



Esophageal strictures in children with recessive dystrophic epidermolysis bullosa: an 11-year experience with fluoroscopically guided balloon dilatation

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Abstract

Background: Recessive dystrophic epidermolysis bullosa (RDEB) is an inherited blistering skin disorder that is associated with significant esophageal strictures, resulting in dysphagia and nutritional failure. Although endoscopically guided balloon dilatation is a widely used treatment, the use of an endoscope carries the risk of oropharyngeal trauma. To minimize this risk, we have eliminated its use. **Method:** We reviewed the charts of all RDEB patients who underwent balloon dilatation for esophageal strictures between August 1993 and March 2005. Balloon dilatation procedures were performed under anesthesia and with fluoroscopic control.

Results: We performed 92 dilatations on 25 RDEB patients. Most patients reported immediate relief of symptoms, rapid recovery, and resumption of adequate food intake within 1 day. The mean interval between dilatations was 1 year. Six patients (24%) have required only 1 dilatation, and 1 of these 6 has had a dilatation-free interval of 25 months. One patient with a history of multiple dilatations has remained dilatation-free for 5 years. No procedure-related complications have occurred.

Conclusions: Fluoroscopically guided balloon dilatation is a gentle, safe, effective, and repeatable technique that should be considered as a first line of treatment.

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1. Background

Recessive dystrophic epidermolysis bullosa (RDEB) is a rare, inherited, blistering disorder that primarily affects the

skin and pharyngoesophageal mucosa. Blistering and scarring occur in response to even minor trauma and have been linked to mutations in the *COL7A1* gene, which resides on the short arm of chromosome 3 [1]. This gene codes for type VII collagen, which is a major component of anchoring fibrils responsible for epidermal-dermal adhesion beneath the basement membrane within the papillary dermis of skin and mucous membranes [2,3]. Because of the high nutritional demands of wound healing and infection, RDEB patients typically have a wide range of nutritional problems. Many patients develop progressive microstomia, contributing to their poor oral intake and making access to the mouth and gastrointestinal tract difficult. In the esophagus and oropharynx, repeated trauma caused by eating and swallowing of solid foods leads to blistering, scar formation, and ultimately esophageal strictures [4-6]. Over time, these strictures may lead to progressive dysphagia, severe malnutrition, and growth disturbances. The long-standing cycle of high nutritional demand, injury, blistering, stenosis, and ongoing nutritional decline has a devastating impact on the quality of life.

Historically, a wide variety of operative and nonoperative treatments such as colon interposition, resection, gastrostomy, and bougienage have been used to interrupt this pathogenic process. During the past 2 decades, however, endoscopically guided balloon dilatation has gradually replaced these more invasive approaches as the first line of treatment [5,7-11]. Published reports reveal a general consensus among clinicians that this approach is superior to bougienage in that it applies only radial stretching forces to the involved area of the esophagus [7,11]. As such, it avoids the bougienage-induced morbidity of the longitudinal shearing forces that can affect the entire length of the esophagus. Nevertheless, use of the endoscope carries the inherent risk of oropharyngeal trauma [10,12,13]. In our own past clinical experience, oropharyngeal blistering after the use of the endoscope was not uncommon and led to a significantly prolonged period of recovery (5-7 days) during which adequate oral intake of food could not be resumed. In an effort to minimize the risk of iatrogenic trauma, we have since routinely eliminated the use of the endoscope when performing balloon dilatations of esophageal strictures in patients with RDEB. This approach not only eliminates the risks associated with the endoscope, but also allows the use of larger balloons that are capable of achieving a greater dilatation diameter. We present our experience with this technique in 25 patients who underwent 92 dilatations over an 11-year period.

2. Patients and methods

We reviewed the medical records of all patients diagnosed with RDEB who underwent nonendoscopic fluoroscopically guided balloon dilatation for esophageal strictures between August 1993 and March 2005 at the Cincinnati Children's Hospital Medical Center. Approval for this study was obtained from our institutional review board.

