

Natural orifice transluminal endoscopic surgery gastrotomy closure in porcine explants with the Padlock-G clip using the Lock-It system

Authors

J. R. Romanelli¹, D. J. Desilets², D. B. Earle¹

Institutions

¹ Department of Surgery, Department of Medicine, Baystate Medical Center, Tufts University School of Medicine, Springfield, Massachusetts, USA

² Division of Gastroenterology, Department of Medicine, Baystate Medical Center, Tufts University School of Medicine, Springfield, Massachusetts, USA

submitted 6 July 2009
accepted after revision
23 December 2009

Bibliography

DOI <http://dx.doi.org/10.1055/s-0029-1243950>
Endoscopy 2010; 42:
306–310 © Georg Thieme
Verlag KG Stuttgart · New York
ISSN 0013-726X

Corresponding author

J. R. Romanelli, MD, FACS
Department of Surgery, S3659
Baystate Medical Center
759 Chestnut Street
Springfield
MA 01199
USA
Fax: +1-413-7941835
john.romanelli@bhs.org

Background and study aims: The success of transgastric surgery depends on reliable, secure closure of the gastrotomy. Few tests of the integrity of these closures have been published. This study aimed to determine whether a gastrotomy suitable for a NOTES procedure can be closed safely and effectively from within the stomach using a novel endoscopically placed device, the Padlock-G with the Lock-It delivery system.

Methods: In a series of eight consecutive porcine gastric explants gastrotomy was performed in an ex vivo animal laboratory, the gastrotomy being closed with the Padlock-G followed by burst pressure testing after completion of the procedure. Gastrotomies were made in porcine explants. T-tags were placed on either side of the gastrotomy,

and, with the T-tags pulled into an endoscopic cap, the Padlock-G was deployed. Gastric transmural pressure gradients at bursting of these closures were measured during insufflation of the explanted stomachs with a high-pressure insufflator.

Results: The mean burst pressure of the gastrotomy closures was 68.0 mm Hg (range: 45–107 mm Hg). All of the stomachs ultimately ruptured at the closure sites, with the exception of the stomach that ruptured at the highest value (107 mm Hg), which ruptured at a site approximately 5 cm away from the closure site. All of the closures were accomplished in 30 minutes or less.

Conclusions: The Padlock-G clip provides a secure gastric closure for natural-orifice surgery.

Introduction

Natural-orifice transluminal endoscopic surgery (NOTES) is an emerging technique whereby abdominal surgery is performed inside the abdomen using minimal or no skin incisions, instead using a natural orifice to provide access. An enterotomy is made across the gut lumen, allowing access to the abdomen in order to perform the surgery. In 2005, gastric closure was identified as a fundamental challenge to the safe introduction of NOTES [1]. There is no current accepted standard method for achieving safe closure of a hollow viscus.

The most commonly available technique to close a gastrotomy with an endoscope is by using mucosal clips, but early animal studies [2–4] show that this can be clumsy, technically difficult, and expensive. One group reports a successful survival study where the gastrotomy was left open [5], but few surgeons would likely be willing to perform this experiment in humans, given that leak pressures in unclosed gastrotomies have been measured to be as low as 2 mm Hg [6], representing minimal gastric distension. Few tests of the

integrity of gastric closure have been published [6–9], and few researchers feel that clip closure alone is safe for human patients. A more reliable, secure closure method is needed before NOTES is ready for widespread adoption.

We have developed a new closure method that uses a 16.5-mm nitinol clip delivered via an over-the-scope delivery pod. This clip is easily deployed, and is retrievable with an endoscopic snare. We performed a pilot study to test bursting pressures in a series of gastric explants utilizing the Padlock-G (◉ Fig. 1).

Methods

In eight explanted porcine stomachs, a site for gastrotomy was selected on the greater curvature near the gastrocolic ligament. Two T-tags (Wilson-Cook, Winston-Salem, North Carolina, USA) were placed endoscopically on either side of the opening to facilitate closure, and the gastrotomy was created at a location across from the gastroesophageal junction using a wire-guided, endoscopic, 12-mm, balloon-dilatation catheter



Fig. 1 Padlock-G clip.

