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Original Article

Hybrid transgastric approach for the treatment of gastroesophageal junction pathologies

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SUMMARY. **Flexible endoscopy has evolved to the point that it includes many endoluminal procedures that once required open or laparoscopic surgery, for instance, antireflux surgery, pyloromyotomy, mucosal and submucosal tumor resections, and even full-thickness resection. However, these procedures remain technically demanding due to flexible technology issues: difficult imaging, limited energy devices, lack of staplers, unsatisfactory suturing abilities, and so on. Transgastric laparoscopy or hybrid laparoscopy/flex endoscopy has been described for almost two decades as an alternative to a pure endoluminal approach, mainly for pancreatic pseudocyst drainage and full-thickness and mucosal resection of various lesions. The approach has never been widely adopted mostly due to cumbersome and difficult to maintain methods of gastric access. We propose to expand the indications of transgastric laparoscopy by using novel endoscopically placed ports to replicate endoscopic procedures particularly in the difficult to access proximal stomach such as endoluminal antireflux surgery. Under general anesthesia, five female pigs (mean weight: 27.6 kg) had endoscopic placement of 3, 5 mm intragastric ports (Endo-TAGSS, Leakwood KS, USA) using a technique similar to percutaneous endoscopic gastrostomy. A 5-mm laparoscope was used for visualization. Laparoendoscopic-assisted plication of the gastroesophageal junction (GEJ) was performed using 3–0 interrupted sutures (Polysorb®, Covidien, Mansfield, MA, USA). A functional lumen imagine probe (EndoFLIP®, Crospon, Inc., Galway, Ireland) was used to measure diameter, cross sectional area (CSA), distensibility, and compliance of GEJ before and after intervention. Once the TAGSS ports were removed, the gastrotomies were closed by using endoscopic over-the-scope clips. At the end of the procedure, animals were euthanized. Five laparoendoscopic-assisted endoluminal plications were performed. The mean operative time was 65.6 min (Endoscopic evaluation: 3.2 min, TAGSS Insertion: 11 min, EndoFLIP evaluation + GEJ Plication: 43.25 min, gastric wall closure: 15 minutes). In all cases, this technique was effective and allowed to achieve an adequate GEJ plication by endoscopic grading and EndoFLIP measurements. Median pre-plication GEJ diameter (D) and median pre-plication GEJ cross-sectional area (CSA) were 11.42 mm (8.6–13.6 mm) and 104.8 mm^2 (58–146 mm^2). After the procedure, these values were decreased to 6.14 mm (5.7–6.6 mm) and 29.8 mm^2 (25–34 mm^2) respectively ($p = 0.0079$). Median pre-plication distensibility (*d*) and compliance (*C*) were 7.87 mm^2/mmHg (2.4–22.69 mm^2/mmHg) and 190.56 mm^3/mmHg (70.9–502.8 mm^3/mmHg). After the procedure, these values decreased to 1.5 mm^2/mmHg (0.7–2.2 mm^2/mmHg) and 52.17 mm^3/mmHg (21.9–98.7 mm^3/mmHg) respectively ($p = 0.0317$). No intraoperative events were observed. Endoscopically, all valves were felt to be transitioned from a Hill grade 3 (normal state for the animal model)**

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to a Hill grade 1 at the procedure completion. A hybrid laparoendoscopic approach is a feasible alternative for performing intragastric procedures with the assistance of conventional laparoscopic instruments; especially in cases where the intervention location limits the access to standard endoscopy or where endoscopic technology is inadequate. Further evaluation is planned in survival models and clinical trials.

KEY WORDS: **fundoplication, GERD, hybrid surgery, laparoendoscopic collaborative surgery.**

INTRODUCTION

Flexible endoscopy has revolutionized the diagnosis and treatment of many gastrointestinal diseases.[1] Newly developed endoscopic approaches are applied to domains like gastroesophageal reflux disease (GERD), morbid obesity, pancreatic necrosis, and cholecystitis, which were once possible only through surgery.[2] However, despite numerous advances in endoscopic surgery, some gastroesophageal pathologies remain too difficult or dangerous for the endoluminal approach alone.

