The role of polyglycolic acid sheets in the management of post-endoscopic submucosal dissection gastrointestinal bleeding and esophageal stricture

A PRISMA compliant systematic review and meta-analysis

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**Abstract**

**Background:** As a relatively minimally invasive technique, endoscopic submucosal dissection (ESD) is widely used for the treatment of gastrointestinal lesions. However, it is associated with complications, such as postoperative bleeding, stricture, and perforation. A covering method using polyglycolic acid (PGA) sheets for ESD-induced ulcers has been reported to be effective in reducing the risk of post-ESD bleeding and esophageal stricture. Herein, we conducted a systematic review and meta-analysis to evaluate the role of PGA sheets in the prevention of gastrointestinal bleeding and esophageal stricture after ESD.

**Methods:** We searched PubMed, Web of Science, and the Cochrane Library databases on October 15, 2019. All eligible articles were selected based on the predefined inclusion and exclusion criteria. The main outcomes were the rates of post-ESD gastrointestinal bleeding and esophageal stricture. Cochrane’s Q statistic and I² test were used to identify heterogeneity between the studies. When there was no obvious heterogeneity (I² < 50%, P > .1), a fixed-effect model was used. When there was obvious heterogeneity (I² > 50%, P < .1), a random effect model was used. Funnel plots and the Egger regression test were used to assess publication bias.

**Results:** Fifteen articles were included in the meta-analysis, of which 7 were exclusively about the use of PGA sheets to prevent postoperative gastrointestinal bleeding, and the remaining reported the use of PGA sheets to prevent postoperative esophageal stenosis. Our analysis showed that preventive therapy with PGA sheets decreased the rates of post-ESD gastrointestinal bleeding (risk ratio [RR] = 0.35, 95% confidential interval [CI]: 0.19–0.64, P < .001) and esophageal stricture (RR = 0.46, 95% CI: 0.27–0.79, P < .001), and the gastrointestinal bleeding and esophageal stricture rates after preventive treatment with PGA sheets were 5.7% (95% CI: 3.6%–8.8%) and 20.6% (95% CI: 14.5%–28.4%), respectively.

**Conclusion:** The utilization of PGA sheets after ESD has an excellent outcome in reducing the risk of postoperative gastrointestinal bleeding and esophageal stricture.

**Abbreviations:** CI = confidential interval, EMR = endoscopic mucosal resection, ESD = endoscopic submucosal dissection, PGA = polyglycolic acid, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses, RCT = randomized controlled trials, RR = risk ratio.

**Keywords:** endoscopic submucosal dissection, esophageal stricture, gastrointestinal bleeding, meta-analysis, polyglycolic acid sheets, systematic review.

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The authors have no conflicts of interest to disclose.

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1. Introduction

Endoscopic submucosal dissection (ESD) was first developed in the 1990s as an advanced technique to overcome the limitations of conventional endoscopic mucosal resection (EMR).[11] Compared with EMR, ESD can resect tumors en bloc regardless of tumor size and shape, leading to a more accurate histological diagnosis and reducing the risk of local recurrence.[2-4] Although ESD has advantages, it is associated with some potential complications, such as bleeding, perforation, and postoperative esophageal stricture. For gastrointestinal ESD, postoperative bleeding, one of the most serious complications, may lead to hemorrhagic shock and require transfusion therapy, interventional therapy, or early gastrointestinal endoscope. Some studies have reported that the incidence of esophageal stenosis in patients with post-ESD mucosal defects greater than three-quarters of the esophageal circumference is 70%-90%,[12-14] which seriously reduces the quality of life of these patients.

Recently, a novel endoscopic tissue covering method using polyglycolic acid (PGA) sheets and fibrin glue has been found to have the potential to reduce the risk of post-ESD gastrointestinal bleeding,[15,16] and prevent esophageal stricture.[17,18] In 2014, Kengo et al first introduced polyglycolic acid sheets combined with fibrin glue to prevent duodenal perforation after ESD.[19] Subsequently, Yoshiro and others reported the potential of PGA sheets to prevent esophageal stricture after ESD.[19,20] In 2015, a controlled study found that prophylactic use of PGA sheets reduced gastric bleeding after ESD.[16] After that, a number of papers about PGA sheets have been published. Herein, we conducted a meta-analysis to investigate the role of PGA sheets in preventing gastrointestinal bleeding and esophageal stricture after ESD, attempting to assess its comparative efficacy with regard to other preventive therapies.

