BMJ Paediatrics Open

Treatment methods for oesophageal strictures in paediatric patients with epidermolysis bullosa: a systematic review

Majid Khademian,[1] Hosein Saneian,[1] Narges Zare ,[1] Fatemeh Famouri,[1] Peiman Nasri,[1] Mehri Moghadasi,[2] Roya Kelishadi[3]

To cite: Khademian M, Saneian H, Zare N, *et al*. Treatment methods for oesophageal strictures in paediatric patients with epidermolysis bullosa: a systematic review. *BMJ Paediatrics Open* 2024;**8**:e002689. doi:10.1136/bmjpo-2024-002689

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjpo-2024-002689).

Received 10 April 2024
Accepted 18 September 2024

For numbered affiliations see end of article.

Correspondence to
Dr Narges Zare; n.zare132@gmail.com

ABSTRACT

Background Epidermolysis bullosa (EB) is a collection of rare, inherited disorders that require treatment in specialised centres by multidisciplinary teams knowledgeable about the unique features and challenges of EB manifestations and complications.
A major gastrointestinal complication in patients with EB is oesophageal strictures. Effective management of oesophageal strictures can significantly improve patients' quality of life. This study systematically reviews the current literature on treatment options for oesophageal strictures in paediatric patients with EB.

Methods In September 2023, we conducted a systematic search for articles on the treatment of oesophageal stricture in patients with EB. We searched PubMed, Scopus, Embase and Ovid database without language or publication date restrictions. We screened 1042 articles, 15 of them were included in the current review. We extracted the following data from these studies: patient demographics, stricture characteristics, procedural details, clinical outcomes, complications and recurrences.

Results Overall, in the reviewed papers, strictures were located mostly in cervical oesophagus followed by thoracic lesions. Moreover, in most of the cases only a single stricture was reported, but multiple strictures were not uncommon. Stricture treatment approaches included medical management, bougienage, as well as fluoroscopic and endoscopic balloon dilation or a combination of these methods. In most studies, fluoroscopic dilation was used as the primary treatment method in 756 procedures. They commonly used general anaesthesia for the procedure, only one study used sedation. Hospital stays were usually brief, with an average duration of 1 day, and in one study patients were discharged after just 4 hours. Most patients experienced symptom relief, could resume oral intake and gained weight soon after the procedure. However, recurrence rates had large variations from 12% to 83%. Studies reported median recurrence intervals ranging from 7 to 18 months. This review showed that complications such as perforation, fever and odynophagia were relatively uncommon, and were controlled by conservative treatment.

Conclusions Both fluoroscopic and endoscopic balloon dilation are widely used methods for the management of oesophageal strictures in patients with EB. Each technique presents its own set of advantages and potential complications. Although the current evidence is notably limited, practical clinical decision-making may favour the fluoroscopic technique over endoscopic balloon dilation due to a comparatively reduced risk of procedural trauma. To ascertain the most effective approach, high-quality randomised controlled trials are imperative to delineate the superiority of one technique over the other.

KEY MESSAGE

Oesophageal strictures in paediatric patients with epidermolysis bullosa (EB) present a significant treatment challenge. This study aims to provide evidence-based recommendations to understand better the effectiveness of various treatment methods for oesophageal strictures in children with EB. The existing literature on this topic is limited and inconclusive, highlighting the importance of this research. The findings of this study can guide healthcare providers in selecting personalised treatment options for these patients. The recommendations from this study may impact future research and help develop standardised treatment protocols for these patients, potentially improving their clinical outcomes and quality of life.

INTRODUCTION

Epidermolysis bullosa (EB) is a rare inherited disorder characterised by tissue fragility. Despite its low prevalence, EB imposes a significant socioeconomic burden and affecting multiple organs. Treatment for patients with EB is best performed in expert centres by multidisciplinary teams.[1–4]

Oesophageal stricture (OS) is among the most prevalent gastrointestinal complications associated with EB.[5] OS and associated symptoms like dysphagia, food impaction and chest pain substantially impede the attainment of a satisfactory quality of life.[6] Effective management of OS improves patients' quality of life and nutritional status, enhanced growth and weight gain, as well as improvement in skin lesions.[7 8]

Effective management of EB in paediatric patients is essential due to its potential to disrupt oral swallowing, hinder growth and lead to complications, given the absence of a cure.[9] Treatment options for OS generally

commence with dietary modifications, a combination of balloon or bougienage oesophageal dilation, pharmacological therapy and surgical intervention.[10 11] Sole reliance on conservative medical treatment may yield suboptimal outcomes.[7] Surgical colonic interposition, as a last-resort measure, carries a high-mortality rate and various complications.[12]

Balloon dilation of OS, the most frequently employed treatment, can be administered through anterograde or retrograde endoscopic and fluoroscopic techniques. Limited research on therapeutic strategies for treating OS in paediatrics patients with EB, prompts ongoing clinical discussion. We aimed to review the current literature on dilation and medical treatment for paediatric patients with EB who have OS.

METHODS

In September 2023, we systematically searched for relevant articles in PubMed, Scopus, Embase and Ovid databases. This search was tailored by restricting the language of studies to English and focusing exclusively on human studies. We did not impose any limitations on the search time frame. The search strategy entailed using a combination of keywords, specifically "Esophageal Stricture", "Esophageal Stenosis", "Treatment", "Management", "Dilatation", "Restenosis" and "Epidermolysis Bullosa". Furthermore, to expand our search scope, we also leveraged the content and references of the identified studies to find additional relevant articles. The screening process involved a sequential assessment based on title, abstract and full text to gauge relevance and eligibility.

The target studies encompassed clinical studies focusing on various treatment modalities for EB paediatric patients (under 18) with OS. First, titles and abstracts of studies were screened and then case report studies investigating fluoroscopic and endoscopic balloon dilatation were excluded due to the abundance of available studies in this field. Then, a comprehensive analysis of selected studies was conducted to identify only relevant articles to be included in this review. Two independent reviewers completed all of the above screening processes. In our review of case series studies that investigated paediatric and adult patients, our primary focus was on paediatric patients. While some original studies exclusively explored paediatric patients, others encompassed the entire age range, including adults.

