sectional area (CSA).[6] Pylorus-directed therapy regimes, including onabotulinumtoxinA injection, transpyloric stent placement, pyloric dilation, and, more recently, endoscopic pyloromyotomy, have been challenged by questionable effect, considerable morbidity, or no long-term follow-up because they are just emerging.[7] Although surgical treatments exist, there is no consensus on the best option; however, gastric resection and/or bypass should be delayed or rather avoided.[8]

Because the pylorus is amenable to endoscopic myotomy, the recent literature has been dominated by studies assessing the therapeutic effect of endoscopic pyloromyotomy (gastric peroral endoscopic myotomy [G-POEM]), whereas other endoscopic treatment modalities such as dilation outside a postoperative setting have only scarcely been evaluated.[9-11] Our group recently published results of achalasia treatment with the esophageal FLIP (EsoFLIP; Crospon Ltd, Galway, Ireland).[12] EsoFLIP is based on FLIP hardware, allowing real-time and dynamic visualization of the pyloric sphincter and intratherapeutic monitoring of diameter, CSA, and intraballoon pressure. This is the first study to present clinical outcomes of a combination of the diagnostic use of endolumenal FLIP (EndoFLIP) with the therapeutic use of EsoFLIP in patients with gastroparesis.

METHODS

Patients not well controlled with pharmaceutical treatment with symptoms suggestive of gastroparesis (ie, gastric emptying time of $t_{1/2} \geq 180$ minutes during ^{13}C-octanoic acid breath test and/or gastric solid remnants during prior gastroscopy after a minimum 12-hour fasting period) were scheduled for EsoFLIP controlled pyloric dilation. All patients were given questionnaires for the subjective assessment of GI symptoms before and after treatment. This study is an analysis of patients treated for gastroparesis with EsoFLIP controlled pyloric dilation from August 2018 until February 2020 at the University Hospital Zurich. The Zurich Ethical Committee (BASEC-No. 2017-00930; amendment submitted on December 31, 2018 and accepted January 16, 2019) approved the study. Exclusion criteria were age <18 years, mechanical gastric outlet obstruction, previous pyloric interventions (such as stent placement, botulinum injection, G-POEM), gastric electric stimulation, and declined informed consent for the use of patient-specific data.

Although technically retrospective, management and data assessment in our functional diagnostic clinic are principally conducted as in prospective trials: Before dilation (T_0), 14 to 21 days (T_1) after dilation, and approximately 3 months (T_2) after dilation, patients were asked to fill out the Patient Assessment of Upper GI Symptoms Severity Index (PAGI-SYM)[13] and the Patient Assessment of Quality of Life Index (PAGI-QOL).[14] PAGI-SYM includes the Gastroparesis Cardinal Symptom Index (GCSI), which assesses abdominal symptoms of gastroparesis including nausea, stomach fullness, loss of appetite, bloating, retching, stomach visibly larger, vomiting, inability to finish a normal-sized meal, and feeling excessively full after meals. Symptoms are graded from 0 (none) to 5 (very severe) over a period of the prior 14 days[14,15]; subscores are averaged to calculate total scores, with higher scores resembling greater symptom severity. At T_1 and T_2 overall treatment response is additionally assessed with the Clinical Patient Grading Assessment Score (CPGAS) ranging from –3 (very considerably worse) over 0 (unchanged) to +3 (completely better). Additionally, at T_1 and T_2 questionnaires are given concerning potential adverse events, including questions regarding abdominal pain (including severity [0-10], number of pain days, and the use of analgesics) and procedure-related visits to physicians. Gastric emptying studies are conducted before (T_0) and 14 to 21 days after dilation (T_1), currently delayed because of coronavirus disease 2019–related measures. Tests are performed in a standardized fashion according to published literature after an overnight fast (at least 8 hours).[16,17] In short, ^{13}C-octanoic acid is ingested mixed into a single scrambled egg, eaten with 2 slices of white bread and 5 g of margarine, followed by 180 mL of water. Results were documented as $t_{1/2}$ (minutes) after a 4-hour measurement period.

Procedure

All patients underwent EsoFLIP controlled pyloric dilation by a single experienced user (D.P.) and an assisting motility-trained fellow or attending. FLIP measurements and treatment were performed according to a self-developed algorithm based on prior experience with EsoFLIP use in achalasia as published by our group.[12] All procedures were conducted as outpatient endoscopies under nurse-assisted propofol sedation.

