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EDITORIAL

Prospects of polyglycolic acid sheets for the treatment of esophageal stricture after esophageal endoscopic submucosal dissection

Qing-Xia Wang, Rui-Hua Shi

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Abstract

Esophageal cancer is the seventh most common type of cancer and the sixth leading cause of cancer -related mortality worldwide. Endoscopic submucosal dissection (ESD) is widely used for the resection of early esophageal cancer. However, post-ESD esophageal stricture is a common long-term complication, which requires attention. Patients with post-ESD esophageal stricture often experience dysphagia and require multiple dilatations, which greatly affects their quality of life and increases healthcare costs. Therefore, to manage post-ESD esophageal stricture, researchers are actively exploring various strategies, such as pharmaceutical interventions, endoscopic balloon dilation, and esophageal stenting. Although steroids-based therapy has achieved some success, steroids can lead to complications such as osteoporosis and infection. Meanwhile, endoscopic balloon dilatation is effective in the short term, but is prone to recurrence and perforation. Additionally, esophageal stenting can alleviate the stricture, but is associated with discomfort during stenting and the complication of easy displacement also present challenges. Tissue engineering has evolved rapidly in recent years, and hydrogel materials have good biodegradability and biocompatibility. A novel type of polyglycolic acid (PGA) sheets has been found to be effective in preventing esophageal stricture after ESD, with the advantages of a simple operation and low complication rate. PGA membranes act as a biophysical barrier to cover the wound as well as facilitate the delivery of medications to promote wound repair and healing. However, there is still a lack of multicenter, large-sample randomized controlled clinical studies focused on the treatment of post-ESD esophageal strictures with PGA membrane, which will be a promising direction for future advancements in this field.

Key Words: Polyglycolic acid; Endoscopic submucosal dissection; Esophageal stenosis; Esophageal cancer; Steroids

Core Tip: Esophageal cancer is the seventh most common type of cancer and the sixth leading cause of cancer death worldwide. Endoscopic submucosal dissection (ESD) is considered a prominent method for early esophageal cancer resection. However, esophageal stenosis is a common complication of esophageal ESD. A novel hydrogel material, polyglycolic acid sheet, is safe and effective for the prevention of esophageal strictures after ESD.

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INTRODUCTION

Endoscopic submucosal dissection (ESD) has become the preferred treatment method for early esophageal cancer, due to its high rate of lesion resection, which is conducive a more accurate pathological diagnosis after surgery[1]. Additionally, ESD causes lesser damage to patients and facilitating faster postoperative recovery compared to traditional surgery. However, it often involves resection of more than 3/4th of the esophageal mucosa, which frequently leads to post-operative esophageal stenosis[2]. Esophageal stenosis is indeed one of the long-term complications of esophageal ESD, often leading to dysphagia. This condition necessitates multiple endoscopic balloon dilatation (EBDs), considerably affecting patients' quality of life[3].

Currently, various strategies are available for treating esophageal strictures, yet each approach has its limitations. Although the effectiveness of oral steroids is well recognized, they potentially cause systemic side effects, such as osteoporosis, immunosuppression, diabetes, peptic ulcers, and infections[4]. Injection of triamcinolone acetonide (TA) has demonstrated good results, but local injection may injure the muscularis propria resulting in complications, such as delayed perforation[5]. Furthermore, the successful use of self-expanding coated metal stents for the prevention of post-ESD esophageal strictures has been reported; however, these stents are associated with the risks of bleeding, perforation, and migration[6].