2.1. Patient management

The Cincinnati Children's Epidermolysis Bullosa Center primarily serves the Midwest and in addition receives referrals from throughout the United States. All patients undergo a thorough medical and nutritional assessment by our multidisciplinary team of pediatric specialists. Patients presenting with dysphagia, nutritional deficiency, or poor weight gain also receive a barium esophagram (Fig. 1). Dilatations are performed on the basis of radiological confirmation of the presence of a stricture(s). Patients with recurrent dysphagia undergo a second barium esophagram to assess the degree of stricture before a second dilatation is considered (Fig. 2).

2.2. Procedure

2.2.1. Barium esophagram

A barium esophagram helps evaluate the number, severity, and level of esophageal strictures. This information assists in determining dilatation strategy and the approximate balloon diameter to be used in the dilatation procedure. This study should be performed in both frontal and lateral projections. It is necessary to evaluate the entire esophagus from the oropharynx through the gastroesophageal junction. Proximal strictures in the cervical esophagus are particularly common in epidermolysis bullosa patients and can be overlooked if proper technique is not followed.

2.2.2. Anesthesia and perioperative care

Epidermolysis bullosa patients with esophageal strictures present the anesthesiologist with significant challenges that

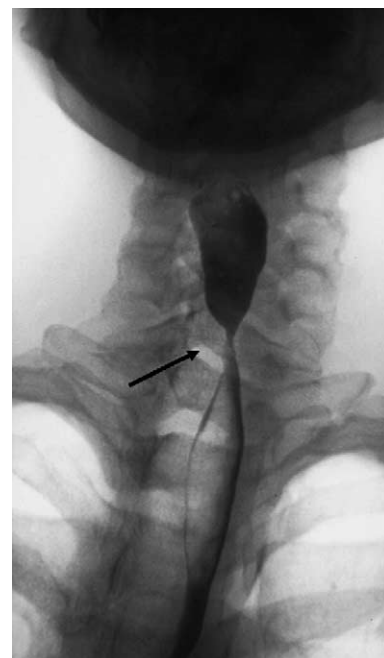


Fig. 1 Barium esophagram, demonstrating a proximal esophageal stenosis (arrow) in a patient with RDEB.

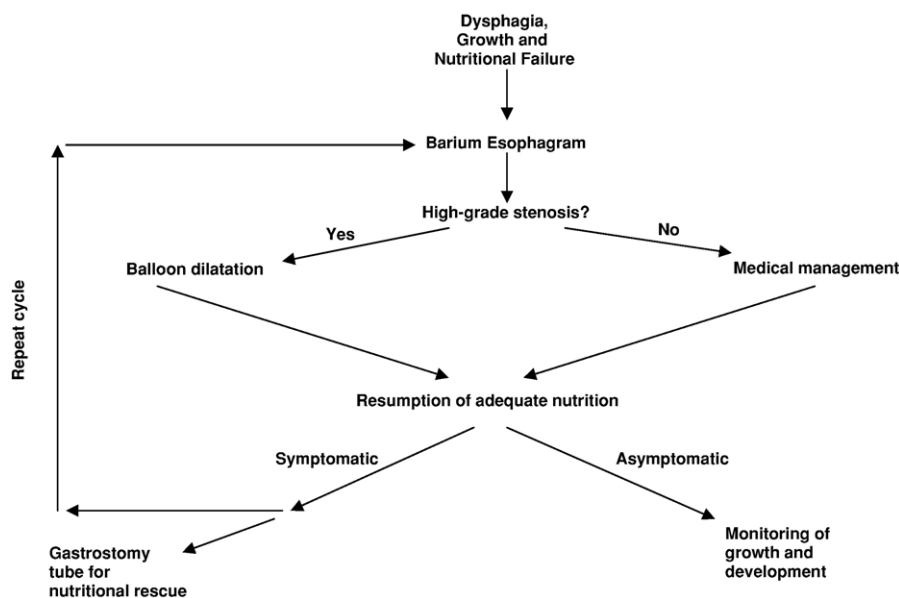


Fig. 2 Treatment algorithm for patients with RDEB.

