

Applying basic principles of surgery may pave the way for more effective endoscopic bariatric techniques

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ABSTRACT

Background and study aims In the last decade, gastroenterologists have been attempting to use endoscopy to reproduce the great success of traditional surgical suture techniques. Despite recent advances, we still lack a reliable method that results in a permanent suture with minimal incidence of suture failure. This was an experimental study in pigs with an innovative technique that applied basic surgical concepts to endoscopy to evaluate the effectiveness of a novel suture technique.

Methods The procedures were performed on six live pigs under general anesthesia. Endoscopic mucosal resection (EMR) first was performed in the stomach, exposing the submucosal or muscularis propria layers. A novel device, a transparent chamber cap (DASE), was developed to aspirate the gastric wall, allowing the sutures to reach deep layers. The aspiration was performed with a standard gastroscope to which the novel cap was distally attached. Three sutures aligned were defined as a plication. Each pig received two or three plications and was placed on a liquid diet for 14 days after the procedure. The pigs were sacrificed at 4 and 8 weeks and the sutures were reviewed.

Results The technique was feasible in all animals. Of 16 plications, only one failed. One perforation occurred after EMR. There were no other complications or adverse events. Permanent fusion of the gastric wall was confirmed by histology in all cases.

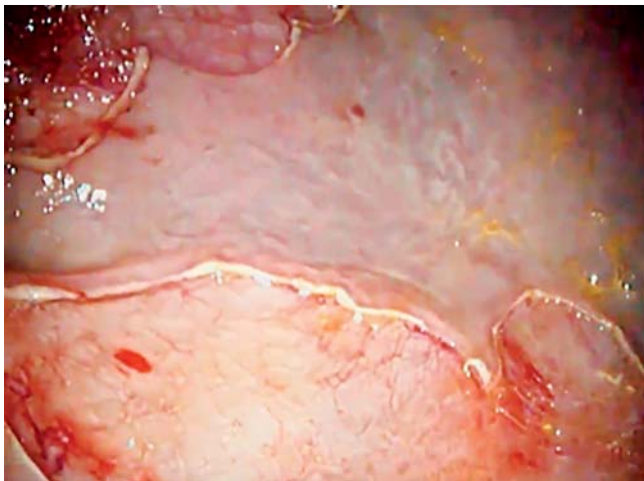
Conclusions This study showed that basic principles of surgery can be applied endoscopically to ensure a permanent suture with reduced chances of failure. These findings can help to pave the way for more effective bariatric endoscopic techniques.

Introduction

It has long been thought that endoscopic approximation of tissues with sutures could be very useful in minimally invasive treatments, especially for obesity. Despite some advances in technology and improved maneuvering capability, the endoscopic suture procedure is still complicated by failures in the

postoperative course. In general, endoscopic sutures are not considered reliably permanent [1].

A study conducted by Hashiba et al showed that for an effective suture between two gastric walls, the point of contact should be an area of submucosa or muscularis propria (without mucosa) measuring $\geq 4\text{ cm}^2$ that is approximated by at least three sutures [2]. This model allows formation of a tunnel in the gastric lumen and serves as a basis for this study that can



► Fig. 1 Gastric wall after EMR.

also be applied to obesity treatment. The aim of the study was to evaluate the feasibility, safety, and efficacy of the basic principles of conventional surgery applied to endoscopic suturing in animal models.

Material and methods

Animal model

Survival experiments were performed on six live pigs (Mini-pigBR, Brazil, body weights 35 kg to 40 kg). Intramuscular midazolam (0.2mg/kg) was used to induce general anesthesia, maintained by using isoflurane and propofol. This procedure was performed by a veterinarian and the animals were housed at an animal research facility. During the procedure, cefazolin sodium hydrate (2g) was administered and repeated for the first 2 days. Analgesics were used in the postoperative course.

The animals were on a liquid diet for 2 weeks after the procedure, after which a normal diet was resumed. The pigs were followed for either 4 or 8 weeks. The study was approved by the Sirio-Libanes Care Institutional Review Board (approval no CEUA-P 2016-17).