In addition to assessing the studies, we made efforts to collect relevant data on paediatric patients, but limited information in the studies often hindered this. We excluded original studies that solely examined adult patients.

Our systematic search identified 1042 articles. Of these, 15 studies were chosen for the final review,[7–9 12–23] as shown in figure 1.

Patient and public involvement

No patient involved.

Risk of bias assessment

In order to assess the risk of biases in our study, we used the National Institutes of Health (NIH) guidelines, which included two questionnaires for before-after (pre-post) studies with no control group and case series studies.[24]

RESULTS

Risk of bias in studies

According to the NIH guidelines, the assessment of biases in the studies conducted by MK and NZ revealed a low risk of bias in intervention studies at 45.4% and a moderate risk at 54.5% (online supplemental table 1). The biases for case series studies are outlined in online supplemental table 2.

Conservative medical treatment (topical corticosteroids—losartan)

Due to the pathophysiology of EB, patients often experience oesophageal involvement, frequent blistering, ulceration and chronic inflammation, resulting in ulceration and stenosis, which are common in most of these patients.[25]

We identified two studies encompassing eight patients, explicitly examining the therapeutic effects of topical budesonide on patients with EB and OS.[13 14] In Dohil *et al*'s study, administering oral viscous budesonide to a 16-year-old boy with EB and recurrent OS reduced the need for dilation from 3 to 5 dilations per year to 2 dilations in 18 months. Notable improvements were observed in the frequency of the patient's choking episodes, symptom severity and the interval between dilations and the onset of symptoms and dysphagia. This study also reported a case of a 9-year-old girl whose need for dilations decreased from three to five times per year to two times within 15 months with this treatment. The patient also did not experience any dysphagia or choking symptoms and could eat regular solid food even on the day before their dilation session.[13] Zanini *et al*'s clinical trial indicated that the administration of oral viscous budesonide caused a statistically significant reduction in OS indicators and improved nutritional status in patients with EB. Despite the small sample size, this constitutes a notable finding. However, it is crucial to consider potential side effects, such as oral mycotic infections and complications resulting from systemic absorption of corticosteroids, especially in long-term treatments. One out of six patients in this study was excluded during the intervention due to the development of oral mycotic infection.[14]

In another study, an attempt to delay the recurrence of OS involved the routine use of an oral steroid treatment regimen before and after the balloon dilation procedure. Although the follow-up period was relatively short, some patients with a history of frequent dilation experienced doubled intervals between dilations.[15] Pope *et al* reported medical treatment around balloon dilatation sessions in approximately half of the stricture episodes,

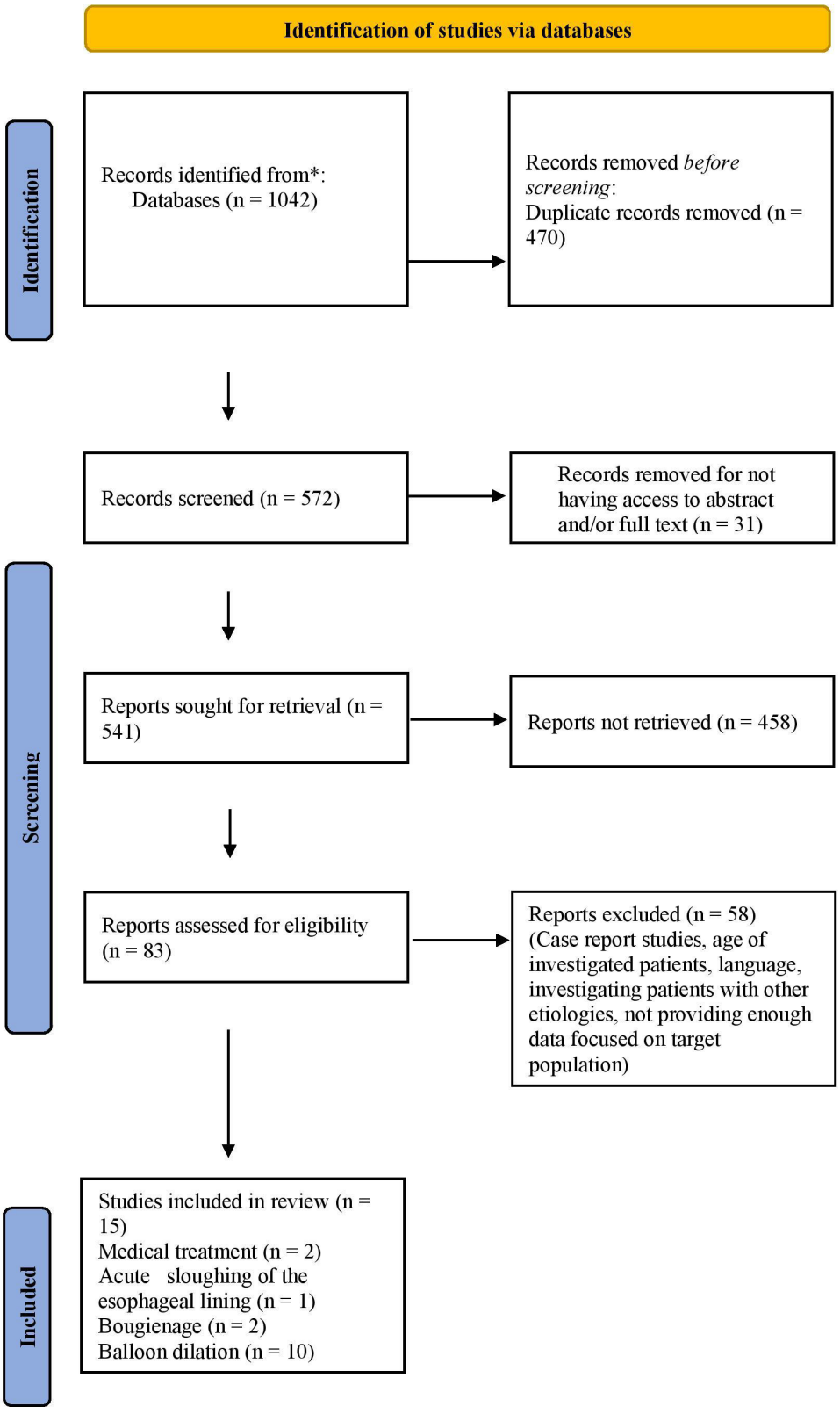

Figure 1 Study selection flow chart.

