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The Efficacy and Safety of Treatment Outcomes for Refractory Benign Esophageal Strictures Using a Novel Combination of Needle-Knife Stricturoplasty, Balloon Dilation, and Steroid Injection (with Video)

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Keywords
Benign strictures · Dysphagia · Esophageal stricture · Stricturoplasty

Abstract

Background and Aims: Benign esophageal strictures often present with dysphagia and can significantly impair a patient's quality of life, especially when refractory to standard endoscopic techniques. When repeat dilations fail to achieve an adequate luminal diameter or resolve dysphagia, further therapy with needle-knife or steroid injections is needed. However, patients can still clinically fail. To manage such strictures, we employed a novel combination of all three techniques. ***Methods:*** Single-center case series of adult patients with benign strictures that were refractory to conventional endoscopic therapy and removable self-expanding metal stenting. Primary clinical success was defined as complete resolution in dysphagia. Secondary outcomes included periodic dilation index (frequency of dilations over the follow-up time), esophageal diameter changes, technical success, and complications. ***Results:*** Four patients (median age 49.7 years old, interquartile range [IQR] 30–59) underwent endoscopic therapy for complex, benign strictures using our triple therapy technique. Etiologies of the strictures included peptic strictures ($n = 3$) and an anastomotic stricture ($n = 1$). There was 100% technical success rate with no associated adverse events. There was a 50% clinical success rate, with 1 additional patient having partial improvement in dysphagia. The median diameter of the esophagus before and after triple therapy was 3.2 mm (IQR 3.5–5.5) and 12.8 mm (IQR 11.7–14.2), respectively. The periodic dilation index was 6.3 before and 1.5 after triple therapy. The median length of follow-up was 362.5 days. ***Conclusion:*** Triple combination therapy may be useful in benign strictures that are refractory to standard techniques. Larger studies are needed to validate these findings.

Eficácia e segurança da combinação de estricturoplastia, dilatação com balão e injeção de corticóides no tratamento de estenoses esofágicas benignas refractárias (com vídeo)

Palavras Chave
Estenoses benignas · Disfagia · Estricturoplastia · Corticosteróides · Dilatação

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Resumo

Introdução e objectivos: As estenoses esofágicas benignas apresentam-se frequentemente com disfagia e podem prejudicar significativamente a qualidade de vida, especialmente quando refractárias às técnicas de dilatação endoscópicas padrão. Quando as dilatações não conseguem isoladamente atingir um diâmetro luminal adequado ou resolver a disfagia, são necessárias terapêuticas adicionais (incisão com faca ou injecções de esteróides), embora a taxa de falha clínica não seja desprezível. Para abordagem destas estenoses refratárias utilizámos uma nova combinação das três técnicas. ***Métodos:*** Série de casos incluindo doentes adultos com estenoses benignas refractárias à dilatação convencional e à colocação de prótese metálica auto-expansível removível. O endpoint primário foi definido como resolução completa da disfagia. Os endpoints secundários incluíram o índice de dilatação periódica (frequência de dilatações ao longo do tempo de seguimento), alterações do diâmetro esofágico, sucesso técnico e complicações. ***Resultados:*** Quatro doentes (idade média 49.7 anos, intervalo interquartil [IQR] 30–59) foram submetidos a terapia endoscópica para estenoses benignas complexas utilizando a técnica de terapêutica tripla. As etiologias das estenoses incluíam estenoses pépticas (n = 3) e estenose anastomótica (n = 1). A taxa de sucesso técnico foi de 100%, sem eventos adversos associados. A taxa de sucesso clínico foi 50%, com um doente adicional apresentando melhoria parcial da disfagia. O diâmetro médio do esófago antes e depois da terapêutica tripla foi de 3,2 mm (IQR 3.5–5.5) e 12.8 mm (IQR 11.7–14.2), respetivamente. O índice de dilatação periódica foi de 6.3 antes e 1.5 após a terapêutica tripla. A duração média do seguimento foi de 362.5 dias. ***Conclusão:*** A terapêutica tripla de combinação pode ser útil em estenoses benignas refractários às técnicas convencionais embora sejam necessários estudos adicionais de validação da técnica.