2. Materials and methods

2.1. Search strategy

The systematic review was carried out according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[21] To identify all relevant studies of the use of PGA sheets for preventing gastrointestinal bleeding or esophageal stricture, a systematic literature search was performed through the databases of PubMed, the Cochrane Library and Web of Science, with the language restricted to English, on October 15, 2019. The following search terms were used for these databases: “polyglycolic acid,” “polyglycolide,” “endoscopic submucosal dissection,” “ESD,” “esophageal stenosis,” “esophageal stricture,” and “bleeding.”

2.2. Selection of studies

The studies were included according to the following criteria: (1) the enrolled patients, who were scheduled for ESD of early-stage esophageal or gastric adenoma or early gastric cancer or early gastrointestinal cancer; (2) the whole procedure was conducted under endoscopy without any surgical intervention, with the ulcer covered with PGA sheets in a single-arm study, or a comparison of postoperative ulcers covered with PGA sheets and without PGA sheets in a controlled study; (3) the main endpoints were post-ESD gastrointestinal bleeding or esophageal stricture; (4) the sample size was >5; and (5) retrospective or prospective, case-control, or cohort studies and clinical trials (including randomized controlled trials). Any comments or review articles without original data were excluded. Studies of oral, hepatic, cardiac or laryngopharyngeal surgery, or esophageal perforation were also excluded. In the case of duplicated reports, only the most recent and comprehensive publication was included.

2.3. Date extraction and study quality assessment

The outcomes assessed were the rates of post-ESD gastrointestinal bleeding and esophageal stricture after preventive treatment with PGA sheets. Post-ESD gastrointestinal bleeding was defined as the occurrence of melena, hematemesis, or hematochezia during the postoperative follow-up period, and confirmed by endoscopy as postoperative ulcer bleeding. Postoperative esophageal stricture was defined as the presence of a stenosis of the esophageal lumen that prevented the passage of a 9.8-mm diameter upper gastrointestinal endoscope.

Basic data were extracted, including name of the first author, year of the publication, country of the study, type of study, location of lesion, procedure, the study duration, the number of patients and lesions, sex, and mean age. Clinical characteristics were extracted according to the assessed outcomes, bleeding or stricture, including the mean resection size, en bloc resection rate, antithrombotic agent therapy rate, technical success rate, bleeding rate, mean time of bleeding onset, rate of circumferential range ≥3/4, stricture rate, and adverse event rate.

2.4. Study quality assessment

We used the JADAD scale to evaluate the quality of the included randomized controlled trials (RCT)[22] and the Newcastle-Ottawa quality assessment scale to evaluate the quality of nonrandomized controlled trials and single-arm trials.[23] The specific components of the JADAD scale include: the generation of random sequences, hiding of randomization, blindness, and withdrawal or exit. The quality evaluation results were divided into high-quality (score 3–7) studies and low-quality (score 1–3) studies by quantitative evaluation. The Newcastle-Ottawa scale consists of 3 major categories: selection (a. representativeness of the exposure cohort; b. selection of the non-exposed cohort; c. determination of exposure; d. no outcome event occurred in the study participants before the study began), comparability (a. the study controlled the main influencing factors; b. the study controlled other confounding factors), and outcomes (a. assessment of outcome events; b. adequacy of follow-up time; c. completeness of follow-up). Each study included in the quality assessment was assessed as high-quality (score 7–9) research, medium-quality (score 5–6), and low-quality (score <5) research.

In addition, the work has been reported in line with PRISMA and AMSTAR (Assessing the methodological quality of systematic reviews) guidelines.