The technical features of the EsoFLIP device, which have been previously described,[18] allow real-time measurements of diameter and CSA. In combination with the use of a computer-controlled electrohydraulic pump, EsoFLIP permits individually titrated dilations with volume increases in milliliter steps, calculated by 15 electrodes incorporated into the shaft with a .1-mm resolution.

Catheters are placed side by side of the endoscope and under visual control across the pylorus (for EndoFLIP, one-third of the balloon positioned inside the gastric lumen, two-thirds placed in the duodenum; for EsoFLIP, positioned half-way through the pylorus) by the endoscopist. Proper balloon placement is verified by an hourglass shape

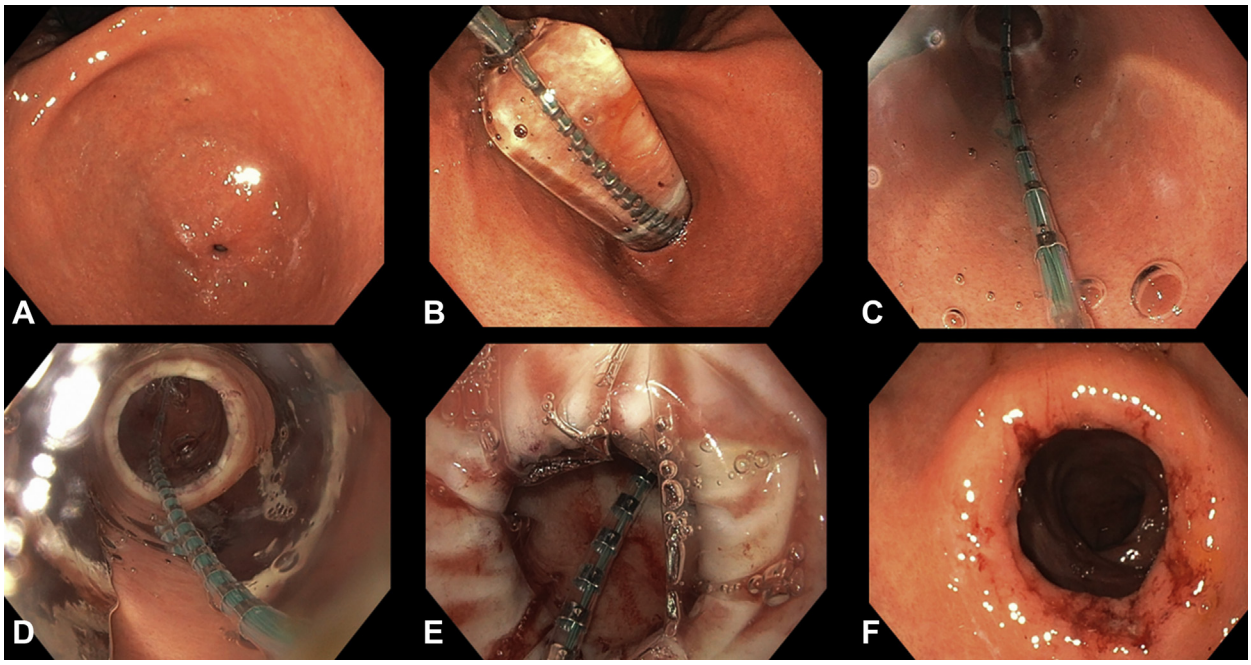

Figure 1. Endoscopic procedure. **A** and **F,** Pylorus pre-/postdilation. **B,** Esophageal functional luminal imaging probe catheter placed in the pylorus with the initial volume of 30 mL. **C-E,** Visualization of the circular pyloric muscle during dilation by pressing the camera into the proximal balloon.

displayed on the device monitor and endoscopically verified in parallel (Fig. 1C-E). The first measurements (diameter, CSA) are documented at a volume of 30 mL. Afterward, the volume is increased stepwise in 5-mL intervals to a volume of 50 mL. To allow stable measurements, balloon volume is kept stable for at least 30 seconds at each step. Further dilation is then tailored individually in 2- to 3-mL steps until a target diameter of about 25 mm is reached, taking into account mucosal lacerations. At the maximum filling volume, balloon position is kept stable for 2 minutes to allow sufficient dilation. After dilation, measurements are routinely repeated at balloon volumes of 30 and 40 mL after the tissue is given at least 30 seconds to readjust at volumes 10 mL below the intended measuring volume.

