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

**Manuscript NO: 35831**

**Manuscript Type: ORIGINAL ARTICLE**

***Randomized Controlled Trial***

**Effect of polyglycolic acid sheet plus esophageal stent placement on preventing esophageal stricture after endoscopic submucosal dissection in patients with early-stage esophageal cancer: A randomized, controlled trial**

Chai NL *et al*. PGA plus stent prevent esophageal stricture in EC patients

Ning-Li Chai, Jia Feng, Long-Song Li, Sheng-Zhen Liu, Chen Du, Qi Zhang, En-Qiang Linghu

**Ning-Li Chai, Jia Feng, Long-Song Li, Sheng-Zhen Liu, Chen Du, Qi Zhang, En-Qiang Linghu**, Department of Gastroenterology, Chinese PLA General Hospital, Beijing 100853, China

**ORCID number:** Ning-Li Chai (0000-0003-0583-4189); Jia Feng (0000-0001-6839-3531); Long-Song Li (0000-0003-4593-7668); Sheng-Zhen Liu (0000-0001-6495-2818); Chen Du (0000-0003-4790-6056); Qi Zhang (0000-0002-6550-9217); En-Qiang Linghu (0000-0002-6311-5265).

**Author contributions:** Chai N and Feng J contributed equally to this article;Linghu EQ contributed to study conception and design; Chai NL and Feng J contributed to data acquisition, data analysis and interpretation; Li LS and Liu SZ drafted initial manuscript; Du C and Zhang Q contributed to editing and revising the article. All authors read and approved the manuscript.

**Institutional review board statement:** The study was reviewed and approved by the Ethics Committee of Chinese PLA General Hospital.

**Clinical trial registration statement:** This study is registered on [www.chictr.org.cn](http://www.chictr.org.cn) with No. chictr-inr-16008709.

**Informed consent statement:** All study participants provided informed written consent prior to study enrolment.

**Conflict-of-interest statement:** The authors have no conflicts of interest to disclose.

**Data sharing statement:** No additional data are available.

**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:** Unsolicited manuscript

**Correspondence to: En-Qiang Linghu, MD, PhD, Chief Doctor,** Department of Gastroenterology, Chinese PLA General Hospital, 28 Fuxing Road, Beijing 100853, China. 0572013@fudan.edu.cn

**Telephone:** +86-10-55499292

**Fax:** +86-10-55499292

**Received:** September 20, 2017

**Peer-review started:** September 21, 2017

**First decision:** September 27, 2017

**Revised:** January 2, 2018

**Accepted:** January 17, 2018

**Article in press:**

**Published online:**

**Abstract**

***AIM***

To assess the effect of polyglycolic acid (PGA) plus stent placement compared with stent placement alone on the prevention of post-endoscopic submucosal dissection (ESD) esophageal stricture in early-stage esophageal cancer (EC) patients.

***METHODS***

Seventy EC patients undergoing ESD were enrolled in this randomized, controlled study. Patients were allocated randomly at a 1:1 ratio into two groups as follows: (1) PGA plus stent group-PGA sheet-coated stent placement was performed; and (2) Stent group-only stent placement was performed. This study was registered on http://[www.chictr.org.cn](http://www.chictr.org.cn) with No. chictr-inr-16008709.

***RESULTS***

The occurrence rate of esophageal stricture in the PGA plus stent group was 20.5% (*n* = 7), which was lower than that in the stent group at 46.9% (*n* = 15) (*P* = 0.024). The mean value of esophageal stricture time was 59.6 ± 16.1 d and 70.7 ± 28.6 d in the PGA plus stent group and stent group (*P* = 0.174), respectively. Time to balloon dilatation in the PGA plus stent group was less than that in the stent group [4 (2-5) *vs* 6 (1-14), *P* = 0.007]. The length (*P* = 0.080) and diameter (*P* = 0.061) of esophageal strictures were numerically decreased in the PGA plus stent group, whereas no difference in location (*P* = 0.232) between the two groups was found. Multivariate logistic analysis suggested that PGA plus stent (*P* = 0.026) was an independent predictive factor for a lower risk of esophageal stricture, while location in the middle third (*P* = 0.034), and circumferential range = 1/1 (*P* = 0.028) could independently predict a higher risk of esophageal stricture in EC patients after ESD.

***CONCLUSION***

PGA plus stent placement is more effective in preventing post-ESD esophageal stricture compared with stent placement alone in EC patients with early-stage disease.

**Key words**: Esophageal cancer; Endoscopic submucosal dissection; Polyglycolic acid plus stent placement; Esophageal stricture

**© The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** This study determines the effect of polyglycolic acid (PGA) plus stent placement compared with stent placement alone on the prevention of post-endoscopic submucosal dissection (ESD) esophageal stricture in early-stage esophageal cancer (EC) patients. Our findings confirm that PGA plus stent placement is more effective in preventing post-ESD esophageal stricture compared with stent placement alone in EC patients with early-stage disease.

