Surg Endosc (2006) 20: 791–793
DOI: 10.1007/s00464-004-2157-8

SURGICAL ENDOSCOPY
and Other Interventional Techniques

The "stamp method": a new treatment for perforated peptic ulcer?

M. J. O. E. Bertleff,[1] R. S. B. Liem,[2] H. L. Bartels,[3] P. H. Robinson,[1] J. F. A. Van der Werff,[4] H. J. Bonjer,[5] J. F. Lange[6]

[1] Department of Plastic Surgery, Academic hospital Groningen, Hanzeplein 1, P.O. Box 30001, Groningen, 9700 RB , The Netherlands
[2] Department of Cell Biology, Section Electron Microscopy, University Groningen, The Netherlands
[3] Laboratory for Animal Research, University of Groningen, The Netherlands
[4] Department of Plastic Surgery, Slotervaart Hospital, Amsterdam, The Netherlands
[5] Erasmus Medical Center Rotterdam, The Netherlands
[6] Department of Surgery, Medical Center Rijnmond Zuid, Rotterdam, The Netherlands

Received: 1 July 2004/Accepted: 11 February 2005/Online publication: 16 March 2006

Abstract
Background: The aim of this study was to develop a simple method for closure of a perforated peptic ulcer, making it more accessible for laparoscopic surgery.
Methods: An experimental pilot study was performed using five male Wistar rats. The perforation was closed by a bioabsorbable patch made of lactide–glycolid–caprolactone fixed with glue onto the outside of the stomach.
Results: Postoperatively, there were no signs of leakage or other complications. Histologically, there were no signs of inflammation on the inside of the stomach, and there was a 50% reduction of the perforation each successive postoperative week. No adverse reactions because of the degradable material or glue were observed.
Conclusions: Treatment of a perforated peptic ulcer by placing a patch of biodegradable material like a "stamp" on the outside of the stomach is a feasible option.

Key words: Perforated peptic ulcer — Laparoscopy — Biodegradable patch — Glue

Introduction

Laparoscopic correction still is not the gold standard for management of a perforated peptic ulcer [4] although many advantages of laparoscopic procedures have been demonstrated during the recent years with regard to postoperative morbidity and pain [1, 8, 9]. During a multicenter Dutch trial (LAMA trial), we compared laparoscopic closure of perforated peptic ulcer with the conventional method using laparotomy. It seemed that one of the problems with the laparoscopic procedure involves the suturing technique [2]. It is especially difficult for surgeons to take big bites, to prevent cutting out of the sutures [9], and to exert sufficient tension on the knot during intra- or extracorporal knotting.

The operation time for laparoscopic correction often is prolonged [2, 6], which is mainly due to the learning curve with regard to suturing technique. This may be the reason why many surgeons (especially during the night) are not even starting up laparoscopically or soon convert to laparotomy. A new method has been developed in which perforation of the stomach in rats was closed with a biodegradable patch fixed with glue, similar to putting a "stamp" on the outside of the stomach. In the current current experiment, this "stamp" method was evaluated.

Methods

Five adult male Wistar rats with an average weight of 255 were used in this trial. With the rats general anesthesia (isoflurangas 2% with oxygen), a median laparotomy was performed. At a fixed point on the ventral side of the stomach, a perforation was created with a diameter of 0.5 cm. A patch, made of lactide–glycolid–caprolactone (LGC) (Polyganics, B.V., Groningen, The Netherlands) was cut into a circle with a diameter of 1 cm and an overlap of 0.5 cm all around the perforation. The patch was glued on the outside of the stomach with Glubran 2 (n-butyl [2] cyanoacrylate, methacryloxysulfolane). The abdomen was closed in two layers with Polysorb 4-0.

After 1week, the first rat underwent relaparotomy under general anesthesia. After inspection of the abdomen, the patch, including the full thickness of the stomach wall, was resected and sent for histology. Each successive postoperative week, one rat underwent the same procedure, resulting in a total clinical and histologic follow-up period of 5 weeks.

