# Steroid pulse therapy prevents restenosis following balloon dilatation for esophageal stricture

Kazuki Yokota [1]

Hiroo Uchida [1,*]

Phone +81-52-744-2959
Email hiro2013@med.nagoya-u.ac.jp

Akihide Tanano [1]

Chiyoe Shirota [1]

Takahisa Tainaka [1]

Akinari Hinoki [1]

Naruhiko Murase [1]

Kazuo Oshima [1]

Ryo Shirotsuki [1]

Kosuke Chiba [1]

[1] Department of Pediatric Surgery, Graduate School of Medicine, Nagoya University, 65 Tsurumai, Showa, Nagoya, 466-8550 Japan

## Abstract

### Purpose

This study aimed to evaluate the effectiveness of intravenous steroid pulse therapy following balloon dilatation for esophageal stenosis and stricture in children.

## Methods

The study enrolled six children, including three with congenital esophageal stenosis and three with anastomotic strictures after surgery for esophageal atresia, all of whom were treated by balloon dilatation combined with high-dose intravenous methylprednisolone pulse therapy. Methylprednisolone was injected intravenously at a dose of 20 mg/kg/day for 2 days, starting from the day of dilatation, followed by 10 mg/kg/day for 2 days, for a total of 4 days.

## Results

Esophageal stricture recurred in all three patients with congenital esophageal stenosis despite repeated balloon dilatation without methylprednisolone. However, the symptoms of dysphagia improved and did not recur after systemic steroid pulse therapy following balloon dilatation. Symptoms also resolved in all three patients with anastomotic strictures following balloon dilatation with systemic steroid pulse therapy. All six patients remained asymptomatic after 6–21 months follow-up, with no complications.

## Conclusion

Intravenous methylprednisolone pulse therapy following balloon dilatation is safe and effective for the treatment of esophageal stenosis and strictures in children.



## Keywords

Esophageal stricture
Congenital esophageal stenosis
Balloon dilatation
Steroid pulse
Systemic administration


## Introduction

Esophageal strictures occur after surgical anastomosis, nasogastric intubation, external trauma, congenital esophageal stenosis (CES), achalasia, caustic injuries, or severe gastroesophageal reflux. Nonsurgical treatment of benign esophageal strictures traditionally involves the use of various types of bougies. Balloon dilatation is currently the first-choice therapy for benign esophageal strictures, and is considered to be safer than bougies and provides an adequate lumen [1]. However, balloon dilatation may need to be performed repeatedly because the strictures usually recur, with some strictures becoming refractory and requiring numerous dilatations [2, 3]. Endoscopic intralesional injection of steroids or systemic steroid administration is used to prevent esophageal strictures after endoscopic submucosal dissection in adults [4–6].

Despite numerous reports of steroid therapy for caustic esophageal strictures, the efficacy of this treatment remains controversial, and few studies have reported on the use of systemic steroid pulse therapy for CES and anastomotic strictures (AS) in children. In this study, we assessed the additional effect of intravenous methylprednisolone pulse therapy following balloon dilatation for esophageal strictures in children.

## Patients and methods

Six pediatric patients were treated with balloon dilatation combined with intravenous methylprednisolone pulse therapy for esophageal stenosis and strictures. The patient characteristics are shown in Table 1. All six patients suffered from dysphagia. Esophagography and esophagoscopy were performed in all six patients. Three patients were diagnosed with CES at 3–27 months. Endoscopic ultrasonography was performed in two CES patients and computed tomography in three. The esophageal wall showed partial muscular thickness and no signs of cartilage, and they were, therefore, diagnosed with fibromuscular thickening-type CES. The other three patients were diagnosed with delayed AS after surgery for esophageal atresia (type C) at 12–38 months. Two of these three patients underwent division of a tracheoesophageal fistula and primary repair of the esophagus. The

other patient had a long gap, and underwent division alone at the first operation, and delayed primary anastomosis at 8 days.