Introduction

Benign esophageal strictures are a common occurrence that present with dysphagia when the lumen diameter is ≤13 mm [1, 2]. Luminal narrowing can significantly worsen a patient's quality of life with complications associated with malnutrition, weight loss, and aspiration pneumonia [3, 4]. Historically, peptic strictures have accounted for up to 80% of benign strictures, though with the increased use of acid suppression therapy the incidence has somewhat decreased [2]. Other etiologies may occur following radiation, caustic ingestion, strictures following endoscopic submucosal dissection, or anastomotic strictures after esophagectomy [4]. These strictures are classified as simple or complex based on the diameter, length, and anatomic abnormalities [2, 4]. Complex stricture is generally longer (>2 cm), irregular, and angulated with severely compromised luminal diameters [5]. Endoscopic dilation is the mainstay of treatment. However, in up to 10% of cases these strictures are refractory to dilation and a luminal diameter >14 mm cannot be achieved [4, 6]. In this setting, the stricture is considered a benign recalcitrant stricture that requires alternative therapy to manage the underlying fibrostenotic disease.

To avoid feeding tube placement or surgery, adjunctive endoscopic therapies including corticosteroid injections or incisional therapy can be used in combination with standard dilation techniques [1]. Removable esophageal stents can also be used to induce stricture remodeling through expansion forces [7]. The use of four quadrant steroid injections (most commonly triamcinolone acetonide) into the stricture has been shown to inhibit matrix proteins that interfere with collagen synthesis and fibrosis [2, 4]. Incisional therapy, such as needle-knife, is a radial incision technique that delivers high-frequency energy to disrupt and remove the rim of stenosis [4]. While these modalities are readily available, the optimal technique remains uncertain, especially due to the heterogenous etiologies of these strictures. Adding needle-knife or steroid injection to standard dilation has produced mixed results [8–14]. No study has investigated a combination of all three modalities in benign refractory strictures. As such, the aim of our case series was to describe treatment outcomes using a novel combination of needle-knife, balloon dilation, and intralesional steroid injection.

Methods

This was a single-center clinical case study of consecutive adult patients (≥18 years old) diagnosed with benign esophageal strictures, refractory to standard dilation therapy, and esophageal stenting between November 2020 and March 2022. All procedures were conducted by a single advanced endoscopist. Baseline demographic and descriptive data were collected, as well as information regarding prior medical, endoscopic, and/or surgical therapies, procedure-related information, and length of follow-up. The stricture length and response to dilation were also recorded. The Institutional Review Board approved the study protocol (HP-00100530).

