TECHNICAL REVIEW

Dilation of refractory benign esophageal strictures

Peter D. Siersema, MD, PhD, Laetitia R.H. de Wijkerslooth, MD

Utrecht, The Netherlands

Benign esophageal strictures are frequently encountered as a problem in endoscopic practice.[1,2] Peptic injury, as a result of chronic exposure of the esophagus to gastric contents, is the most common cause of esophageal strictures, accounting for approximately 60% to 70% of cases.[3] Other etiologies include Schatzki's rings, esophageal webs, radiation injuries, caustic ingestions, photodynamic therapy-induced strictures, and anastomotic strictures.[2,4] For centuries, the cornerstone of treatment for esophageal strictures has been dilation therapy. The first documented treatment dates back to 1674 when the passing of a whale bone through a stricture in the esophagus was reported.[5] Since then, esophageal dilation devices have evolved and have continued to improve in efficacy and safety.[6]

Although dilation usually relieves symptoms of dysphagia, recurrent strictures do occur. Benign esophageal strictures can be classified according to complexity. Strictures that are short, focal, straight, and, in most cases, allow passage of a normal-diameter endoscope are considered simple strictures. Examples of these include Schatzki's rings, esophageal webs, and peptic strictures.[1] In general, one to 3 dilations are needed to relieve dysphagia because of simple strictures, with only 25% to 35% requiring additional sessions, with up to 5 dilations.[7] There is a subgroup of strictures that are more difficult to treat and tend to be refractory or tend to recur despite dilation therapy. These strictures are usually longer (>2 cm), angulated, irregular, or have a severely narrowed diameter.[1] The more complex strictures are defined as anatomic restrictions because of a cicatricial luminal compromise or fibrosis that results in symptoms of dysphagia in the absence of endoscopic evidence of inflammation. This may occur as the result of either an inability to successfully remediate the anatomic problem to a diameter of 14 mm during 5 sessions at 2-week intervals (refractory), or as a result of an inability to maintain a satisfactory luminal diameter for 4 weeks once the target diameter of 14 mm has been achieved (recurrent). It is important to note that this definition is not meant to include patients with an inflammatory stricture that will not resolve successfully until the inflammation subsides, or those with a satisfactory diameter who have dysphagia on the basis of neuromuscular dysfunction (eg, those with postoperative and postradiation therapy dysphagia).[8] The most common etiologies include anastomotic strictures, radiation-induced strictures, caustic strictures, and photodynamic therapy-related strictures.[1,6]

This review summarizes techniques for optimal dilation, and discusses alternative approaches for treating refractory benign esophageal strictures, such as dilation therapy combined with steroid injection, stent placement, and incisional therapy.

Abbreviations: SEMS, self-expanding metal stent; SEPS, self-expanding plastic stent.

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REVIEW METHODOLOGY OF PUBLISHED STUDIES

Key words, including "esophageal stricture," "benign," "refractory," "anastomotic," "caustic," "radiation," "peptic," "photodynamic therapy," "bougie dilation," "balloon dilation," "retrograde and antegrade dilation," "steroid injection," "stent," and "incisional therapy" with limits to studies in English, were used to search the PubMed database from 1975 to December 2008. In addition, a manual search of citations from relevant articles was performed.

DILATION

Treatment of benign esophageal strictures aims to relieve symptoms of dysphagia, with avoidance of complications and prevention of recurrences. Dilation used to be and still is the first-line option to treat benign esophageal strictures.[2] Various types of dilators are available and can be categorized into mechanical (bougie) or balloon-type dilators. Mechanical dilators can further be subdivided into those that are passed down the esophagus with or without a guidewire and/or fluoroscopy.[2,3,6] Bougies that do not need a guidewire for introduction into the esophagus are filled with mercury or tungsten (eg, Maloney dilators; Medovations, Germantown, WI). These types of bougies have a tapered tip and are available in multiple sizes. The most commonly used guidewire-assisted mechanical bougie is the polyvinyl Savary-Gilliard dilator (Wilson-Cook Medical, Winston-Salem, NC). Balloon dilators

can be passed through the scope and are available with or without a guidewire. Both Savary-Gilliard and balloon dilators are currently by far the most frequently used dilators.[6,7,9]