**Table 1**

Characteristics of the patients

| Patients | Sex | Age at diagnosis (months) | Diagnosis | Dilation without steroid (times) | Dilation with steroid (times) | Observation (months) |
|---|---|---|---|---|---|---|
| 1 | M | 6 | CES | 2 | 1 | 21 |
| 2 | M | 3 | CES | 2 | 3 | 19 |
| 3 | F | 27 | CES | 2 | 3 | 15 |
| 4 | F | 22 | AS | 0 | 1 | 17 |
| 5 | M | 12 | AS | 1 | 1 | 6 |
| 6 | F | 38 | AS | 0 | 2 | 6 |

*M* male, *F* female, *CES* congenital esophageal stenosis, *AS* anastomotic strictures

All three patients with CES initially underwent balloon dilatation twice without steroid administration, followed by balloon dilatation with steroid pulse therapy. The three patients with AS underwent balloon dilatation with steroid pulse therapy at the initial dilatation. The balloon diameter was determined by the diameter of the no-stricture site. Dilatation was maintained for 3–5 min and repeated three times in one operation.

The protocol for steroid pulse therapy was as follows. Methylprednisolone was injected intravenously at a dose of 20 mg/kg/day for 2 days, starting from the day of dilatation, followed by 10 mg/kg/day for 2 days, finishing on day 4.

This retrospective study was approved by the ethics committee at Nagoya University Hospital (2015-0508).

# Results

Three patients with CES underwent balloon dilatation twice without steroid therapy. Each dilatation (maximum diameter 8–12 mm) effectively resolved the stenosis temporarily. However, dysphagia recurred 1–5 months after the second dilatation, and esophagography and esophagoscopy showed that the esophageal strictures had recurred (Fig. 1). We, therefore, performed balloon dilatation with systemic methylprednisolone pulse therapy, with no recurrence of dysphagia. The procedure was repeated three times in two of these three patients to enlarge the diameter comparable to that in the normal esophagus, while the stenosis was sufficiently enlarged after the first procedure in the other patient. The esophageal strictures were eventually resolved in all three CES cases (Figs. 2, 3), who remained symptom free at 15–21 months after the last dilatation.

**Fig. 1**

Esophagography in patient no. 2. **a** Endoscopic ultrasonography before therapy showed partial muscular thickness and no signs of cartilage in the esophageal wall. The lesion was, therefore, classified as fibromuscular thickening-type CES. **b** Balloon dilatation procedure. The notch of the balloon has disappeared. **c** Esophageal stricture and dysphagia recurred 2 months after the initial balloon dilatation without steroid therapy. **d** There was no sign of esophageal stricture and no recurrence of dysphagia 2 months after balloon dilatation with systemic steroid pulse therapy