2.5. Statistical analysis

Review Manager 5.3 (London, UK) and Comprehensive Meta-Analysis software version 3.0 were used to analyze the data. Given that the main purpose of this study was to evaluate whether preventive treatment with PGA sheets can reduce the incidence of outcome events, and to report the incidence of outcome events after prophylactic use, we used forest plots for statistical analysis. The risk ratio (RR) with 95% confidence interval (CI) was recommended for dichotomous variables, such as bleeding rate and stricture. In this study, we estimated heterogeneity with $\chi^2$ and I$^2$ tests; I$^2$ > 50% or P < .1 were considered to indicate obvious heterogeneity.[24] When there was obvious heterogeneity, we used a random effect model, otherwise we used a fixed-effect model. Publication bias was detected by funnel plots and the Egger regression test. For the sensitivity analysis, we repeated the method of eliminating variables one by one and then combining the effect size. A 2-tailed P value <.05 was considered statistically significant.
3. Results

3.1. Baseline characteristics of enrolled studies

A total of 144 records were identified from the 3 electronic databases; 15 articles were included in the final analysis based on the inclusion and exclusion criteria (Fig. 1). The basic characteristics of the included studies were shown in Table 1. All of the studies were performed between 2014 and 2019. Most of the studies (n = 12) were conducted in Japan, and the others (n = 3) were performed in China. They included randomized controlled trials (n = 3), nonrandomized controlled trials (n = 5), and single-armed trials (n = 7). Some of them (n = 7) focused exclusively on gastrointestinal bleeding and the remainder (n = 8) exclusively on esophageal stricture. The location of lesions in the study included the esophagus (n = 8), stomach (n = 5), colorectum (n = 1), and the whole gastrointestinal tract (n = 1). Most of the studies (n = 13) included >10 cases. A total of 814 patients were included, and the majority of patients were male (n = 513, 63.0%). The mean age ranged from 59.9 to 78.5 years.

The clinical characteristics and outcomes of using PGA sheets to prevent post-ESD gastrointestinal bleeding were summarized in Table 2. Most patients (n = 419, 74.7%) included in our analysis took long-term antithrombotic drugs. The mean size of ESD resection was >20 mm in most of the studies. The time of bleeding onset post-ESD in patients undergoing preventive treatments with PGA sheets and fibrin glue varied from 7 to 17 days. The adverse event rates ranged from 0% to 3%.
Table 3 showed the clinical characteristic and outcomes of the use of PGA sheets for preventing esophageal stricture. In these studies, most patients (n = 233, 88.3%) had a circular resection of the esophageal mucosa of more than three-quarters of the circumference. The resected lesions were located in the upper (n = 20, 7.6%), middle (n = 126, 47.7%), and lower (n = 118, 44.7%) thirds of the esophagus. The technical success rate of PGA was 100%. Postoperative follow-up time varied from 6 to 131 weeks. The rate of adverse events ranged from 0% to 9.1%.

### 3.2. Risk of bias within studies

#### 3.2.1. Risk of bias

The quality scores of each included study according to the JADAD scale or the Newcastle–Ottawa quality assessment scale were shown in Table 4. The 3 RCTs[26,28,31] were all high-quality trials (scores ranged from 6 to 7). The final methodological quality evaluation revealed that 1 study was of low quality, 8 of medium quality, and 6 of high quality.