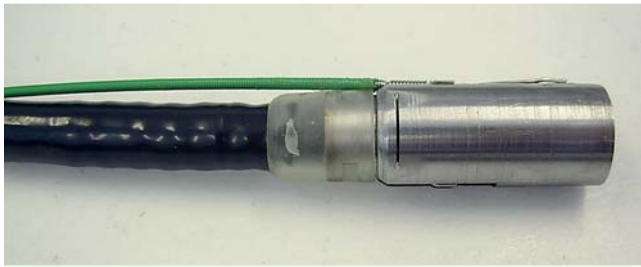


Fig. 2 Lock-It system for Padlock-G clip deployment.

(Wilson-Cook) to accommodate a diagnostic gastroscope. The deployment pod (Lock-It system, ● Fig. 2) was then placed at the tip of the gastroscope, allowing maneuverability, and the T-tags were pulled into the pod.

The Padlock-G was then deployed by depressing a handle, which activates a trigger cable (see schematics, ● Fig. 3).

The cable pushes the clip out of the pod; since it is deformed to fit the pod, the Padlock-G returns to its normal shape as it leaves it. This causes the barbs on the inside of the pod to pucker the tissue inward, similar to a purse-string closure (● Fig. 4).

Closure integrity was assessed by submerging each explant under water, and insufflating with carbon dioxide with a transmural Veress needle until gas leakage occurred. The pressure gradients across the gastric wall, using ambient atmospheric pressure in the laboratory as a reference standard, were recorded using a

hand-held digital manometer (Extech Instruments Corporation, Waltham, Massachusetts, USA).

The experiment was repeated in exactly the same manner in a single live animal. This was done as a test to replicate our ex vivo work. At necropsy, the stomach was explanted, and burst testing was done in an identical fashion.

Results



The results of the burst pressure measurements are shown in ● Table 1.

All attempts to close the gastrotomies were successful in this experiment. There were no gastrotomies that were judged to be inaccurately closed by a single deployment of the Padlock-G. No attempts were needed or made to deploy a second clip to close the gastrotomy.

Mean burst pressure of the gastrotomy closures in ex vivo stomachs was 68 mm Hg. One explant achieved a burst pressure of 107 mm Hg, which caused gastric rupture approximately 5 cm away from the gastrotomy site, while the Padlock-G remained intact. The in vivo gastrotomy closure ruptured at 98 mm Hg. All of the closures were accomplished in 30 minutes or less.

Discussion



Our specific aim was to determine whether a gastrotomy suitable for a NOTES procedure can be closed effectively from within the stomach using the Padlock-G with the Lock-It system. A key issue that will determine whether NOTES can be performed safely is the reliability of the enterotomy closure upon its completion. Most gastric or colonic closure methods employ either endoscopic clips, loops [2–4, 7–11], or T-anchors [12]. Two studies used a self-approximating submucosal tunnel which was closed with an endoscopic clip [6, 13]. Relatively few papers focus specifically on gastrotomy closure [7–9, 14–21]. Other ideas have been proposed for gastrotomy closure including tissue anchors [15], endoscopic suturing devices [7, 8, 16, 17], endoscopic transoral stapling [8, 18, 19], or an over-the-scope clip [21]. Newer

