**Name of journal:** ***World Journal of*** ***Gastroenterology***

**Manuscript NO: 33044**

**Manuscript Type: EDITORIAL**

**Endoscopic shielding technique, a new method in therapeutic endoscopy**

Bon I *et al*. Endoscopic shielding technique

Ignacio Bon, Ramon Bartolí, Vicente Lorenzo-Zúñiga

**Ignacio Bon**, **Ramon Bartolí, Vicente Lorenzo-Zúñiga,** Institut Investigació en Ciències de la Salut Germans Trias i Pujol, Badalona, 08916 Badalona, Spain

**Ramon Bartolí**, **Vicente Lorenzo-Zúñiga,** Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, 08916 Badalona, Spain

**Vicente Lorenzo-Zúñiga,** Endoscopy Unit, Department of Gastroenterology, Hospital Universitari Germans Trias i Pujol, 08916 Badalona, Spain

**Author contributions:** Bon I, Bartolí R and Lorenzo-Zúñiga V contributed in equally form to this paper.

**Conflict-of-interest statement:** Bon I, Bartolí R and Lorenzo-Zúñiga V declare no conflict of interest related to this publication.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

**Manuscript source:** Invited manuscript

**Correspondence to:** **Vicente Lorenzo-Zúñiga, MD, PhD, Professor,** Endoscopy Unit, Department of Gastroenterology, Hospital Universitari Germans Trias i Pujol, Carretera de Canyet, s/n, 08916 Badalona, Spain. vlorenzo.germanstrias@gencat.cat

**Telephone:** +34-93-4978443

**Received:** January 27, 2017

**Peer-review started:** February 6, 2017

**First decision:** March 3, 2017

**Revised:** March 21, 2017

**Accepted:** May 4, 2017

**Article in press:**

**Published online:**

**Abstract**

Prevention of late complications after large endoscopic resection is inefficient with current methods. Endoscopic shielding, as a simple and safe technique, has been proposed to improve the incidence of these events. Different methods, sheets or hydrogels, have showed proven efficacy in the prevention of late bleeding and perforation, as well as the improvement of tissue repair, in experimental models and in clinical practice.

**Key words:** Endoscopic shielding technique; Late complication; Therapeutic endoscopy

**© The Author(s) 2017.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Prevention of late complications after large endoscopic resection is inefficient with current methods. Endoscopic shielding technique is a simple and safe method to reduce the incidence of late bleeding and perforation.

Bon I, Bartolí R, Lorenzo-Zúñiga V. Endoscopic shielding technique, a new method in therapeutic endoscopy. *World J Gastroenterol* 2017; In press

**INTRODUCTION**

Endoscopic resection of large lesions leads to extensive mucosal defects and submucosal exposure, with a substantial risk of complications. Late complications (bleeding, stricture, and perforation) are well known by endoscopists that perform advanced techniques[1]. There are several techniques can be used to prevent these adverse effects, such as adding adrenaline to the submucosal cushion, applying argon plasma coagulation, or clipping closure of the mucosal defect. However, these approaches are inefficient in the management of extensive submucosal exposure[2].

A shielding technique refers to the application of different biocompatible substances with proven biological activity to cover the lesion after therapeutic endoscopy. There are different techniques to perform this procedure. All of them are simple and safe methods to provide shielding protection of the resected area as a way to prevent late complications[3]. Due to the experience we have gained using this technique, we aim to review our evidence, as well as the experimental models used in clinical practice.

***Search strategies***

Studies in English studies were identified by using a comprehensive search of PUBMED. The key words and search strategies were as follows: 1, (“endoscopy” [All Fields] AND (“shielding” [All Fields]). 2, (“hydrogel” [All Fields] AND “mucosectomy” [All Fields]). The Reference lists of primary study publications were searched manually. We did not consider abstracts or unpublished reports for inclusion.

**EXPERIMENTAL MODELS**

Endoscopic shielding techniques have been evaluated in some preclinical models (Table 1). Aimed to increase mucosal healing, to prevent late bleeding secondary to acetic acid or EMR-induced gastric ulcers, a hydrogel based on epidermal growth factor-containing chitosan hydrogel was tested in rabbits and pigs[4]. Feasibility of endoscopic application of this hydrogel was observed in both models, with a significant reduction in the ulcer size in animals treated with this hydrogel. Moreover, the depth of the untreated ulcers was greater, and the underlying muscle layer remained exposed one week after treatment, with deep scar formation and fibrotic submucosa six weeks after endoscopic resection. Other studies refer to the use of Polyglycolic acid sheets (PGA) and Fibrin Glue (FG) to prevent late complications of ESD-induced ulcers in the stomach of two animal models, porcine[5] and canine[6]. PGA-FG exhibited a protective effect against gastric juice, and no peeling of the sheet was observed despite the influence of peristalsis and gastric acid. Histopathological examination revealed excellent long-term tissue repair, with no adverse events.

