

Benefits of precise endoscopic incision on post-dilation mucosal scars to treat refractory esophageal stricture after endoscopic submucosal dissection




Authors

Jiaoyang Lu^{*1}, Ruozi Pan^{*1}, Jindong Fu², Shuhua Li¹, Rui Ji¹, Xuefeng Lu¹

Institutions

- 1 Department of Gastroenterology, Qilu Hospital, Cheeloo College of Medicine, Shandong University, Jinan, Shandong, China
- 2 Department of Gastroenterology, Rizhao People's Hospital, Rizhao, Shandong, China

submitted 11.11.2022

accepted after revision 2.3.2023

published online 6.3.2023

Bibliography

Endosc Int Open 2023; 11: E409–E412

DOI 10.1055/a-2048-1532

ISSN 2364-3722

© 2023. The Author(s).

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)

Georg Thieme Verlag KG, Rüdigerstraße 14,
70469 Stuttgart, Germany

Corresponding author

Xuefeng Lu, Department of Gastroenterology, Qilu Hospital, Shandong University, Wenhuxi Road #107, Jinan, Shandong 250012, China

Fax: +86-53182166095

lu0801shanyi@163.com

ABSTRACT

Endoscopic dilation (ED) is the mainstream treatment for esophageal stricture after endoscopic submucosal dissection (ESD). However, some complex esophageal strictures do not respond well to dilation. Endoscopic radial incision (ERI) has proved to be effective in treating anastomotic strictures, but it is rarely used to treat post-ESD esophageal strictures due to technical difficulties and risks, not to mention the optimal method and timing to perform ERI. Here, we developed an integrated procedure in which ED was performed first, followed by ERI on the stiff scars that remained intact after dilation. The ED+ERI procedure resulted in complete, uniform expansion of the esophageal lumen. Between 2019 and 2022, 5 post-ESD patients who received a median number of 11 sessions of ED (range, 4–28) of ED over a period of 322 days (range, 246–584) but still had moderate to severe dysphagia were admitted. 2 or 3 sessions of ED+ERI were performed for each patient interspersed with ED. After a median number of 4 treatments (range, 2–9), all patients were symptom-free or had minimal symptoms. No serious complications occurred in any patients who underwent ED+ERI. Therefore, ED+ERI is safe, feasible, and may serve as a useful therapeutic method for refractory esophageal stricture after ESD.

Introduction

Endoscopic submucosal dissection (ESD) has become a standard treatment for early esophageal cancer. However, ESD may cause a series of complications, such as perforation, bleeding and stenosis. Among them, esophageal stricture is common and probably one of the most challenging complications. The incidence of esophageal stricture after ESD is 6% to 18% and soars to 100% after removal of circumferential or near-circum-

ferential neoplastic lesions [1]. Regardless of the causes, endoscopic dilation (ED) using balloons or bougies is the most common treatment for esophageal strictures and optimal treatment by default. Esophageal stenosis after ESD is usually complex esophageal stenosis, which requires repeated dilation [2]. For strictures that do not respond well to dilations, other treatment methods have been reported, such as endoscopic radial incision (ERI), steroid injection, and esophageal stent placement [3].

ERI is traditionally performed safely and effectively in patients with simple esophageal strictures or anastomotic stric-

* These authors contributed equally.

tures, and is considered an alternative therapy for patients who have relatively short strictures [4]. For esophageal strictures after ESD, the strictures are usually longer and more angulated than anastomotic strictures. Due to the technical challenges and risks of ERI, it is usually reserved as a second-line treatment for refractory esophageal stenosis after ESD. Currently, there are only a few reports evaluating the role of ERI in treating esophageal stenosis [5–7].

We have noticed that, after each session of ED, only the relatively “weak” and fresh scar tissue is torn apart, whereas the whitish, older and stiffer tissue remains intact. These “tough” scars are ideal targets for ERI, and by combining initial ED and subsequent ERI, the narrowed esophagus can expand completely and uniformly. Here, we report our experience with using ED+ERI, and demonstrate that compared to ED only in previous cases, ED+ERI can reduce the number of treatment cycles and eventually shorten the course of treatment.