### 3.3. Clinical outcomes

#### 3.3.1. Bleeding

As shown in Table 2, the rate of bleeding varied from 0% to 22.0%. Seven studies[15,16,25–29] were composed of 323 patients who underwent preventive treatment with PGA sheets after ESD. The estimated pooled bleeding rate was 5.7% (95% CI: 3.6%–8.8%) (Fig. 2). There was no obvious heterogeneity among the studies (Q = 2.805, I² < 0.001, P = .833). No significant publication bias was detected by the funnel plot (Fig. 3A) and the Egger test (P = .46). Based on the study quality, the subgroup analysis showed that the rate of bleeding was 6.7% (95% CI: 3.6%–12.0%, I² < 0.001) in high-quality studies (n = 3), 4.6% (95% CI: 2.3%–9.2%, I² ≤ 0.001) in moderate-quality studies (n = 3), and 4.5% (95% CI: 0.3%–44.8%, I² ≤ 0.001) in the low-quality study (n = 1), respectively (Fig. 4A). Based on the study type, the subgroup analysis showed that the rate of bleeding was 5.0% (95%
CI: 2.9%–8.4%, \( F < 0.001 \) in controlled studies (\( n = 4 \)) and 8.1% (95% CI: 3.4%–18.1%, \( F < 0.001 \)) in single-arm studies (\( n = 3 \)) (Fig. 4B). Four studies\(^{[16,25,28]}\) compared the bleeding rate between patients with and without PGA sheets: the RR was 0.35 (95% CI: 0.19–0.64, \( F = 0\%), \chi^2 = 1.43, P < .001\), indicating that the preventive therapy with PGA sheets decreased the risk of gastrointestinal bleeding after ESD (Fig. 5), and there was no obvious heterogeneity. For the sensitivity analysis, no single study significantly changed the outcome or the heterogeneity. No significant publication bias was detected by the funnel plot (Fig. 3B) and the Egger test (\( P = .24\)).

### 3.3.2. Esophageal stricture

The rate of esophageal stricture after ESD ranged from 7.7% to 46.9% (Table 3). Eight studies\(^{[17,18,20,30–34]}\) with a total of 164 patients who underwent preventive treatment with PGA sheets after ESD were included. The estimated pooled esophageal stricture rate was 20.6% (95% CI: 14.5%–28.4%) (Fig. 6). In the sensitivity analysis, the largest change in the rate of esophageal stricture occurred when the study by Nagami et al\(^{[32]}\) was removed, which reduced the heterogeneity level from high to low and changed the effect size from 20.6% to 17.9% (\( Q = 6.552, P = .364, F = 8.430\)). However, overall, there was no obvious heterogeneity. No significant publication bias was detected by the funnel plot (Fig. 3C) and the Egger test (\( P = .84\)). Based on the study quality, the subgroup analysis showed that the rate of esophageal stricture was 14.9% (95% CI: 9.2%–23.3%, \( F < 0.001 \)) in high-quality studies (\( n = 3 \)) and 31.1% (95% CI: 19.9%–46.5%, \( F = 23.241 \)) in medium-quality studies (\( n = 5 \)) (Fig. 7A). Based on the study type, the subgroup analysis showed that the rate of esophageal stricture was 14.9% (95% CI: 9.2%–23.3%, \( F < 0.001 \)) in controlled studies (\( n = 3 \)) and 31.1% (95% CI: 19.9%–46.5%, \( F = 23.241 \)) in single-arm studies (\( n = 5 \)) (Fig. 7B). Three studies\(^{[25,31,34]}\) compared the stricture rate between patients with and without PGA sheets. The RR was 0.46 (95% CI: 0.27–0.79, \( F = 0\%), \chi^2 = 0.90, P = .005\) (Fig. 8), which demonstrated that preventive therapy with PGA sheets decreased the risk of esophageal stricture after ESD, and there was no obvious heterogeneity. In the sensitivity analysis, no single study significantly changed the outcome or the heterogeneity. No significant publication bias was detected by the funnel plot (Fig. 3D) and the Egger test (\( P = .13\)).

### 4. Discussion

Although ESD has many advantages over other treatments in cases of upper gastrointestinal lesions, and some guidelines have

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**Table 3**

Clinical outcomes of studies on stricture rates after esophageal ESD.