Shielding with Platelet Rich Plasma (PRP) has been successfully tested in colonic EMR-induced ulcers to prevent late perforations in rats and pigs[7]. On the other hand, PRP showed strong healing properties in both models, with a significant reduction of the ulcer size (2.4% in control groups *vs* 80% in treated animals). More recently, the application of other new hydrogel based on the combination of hyaluronic acid, methylcellulose, poloxamer 407 and a non-absorbable antibiotic, is able to increase mucosal healing rate and to prevent late perforation secondary to deep thermal injury in two experimental models, murine and porcine[8].

**CLINICAL EXPERIENCE**

According to our study, 9 articles were identified with around one hundred patients included, and are summarized in Table 2. The first report was published in 2012[3] as a case report using PGA-FG to prevent late perforation associated with ESD for a duodenal tumor 20mm in diameter. The ulcer was covered with pieces of PGA sheets using biopsy forceps and fixed in place with sprayed FG, that were spontaneously absorbed within 4-15 wk. FG is the result of spraying fibrinogen and thrombin with different tubes. This method, considered to be useful, simple and safe, can sometimes present problems because of gravitational influence, with early slipping of the sheets. To resolve this and to improve the coverage, adding clips to PGA-FG has been successfully assessed in endoscopic resection of duodenal lesions, with a median covering procedure time of 22 minutes[9,10].

The usefulness of the shielding technique in the prevention of late complications has been evaluated in colorectal ESD with large sheets of PGA-FG[10] or Surgicel®[12]. Both substances showed a success rate of 100%. Regarding total procedure time, Surgicel®, an oxidized cellulose polymer that swells into a gelatinous mass with hemostatic and bactericidal effects, showed the best results as a rapid technique (mean time 5 min), in comparison with PGA-FG (19 min). Despite the use of large PGA sheets being less time consuming than many small PGA sheets, is not comparable with the use of a gel agent.

PGA-FG decreased the risk of bleeding after ESD of a large gastric neoplasm, with a mean resection size of 40mm[13]. The post-ESD bleeding occurred at a rate of 6.7% in the study group, compared to 22% in the historical control group. Furthermore, another study[14] reported the efficacy of PGA-FG in the closure of postoperative gastric perforations without large and deep cavities.

The prevention of late esophageal strictures after circumferential ESD has been evaluated with the combination of intra-lesional steroid injections (triamcinolone 40mg, 5 mg/mL) and shielding with PGA sheets and FG[15,16] with and incidence of stricture around 18%.

**CONCLUSION**

Significant technological advancements have led to a rapid expansion of the indications of therapeutic endoscopy, which carries a small, but significant, risk of complications. Adverse events associated with large endoscopic resections cannot be overlooked. To prevent these events we should close the submucosal exposure, although it is difficult to completely close ones > 30 mm in diameter with clipping closure[17]. In our opinion, endoscopic shielding technique is a very promising method that does not require special or complex devices. Shielding large mucosal defects has been demonstrated in experimental models and in clinical practice with around one hundred patients included, showing effectiveness in the prevention of late complications (perforation, bleeding or stricture). There are now different substances, sheets or hydrogels, with different mechanisms of action, which can be used as covering agents. We believe that the use of a single gelling agent seems to have more advantages, as it is the simplest and quickest method to cover large lesions. Moreover, these agents typically have bioactive properties that can accelerate mucosal healing. However, larger prospective studies with control groups are needed to perform a comparison of the different substances.

**REFERENCES**

1 **Paspatis GA**, Dumonceau JM, Barthet M, Meisner S, Repici A, Saunders BP, Vezakis A, Gonzalez JM, Turino SY, Tsiamoulos ZP, Fockens P, Hassan C. Diagnosis and management of iatrogenic endoscopic perforations: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. *Endoscopy* 2014; **46**: 693-711 [PMID: 25046348 DOI: 10.1055/s-0034-1377531]

2 **Toyonaga T**, Man-i M, East JE, Nishino E, Ono W, Hirooka T, Ueda C, Iwata Y, Sugiyama T, Dozaiku T, Hirooka T, Fujita T, Inokuchi H, Azuma T. 1,635 Endoscopic submucosal dissection cases in the esophagus, stomach, and colorectum: complication rates and long-term outcomes. *Surg Endosc* 2013; **27**: 1000-1008 [PMID: 23052530 DOI: 10.1007/s00464-012-2555-2]

3 **Takimoto K**, Toyonaga T, Matsuyama K. Endoscopic tissue shielding to prevent delayed perforation associated with endoscopic submucosal dissection for duodenal neoplasms. *Endoscopy* 2012; **44** Suppl 2 UCTN: E414-E415 [PMID: 23169042 DOI: 10.1055/s-0032-1325739]