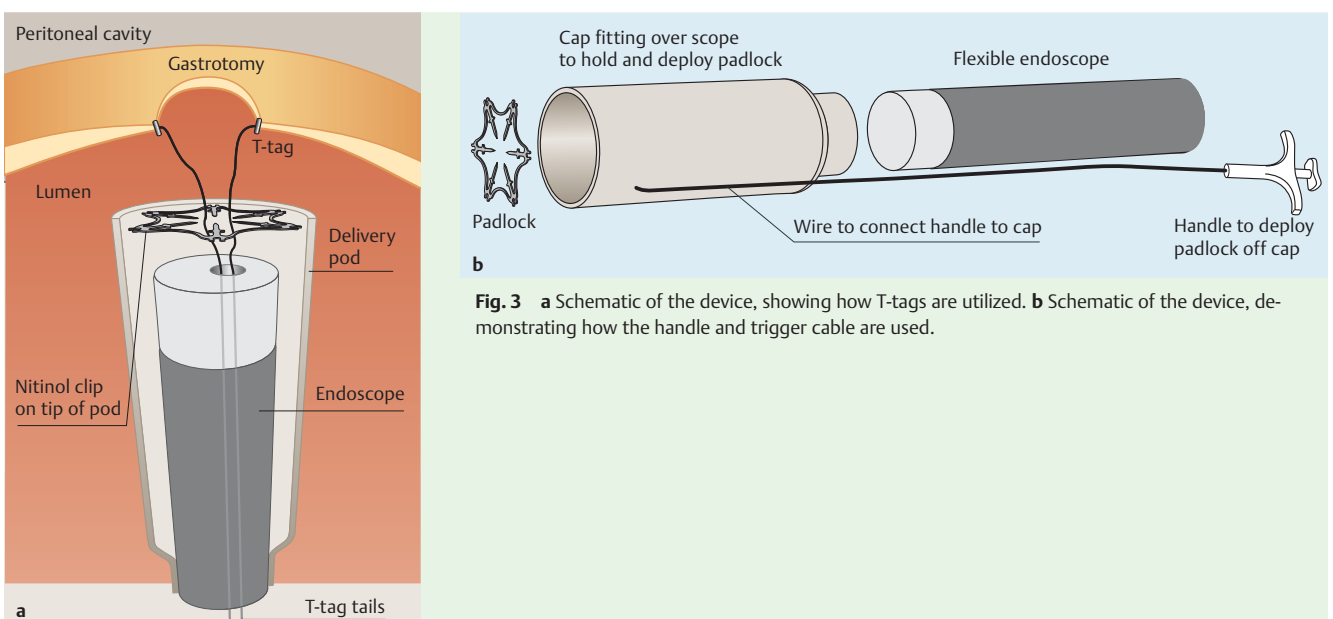


Fig. 3 a Schematic of the device, showing how T-tags are utilized. b Schematic of the device, demonstrating how the handle and trigger cable are used.

concepts involve plugging the gastrotomy, with materials such as an atrial septal occluder [22] or a bioabsorbable plug [23]. Only four reports actually test the intragastric pressures needed to cause failure of gastric closure, all in explanted porcine stomachs [6–9].

It remains unknown how high enteric closure pressure must be. NOSCAR (Natural Orifice Surgery Consortium for Assessment and Research) proposed that whatever technique is employed should withstand burst pressures as high as cough pressures, which have been measured to be as high as 200 mm Hg [24]. Jagannath et al. did not close gastrotomies after porcine transgastric uterine horn resection, with openings as large as 20 mm [5]. The pigs apparently showed no septic complications after 2 weeks of survival. This intriguing report compels us to suspect that, at least in swine, closures may not need to be as robust as initially believed. Human data in this regard are lacking, with a need for better physiologic understanding of the mechanics of gastric pressures.

Several recent studies have looked at burst pressures after gastric closure techniques [6–9]. The technique employed to record pressures varied within each experiment, yielding different results. Von Delius et al. [6] found that negative controls leaked at only 2 mm Hg pressure, whereas Ryou et al. [7] established that leakage occurred at 15 mm Hg pressure in unclosed stomachs. Such wide variance in results can make interpretation difficult. The only widely available modality at the current time utilizes mucosal clips. Von Delius et al. [6] reported that gastrotomy closure with mucosal clips had burst pressures ranging from means of 37 to 44 mm Hg. This data range was similar in the work of Ryou et al. [7,8], who found median burst pressures of 33 mm Hg [7] and 40 mm Hg [8]. Interestingly, Voermans et al. [9] have shown burst pressures to be significantly higher, at 202 mm Hg. The method they employed to record these pressures involved only the gastric wall itself, stretched over an “experimental apparatus.” One must wonder whether the values reflect the type of experiment rather than the closure technique.