Chai NL, Feng J, Li LS, Liu SZ, Du C, Zhang Q, Linghu EQ. Effect of polyglycolic acid sheet plus esophageal stent placement on preventing esophageal stricture after endoscopic submucosal dissection in patients with early-stage esophageal cancer: A randomized, controlled trial.*World J Gastroenterol* 2018*;* In press

**INTRODUCTION**

Esophageal cancer (EC) is one of the most common carcinomas with high mortality and has been identified as the sixth leading cause of cancer-related death worldwide[1]. Based on 2015 global cancer statistics, an estimated 455800 new EC cases and 400200 deaths occurred in 2012. In the United States, approximately 16940 new EC cases and 15690 deaths will be seen in 2017[2,3]. Endoscopic submucosal dissection (ESD), performed as an endoscopic resection technique, has been widely utilized in the treatment of EC patients with early-stage disease, due to its minimal invasiveness and high rate of *en bloc* resection[4,5]. However, more than 30% of EC patients after ESD still experience postoperative esophageal stricture, which is characterized by dysphagia, dramatically decreasing the quality of life[6,7].

To prevent post-ESD esophageal stricture, various treatments have been implemented, such as polyglycolic acid (PGA) sheet, stent placement and esophageal balloon dilatation[8]. Among these, PGA sheet, a biodegradable suture material, could be used to prevent post-ESD esophageal stricture because of its advantages of reinforcing suture and minimal scar contracture, although the limitation of instability between the PGA sheet and wound surface after long-term pasting still exists[9-11]. Another popular method is stent placement, which is frequently used with covered self-expandable metal material, and has been verified to have curative effects on refractory stricture to some extent, although its complications, such as translocation and promotion of granulation tissue proliferation, still affects its clinical outcomes in EC patients[12,13].

Although some studies on the applications of combinations of two or three treatments in the prevention of esophageal stricture after ESD have been investigated, no study has explored the effect of the combination of PGA and stent placement on the prevention of post-ESD esophageal stricture[9,14]. Therefore, the aim of this study was to assess the effect of PGA plus stent placement compared with stent placement alone on the prevention of post-ESD esophageal stricture in early-stage EC patients.

**MATERIALS AND METHODS**

***Patients***

A total of 70 early-stage EC patients receiving ESD at Department of Gastroenterology, China PLA General Hospital from July 2016 to May 2017 were consecutively enrolled in this randomized controlled study. The inclusion criteria were as follows: (1) Circumferential range above 3/4; (2) Longitudinal length above 3 cm; (3) Lesion depth no more than M2; and (4) Tumor lesion could be completely removed. The exclusion criteria were as follows: (1) Patients with coagulative dysfunction, hepatic failure, renal failure or cardiopulmonary dysfunction; (2) Complicated with malignant hematological disease or other solid tumors; (3) Patients who had a previous history of esophagectomy or radiation therapy; (4) Patients who were unable to complete the ESD operation; (5) Pregnant or lactating women; (6) Patients who could not be followed up regularly; and (7) Patients who refused to participate in this study.

This study was approved by the Ethics Committee of China PLA General Hospital with approval No. S2016-059-01, and all participants provided written informed consent. This study was registered on http://[www.chictr.org.cn](http://www.chictr.org.cn) (Chinese Clinical Trial Registry conducted by World Health Organization) with registration No. chictr-inr-16008709.

***Randomization***

The randomization code was generated by a statistician using the blocked randomization method with block length set as 4 because of the need for allocation balance between two groups (1:1 ratio). The documents were subsequently sent and kept in Shanghai Qeejen Bio-tech Company (a medical and statistical service company). After screening, when a patient was eligible for the study, a call was made to the Qeejen Company, and a unique subject identification number was provided from the randomized module.

***Treatment***

After the randomization, patients were allocated to the PGA plus stent treatment group or stent treatment group at a 1:1 ratio. In the PGA plus stent group, the patients received a PGA sheet-coated stent placement to prevent esophageal stricture post ESD operation; in the stent group, the patients received only stent placement to prevent esophageal stricture post ESD operation.

***ESD procedure***

After intravenous anesthesia, patients with tracheal intubation and oropharyngeal tube placement underwent endoscope (Olympus, Japan) insertion to the area of the tumor lesion. Subsequently, the lesion margins were stained with iodine, and the submucosa was labeled. Then, the lesion dissections were performed, and endoscopic submucosal tunnel dissection was used for lesion stripping, followed by hemostasis.

***Combination of PGA membrane and stent***

According to the ESD wound length (Figure 1A), the length of stent (Derman Science, China, 1.7 cm of diameter, stainless steel, silicone rubber membrane) was selected (Figure 1B), followed by PGA sheet selection (NEOVEIL, Japan, 100 mm × 100 mm × 0.15 mm) (Figure 1C). Subsequently, the stent was coated with the PGA sheet (Figure 1D), and the covered place was designed to the ESD wound site after stent release. Then, this stent covered with a PGA sheet was mounted on the conveyer for the esophageal stent ring supporter (Figure 1E and F) and inserted under endoscopic observation (Figure 1G).