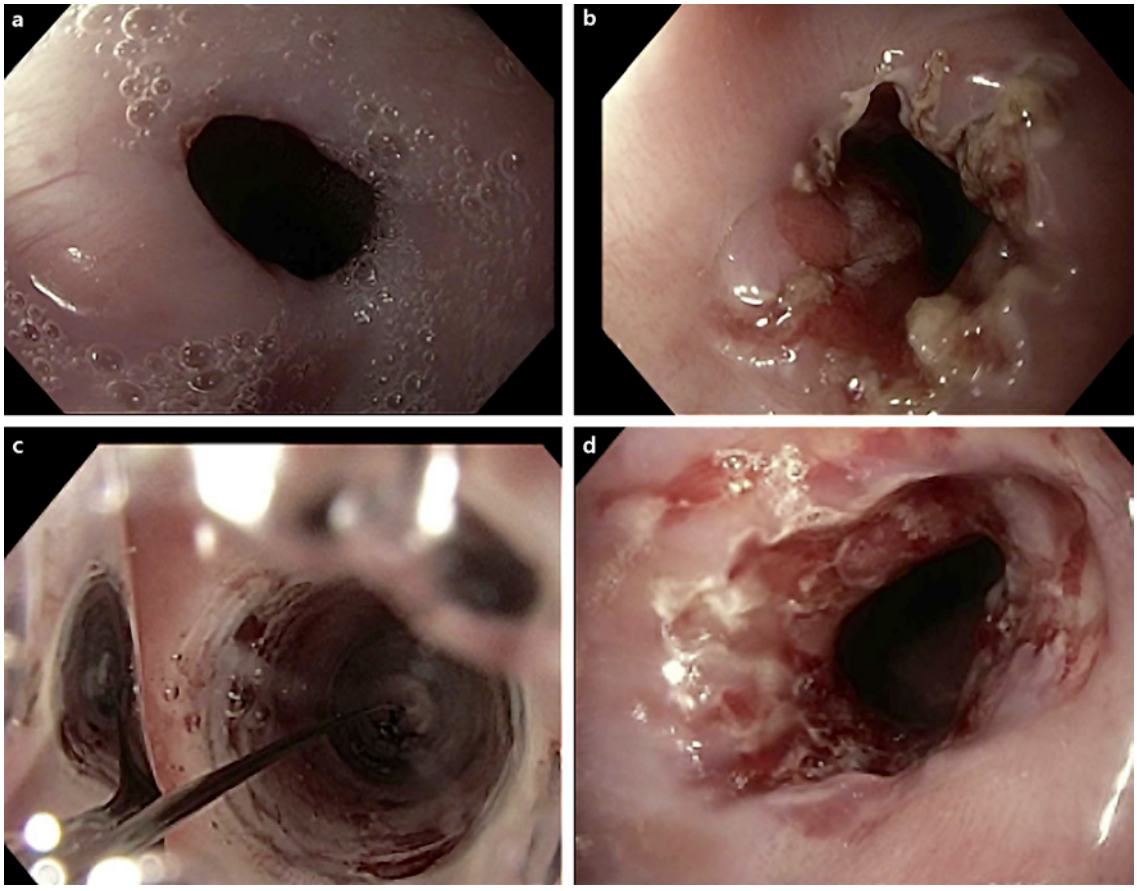

Fig. 1. Esophageal stricture (**a**) that was treated with needle-knife (**b**), balloon dilation (**c**), and then steroid injections (**d**).

The primary outcome was clinical success, defined as complete resolution dysphagia with an ability to tolerate a regular diet. Secondary outcomes included technical success, changes in the esophageal diameter, and a decrease in periodic dilation index needed. The periodic dilation index was defined by the frequency of dilations over the follow-up time in months. Procedure-related adverse events were defined by the American Society for Gastrointestinal Endoscopy lexicon severity scoring system [15].

Statistical Analysis

This was a descriptive study. Nonparametric data were presented as a median with an interquartile range (IQR). Due to a small size, logistic regression analysis was not incorporated.

Procedural Description

All patients underwent the same procedural technique (online suppl. Video 1; for all online suppl. material, see www.karger.com/doi/10.1159/000527770). First, longitudinal needle-knife XL (triple lumen needle-knife – 5.5 Fr Boston Scientific, Natick, MA, USA) incisions were performed at 3–4 mm in depth along the length of the stricture, circumferentially with at least four separate incisions. The incisions were made distal to proximal for optimal control. The needle-knife settings included ERBE Vio 3 with an endocut setting of 2 and forced coagulation setting of 1.5. Next, balloon dilation using a CRE balloon dilators (Boston Scientific) was done in a serial manner to allow the endoscope to pass. Finally, targeted four quadrant intralesional steroids (triamcinolone 40 mg/mL, 2 mL in total) were then injected (Fig. 1, 2).

Repeat endoscopy was done every 4–6 weeks until persistent esophageal dilation was obtained to pass the GIF H-160/H180 scope (~9.4 mm) through the stricture without intervention. From there, the procedures were repeated based upon symptoms and/or resolution of dysphagia.