Before and immediately after dilation, the pylorus is examined with the EndoFLIP. For logistic reasons, 2 different EndoFLIP systems were used during the study period: EndoFLIP-325 (8 patients) and EndoFLIP-322 (38 patients), differing by measurement segments of 8 cm (EndoFLIP-325) or 16 cm (EndoFLIP-322) and balloon filling. Diameter, CSA, and pyloric DI were measured at 30, 40, and 50 mL (EndoFLIP-325) or 50, 60, 65, and 70 mL (EndoFLIP-322), with a goal of intraballoon pressure >15 mm Hg, ideally >20 mm Hg, to allow for a valid measurement.

Endpoints

The primary endpoint was the clinical response after a singular EsoFLIP controlled pyloric dilation, defined as a reduction in gastric emptying time and GCSI. Secondary outcomes were the change of pyloric DI and diameter before and after dilation, changes in PAGI-SYM/PAGI-QOL, evaluation of CPGAS, and incidence of adverse events.

Statistical analysis

According to the literature, we regarded a GSCI reduction of .5 points as clinically meaningful, requiring a total of 41 patients, according to a sample size calculation performed with a (2-sided) Type I error of .05 and a power of .85. Statistical analysis was conducted with R version 3.5.1. (R Foundation for Statistical Computing, Austria, Vienna). The Friedman test was used to compare changes of median GCSI, PAGI-SYM, and PAGI-QOL values over time. Wilcoxon signed-rank test (Bonferroni corrected) was used to compare non-normally distributed paired (pre- and post-treatment) data. A $P < .05$ was regarded as statistically significant. Results are expressed as median and range or mean and standard deviation.

RESULTS

Forty-six patients (median age, 39 years [range, 18-88]; 33 women [72%]; median body mass index, 24 kg/m^2 [range, 17.5-37.7]) underwent EsoFLIP controlled pyloric dilation for clinically relevant gastroparesis (diabetic, 10 patients [22%]; idiopathic, 33 [72%]; postoperative, [6%]; upside-down stomach and hiatal hernia repair, 1; Nissen fundoplication, 1; and distal esophagectomy with esophagogastrostomy, 1). All patients underwent prior endoscopy before additional testing. In 41 patients (89%), gastric

TABLE 1. Effect of pyloric dilation on gastric emptying time, pyloric distensibility, and diameter

	Before dilation	After dilation	*P* value
^{13}C-octanoic acid breath test, min ($t_{1/2}$)	43/46 211 (132-513)	41/46* 179 (88-441)*	.001
Pyloric distensibility,† mm^2/mm Hg	46/46 9 (2.8-21.8)‡	39/46 13 (2.4-24.8)	<.001
Pyloric diameter,§ mm	46/46 17 (13.2-22.1)	45/46 20 (10.8-23.0)	<.001

Values are n/N, median (range).
*Measurement at T_1 (median 21 days after dilation; range, 6-93).
†Measured with the EndoFLIP-325 (n = 8) at 40 mL volume and at 60 mL with the EndoFLIP-322.
‡Patients with distensibility values ≥10 mm^2/mm Hg (n = 15) had a gastric emptying time ($t_{1/2}$) of ≥180 minutes.
§Measured with the esophageal functional luminal imaging probe at 40 mL volume.

emptying time was >180 minutes, whereas the remaining 5 patients (11%) were included based on suggestive previous endoscopic findings only (no gastric emptying study performed in 3; gastric emptying time <180 minutes in 2 patients). At T_0 median gastric emptying time was 211 minutes (range, 132-513) and median GCSI was 2.78 (range, 1.0-4.2). Based on a simple clinical grading scale,[19] gastroparesis was classified as mild in 74% (n = 34), compensated (daily medication, dietary adjustments) in 24% (n = 11), and gastric failure (frequent medical consultation, hospitalization, and/or inability to maintain nutrition) in 2% (n = 1) of all patients.

The first postinterventional clinical assessment (gastric emptying studies and questionnaires) was conducted after a median of 21 days (range, 6-93), resembling T_1. The median clinical follow-up was 3.9 months (range, 2.2-12.2), resembling T_2. Specific details of pre- and postinterventional characteristics regarding gastric emptying time, pyloric DI, and diameter and a detailed analysis of questionnaires are listed in Tables 1 to 3.

Outcomes of gastric emptying time, pyloric DI, and diameter

Dilation was conducted up to a median pyloric diameter of 25.5 mm (range, 23.1-26.5) with a median balloon filling volume of 60 mL. Postinterventional mucosa lacerations (Fig. 1F) were observed in all but 1 patient. Of these, 66% had lacerations in 3 quadrants and 33% in all 4 quadrants.

