Endoscopic balloon dilation and submucosal injection of triamcinolone acetonide in the treatment of esophageal stricture: A single-center retrospective study

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Abstract. Effect and prognosis of endoscopic balloon dilatation combined with submucosal triamcinolone acetonide on treating benign esophageal lesions were explored. This retrospective study included patients with esophageal stricture treated in the Department of Gastroenterology, the Third Affiliated Hospital of Soochow University from March 2012 to March 2015. Enrolled patients were divided into the treatment and control group depending on the therapy differences. Endoscopic balloon dilation combined with submucosal injection of triamcinolone acetonide was performed in the treatment group and the endoscopic balloon dilatation was performed in the control group. In addition, the treatment group was further divided into the <16- and >16-mm subgroup according to the degree of balloon dilatation. During 1-year follow-up, changes of esophageal stenosis, esophageal stenosis recurrence rate, postoperative complications and adverse reactions were observed and analyzed. The improvement of esophageal stenosis of the treatment group was significantly superior to that of the control group at 2 and 4 months after operation, respectively (P=0.002, 0.013). The esophageal stenosis recurrence rate was 62.2 and 77.2% in the treatment and control group, respectively (P=0.027); the recurrence time of stenosis was 101.4±8.6 days in the treatment group and 75.4±5.2 days in the control group (P=0.006). Additionally, the recurrence time of esophageal stenosis was significantly shorter in the >16-mm subgroup compared with that of the <16-mm subgroup (P<0.001). Endoscopic balloon dilatation combined with local injection of triamcinolone acetonide in the treatment of esophageal stricture had a better therapeutic effect than that of the simple balloon dilatation, which was more effective when the balloon dilatation was >16 mm. It could significantly prolong the recurrence time of esophageal stricture.

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Introduction

Esophageal benign stenosis can be induced by a variety of reasons, such as esophageal anastomotic stenosis, gastroesophageal reflux, corrosive stenosis and radioactive injury (1). Recently, more and more studies have indicated that surgeries can also lead to benign esophageal stenosis, including endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) (2). Under various physical and chemical effects, activation of fibroblast proliferation enhances collagen deposition and scar formation, thus eventually leading to esophageal contracture. Clinical treatments of benign esophageal stenosis are varied, including surgery, expansion, stents and drugs (3). Most esophageal stenosis can achieve long-term relief by endoscopic distension 3 times. However, there are still some unrelieved cases that require repeated treatments, which is called refractory esophageal stricture or relapse esophageal stenosis (4). It is worth mentioning that esophageal stricture is a common complication of esophageal ESD. Particularly, esophageal stricture with >3/4 peeled lesion is more prone to postoperative stenosis. Some stenosis needs to be repeatedly expanded, which is known as the intractable narrow (5).

Currently, there are some methods that can prevent esophageal stenosis, including endoscopic balloon dilation, glucocorticoid, tissue engineering, amniotic membrane transplantation, gastric mucosa transplantation, polyglycolic acid tablets transplantation, and local injection of botulinum toxin. Prevention of esophageal stenosis with glucocorticoids has been demonstrated in several studies (2,5-11). In the present study, we explored the efficacy and safety of endoscopic balloon dilatation combined with glucocorticoid therapy on the treatment of esophageal stricture.

Patients and methods

Patients. A total of 183 patients aged from 35 to 76 years with a mean age of 58.6 years were enrolled in our study, including 97 males and 86 females. Patients with benign

Table I. Basic patient characteristics of the control group.

Characteristics	Triamcinolone group (n=82)	Hormone-free group (n=101)	P-value
Sex			0.873
Male	44	53	
Female	38	48	
Age (years)	55.9±7.3	60.2±6.8	0.368
Narrow parts			
Cervical oesophagus	14	12	0.317
Upper thoracic esophagus	18	26	0.551
Middle thoracic esophagus	27	36	0.700
Lower thoracic esophagus	23	27	0.843
Narrow etiology			
Esophageal cancer early after ESD	26	36	0.575
Esophageal cancer anastomotic stenosis after radical surgery	38	52	0.489
Others	18	13	0.103

ESD, endoscopic submucosal dissection.

Table II. Basic information of the treatment group.