require thorough preoperative planning and meticulous perioperative care. Management of a potentially difficult airway and the fragility of the skin and mucous membranes are of the highest priority. To avoid unanticipated difficulties with intubation, a thorough preoperative airway evaluation must be performed. When possible, we perform endotracheal anesthesia. We feel that this is the safest and most effective technique, protecting against aspiration and providing optimal conditions for balloon dilatation. In patients with microstomia, the tongue is often scarred down to the floor of the mouth, and the teeth are often angled inward, making endotracheal intubation more difficult. This difficulty increases with age as the cycle of scarring progresses. In some patients with microstomia, oral fiberoptic intubation may be necessary.

To minimize trauma to the skin and mucous membranes, patients are placed on and remain on an egg-crate foam mattress for the entire procedure. Premedication with oral midazolam helps promote a calm anesthetic induction with minimal anxiety, movement, and restlessness. Because of repeated blistering and scarring, establishing peripheral venous access can be difficult. Anesthesia is thus usually induced by mask with inhalation anesthetics. Alternatively, if peripheral veins are accessible and a patient is cooperative, a peripheral intravenous line may be placed with the patient awake before intravenous induction of anesthesia. The tourniquet is placed gently over layers of gauze. Intravenous lines are secured with a nonadhesive dressing (Mepitel or Mepiform, Mölnlycke Healthcare, Göteborg, Sweden) and gently wrapped with gauze and Coban wrap (3M, St. Paul, MN). The anesthesia mask is gently handled and lubricated with Aquaphor ointment (Beiersdorf Inc, Wilton, CT). Gentle laryngoscopy with a lubricated blade is important to minimize oral trauma. The endotracheal tube is secured with cotton tape that is initially placed behind the neck; the ends

are then tied around the endotracheal tube at the level of the lips. The eyes are lubricated and covered with saline-moistened gauze pads. No adhesive tape of any kind is used. Skin fragility also requires special precautions in the use of routine anesthesia monitors. Oxygen saturation is measured with a clip pulse oximeter probe rather than the adhesive-style probes; the blood pressure cuff is applied over several layers of Webril (Tyco Healthcare, Mansfield, MA) wrapped around the extremity. Electrocardiogram leads, if used, must have the adhesive portions removed and are secured to the patient with gauze or other nonadhesive wraps. The precordial stethoscope should be placed on the chest without adhesive.

We typically use a combination of intravenous and inhalation anesthetics. Muscle relaxants may help facilitate intubation, and antiemetics are given to prevent postoperative nausea and vomiting. Although awake extubation at the end of the procedure may be associated with coughing, it minimizes the risk of aspiration and the need for continued mask pressure on the face after extubation.

2.2.3. Radiation safety

Extreme care is taken to minimize patient and operator exposure to ionizing radiation. Our interventional suites are equipped with state-of-the-art equipment calibrated for our pediatric population. Because esophageal balloon dilatation typically does not require the same anatomical resolution as required in angiography, we routinely perform this procedure on a low-dose setting. As with all fluoroscopic procedures, the x-ray beam is carefully collimated to expose only the smallest anatomical area necessary.

2.2.4. Balloon dilatation

Using fluoroscopic guidance, we initially place a 5F to 8F umbilical artery catheter (Boston Scientific Corp, Natick, Mass) transorally into the stomach. We then insert a flexible,