***Stent placement***

The length of the ESD wound was measured, and then the appropriate length of metal coated stent was selected (Derman Science, China, 1.7 cm of diameter, stainless steel, silicone rubber membrane), which was beyond the top and bottom edge of the lesion by more than 2 cm. Subsequently, the guide wire was placed under the endoscope, and then the endoscope was pulled out and the conveyer was inserted for the esophageal stent ring supporter along with the guide wire for the stent placement. After stent placement, the endoscope was inserted again to observe the stent position. A chest X-ray was performed after the stent placement, and the stent position was recorded.

***Stent removal***

In the PGA plus stent group, the stent was removed by endoscopy at 4 wk, whereas in the stent group, the stent was removed at 8 wk after operation. Endoscopic evaluation of the ESD wound was performed (Figure 2A-C). The time to remove the stent between the two groups was different because PGA is a biodegradable suture material, which would be degraded after a period of time. According to a preliminary study with a small sample size, we found that when PGA plus stent placement was used to prevent post-ESD esophageal stricture in early-stage EC patients, the PGA was degraded at approximately 3 wk or 4 wk after ESD, and therefore, the previous clinical experiences suggested that removing PGA plus stent placement at 4 wk might be a good choice in EC patients.

***Assessment***

The primary endpoint was esophageal stricture occurrence after ESD operation, which was defined as diameter of stricture section below 1 cm (endoscopy could not pass through) under endoscopy. The secondary endpoints were as follows: time to esophageal stricture; location, length and diameter of esophageal stricture; balloon dilatation times for the esophageal stricture.

***Follow-ups***

All patients were followed up through clinic visits or telephone interviews. Each patient was asked if dysphagia or other symptoms occurred at each visit or call, and if distinct dysphagia was determined, endoscopy was performed to examine the esophageal stricture. Chest X-ray examination was performed every 2 wk to monitor the position of esophageal stent, and if a stent shifted more than 2 cm, endoscopy was performed to adjust the stent to the original place.

***Balloon dilatation***

All patients with esophageal stricture received endoscopic balloon dilation treatment (balloon diameter: 8 mm/10 mm/12 mm/15 mm, Boston Scientific, United States). The esophageal stricture section was repeatedly dilated until the endoscope could successfully pass through at each endoscopic examination, and balloon dilation was performed every week until the endoscope could pass through the section before dilation.

***Statistics***

Statistical analysis was performed using SPSS 22.0 (IBM, United States) and OFFICE 2010 (Microsoft, United States). Data are mainly presented as mean value ± SD, median value (range) or count (percentage). The comparison between two groups was determined by t-test, Chi-square test or Wilcoxon rank sum test. Factors affecting esophageal stricture occurrence were evaluated by univariate logistic regression analysis, and all factors with a *P* value below 0.1 were further detected by multivariate logistic regression analysis. *P* < 0.05 was considered significant.

**RESULTS**

***Study flow***

In the current study, 109 EC patients were screened for eligibility, while 39 cases were excluded as follows: 21 patients for exclusions and 10 patients who refused to participate in this study (Figure 3). Subsequently, these remaining 70 patients were randomized at a 1:1 ratio into two groups as follows: PGA plus stent group and stent group. In the PGA plus stent group, 1 case withdrew during the study due to a lesion depth > m2 post-ESD operation, and 34 (97%) cases completed the entire study. In the stent group, there were 3 total withdrawals; 3 patients with lesion depth more than M2 after ESD operation withdrew, and 32 (91%) cases completed the entire study. Ultimately, a total of 66 EC patients completed the final analysis. After the operation, the stent was removed by endoscopy at 4 wk in the PGA plus stent group, and it was removed at 8 wk in the stent group. During the study, stent displacement was adjusted by endoscopy. Chest X-ray examination was performed every 2 wk. Endoscopy was performed to check the esophageal stricture. All patients with esophageal stricture received endoscopic balloon dilation treatment.

***Baseline characteristics***

As shown in Table 1, no difference in patients’ characteristics and tumor lesion features between the PGA plus stent group and stent group were observed (All *P* > 0.05). The numbers of patients with tumor location upper, middle and lower third were 0 (0%), 12 (35%) and 22 (65%), respectively, in the PGA plus stent group, while 0 (0%), 17 (53%) and 15 (47%) in the stent group (*P* = 0.145). In terms of tissue depth (*P* = 0.331), there were 20 (59%) patients with M1 and 14 (41%) patients with M2 in the PGA plus stent group and 15 (47%) patients with M1 and 17 (53%) patients with M2 were in stent group. The mean value of longitudinal length was 5.97 ± 2.68 cm in PGA plus stent group and 6.06 ± 2.12 cm in the stent group (*P* = 0.878). Other baseline characteristics are presented in Table 1.

***Comparison of post-ESD stricture in PGA plus stent and stent groups***

The occurrence rate of patients with esophageal stricture in the PGA plus stent group was 20.5% (*n* = 7), which was lower than in the stent group at 46.9% (*n* = 15) (*P* = 0.024, Figure 4A). Regarding time to esophageal stricture, the mean value was 59.6 ± 16.1 d and 70.7 ± 28.6 d in the PGA plus stent group and stent groups, respectively (*P* = 0.174, Figure 4B).