The exact mechanism by which the luminal diameter is increased during dilation has not been fully elucidated, but the most likely mechanism is that the esophagus is widened by circumferential stretching and/or splitting of the stricture.[1,10] Bougie dilators enable dilation of a stenotic segment by using gradually increasing dilator diameters. This results not only in a longitudinal force, but also in a radial, more shearing, force on the stricture. Balloon dilators can be passed through the working channel of an endoscope, which enables the procedure to be performed under direct vision. The balloon is inflated with water (or contrast if fluoroscopy is used) to a pressure that corresponds to a specific diameter. The middle part of the balloon is positioned at the narrowest part of the stricture. A guidewire and/or fluoroscopy can be used to position the balloon. In contrast to bougie-type dilators, balloon dilators only deliver a radial force, resulting in a simultaneously applied dilating force across the entire length of the stricture.[3,6,10]

Despite these mechanistic differences, no clear advantage of either balloon or bougie (Savary-Gilliard) dilation has been demonstrated. Scolapio et al[9] compared safety and efficacy of Savary-Gilliard dilation with balloon dilation in the treatment of peptic strictures and Schatzki rings. No differences in relief of dysphagia or in need for repeat dilation were observed. Moreover, both methods were found to be safe with no major complications observed in 251 patients. Also, other authors did not find functional differences between bougie and balloon dilation.[11-13] An advantage of Savary-Gilliard dilators is that they are more cost-effective because they are reusable, compared with balloon dilators that are intended for single use only.

The most frequently reported complications of esophageal dilation include perforation, hemorrhage, and bacteremia. Perforation rates varying between 0.1% and 0.4% have been reported.[2,7,14,15] In general, it is accepted that the risk of perforation is only minimal when ''the rule of 3'' is applied, meaning that no more than 3 dilators of progressively increasing diameter should be passed in a single session (corresponding with a total of $3 \times 1 = 3$ mm increase in diameter).[1,6] Although this ''rule'' is easily applicable as a clinical guideline, no studies have demonstrated that it indeed improves safety and efficacy.[3] Therefore, one could argue that in very tight or long strictures, only one or two dilators should be passed in each dilation session. It is commonly advised to limit initial dilation to 39F to 45F (corresponding to a diameter of 13 to 15 mm). Nonetheless, in a small series of 35 patients with predominantly peptic strictures, it was found that dilation with Rigiflex balloons (Rigiflex esophageal balloon dilator; KeyMed, Southend-on-Sea, UK), which were inflated up to 60F (20 mm) during the first session, did not result in complications.[11]

With such low complication rates it is hard to demonstrate a safety benefit of any dilation device. One study retrospectively compared the balloon-type Maloney device (both the hydrostatic and pneumatic type) and Savary-Gilliard dilators in 102, 156, and 90 sessions, respectively. An increased perforation rate was found with Maloney dilators that were passed blindly into complex strictures.[15] Therefore, using Maloney bougies only in patients with simple strictures is advisable.[2,15,16] The efficacy and safety of endoscopic dilation without fluoroscopy has been shown in several studies.[7,17-19] Nonetheless, it is generally advocated to use fluoroscopic guidance to enhance safety during dilation of complex strictures.[6]

The majority of complex strictures can be endoscopically passed with a guidewire, followed by dilation. Occasionally, it can be difficult to identify the true lumen of a stenotic esophagus, for instance in postradiation strictures in the cervical esophagus. In these circumstances, the passing of a guidewire for dilation through antegrade endoscopy is unsuccessful. To reduce the potential risk of perforation, the combined antegrade and retrograde dilation technique can be applied.[20,21] The principle of the combined antegrade and retrograde dilation technique is dual endoscopic access to the proximal and distal end of the stricture, resulting in better control during dilation. As a first step, a small-diameter endoscope is passed retrogradely into the patient's esophagus through the gastric lumen by using a mature gastrostomy or jejunostomy tract for access. Then a guidewire is passed from the distal side under fluoroscopic guidance across the stricture. If the lumen is not detected from the distal side, a guidewire puncture or the use of a pre-cut knife to provide a small access hole in the stricture under fluoroscopic guidance followed by passing a guidewire has been reported.[22-24] The guidewire is antegradely detected and picked up with a proximally positioned endoscope. Dilation can be performed by using either Savary-Gilliard or balloon dilation. Two studies in small groups of patients have demonstrated that the combined antegrade and retrograde dilation technique is indeed an effective and safe method.[20,21]

In summary, (repeat) dilations are effective in the majority of benign esophageal strictures, irrespective of the underlying disorder. In a minority of patients, however, strictures recur and are defined as refractory; in these patients, an alternative treatment strategy should be considered.