| Author          | Year | Procedure            | Circumferential range (≥3/4 rate) (%) (n/N) | Location of lesion (U/M/L) | Technical success rate (%) (n/N) | Stricture rate (%) (n/N) | Follow-up time (wk) | Adverse event (%) (n/N) |
|-----------------|------|----------------------|-------------------------------------------|---------------------------|---------------------------------|------------------------|-----------------------|------------------------|
| Li et al\(^{[30]}\) | 2018 | TS-PGA+FCMS          | 100 (9/9)                                 | 0/8/1                     | 100 (9/9)                       | 33.3 (3/9)             | Dec-22                | 0                      |
| Chao et al\(^{[31]}\) | 2018 | TS-PGA+FCMS          | 100 (34/34)                               | 0/12/22                   | 100 (34/34)                     | 20.5 (7/34)            | 6                     | 0                      |
| Iizuka et al\(^{[32]}\) | 2017 | TS-PGA+FCMS          | 74.4 (29/39)                               | 5/23/11                   | 100 (33/33)                     | 9.1 (3/33)             | 6                     | Jan-33                 |
| Blank           |      | Stent                | 64.5 (20/31)                               | 6/14/11                   | 100 (29/29)                     | 10.3 (3/29)            | 6                     | 0                      |
| Blank           |      | Steroid injection    | 33.3 (6/19)                               | 0/10/5                    | 100 (13/13)                     | 7.7 (1/13)             | 6                     | Jan-13                 |
| Nagami et al\(^{[33]}\) | 2015 | MCFP                 | 100 (10/10)                               | 05-03-02                  | 100 (10/10)                     | 50 (5/10)              | 10-131                | 0                      |
| Sakaguchi et al\(^{[34]}\) | 2015 | MCFP                 | 100 (8/8)                                 | 02-04-02                  | 100 (8/8)                       | 37.5 (3/8)             | 8                     | 0                      |
| Blank           |      | MCFP                 | 100 (11/11)                               | 0/9/2                     | 100 (11/11)                     | 18.2 (2/11)            | 12                    | 01 November            |
| Yang et al\(^{[35]}\) | 2019 | PGA+stent            | 100 (38/38)                                | 01-11-26                  | 100 (38/38)                     | 13.2 (5/38)            | NA                    | NA                     |
| Blank           |      | Stent                | 100 (37/37)                                | 1/15/21                   | 100 (37/37)                     | 35.1 (13/37)           | NA                    | NA                     |

ESD = endoscopic balloon dilatation, ESD = endoscopic submucosal dissection, Hybrid therapy = locoregional steroid injection and polyglycolic acid sheets with fibrin glue, MCFP = mucosal defect covered with fibrin glue and polyglycolic acid sheets, TS-PGA+FCMS = trimcoonelone-soaked polyglycolic acid sheet plus fully covered metal stent, U/M/L = upper/middle/lower.
adopted it as a standard treatment for upper gastrointestinal tumors, we cannot ignore its intraoperative or postoperative complications, such as bleeding, perforation, and stricture.\[35\] Recently, a novel endoscopic shielding method using PGA sheets and fibrin glue has been reported be effective in reducing the post-ESD bleeding and stricture rates.\[15,16\] However, some studies have suggested that prophylactic use of PGA sheets was not effective in reducing the rates of bleeding or esophageal stricture after ESD.\[20,28\] Therefore, we performed this meta-analysis to evaluate the effect of PGA sheets in prevention of post-ESD gastrointestinal bleeding and esophageal stricture.

In this study, our results showed that the rates of gastrointestinal bleeding and stricture in the PGA sheets group were significantly lower than in the control group. Regarding the complication of bleeding, this finding was consistent with a recent study,\[36\] which demonstrated that the rate of delayed bleeding was much lower in the shielding group (2.6%, 1/38) than that in the conventional group (14.1%, 12/85). Mori et al\[26\] pointed out that in the healing process of artificial ulcers after ESD, PGA sheets played an anti-inflammatory role and promote the production of rich granulation tissue. At the same time, PGA sheets promoted the migration of epidermal cells on rich granulation tissue, accelerated the activity of fibroblasts, and formed collagen scar tissue. Such a coating method can also protect surfaces from physical and chemical factors such as ulcer stimulants in food, gastric acid, bile, and pancreatic juice.\[13\]

However, our result is not consistent with Kataoka et al’s report.\[28\] They suggested that the possible reasons for the different findings were: (a) patient inclusion criteria not ideal, resulting in a low overall rate of bleeding after ESD; (b) technological advances in ESD have led to reduced rates of postoperative bleeding; and (c) small sample size—increasing the sample size may produce different results.