Postprocedural gastric emptying time decreased significantly (P = .001) from a median of 211 minutes to 179 minutes (Table 1 and Fig. 2). After dilation, $t_{1/2}$ was reduced to under 180 minutes in 41% of patients with completed gastric empting studies (17/41) in which $t_{1/2}$ was >180 minutes before intervention. Three further patients (3/41) with unknown preprocedural gastric emptying time showed a postprocedural $t_{1/2}$ of <180 minutes. Two other patients (2/41) had pre- and postprocedural $t_{1/2}$ below 180 minutes. In accordance, pyloric DI increased significantly (P < .001) from a median of 9 to 13 mm^2/mm Hg after dilation (Table 1 and Fig. 2). In addition, postdilation pyloric diameter was significantly larger (median 17 vs 20 mm; P < .001) (Table 1 and Fig. 2).

Patient self-assessment of symptom response

Questionnaires were returned by 85% of all treated patients (39/46) at T_1 and by 61% (28/46) at T_2. Quality of life markers GCSI and PAGI-SYM values improved significantly over time (P = .012 and P = .002, respectively), and PAGI-QOL improved significantly from T_0 to T_1 (P = .028) and from T_0 to T_2 (P = .020) (Table 2 and Figs. 3-5). After a median follow-up of 3.9 months, 57% of all treated patients with returned questionnaires reported global symptom improvement (CPGAS at T_2).

The GCSI improved significantly after dilation (P = .012) from a median of 2.78 before dilation (T_0) to 2.44 at T_1 (P < .001) with a further reduction to a median of 1.95 at T_2 (P < .001). Accordingly, the GCSI postprandial fullness subscore improved from a median of 3 before dilation to a median of 2.5 at T_1 (P = .002) and a median of 2 at T_2 (P = .004). A reduction of the mean GCSI of >.5 points was achieved in 53% of patients (15/28) at T_2.

Table 3 and Figure 6 list the changes of the 9 individual GCSI-symptoms in detail. In general all symptoms showed a reduction in the mean value over time ($T_0 > T_1$ and $T_1 > T_2$). At T_2, 6 of 9 symptoms (nausea, stomach fullness, bloating, stomach or belly visibly larger, not able to finish a normal-sized meal, and feeling excessively full after meals) improved significantly. The remaining 3 symptoms (loss of appetite, retching, and vomiting) showed a decreased mean value but without reaching statistical significance.

Association between pyloric distensibility and GCSI

There was a significant GCSI decrease of .9 points (standard deviation, .03) per 10 mm^2/mm Hg postinterventional DI increase (P = .012).

Adverse events

At T_1 patients were specifically asked to fill out a standardized questionnaire assessing postprocedural adverse

TABLE 2. Effect of pyloric dilation on patient questionnaires

	T_0 42/46 patient	T_1 39/46 patients	*P* value*	T_2 28/46 patients	*P* value*
Patient Assessment of Upper GI Symptoms Severity	2.45 (.7-4.6)	2.05 (.5-3.6)	<.001	1.65 (.6-3.4)	<.001
Gastroparesis Cardinal Symptom Index	2.78 (1.0-4.2)	2.44 (.6-3.8)	<.001	1.95 (.3-3.1)	<.001
Gastroparesis Cardinal Symptom Index, postprandial fullness	3 (1.0-5.0)	2.5 (.8-4.0)	.002	2 (.5-4.5)	.004
Patient Assessment of Quality of Life	1.92 (.4-4.5)	1.43 (.4-3.7)	.028	1.27 (0-3.6)	.02
		T_1		T_2	
Clinical Patient Grading Assessment Score	Positive ($\geq +1$)	25/39 (64)		16/28 (57)	
	Neutral (0)	8/39 (21)		8/28 (29)	
	Negative (≤ -1)	6/39 (15)		4/28 (14)	

Values are median (range) or n/N (%).
T_0, Before dilation; T_1, median 21 days after dilation (range, 6-93); T_2, median 3.9 months after dilation (range, 2.2-12.2).
*P value (T_0 – T_1/ T_2) according to the Wilcoxon rank sum test, Bonferroni corrected.