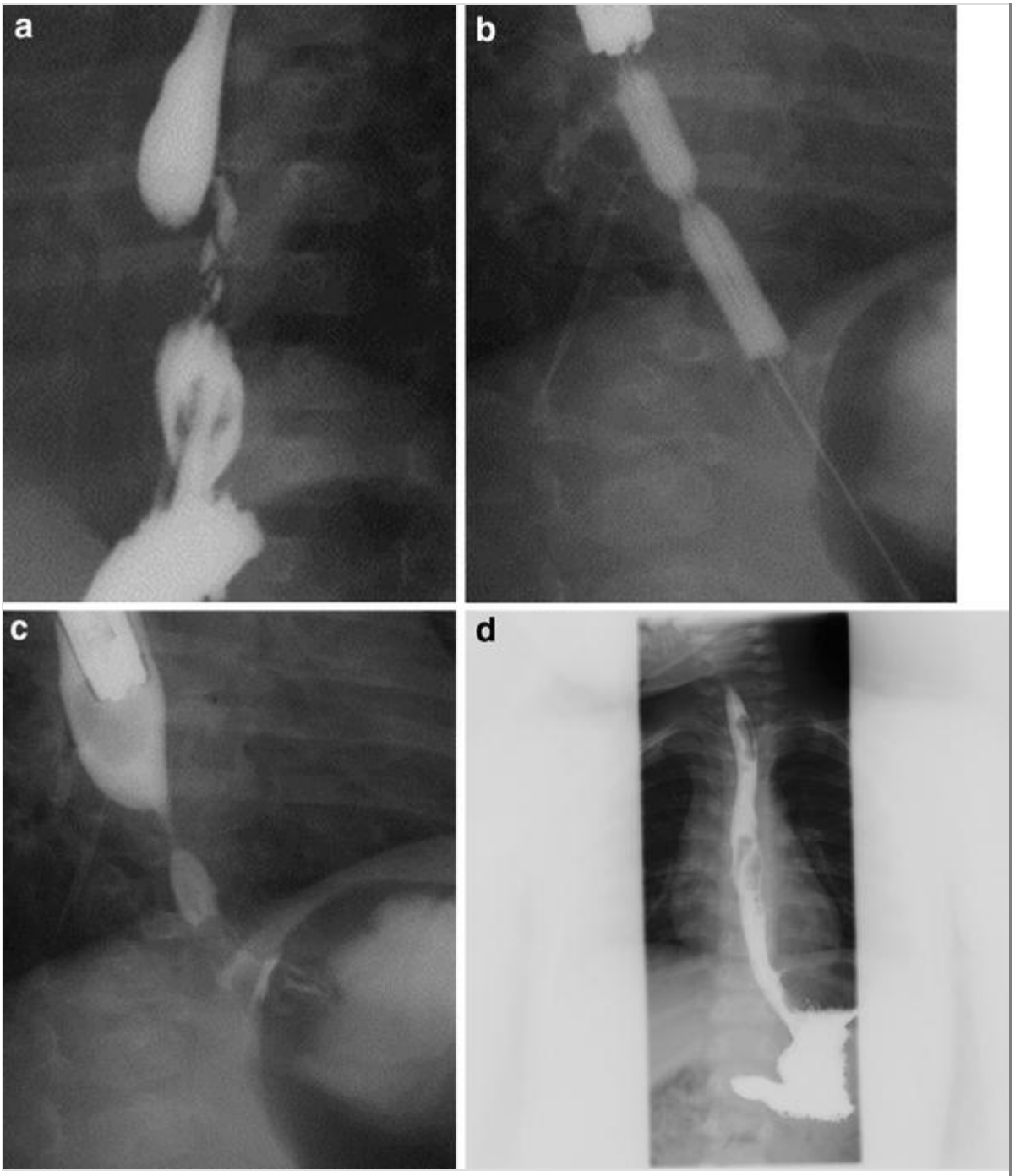



**Fig. 2**

Esophagography and endoscopic ultrasonography in patient no. 3. **a** Endoscopic ultrasonogram before therapy showed partial muscular thickness (*plus dots plus*) and no signs of cartilage in the esophageal wall. The lesion was, therefore, classified as fibromuscular thickening-type CES. **b** Esophagogram before therapy showing esophageal stricture. **c** Esophageal stricture and dysphagia recurred 4 months after the initial balloon dilatation without steroid therapy. **d** There was no sign of

esophageal stricture and no recurrence of dysphagia 9 months after the last balloon dilatation with systemic steroid pulse therapy