Information	Expansion <16 mm (n=39)	Expansion >16 mm (n=43)	P-value
Sex			0.681
Male	20	24	
Female	19	19	
Age (years)	53.6±6.4	51.2±5.6	0.425
Narrow parts			
Cervical oesophagus	6	8	0.699
Upper thoracic esophagus	9	9	0.815
Middle thoracic esophagus	14	13	0.586
Lower thoracic esophagus	10	13	0.644
Narrow etiology			
Esophageal cancer early after ESD	12	14	0.862
Esophageal cancer anastomotic stenosis after radical surgery	18	20	0.974
Others	9	9	0.815

ESD, endoscopic submucosal dissection.

esophageal stenosis received digestive medicine in the hospital from March 2012 to March 2015. This study was approved by the Ethics Committee of the Third Affiliated Hospital of Soochow University (Changzhou, China). Signed written informed consents were obtained from all participants before the study. Inclusion criteria were applied in patients with significant dysphagia, esophageal or anastomotic stricture diagnosed by endoscopy or X-ray and benign esophageal stricture confirmed by endoscopic esophageal mucosal biopsy. Patients with esophageal pressure and esophageal benign tumor were excluded by ultrasound endoscope. Exclusion criteria were applied in patients with achalasia cardia and severe cardiopulmonary insufficiency. Pregnancies and breastfeeding women were also excluded.

Methods. All enrolled patients were divided into endoscopic balloon dilatation combined with triamcinolone acetonide group (treatment group) and simple balloon dilatation group (control group). There were 82 cases aged 43-74 years with a mean age of 55.9 years in the treatment group, and 101 cases aged from 35 to 76 years with an average age of 60.2 years in the control group. Treatment group was further divided into the <16- and >16-mm subgroup based on the expansion degree. Among them, 39 cases were expanded <16 mm and 43 cases were >16 mm.

In treatment group, the gastroscopy was placed to the site of esophageal stricture. Briefly, guide wire was crossed into the stenosis and retained in the human gastric cavity guided with endoscopy. With X-ray imaging, the balloon catheter was placed alongside the guide wire. The diluted contrast medium was then injected into the balloon until the balloon struts disappeared at the stenosis site. When the central portion of the balloon reached the narrow central region, triamcinolone acetonide with 1 ml/10 mg per point was injected at four points around the esophageal dilatation or stenosis through biopsy tracts. Simple esophageal balloon dilatation was performed to patients in control group.

Observation. Esophageal stenosis diameter and stenosis at 15 days, 1, 2 and 4 months after operation were recorded by upper gastrointestinal angiography. During the 12-month follow-up, postoperative complications and prognosis were observed.

Statistical analysis. Statistical Product and Service Solutions (SPSS) 22.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The data are presented as mean ± SD. The independent t-test was used for the difference analysis of the two groups. Enumeration data were presented by numbers and percentages and analyzed by the Chi-square or rank sum test. $P<0.05$ was considered statistically significant ($P<0.05$, $P<0.01$, $P<0.001$).

Results

Patient characteristics. Patients were divided into endoscopic balloon dilatation combined with triamcinolone acetonide group (treatment group) and simple balloon dilatation group (control group). There were 82 cases in the treatment group with 44 males and 38 females aged from 43 to 74 years (55.9±7.3 years) and 101 cases in the control group with 53 males and 48 females aged from 60 to 64 years (60.2±6.8 years). No significant differences were observed in sex, age, location and causes of stenosis between the treatment and control group (Table I). Treatment group was further