TABLE 3. Effect of pyloric dilation on individual symptoms (included in the Gastroparesis Cardinal Symptom Index)

	T_0 42/46	T_1 39/46	*P* value T_0 vs T_1	T_2 28/46	*P* value T_0 vs T_2
Nausea	3.3 ± 1.4	2.7 ± 1.5	.138	2.3 ± 1.6	.013
Stomach fullness	3.2 ± 1.3	2.9 ± 1.2	.193	2.3 ± 1.5	.013
Loss of appetite	2.3 ± 1.6	1.8 ± 1.6	.008	1.7 ± 1.5	.061
Bloating	3.3 ± 1.7	2.7 ± 1.4	.024	2.4 ± 1.5	.003
Retching	1.7 ± 1.7	1.4 ± 1.7	.153	1.1 ± 1.3	.204
Stomach or belly visibly larger	2.6 ± 1.9	2.0 ± 1.6	.006	1.7 ± 1.5	.004
Vomiting	1.7 ± 1.8	1.1 ± 1.6	.005	1.1 ± 1.6	.465
Not able to finish a normal-sized meal	2.5 ± 1.8	2.1 ± 1.6	.161	1.8 ± 1.4	.041
Feeling excessively full after meals	3.3 ± 1.5	2.7 ± 1.6	.052	2.4 ± 1.6	.008

Values are mean ± standard deviation.
T_0, Before dilation; T_1, median 21 days after dilation (range, 6-93); T_2, median 3.9 months after dilation (range, 2.2-12.2).

events to ensure proper documentation, which was completed by 37 of 46 treated patients. Twenty-three patients (62%) reported postprocedural epigastric pain for a median of 1 day with a median intensity of 3 (scale, 0-10). Six patients reported the use of analgesics (nonsteroidal anti-inflammatory drugs, 3; metamizol, 2; acetaminophen, 1), and none required opioids. No significant side effects, especially no perforations, hospitalizations, or hemodynamically relevant bleeding, were documented.

DISCUSSION

This study is the first to demonstrate the feasibility of pyloric EsoFLIP dilation for patients with gastroparesis. Our results show EsoFLIP pyloric dilations to be well tolerated and comparatively effective both in objective (significant reduction in gastric emptying time and FLIP parameters such as pyloric DI and diameter) and subjective (significant reduction in GCSI, positive CPGAS and quality of life) outcome markers.

Unsatisfactory pharmaceutical treatment options, new insights into the mechanism of gastroparesis, and new technical developments have led to renewed interest in pyloric-directed therapy regimes in recent years. In short, gastric emptying depends on the trituration of solids by antral contractions to particle sizes of approximately 2 mm.[20] Those particles then leave the stomach as chyme through the pylorus into the small bowel. Pathophysiologically, pyloric dysfunction may contribute to gastroparesis because the interstitial cells of Cajal, resembling "pyloric pacemaker cells," were shown to be depleted in the pylorus in most gastroparetic patients.[21] At least since 1986, pylorospasm is linked to gastroparesis.[22] However, because of the infrequent clinical use of antral manometry, little progress has been made concerning pyloric-directed diagnostics.

The development of the FLIP technology has started to change this. In gastroparetic patients, Malik et al[3] demonstrated an inverse correlation between pyloric diameter and CSA and early satiety. Gourcerol et al[5] reported reduced pyloric DI in patients with prolonged

