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Endoscopic management of esophageal stenosis in children: New and traditional treatments

Luigi Dall'Oglio, Tamara Caldaro, Francesca Foschia, Simona Faraci, Giovanni Federici di Abriola, Francesca Rea, Erminia Romeo, Filippo Torroni, Giulia Angelino, Paola De Angelis

Luigi Dall'Oglio, Tamara Caldaro, Francesca Foschia, Simona Faraci, Giovanni Federici di Abriola, Francesca Rea, Erminia Romeo, Filippo Torroni, Giulia Angelino, Paola De Angelis, Digestive Endoscopy and Surgery Unit, Bambino Gesù Children Hospital, IRCCS, 00165 Roma, Italy

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Correspondence to: Luigi Dall'Oglio, MD, Digestive Endoscopy and Surgery Unit, Bambino Gesù Children Hospital, IRCCS, Piazza Sant'Onofrio 4, 00165 Roma, Italy. luigi.dalloglio@opbg.net
Telephone: +39-06-68592841
Fax: +39-06-68593910

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Abstract

Post-esophageal atresia anastomotic strictures and post-corrosive esophagitis are the most frequent types of cicatricial esophageal stricture. Congenital esophageal stenosis has been reported to be a rare but typical disease in children; other pediatric conditions are peptic, eosinophilic esophagitis and dystrophic recessive epidermolysis bullosa strictures. The conservative treatment of esophageal stenosis and strictures (ES) rather than surgery is a well-known strategy for children. Before planning esophageal dilation, the esophageal morphology should be assessed in detail for its length, aspect, number and level, and different conservative strategies should be chosen accordingly. Endoscopic dilators and techniques that involve different adjuvant treatment strategies have been reported and depend on the stricture's etiology, the availability of different tools and the operator's experience and preferences. Balloon and semirigid dilators are the most frequently used tools. No high-quality studies have reported on the differences in the efficacies and rates of complications associated with these two types of dilators. There is no consensus in the literature regarding the frequency of dilations or the diameter that should be achieved. The use of adjuvant treatments has been reported in cases of recalcitrant stenosis or strictures with evidence of dysphagic symptoms. Corticosteroids (either systemically or locally injected), the local application of mitomycin C, diathermy and laser ES sectioning have been reported. Some authors have suggested that stenting can reduce both the number of dilations and the treatment length. In many cases, this strategy is effective when either metallic or plastic stents are utilized. Treatment complications, such as esophageal perforations, can be conservatively managed, considering surgery only in cases with severe pleural cavity involvement. In cases of stricture relapse,

even if such relapses occur following the execution of well-conducted conservative strategies, surgical stricture resection and anastomosis or esophageal substitution are the only remaining options.

Key words: Esophageal stenosis; Esophageal stricture; Esophageal dilation; Esophageal stent; Caustic stricture

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Core tip: The paper reviews the conservative treatment of esophageal stenosis and strictures (ES) in children. Different types of ES are discussed, including post-esophageal atresia anastomotic strictures, congenital esophageal stenosis and dystrophic recessive epidermolysis bullosa strictures. Endoscopic techniques are reviewed, including balloon and semirigid dilators, esophageal stents and different adjuvant treatment strategies, like corticosteroids (either systemically or locally injected), the local application of mitomycin C, and ES incision. Conservative management must be considered also for complications, such as esophageal perforations, except for patients with severe pleural cavity involvement, who require surgery.

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INTRODUCTION

The endoscopic treatment of esophageal strictures or stenosis (ES) has been reported to be the most frequently used strategy in children and adults. Improvements in endoscopes and accessories have supported an increase in the number of patients who are conservatively treated with endoscopic dilations (ED) rather than surgical treatment.

In the past, patients with severe cicatricial strictures, particularly cases that occurred following the ingestion of caustic agents, have generally undergone esophageal substitutions with or without esophagectomy. The conservative option was complicated by the difficulty of passing the bougie through the stricture without clear endoscopic control and without a guide wire. The mortality risks of these procedures was elevated because of high incidence of complicated esophageal perforations and consequently severe mediastinal infections.

Safe and effective ED performed with flexible endoscopes, guide wires with differing stiffnesses, balloon dilators or semirigid bougie dilators have drastically improved the outcomes and the quality of life of these

patients. Further, the rates of ES resolution with a stable esophageal caliber that is suitable for normal food intake without dysphagia are high.

Normal food intake is the only achievable target of conservative treatment because there are no treatments that can achieve a true normal esophagus with normal motility at the level of the cicatricial tissue.