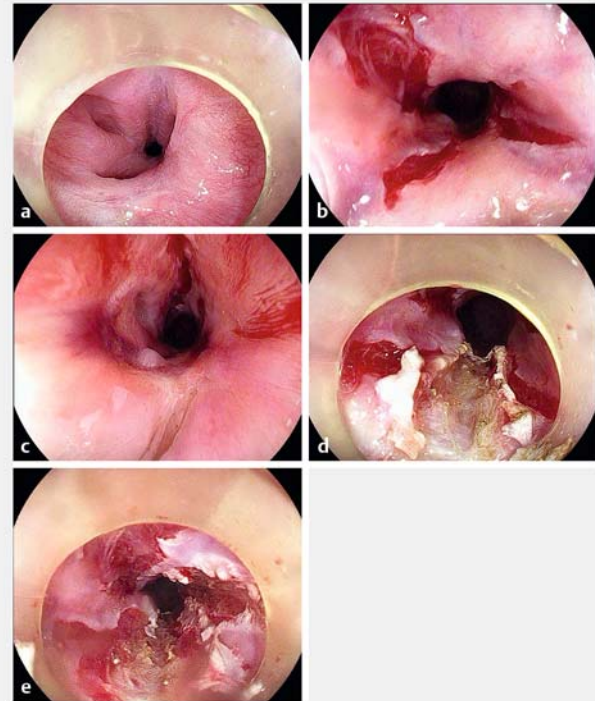
Patients and methods

Patients

This pilot study included 5 patients with post-esophageal ESD who had received ED more than 3 times but still had recurrent dysphagia. All patients underwent ED+ERI interspersed with ED. Some patients with anastomotic stricture also received ED+ERI but were excluded from this study. This study was performed in compliance with the ethical principles of the Declaration of Helsinki and approved by the Ethics Committee of Qilu Hospital of Shandong University. Informed consent was obtained from all patients or their authorized relatives before the procedure was performed. All patients or their authorized relatives were informed of possible adverse events and other possible treatment options.

Endoscopic incision and dilation procedure

Conventional ED was performed without general anesthesia; ED+ERI requires general anesthesia with endotracheal intubation. For ED, Savary-Gilliard dilators (Cook Medical) following guidewire placement was used. Severely narrowed, angulated strictures may require fluoroscopy guidance or even pre-incision to allow passage of the guidewire (► Fig. 1a). Savary-Gilliard dilations followed the “rule of three”: in each treatment session, starting from the size when moderate resistance was felt, usually 5 mm or 7 mm, then increased by 2 mm each time until the third dilation. Active hemorrhage after dilation, although rare, should be managed with electrocoagulation, but not metal clips, to avoid hindering subsequent incision. Most patients will be symptom-free if their strictures are dilated to 11 mm. ED usually resulted in 3 reddish longitudinal mucosal lacerations, but some old white scar tissue between the lacerations remained intact (► Fig. 1b). It seems that ED is only capable of repeatedly tearing up relatively fresh scars, but not the older, stiffer scars. The latter type of scars may contribute to recurrence of strictures and, hence, the target for ERI (► Fig. 1c). We used an IT knife to cut through the scar tissue and expose the underlying muscularis propria. Care should be taken not to injure the smooth muscle fibers (► Fig. 1d). Scar tissue ridges



► **Fig. 1** Endoscopic dilation combined with incisional therapy for refractory esophageal stricture after endoscopic submucosal dissection. **a** Refractory esophageal stricture after multiple sessions of endoscopic dilation after endoscopic submucosal dissection. **b** Endoscopic dilation resulted in reddish longitudinal mucosal lacerations. **c** White, old scar tissue remained intact between the mucosal lacerations. **d** Radial incision of the white, old scar tissue deep into the muscularis propria layer. **e** Complete expansion of the esophageal lumen after the procedure.

► VIDEO



► **Video 1** Endoscopic dilation combined with incisional therapy for refractory esophageal stricture after endoscopic submucosal dissection.

between esophageal wall indents should be cut and released as well to prevent food retention. The ED+ERI procedure resulted in complete, uniform expansion of the esophageal lumen (► Fig. 1e, ► Video 1).