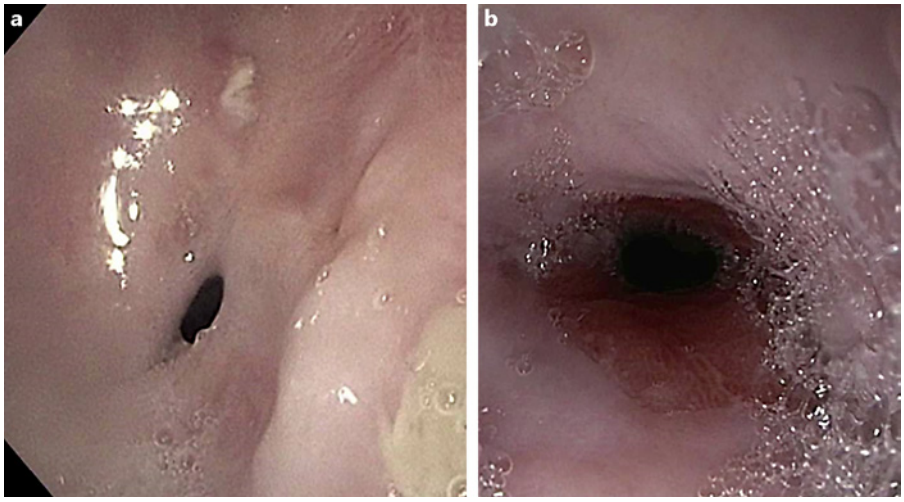

Fig. 2. Endoscopic evidence of a stricture treated before (**a**) and after (**b**) triple therapy 2 months apart.

Table 1. Patient characteristics

Patient	Age/sex	Body mass index, kg/m^2	Stricture etiology	Stricture distance from incisors	Total procedures before triple therapy	Total procedures after triple therapy	Length of follow-up, days
1	30/male	20.3	GERD	39 cm	15[b]	5	425
2	59/male	25.3	Anastomotic[a]	24 cm	8	0	421
3	57/male	19.6	GERD	35 cm	4[b]	0	304
4	53/male	26.1	GERD	30 cm	2[b]	1	116

GERD, gastroesophageal reflux disease. [a] Underwent esophagogastrectomy for gastric adenocarcinoma. [b] Required PEG tube at one point, that procedure is not counted here.

Table 2. Procedure outcomes and clinical success

Patient	Initial stricture diameter × length before triple therapy	Stricture diameter after triple therapy	Triple therapy procedures,[1] *n*	Symptom resolution
1	7 mm × 5 cm	13.5 mm	1	Partial
2	3 mm × 1 cm	15 mm	2	Yes
3	3 mm × 1 cm	11.5 mm	4	No
4	4 mm × 1 cm	12 mm	2	Yes

[1] Combination of needle-knife, balloon dilation, steroid injection.

Results

Four patients (median age 55 [IQR 30–59], 4 males, median body mass index 22.8 kg/m^2 [IQR 19.9–25.7], 2 Caucasians) underwent endoscopic therapy for a benign refractory stricture using our triple therapy technique for symptoms of dysphagia (Table 1). Etiologies of the strictures included peptic stricture ($n = 3$) and a post-surgical anastomotic stricture ($n = 1$). Prior to triple therapy, the patients underwent periodic dilation an average of 6.3 times, typically every month. All patients previously required esophageal stenting ranging from 1 to 3 times; 1 patient (# 4) was managed primarily with stenting and only underwent dilation once. Of note, the option for stent placement before incisional therapy was primarily because these patients were referred to our center with prior therapy. In cases of stent placement, we placed an 18-mm fully covered metallic stent (WallFlex; Boston Scientific).

Clinical success was achieved in 2 patients over a median length of follow-up of 362.5 days (IQR 210–423). One patient (#1) had a brief resolution in his solid food dysphagia; however, his symptoms returned 24 days later following triple therapy in which he reported occasional dysphagia to solids but was able to tolerate a soft diet. There was 100% technical success rate with no associated

adverse events. The median diameter of the esophagus before triple therapy was 3.2 mm (IQR 3.5–5.5) and improved to 12.8 mm (IQR 11.7–14.2) following triple therapy (Table 2). The periodic dilatation index decreased to 1.5 following triple therapy. The patients underwent a median of 2 (IQR 2–3) triple therapy procedures total.

Discussion

To our knowledge, this is the first case series to describe triple combination therapy in patients with benign refractory strictures. Clinically, 3 patients improved with no procedure-related complications. Furthermore, the median stricture diameter improved from 3.2 to 12.8 mm with a decrease in periodic dilations needed. The order of triple therapy chosen allowed for the balloon dilation to open the needle-knife tract so that targeted four quadrant steroid injections could provide optimal results.