Basic materials and preparation

All procedures were performed by a skilled endoscopist with the pig in the supine position. A standard gastrointestinal endoscope (Silver Line Karl Storz Video endoscope, Tuttlingen, Germany) was used. The endoscope was introduced into the gastric lumen and two wide areas of the gastric body were selected, one in the anterior wall and another one in the posterior wall. The selected areas were marked with the tip of a polypectomy snare (Captivator, Boston Scientific, Natick, Massachusetts, United States). The proximal limit of these areas was approximately 2.0 cm distal to the cardia level in the anterior and posterior wall; the distal limit was the gastric incisura.



► Fig. 2 DASE chamber with the needle appearing in the window.

Endoscopic mucosal resection

Exposition of the submucosa/muscular propria was done using the snare placed around a transparent cap used for variceal band ligation. When the cap suctioned the gastric wall to the maximum, the snare was released and subsequently closed, grasping the aspirated tissue. The suction was interrupted with the snare still grasping the tissue outside of the cap. A pulling maneuver was applied to avoid the deep layers of the gastric wall, followed by resection using electrocoagulation (► Fig. 1). No fluid was injected into the submucosa. The procedure was repeated many times in the demarcated area, until total exposition of the submucosa/muscular propria layers in the previously marked area.

Novel suture device

A novel device termed DASE was used (prototype, G-Flex, Sao Paulo, Brazil), which comprised a plastic chamber for tissue aspiration and T-tag placement (Tissue Apposition System (TAS), Ethicon EndoSurgery, Cincinnati, Ohio, United States). The device is a 3-cm-long, transparent plastic tube that is closed at the distal end by a transparent wall (► Fig. 2).

Laterally, the DASE has a window that is 1.0×1.2 cm wide. The endoscope was inserted into the proximal end. The chamber distal wall has a thin channel, which allows for insertion of the metallic needle that carries the T-tag suture. The T-tag is a device consisting of a small magnetic resonancing imaging-compatible steel tag that is loaded onto a needle.

Suture and plication

The sutures were placed approximating the anterior and posterior wall. The procedure began after EMR and the steps performed were as follows. The gastric wall was aspirated through the DASE window until it no longer penetrates into the chamber (► **Fig. 3**). Once the T-tag was loaded inside of the needle, the needle was inserted through the captured tissue. The needle was pushed through the aspirated tissue and the T-tag was released by the needle stylet (► **Fig. 4**). A small amount of traction then was applied to the surgical stitch while the injected needle was withdrawn, which caused the T-tag to be deployed from the needle and assume a T-shaped position perpendicular to the thread direction, anchoring it in situ (► **Fig. 5**). This procedure was repeated in the posterior wall. At that time, both gastric walls without mucosa (anterior and posterior) were crossed with a T-tag surgical thread at the distal tip. The two proximal tips of the T-tag thread were exteriorized through the mouth. Finally, the two threads were cinched together with a tie-knot that completed the suture (► **Fig. 6**). The thread above the tie-knot was cut with scissors. Plication consisted of a group of three aligned sutures.

Procedure completion

Each plication was made with three sutures. Three plications were used to make a pig model gastropasty. In each plication, the first step was insertion of the T-tag through the tissue in both walls, as previously described.

It is worth mentioning that in the central suture of each plication, between the gastric wall and the T-tag, the two T-tags were approximated using a metallic clip and subsequently the tie-knot was used to close the suture, as we previously described. The two remaining sutures of the plication were cinched straight together by pulling the surgical threads and placing the tie-knot (prototype, Cook Endoscopy, Winston-Salem, NC, USA) that completed the suture, followed by cutting the thread with scissors (► **Fig. 7a**, ► **Fig. 7b**, and ► **Fig. 7c**).

Two plications were performed in two animals, the first two in this series, and the remaining four animals received three plications.

Results

Plication placement was successful in all animals (► **Fig. 8**). In the second animal in this series, one plication failed 4 weeks later. The remaining 15 plications were stable 4 to 8 weeks later. One perforation occurred during the EMR and it was closed with one clip. A Veress needle was used to treat the pneumoritoneum. The procedure was conducted normally after the event. There were no other early or late adverse events. All animals were submitted to an esophagogastroduodenoscopy (EGD) and sacrificed.