Recently, it has been shown that simultaneous laparoscopic support allows endoscopists to treat pathological findings that are not easily accessible with an exclusively endoluminal treatment. Combined endoscopic/laparoscopic intervention techniques that incorporate both the safety and efficiency of laparoscopy and the diagnostic accuracy and minimally invasive nature of endoscopy could expand the possibilities of new minimally invasive procedures.[3]

We hypothesized that to reach this goal, a dedicated system is required, one that provides stable and secure access to the gastric lumen allowing the interventionalist to overcome the limitations of available flexible endoscopy platforms and facilitating endoscopic procedures, especially for large lesions or in less accessible locations.

For this reason, we propose to expand the indications of endoluminal surgery by using novel endoscopically placed access ports to permit hybrid transgastric laparoscopy. This study represents a proof of concept by the performance of endoluminal antireflux surgery in a porcine model.

MATERIALS AND METHODS

Animals

The present preclinical acute study (No. 38.2015.01.069) was approved by our local animal experimentation ethics committee. All animals used in the laboratory were managed according to the French laws for animal use and care and according to the directives of the European Community Council (2010/63/EU).

Five female pigs (*Sus scrofa domesticus*, ssp large white, mean weight 27.6 kg) were included in the study. The animals were allowed to eat and drink water up to 1 hour prior to the surgery. Cefalexin (300 mg) was used as prophylaxis during induction. Ketamine (7 mL) and azaperone (3 mL) were administered intramuscularly as premedication 1 hour before the procedure. Induction of anesthesia was achieved using intravenous propofol combined with pancuronium (2 mL) and maintained with 2% isoflurane after endotracheal intubation.

Procedures

Upper endoscopy and TAGSS port placement

Animals were placed in a supine position under general anesthesia and mechanical ventilation. Upper endoscopy was performed using a high-definition gastroscope (Olympus Medical Systems, Tokyo, Japan). The stomach was washed and carefully surveyed.

Under endoscopic control, 3 intragastric trocar TAGSS® ports (Endo-TAGSS, Leakwood KS, USA) were inserted. TAGSS device is a 5-mm plastic trocar that is placed through the mouth, by using a flexible endoscope. It has four components: (1) a cannula with a flexible bumper, (2) an introducer cap, (3) an external disc for fixation, and (4) a working cap that seals around the instrument during use (Fig. 1).

The conical shape of the introducer cap allows the insertion of the cannula using the same 'pull method' and tools used for the placement of a percutaneous endoscopic gastrostomy (PEG) tube, as described in a previous report.[4] Once the cannula is in place, the introducer cap is removed and replaced with the working cap. The bumper rests against the internal gastric wall, while the external disc of the cannula

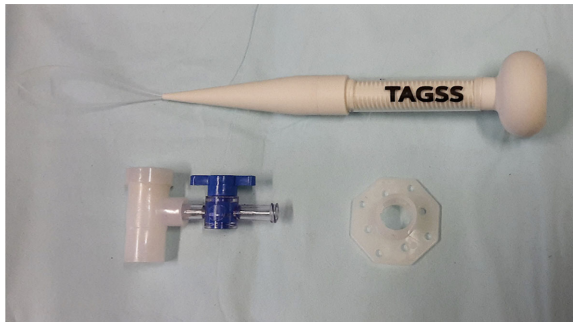

Fig. 1 Trans-abdominal gastric surgical system (TAGSS®) ports (Endo-TAGSS, Leakwood KS, USA).