with 90% involving corticosteroid treatment with a mean (SD) treatment duration of 5.2 days following dilation. Notably, no significant relationship was found between medical treatment and the risk of recurrent strictures. Further investigation is needed to explore the potential of budesonide as a preventive intervention in high-risk individuals, given the limited opportunity to alter the natural course of the disease and the risk of OS.[12]

Oldakovskiy *et al* conducted a study to investigate the efficacy of losartan in preventing the recurrence

of strictures in patients with dystrophic epidermolysis bullosa undergoing balloon dilation. After 1 year, the recurrence rate of strictures was 11% (1 out of 9 patients) in the group treated with losartan and 40% (4 out of 10 patients) in the control group. In a study comparing the effects of losartan versus a control group on children with dysphagia, both groups showed improvements in dysphagia scores and nutritional deficiency indicators. However, the losartan group had significantly greater reductions in dysphagia scores and lower levels of Epidermolysis Bullosa Disease Activity and Scarring Index both before and after treatment. The study had limitations in sample size, follow-up duration and lack of thorough investigation into certain variables.[26]

Acute sloughing

Acute sloughing of the oesophageal lining can occur in patients with EB, constituting a critical emergency. This aspect has received less attention in previous studies. Bageta *et al* reported six cases of patients with EB experiencing acute sloughing of the oesophageal lining, with a mean age of 2.7 years. Online supplemental table 3 provides a summary of the condition of the examined patients. Most of the patients in the study responded well to medical, while two cases necessitated gastrostomy tube insertion due to persistent symptoms. Notably, none of the OS cases were reported prior to hospitalisation due to sloughing. Subsequent strictures were observed in five patients, and these were promptly treated with dilation following the sloughing episode, extending up to 1 year later.[16]

Bougienage

The primary adverse effects of bougienage include mucosal damage and oesophageal perforation.[17 27 28] During bougienage, the dilatation occurs by applying axial force to the stricture, progressing from proximal to distal. Conversely, when using balloon dilation, a radial force is simultaneously applied across the entire length. Consequently, balloon dilation is generally considered a safer option than bougienage dilation. Currently, limited studies have investigated oesophageal dilatation's outcomes and adverse effects using the bougienage method in children, including those with EB, and compared it with balloon dilatation.[29]

Kern *et al* reported on seven children with recessive dystrophic epidermolysis bullosa (RDEB) and OS who were treated with endoscopic bougienage dilatation. Re-dilatation was required for all patients within a year of the initial treatment, with intervals ranging from 5 weeks to 1 year. Following this, most patients remained asymptomatic for several years, with some remaining symptom-free for up to 10 years. Unfortunately, one patient experienced a fatal outcome due to oesophageal perforation.[17] Study by Lee *et al* reported successful treatment of OS in a 15-year-old patient with RDEB using endoscopic bougienage. Limited information on long-term outcomes was provided. Medical treatments included corticosteroids and phenytoin.[18]

Endoscopic and fluoroscopic balloon dilatation

Patients, lesions, interventions and outcomes

As mentioned in the Methods section, case reports in this field were excluded. As shown in table 1, 10 case series on fluoroscopy and balloon dilatation were ultimately retained for further investigation.[7–9 12 15 19–23] These studies encompassed a total of 325 patients. Excluding the two studies by Anderson *et al*[7] and Vowinkel *et al*,[9] in which sex distribution was not precisely determined, approximately 48% of the studied patients were males.[8 12 15 19–23] In the study of Vowinkel *et al*, overall, 756 fluoroscopic and 503 endoscopic interventions were performed.[9] The studied lesions were primarily located in the proximal section of the oesophagus, followed by the middle part, with a limited number of lesions in the distal part. Most studied patients had single lesions.[7–9 12 15 19–23] The follow-up period for the studied patients was relatively long, with a minimum follow-up duration of 6 months.[22]

The procedures performed in three studies differed from the others. Castillo *et al*'s therapeutic approach involved a combination of endoscopy, fluoroscopy and endotracheal intubation.[21] (A chest X-ray is taken to confirm the endotracheal tube's placement and check for lung issues. An endoscope was inserted into the oesophagus, marked at the stricture site, and a guide wire was passed through it into the stomach. A balloon dilator was passed over the wire to dilate the stricture. Fluoroscopy ensured success and lack of perforation following the procedure.) In Vowinkel *et al*'s study, a two-step multidisciplinary approach was introduced in which patients initially underwent anterograde endoscopic dilation under general anaesthesia with the insertion of a gastrostomy during the same session. Further dilations were performed fluoroscopically by a retrograde manner through the gastrostomy during a brief sedation period.[9] In De Angelis *et al*'s study, the endoscopic method was employed in conjunction with gastrostomy insertion for cases of severe stricture in the proximal or middle oesophagus.[22]

Eight studies used general anaesthesia and endotracheal intubation as the primary anaesthetic approach, whereas two used sedations with no intubation.

Hospitalisation, recurrence, outcome and treatment success

Notably, the frequency, severity and intervals of recurrences cannot be solely attributed to the intervention method and the extent of dilatation. Recurrence rate and intervals can also be influenced by factors such as the follow-up period, stricture length, patients' age, diet, sex, medical treatment and the severity of the disease.[12 14 30–33] Not all reviewed studies provided accurate recurrence rates. The highest recurrence rate, at 83.3%, was observed in the 2018 study by Anderson *et al*, which primarily focused on paediatric patients. This study boasted a relatively extended follow-up period compared with others,

Table 1 A summary of studies on different management strategies of oesophageal strictures in patients with EB