4 **Maeng JH**, Bang BW, Lee E, Kim J, Kim HG, Lee DH, Yang SG. Endoscopic application of EGF-chitosan hydrogel for precipitated healing of GI peptic ulcers and mucosectomy-induced ulcers. *J Mater Sci Mater Med* 2014; **25**: 573-582 [PMID: 24338378 DOI: 10.1007/s10856-013-5088-x]

5 **Takao T**, Takegawa Y, Shinya N, Tsudomi K, Oka S, Ono H. Tissue shielding with polyglycolic acid sheets and fibrin glue on ulcers induced by endoscopic submucosal dissection in a porcine model. *Endosc Int Open* 2015; **3**: E146-E151 [PMID: 26135658 DOI: 10.1055/s-0034-1391391]

6 **Hiroyuki T**, Kohki Y, Hiroe M, Tsunehito H, Rie A, Shota T, Hiroko T, Yuki O, Takagi T, Kengo T, Takashi T, Hideyuki K, Hideki T, Akeo H. A basic study of the effect of the shielding method with polyglycolic acid fabric and fibrin glue after endoscopic submucosal dissection. *Endosc Int Open* 2016; **4**: E1298-E1304 [PMID: 27995192 DOI: 10.1055/s-0042-118208]

7 **Lorenzo-Zúñiga V**, Boix J, Moreno de Vega V, Bon I, Marín I, Bartolí R. Efficacy of platelet-rich plasma as a shielding technique after endoscopic mucosal resection in rat and porcine models. *Endosc Int Open* 2016; **4**: E859-E864 [PMID: 27540573 DOI: 10.1055/s-0042-109170]

8 **Lorenzo-Zúñiga V**, Boix J, Moreno de Vega V, Bon I, Marín I, Bartolí R. Endoscopic shielding technique with a newly developed hydrogel to prevent thermal injury in two experimental models. *Dig Endosc* 2017; Epub ahead of print [PMID: 28294423 DOI: 10.111/den.12864]

9 **Doyama H**, Tominaga K, Yoshida N, Takemura K, Yamada S. Endoscopic tissue shielding with polyglycolic acid sheets, fibrin glue and clips to prevent delayed perforation after duodenal endoscopic resection. *Dig Endosc* 2014; **26** Suppl 2: 41-45 [PMID: 24750147 DOI: 10.1111/den.12253]

10 **Takimoto K**, Imai Y, Matsuyama K. Endoscopic tissue shielding method with polyglycolic acid sheets and fibrin glue to prevent delayed perforation after duodenal endoscopic submucosal dissection. *Dig Endosc* 2014; **26** Suppl 2: 46-49 [PMID: 24750148 DOI: 10.1111/den.12280]

11 **Tsuji Y**, Ohata K, Gunji T, Shozushima M, Hamanaka J, Ohno A, Ito T, Yamamichi N, Fujishiro M, Matsuhashi N, Koike K. Endoscopic tissue shielding method with polyglycolic acid sheets and fibrin glue to cover wounds after colorectal endoscopic submucosal dissection (with video). *Gastrointest Endosc* 2014; **79**: 151-155 [PMID: 24140128 DOI: 10.1016/j.gie.2013.08.041]

12 **Myung YS**, Ko BM, Han JP, Hong SJ, Jeon SR, Kim JO, Moon JH, Lee MS. Effectiveness of Surgicel® (Fibrillar) in patients with colorectal endoscopic submucosal dissection. *Surg Endosc* 2016; **30**: 1534-1541 [PMID: 26201411 DOI: 10.1007/s00464-015-4369-5]

13 **Tsuji Y**, Fujishiro M, Kodashima S, Ono S, Niimi K, Mochizuki S, Asada-Hirayama I, Matsuda R, Minatsuki C, Nakayama C, Takahashi Y, Sakaguchi Y, Yamamichi N, Koike K. Polyglycolic acid sheets and fibrin glue decrease the risk of bleeding after endoscopic submucosal dissection of gastric neoplasms (with video). *Gastrointest Endosc* 2015; **81**: 906-912 [PMID: 25440679 DOI: 10.1016/j.gie.2014.08.028]

14 **Takimoto K**, Hagiwara A. Filling and shielding for postoperative gastric perforations of endoscopic submucosal dissection using polyglycolic acid sheets and fibrin glue. *Endosc Int Open* 2016; **4**: E661-E664 [PMID: 27556075 DOI: 10.1055/s-0042-105867]