In 2017, Mori et al\[24\] used RCTs to evaluate the effect of different delivery systems on the use of PGA sheets to prevent bleeding after ESD. The results showed that a new delivery system can reduce bleeding after ESD when compared with traditional delivery methods. However, because all patients received treatment with PGA sheets, this RCT was regarded as a single-armed trial and we included it in our pooled analysis, which may have produced heterogeneity. As PGA sheets have been widely used as an absorbable biomaterial in the surgical field, the incidence of adverse events related to PGA sheets is close to zero, so we did not analyze the incidence of adverse events in our study.

ESD has been widely used for resection of esophageal lesions, especially esophageal squamous cell carcinoma.\[17\] However, esophageal stricture is a major complication that can occur following ESD in patients left with large mucosal defects, and leads to a poor quality of life.\[14\] Our meta-analysis showed that prophylactic use of PGA sheets can effectively reduce the rate of esophageal stricture after ESD. By pooled analysis, the results showed that the esophageal stricture rate after prophylactic use of PGA sheets is 17.1%. This is consistent with the results of a randomized controlled trial in 2018,\[31\] which reported that the postoperative stricture rate (20.5%) of ulcers covered with PGA sheets was lower than in the non-covered group (46.9%; P = .024). The development of esophageal stricture after ESD mainly involves 3 overlapping pathological processes: inflammatory response, epidermal cell proliferation, and tissue reconstruction.\[38\] The mechanism of action of PGA sheets in preventing esophageal stricture after ESD may involve: (a) PGA sheets protect the ulcer

| Study name                | Event rate | Lower limit | Upper limit | Z-Value | p-Value | Total |
|---------------------------|------------|-------------|-------------|---------|---------|-------|
| Noboru Kawata, 2018       | 0.058      | 0.019       | 0.164       | -4.696  | 0.000   | 3/52  |
| Hirohito Mori, 2017       | 0.103      | 0.039       | 0.243       | -4.110  | 0.000   | 4/39  |
| Yosuke Tsuji, 2015        | 0.067      | 0.022       | 0.187       | -4.416  | 0.000   | 3/45  |
| Yosuke Tsuji, 2014        | 0.045      | 0.003       | 0.448       | -2.103  | 0.035   | 0/10  |
| Yosuke Kataoka, 2019      | 0.045      | 0.015       | 0.130       | -5.181  | 0.000   | 3/67  |
| Hiroko Fukuda, 2016       | 0.038      | 0.015       | 0.098       | -6.313  | 0.000   | 4/104 |
| Daisuke Kikuchi, 2018     | 0.024      | 0.001       | 0.287       | -2.594  | 0.009   | 0/20  |
| Event rate and 95% CI     |            |             |             |         |         |       |

**Meta Analysis**

Figure 2. Forest plot of gastrointestinal bleeding rate after endoscopic submucosal dissection using polyglycolic acid sheets. CI = confidence interval.
Figure 3. (A) Funnel plot on the study of gastrointestinal bleeding rate after endoscopic submucosal dissection using polyglycolic acid sheets; (B) Funnel plot for 4 studies comparing gastrointestinal bleeding rates with or without polyglycolic acid sheets after endoscopic submucosal dissection; (C) Funnel plot for stricture rate after esophageal endoscopic submucosal dissection using polyglycolic acid sheets; (D) Funnel plot of controlled studies on whether polyglycolic acid sheets prophylactic use can reduce esophageal stricture after endoscopic submucosal dissection.