Study	Intervention	Patients and time of F/U	Lesions and procedures	Recurrence—success rate	Major/minor AEs
Anderson *et al*[7]	231 fluoroscopy BD (8.6% retrograde due to microstomia), 4[5–12] dilation per patient, GA+fibreoptic nasotracheal intubation	In 13 years of survey 24 patients with a median age of 4 years[3–9] at initial dilation (1–19). 23 RDEB and 1 KS	More common in proximal, median 13 cm from lips. A single stricture was found in 73.2% of procedures whereas multiple strictures were dilated in 26.8% of procedures	20 patients (83.3%) underwent repeated dilations with a median interval of 164 days (117–273). Among those with multiple dilations, 1 remained dilatation-free for 5 years, 2 were non-dilated for 2 years and 6 have not been dilated for over 1 year	46% experienced ≥1 AEs during a dilation session. 10% of dilations had 29 AEs, with significant AEs (grade ≥2) in 8.7% of all procedures. Common grade ≥2 AEs included fever, pain and vomiting*
De Angelis *et al*[22]	Total 93 dilations (mean 3.3 per patient, 1–11), 87 (93.5%) fluoroscopy BD and 6 endoscopic BD were performed with sedation and anaesthetic facemask. 38.2% of patients underwent one dilation	34 patients (18 (52.9%) male; mean age of onset of 18 years; 3–45). The mean (SD) age at the initial procedure was 10 (8) (2–38) years. Mean F/U time of 5.5 years (6 months to 14 years). 32 (94.1%) patients with RDEB, 1 with simplex EB and 1 with KS	17 (50%) patients had one lesion (10 (58.8%) in the middle and rest in cervical oesophagus), 17 had multiple lesions (21 cervical (<1 cm), 21 middle, 3 lower (mean length of middle and lower strictures were 2.4 cm (1–6))	In 95.5% of patients, fluoroscopic BD without the endoscopy were successfully performed (effectiveness, 93.5%)	Two perforations 10.7% had transient dysphagia. No patients experienced cutaneous issues, such as erythema, skin desquamation, delayed necrosis or worsening of skin lesions due to our procedure
Azizkhan *et al*[15]	92 fluoroscopic BD, mean of 4 per patient (1–14)	25 patients with RDEB (36.0% males), mean (SD) age at first procedure was 10 (8) (2–38) years, median F/U time was 3.2 years (1–11 years)	15 (60%) patients had single strictures (13 (86.7%) proximal, 1 (6.7%) distal), 7 (28%) had two strictures (5 (71.4%) in proximal and midsection, 2 (28.6%) in mid and distal), 3 (12.0%) had three lesions, each in three sections	Six (24%) patients required only one dilatation, the mean interval between dilatations was 1 year (range, 1.5 months–4.5 years)	No major complication. One patient, post-dental extractions, aspirated 12 after procedure, necessitating a week of intensive respiratory care, with full recovery

Continued

Table 1 Continued

Study	Intervention	Patients and time of F/U	Lesions and procedures	Recurrence—success rate	Major/minor AEs
Castillo *et al*[21]	109 combining upper endoscopy using small calibre endoscopes, EI and fluoroscopic balloon dilatation. Mean of five dilations per patient (1–18) with GA and EI	22 patients (12 men), age of 20 months to 16 years (48±34 months), 9 years of F/U	14 single lesions (9 (64.3%) located in proximal-cervical and 5 (35.7%) in mid-section), 8 (36.4%) patients had two lesions (cervical-mid section)	Six (27.2%) required only one dilatation. Mean (SD) interval between dilatations was 11±9 months (1 month to 3 years)	In the first year, one intramural oesophageal tear and one contrast aspiration occurred, both requiring medical treatment and a short hospital stay. No complications in the next 8 years, including those related to EI, post-intubation stridor or respiratory complication requiring intubation
Pope *et al*[12]	451 dilations: 45.2% fluoroscopic balloon, 33.0% retrograde endoscopy, 19.0% antegrade endoscopy. Median stricture episodes: 2.[1–7] GA with intubation was preferred in 87.58%, while 2.4% underwent sedation	125 patients (53% male), mean age at first episode of 12.6 years (8.2), 497 stricture episodes, mean F/U of 16.9 years (11.9). 123 with RDEB, and 1 with JEB and KS each	76.7 lesions were upper, 56.7 were middle and 9.6 were abdominal, with long segment involvement (>1 cm) being the predominant presentation	Median (IQR) dilation interval: 7 months.[4–12] Success rate: 99.33% (448/451), 96% fully dilated to oesophageal calibre and 3.33% partially dilated. No outcome difference based on the dilation method. 10 fluoroscopy and 8 endoscopy patients had partial or unsuccessful dilation	Rare transient complications (12 of 451 (2.66%)) included haemorrhage (3), tear (1), chest pain (2) and non-specified (9). Endoscopic approach had more complications (4.2%) (8/86 antegrade (9.3%), 2/149 retrograde (1.3%)) than 2/204 fluoroscopy (1%)
Anderson *et al*[19]	182 endoscopic balloon dilations (median 2[1–4] per patient) with sedation and a nasal mask. Five patients had prior gastrostomy tube	53 patients (41.6% men), median age at index endoscopy of 16 years (9.5–28), 3.5 years F/U. 49 (92.3%) RDEB, 1 dominant dystrophic EB, 1 acquired EB; 1 patient had an uncertain genotype	75% had a single stricture (1–6), median 20 cm from incisors	45% (24) needed one dilation, with a median (IQR) interval of 18 months (14 day–24.5 months). Initial unsuccessful dilation in three patients (no improvement in dysphagia score) with later succeess	No mortality or perforation. Self-limiting odynophagia occurred in three (5.7%) patients