In recent years, rapid advancements in tissue engineering have led to the introduction of hydrogel materials with controllable physicochemical properties and biocompatibility[7,8]. Polyglycolic acid (PGA) membranes, a type of hydrogel material, are increasingly being used for preventing post-ESD esophageal strictures[9,10]. Extensive endoscopic resections, often employed for the treatment of early esophageal neoplasia, can result in fibro-inflammatory strictures. The mechanisms behind post-ESD esophageal stricture formation are as follows: (1) Initial secretion of tissue invasive factors; (2) disruption of the protective barrier; and (3) activation of inflammatory pathways; and (4) inflammatory proliferation of myofibroblasts[11,12]. Creating a barrier over large exposed areas of submucosa after resection not only protects it from endoluminal stress factors but also shields the residual submucosa and muscularis propria while serving as a matrix for epithelial cell migration. Among the various wound-protective strategies, PGA sheets have shown the most convincing evidence with a 37.5% stricture rate and excellent safety[13].

CLINICAL IMPLICATIONS

PGA membranes serves as a biophysical barrier for covering wounds, as well as it facilitates delivery of medications to promote wound repair and healing[9,10]. Kim *et al*[14] reported good results in preventing esophageal strictures using PGA patches to cover postoperative defects. Sakaguchi *et al*[15] evaluated the application of PGA sheets with fibrin glue and found it to be an effective and safe method for preventing post-ESD esophageal stricture and reducing the need for EBDs. Sakaguchi *et al*[16] suggested that the administration of PGA and basic fibroblast growth factor suppresses myofibroblast activation in the acute phase, thereby preventing esophageal constriction. A randomized controlled trial conducted in 2018 reported a lower postoperative stricture rate (20.5%) with the application of PGA sheets for wound coverage in the coverage group than in the non-covered group[17]. Sakaguchi *et al*[18] proposed the efficacy of PGA combined with steroid injections for preventing post-ESD esophageal stenosis, revealing a significantly lower stenosis rate with the use of combination therapy than with PGA alone. A study by Iizuka *et al*[19] suggested that PGA sheets and fibrin glue are promising option for preventing esophageal stricture, showing similar efficacy to that of intralesional steroid injections. Hwang *et al*[20] reported favorable outcomes, noting that the stricture rate in the PGA group (12.5%) was significantly lower than that of the historical control group (66.7%). Yang *et al*[21] demonstrated that the combined PGA plus stent placement therapy yielded a lower occurrence and milder severity of post-ESD esophageal stricture than that of stent placement therapy alone in patients with early-stage esophageal cancer. Additionally, a recent study employed a triamcinolone-soaked PGA combined with a fully covered metal stent to prevent stricture after extensive dissection of the esophageal mucosa. The study demonstrated that the method is safe and may decrease the incidence of esophageal stricture and the number of EBD sessions required after large esophageal ESD[22].

However, Iizuka *et al*[23] suggested that PGA sheets do not reduce the incidence of esophageal strictures after ESD, proposing that potential reasons for this to be premature detachment of the PGA sheets and insufficient follow-up period.

CONCLUSION

A growing number of studies have demonstrated that PGA membranes can significantly reduce the rate of esophageal strictures after esophageal ESD, decrease the number of EBDs needed by patients, and improve their quality of life. Some studies have suggested that the efficacy of PGA membrane in preventing esophageal stricture after ESD is not superior to that of a local TA injection; however, this observation also reinforces the fact that PGA membranes indeed play a role in preventing esophageal stricture. The primary mechanism by which PGA membranes prevent esophageal strictures appears to be the physical protection of the wound, leading to a consequent reduction in inflammatory exudation.

To address the challenge of PGA membranes being easily dislodged numerous researchers have combined PGA membranes with fibrin glue or stent, achieving positive effects. Other researchers have used PGA membranes in combination with TA to prevent stenosis after ESD and have also achieved effective results. These combined treatments can address the shortcomings of monotherapy and enhance overall therapeutic effectiveness, thereby demonstrating the promising application potential of PGA membranes.

In conclusion, PGA sheets are safe and effective in preventing post-ESD esophageal strictures. However, a notable gap exists in the form of multicenter, large-sample randomized controlled clinical studies focusing on the treatment of post-ESD esophageal strictures with PGA membranes. Addressing this gap represents, a promising direction for future development in this field.

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