Other gastric closures have resulted in similar burst strengths. Hand-sewn closures ruptured at a mean of 50 mm Hg [6]. Interestingly, Ryou et al. [8] looked at different methods of sutured closure, with full-thickness closure leaking at the lowest pressure (mean: 37.2 mm Hg) compared to double-layer closure (mean: 81.8 mm Hg) and purse-string closure (mean: 69 mm Hg). The authors concluded that needle holes were potential conduits for air leakage. This may imply that closure without serosal involvement may be strong enough following a NOTES procedure. Ryou et al. [8] also found endoluminal stapled closure (Power Medical Interventions, Langhorne, Pennsylvania, USA) to have a similar closing pressure (mean: 64.6 mm Hg).

Our results reveal mean burst pressures of 68 mm Hg with the Padlock-G. One of our stomachs ruptured at a site away from the gastric closure, a phenomenon also observed by Ryou et al. [7]. We further tested the device in an in vivo stomach, utilizing a similar technique. At necropsy, we explanted the stomach, and burst pressure was found to be 98 mm Hg. While this value would have raised our mean burst pressure higher, we did not include it in this analysis, as we were concerned that a difference in structural integrity in comparison to explanted stomachs would confound the data. We were encouraged by the successful result of in vivo deployment; survival studies with the device are ongoing.

One concern with the device is how to handle its inaccurate deployment. We have successfully utilized a snare to remove the Padlock-G with minimal mucosal trauma. If a gastrotomy was incompletely closed, a side-by-side application of a second Padlock-



Fig. 4 Internal view (after excision) of a Padlock-G clip deployed in a non-survival in vivo porcine stomach.

Table 1 Burst pressures from Padlock-G closures in gastric explants.

	Attempt	Pressure, mm Hg*
Ex vivo procedures	1	57
	2	107†
	3	45
	4	72
	5	69
	6	62
	7	66
	8	66
Mean		68
In vivo procedure	1	98

*Pressures are measured in mm Hg compared to laboratory atmospheric pressure as a reference standard.

†Stomach ruptured at site away from Padlock-G clip closure.



Fig. 5 Padlock-G clip loaded in a clear version of the Lock-It system.

G could be considered, although it was unnecessary in this study. Attention must be made not to overlap the clips, however, as they could become entangled in one another and thus deliver a suboptimal closure. Also, visibility is somewhat hindered, although no more so than with other available off-the-shelf, over-the-scope devices, such as an endoscopic cap. A future iteration of the device will have a clear pod (● Fig. 5), rather than the metal pod shown (● Fig. 2), which may enable better visualization.

Another theoretical concern is late trauma to the mucosa or the gastrointestinal tract, should it slough off of the closure, but long-term survival studies, as well as studies testing its transit through the gastrointestinal tract, would need to be performed to investigate this, placing this concern outside the scope of this experiment.

The decision to utilize T-tags was done with the aim of centering the Padlock-G over the gastrotomy site. The T-tags were not used to close the gastrotomy prior to application of the clip. We have successfully deployed the Padlock-G without T-tags; however, the iteration of the device used in this experiment only fits over an endoscope with a single working channel. When only one side of the gastrotomy is grasped, the Padlock-G can deploy off-center, creating a suboptimal closure.