Table 1 Balloon size for patient age

Patient age (y)	Balloon diameter (mm)
≤4 y	12-18
4-12	18-22
≥12	20-26

soft-tip, 0.035-in guidewire through the umbilical artery catheter into the stomach. Once the position of the guidewire is fluoroscopically verified, it remains in place throughout the entire procedure. We then remove the umbilical artery catheter and replace it with a high-pressure hydrostatic balloon catheter. Selection of balloon diameter is based on the patient's age and the appearance of the esophagus as seen on barium esophagram (Table 1). Selection of balloon length, which typically varies from 40 to 80 mm, depends on the length of the stricture and whether one or multiple strictures are present. If a single stricture is present, the balloon catheter is carefully positioned at the stricture site in the esophagus and inflated with 50% diluted water-soluble contrast. If multiple strictures are present, the most distal stricture is treated first. Balloon inflation with simultaneous fluoroscopic monitoring allows the visualization of strictures (Fig. 3A) and their effacement with the dilatation process. Optimally, we position the central portion of the balloon at the stricture site. To avoid aboral migration of the balloon during inflation, gentle traction is applied. The balloon is inflated to the minimally necessary pressure at which complete effacement of the stricture is observed (Fig. 3B). Inflation pressure is monitored by a manometer; 1.5 to 2 atm of pressure is generally sufficient for complete dilatation, and an upper limit of 3 atm of pressure is not exceeded. Pressure is maintained for a minimum of 30 seconds; the balloon is then deflated. If another stricture is present, the balloon is subsequently repositioned proximal to the first

treated site, and the dilatation procedure is repeated. In the event that preoperative radiographic visualization of the esophagus is inadequate, this technique allows for complete and precise mapping of the entire length of the esophagus and subsequent treatment of additional strictures. Upon completion of the procedure, the balloon catheter is replaced by the initially used umbilical artery catheter. To ensure adequate lumen size and to rule out esophageal perforation or leakage, we perform a postprocedure esophagram with diluted water-soluble contrast through the umbilical artery catheter. This is accomplished by injecting the contrast through the catheter as it is pulled from the distal to proximal esophagus. Residual contrast in the esophagus is aspirated to minimize the risk of postoperative regurgitation.

2.2.5. Postoperative protocol

Once patients are awake and alert, they resume a liquid diet. When they are comfortably able to swallow (within 2-4 hours), they are given soft solid food. RDEB patients who have not previously undergone dilatations at our institution are monitored overnight in the hospital and discharged on the following day. Those on whom we have previously performed dilatations are discharged within 8 hours. Patients who require additional concurrent dental procedures remain in the hospital for a 23-hour period. In 2001, we began administering perioperative and postoperative steroid treatment, postulating that this would delay the recurrence of stenoses. Patients receive an intraoperative 1 to 2 mg/kg intravenous dose of dexamethasone. This is followed by a 5-day tapered dose of liquid prednisolone, with the initial dose of 2 mg/kg being reduced by 20% daily. To minimize the consequences of gastroesophageal reflux, we also prescribe a proton pump inhibitor (pantoprazole) or H-2 blocker (ranitidine); first-dilatation patients are treated with this regimen for 6 months. Those who require frequent dilatations remain on the regimen for an indefinite period.

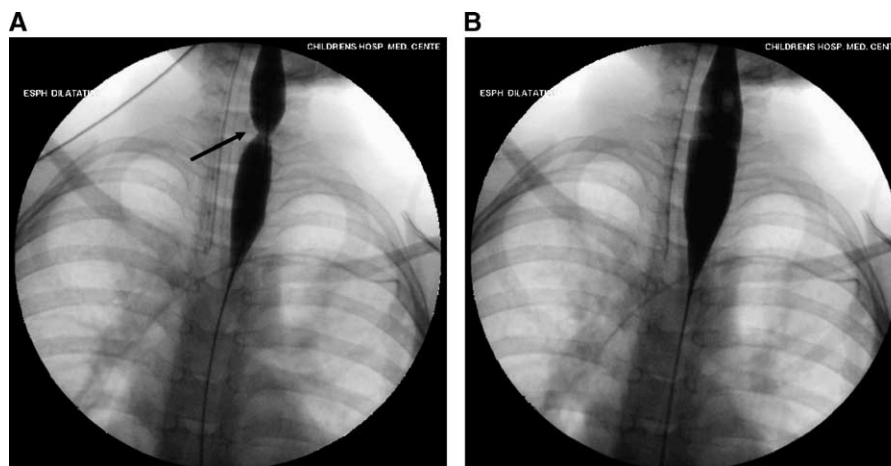


Fig. 3 A, Balloon dilatation of proximal esophageal stricture: balloon partially inflated, showing stricture site (arrow). B, Stricture effacement after complete balloon inflation.