ESOPHAGEAL DILATIONS

Conservative treatments of ES with ED utilizing different strategies have been reported, and the indications for each treatment depend on the operator's experience and preferences and the etiology of the ES.

General anesthesia represents a widespread strategy that is used in children both to reduce patient discomfort and to allow for proper airway protection during dilation maneuvers. In teenagers, repeated ED under conscious sedation can be used. In indwelling balloon dilation program, the patient requires neither sedation nor anesthesia^[1].

A guide wire that is inserted under endoscopic control through the stricture represents an important and effective tool for avoiding an incorrect path of the preferred dilator tip.

Different dilators are now available; for example, reusable dilators that are applied over the wire such as semirigid Savary-Giliard bougies and disposable balloon dilators have been used. Balloon dilators pass over a guide wire or through the channel of the endoscope. All of these dilators are available in different lengths and diameters.

There is no consensus regarding the use of balloon dilators or semirigid Savary-Giliard bougies. No prospective studies have directly compared the safety and efficacy of these types of dilators. However, retrospective studies have reported different results regarding perforation rates^[2,3].

Based on our more than thirty-five years of experience with thousands of dilations, we generally use balloon dilators in cases that involve inflammatory strictures, *e.g.*, in the early treatment of caustic, epidermolysis bullosa and peptic strictures.

Savary dilators are safer and more effective than balloon dilators in the treatment of consolidated and old cicatricial strictures and in cases of resistant esophageal narrowing due to, *e.g.*, congenital esophageal stenosis (CES) with cartilaginous remnants^[4].

The advantages of balloon dilators include the radial force that is applied to the ES and the avoidance of the application of axial force^[5]. Balloon dilators can be advanced through the endoscope channel and carefully pushed forward into and through the ES under direct vision. Balloon dilators may also be inserted, on the side of the endoscope itself or under fluoroscopic control, over a guide wire that has previously been inserted through the scope.

Inflating balloon devices allow for the application of a standard force (PSI or ATM) at a standard diameter

Table 1 How to prevent esophageal perforation

Accurate stricture/stenosis morphology with X-ray-esophagram, MEUS
Stricture/stenosis etiology
General anesthesia
Fluoroscopy available
Guide wire in correct position
Correct dilator type and size
Carefully dilator passage or inflation
Endoscopic/contrast X-ray evaluation for possible perforation

MEUS: Miniprobe ultrasonography.

and with one specific pressure. The balloon filled with contrast medium allows for the verification of the disappearance of the hourglass image or the waist in the balloon caused by the stricture, under the fluoroscopic control^[5]. The persistence of a portion of the "waist" is an indication that the procedure was partially successful^[6].

There is no consensus regarding the duration, which can range from 10 to 120 s, that the balloon should remain inflated, and there are no published pediatric studies on this topic. An adult study^[7] revealed no difference in the outcomes of patient regardless of whether the balloon was dilated for 10 or 120 s.

Semirigid Savary-Giliard dilators require an expert operator to conduct progressive dilations and thus avoid esophageal perforation by carefully inserting the dilators without excessive force or hastiness.

The problem of the optimum dilator is difficult to solve, because of the different esophageal size during the pediatric age. The "tumble rule" was proposed, comparing the size of the thumb with the esophageal size. The most frequently used rule in children is to dilate no more than two sizes for each dilation session. Dilation can be repeated, with increasing diameter, after at least 3 d. Only the tissue damage after the previous dilation could represent a guide for the treatment. Personal experience plays a fundamental role in the choice of the optimal dilator size.

In patients operated for esophageal atresia (EA) the opportunity and the timing of the first endoscopic control of esophageal anastomosis is debated. Due to the absence of evidence of routine endoscopic control utility, the most used strategy is to evaluate with barium swallow or endoscopy only the patient that are not able to eat the normal food for the age. In case of dysphagia and stricture evidence the patient starts with a dilations program.

There is no consensus regarding the interval between repeated ED with either a balloon or a bougie. An average of two to three weeks is the most frequently reported interval^[2,3]. This interval should be individualized based on the stricture size, the resistance against the dilations, the post-dilation bleeding, the symptoms and the local or patient's logistical environment. Patients who require treatment in a level III endoscopic center may request a special dilation setting and an increased frequency of dilations to reduce difficult or expensive travel from the country of origin, if they are located far

Table 2 Type of esophageal strictures in children

Caustic
Anastomotic
Congenital stenosis
Epidermolysis bullosa
Peptic
Eosinophilic esophagitis
Actinic
Neoplastic

from the level III center. In many cases the interval between ED can be progressively elongated, according with symptoms relapse, to reduce the patient's stress.