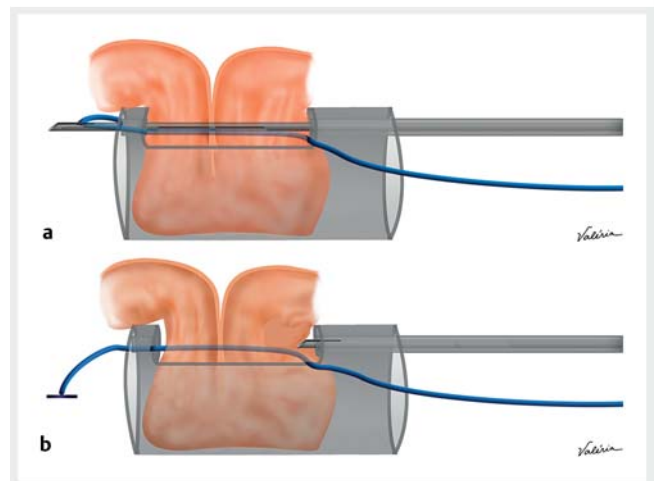
Four animals were sacrificed within 4 weeks and two animals were followed up for another 4 weeks (8 weeks total). On EGD, the plications remained stable, but the wall retraction increased, mainly on the side of the greater curvature. The spaces between the plication were closed with scar tissue, probably due to tissue retraction.



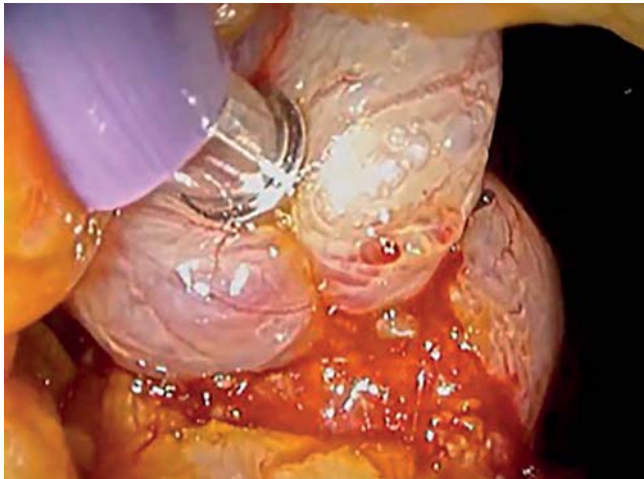
► **Fig. 3** View of the gastric wall through the DASE chamber window.



► **Fig. 4** Gastric wall without mucosa inside the DASE chamber.



► **Fig. 5** Illustration of the gastric walls showing the sutures and plications.



► **Fig. 6** Joining of the anterior and posterior gastric walls with a suture cinched by a tie-knot.

Externally, the stomach showed some deformity with three retraction areas, but the organ shape was not significantly altered (► **Fig. 9**). Necropsy showed only adhesions between the great omentum and the stomach, proving that the adjacent organs were not affected by the sutures. There were signs of retraction, even where the serosa was not involved. Histology showed two muscularis propria layers joined by dense fibrotic tissue (► **Fig. 10**).

The present study included 16 plications performed in six animals. The number of plications per animal ranged from three ($n=4$) to two ($n=2$). Only one plication failed after 4 weeks.

The hypothetical likelihood of procedure failure or success was 50% but the observed incidence of individual suture failure was 6.25% ($n=16$). This was a very significant difference ($P < 0.001$, Fisher exact test). Thus, the total incidence of suture failure after 4 weeks was 6.25%.