Continued

Table 1 Continued

Study	Intervention	Patients and time of F/U	Lesions and procedures	Recurrence—success rate	Major/minor AEs
Gollu *et al*[20]	56 endoscopic balloon dilations (mean 5 procedures per patient) under GA with EI	11 patients (36.3% males), median age of 14 years[2–32] median (IQR) F/U of 41 months (19–60)	All but one (9.0%) child had a single lesion. Seven (64%) patients had middle, three (27%) had cervical oesophageal and one (9%) had cervical and middle OS. 72.7% of lesions were middle, the rest were proximal	Not achieving optimal nutritional status in a 32 years female led to colon interposition. 2/7 of remained patients in the programme have dysphagia to solid food between dilations	One patient underwent gastrostomy after a perforation during dilatation; another quit the programme, and a third declined colon interposition, later succumbing to complications from amyloidosis
Vowinkel *et al*[9]	Two-step approach: general anaesthesia with endotracheal intubation in the first step, followed by sedation in the second step	12 children with RDEB (median age: 7.8 years, range: 6 weeks to 17 years), with a median F/U of 6.4 years (range: 9 months to 12 years)	N/A	During follow-up, five children (median age: 10.9 years) had recurrent lesions and underwent step 2	Two uncomplicated wound infections were treated conservatively. One child's gastrostomy removed after 10 days due to skin ulcerations
Spiliopoulos *et al*[8]	121 fluoroscopic dilations averaged 1.19 per patient per year. 48.7% dilations in upper, 5.0% in lower segment	19 dystrophic EB (18 (94.7%) recessive and 1 dominant) patients (42.1% males) aged 10–51 years (mean±SD: 30±12.2), with a mean F/U of 47.51±16.64 months (17–73)	28 lesions: 16 upper, 2 lower; all short, tight focal strictures	Procedures technical success: 96.7% (87/90). Reintervention rate for clinical recurrence: 94.7% (18/19), lesion reintervention rate: 92.8% (26/28). 31.6% had a dilation-free interval >2 years, 10.5% >3 years; 2 patients had intervals >4 and 5 years	No—N/A
Zanini *et al*[14]	4 months of two times per day oral budesonide nebuliser solution (0.5 mg/2 mL) with maltodextrin (5 g)	Six patients with dystrophic EB (three males) aged 8–17 years	Six moderate-to-severe lesions (five proximal and one distal)	Significant decrease in stricture index scores Improved food intake status	Oral candidiasis halted treatment
Mavili *et al*[23]	27 fluoroscopically dilatation	Seven patients aged from 6 to 18 years (four boys and three girls)	Different levels of strictures in six patients, ranging from 70% to 90% severity, at the cervical, midoesophagus and multiple levels	Five out of seven needed multiple dilatations. Time intervals: 3–57 months (average of 16.5 months)	Fever, vomiting and aspiration, self-limiting haemorrhage, severe oesophageal stenosis 13 days after procedure (one case)

*Complications were graded from 1 to 5, with higher grades requiring more severe interventions. Grade 1 involved home care, grade 2 needed outpatient treatment, grade 3 required hospitalisation, grade 4 involved intensive care or surgery and grade 5 led to death. Grades 2 and above posed significant risks and increased medical costs.
AEs, adverse events; BD, balloon dilatation; EB, epidermolysis bullosa; EI, endotracheal intubation; OS, oesophageal strictures; F/U, follow-up; GA, general anaesthesia; JEB, junctional epidermolysis bullosa; KS, Kindler syndrome; RDEB, recessive dystrophic epidermolysis bullosa.

with 95.8% of the participants suffering from RDEB, which can be highly susceptible to OS.[7] Conversely, in the 2004 study by Anderson *et al*, encompassing children and adults, the recurrence rate was 45%, with a median (IQR) interval of 18 months. Differences in participant age, follow-up duration and intervention methods, and the choice of procedure, may impact recurrence rates between the two studies.[19] The study by Vowinkel *et al*[9] reported the lowest recurrence rate at 41.6%. In five other studies, the recurrence intervals were reported in a range of 5.5–18 months.[7 12 15 19 21]

Outcome measurement methods varied among studies. In Azizkhan *et al*'s study, most patients reported immediate relief of symptoms and showed the ability to resume adequate oral nutrition within 1 day of fluoroscopic dilation, with nearly all patients experiencing significant weight gain within 4–6 weeks.[15] In the study by Anderson *et al*,[7] dilation repetition within a few days was observed in only one patient, and the highest dilation rate per year was 6. A study conducted by Anderson *et al*[19] found that 38 patients experienced a significant mean weight gain of 2.9 kg, mean increase in body mass index of 1.9 and a decrease in dysphagia scores over a median follow-up of 29 days. Furthermore, five patients had a gastrotomy tube inserted before the study, and their weight gain did not significantly differ from the other participants. Notably, less than half of the patients in this study were adults, and detailed information on outcome and intervention complications based on age and other demographic variables was not provided.[19]

In De Angelis *et al*'s study, 30 patients could resume oral feeding within 24 hours after dilation, while 4 patients, 2 of whom had suffered perforations, resumed oral feeding within 7 days. 10 patients reported mild and transient dysphagia within 12 hours of dilation but could still consume a soft diet. The success rate of fluoroscopic method in this study was reported to be 93.5%.[22] The two-step multidisciplinary approach performed in Vowinkel *et al*'s study facilitated height and weight percentile in children with EB. Gastrostomy significantly reduces the physical and emotional stress experienced by parents and children, especially concerning eating.[9] Eight patients were observed by Gollu *et al* following an intervention, which resulted in an average weight gain of 12.3 kg over an average follow-up period of 41 months. Out of nine patients, seven showed significant improvement in dysphagia severity, with both patients and their parents reporting improved swallowing, reduced symptoms and even better skin conditions.[20] In the study by Spiliopoulos *et al*, which primarily focused on adults, the success rate was reported to be 96.7%. Dysphagia scores after dilatation were significantly lower than at baseline. Three patients had to undergo gastrostomy to ensure adequate nutrition, whereas another required it due to a stricture that could not be dilated. Three cases of treatment failure were encountered, including a severe stricture, obstruction of the guide wire by an artificial airway and a missed second stenosis during pre-dilatation imaging. In all three instances, additional procedures were successfully performed. The survival rate among patients after 6 years of follow-up was 89.2%, with two patients dying from metastatic squamous cell carcinoma.[8]

In a study that considered a combined approach, post-dilation oesophageal endoscopy consistently indicated a notable improvement in oesophageal calibre (easier endoscope passage through the dilated stricture site compared with pre-dilation endoscopy). Postoperative dysphagia was minimal, as all children could tolerate oral liquids intake before discharge from the recovery ward and solid food within 6 hours postoperatively. Weight gain was observed and no gastrostomy placement or medical treatments were needed.[21] In Pope *et al*'s study, dilation was successful in 99.3% of cases, regardless of the procedure method (chosen based on patient preference). Complete dilation was achieved in approximately 96% of cases, while only 3.33% achieved partial dilation.[12]