INTRALESIONAL STEROID INJECTION THERAPY

In 1966, the first reports of the successful treatment of cutaneous hypertrophic scars, burn contractures, and keloids by the local infiltration of triamcinolone diacetate were published. The intralesional injection of corticosteroids was shown to soften scars and keloids.[25,26] A few

years later, Holder et al[27] were the first to report the use of intralesional corticosteroid injections into benign esophageal strictures of dogs and children. Although the effectiveness of intralesional steroid injections in short strictures was demonstrated, initially the effectiveness was not a frequently applied treatment for (refractory) benign esophageal strictures.[28] However, during the last decade, this treatment is increasingly being used in the treatment of refractory benign esophageal strictures.[29-31]

Kochhar and Makharia[29] showed an increase in intervals between dilations and a reduction in the frequency of dilations in 71 patients with various types of benign esophageal strictures when dilation was combined with 4 intralesional injections in all 4 quadrants with triamcinolone acetonide (40 mg/mL, diluted 1:1 with saline solution) by using a 23-gauge, 5-mm long sclerotherapy needle in aliquots of 0.5 mL at the proximal margin of the stricture and another 4 injections into the strictured segment whenever possible. Altintas et al[30] demonstrated a statistically significant increase in the interval between dilations and a longer symptom-free period in a small group of 21 patients with refractory benign esophageal strictures randomized between dilation alone (n = 11) or dilation combined with intralesional 4-quadrant injections with triamcinolone acetate (8 mg into each quadrant) (n = 10). Ramage et al[31] performed a randomized study in 30 patients with peptic strictures and recurrent dysphagia who had undergone at least one dilation session. They found that an intralesional 4-quadrant injection of 0.5 mL/quadrant triamcinolone (40 mg/mL), combined with dilation and acid suppression, reduced the need for repeat dilation and the average time to repeat dilation. Perforation was not reported in any of these studies.[29-31] The mechanism of action is suggested to be the local inhibition of the inflammatory response, resulting in a reduction of collagen formation.[31]

In summary, there is evidence that intralesional steroid injection prior to dilation reduces the risk of recurrent stricture formation in refractory benign esophageal strictures. However, this comes from studies with poorly defined patient populations in which it was not clear whether patients truly had a refractory benign esophageal stricture. In addition, it remains to be defined what the optimal injection technique and frequency is, and at what dose triamcinolone should be injected.

STENTS

Placement of a self-expanding metal stent (SEMS) is the most frequently used method for palliation of dysphagia from esophageal or gastric cardia cancer. The use of a SEMS in malignant dysphagia is effective and relatively safe with complications in as many as 30% to 40% of patients.[32] Recently, self-expanding plastic stents (SEPSs) have been introduced. Results with SEPSs in malignant dysphagia are comparable to those with SEMSs; however, recurrent dysphagia because of stent migration has been reported to occur more frequently.[33]

During the last few years, stents have become increasingly important in various clinical applications, such as sealing benign esophageal leaks or perforations, and dilating refractory benign esophageal strictures. In the latter, the idea is that dilation for a prolonged period of time will ultimately reduce the risk of recurrent stricture formation. Stent types that have been used for benign esophageal strictures include uncovered, partially covered, or fully covered SEMSs, and fully covered SEPSs.[34]

SEMSs

Until now, more than 150 patients have been reported with a SEMS placed for a benign esophageal stricture (Table 1).[35-45] In the majority of patients, the strictures were resistant to repeated dilations. Indications for the SEMS placement included a variety of indications, with achalasia being the most common. Other indications included caustic strictures, postradiation strictures, anastomotic strictures, peptic strictures, and some other causes. In the initial studies, mainly uncovered SEMSs were used[35,36,38,39,41,43]; however, in the more recent studies, partially or fully covered SEMSs were more common.[37,38,40,42-45]