The steps to reduce the risk of esophageal perforation are listed in Table 1.

TYPE OF STRICTURES

Table 2 shows the most frequent ES in children listed in order of frequency.

In EA anastomotic strictures, there are no clear indications for dilations, as a routine post-operative procedures^[8]; indeed, the only indication is the presence of dysphagia symptoms.

This second strategy has been reported to be as effective as the first one and with fewer dilations^[9-11].

Due to the high risk of severe stricture that has reportedly been associated with long gaps EA with anastomotic tension^[12,13], patients with this condition require strict clinical follow-up to prevent sudden, full and potentially dramatic anastomotic occlusions that can only be dilated with special strategies. In very difficult situations that lack evidence of an anastomotic lumen, the simultaneous insertion of two endoscopes, one *via* the mouth and the second through a preexisting gastrostomy, could provide an opportunity to reestablish esophageal patency^[14].

In very thin anastomotic stricture it may be impossible to pass the guide wire through. Under fluoroscopy, using an ERCP cannula and strategy, filling water-soluble contrast medium it is possible to verify the correct way and then the correct wire passage through the cannula into the stricture.

In CES, different subtypes have been described. The two most important subtypes in terms of frequency are the fibromuscular (FMS CES) and tracheal cartilaginous remnant (TBR CES) subtypes.

The differential diagnosis, to rule out other esophageal narrowing etiologies, is necessary for selecting the correct therapeutic strategy. Miniprobe ultrasonography (MEUS) currently represents the only diagnostic tool that can provide an accurate evaluation of esophageal wall thickness and can differentiate the CES subtype^[4,15,16]. Different therapeutic options have been reported for CES. In case of TBR, some authors have suggested surgical stenosis resection and anastomosis^[15-17]. The conservative treatment with ED has been reported to be effective^[4] in a large series of 47 patients. An overall

success rate of 95% has also been reported in cases of TBR CES.

The reported incidences of perforation following stenosis dilation in CES are higher than those reported for other types of ES and range from 10%^[4] to 33%^[18] and 44%^[19]. These higher incidences are likely due to the high resistance of the stenosis and the risk of the sudden cracking of the stenosis during dilations, particularly with balloon dilators^[4]. In the reviews of Michaud *et al.*^[16] and Takamizawa *et al.*^[17], the authors reported many cases and studies of the surgical resection of TBR CES as the first option when diagnoses of TBR CES were obtained; but in many reported cases^[16] the TBR diagnosis was based only on post-operative histology and not preoperatively. Indeed, the surgical option has been reported to be the first option in surgical environments, whereas dilation options are more frequently employed in gastroenterological centers^[16]. The numbers of patients with diagnoses of cartilaginous remnants on endoscopic ultrasound with miniprbes that were reported in these two reviews were low, even if this tool is currently the only diagnostic tool that can identify cartilaginous remnants.

Romeo published results supporting conservative strategy as an effective treatment for CES, either FMS or TBR CES. Special care must be taken, in particular in previously MEUS detected TBR CES, to prevent esophageal perforation. Surgery should be reserved only for cases in which conservative treatment has been ineffective^[4].

In recessive dystrophic epidermolysis bullosa, the ES result from bullous lesions and tend to relapse. In these patients, it is important to reduce the esophageal trauma to avoid new blisters and the resultant risk of strictures^[20,21]. To minimize these risks, balloon dilation under only fluoroscopic control allows for ED without a high risk of blisters in non-stenotic esophageal areas^[21-23]. The first step is to pass a soft guide wire through the nostril, the pharynx and the esophageal stricture into the stomach. Under fluoroscopic control, the passage of the guide wire (0.032-0.035 mm hydrophilic wire) through the cricopharyngeal junction can occasionally be very difficult, but this difficulty can be resolved by using a thin tube, over-the-wire. In rare cases, the only option is endoscopic control. An over-the-wire-balloon dilator is then progressively introduced to reach the stomach. The balloon is partially filled with water and contrast medium and is slowly retracted to identify the stricture *via* the appearance of an "hourglass shape" that disappears with progressive balloon inflation. The balloon is then deflated and pulled back to identify any possible additional strictures. It is very important that the completely inflated balloon is not pulled back, to prevent the formation of blisters and new scars^[21-23]. Adjuvant treatment with dexamethasone (2 mg/kg per day for 3 d) reduces patient discomfort and can reduce the formation of scar tissue^[21].