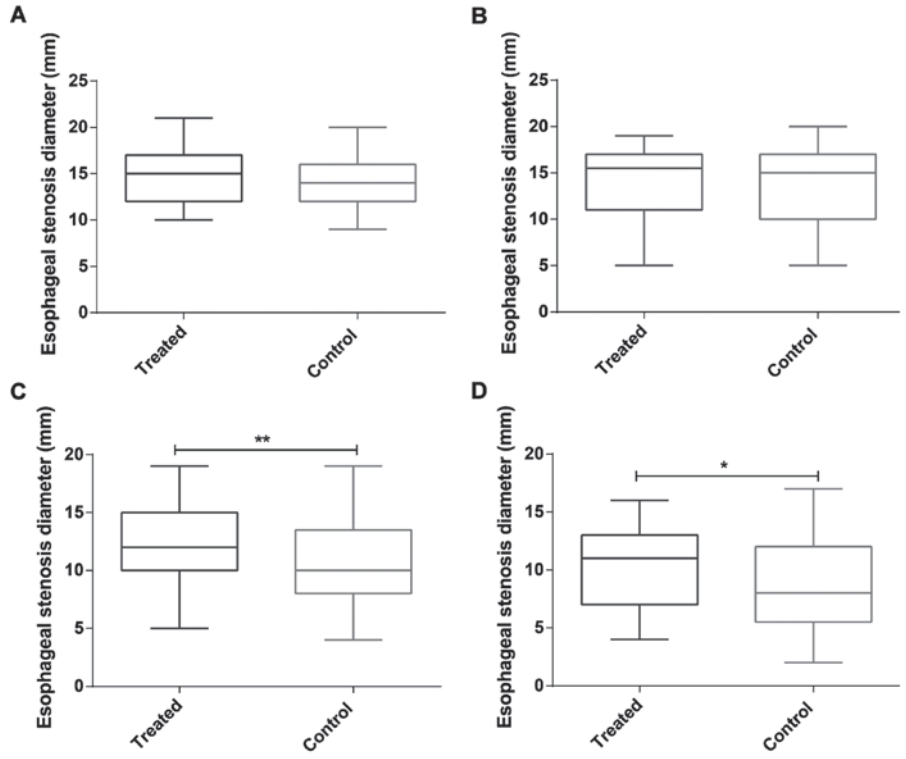

Figure 1. Postoperative esophageal stenosis assessment. (A and B) There was no significant difference in esophageal stenosis between the treatment and control group at 15 days and 1 month after surgery. (C and D) The improvement of esophageal stenosis in the treatment group was better than that of the control group at 2 and 4 months after surgery. *P<0.05, **P<0.01.

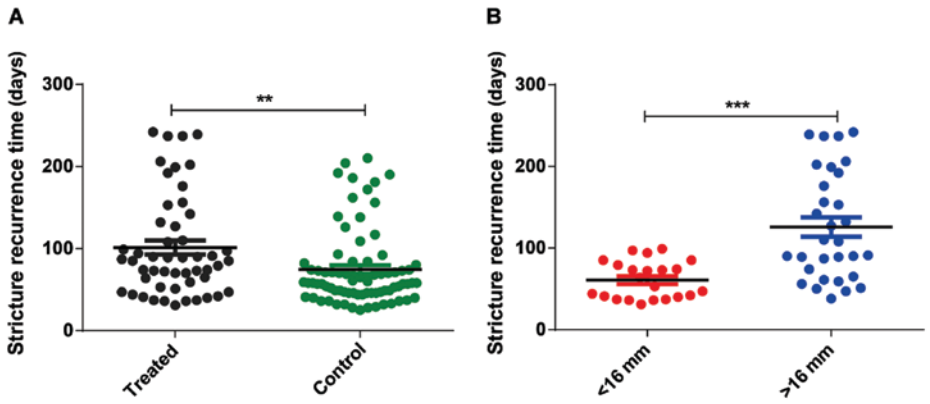

Figure 2. Comparison of postoperative recurrence of stenosis. (A) The recurrence time of the treatment group was longer than that of the control group. (B) The recurrence time of patients in the treatment group with a balloon expansion >16 mm was longer than that with an expansion <16 mm. **P<0.01, ***P<0.001.

divided into the <16- and >16-mm subgroups according to the expansion degree. There were 39 cases in the <16-mm subgroup with 20 males and 19 females and 43 cases in the >16-mm subgroup with 24 males and 19 females (Table II).

Improvement of postoperative esophageal stricture. In this study, patients with esophageal stricture were diagnosed by esophageal angiography. The improvement of esophageal stenosis in the treatment group was significantly better than that of the control group at 2 and 4 months after treatment, respectively (P=0.002, 0.013). However, there was no significant difference in esophageal stenosis between the two groups at 15 days and 1 month after operation, respectively (P=0.107, 0.128, Fig. 1).

Recurrence time of postoperative esophageal stricture. The recurrence rate of esophageal stricture in the treatment and control group was 62.2% (51/82) and 77.2% (78/101) within the 1-year follow-up, respectively (P=0.027). The recurrence time of stenosis in the treatment group (101.4±8.6 days) was markedly longer than that of the control group (75.4±5.2 days, P=0.006). Furthermore, the recurrent time of the >16-mm subgroup was also significantly longer than that of the <16-mm subgroup (P<0.001, Fig. 2).