Patients without complications were typically discharged from the hospital the day following the procedure. The shortest hospitalisation duration, at 4 hours, was noted in the study by Castillo *et al*.[21]

In Mavili *et al*'s study, out of the 87 interventional procedures, 27 (31%) were oesophageal dilatations conducted on seven patients (four boys and three girls) due to symptoms of dysphagia and confirmed OS on previous oesophagograms. Five out of seven patients needed to undergo more than one oesophageal dilatation procedure, with the number of dilatations ranging from 2 to 13. All patients underwent post-procedure overnight observation for 24 hours before being discharged. In terms of complications, tracheal aspiration, submucosal tearing, small self-limited bleeding and acute blistering leading to dysphagia were reported.[23]

Complications

The complications caused by the interventions in the studied patients can be considered limited. In investigating minor side effects, it is necessary to acknowledge that the reviewed studies were often conducted retrospectively, limiting the study in many aspects, such as assessing minor complications during the follow-up. Five studies reported minor complications such as pain, fever, vomiting, nausea, transient odynophagia and dysphagia. These complications did not prolong hospitalisation and were manageable with supportive treatment.[7 12 19 22 23]

Anderson *et al*'s 2018 study evaluated side effects up to 72 hours post-procedure. None of the complications were observed in 54% of patients. 8.7% had significant side effects, with fever, pain and vomiting being the most common. 6.9% experienced complications needing monitoring or treatment. All patients were discharged within 24 hours after the procedure. Complications were more common in antegrade endoscopic dilation patients but not statistically significant. Endoscopic assessment before the primary procedure (performed in 25%) did not significantly affect side effects.[7]

In patients with EB, balloon dilation for strictures requires less pressure and a shorter duration, leading to a low perforation rate.[8 22] Oesophageal perforation/tearing was identified as a significant complication in four studies and five patients (all under endoscopy).[12 20–22] De Angelis *et al*'s study observed two cases of oesophageal perforation; one was a 3-year-old patient, in whom perforation was managed with soft pharyngeal aspiration, complete parenteral nutrition and antibiotic therapy. The patient later underwent successful dilation. Another case was a patient unable to undergo dilation due to the severity of the stricture and instead underwent a gastrostomy. Then, a combined attempt using two endoscopes (anterograde and retrograde) to pass the guide wire failed but resulted in perforation of the cervical oesophagus. This perforation was also managed conservatively.[22] Castillo *et al* observed one case of contrast aspiration and one case of oesophageal rupture in their study. Both cases were successfully treated with medical intervention and short hospital stays.[21]

In patients with gastrostomy, performing the balloon dilation procedure using the retrograde method, considering the lower risk of trauma to the mouth, pharynx and upper oesophagus exposed to stricture may be preferable due to the higher likelihood of severe and frequent strictures in these patients.[34] In Gollu *et al*'s study, a case of oesophageal perforation was managed with medical care and gastrotomy tube insertion. Following a 10-day hospitalisation, the patient was discharged after successfully restoring their ability to consume food orally.[20] Therefore, all cases of perforation in patients undergoing endoscopy were mainly caused by trauma from the endoscope's movement and not directly by the dilation of the balloon. These cases were successfully managed with medical treatment, soft pharyngeal aspiration, complete parenteral nutrition and gastrostomy tube insertion, but they did undergo prolonged hospitalisation.[12 20–23] The primary complications observed in Vowinkel *et al*'s study included wound infection and severe skin ulcers caused by gastrostomy tube insertion. In Spiliopoulos *et al*'s study, one of the examined patients had an oesophageal injury during endoscopy before entering the study, and OS in this patient also improved with the help of the fluoroscopic method.[9]

Summary, insights

Studies conducted on children primarily focused on the fluoroscopic balloon dilation method and explored the use of the endoscopic method in combination with or as a complement to the fluoroscopic method.[7 9 12 21] Generally, both methods can be used for patients with EB and OS. As physicians have shifted away from the more invasive approaches used in the past, like bougienage, balloon dilation of OS has become the most widely used treatment, especially in patients with benign aetiologies.[20 35] The endoscopic method offers the advantage of direct visualisation of the oesophagus, allowing for more accurate assessment of the balloon's calibre and pressure, prompt detecting of perforations or bleeding, as well as identifying additional strictures and potential pathologies that may be missed by other imaging methods.[20] Endoscopic balloon dilation is effective but can cause trauma to the mouth, pharynx and oesophagus. Fluoroscopic technique offers a way to minimise this trauma.[12 20–23] According to the findings of reviewed studies and similar research on patients with various aetiologies of OS, endoscopy can independently lead to oesophageal perforation, irrespective of the balloon extension effect.[19–22 36]

On the contrary, fluoroscopic method is the most employed management strategy for patients with EB.[7–9 12 15 19–23] Fluoroscopic-guided balloon dilation offers better visual monitoring and precise positioning compared with endoscopic methods, making it more effective and precise for treating narrow structures in oesophagus.[37] Despite many potential benefits, fluoroscopy can have potential disadvantages, such as exposing patients to radiation. Minimising radiation exposure is crucial because patients with EB, especially the dystrophic type, may already be predisposed to squamous cell carcinoma. However, no studies have established a direct correlation between elevated rates of skin cancer and fluoroscopy in patients with EB.[38] One limitation of endoscopic dilation is use of small balloons, restricting the diameter of oesophageal dilation. In contrast, fluoroscopic dilation allows for larger balloon sizes, potentially leading to longer intervals between dilations, although this may not be the case for children.[15 19 21 39]

Fluoroscopic method is currently the preferred choice for children due to its high success rate and minimal complications, but more research is needed to assess its effectiveness in preventing recurrence and improving patient outcomes. It is crucial to be proactive in preventing oesophageal perforation and extended hospital stays, especially in paediatric patients with EB who are already prone to complications and a reduced quality of life.[40] Combining these two dilation methods, using minimum calibre endoscope and employing the retrograde method in patients with gastrostomy may partially overcome the limitations associated with each method. Concurrently, exploring medical treatments to prevent recurrence, improve outcomes and extend the intervals between dilations is imperative.

CONCLUSION

Although few case studies and small clinical trials have shown benefit of short-term periprocedural administration of oral corticosteroids, in patients with EB, this issue has not been confirmed by a larger cohort study. Further investigation is needed to explore the potential of corticosteroids as an adjuvant therapy in dilatation sessions.