***Comparison of esophageal stricture features in PGA plus stent and stent groups***

T-test or Wilcoxon rank sum test was used to compare esophageal stricture features between the PGA plus stent and stent groups (Table 2). The balloon dilatation times for esophageal stricture in the PGA plus stent group was less than that in the stent group (4 (2-5) *vs* 6 (1-14), *P* = 0.007). Length (*P* = 0.080) and diameter (*P* = 0.061) of esophageal stricture were numerically decreased in PGA plus stent group compared with the stent group, whereas there was no difference in location (*P* = 0.232) between the PGA plus stent and stent groups (Table 2).

***Comparison of tumor lesion features in patients occurred esophageal stricture***

As presented Table 3, comparison of tumor lesion features in patients with esophageal stricture between the PGA plus stent and stent groups was evaluated. No difference of location (*P* = 0.899), tissue depth (*P* = 0.823), longitudinal length (*P* = 0.360) or circumferential range (*P* = 0.181) in patients with esophageal stricture between the two groups (Table 3).

***Analysis of factors affecting esophageal stricture occurrence***

Factors affecting esophageal stricture occurrence were determined by univariate logistic regression analysis (Table 4). PGA plus stent (*P* = 0.027) was correlated with a lower possibility of esophageal stricture occurrence, whereas circumferential range = 1/1 (*P* = 0.008) and tissue depth M2 (*P* = 0.017) were associated with a higher probability of esophageal stricture occurrence. Location in the middle third (*P* = 0.083) and longitudinal length ≥ 6 cm (*P* = 0.059), were two factors that appeared to be correlated with a higher risk of esophageal stricture but without statistical significance. All factors with *P* value not above 0.1 were further detected by multivariate logistic regression analysis. PGA plus stent (*P* = 0.026) was an independent predictive factor for a lower risk of esophageal stricture, whereas location in the middle third (*P* = 0.034) and circumferential range = 1/1 (*P* = 0.028) could independently predict a higher risk of esophageal stricture in EC patients after ESD.

**DISCUSSION**

In the current study, we found the following: (1) The occurrence rate of patients with esophageal stricture in the PGA plus stent group was lower compared with the stent group, and the balloon dilatation times of esophageal stricture in the PGA plus stent group were less compared with the stent group; and (2) PGA plus stent could independently predict a lower occurrence rate of esophageal stricture, while location in the middle third and circumferential range = 1/1 were independent predictive factors for a higher possibility of post-ESD esophageal stricture occurrence in EC patients.

ESD, which is considered an effective method to completely resect lesions of mucous membranes, has been popularly applied in EC patients with early-stage disease, although due to the physiological characteristics of the esophageal cavity, esophageal stricture frequently occurs after ESD[4,15,16]. Recent data indicate that the appearance of several fibroblasts and the shrinking of the natural muscle layer are present in the formation of post-ESD esophageal stricture, which suggests that fiber proliferation, scar formation and wound contracture might contribute to the formation of post-ESD esophageal stricture[17].

Stenting has been regarded as a useful way to prevent post-ESD esophageal stricture, although a high recurrence rate still exists in most patients after removing the stent, and some patients with long-term stent placement experience several complications, such as displacement and granulation tissue hyperplasia[18,19]. In clinical practice, stent insertion has been reported to decrease the dysphagia score and the mean diameter of esophageal stricture[20]. PGA sheet, a polymer with a fiber mesh structure, could (1) provide abundant cytoskeletons to support cell crawling during the repair process, and inhibit rejection reaction by its strong degradative function, thereby leading to a decreased risk of scar germination and stricture formation; and (2) carry cells and medicines to promote cell repair and wound healing. An interesting study revealed that PGA sheets could shield mucosal defects and prevent scarring, reducing postoperative adverse events in patients with colorectal ESD[21]. However, some limitations of PGA sheets still exist, which is easy to fall off for long-term utilization[9,10]. Therefore, both stents and PGA can decrease the risk of esophageal stricture to some extent. However, there remain several limitations. No study on the effects of the combined application of PGA and stent has been reported. Our study compared the occurrence rate of post-ESD esophageal stricture between PGA plus stent and stent groups and indicated that the percentage of post-ESD esophageal stricture in the PGA plus stent group was lower compared with the stent group. Balloon dilatation, which is one of the most common treatments for esophageal stricture, has been identified to have good short-term efficacy, whereas the long-term curative effect is still far from satisfactory. One previous study suggested that the average usage rate of balloon dilatation is estimated to be 16 times for post-ESD esophageal stricture[22]. The results of our study also found that the balloon dilatation times for esophageal stricture in the PGA plus stent group were less than in the stent group [4 (2-5) *vs* 6 (1-14) times]. Therefore, these findings indicated that PGA plus stent could decrease the risk of esophageal stricture and the balloon dilatation times for esophageal stricture compared with stent placement alone. Possible explanations might be as follows: (1) The stent could provide radial force to fix the PGA sheet, thereby preventing the defluvium of the PGA sheet[18,19]; and (2) The PGA sheet could increase the friction between the stent and wound surface, reducing stent displacement, and also provide cytoskeleton and carry medicine to accelerate cell repair and wound healing. Therefore, the interaction of the PGA sheet with the stent could decrease the occurrence rate of post-ESD esophageal stricture[9,11]. However, 7 patients still reported the formation of esophageal stricture in the PGA plus stent group. This occurrence might be explained by the fact that during the process of wound repair, epithelial cells usually crawl from the edge of the wound to the central area. Because of the long-term repair, the PGA sheet might be degraded to result in frameless support, leading to its defluvium and increasing the occurrence rate of esophageal stricture in the central area (Figure 5A-D). As to the predictive value, the results of the present study showed that PGA plus stent could be an independent factor to predict a lower possibility of esophageal stricture occurrence. The possible reasons are that the stent contributes to fixing the PGA sheet and the PGA sheet increases the friction to reduce stent displacement, thereby preventing the occurrence of post-ESD esophageal stricture[9,11,18,19]. Although there is no report on the effects of PGA plus stent on the prevention of post-ESD esophageal stricture in EC patients, further studies investigating other combined treatments, such as PGA plus stent plus corticosteroids, are greatly needed. Furthermore, the results of our study also found that shorter length (*P* = 0.080) and diameter (*P* = 0.061) were observed in the PGA plus stent group compared with the stent group, which suggests that the interaction of PGA and stent might decrease the severity of the degree of esophageal stricture.