A limitation of uncovered and partially covered SEMSs is the occurrence of hyperplastic tissue ingrowth through the uncovered stent meshes (Fig. 1). Tissue ingrowth has been considered because of a combination of factors, particularly the type of metal (stainless steel or nitinol) used, the size, and the radial force of the stent and duration of stenting.[46] Although the risk of tissue ingrowth increases with stent time, it can already be observed as soon as 2 to 6 weeks after stent placement. This tissue reaction causes the uncovered stent parts to embed in the esophageal wall, which precludes easy removal. An obvious advantage of this anchoring is that migration of uncovered or partially covered SEMSs is uncommon, although it is more frequent with fully covered SEMSs. We and others have observed that tissue ingrowth can successfully be treated by placing a fully covered stent in the previously placed stent. The fully covered stent should have a length that overlaps and a size that is at least equal to that of the uncovered or partially covered stent.[47] During a period of 10 to 14 days, pressure necrosis of the hyperplastic tissue occurs as a result of friction between the two stents. Hence, removal of both stents can in most cases be performed without any friction. Apart from tissue ingrowth, hyperplastic tissue overgrowth at both stent ends can also be observed. This is a complication that occurs with all stent types. As can be seen in Table 1, hyperplastic tissue ingrowth or overgrowth was the cause of recurrent dysphagia in 26 patients (16%), whereas stent migration was seen in 19 patients (12%) treated with SEMSs. The use of a SEMS is relatively safe, with major complications seen in 17% of patients. The most frequent complications

TABLE 1. Reported results of self-expanding metal stents (SEMSs) for benign esophageal stricture. Dysphagia improvement is defined according to the dysphagia scoring system developed by Atkinson et al[74]*

Author	Patients (n)	Stricture type	Previous therapy	SEMSs (n)	Dyshagia improvement	Stenting time	Complications (%)	Long-term effect (%)
Cwikiel et al[35]	5	Caustic (n = 3)	>> dilations	Strecker (uncov) (n = 5)	Significant improvement	Stents not removed	2/5 (40): Hyperplastic tissue growth	2/5 (40): No recurrent stricture
		Peptic (n = 2)					1/5 (20): Pain	
Tan et al[36]	4	Peptic (n = 3)	4-14 dilations	Wallstent (uncov) (n = 5)	3.5 → 1	Stents not removed	2/4 (50): Hyperplastic tissue growth	2/4 (50): No recurrent stricture
		Protracted nasogastric tube (n = 1)						
Song et al[37]	5	Caustic (n = 3)	>> dilations	Custom-made Z-type stent (n = 3)	3 → 1	2 months	1/5 (20): Migration	3/5 (60): Improvement of dysphagia
		Peptic (n = 1)					1/5 (20): Pain	
		Extrinsic mass (n = 1)						
Song et al[38]	12	Caustic (n = 6)	Unknown	Strecker (uncov) (n = 1)	3 → 1	Stents not removed	6/12 (50): Migration	Unknown
		Anastomotic (n = 5)		Modified Z-stent (uncov) (n = 2)			5/12 (42): Hyperplastic tissue growth	
		Unknown (n = 1)		Song stent (cov) (n = 11)			1/12 (8): Migration + hyperplastic tissue growth	
Lee et al[39]	2	Achalasia (n = 2)	Myotomy (n = 1)	Esophacoil (uncov) (n = 2)	3 → 1	Stents not removed	1/2 (50): Ulcerative esophagitis	0/2 (0): No recurrent stricture
			Pneumatic dilation (n = 1)				1/2 (50%): Migration	
Mukherjee et al[40]	4	Achalasia (n = 4)	2-6 Pneumatic dilations	Wallstent (part. cov.) (n = 5)	Unknown	Stents not removed	1/4 (25): Migration	2/4 (50): No recurrent stricture
				Gianturco-Z (cov.) (n = 3)			1/4 (25): Stent occlusion	
							1/4 (25): Food bolus obstruction	
							1/4 (25): Hyperplastic tissue growth	

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TABLE 1 (*Continued*)