Losartan, has shown positive effects in reducing the risk of recurrent OS in patients with EB. Also, other benefits such as decrease in the disease severity index and dysphagia score have been shown, which need to be confirmed by future studies.

Bougienage treatment of OS with multiple aetiologies has the benefits of shorter operation duration, lower cost and low complication, while a high success rate. Bougienage treatment on eight patients with EB in the form of two studies showed acceptable results after two dilation sessions, but with a high mortality rate (one out of eight).

Endoscopic advantages are direct visualisation of the oesophagus, assessment of the balloon's calibre and pressure, prompt detection of perforations or bleeding during procedure, identification of additional strictures and potential pathologies. During the procedure, mucosal trauma of oropharynx and small risk of perforation may occur, independent of the balloon expansion effect.

Gastrostomy can be inserted with benefits of improving nutritional state and reduction of stress for parents and children during endoscopy. It also provides a route for retrograde dilation with less trauma in subsequent sessions performed under brief sedation.

Compared with the endoscopic method, fluoroscopic-guided balloon dilation provides superior visual monitoring during balloon expansion.

Outcome measurement methods varied among studies, so it is not possible to accurately compare the success rate of dilatation in existing studies.

Minor complications such as: pain, fever, vomiting, odynophagia and dysphagia had been reported in some studies which did not prolong hospitalisation. In few cases, significant complications such as oesophageal perforation were seen, all managed with conservative treatment. Perforations were seen mostly in antegrade endoscopic dilation method.

One limitation of this review is the scarcity of literature on the management of OS in individuals with EB. The existing research mainly consists of retrospective case series and cohort studies with a limited number of participants, reflecting the rarity of the condition.

Author affiliations
[1]Pediatrics Department, Metabolic Liver Disease Research Center, Research Institute of Primordial Prevention of Non-Communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran (the Islamic Republic of)
[2]Research Institute of Primordial Prevention of Non-Communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran (the Islamic Republic of)
[3]Pediatrics Department, Metabolic Liver Disease Research Center, Child Growth and Development Research Center, Isfahan University of Medical Sciences, Isfahan, Iran (the Islamic Republic of)

Contributors MK: supervisor author; provided overall supervision and guidance for the research project. HS: contributed to planning the study; involved in designing the research framework and methodology. NZ: corresponding author, responsible for reporting the work described in the article; involved in drafting and revising the manuscript. FF: served as a scientific advisor; provided critical insights and feedback throughout the study. PN: served as a scientific advisor; offered expertise and guidance in specific areas of the research. MM: collected data; actively involved in the acquisition and management of research data. RK: guarantor; accepts full responsibility for the finished work and the conduct of the study, had access to the data, and controlled the decision to publish. All individuals named in this statement have given their permission to be included, as their contributions are acknowledged. Each contributor's nature of involvement has been agreed upon through open discussions among the participants. Additionally, we recognise the importance of contributions by patients and the public, if applicable, and appropriately acknowledge their roles in the research.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study was evaluated by Research Ethics Committees of School of Medicine—Isfahan University of Medical Sciences and was found to be in accordance to the ethical principles and the national norms and standards for conducting Medical Research in Iran (approval ID: IR.MUI.MED.REC.1402.331).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. In accordance with the guidelines provided, we require that the data generated from our research on this article be made openly and publicly available upon publication of our article. We understand the importance of transparency and accessibility in academic research and are committed to supporting this initiative. In cases where it is not feasible to make this data openly available, we will ensure that the data is shared through a controlled access repository. This approach will allow us to protect sensitive information while still making our findings accessible to the broader research community. We affirm our commitment to adhering to these standards, ensuring that our research contributes to the ongoing dialogue and advancements in the treatment of paediatric oesophageal strictures associated with epidermolysis bullosa.

ORCID iD
Narges Zare http://orcid.org/0009-0004-4123-5401

REFERENCES

1 Fine J-D. Inherited epidermolysis bullosa. *Orphanet J Rare Dis* 2010;5:12.
2 Forghani SF, Jahangiri R, Ghasemi F, *et al*. Economic Burden of Epidermolysis Bullosa Disease in Iran. *Med J Islam Repub Iran* 2021;35:146.
3 du Rand A, Hunt JMT, Feisst V, *et al*. Epidermolysis Bullosa: A Review of the Tissue-Engineered Skin Substitutes Used to Treat Wounds. *Mol Diagn Ther* 2022;26:627–43.
4 El Yacoubi O, Chbicheb S. Recessive dystrophic epidermolysis bullosa (RDEB): Oral manifestation and management rules in oral surgery: A case report. *Int J Surg Case Rep* 2023;102:107848.
5 Fine J-D, Johnson LB, Weiner M, *et al*. Gastrointestinal complications of inherited epidermolysis bullosa: cumulative experience of the National Epidermolysis Bullosa Registry. *J Pediatr Gastroenterol Nutr* 2008;46:147–58.
6 Anand N, Sharma A, Shah J, *et al*. Quality of life in patients of corrosive esophageal stricture treated with endoscopic dilatation. *JGH Open* 2021;5:301–6.
7 Anderson BT, Feinstein JA, Kramer RE, *et al*. Approach and Safety of Esophageal Dilation for Treatment of Strictures in Children With Epidermolysis Bullosa. *J Pediatr Gastroenterol Nutr* 2018;67:701–5.
8 Spiliopoulos S, Sabharwal T, Krokidis M, *et al*. Fluoroscopically guided dilation of esophageal strictures in patients with dystrophic epidermolysis bullosa: long-term results. *AJR Am J Roentgenol* 2012;199:208–12.