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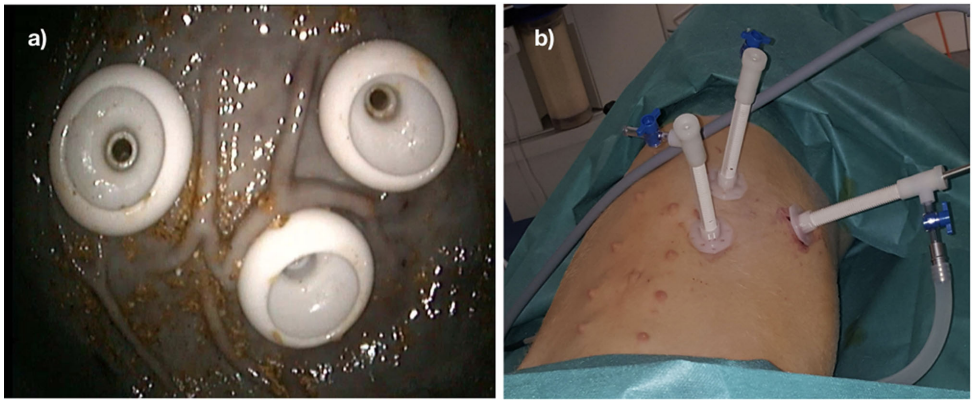

Fig. 2 Final location of TAGSS® for intraluminal gastroesophageal junction (GEJ) plication: (a) Internal visualization. (b) External visualization.

is anchored to the external abdominal wall by the external disc (Fig. 2a).

A laparoscopic instrument may then be inserted through the lumen of the TAGSS cannula into the stomach. An endoscope may also be used at the same time to provide visualization from different points.

After port placement, the ports were connected to a laparoscopic insufflator and a combination of flexible endoscopy and laparoscopic instruments were used for the rest of the procedure (Fig. 2b).

Endoscopic valve grading

Endoscopic grading of the GEJ under endoscopic retroflexed view was performed at the beginning of the procedure and repeated at the end. Valves were graded according to the Hill criteria.[5]

GEJ plication

Under laparoscopic view using a 5-mm laparoscope and/or the flexible endoscope, laparoendoscopic-assisted enplication of the GEJ was performed using 3–0 lactomer glycolide/lactide copolymer interrupted suture (Polysorb®, Covidien, Mansfield, MA, USA). The stitches were placed separately and lengthwise in the anterior portion of the esophagogastric junction until a competent gastroesophageal flap valve (Hill Grade I valve) was obtained. This was defined as a prominent fold of tissue, closely approximated to the axis of the endoscope and extending 3–4 cm along the minor curve at the entrance of the esophagus into the stomach.[5]

EndoFLIP® protocol

A functional lumen imaging probe (EndoFLIP, Crospon, Inc., Galway, Ireland) was introduced to the distal esophagus through the mouth and used to calibrate the endoplication. EndoFLIP is a measurement system in the form of a balloon catheter that measures cross-sectional area at 16 points along the shaft using impedance planimetry and that allows the measurement of the shape and compliance

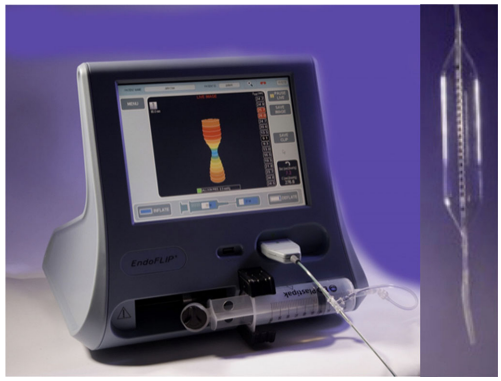

Fig. 3 Functional lumen imaging probe (EndoFLIP®), Crospon, Inc., Galway, Ireland.

of the GEJ during surgery. Results are displayed in an intuitively interpretable 2-dimensional topographical format[6] (Fig. 3).