Discussion

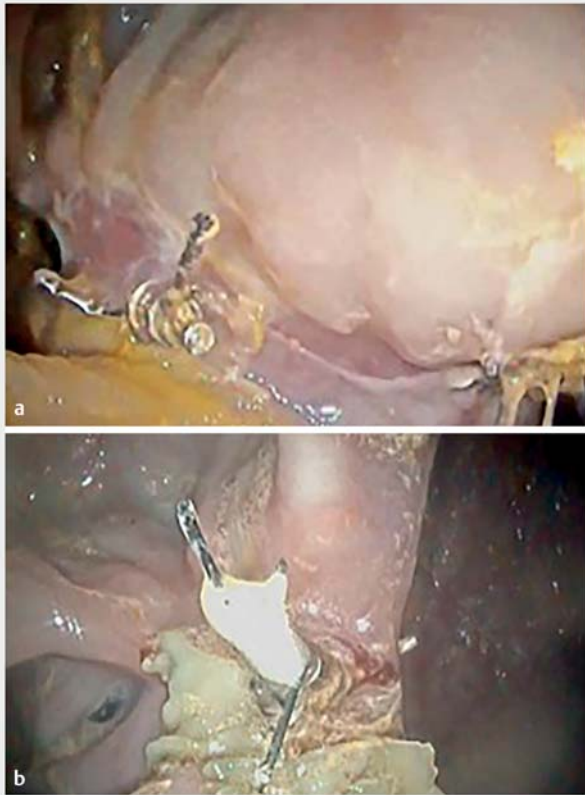
Development of an effective, fast, and cost-efficient method of endoscopic gastrointestinal wall apposition and permanent fusion has long been desired. Endoscopic suturing is a surgical procedure and should be performed based on basic scientific principles [3].

To ensure the success of suturing, important details should be considered, such as the area, depth, and conditions of the sutured tissue [1, 4]. Furthermore, the healing process has not changed since Lembert stated in 1826 that suturing the mucosal surfaces on both sides does not lead to fusion of the walls [4], as this does not trigger a strong healing process, which only occurs if the submucosa is extensively involved [5, 6]. Gross and Halsted's seminal studies at the end of the 19th century also demonstrated the importance of submucosal involvement [5, 6]. These and several other studies [7, 8] have demonstrated that to achieve fusion of the gastrointestinal walls, trauma is required because it triggers an organized and complex cascade of cellular and biochemical events, starting with hemostasis and an inflammatory phase, which is characterized by increased vascular permeability, chemotaxis of cells from the circulation into the wound, local release of cytokines and growth factor, activation of migrating cells like macrophages and wound fibroblasts, and a phenotypic change in the dermal fibroblast with increased collagen synthesis capacity. The proliferative phase, in which fibroblasts and endothelial cells proliferate, is followed by the maturation phase, which starts 1 week after the injury [7]. This provides necessary resistance to tissue fusion [8]. Sutures involving the deep muscularis propria layer would guarantee the initial support required for all these steps to occur.

The endoscopic suturing currently being performed has not respected the traditional rules created by surgeons who extensively studied anastomoses [3], given that suturing mucosa to mucosa would explain the findings of suture failure are 1-year follow-up that have been reported in studies [9]. This means that approximation of tissues without prior trauma does not trigger a sufficient inflammatory process and, therefore, will not lead to effective tissue fusion [7, 8].

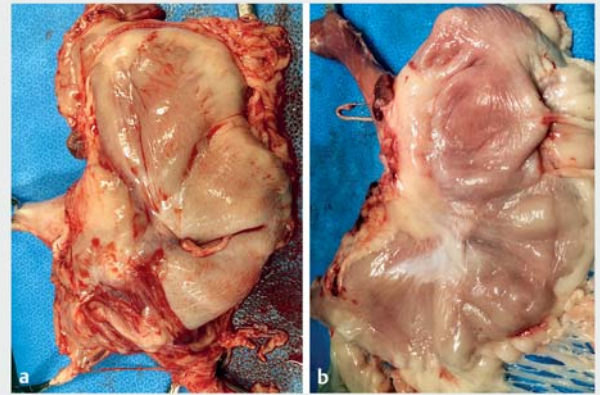


► **Fig. 7 a** Sutures with T-tag caught by a metallic clip. **b** The sutures are pulled through the tie-knot and the gastric walls are joined together. **c** Three sutures together forming one plication.



► **Fig. 8** The wall created by the plication between: **a** a tunnel on the lesser curvature side and **b** the tunnel of the greater curvature.