Oral budesonide was recently reported in a short

series as adjuvant treatment in these special patients^[24].

In children during chemotherapy for leukemia or other hematologic diseases ES have been reported^[25,26], due to deep mucositis and esophageal wall damage. Conservative treatment with ED and stenting represents the first option but esophageal substitution could be necessary because of the stricture length and its recurrence. In our experience two, out three, ES resolved with stenting; the other underwent jejunum esophageal substitution.

ADJUVANT TREATMENTS

Different adjuvant treatments have been proposed for cases of refractory or recurrent ES. These solutions can reduce fibroblastic activity in scar tissue production and reduce the damage to the injured esophageal wall due to acid gastro esophageal reflux. The role of these treatments is very important because they could give the chance to avoid a surgical procedure, with esophageal resection and anastomosis, a partial or total esophageal substitution or a gastric pull-up procedure. Before planning a surgical strategy in a refractory or relapsed ES a treatment with one or more combined adjuvant strategies is mandatory.

Proton pump inhibitors (PPI) are commonly used, although there are no studies of their efficacy in the prevention of stricture relapse. In one prospective study^[27], the authors reported no prophylactic effect of omeprazole (2 mg/kg) on post-esophageal atresia ES and no effect on reducing the number of ED.

In contrast, severe gastro esophageal reflux disease (GERD) is frequently observed in cases of severe ES due to corrosive esophagitis or long-gap esophageal atresia anastomosis strictures. Cicatricial shortening of the esophagus represents an important cause of GERD and consequent stricture worsening. In these patients, PPI treatment is very helpful to treat esophagitis and acid damage on the stricture wall; a correct evaluation is necessary for potential anti reflux surgery.

Mitomycin C is an antineoplastic antibiotic with *in vivo* and *in vitro* anti fibroblastic activities that has been described to exert inconsistent results at different drug concentrations. Good results in two patients with caustic ES and two patients with anastomotic ES who were treated with ED plus 1 mg/mL mitomycin C have been reported^[28]. The authors of one study reported results that were similar to those of an ED-only treated group in 11/21 anastomotic ES patients who were treated with ED plus mitomycin C (0.1 mg/mL)^[29]. In a review of 11 papers with 31 patients with ES, no direct or indirect side effects were reported. The mitomycin C concentrations varied from 0.1 mg/mL to 1 mg/mL. After a mean follow-up of 22 mo, good results in terms of symptom relief were reported for 21 children (67.7%), and 6 (19.4%) children experienced partial relief. In four children (12.9%), the mitomycin C treatment failed^[30].

In a recent prospective study, the authors described significant improvements in dysphagia in 18/30 corrosive ES patients who were treated with ED plus mitomycin C at 0.4 mg/mL^[31]. In two papers by El-Asmar *et al.*^[32,33], the authors described a significant effectiveness of 0.4 mg/mL of mitomycin C in caustic stricture.

No direct or indirect adverse effects were reported in any of these series.

Different techniques for the topical application of mitomycin C application have been reported. Cotton pledgets soaked in mitomycin C solution have generally been used. Other techniques, such as drug-eluting stents or, in our own experience, the local instillation of a mitomycin C solution at the stricture level with a cotton swab, have produced accurate solution aspiration and lavage after 4-5 min.

Until larger prospective studies are published, topical mitomycin C solutions (0.4 mg/mL) may help improve symptoms and reduces both the number of dilations and their frequency. There are no reports of direct or indirect adverse effects of the topical use of mitomycin C topical, but additional long-term follow-up studies are needed.

The use of corticosteroids, both systemically and intralesionally, has been described. In two ES patients, one post-anastomotic and one corrosive, who were previously treated with repeated intralesional dexamethasone injections, the systemic intravenous administration of prednisolone (2, 1, and 0.5 mg/kg daily for 1 wk each) improved the dysphagia in both patients^[34].

Adjuvant dexamethasone (2 mg/kg for 3 d, tapered over six additional days) has been used in the successful treatment of patients with "dynamic" custom plastic stents^[35,36].

Intralesional triamcinolone acetonide (TAC) injection has been described in adults and children. A prospective study of 60 adult patients with post-esophagectomy esophagogastric anastomotic strictures described non-significant improvement in the number of ED and the dysphagia-free period^[37]. Ten patients with intractable corrosive ES received 2 mL of TAC (40 mg/mL) injected in 3 or 4 quadrants and achieved symptom resolution^[38].