These findings are important, especially since recurrent symptoms of dysphagia can be seen in up to 40% of patients undergoing dilation [16]. Typically, these patients undergo serial dilation to alleviate symptoms, though complex stricture can be refractory and persistent dysphagia often poses as a significant challenge for the endoscopist [4]. Recently, anastomotic strictures have emerged as common cause of complex strictures that are often difficult to treat with limited improvement following steroid use [17, 18].

Data regarding combination steroid use and dilation in these strictures are variable, especially since there is no standardized technique with volumes per injection of triamcinolone ranging from 0.5 mL to 2.8 mL [4]. One comparative study of 21 benign strictures of varying etiologies found that steroids plus boogie dilation decreased the number of periodic dilations while prolonging dysphagia-free periods [12]. Yet, another prospective randomized study looking at 14 patients with caustic stricture found no difference in such outcomes [13]. That being said, a more recent prospective study (also evaluating caustic-related strictures) reported an improvement in dysphagia scores and periodic dilation index over a 1-year follow-up period [14]. It is possible that injecting steroids following dilation can enhance clinical outcomes. In fact, two randomized controlled studies analyzing anastomotic strictures produced conflicting results when analyzing steroid injections before or after dilation [18, 19]. Similar to our findings, the study with steroid injection after dilation found significant symptomatic improvement to the point that the study was ended early [19]. All patients in our cohort received steroid injections after dilation since the incisions were easier to place once the lumen was more open and the steroid was used to prevent restenosis by softening the fibrotic tissue.

Needle-knife therapy with dilation can improve long-term outcomes, especially in shorter anastomotic strictures [20]. A few studies have demonstrated favorable results [9, 10, 20, 21]. In fact, one study comparing needle-knife to balloon dilation reported longer term luminal patency in 62% and 20% of patients, respectively, at 12-month follow-up [9]. Another comparative study of 50 patients with Schatzki rings found that electrosurgical incisions allowed for longer symptom-free periods (8 vs. 5.8 months) compared to boogie dilation [10]. It also appears that short anastomotic strictures are particularly responsive to needle-knife [20]. However, one randomized study of 62 patients with anastomotic strictures found no differences in clinical outcomes or number of dilations needed when comparing Savary-Gilliard dilation to electrocautery incision [11]. Longer strictures (>1.5 cm) usually require re-treatment and are more difficult to manage [22]. As such, caution is needed when directly comparing these study outcomes. However, in our study 4 incisions were typically performed for the short segment strictures with a moderate clinical success rate when steroid injections were added to the procedure protocol.

Due to the varying complexity and etiologies of strictures, it is still difficult to interpret the current literature. However, given the possible long-term benefits of our triple therapy technique we do recommend needle-knife before dilation as a means to enhance the efficacy of steroid injections. In our cohort, 3 out of 4 patients had initial stricture lengths of 1 cm, and these longer strictures may respond differently. Additionally, deciding when to employ this technique should be determined on a case-by-case basis. Given our positive outcomes with no associated complications, we believe that this method should be considered when strictures are refractory after 2–3 dilation sessions and/or stent therapy.

There are a few limitations to highlight in this study. As a retrospective case series, there are inherent biases that can occur. Our limited sample size may also confound our findings; yet, this study was done at a large tertiary center with patients who failed numerous endoscopic therapies leading up to our novel technique. The majority of these strictures were secondary to peptic strictures, and there may be different outcomes based on varying stricture etiologies. Yet, all procedures were performed by the same endoscopist with the same technique used with long-term follow-up.

In conclusion, utilizing triple therapy for refractory benign strictures can improve therapeutic outcomes while reducing the need for repeat dilations. Further larger studies are needed to validate these findings and determine the optimal technique.

Statement of Ethics

This study protocol was reviewed and approved by the University of Maryland Institutional Board Review, approval number HP-00100530. Informed consent was obtained from the patients.

Conflict of Interest Statement

Eric M. Goldberg is a consultant for Medtronic and Ambu. All other authors have no potential conflicts (financial, professional, or personal) that are relevant to the content presented in this manuscript.

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Author Contributions

Andrew Canakis performed research, collected and analyzed data, and wrote the paper. Varun Kesar, Benjamin Twery, Osman Ali, Justin Canakis, and Caleb Hudspath collected data and revised the paper. Eric Goldberg designed the study and revised the paper.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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