The air insufflated during endoscopy was removed and the intrabag pressure was zeroed in the stomach. Therefore, subsequent pressure measurements were relative to the baseline gastric pressure. Diameter (D), cross sectional area (CSA), distensibility (d), and compliance (c) measurements were made with the bag filled up to 30 mL. EndoFLIP data were monitored in real time to ensure proper bag placement using the laparoscope. If the bag was migrated, it was repositioned, and the measurement was repeated.

The values obtained during the EndoFLIP protocol before and after the endoplication of the gastroesophageal junction (GEJ) were compared and registered (Fig. 4).

Gastric wall closure

After the endoplication was completed, the gastric access sites were closed by an over-the-scope endoscopic clip (Ovesco, Tubingen, Germany) (Fig. 5). The abdominal wall was closed in layers externally.

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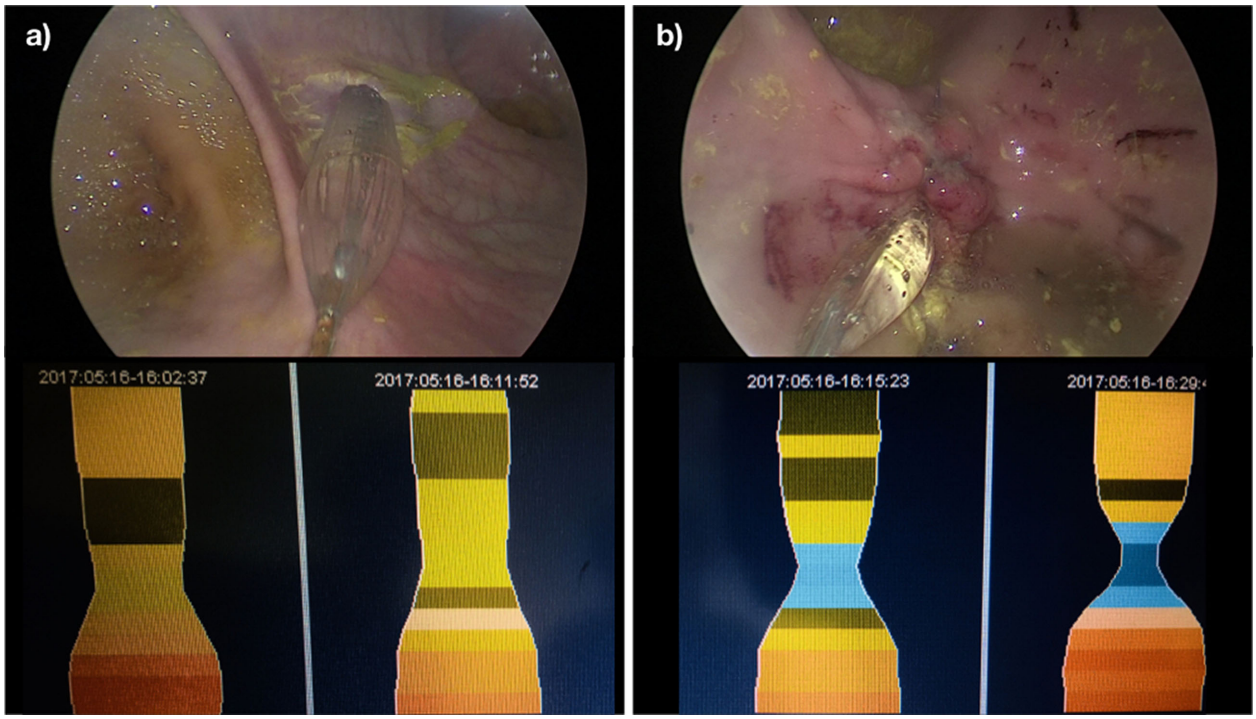

Fig. 4 Visualization of the Hill grade and calibration of gastroesophageal junction with EndoFLIP® probe: (a) before endoplication—Hill grade III valve. (b) after plication—Hill grade I Valve.