In clinical practice, glucocorticoids have established their value in inhibiting the inflammatory response, repressing collagen synthesis, and promoting collagen decomposition, thereby preventing the formation of post-ESD esophageal stricture[23,24]. Although glucocorticoid injection is a good way to decrease the occurrence of systemic adverse reactions, it still leads to several complications in EC patients after ESD, including perforation, bleeding, and mediastinal abscess[23,25]. Therefore, a PGA sheet infiltrated with a glucocorticoid (triamcinolone acetonide) might decrease the occurrence of post-ESD esophageal stricture while reducing adverse reactions. Furthermore, to optimize the methods to prevent esophageal stricture, we explored the combined application of PGA, stent and glucocorticoid in three EC patients after ESD (Figure 6A-C). After stent removal, no formation of esophageal stricture occurred and good effectiveness was achieved during a 3 mo follow-up (Figure 6D and E). However, further study with a larger sample size and a longer follow-up is necessary.

One limitation in the present study was that the total number of recruited EC patients was relatively small, which might cause lower statistical efficiency compared with a study with a large sample size. Therefore, a study with a larger sample size is needed to further confirm the efficacy of PGA plus stent in preventing esophageal stricture.

In conclusion, PGA plus stent placement is more effective in preventing post-ESD esophageal stricture compared with stent placement alone in EC patients with early-stage disease.

**ARTICLE HIGHLIGHTS**

***Research background***

Esophageal cancer (EC) is one of the most common carcinomas with high mortality; and more than 30% of EC patients after endoscopic submucosal dissection (ESD) still experience postoperative esophageal stricture which dramatically decreasing the quality of life.

***Research motivation***

The applications of combinations of two or three treatments in the prevention of esophageal stricture after ESD have been investigated in some studies. However, no study explored the effect of the combination of PGA and stent placement on the prevention of post-ESD esophageal stricture.

***Research objectives***

This study aimed to assess the effect of PGA plus stent placement *vs* stent placement alone on the prevention of post-ESD esophageal stricture in early-stage EC patients.

***Research methods***

About 70 EC patients undergoing ESD were enrolled in this study. Patients were allocated randomly at a 1:1 ratio into PGA plus stent group (PGA sheet-coated stent placement was performed) and stent group (only stent placement was performed). All patients were followed up, if dysphagia or other symptoms occurred, if distinct dysphagia was determined, and endoscopy was performed to examine the esophageal stricture.

***Research results***

The occurrence rate of esophageal stricture in the PGA plus stent group was lower than that in the stent group. Time to balloon dilatation in the PGA plus stent group was less than that in the stent group. Multivariate logistic analysis suggested that PGA plus stent was an independent predictive factor for a lower risk of esophageal stricture, while location in the middle third, and circumferential range = 1/1 could independently predict a higher risk of esophageal stricture in EC patients after ESD.

***Research conclusions***

The PGA plus stent placement is more effective in preventing post-ESD esophageal stricture *vs* stent placement alone in early-stage EC patients.

***Research perspectives***

The total number of recruited EC patients in the present study was relatively small. And a larger sample size study is needed to further confirm the efficacy of PGA plus stent in preventing esophageal stricture.