3. Results

Between August 1993 and March 2005, we performed a total of 92 hydrostatic balloon dilatations on 25 RDEB patients (9 male and 16 female). The median fluoroscopy time required for these procedures was 3.8 minutes. The mean age at first procedure was 10 ± 8 years (range, 2-38 years). Fifteen (60%) of our 25 patients had single strictures; 13 of these 15 strictures were found in the proximal esophagus, 1 in the midesophagus, and 1 in the distal esophagus. Seven patients (28%) had 2 strictures; 5 were found in the proximal and midesophagus, and 2 in the midesophagus and distal esophagus. The remaining 3 patients (12%) had 3 strictures, each in proximal, middle, and distal locations. Balloon diameter varied from 12 to 22 mm, with a median diameter of 18.0 mm. We performed an average of 4 procedures per patient; however, the number of procedures ranged from 1 to 14.

Cannulating the esophagus through the stricture was difficult in several patients. In some, to facilitate initial placement, the umbilical artery catheter was passed from the oropharynx into the esophagus, with the flexible guidewire positioned inside the catheter so that the distal tip of the catheter and that of the guidewire were at the same level. The guidewire provides a degree of stiffness, allowing the clinician to more successfully traverse the strictured area. In some patients with a very proximal high-grade stenosis, this technique was not workable, and a steerable angiography catheter with a guidewire was used. Such patients may require 1 to 2 mL of diluted water-soluble contrast in the pharynx to outline posterior pharyngeal anatomy to facilitate esophageal cannulation. In 1 patient, direct laryngoscopy was required to place the guidewire through a distal pharyngeal stricture. Three patients had very severe microstomia. One was treated by accessing the esophagus transnasally, and in 2 others who presented with a percutaneous gastrostomy tube in place, we opted to perform retrograde cannulation and dilatation of the esophagus through the mature gastrostomy stoma.

Most patients reported immediate relief of symptoms and the ability to resume adequate oral feeding within a day of the dilatation procedure, and virtually all patients had significant weight gain within 4 to 6 weeks. The mean interval between dilatations was 1 year (range, 1.5 months to 4.5 years). The median follow-up time was 3.2 years (range, 1-11 years). To date, 6 patients (24%) have required only 1 dilatation; 1 of these 6 has had a dilatation-free interval of 25 months. In patients who have had multiple dilatations at our institution, one has remained dilatation-free for 5 years. Two others have been dilatation-free for 2 years, and 6 have not been dilated in more than 1 year. Over the 11-year duration of the study, we have incurred no complications from the dilatation procedure; however, 1 patient who had undergone concurrent dental extractions aspirated 12 hours postoperatively and required 1 week of intensive respiratory management from which she fully recovered.

4. Discussion

Our extensive experience with fluoroscopically guided balloon dilatation has shown this to be a safe, gentle, effective, repeatable, and minimally invasive technique. Patients and their families have reported immediate relief of symptoms, rapid recovery, and dramatic improvements in the quality of life. Furthermore, many patients who have previously undergone endoscopic procedures have reported this experience to be superior in terms of the level of oropharyngeal comfort and unencumbered swallowing. In light of our findings, we recommend that this approach be considered as a first-line treatment option.

Most patients with RDEB eventually develop scarring of the esophagus [12]. In that most strictures are high in the esophagus, it is imperative that clinicians specifically request that the diagnostic barium esophagram include the neck. Strictures frequently result in progressive dysphagia, which severely compromises the ability to maintain adequate hydration and nutrition and predisposes patients to repeated aspiration. Allowing for adequate nutritional intake by effectively dilating symptomatic strictures is thus a central aim of treatment. As clinicians have moved away from the more invasive approaches used in the past, endoscopic dilatation of esophageal strictures has become the most widely used treatment. Although this approach has been successful, many patients still experience a significant degree of pharyngoesophageal trauma from endoscopy. Our technique largely avoids this trauma.