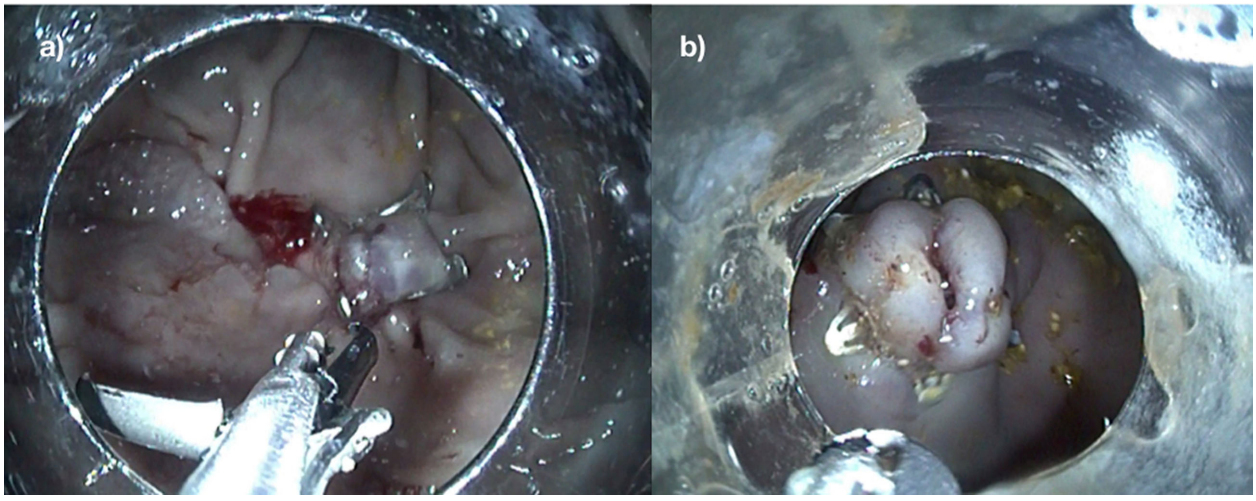

Fig. 5 Gastric access site closure.

Procedure time, complications and physiologic results were registered. At the end of the experimental protocol, animals were euthanized by intravenous injection of a lethal dose of potassium chloride.

RESULTS

Five GEJ endoplications were performed. The mean operative time was 65.6 min. The mean time for endoscopy and placement of intragastric portals was 14.2 minute (13–44 minute). Endoplication under EndoFLIP evaluation took 54 minute, as for gastric wall closing, the mean time was 15 minute. The insertion of the TAGSS ports was feasible and without complications in all cases.

The mean pre-plication GEJ diameter was 11.42 mm (8.6–13.6 mm) and the post-plication diameter was 6.14 mm (5.7–6.6 mm) ($p = 0.0152$) (Fig. 6a). The pre-plication CSA of GEJ was 104.8 mm^2 (58–146 mm^2), while the postplication one was 29.8 mm^2 (25–34 mm^2) ($p = 0.0152$) (Fig. 6b). Median preplication distensibility (d) and compliance (C) were 7.87 mm^2/mmHg (2.4–22.69 mm^2/mmHg) and 190.56 mm^3/mmHg (70.9–502.8 mm^3/mmHg),