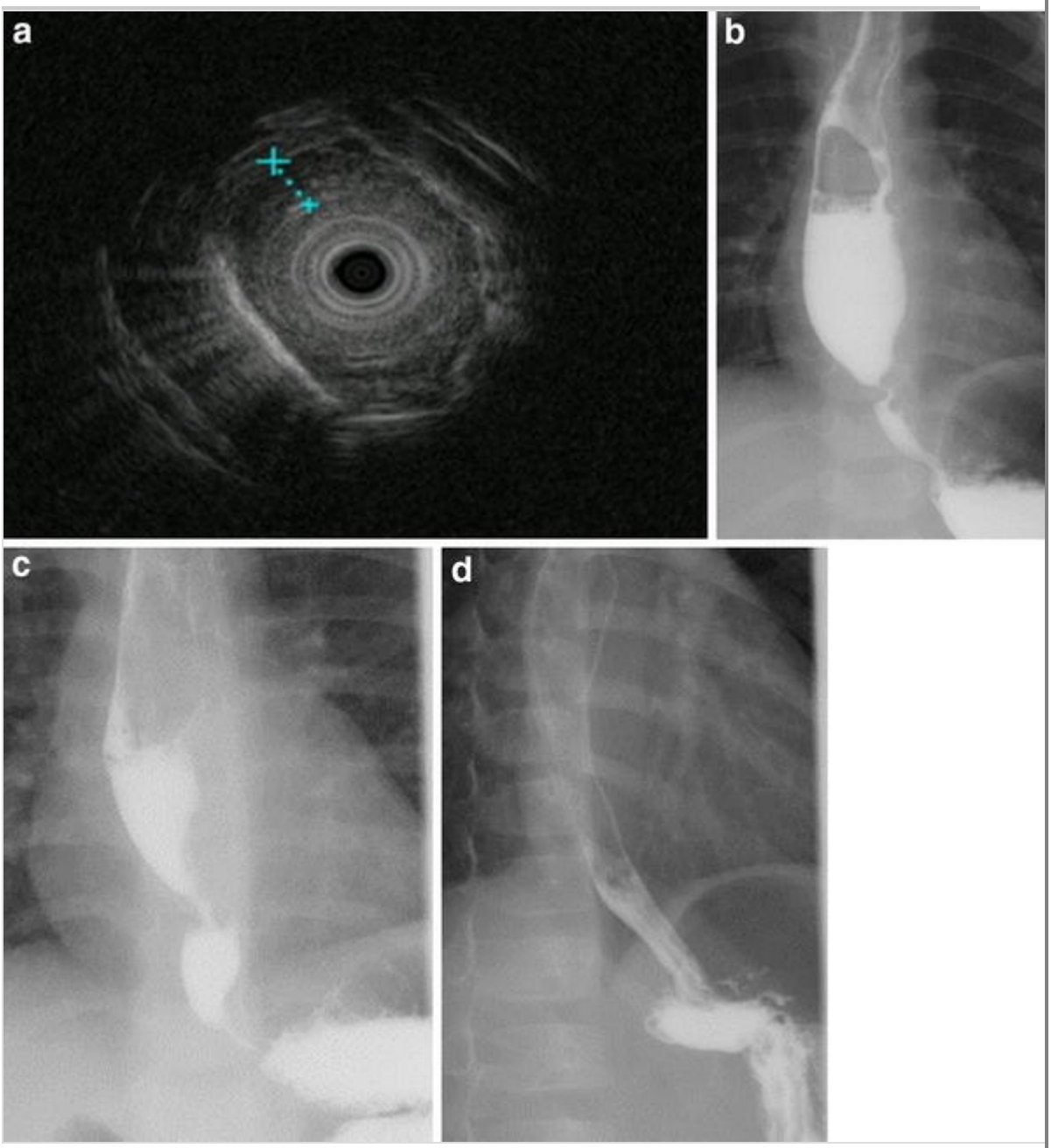
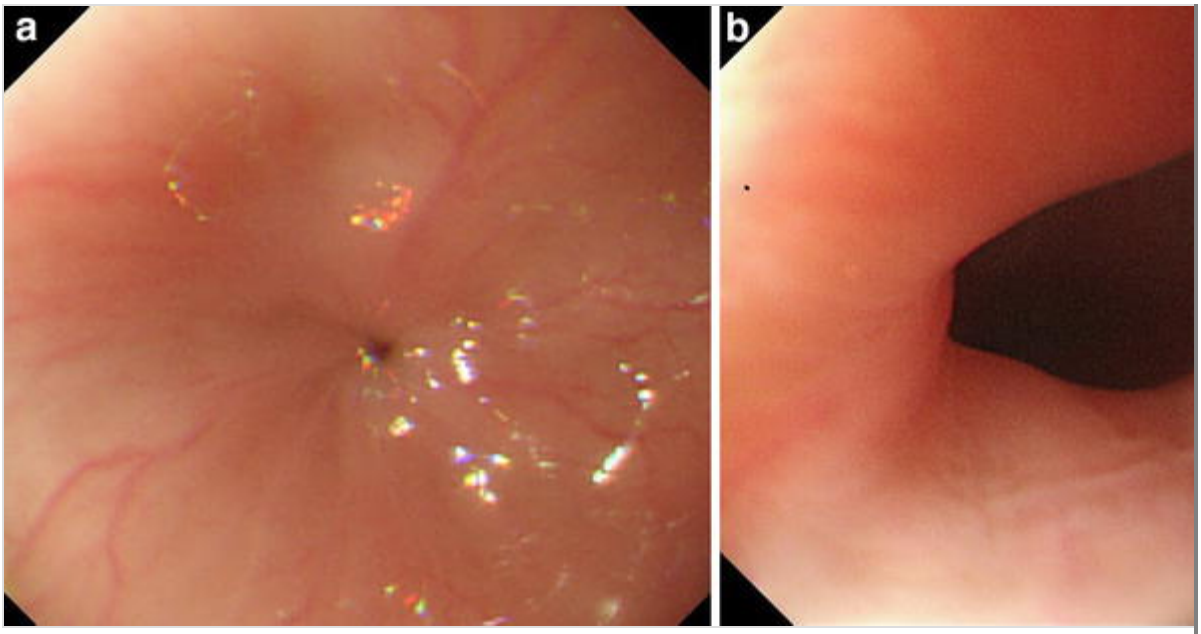