For histology, tissue specimens were rinsed in saline and placed into a fixative containing 2% glutardialdehyde buffered with 0.1 mol/ phosphate buffer, pH 7.4. Then the specimens were dehydrated through a graded concentration of ethanol and embedded in glycol methacrylate. From all samples, 2-μm-thick sections were prepared using a disposable histoknife and a Reichert–Jung "2050 supercut"

Correspondence to: M. J. O. E. Bertleff

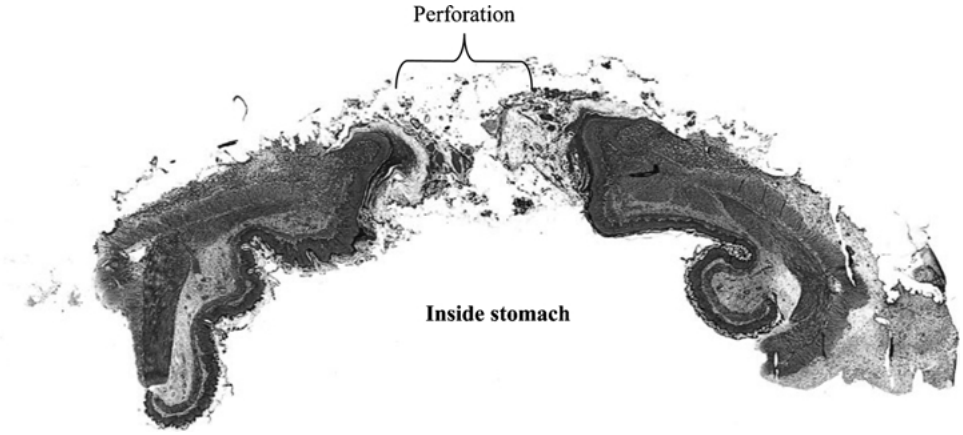

Fig. 1. Histology at week 1.

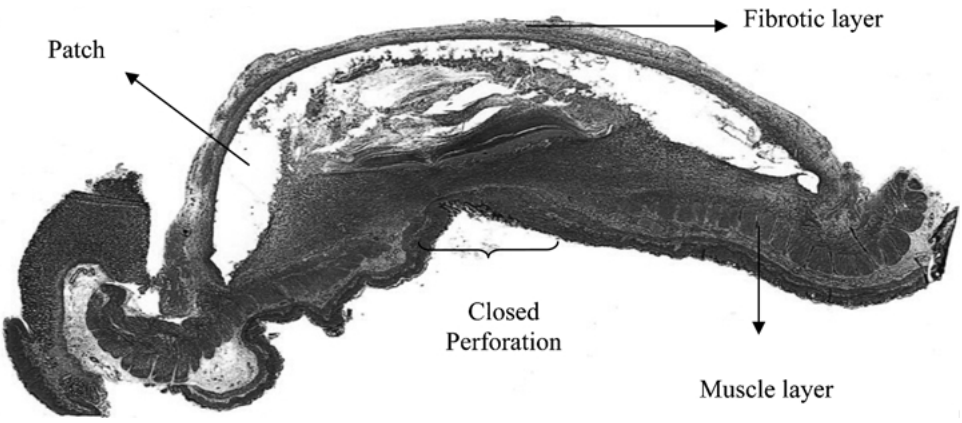

Fig. 2. Histology at week 5.

microtome. The sections were mounted on glass slides and stained with toluidine blue and alkaline fuchsin (Merck, Darmstadt, Germany). All the sections were evaluated and photomicrographed using a Olympus BX-50 microscope (Olympus Optical Co., Japan)

Results

All the rats survived the first operation without complications. The mean operating time was 10 min. At relaparotomy, there were neither signs of leakage nor evidence of peritonitis. There were small adhesions, mainly to the liver, and in the first two rats there also were small adhesions between the spleen and the stomach. From week 1, the patch was covered by omentum. Biodegradation of the patch was visible at week 5. The diameter of the perforation, as observed from the inside of the stomach, decreased by 50% every week. After 5 weeks, only a pinpoint perforation could be found. All the rats gained weight during their weeks of follow-up evaluation, with an average weight of 348 g (range, 313–392 g), on the day of re-operation meaning they were in good condition.

Histology

At 1 week postoperatively, no inflammatory cells were detected on the inside of the stomach. Bacteria were found in the superficial mucous layer of the epithelium, and among the microvilli of epithelial cells. They were distributed irregularly, patchy and with heavy colonization, in some areas but did not invade the epithelium. The mucosa consisted of dense connective tissue and numerous blood vessels. The basement membrane underlying the epithelial basal cells was clearly visible. The muscular layer and submucosal glands were present, but did not continue, as was to be expected.

At 2 weeks postoperatively, cellular ingrowth of inflammatory cells, especially granulocytes, was seen lying against the LGC patches. Multinucleated giant cells also were seen at the interface of the patches.

At 3 weeks postoperatively, the LGC patches were covered by a capsule of fibrotic tissue. This capsule consisted of 14 to 15 layers of fibroblasts, collagen fibers, extracellular matrix, and numerous blood vessels. Still, some multinucleated giant cells were observed in the patches, and degradation of the LGC patches had begun.