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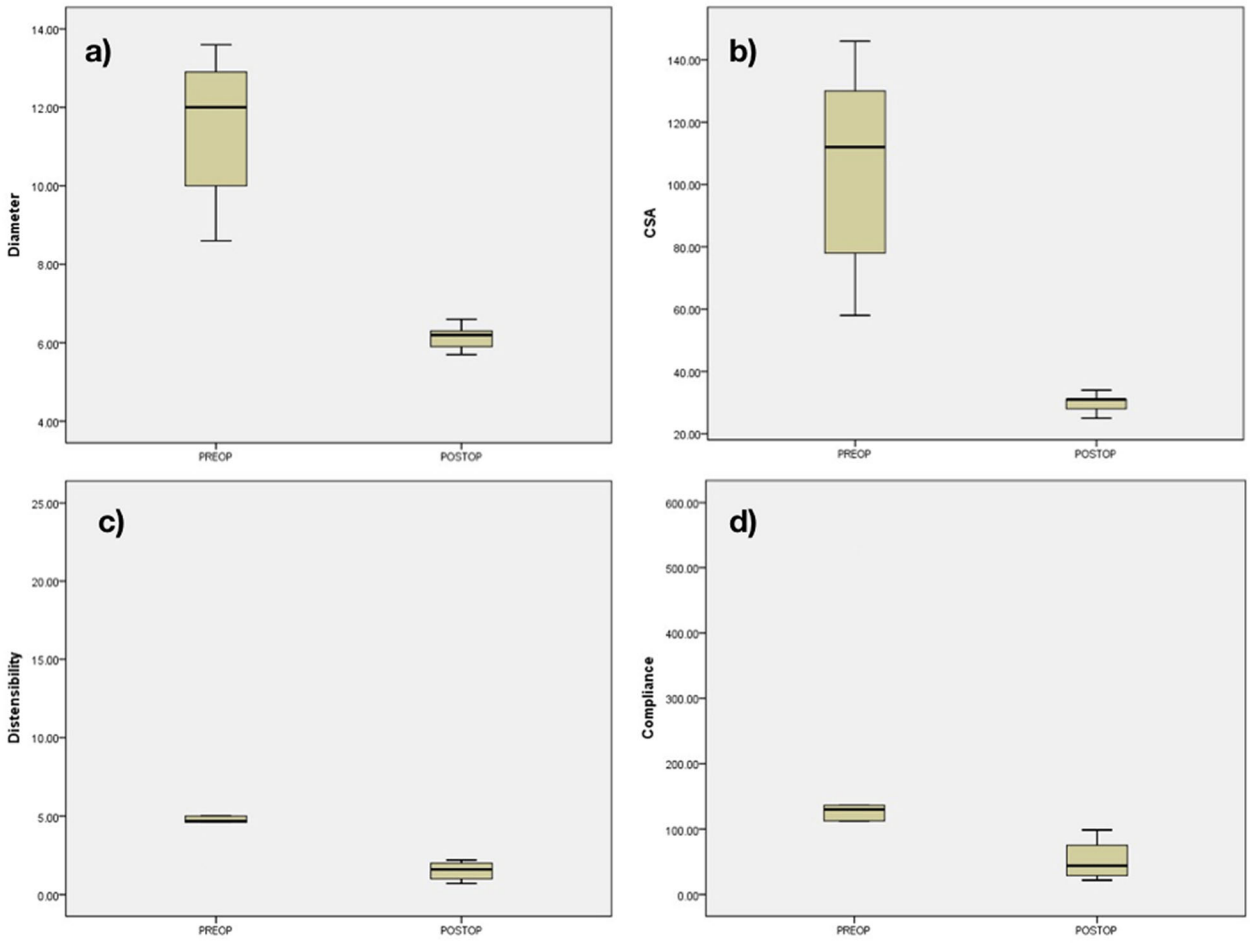

Fig. 6 Comparison of EndoFLIP® values before and after plication: (a) diameter. (b) cross-sectional area, (c) distensibility, (d) compliance.

respectively. After the procedure, these values were decreased to 1.5 mm^2/mmHg (0.7–2.2 mm^2/mmHg) and 52.17 mm^3/mmHg (21.9–98.7 mm^3/mmHg) correspondingly ($p = 0.0317$) (Fig. 6c,d).

Endoscopic Hill grades changed from Hill grade 3 in all cases before plication to Hill grade 1 in all cases at completion (100%).

No intraoperative complications were observed. Gastric wall closure was performed with over-the-scope clips and took 15 minute (14–16 minute).