15 **Sakaguchi Y**, Tsuji Y, Fujishiro M, Kataoka Y, Takeuchi C, Yakabi S, Saito I, Shichijo S, Minatsuki C, Asada-Hirayama I, Yamaguchi D, Niimi K, Ono S, Kodashima S, Yamamichi N, Koike K. Triamcinolone Injection and Shielding with Polyglycolic Acid Sheets and Fibrin Glue for Postoperative Stricture Prevention after Esophageal Endoscopic Resection: A Pilot Study. *Am J Gastroenterol* 2016; **111**: 581-583 [PMID: 27125718 DOI: 10.1038/ajg.2016.60]

16 **Kataoka Y**, Tsuji Y, Sakaguchi Y, Kodashima S, Yamamichi N, Fujishiro M, Koike K. Preventing esophageal stricture after endoscopic submucosal dissection: steroid injection and shielding with polyglycolic acid sheets and fibrin glue. *Endoscopy* 2015; **47** Suppl 1 UCTN: E473-E474 [PMID: 26465191 DOI: 10.1055/s-0034-1392975]

17 **Liaquat H**, Rohn E, Rex DK. Prophylactic clip closure reduced the risk of delayed postpolypectomy hemorrhage: experience in 277 clipped large sessile or flat colorectal lesions and 247 control lesions. *Gastrointest Endosc* 2013; **77**: 401-407 [PMID: 23317580 DOI: 10.1016/j.gie.2012.10.024]

**P-Reviewer:** Phillips HN, Tallon-Aguilar L **S-Editor:** Qi Y **L-Editor: E-Editor:**

**Specialty type:** Gastroenterology and hepatology

**Country of origin:** Spain

**Peer-review report classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

**Table 1 Outcomes of endoscopic shielding techniques with different experimental models**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Ref.** | **Year** | ***n*** | **Species** | **Location of lesions** | **Substance** | **Primary endpoint** | **Efficacy**  |
| Maeng *et al*[4] | 2014 | 12/2 | Rabbit/Pigs | Stomach | EGF-CS | Mucosal healing  | 90%-95% |
| Takao *et al*[5] | 2015 | 9 | Pigs | Stomach | PGA-FG  | Prevent late complications | 100% |
| Hiroyuki *et al*[6] | 2016 | 20 | Canine | Stomach | PGA-FG with suture | Prevent late complications | 100% |
| Lorenzo-Zúñiga *et al*[7] | 2016 | 4/16 | Pigs/Rats | Colon | PRP | Prevent late perforation and mucosal healing | 100% and 2.4% (control) *vs* 80% (treated) |
| Lorenzo-Zúñiga *et al*[8] | 2017 | 8/24 | Pigs/Rats | Colon | HAMPA | Prevent late perforation  | 100% |

PGA: Polyglycocolic acid sheets; FG: Fibrin glue; EGF-CS: Hydrogel Epidermal Growth Factor with Chitosan; PRP: Platelet rich Plasma; HAMPA: Hydrogel based on the combination of hyaluronic acid, methylcellulose, poloxamer 407 and a non-absorbable antibiotic.

**Table 2 Outcomes of endoscopic shielding with different substances to prevent late complications after endoscopic resection**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Ref.** | **Year** | ***n*** | **Location of lesions** | **Size (mm)** | **Substance** | **Procedure time (min)** | **Primary endpoint** | **Efficacy**  |
| Takimoto *et al*[3] | 2012 | 1 | Duodenum | 20 | PGA-FG | NR | Prevent late perforation | 100% |
| Doyama *et al*[9] | 2014 | 3 | Duodenum | 17.5 | PGA-FG with clips | 22 | Prevent late perforation | 100% |
| Takimoto *et al*[10] | 2014 | 2 | Duodenum | 17.5 | PGA-FG with clips | NR | Prevent late perforation | 100% |
| Tsuji *et al*[11] | 2014 | 10 | Colorectal | 39.7 | PGA-FG | 18.7 | Prevent late complications | 100% |
| Tsuji *et al*[13] | 2015 | 41 | Stomach | 40.1 | PGA-FG | 20.4 | Prevent late bleeding | 93.3% |
| Kataoka *et al*[16] | 2015 | 1 | Esophagus | 55 | PGA-FG-T | NR | Prevent late stricture | 100% |
| Myung *et al*[12] | 2016 | 35 | Colorectal | 38.8 | Surgicel® | 5 | Prevent late complications | 100% |
| Sakaguchi *et al*[15] | 2016 | 11 | Esophagus | 38.3 | PGA-T | 12 | Prevent late stricture | 81.8% |
| Takimoto *et al*[14] | 2016 | 3 | Stomach | 25 | PGA-FG | NR | Treatment of postoperative perforations | 100% |

PGA: Polyglycocolic acid sheets; FG: Fibrin glue; T: Triamcinolone; NR: Not reported.