**REFERENCES**

1 **Mohammed F**. Esophageal cancer. *N Engl J Med* 2004; **350**: 1363-1364; author reply 1363-1364 [PMID: 15044652 DOI: 10.1056/NEJMc033106]

2 **Torre LA**, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin* 2015; **65**: 87-108 [PMID: 25651787 DOI: 10.3322/caac.21262]

3 **Scott DL**, Wolfe F, Huizinga TW. Rheumatoid arthritis. *Lancet* 2010; **376**: 1094-1108 [PMID: 20870100 DOI: 10.1016/S0140-6736(10)60826-4]

4 **Ning B**, Abdelfatah MM, Othman MO. Endoscopic submucosal dissection and endoscopic mucosal resection for early stage esophageal cancer. *Ann Cardiothorac Surg* 2017; **6**: 88-98 [PMID: 28446997 DOI: 10.21037/acs.2017.03.15]

5 **Yu JP**, Liu YJ, Tao YL, Ruan RW, Cui Z, Zhu SW, Shi W. Prevention of Esophageal Stricture After Endoscopic Submucosal Dissection: A Systematic Review. *World J Surg* 2015; **39**: 2955-2964 [PMID: 26335901 DOI: 10.1007/s00268-015-3193-3]

6 **Shi KD**, Ji F. Prophylactic stenting for esophageal stricture prevention after endoscopic submucosal dissection. *World J Gastroenterol* 2017; **23**: 931-934 [PMID: 28246466 DOI: 10.3748/wjg.v23.i6.931]

7 **Jain D**, Singhal S. Esophageal Stricture Prevention after Endoscopic Submucosal Dissection. *Clin Endosc* 2016; **49**: 241-256 [PMID: 26949124 DOI: 10.5946/ce.2015.099]

8 **ASGE Technology Committee.**, Maple JT, Abu Dayyeh BK, Chauhan SS, Hwang JH, Komanduri S, Manfredi M, Konda V, Murad FM, Siddiqui UD, Banerjee S. Endoscopic submucosal dissection. *Gastrointest Endosc* 2015; **81**: 1311-1325 [PMID: 25796422 DOI: 10.1016/j.gie.2014.12.010]

9 **Sakaguchi Y**, Tsuji Y, Ono S, Saito I, Kataoka Y, Takahashi Y, Nakayama C, Shichijo S, Matsuda R, Minatsuki C, Asada-Hirayama I, Niimi K, Kodashima S, Yamamichi N, Fujishiro M, Koike K. Polyglycolic acid sheets with fibrin glue can prevent esophageal stricture after endoscopic submucosal dissection. *Endoscopy* 2015; **47**: 336-340 [PMID: 25314328 DOI: 10.1055/s-0034-1390787]

10 **Kim YJ**, Park JC, Chung H, Shin SK, Lee SK, Lee YC. Polyglycolic acid sheet application to prevent esophageal stricture after endoscopic submucosal dissection for recurrent esophageal cancer. *Endoscopy* 2016; **48**: E319-E320 [PMID: 27706540 DOI: 10.1055/s-0042-117224]

11 **Iizuka T**, Kikuchi D, Yamada A, Hoteya S, Kajiyama Y, Kaise M. Polyglycolic acid sheet application to prevent esophageal stricture after endoscopic submucosal dissection for esophageal squamous cell carcinoma. *Endoscopy* 2015; **47**: 341-344 [PMID: 25412087 DOI: 10.1055/s-0034-1390770]

12 **Yamasaki T**, Tomita T, Takimoto M, Ohda Y, Oshima T, Fukui H, Watari J, Miwa H. Esophageal stricture after endoscopic submucosal dissection treated successfully by temporary stent placement. *Clin J Gastroenterol* 2016; **9**: 337-340 [PMID: 27687827 DOI: 10.1007/s12328-016-0685-0]

13 **Vleggaar FP**. Stent placement in esophageal cancer as a bridge to surgery. *Gastrointest Endosc* 2009; **70**: 620-622 [PMID: 19788979 DOI: 10.1016/j.gie.2009.03.025]

14 **Nagami Y**, Shiba M, Tominaga K, Ominami M, Fukunaga S, Sugimori S, Tanaka F, Kamata N, Tanigawa T, Yamagami H, Watanabe T, Fujiwara Y, Arakawa T. Hybrid therapy with locoregional steroid injection and polyglycolic acid sheets to prevent stricture after esophageal endoscopic submucosal dissection. *Endosc Int Open* 2016; **4**: E1017-E1022 [PMID: 27652294 DOI: 10.1055/s-0042-111906]

15 **Nagami Y**, Ominami M, Shiba M, Minamino H, Fukunaga S, Kameda N, Sugimori S, Machida H, Tanigawa T, Yamagami H, Watanabe T, Tominaga K, Fujiwara Y, Arakawa T. The five-year survival rate after endoscopic submucosal dissection for superficial esophageal squamous cell neoplasia. *Dig Liver Dis* 2017; **49**: 427-433 [PMID: 28096057 DOI: 10.1016/j.dld.2016.12.009]

16 **Kanai N**, Yamato M, Ohki T, Yamamoto M, Okano T. Fabricated autologous epidermal cell sheets for the prevention of esophageal stricture after circumferential ESD in a porcine model. *Gastrointest Endosc* 2012; **76**: 873-881 [PMID: 22867446 DOI: 10.1016/j.gie.2012.06.017]