DISCUSSION

Laparoscopic Nissen fundoplication is the gold standard of treatment for patients who have no response or intolerance to proton pump inhibitors (PPIs), who are concerned about long-term PPIs side-effects or who have complications of GERD. This procedure is highly effective at preventing reflux. However, it impedes the normal venting of swallowed air, reduces the number of normal reflux episodes, and dramatically alters the anatomy of the digestive tract.[7] For this reason, Nissen surgery is frequently associated with significant side effects that include gas bloat syndrome, flatulence, inability to belch or vomit, and dysphagia.[8]

Recently, innovative endoscopic and surgical techniques have emerged to bridge the gap between fundoplication and chronic medical treatment, including endoscopic fundoplication techniques (transoral incisionless fundoplication [TIF, EsophyX, Endogastric Solutions] and SRS Endoscopic Stapling System [Medigus]), radiofrequency energy delivery (Stretta, Mederi Therapeutics), magnetic sphincter augmentation (LINX®, Torax® Medical) and implanted pacemaker (Endostim, Endostim BV), and most recently the ARMS procedure (AntiReflux Endoscopic Mucosectomy).[9] However, the efficacy of these methods has been somewhat variable in controlling reflux, improving symptoms, and reducing the use of PPI.[7] Therefore, their usefulness is still under evaluation and there remains a need for a minimally invasive, highly effective treatment with little or no anatomical distortion, safe and long-term sequel-free. The GEJ intraluminal approach may be a method of achieving this objective.

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In 1992, Jennings *et al*. published an article on the transgastric access technique for the treatment of GERD using staplers to produce a full thickness plication of the esophagogastric junction.[10] This technique was the precursor to some of the endoscopic methods currently available. However, the use of suture materials to emulate this type of procedures has not been as successful so far.

The technical inability to secure a full thickness robust tissue apposition was the reason why some devices, such as EndoCinch® did not show satisfactory long-term results.[11] Intermediate and long-term EndoCinch performance was considered poor after endoscopic re-evaluation, which revealed loosening of the sutures due to the lack of full-thickness fundoplication and mucosal apposition, even after improved modifications.[12] The same was evidenced in animals by Chang *et al*. when it was found out that the use of endoluminal plication with mucosal ablation did not improve low esophageal sphincter pressure, gastric yield pressure, or GEJ compliance.[13] They concluded that since endoluminal plications (even with reinforcing pledgets and pre-plication mucosal ablation) do not retain the suture or plicatures within 6 weeks, do not improve the basal pressure of lower esophageal sphincter, and do not improve the GEJ compliance, any endoscopic approaches should look beyond this type of endoluminal plication in GERD therapy.

The transgastric hybrid approach may favor a more robust and full-thickness plication anchorage due to the maneuverability offered by laparoscopic instruments. In addition, monitoring the procedure with EndoFLIP could allow the surgeon to standardize the technique and objectively calibrate the repair, helping to reduce the variability of observed laparoscopic or endoscopic plications.[6] This device uses impedance planimetry to determine multiple adjacent CSAs within a compliant balloon placed across the GEJ during volumetric distention. The additional measure of the corresponding intrabag pressure allows for the assessment of the CSA pressure response (distensibility) in the distended area.[14] Although patients with GERD may be heterogeneous in terms of GEJ distensibility, their stratification according to these physiological measurements has been shown to correlate to successful response to endoluminal or surgical therapies and also allows intraoperative monitoring of the quality of the treatment performed.[6]

In our experiment, we were able to access the GEJ with the TAGSS system and perform suture plication under EndoFLIP guidance. This proof of concept demonstrates that the combined laparoscopic and endoscopic approach brings laparoscopic abilities to intragastric procedures, especially in the areas difficult to access by flexible endoscopy alone. It gives the opportunity to evaluate this technique and/or its modifications as a possible alternative treatment in patients with GERD. This approach may also facilitate other types of intragastric procedures (i.e., EMR, ESD, full-thickness resection or procedures such as pseudocyst drainage or pyloroplasty/myotomy).