No direct or indirect adverse effects were reported in any of these series, and despite the lack of prospective pediatric studies, local TAC injections could aid the treatment of ES.

STENTING

Surgical ES resection and anastomosis with partial or total esophageal substitution may represent the only therapeutic option for refractory or recurrent ES.

Intra- and post-operative complications, anastomotic strictures, severe GERD, bronchopulmonary disease, chronic dysphagia due to esophageal motility disorders and frequent long-term low quality of life have prompted the use of more aggressive conservative strategies in the

treatment of ES with the goal of avoiding surgery and the goal to save the own patient's esophagus.

Two different strategies for stenting have been described. The metal and plastic stents press against the esophageal wall, with food and secretions that pass through the stent itself. The stents pressing against the cicatricial ES allow for the ES healing.

The second stenting strategy consists of a plastic or silicon tube, customized in different length and diameter according with the stricture size and level, affixed to a nasogastric tube. This type of stent allows the food and secretions to pass in the space between the ES and the stent itself. Such continuous passages seem to effectively maintaining lumen patency^[35,36,39-41]. In one review^[42], experiences with different stents were reported. There are three studies that have reported on second type PTFE or silicon custom stents and three that have reported on self-expanding metallic or plastic stents. Migration of the first type stent was the most commonly cited complication of metallic stents and occurred in 0% to 29% of the patients^[43,44]. The softening of the esophageal wall allowed for the distal displacement of the stent. Plastic stents affixed to nasogastric tubes are associated with a reduced risk of dislocation risks but are also associated with the increased discomfort of a nasal tube.

Results related to one of the second type of stent, the custom "dynamic stent", have been reported in two retrospective studies^[35,36] of patients with post-anastomotic (25 patients) and corrosive (55 patients) ES. The implantation of the stents was followed by high-dose dexamethasone therapy (2 mg/kg per day for 3 d tapered in 6 d more). This stenting strategy was reported to be effective in 88% of the patients. The authors underlined that this type of stent allows for continuous swallowing and food passage, which resulted in a type of gym for the esophageal wall. These dynamic custom stents might aid in stricture healing, but at a minimum, they aid in stricture shortening. This aspect has been reported to be important with respect to possible surgical resection and anastomosis. Indeed, total or long esophageal resection with partial or total esophageal substitution can be avoided^[35].

In a study of plastic and metallic stents^[45], the authors reported stent appositions in refractory ES and esophageal perforation of 23 and 14, respectively. These authors reported that the stents were effective in all patients with esophageal perforations. In the treatment of ES, the stents were effective in 6 of the 23 patients who did not receive further treatment following stent removal. The authors concluded that in anastomotic ES, self-expanding stents are very effective for treating post-dilation perforations and post-anastomotic leaks but are not effective in the treatment of ES with ES relapse after stent removal.

In a recent paper^[46], the authors reported on eleven patients with perforations or anastomotic strictures (7 and 4 patients, respectively) who were treated with

covered metal stents. No stent-related complications were observed during stent insertion or removal. Two patients underwent one additional ED. These authors concluded that stenting represents a safe and effective strategy for healing esophageal perforations.

Severe stent related complication has been described in esophageal atresia patients with post anastomotic ES. In three patients with stent (metallic and dynamic custom stent) massive bleeding from arterial-esophageal fistula has been reported. One patient with metallic stent had fatal outcome and two, with dynamic custom stent, needed thoracic surgery for subclavian anomaly^[47]. Because of the higher incidence of vascular anomalies in patients with post esophageal atresia, it is mandatory to rule out vascular anomalies with CT or MR angiography before implanting a stent.

Biodegradable esophageal stent use was described in children^[48]. The opportunity of progressive reduction of stent compression on the esophageal wall represents an important advantage of this special stent. The published inconstant results in children didn't show a significant advantage in the treatment of recalcitrant esophageal stricture. The most frequent described complications are the gastric dislocations and the mucosal overgrowth with consequent stent obstruction^[49].

ES incision has been reported in some case reports. In a recent retrospective paper, the authors reported on seven anastomotic ES patients.

In two patients ES relapsed and patients underwent one more successful incision. Three patients with ES longer than 1.5 cm underwent metallic stenting after the incision^[50].

This strategy, as the others above reported, should be performed only in III level referral centers in a pediatric medical-surgical setting, for individualized conservative strategy. Before planning surgery, in refractory or recurrent ES, all these conservative strategies must be considered.

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