17 **Nonaka K**, Miyazawa M, Ban S, Aikawa M, Akimoto N, Koyama I, Kita H. Different healing process of esophageal large mucosal defects by endoscopic mucosal dissection between with and without steroid injection in an animal model. *BMC Gastroenterol* 2013; **13**: 72 [PMID: 23617935 DOI: 10.1186/1471-230X-13-72]

18 **Wagh MS**, Forsmark CE, Chauhan S, Draganov PV. Efficacy and safety of a fully covered esophageal stent: a prospective study. *Gastrointest Endosc* 2012; **75**: 678-682 [PMID: 22243830 DOI: 10.1016/j.gie.2011.10.006]

19 **Shah MB**, Jajoo K. Endoscopic retrieval of a migrated esophageal stent in the cecum. *Endoscopy* 2010; **42 Suppl 2**: E245-E246 [PMID: 20931463 DOI: 10.1055/s-0030-1255604]

20 **Cheng YS**, Li MH, Chen WX, Chen NW, Zhuang QX, Shang KZ. Temporary partially-covered metal stent insertion in benign esophageal stricture. *World J Gastroenterol* 2003; **9**: 2359-2361 [PMID: 14562413]

21 **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]

22 **Yamaguchi N**, Isomoto H, Nakayama T, Hayashi T, Nishiyama H, Ohnita K, Takeshima F, Shikuwa S, Kohno S, Nakao K. Usefulness of oral prednisolone in the treatment of esophageal stricture after endoscopic submucosal dissection for superficial esophageal squamous cell carcinoma. *Gastrointest Endosc* 2011; **73**: 1115-1121 [PMID: 21492854 DOI: 10.1016/j.gie.2011.02.005]

23 **Hanaoka N**, Ishihara R, Takeuchi Y, Uedo N, Higashino K, Ohta T, Kanzaki H, Hanafusa M, Nagai K, Matsui F, Iishi H, Tatsuta M, Ito Y. Intralesional steroid injection to prevent stricture after endoscopic submucosal dissection for esophageal cancer: a controlled prospective study. *Endoscopy* 2012; **44**: 1007-1011 [PMID: 22930171 DOI: 10.1055/s-0032-1310107]

24 **Nagami Y**, Shiba M, Tominaga K, Minamino H, Ominami M, Fukunaga S, Sugimori S, Tanigawa T, Yamagami H, Watanabe K, Watanabe T, Fujiwara Y, Arakawa T. Locoregional steroid injection prevents stricture formation after endoscopic submucosal dissection for esophageal cancer: a propensity score matching analysis. *Surg Endosc* 2016; **30**: 1441-1449 [PMID: 26123341 DOI: 10.1007/s00464-015-4348-x]

25 **Hashimoto S**, Kobayashi M, Takeuchi M, Sato Y, Narisawa R, Aoyagi Y. The efficacy of endoscopic triamcinolone injection for the prevention of esophageal stricture after endoscopic submucosal dissection. *Gastrointest Endosc* 2011; **74**: 1389-1393 [PMID: 22136782 DOI: 10.1016/j.gie.2011.07.070]

**P-Reviewer:** Sato Y, Rodrigo L **S-Editor:** Wang JL

**L-Editor: E-Editor:**

**Specialty type:** Gastroenterology and hepatology

**Country of origin:** China

**Peer-review report classification**

Grade A (Excellent): A

Grade B (Very good): B

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

**Table 1 Baseline characteristics *n* (%)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **PGA + Stent group**  **(*n* = 34)** | **Stent group**  **(*n* = 32)** | ***P* value** |
| Patients characteristics |  |  |  |
| Age (yr) | 62.74 ± 8.38 | 59.91 ± 8.80 | 0.186 |
| Gender (Male/Female) | 22/12 | 18/14 | 0.482 |
| Tumor lesion features |  |  |  |
| Location |  |  | 0.145 |
| Upper third | 0 (0) | 0 (0) |  |
| Middle third | 12 (35) | 17 (53) |  |
| Lower third | 22 (65) | 15 (47) |  |
| Tissue depth |  |  | 0.331 |
| M1 | 20 (59) | 15 (47) |  |
| M2 | 14 (41) | 17 (53) |
| Longitudinal length (cm) | 5.97 ± 2.68 | 6.06 ± 2.12 | 0.878 |
| Circumferential range |  |  | 0.684 |
| 3/4 | 12 (35) | 14 (44) |  |
| 4/5 | 8 (24) | 8 (25) |  |
| 1/1 | 14 (41) | 10 (31) |  |

Data was presented as mean ± SD or count (with or without percentage). Comparison was determined by *t*-test or Chi-square test. *P* < 0.05 was considered significant. PGA: Polyglycolic acid.

**Table 2 Comparison of esophageal stricture features in polyglycolic acid + stent and stent groups**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **PGA + stent group**  **(*n* = 7)** | **Stent group**  **(*n* = 15)** | ***P* value** |
| Length (cm) | 0.97 + 0.59 | 1.47 + 0.59 | 0.080 |
| Diameter (cm) | 0.37 + 0.17 | 0.51 + 0.14 | 0.061 |
| Location (distance from the incisors, cm) | 31.71 + 3.20 | 29.07 + 5.20 | 0.232 |
| Balloon dilatation times | 4 (2-5) | 6 (1-14) | 0.007 |

Data was presented as mean ± SD or median (range). Comparison was determined by *t*-test or Wilcoxon rank sum test. *P* < 0.05 was considered significant. PGA: Polyglycolic acid.