An additional limitation of the endoscopic dilatation procedure is that only catheters with small balloons fit through the endoscope, thereby limiting the diameter of the esophageal dilatation. By contrast, our technique allows for the use of much larger balloon sizes (up to 26 mm), achieving larger functional esophageal diameter. As such, this technique increases the likelihood of more prolonged intervals between repeated dilatations. We achieved a mean interval between treatments of 1 year, which compares favorably to or exceeds treatment intervals previously reported in the literature [5-7]. Six patients have thus far not required a second dilatation, and to date, 1 has remained dilatation-free for 25 months. Of patients who have undergone multiple dilatations, 1 patient has remained dilatation-free for 5 years, 2 patients have been dilatation-free for 2 years, and 6 patients have been dilatation-free for more than 12 months. In a further effort to delay the recurrence of stenosis, since 2001, we have routinely used a regimen of perioperative and postoperative oral steroid treatment. Despite the relatively brief follow-up time, we have observed that in some patients with a history of frequent dilatations, the interval between dilatations has more than doubled. One potential disadvantage of our approach lies in the repeated exposure of RDEB patients to radiation, particularly in view of the fact that they are known to be predisposed to squamous cell carcinoma of the skin [14,15]. We have partially addressed this issue by instituting developing protocols that limit radiation exposure.

Maintaining gentle handling of the patient and generating minimal physical injury to the skin and gastrointestinal tract from the oropharynx to the stomach throughout the entire perioperative process are fundamental to our approach. At our institution, this procedure is generally performed by an experienced team, including an attending pediatric surgeon and pediatric radiologist. Because the procedure has a steep learning curve, we feel that it could be performed by either specialty, provided that the clinicians performing the dilatation procedure have a broad repertoire of skills as well as the ability to modify technique according to a patient's unique anatomic and physiologic needs. In particular, achieving oropharyngeal access in patients with severe microstomia is extremely challenging, and performing endotracheal intubation to minimize the risk of aspiration and maintain a secure airway cannot always be achieved. Some patients with severe microstomia may require endoscopically guided intubation of the trachea. Others may require management with laryngeal mask or regular mask anesthetic techniques, which are of concern in that the airway is not protected. Rarely, transnasal or retrograde esophageal cannulation through a gastrostomy is required.

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Discussion

Arnold Coran, MD (Ann Arbor, MI): Thank you for this presentation. A number of these children after they have had multiple strictures shorten their esophagus and then develop significant gastroesophageal reflux. My question to you is, in this large series, how many developed reflux that you demonstrated, and did you do any fundoplications in any of them, because I do think some of them need a fundoplication. Otherwise, you end up with a combination of stricture from the underlying disease and possibly stricturing from reflux.

Wolfgang Stehr, MD (response): Thank you very much for your question. You are absolutely correct. We treat many of these patients, especially patients presenting with distal esophageal strictures with proton pump inhibitors to limit the effects of their reflux. So far I am not aware that any of our patients have undergone Nissen fundoplication, but we have started a protocol where all patients with reflux are being treated with proton pump inhibitors after dilatation of these distal strictures.

Patricia Donahoe, MD (Boston, MA): I commend your recommendations and your study. It is often possible to do the first few procedures in the fluoroscopy suite and at the same time instruct the parents to do the dilatations, first under fluoroscopy and then without so that they feel comfortable doing the procedure. They take the devices home where they can dilate more often, as necessary. Repeated dilations at home can be quite effective in severe cases. In our experience, like yours, the lesions are more often high, so doing the balloon dilatations at home is safe and effective. Thank you.

Wolfgang Stehr, MD (response): Thank you very much.