Adverse events and complications. There were 3 and 4 cases of postoperative bleeding in the treatment and control group, respectively (P=0.916). Local spraying of norepinephrine was administered to those patients for hemostasis. Five

patients in the treatment group experienced postoperative fever but recovered after given physical cooling. No patient had mediastinal emphysema, peri-esophageal abscess or esophageal perforation during follow-up.

Discussion

The impact of esophageal stricture has been increasingly expanding with the clinical application of esophageal cancer surgery, radiotherapy and ESD and other new technologies. Esophageal stenosis dilatation includes the probe dilation and the balloon dilatation. Probe dilation was first developed dating back to the 16th century, represented by Savary-Gilliard. Balloon dilatation, performed in our study, was first proposed by Scolapio (12). Hagel *et al* (13) retrospectively analyzed 368 cases of esophageal stenosis from January 2002 to December 2011. A total of 8 cases experienced perforation, of which 1 patient in the probe expansion group died. The total perforated rate was 0.54% (8/1479), and the perforation rate of benign esophageal stenosis was 0.3% (3/912). The results showed that despite lower perforation rate, the balloon dilatation was much safer than that of the probe dilation, which might be explained by the stronger destructive effect of the probe. Glucocorticoids can not only inhibit the exudation of inflammatory cells, granulation tissue proliferation and submucosal tissue fibrosis, but also attenuate the activation and migration of inflammatory cells and fibroblasts, reduce the collagen synthesis and collagen degradation, and finally inhibit the esophageal stenosis after the expansion of scar formation (14). In this study, local injection of triamcinolone acetonide was introduced to reduce the scar formation after esophageal balloon dilatation.

It has been reported that steroid combined with endoscopic distension is applied in esophageal benign stenosis (15,16). The application of endoscopic dilation and submucosal injection of triamcinolone acetonide in the treatment of benign esophageal stenosis also achieved better curative effect. However, some studies have found that the effect of the combination treatment may be related to the stenosis extent.

Our data showed that all patients had significant improvement in swallowing and dilated symptoms at the end of treatment. The combination treatment group showed a better relief compared to that of the control group at 15 days and 1 month after operation, but the difference was not statistically significant. However, the degree of esophageal stenosis in the treatment group at 2 and 4 months after treatment was significantly better than that of the control group, the difference was statistically significant. The recurrence time of treatment group was significantly longer than that of control group, indicating that hormone treatment combined with balloon dilatation had a better effect than that of simple esophageal dilation treatment. Long-term prognosis achieved the same result. The incidence of short-term restenosis after endoscopic dilatation was higher in the control group than that of the treatment group, suggesting that endoscopic balloon dilation and submucosal triamcinolone acetonide injection could prolong the short-term restenosis of esophagus and reduce the incidence rate of recent restenosis.

In addition, the injection of triamcinolone acetonide after endoscopic dilation could effectively reduce tissue damage, inflammatory exudation and inflammatory cell aggregation, inhibit fibroblast activity, and finally reduce or alleviate the forming of scars. The specific mechanisms, however, need to be further clarified. Clinical evidence also revealed that the expansion extent is positively correlated with recurrence time of esophageal stricture (17-19), which was consistent with our findings. In our study, the recurrence time of esophageal stricture in the <16-mm subgroup was significantly shorter than that in the expanded >16-mm subgroup.

In this study, no patient had mediastinal emphysema, esophageal abscess, esophageal perforation and other complications, indicating that the degree of balloon expansion may not be associated with the risk of esophageal perforation, which was consistent with other researches (17,20).

In conclusion, our study showed that endoscopic balloon dilatation combined with local injection of triamcinolone acetonide in the treatment of benign esophageal stenosis is superior to the simple balloon dilatation, which significantly prolongs esophageal restenosis and reduces the duration of esophageal dilatation. In addition, the effect of the combination therapy is better when the degree of balloon dilatation is >16 mm.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

LQ and JC designed the study and performed the experiments, WH, JY and YG collected the data, LQ and YG analyzed the data, LQ and JC prepared the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Third Affiliated Hospital of Soochow University (Changzhou, China). Patients or their guardians provided written informed consents for publication.

Patient consent for publication

Not applicable

Competing interests

The authors declare they have no competing interests.

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