Limitations of this study include its small sample size, lack of objective evidence of a true anti-reflux barrier and its nonsurvival nature, survival being needed to confirm a lasting procedure. Also, so far, we cannot estimate the real costs of this procedure as TAGSS devices are not commercially available. Likewise, the incorporation of new technological resources for the calibration of the endoplication and the need for special materials for the closure of the gastric wall are factors that, by raising the costs, could limit the implementation of this type of procedure. Our objective however was in fact less to validate a new treatment for GERD and more to validate the ease of use and utility of this hybrid endoluminal approach.

CONCLUSIONS

We present an acute animal study using novel endoscopically placed intragastric ports to allow a hybrid collaborative laparo/endoscopic GEJ endoplication under EndoFLIP guidance. Ease and security of access were demonstrated and feasibility of an effective sutured antireflux procedure based on physiologic and endoscopic criteria was confirmed. This new approach may advance the capabilities of endoluminal procedures at least until technical solutions to totally endoscopic interventions are available.

ACKNOWLEDGEMENTS

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References

1 Banerjee R, Reddy D N. Advances in endoscopic imaging: advantages and limitations. J Dig Endosc 2012; 3: 7–12.
2 Feussner H, Becker V, Bauer M *et al.* Developments in flexible endoscopy surgery: a review. Clin Exp Gastroenterol 2015; 8: 31–42.
3 Kim H H, Uedo N. Hybrid NOTES. Gastrointest Endosc Clin N Am 2016; 26: 335–73.
4 Soares R V, Molos M, Donepudi P *et al.* Transgastric hybrid surgery for the flexible endoscopist: early experience with the TAGSS system. Gastrointest Endosc 2016; 84: 852–3.
5 Hill L D, Kozarek R A, Kraemer S J, et al . The gastroesophageal flap valve: in vitro and in vivo observations. Gastrointest Endosc 1996; 4: 541–7.
6 Perretta S, Mc Anena O, Botha A *et al.* Acta from the ENdoFLIP symposium. Surg Innov 2013; 20: 545–52.
7 Ganz R A. A review of new surgical and endoscopic therapies for gastroesophageal reflux disease. Gastroenterol Hepatol 2016; 12: 424–31.

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8 Lundell L, Miettinen P, Myrvold H E *et al.* Nordic GERD Study Group. Comparison of outcomes twelve years after antireflux surgery or omeprazole maintenance therapy for reflux esophagitis. Clin Gastroenterol Hepatol 2009; 7: 1292–8.
9 Inoue H, Ito H, Ikeda H, et al . Anti-reflux mucosectomy for gastroesophageal reflux disease in the absence of hiatus hernia: a pilot study. Ann Gastroenterol 2014; 27: 346–51.
10 Jennings R W, Flake A W, Mussan G. A novel endoscopic transgastric fundoplication procedure for gastroesophageal reflux: an initial animal evaluation. J Laparoendosc Surg 1992; 2: 207–13.
11 Schiefke I, Zabel-Langhennig A, Neumann S, Feisthammel J, Moessner J, Caca K. Long term failure of endoscopic gastroplication (EndoCinch). Gut 2005; 54: 752–8.
12 Mosler P, Abdel Aziz A M, Hieston K *et al.* Evaluation of supplemental cautery during endoluminal gastroplication for the treatment of gastroesophageal reflux disease. Surg Endosc 2008; 22: 2158–63.
13 Chang K J, Nguyen N T, Pandolfino J E, Nguyen P T. Endoluminal plication with mucosal ablation of the gastroesophageal junction (GEJ) does not improve LES pressure, gastric yield pressure or GEJ compliance: is it time to give it up? Gastrointest Endosc 2005; 61: 129.
14 Kwiatek M A, Pandolfino J E, Hirano I, Kahrilas P J. Esophagogastric junction distensibility assessed with an endoscopic functional luminal imaging probe (EndoFLIP). Gastrointest Endosc 2010; 72: 272–8.

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