9 Vowinkel T, Laukoetter M, Mennigen R, *et al*. A two-step multidisciplinary approach to treat recurrent esophageal strictures in children with epidermolysis bullosa dystrophica. *Endoscopy* 2015;47:541–4.
10 Chahed J, Mekki M, Ksia A, *et al*. Management of digestive lesions associated to congenital epidermolysis bullosa. *Afr J Paediatr Surg* 2015;12:221–6.
11 Feinstein JA, Jambal P, Peoples K, *et al*. Assessment of the Timing of Milestone Clinical Events in Patients With Epidermolysis Bullosa From North America. *JAMA Dermatol* 2019;155:196–203.
12 Pope E, Mansour M, Berseneva M, *et al*. Outcomes and Predictors for Re-stenosis of Esophageal Stricture in Epidermolysis Bullosa: A Multicenter Cohort Study. *J Pediatr Gastroenterol Nutr* 2020;71:310–4.
13 Dohil R, Aceves SS, Dohil MA. Oral viscous budesonide therapy in children with epidermolysis bullosa and proximal esophageal strictures. *J Pediatr Gastroenterol Nutr* 2011;52:776–7.
14 Zanini A, Guez S, Salera S, *et al*. Oral viscous budesonide as a first-line approach to esophageal stenosis in epidermolysis bullosa: an open-label trial in six children. *Paediatr Drugs* 2014;16:391–5.
15 Azizkhan RG, Stehr W, Cohen AP, *et al*. Esophageal strictures in children with recessive dystrophic epidermolysis bullosa: an 11-year experience with fluoroscopically guided balloon dilatation. *J Pediatr Surg* 2006;41:55–60; .
16 Bageta ML, Yerlett N, Rybak A, *et al*. Management of acute sloughing of the esophageal lining in patients with dystrophic epidermolysis bullosa-A series of six pediatric patients. *Pediatr Dermatol* 2023;40:1010–4.
17 Kern IB, Eisenberg M, Willis S. Management of oesophageal stenosis in epidermolysis bullosa dystrophica. *Arch Dis Child* 1989;64:551–6.
18 Lee CW, Song KH, Kim KH. A case of recessive dystrophic epidermolysis bullosa with esophageal stenosis treated with endoscopic bougienage. *J Dermatol* 2002;29:628–32.
19 Anderson SHC, Meenan J, Williams KN, *et al*. Efficacy and safety of endoscopic dilation of esophageal strictures in epidermolysis bullosa. *Gastrointest Endosc* 2004;59:28–32.
20 Gollu G, Ergun E, Ates U, *et al*. Balloon dilatation in esophageal strictures in epidermolysis bullosa and the role of anesthesia. *Dis Esophagus* 2017;30:1–6.
21 Castillo RO, Davies YK, Lin Y-C, *et al*. Management of esophageal strictures in children with recessive dystrophic epidermolysis bullosa. *J Pediatr Gastroenterol Nutr* 2002;34:535–41.
22 De Angelis P, Caldaro T, Torroni F, *et al*. Esophageal stenosis in epidermolysis bullosum: a challenge for the endoscopist. *J Pediatr Surg* 2011;46:842–7.
23 Mavili E, Amaral J, Healey A, *et al*. Percutaneous Interventional Radiology Procedures in Patients With Epidermolysis Bullosa: Modifications and Challenges. *Am J Roentgenol* 2010;195:468–75.
24 Study quality assessment tools, Available: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools
25 Gupta R, Woodley DT, Chen M. Epidermolysis bullosa acquisita. *Clin Dermatol* 2012;30:60–9.
26 Oldakovskiy V, Murashkin N, Lokhmatov M, *et al*. Our experience of using Losartan for esophageal stenosis in children with dystrophic form of congenital epidermolysis bullosa. *J Pediatr Surg* 2023;58:619–23.
27 Gryboski JD, Touloukian R, Campanella RA. Gastrointestinal manifestations of epidermolysis bullosa in children. *Arch Dermatol* 1988;124:746–52.
28 Griffin RP, Mayou BJ. The anaesthetic management of patients with dystrophic epidermolysis bullosa. A review of 44 patients over a 10 year period. *Anaesthesia* 1993;48:810–5.
29 Kay M, Wyllie R. Endoscopic dilatation of esophageal strictures in recessive dystrophic epidermolysis bullosa: new equipment, new techniques. *J Pediatr Gastroenterol Nutr* 2002;34:515–8.
30 Agha FP, Francis IR, Ellis CN. Esophageal involvement in epidermolysis bullosa dystrophica: clinical and roentgenographic manifestations. *Gastrointest Radiol* 1983;8:111–7.
31 Okada T, Sasaki F, Shimizu H, *et al*. Effective Esophageal Balloon Dilation for Esophageal Stenosis in Recessive Dystrophic Epidermolysis Bullosa. *Eur J Pediatr Surg* 2006;16:115–9.
32 Hammoudi N, Giaoui A, Lambert J, *et al*. Predictive factors for the success of endoscopic dilation of esophageal caustic stricture: the experience of a French tertiary reference center. *Surg Endosc* 2022;36:5660–8.
33 Said A, Brust DJ, Gaumnitz EA, *et al*. Predictors of early recurrence of benign esophageal strictures. *Am J Gastroenterol* 2003;98:1252–6.
34 Hawkins DB. Dilation of esophageal strictures: comparative morbidity of antegrade and retrograde methods. *Ann Otol Rhinol Laryngol* 1988;97:460–5.
35 Henkens N, Wauters L, Vanuytsel T. Intralesional steroid injections in addition to endoscopic dilation in benign refractory esophageal strictures: a systemic review. *Acta Gastroenterol Belg* 2020;83:432–40.
36 Salo JA, Sihvo EI. *Surg treat evid-based probl-oriented zuckschwerdt*. In: *Instrumental perforation of the esophagus*. 2001.
37 Blount KJ, Lambert DL, Shaffer HA, *et al*. De Lange EE. *Semin Intervent Radiol* 2010.
38 Fasulakis S, Andronikou S. Balloon dilatation in children for oesophageal strictures other than those due to primary repair of oesophageal atresia, interposition or restrictive fundoplication. *Pediatr Radiol* 2003;33:682–7.
39 Heyman MB, Zwass M, Applebaum M, *et al*. Chronic recurrent esophageal strictures treated with balloon dilation in children with autosomal recessive epidermolysis bullosa dystrophica. *Am J Gastroenterol* 1993;88:953–7.
40 García-Espinosa L, del Rosal T, Quintana L, *et al*. Bloodstream Infection in Children With Epidermolysis Bullosa. *Pediatr Infect Dis J* 2023;42:510–4.