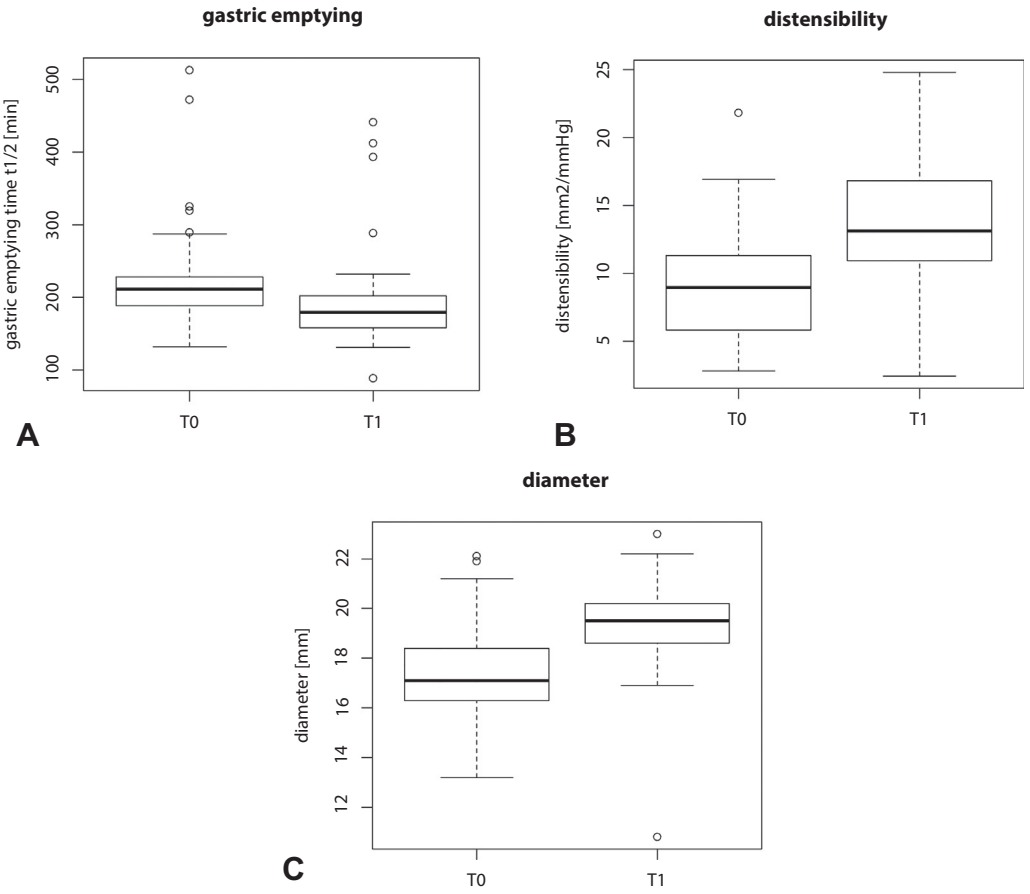

Figure 2. Boxplots of statistical analysis of gastric emptying time, distensibility, and diameter. **A,** Gastric empting time decreases from a median of 211 minutes to 179 minutes ($P = .001$). **B,** Pyloric distensibility increased from a median of 9 to 13 mm^2/mm Hg ($P < .001$). **C,** Diameter decreased from a median of 17 to 20 mm ($P < .001$). T_0, Before dilation; T_1, median 21 days after dilation (range, 6-93).

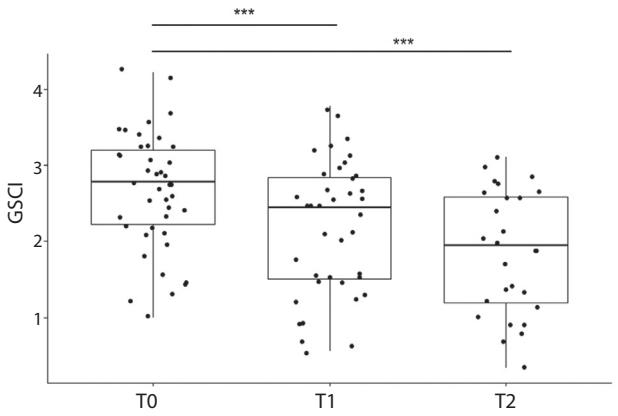

Figure 3. Boxplots of statistical analysis of changes of the Gastroparesis Cardinal Symptom Index (GCSI)). The GCSI improved significantly from a median of 2.78 before dilation to 2.44 at T_1, with a further reduction to a median of 1.95 at T_2. ***$P < .001$ (Wilcoxon rank sum test, Bonferroni corrected). T_0, Before dilation; T_1, median 21 days after dilation (range, 6-93); T_2, median 3.9 months after dilation (range, 2.2-12.2).

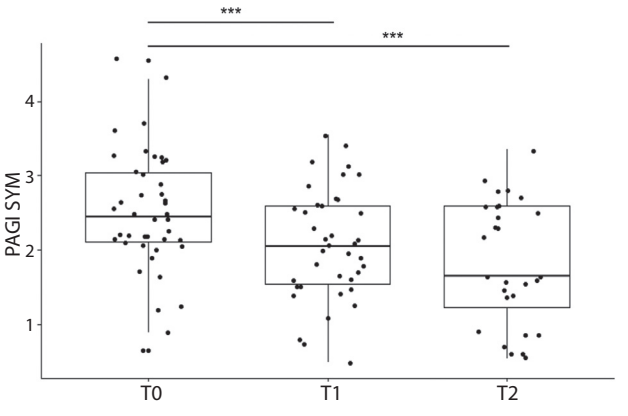

Figure 4. Boxplots of statistical analysis of changes of the Patient Assessment of Upper GI Symptoms Severity Index (PAGI-SYM). The PAGI-SYM improved significantly from a median of 2.45 before dilation to 2.05 at T_1, with a further reduction to a median of 1.65 at T_2. ***$P < .001$ (Wilcoxon rank sum test, Bonferroni corrected). T_0, Before dilation; T_1, median 21 days after dilation (range, 6-93); T_2, median 3.9 months after dilation (range, 2.2-12.2).

