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Endoscopic shielding technique, a new method in therapeutic endoscopy

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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

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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.

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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

Table 1 Outcomes of endoscopic shielding techniques with different experimental models

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

PGA: Polyglycolic 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.

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 min^[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^[11] 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

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

Ref.	Year	<i>n</i>	Location of lesions	Size (mm)	Substance	Procedure time (min)	Primary endpoint	Efficacy
Takimoto <i>et al</i> ^[3]	2012	1	Duodenum	20.0	PGA-FG	NR	Prevent late perforation	100%
Doyama <i>et al</i> ^[9]	2014	3	Duodenum	17.5	PGA-FG with clips	22	Prevent late perforation	100%
Takimoto <i>et al</i> ^[10]	2014	2	Duodenum	17.5	PGA-FG with clips	NR	Prevent late perforation	100%
Tsuji <i>et al</i> ^[11]	2014	10	Colorectal	39.7	PGA-FG	18.7	Prevent late complications	100%
Tsuji <i>et al</i> ^[13]	2015	41	Stomach	40.1	PGA-FG	20.4	Prevent late bleeding	93.3%
Kataoka <i>et al</i> ^[16]	2015	1	Esophagus	55.0	PGA-FG-T	NR	Prevent late stricture	100%
Myung <i>et al</i> ^[12]	2016	35	Colorectal	38.8	Surgicel®	5	Prevent late complications	100%
Sakaguchi <i>et al</i> ^[15]	2016	11	Esophagus	38.3	PGA-T	12	Prevent late stricture	81.8%
Takimoto <i>et al</i> ^[14]	2016	3	Stomach	25.0	PGA-FG	NR	Treatment of postoperative perforations	100%

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

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 40 mm^[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 40 mg, 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.

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