► **Table 1** Baseline characters and treatment parameters of five patients with refractory esophageal stenosis after ESD.

Case	Sex	Age	Before dilation + incision				After dilation + incision			
			Time (days)	Number	Interval (days) ¹	Dysphagia score ²	Time (days)	Number	Interval (days)	Dysphagia score
1	F	64	584	28	21	3	277	5	69	0
2	M	66	246	10	25	3	188	9	24	0
3	M	62	267	12	22	4	98	4	33	0
4	F	70	322	11	29	3	100	4	33	1
5	F	65	329	4	82	3	203	2	203	0

¹ Before dilation + incision, time interval between treatments was calculated by treatment time/number of treatments, because patients were referred to our center when dysphagia recurred after the last time of treatment. After dilation + incision, time interval between treatments was calculated by treatment time/(number of treatments-1).

² Dysphagia score originally described by Knyrim et al. in the *New England Journal of Medicine* in 1993. Grade 0: able to eat normally; grade I: unable to swallow some solid foods; grade II: only able to swallow semi-liquid food; grade III: only able to swallow liquid food; grade IV: unable to swallow liquid food.

Postoperative management and follow-up

After the procedure, patients were routinely monitored for vital signs. Alarming symptoms such as chest pain could indicate esophageal perforation. The fasting time of patients depended on the type of treatment. Patients who underwent ED only fasted for 2 to 4 hours before resuming a liquid diet. For those who underwent ED+ERI, fasting was required for 24 hours, during which proton pump inhibitors and prophylactical antibiotics were administered intravenously. Patients were regularly followed up in the outpatient department, and endoscopy was performed when dysphagia recurred. If confirmed, we still prefer ED as a first-line treatment because it is simple and does not require hospitalization. If ED was not optimal due to remained fibrotic scar tissue, then additional ERI was performed. Patients were followed up 6 months after the last treatment if they failed to receive further treatment, and then every year thereafter.

Outcome measures

Criteria for evaluating treatment methods were total treatment time, number of treatments as well as time interval between treatments. Dysphagia score described by Knyrim, et al. was used to grade dysphagia before surgery and during follow-up [8]. The following grading was applied: grade 0, able to eat normally; grade I, unable to swallow some solid foods; grade II, only able to swallow semi-liquid food; grade III, only able to swallow liquid food; grade IV, unable to swallow liquid food. Relief of symptoms was defined as a dysphagia score <2 or no stenosis confirmed by endoscopy.

Statistical analysis

SPSS26.0 was used for statistical analyses and for illustrations. Measurement data were expressed as median ranges.

Results

Baseline characteristics and treatment parameters of the 5 patients with refractory stenosis are shown in ► **Table 1**. The patients underwent 11 ED sessions (range, 4–28) in 322 days (range, 246–584) before being referred to our center; the time interval between ED was typically within 1 month, except for the last patient. 2 or 3 sessions of ED+ERI were performed on each patient interspersed with additional ED at local hospitals. After 4 treatments (range, 2–9) in 188 days (range, 98–277), all patients were symptom-free. The first and last patient also benefited from an elongated time interval between treatments (21 to 69 days and 82 to 203 days, respectively). No complications such as major bleeding or perforation occurred. The median follow-up time was 688 days (range, 188–1255), and all 5 patients were symptom-free. Therefore, ED+ERI is a feasible method to treat refractory esophageal stenosis after ESD.

Discussion

ERI is a second-line treatment for esophageal stenosis and has shown good safety and efficacy, mainly in patients with simple stenosis or anastomotic strictures [4]. ERI can be conventionally performed by making radial incisions on fibrotic tissue, or in recent years, radial incision and cutting (RIC) to remove the scar tissue [4, 7, 9]. However, RIC leaves a circumferential wound that resembles the post-ESD wound, raising concerns for further strictures if applied to treat long-segment, angulated strictures after ESD. Also, because it is difficult to inject medium beneath scar tissue, dissection can be arduous and risky. Nevertheless, there have been a few reports about using ERI or RIC to treat refractory esophageal stenosis after ESD, all with favorable results, although with relatively high perforation rate, demonstrating the feasibility of this technique [5, 7, 9].