**Fig. 3**

Esophagoscopy in patient no. 3. **a** Esophagoscopy before therapy showed a severe esophageal stricture. **b** The esophagus diameter was sufficiently enlarged 1 month after the last balloon dilatation with systemic steroid pulse therapy




The three patients with AS were treated with intravenous methylprednisolone pulse therapy following balloon dilatation from the initial treatment. The maximum dilatation diameter was 12–15 mm. Symptoms of dysphagia improved in all three patients. The procedure was repeated twice in two of the three AS patients to enlarge the diameter comparable to that of the normal esophagus. All three AS patients remained asymptomatic at 6–17 months following the initial dilatation with steroid pulse therapy.

No side effects or complications related to balloon dilatation with steroid pulse therapy were noted during the 21-month follow-up.

## Discussion

There is currently no consensus treatment for CES. Several studies have reported that esophageal balloon dilatation is a safe and effective treatment for esophageal strictures in children. However, although a small study reported success rates of 65–100 % [7], a large study of balloon dilatation outcomes in patients with CES found that only 27 % of patients became asymptomatic [8]. However, these studies did not report on the patients' pathology. CES can be distinguished as fibromuscular thickening, tracheobronchial remnants, and membranous web types. Endoscopic ultrasonography is useful for distinguishing between tracheobronchial remnants and other types, and the overall success rate of balloon dilatation for CES, excluding tracheobronchial

remnants, is as high as 89.7 % [9]. However, a proportion of esophageal strictures recurs after balloon dilatation, and balloon dilatation was found to be ineffective in our patients with fibromuscular thickening-type CES, diagnosed by endoscopic ultrasonography. Symptoms of dysphagia or vomiting persisted 1–5 months after dilatation.

Therapy for AS is similar to that for CES [10]. Said et al. [11] reported that strictures were relieved in all 25 patients with AS following 1–14 dilatation procedures per patient. However, this is an unacceptably high number of procedures, and some studies have suggested that surgical resection should be considered if the lesion fails to respond to a series of dilatations [12–14]. Nevertheless, surgery is an invasive procedure and is thus not an ideal solution. Michaud et al. [8] indicated that surgery should not be considered a definite curative option, given that 66 % of their patients with CES remained symptomatic after surgery. Surgery should thus only be considered as a last option.

Gandhi et al. [14] reported that balloon dilatation with intralesional steroid injection was effective in patients with esophageal strictures, a finding supported by some subsequent studies in adult and pediatric patients [1, 3, 4]. However, this technique has not been used routinely at our institute because we considered that the esophageal wall would be too thick to perform uniform injections in patients with strictures. Furthermore, some studies have reported that balloon dilatation with intralesional steroid injection was ineffective in some patients [3, 13].

Some studies have reported on the successful treatment of refractory esophageal strictures using a combination of balloon dilatation and systemic steroid administration [2, 13, 15], including the advantage of high-dose systemic steroids for the prevention of stricture recurrence [1, 3, 13, 15]. We, therefore, investigated the use of short-term intravenous steroid pulse therapy, with successful results.

We only administered steroids for 4 days, while to the best of our knowledge all previous studies have used long-term steroid administration for 3–6 weeks. Steroids administered immediately after dilatation suppress the initial inflammation, which is the first step in

stricture formation. Stricture formation occurs within the first 3 days of wound healing, and steroids reduce the tissue collagen content and anti-inflammatory activity [13]. Administration of steroids for the first 3–4 days should thus be sufficient to prevent restenosis. The increased risk of side effects may be an important consideration for long-term steroid administration. Furthermore, given that short-term steroid pulse treatment is currently used for various diseases, we chose to use this protocol instead of longer term steroid administration as reported in previous studies [3–6, 13, 15]. None of the patients in the current study experienced any serious side effects, such as adrenal insufficiency, gastrointestinal ulcers, or severe infection, suggesting that short-term administration does not present a major systemic risk.