The following limitations in this study should be highlighted. First, we did not have a control group for closure comparison. We have historical data regarding mucosal clips, which were compared to a loop-anchor purse-string (Wilson-Cook) closure technique [26] that was in part developed in our lab. As these data were part of another study, we chose not to report the results here. Second, we had several attempts at deploying the Padlock-G in vivo prior to conducting this experiment, and our work led to design refinements to maximize its success: our experience with the device may have contributed to the successful results. Third, we chose to place T-tags on either side of the gastrotomy to pull the visceral opening into the Lock-It system to help deploy the device. This step may have improved our results, and was based on prior in vivo work. T-tags are costly, require a steep learning curve (which also adds to closure time), and can cause visceral injury across the gastric wall, but future iterations of the device may obviate the need for them. Fourth, gastrotomies were made in endoscopically advantageous areas on the stomach. While in vivo gastrotomies tend to be made anteriorly to avoid entry into the lesser sac, the gastrotomies in this experiment were made across from the esophageal opening, avoiding difficulties with undue torque either on the scope or on the Padlock-G and Lock-It system. Fifth, we have not obtained histologic data demonstrating healing of the gastrotomy, as this study was merely an explant study. Surely such data would represent confirmatory evidence that the device does successfully close a gastrotomy; survival studies with the device are ongoing and will include such data. Lastly, we recognize that the study size is small, but as this was not a comparative study, we did not attempt to power it statistically. While it would have been optimal to do a comparative study with unclosed controls or gastrotomies closed by other methods, we felt that this would duplicate previously published work. Further, the intent of the study was merely to test the feasibility of the device.

This pilot study shows that gastrotomy closure with the Padlock-G and Lock-It system is feasible, with comparable burst pressures to other published methods. Further studies are ongoing to continue to assess the safety of the device's use. Assessing transit time through the gastrointestinal tract, assuming the Padlock-G does slough, will be an important area of future study. How the Padlock-G performs in the human gastrointestinal tract remains as yet unknown.

Summary



A current limitation of NOTES is the ability to close the visceral opening. In early human cases the focus has mostly been on transvaginal approaches, in order to sidestep this problem. Most published studies involving enterotomy closure utilize endoscopic clips. The disadvantages of this approach include cost, technical difficulty, and the potentially poor mechanical strength of these closures, which by definition are mucosal only. A safer, stronger, more reliable method of closing the stomach, preferably using a full-thickness approach, is highly desirable.

The Padlock-G deployed via the Lock-It system is an easy-to-use system which resulted in successful gastrotomy closures both in explanted porcine stomachs and in an in vivo model. Further survival studies are warranted to determine whether the clips remain in place or slough, before they can be considered for human use. In addition, histologic study of the closure would be of value to understand how much of the gastric wall is incorporated into the closure.

Competing interests: None

References

- 1 Rattner D, Kalloo A and SAGES/ASGE Working Group on Natural Orifice Transluminal Endoscopic Surgery. ASGE/SAGES Working Group on Natural Orifice Transluminal Endoscopic Surgery. *Surg Endosc* 2006; 20: 329–333
- 2 Wagh MS, Merrifield BF, Thompson CC. Endoscopic transgastric abdominal exploration and organ resection: initial experience in a porcine model. *Clin Gastroenterol Hepatol* 2005; 3: 892–896
- 3 Wagh MS, Merrifield BF, Thompson CC. Survival studies after endoscopic transgastric oophorectomy and tubectomy in a porcine model. *Gastrointest Endosc* 2006; 63: 473–478
- 4 Merrifield BF, Wagh MS, Thompson CC. Peroral transgastric organ resection: a feasibility study in pigs. *Gastrointest Endosc* 2006; 63: 693–697
- 5 Jagannath SB, Kantsevov SV, Vaughn CA et al. Peroral transgastric endoscopic ligation of fallopian tubes with long-term survival in a porcine model. *Gastrointest Endosc* 2005; 61: 449–453
- 6 Von Delius S, Gillen S, Doundoulakis E et al. Comparison of transgastric access techniques for natural orifice transluminal endoscopic surgery. *Gastrointest Endosc* 2008; 68: 940–947
- 7 Ryou M, Pai R, Sauer J et al. Evaluating an optimal gastric closure method for transgastric surgery. *Surg Endosc* 2007; 21: 677–680
- 8 Ryou M, Fong D, Pai R et al. Transluminal closure for NOTES: an ex vivo study comparing leak pressures of various gastrotomy and colotomy closure modalities. *Endoscopy* 2008; 40: 432–436
- 9 Voermans RP, Worm AM, van Berge Henegouwen MI et al. In vitro comparison and evaluation of seven gastric closure modalities for natural orifice transluminal endoscopic surgery (NOTES). *Endoscopy* 2008; 40: 595–601
- 10 Pai RD, Fong DG, Bundga ME et al. Transcolonic endoscopic cholecystectomy: a NOTES survival study in a porcine model. *Gastrointest Endosc* 2006; 64: 428–434
- 11 Fong DG, Pai RD, Thompson CC. Transcolonic endoscopic abdominal exploration: a NOTES survival study in a porcine model. *Gastrointest Endosc* 2007; 65: 312–318
- 12 Sumiyama K, Gostout CJ, Rajan E et al. Pilot study of the porcine uterine horn as an in vivo appendicitis model for development of endoscopic transgastric appendectomy. *Gastrointest Endosc* 2006; 64: 808–812
- 13 Pauli EM, Moyer MT, Haluck RS, Mathew A. Self-approximating transluminal access technique for natural orifice transluminal endoscopic surgery: a porcine survival study. *Gastrointest Endosc* 2008; 67: 690–697
- 14 Sclabas GM, Swain P, Swanstrom LL. Endoluminal methods for gastrotomy closure in natural orifice transenteric surgery (NOTES). *Surg Innov* 2006; 13: 23–30
- 15 Seaman DL, Gostout CJ, de la Mora Levy JG, Knipschildt MA. Tissue anchors for transmural gut-wall apposition. *Gastrointest Endosc* 2006; 66: 577–581