Our method, for the first time, integrates ED and ERI, leveraging the advantages of the 2 techniques. ED is used for initial dilation and ERI is used for subsequent, targeted incision of stiff scars that remain after ED to achieve complete expansion of the

esophagus. In general, although there were only 5 cases, patients seemed to benefit more when ED+ERI was more frequently performed. Basic science research has demonstrated that mechanical forces play an important role in the fibrosis process: A constant high level of tissue matrix tension promotes fibrosis progression whereas relieving mechanical tension can reduce fibrosis and scar formation [10]. Therefore, the stiff scars left by ED may contribute to subsequent scarring by maintaining high tension locally, and removing such scars can provide a tension-less environment to promote normal healing. This could be a theoretical explanation for the effect of ED+ERI as well as the established RIC. The fact that ED+ERI enabled longer symptom-free time between treatments supports this hypothesis.

Compared with ED, ED+ERI still has certain limitations, such as the need for general anesthesia, difficulty of the procedure, risk of perforation, need for hospitalization after operation, and high cost. Therefore, ED+ERI may be particularly beneficial for esophageal strictures that are at high risk of becoming refractory, such as circumferential, long-segment lesions, injury to the muscularis propria during ESD or even perforation.

Conclusions

The current pilot study has demonstrated the feasibility and potential of ED+ERI. Well-designed, prospective cohorts with more patients are needed to better elucidate the benefits or disadvantages of this procedure.

Acknowledgments

The authors thank the Natural Science Foundation of Shandong Province (ZR2020QH184) and the China Postdoctoral Science Foundation (2020M670044ZX) for funding support.

Competing interests

The authors declare that they have no conflict of interest.

Funding

Natural Science Foundation of Shandong Province ZR2020QH184
China Postdoctoral Science Foundation 2020M670044ZX

References

- [1] Ono S, Fujishiro M, Niimi K et al. Predictors of postoperative stricture after esophageal endoscopic submucosal dissection for superficial squamous cell neoplasms. *Endoscopy* 2009; 41: 661–665
- [2] Shah JN. Benign refractory esophageal strictures: widening the endoscopist's role. *Gastrointest Endosc* 2006; 63: 164–167
- [3] de Wijkerslooth LR, Vleggaar FP, Siersema PD. Endoscopic management of difficult or recurrent esophageal strictures. *Am J Gastroenterol* 2011; 106: 2080–2091; quiz 2092
- [4] Muto M, Ezoe Y, Yano T et al. Usefulness of endoscopic radial incision and cutting method for refractory esophagogastric anastomotic stricture (with video). *Gastrointest Endosc* 2012; 75: 965–972
- [5] Huang Z, Wei W, Cheng F. Endoscopic radial incision method for two strictures of the esophagus after endoscopic submucosal dissection: a case report. *World J Surg Oncol* 2020; 18: 38
- [6] Zeng QS, Yang J, Liu W et al. Endoscopic incision method for treatment of refractory esophageal stricture. *VideoGIE* 2017; 2: 76–78
- [7] Yano T, Yoda Y, Satake H et al. Radial incision and cutting method for refractory stricture after nonsurgical treatment of esophageal cancer. *Endoscopy* 2013; 45: 316–319
- [8] Knyrim K, Wagner HJ, Bethge N et al. A controlled trial of an expansile metal stent for palliation of esophageal obstruction due to inoperable cancer. *N Engl J Med* 1993; 329: 1302–1307
- [9] Zhu Y, Shrestha SM, Yu T et al. Modified endoscopic radial incision and cutting method (M-RIC) for the treatment of refractory esophageal stricture. *Surg Endosc* 2022; 36: 1385–1393
- [10] Yamada KM, Doyle AD, Lu J. Cell-3D matrix interactions: recent advances and opportunities. *Trends Cell Biol* 2022; 32: 883–895