The present study demonstrated postoperative fusion of anterior and posterior gastric walls with dense fibrosis between the muscularis propria layers of the stomach and showed that

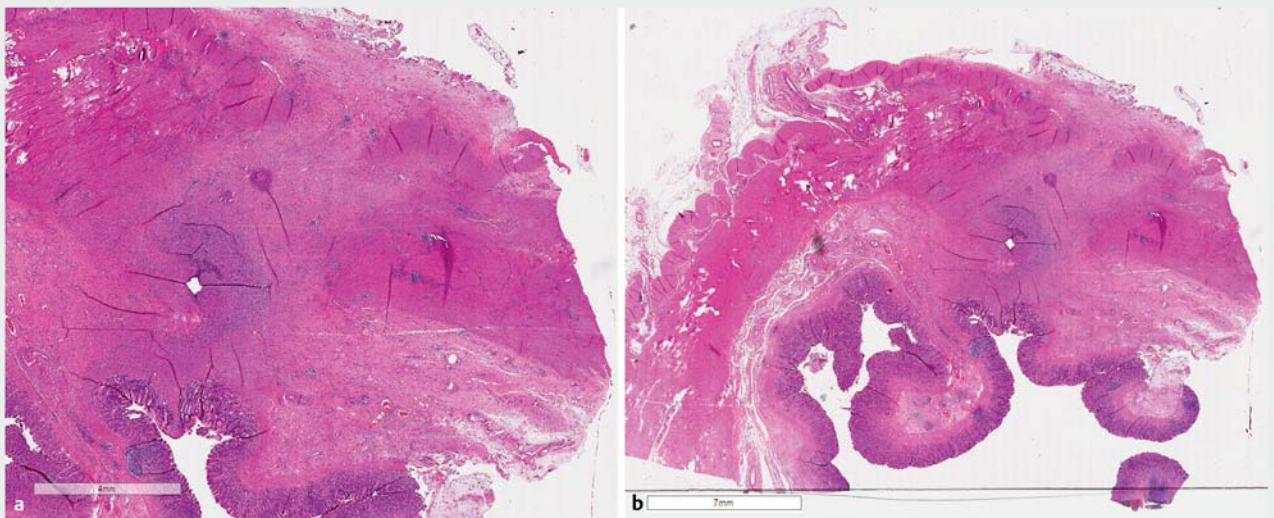


► **Fig. 9 a, b** Anterior and posterior views of the stomach 3 weeks after the suture. Many retracted areas were created by the procedure.

the suture material remained in place. These results, verified by endoscopy and histology, suggest that separation of the sutured tissues can only be done surgically.

Based on established surgical practice as well as studies by Hashiba et al (2), certain rules must be applied if a permanent suture is desired. The apposition must be in an area of the submucosa/muscularis propria that measures $\geq 4\text{cm}^2$, two to five sutures made of non-absorbable material should be used, and the muscularis propria layer must be incorporated into all sutures. Despite the involvement of the serosa, detected in the laparotomy post-mortem, the study showed it is not important to plicate the serosa during suture placement [2].

From a technical point of view, the technique used in the present study is particularly relevant as it was performed using a conventional gastrointestinal endoscope.



► **Fig. 10 a, b** Histologic images of a transverse section of the suture. The muscularis propria layers are separated by the scar (dense fibrotic tissue).

As the aspirated wall lacked mucosa because of the previous EMR, it is reasonable to assume that the muscularis layer was strongly represented (► **Fig. 6**). The author's previous study, described above, showed that the muscularis propria layer is always included [2]. When the serosa was reached, no more than 2.3 mm of the suture was exposed. Even pathological evaluation of the stomach after euthanasia did not allow definitive conclusions, although the serosa often was seen or encompassed in the suture or the inflammatory process.

The maintenance of intact plication in 15 of 16 attempts at 4 and 8 weeks was highly significant. Distention of the stomach with solid foods also should be avoided in the early postoperative period. As this method is developed, the length of time during which solid folds are restricted may be reduced, as has been the case with conventional open surgery.

Some improvements can be made in the devices used in this study to make the procedure more practical and less time-consuming. Development of the tie-knot to allow for automatic suture cutting could eliminate the need for use of scissors.

Conclusions

In conclusion, this study showed that endoscopists performing permanent endoluminal suturing need to follow some fundamentals. Our results also suggest that endoscopic sutures can be used in different ways, such in situations involving large fistulas in the gastrointestinal tract, for gastroesophageal reflux therapy, and for gastropasty and gastric restriction in treatment of obesity. Although novel and effective, the suturing method as a whole may not be as important as understanding that exposing the submucosa with EMR and ensuring that suturing is effective by providing adequate support for the wound healing cascade are fundamental steps for successful tissue fusion.

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Competing interests

The authors declare that they have no conflict of interest.

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