At 4 weeks postoperatively, the amount of inflammatory infiltrate had increased, while other cells such as macrophages and multinucleated giant cells were seen infiltrating the LGC-patches. The capsule of fibrotic layer became ticker. Fibroblasts as well as collagen fibers and blood vessels were found more frequently and denser, as compared with findings 3 weeks postoperatively.

At 5 weeks postoperatively, the fibrotic layer on the patch had increased Macrophages and giant cells still were found infiltrating and phagocytosing the LGC patches. There were epithelial cells close to the perforation. The muscular layer still showed perforation. There were no signs of rejection (Figs. 1 and 2).

Discussion

A new method for closure of peptic ulcer perforation was tested in rats, and the first results seem promising. Sealing of the perforation with a glued biodegradable patch seemed sufficient because no leakage occurred. Furthermore, no inflammation or other side effects to the abdominal wall were observed. It was decided that at this phase, the use of an iatrogenically made perforation would be sufficient, because we wanted only to evaluate whether this new technique would work.

Of course, this test did not completely mimic the clinical situation. There was no edema, no fibrin deposition, and no inflammation of surrounding tissue. However, no clinical evidence so far had proved that a perforation of any longer duration with fibrin deposition has a worse outcome with regard to healing of the perforation itself and a higher risk for reperforation. It could even be suggested that fibrin deposition helps in sealing the perforation, but more research on this topic is needed.

Closure of a perforated peptic ulcer by a Graham omental patch or mere sutures has been performed for many years [7, 8]. Several alternative techniques have been tried [7, 9]. The incentive for introducing these new operations was to simplify the procedure and make it suitable for minimal invasive therapy [9]. A few procedures can be accomplished by endoscopy, but often it still is necessary to combine it with laparotomy or laparoscopy [3, 6]. Lau et al. [5] described a method for closing the perforation using spongostan fixed with fibrin glue. This seemed to be suitable only for smaller perforations. The patch used in this study can be introduced through a trocar and unfolded with ease because it has no memory. Glubran 2, the glue used in this trial, is a synthetic surgical glue european conformity (CE) certified for internal use. It is liquid, does not need any preparation and can be applied to the patch inside the abdomen using a laparoscopic needle. The size of the perforation does not matter because the patches can be cut easily into any desired size.

In conclusion we propose a simple technique for closure of a perforated peptic ulcer, making laparoscopic correction of a perforated peptic ulcer more accessible. A randomized clinical trial will be initiated in due course.

Acknowledgement. The authors thank Polyganics, BV (Gronigen, The Netherlands) for providing the patches and (Global Entrepreneurship Monitor) GEM (Italy) for providing the glue and Mr. G. Kors for the technical assistance.

References

1. Agresta F, Michelet I, Coluci G, Bedin N (2000) Emergency laparoscopy: a community hospital experience. Surg Endosc 14: 484–487
2. Bertleff MJOE, Bemelman W, Oei I, Smulders J, vanderHam A, Bonjer H, Lange J (2002) Laparoscopic correction versus open surgery of perforated peptic ulcer: first results of the LAMA trial. Surg Endosc 16: S3
3. Hashiba K, Carvaiho AM, Diniz G, Barbosa de Aridrade N, Guedes CAF, Filho LS, Lima CAP, Coetho HE, Oliveira RA (2001) Experimental endoscopic repair of gastric perforations with an omental patch and clips. Gastrointest Endosc 54: 500–504
4. Lagoo SA (2002) Laparoscopic repair for perforated peptic ulcer. Ann Surg 235: 320–321
5. Lau WY, Leung KL, Kwong KH, Davey IC, Robertson C, Dawson JJ, Chung SCS, Li AKC (1996) A randomized study comparing laparoscopic versus open repair of perforated peptic ulcer using suture or sutureless technique. Ann Surg 224: 131–138
6. Pescatore P, Halkic N, Calmes JM, Blum A, Gillet (1998) Combined laparoscopic–endoscopic method using an omental plug for therapy of gastroduodenal ulcer perforation. Gastrointest Endosc 48: 411–414
7. Siu WT, Leong HT, Law BKB, Chau CH, Li ACN, Fung KH, Tai YP, Li MKW (2002) Laparoscopic repair for perforated peptic ulcer: a randomized controlled trial. Ann Surg 235: 313–319
8. Sø JBY, Kum CK, Fernandes ML, Goh P (1996) Comparison between laparoscopic and conventional omental patch repair for perforated duodenal ulcer. Surg Endosc 10: 1060–1063
9. Wemyss-Holden S, White SA, Robertson G, Lloyd D (2002) Color coding of sutures in laparoscopic perforated duodenal ulcer: a new concept. Surg Laparosc Endosc Percutan Tech 2002 12: 177–179