gastric emptying time. Later, Snape et al[4] confirmed a significant decrease in pyloric compliance in patients with gastroparesis-associated symptoms. Pyloric sphincter myotomy performed laparoscopically[23-25] or, more recently, endoscopically[9-11,26] has demonstrated clinical benefit in gastroparetic patients with success rates

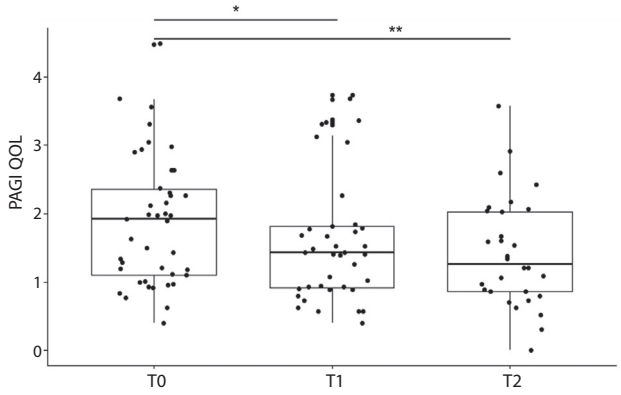

Figure 5. Boxplots of statistical analysis of changes of the Patient Assessment of Quality of Life Index (PAGI-QOL). The PAGI-QOL improved significantly from a median of 1.92 before dilation to 1.43 at T_1, with a further reduction to a median of 1.27 at T_2. *$P < .028$ and **$P < .020$ (Wilcoxon rank sum test, Bonferroni corrected). T_0, Before dilation; T_1, median 21 days after dilation (range, 6-93); T_2, median 3.9 months after dilation (range, 2.2-12.2).

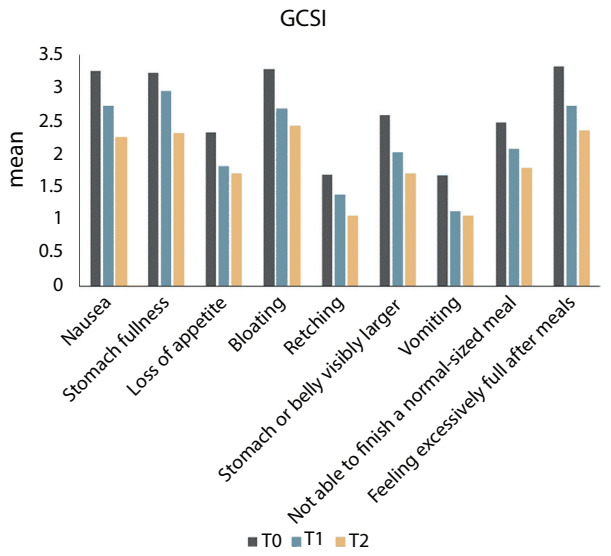

Figure 6. Changes of individual GCSI. Symptoms at T_1 (median 21 days after dilation, range 6-93) and T_2 (median 3.9 months after dilation, range 2.2-12.2). GCSI, Gastroparesis Cardinal Symptom Index.

ranging around 70%. In contrast, electric stimulation and onabotulinumtoxinA injections have not shown consistent clinical efficacy.[20] Gourcerol et al[5] conducted the only prospective trial evaluating hydraulic balloon dilation using a 20-mm through-the-scope balloon and showed an increased pyloric compliance, an accelerated gastric emptying time, and an improved quality of life after a follow-up of 10 days in a cohort of 10 patients. In general, it seems that using larger balloons (30 vs 20 mm) led to a better treatment outcome,[27] whereas balloon sizes of up to 30 to 35 mm seem to be safe according to the literature available on this topic.[28] This was the primary reason, apart from the possibility of data acquisition and better control over the dilation process, that we chose the EsoFLIP system that technically currently allows for a maximum dilation diameter of 30 mm.

Our results show that EsoFLIP controlled pyloric dilation leads to significant reduction of gastric emptying time and GCSI and a 57% positive patient global assessment after a median of 3.9 months. Specifically, a clinically meaningful GSCI reduction of .5[15] was achieved in 53% of patients, with an improvement of all 9 individual GCSI symptoms (6 with significance). When comparing GCSI scores at T_1 and T_2, the effect of pyloric dilation seems to increase over time (at least during this rather short follow-up), which, given a sizeable to be expected placebo response, hints at an actual effect of the intervention. In accordance, quality of life improved significantly.