Figure 4. (A) Forest plot of the postesophageal endoscopic submucosal gastrointestinal bleeding rate based on study quality; (B) Forest plot of the postesophageal endoscopic submucosal gastrointestinal bleeding rate based on study type. CI = confidence interval.
surface resulting from ESD from exogenous materials, reducing the local inflammatory response; (b) acting as a scaffold for cell adhesion and promoting tissue regeneration; and (c) strengthening adhesions and reducing scar contracture.[17,18,20,27,30–32,39,40] However, a controlled study by Iizuka et al.[20] demonstrated that PGA sheets cannot reduce the rate of esophageal stricture after ESD. The study also suggested that possible reasons may be the premature detachment of PGA sheets and insufficient study follow-up time. It should be noted that the control group in this study received topical steroid injection to prevent esophageal stricture. Local injection of glucocorticoids prevents esophageal stricture after ESD by inhibiting inflammation, inhibiting collagen synthesis, and promoting collagen degradation[14,41]; however, it can cause complications such as perforation, bleeding, and mediastinal abscess.[13,14] PGA sheets not only avoid these complications caused by local steroid injections but also can be safely applied to patients with contraindications to steroid use such as latent tuberculosis infection.[42] Stent implantation is considered to be a safe and effective method to prevent esophageal strictures after ESD, but we cannot ignore its complications, such as esophageal perforation, severe bleeding, stent displacement, and fractures.[43–46] Some studies[31,34] have overcome these shortcomings by using stents combined with PGA sheets, or a combination of stents, steroids, and PGA sheets. There has been no controlled study of the effectiveness of each method of prevention, so we cannot determine which method is associated with a lower incidence of esophageal stenosis after ESD. Furthermore, there were few complications and no adverse reactions related to PGA sheets in any study. In other words, PGA sheets are safe when used to prevent esophageal stricture after ESD.

Our study had several limitations. First, some studies had small sample sizes[17,20,27,30,33] and smaller total sample sizes (n = 837), so our results may be less clinically relevant. Second, some factors such as resection area and resection circumference may affect the assessed endpoints, and subgroup analysis was not performed due to incomplete data, which may affect its clinical application subdivision criteria. Third, only 3 RCTs[26,28,31] were included in the analysis. Fourth, in the study of PGA sheets to prevent esophageal stricture after ESD, other interventions such as stents, steroid injection, steroid-soaked PGA sheets, and fibrin glue were also included, which can cause great heterogeneity in our meta-analysis.

5. Conclusion
In conclusion, the utilization of PGA sheets after ESD has an excellent outcome in reducing the risk of postoperative

| Study name | Event rate | Lower limit | Upper limit | Z-Value | p-Value | Total |
|------------|------------|-------------|-------------|---------|---------|-------|
| Longsong Li, 2018 | 0.333 | 0.111 | 0.667 | -0.980 | 0.327 | 3 / 9 |
| Ning-Li Chai, 2018 | 0.206 | 0.101 | 0.373 | -3.183 | 0.001 | 7 / 34 |
| T. Iizuka, 2017 | 0.091 | 0.030 | 0.247 | -3.803 | 0.000 | 3 / 33 |
| Toshiro Iizuka, 2015 | 0.077 | 0.011 | 0.391 | -2.387 | 0.017 | 1 / 13 |
| Yasuaki Nagami, 2016 | 0.500 | 0.225 | 0.775 | 0.000 | 1.001 | 5 / 10 |
| Yoshiki Sakaguchi, 2015 | 0.375 | 0.125 | 0.715 | -0.699 | 0.484 | 3 / 8 |
| Yoshiki Sakaguchi, 2016 | 0.182 | 0.046 | 0.507 | -1.924 | 0.054 | 2 / 11 |
| Yanguo Yang, 2019 | 0.132 | 0.056 | 0.280 | -3.932 | 0.000 | 5 / 38 |

Figure 5. Forest plot comparing gastrointestinal bleeding rates with or without polyglycolic acid sheets after endoscopic submucosal dissection. CI = confidence interval, PGA = polyglycolic acid.

Figure 6. Forest plot of stricture rate after esophageal endoscopic submucosal dissection using polyglycolic acid sheets. CI = confidence interval.

Meta Analysis

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gastrointestinal bleeding and esophageal stricture. More high-quality clinical trials are warranted in the future.

**Author contributions**

Study conception and design: Xiaowei Tang and Muhan Lü.

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Revision of manuscript, and final approval of manuscript: Muhan Lü and Xiaowei Tang

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