**Table 3 Comparison of tumor lesion features in patients occurred esophageal stricture *n* (%)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **PGA + stent group (*n* = 7)** | **Stent group**  **(*n* = 15)** | ***P* value** |
| Location |  |  | 0.899 |
| Upper third | 0 (0) | 0 (0) |  |
| Middle third | 4 (57) | 9 (60) |  |
| Lower third | 3 (43) | 6 (40) |  |
| Tissue depth |  |  | 0.823 |
| M1 | 2 (29) | 5 (33) |  |
| M2 | 5 (71) | 10 (67) |  |
| Longitudinal length (cm) | 7.71 + 3.50 | 6.60 + 2.10 | 0.360 |
| Circumferential range |  |  | 0.181 |
| 3/4 | 0 (0) | 4 (27) |  |
| 4/5 | 1 (14) | 4 (27) |  |
| 1/1 | 6 (86) | 7 (47) |  |

Data was presented as mean ± SD or count (percentage). Comparison was determined by *t* test or Chi-square test. *P* < 0.05 was considered significant. PGA: Polyglycolic acid.

**Table 4 Logistic analysis of factors affecting esophageal stricture occurrence**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Parameters** | **Univariate logistic regression** | | | | **Multivariate logistic regression** | | | |
| ***P* value** | **OR** | **95%CI** | | ***P* value** | **OR** | **95%CI** | |
| **Lower** | **Higher** | **Lower** | **Higher** |
| PGA + Stent (*vs* Stent) | 0.027 | 0.294 | 0.099 | 0.868 | 0.026 | 0.197 | 0.047 | 0.820 |
| Age ≥ 62 yr | 0.298 | 1.733 | 0.615 | 4.887 | - | - | - | - |
| Location - middle third (*vs* lower third) | 0.083 | 2.528 | 0.886 | 7.214 | 0.034 | 5.148 | 1.135 | 23.344 |
| Longitudinal length ≥ 6 cm | 0.059 | 2.779 | 0.963 | 8.019 | 0.092 | 3.826 | 0.801 | 18.270 |
| Circumferential range = 1/1 (*vs* others) | 0.008 | 4.333 | 1.457 | 12.888 | 0.028 | 5.113 | 1.194 | 21.892 |
| Tissue depth M2 (*vs* M1) | 0.017 | 3.750 | 1.264 | 11.123 | 0.069 | 3.284 | 0.912 | 11.822 |

Data was presented as *P*-value, OR (odds ratio) and 95% CI. Factors affecting esophageal stricture occurrence were determined by univariate logistic regression analysis, while all factors with *P* value less than 0.1 were further detected by multivariate logistic regression analysis. *P*-Value < 0.05 was considered significant. PGA: Polyglycolic acid.

****

**Figure 1 Combination of polyglycolic acid sheet and stent.** A: Measurement of endoscopic submucosal dissection wound length; B: Adjustment of stent length; C: Polyglycolic acid sheet selection based on lesion length; D: Stent coating with polyglycolic acid (PGA) sheet; E-F: Stent covered with PGA sheet mounted on the stent support; G: Insertion of stent covered with PGA sheet under endoscopic observation.

****

**Figure 2 The management of one of the study patients showing.** A: Stent covered with polyglycolic acid sheet inserted after 1 wk; B: Stent removed after 4 wk with portion of wound not healed; C: No formation of esophageal stricture observed after 2 mo.



**Figure 3 Study flow.** ESD: Endoscopic submucosal dissection.

****

**Figure 4 Comparison of post-endoscopic submucosal dissection stricture in polyglycolic acid plus stent and stent groups.** A: Patients in the polyglycolic acid (PGA) plus stent group had a lower occurrence rate of esophageal stricturet than that in stent group; B: No difference in time to esophageal stricture was observed between the PGA plus stent and stent groups.Comparison of post-endoscopic submucosal dissectionstricture in the PGA plus stent and stent groups was analyzed by *t*-test. *P* < 0.05 was considered significant.



**Figure 5 The endoscopic submucosal dissection wound before and after the polyglycolic acid sheet plus stent placement.** A: The esophageal lesion before endoscopic submucosal dissection (ESD); B: The mucosal defect after ESD; C: The ESD wound after the PGA sheet plus stent placement; D: The PGA sheet plus stent placement was inserted after 3 wk.



**Figure 6 The management of one of the study patients showing.** A: Stent covered with polyglycolic acid (PGA) sheet was injected with glucocorticoid before insertion; B: The mucosal defect after endoscopic submucosal dissection (ESD); C: The combination of PGA, stent and glucocorticoid was applied after 1 wk; D: The endoscopic appearance of the esophagus 4 wk after ESD; E: The endoscopic appearance of the esophagus 3 mo after ESD.