Despite the growing number of therapeutic studies, patient selection for pylorus-directed treatment remains a matter of debate, especially because most patients with suspected gastroparesis have normal gastric emptying[29] and because of the clinical dilemma of an overlap of functional dyspepsia and gastroparesis. This dilemma was recently evaluated in a prospective trial with 944 patients with chronic upper GI symptoms.[30] In this trial, 37% of patients initially classified as having functional dyspepsia were reclassified as gastroparesis and 42% initially diagnosed with gastroparesis were reclassified as suffering from functional dyspepsia after a 48-week follow-up.[30] Also, even in documented delayed gastric emptying and suggestive symptoms, the correlation between subjective outcomes and treatment efficacy is low.[31,32]

The subjective endoscopic visualization of the pylorus with a diagnosis of "pylorospasm" is not reliable and not based on solid data. Although initially promising, botulinum toxin injections used as a screening test for pyloric-directed therapies are currently not recommended.[7] EndoFLIP metrics might be able to predict clinical efficacy of pyloric-directed approaches. Vosoughi et al[9] confirmed the earlier results by Malik et al[3] showing that pyloric CSA is associated with clinical success and improvement in gastric emptying. Other studies demonstrated an impaired pyloric DI to predict a meaningful effect of pyloric treatment[33,34] but with a low negative predictive value of preprocedural values.[34] Our results did not show a relevant relationship of pre- or postinterventional DI with the corresponding GCSI, currently leaving the question of which patients to treat best with this entity unanswered. However, an increase in postdilation DI (delta pre-/postdilation) was significantly associated with a GCSI decrease. Measuring postprocedural DI might therefore help to decide whether the degree of pyloric dilation or myotomy was sufficient. This is in line with the findings of Vosoughi et al,[9] who demonstrated that measuring pyloric DI immediately after G-POEM predicted clinical success better than the DI change measured 3 months later.

However, it remains unclear what delta size needs to be achieved: Our data merely suggest that with every 10-mm^2/mm Hg increase, the GCSI decreases by .9. We believe that enlarging the pyloric diameter and DI, as demonstrated in this study, enables gastric emptying with less antral pressure and may therefore alter gastroparetic symptoms, especially in patients with antral hypomotility, leading to a better quality of life in a patient cohort with debilitating symptoms.

Currently, the literature regarding pyloric-directed therapies is dominated by G-POEM, which has been shown to be effective and, compared with laparoscopic procedures, associated with shorter hospitalizations, less blood loss, and fewer adverse events.[8] No study comparing G-POEM and EsoFLIP or other dilation modalities exists. However, EsoFLIP might resemble a valuable alternative to G-POEM, which is available in few centers, is technically challenging, and is still considered experimental, per European Society of Gastrointestinal Endoscopy guidelines.[7] Despite having a rather favorable safety profile, the technically highly complex G-POEM procedures are associated with moderate and severe rates of adverse events of 16% and 6%, respectively, with significantly higher rates for less-experienced endoscopists,[35] usually leading to procedures conducted in specialized tertiary centers. Because of the possibility of adverse events, patients are usually monitored for a few days in the hospital.[26,34] In contrast, no patient in this study or in a study evaluating the treatment effect of EsoFLIP in achalasia by our group[12] had to be hospitalized (100% outpatient treatments), and no serious adverse events occurred. One other advantage might be the possibility of individualized treatment regimes. The EsoFLIP technology allows visually controlled dilations with the possibility of instantly identifying mucosal lacerations and changes in diameter and CSA. Additional and more aggressive pylorus-directed therapies should still be possible, yet no data for G-POEM after dilation currently exist.

One limitation of this cross-sectional study is its retrospective nature with a rather short follow-up and a medium sample size. Furthermore, T_2 resembles a clinical follow-up without another EndoFLIP evaluation of pyloric DI, which would be a valuable endpoint. In addition, because our study was not sham-controlled, a placebo effect, which has been shown for onabotulinumtoxinA-directed therapies,[36] is certainly part of our patient-reported outcome and symptom data. Finally, the motor function of the antrum and small bowel were not studied; however, the effect of pylorus-directed therapy in such patients in largely unknown.

Pyloric EsoFLIP dilation for gastroparesis appears to be feasible, well tolerated, and, acknowledging the limitations discussed, effective using both objective and subjective outcome markers. With its potential for individualized treatment regimes, good handling, and larger dilation diameter to conventional through-the-scope balloons, EsoFLIP constitutes a very interesting alternative to existing interventional modalities. Long-term follow-up to assess efficacy and sham-controlled studies and comparison with other pylorus-directed treatment strategies are warranted. Finally, patient selection is likely the cornerstone for the success of this technique, however good it is.

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