- 16 McGee MF, Marks JM, Onders RP *et al.* Complete endoscopic closure of gastrotomy after natural orifice transluminal endoscopic surgery using the NDO Plicator. *Surg Endosc* 2008; 2: 214–220
- 17 McGee MF, Marks JM, Jin J *et al.* Complete endoscopic closure of gastric defects using a full-thickness tissue plicating device. *J Gastrointest Surg* 2008; 12: 38–45
- 18 Magno P, Giday SA, Dray X *et al.* A new stapler-based full-thickness transgastric access closure: results from an animal pilot trial. *Endoscopy* 2007; 39: 876–880
- 19 Meireles OR, Kantsevov SV, Assumpcao LR *et al.* Reliable gastric closure after natural orifice transluminal endoscopic surgery (NOTES) using a novel automated flexible stapling device. *Surg Endosc* 2008; 22: 1609–1613
- 20 Sporn E, Miedema BW, Astudillo JA *et al.* Gastrotomy creation and closure for NOTES using a gastropexy technique (with video). *Gastrointest Endosc* 2008; 68: 948–953
- 21 Schurr MO, Arezzo A, Ho CN *et al.* The OTSC clip for endoscopic organ closure in NOTES: device and technique. *Minim Invasive Ther Allied Technol* 2008; 17: 262–266
- 22 Perretta S, Sereno S, Forgione A *et al.* A new method to close the gastrotomy by using a cardiac septal occluder: long-term survival study in a porcine model. *Gastrointest Endosc* 2007; 66: 809–813
- 23 Cios TJ, Reavis KM, Renton DR *et al.* Gastrotomy closure using bioabsorbable plugs in a canine model. *Surg Endosc* 2008; 22: 961–966
- 24 Man WD-C, Kyroussis D, Fleming TA *et al.* Cough gastric pressure and maximum expiratory mouth pressure in humans. *Am J Resp Crit Care Med* 2003; 168: 714–717
- 25 Fritscher-Ravens A, Patel K, Ghanbari A *et al.* Natural orifice transluminal endoscopic surgery (NOTES) in the mediastinum: long-term survival animal experiments in transesophageal access, including minor surgical procedures. *Endoscopy* 2007; 39: 870–875
- 26 Desilets DJ, Romanelli JR, Surti VC *et al.* The ties that bind: durable, transmural, purse-string-like gastrotomy closure using a novel device [abstract]. *Gastrointest Endosc* 2007; 65: AB292