Our study had some limitations, including a short follow-up period and small number of patients. Further studies with more patients and a longer follow-up are, therefore, required to define the role of this procedure.

In conclusion, the combination of balloon dilatation and intravenous methylprednisolone pulse therapy may provide a safe and effective treatment for esophageal strictures in children. All patients with esophageal strictures should be considered as potential candidates for this treatment option.

### Compliance with ethical standards

*Conflict of interest* The authors declare that they have no conflicts of interest.

## References

1. Miyashita M, Onda M, Okawa K et al (1997) Endoscopic dexamethasone injection following balloon dilatation of anastomotic stricture after esophagogastrostomy. Am J Surg 174:442–444. doi:10.1016/S0002-9610(97)00116-5

2. Said A, Brust DJ, Gaumnitz EA et al (2003) Predictors of early recurrence of benign esophageal strictures. Am J Gastroenterol 98:1252–1256. doi:10.1016/S0002-9270(03)00269-7

3. Hishiki T, Kouchi K, Saito T et al (2009) Successful treatment of severe refractory anastomotic stricture in an infant after esophageal atresia repair by endoscopic balloon dilation combined with systemic administration of dexamethasone. Pediatr Surg Int 25:531–533. doi:10.1007/s00383-009-2367-1

4. Kobayashi S, Kanai N, Ohki T et al (2014) Prevention of esophageal strictures after endoscopic submucosal dissection. World J Gastroenterol 20:15098–15109. doi:10.3748/wjg.v20.i41.15098

5. Wang W, Ma Z (2015) Steroid administration is effective to prevent strictures after endoscopic esophageal submucosal dissection. Medicine. doi:10.1097/MD.0000000000001664

6. Nonaka K, Ban S, Aikawa M et al (2013) Electrocautery therapy combined with oral steroid administration for refractory corrosive esophageal stenosis prevents restenosis. Esophagus 10:230–234. doi:10.1007/s10388-013-0375-7

7. Hu HT, Shin JH, Kim JH et al (2015) Fluoroscopically guided large balloon dilatation for treating congenital esophageal stenosis in children. Jpn J Radiol 33:418–423. doi:10.1007/s11604-015-0441-2

8. Michaud L, Coutenier F, Podevin G et al (2013) Characteristics and management of congenital esophageal stenosis: findings from a multicenter study. Orphanet J Rare Dis 8:186–190. doi:10.1186/1750-1172-8-186

9. Terui K, Saito T, Mitsunaga T et al (2015) Endoscopic management for congenital esophageal stenosis: a systematic review. World J Gastrointest Endosc 16:183–191. doi:10.4253/wjge.v7.i3.183

10. Ko HK, Shin JH, Song HY et al (2006) Balloon dilation of anastomotic strictures secondary to surgical repair of esophageal atresia in a pediatric population: long-term results. J Vasc Interv Radiol 17:1327–1333. doi:10.1097/01.RVI.0000232686.29864.0A

11. Said M, Mekki M, Golli M et al (2003) Balloon dilatation of anastomotic strictures secondary to surgical repair of oesophageal atresia. Br J Radiol 76:26–31. doi:10.1259/bjr/64412147

12. Jones DW, Kunisaki SM, Teitelbaum DH et al (2010) Congenital esophageal stenosis: the differential diagnosis and management. Pediatr Surg Int 26:547–551. doi:10.1007/s00383-010-2568-7

13. Morikawa N, Honnna T, Kuroda T et al (2008) High dose intravenous methylprednisolone resolves esophageal stricture resistant to balloon dilatation with intralesional injection of dexamethasone. Pediatr Surg Int 24:1161–1164. doi:10.1007/s00383-008-2224-7

14. Gandhi RP, Cooper A, Barlow BA (1989) Successful management of esophageal strictures without resection or replacement. J Pediatr Surg 24:745–749. doi:10.1016/S0022-3468(89)80529-9

15. Cadranel S, Scaillon M, Goyens P et al (1993) Treatment of esophageal caustic injuries: experience with high-dose dexamethasone. Pediatr Surg Int 8:97–102. doi:10.1007/BF00184209