Author	Patients (n)	Stricture type	Previous therapy	SEMSs (n)	Dyshagia improvement	Stenting time	Complications (%)	Long-term effect (%)
Fiorini et al[41]	10	Postradiation (n = 5)	Unknown	Esophacoil (uncov) (n = 11)	3.5 → 1	Stents not removed	3/10 (30): Migration	5/10 (50): No recurrent stricture
		Anastomotic (n = 2)		CMD-F (uncov) (n = 3)			1/10 (10): Perforation by stent	
		Peptic (n=2)					1/10 (10): Pain	
		Achalasia (n = 1)					1/10 (10): Recurrent stricture	
Song et al[42]	25	Caustic (n = 22)	>> dilations	Type A (custom-made)	3 → 0-1	1-8 weeks	5/25 (20): Pain	Unknown
		Postradiation (n-1)		24-16-20 mm (cov) (n = 12)			12/25 (48): Hyperplastic tissue growth	
		Post-sclerotherapy (n = 1)		Type B (custom-made):			3/25 (12): Migration	
		Peptic (n = 1)		26-16-26 mm (cov) (n = 13)				
De Palma et al[43]	8	Achalasia (n = 8)	Myotomy (n = 2)	Esophacoil (uncov) (n = 4)	After stent plac: 0	Stents not removed	Early:	Unknown
			Pneumatic dilation (n = 2)	Ultraflex (part cov) (n = 4)			3/8 (38): Migration	
			Botox + dilation (n = 2)				1/8 (12): Pain	
			Myotomy + dilation (n = 2)				1/8 (12): Reflux	
							Late:	
							2/8 (25): Pain	
							1/8 (12): Migration	
							1/8 (12): Reflux esophagitis	
Wadhwa et al[44]	3	Anastomotic (n = 2)	>> dilations	Ultraflex (part cov) (n = 1)	Symptom relief	Unknown	1/3 (33): Cervical discitis	Unknown
		Peptic (n = 1)		Diamond (part cov) (n = 1)			1/3 (33): Stent erosion into aorta	
				Gianturco-Z (cov) (n = 1)			2/3 (66): Hyperplastic tissue growth	

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TABLE 1 (*Continued*)

Author	Patients (n)	Stricture type	Previous therapy	SEMSs (n)	Dyshagia improvement	Stenting time	Complications (%)	Long-term effect (%)
Cheng et al[45]	83	Achalasia (n = 70)	Unknown	Nitinol stent (part cov) (n = 85)	3 → 1	3-7 days	37/83 (45): Path	Unknown
		Anastomotic (n = 5)					12 (14) Bleeding (after stent removal)	
		Postradiation (n = 5)					13 (16) reflux	
		Caustic (n = 3)						

>>, Multiple dilations; *COV*, covered; *UNCOV*, uncovered.
*Please see Table 3.

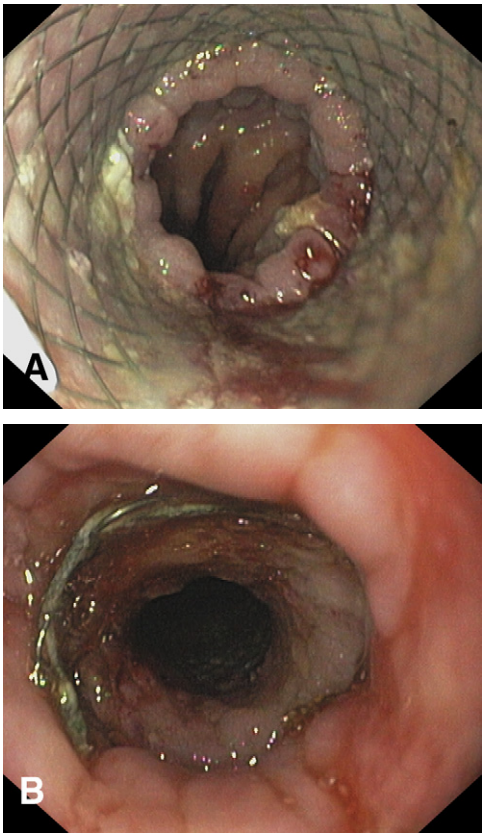

Figure 1. Hyperplastic tissue ingrowth through uncovered stent meshes at the distal (**A)** and proximal (**B)** end of a partially covered self-expanding metal stent.

included pain, followed by reflux (esophagitis), and, rarely, perforation.

Although stent removal after a limited timeframe is considered to be part of the treatment, more than 30% of patients had an SEMS that was not removed and was left in the esophagus for a prolonged period (Table 1). We believe that patient-related factors were predominantly involved in not having stents removed, with the most prominent of these being old age and comorbidity of patients. Some patients were probably also unwilling to have their stent removed because they were able to eat, which was not the case before stent placement. Finally, if faced with a stent embedded into the esophageal wall, physicians might be reluctant to remove the SEMS. Long-term effects of SEMS placement were only reported in less than 20% of patients. Of these, 47% had no clinical evidence of a recurrent stricture.[35-37,39-41] Factors related to long-term success were type of stricture, with postradiation strictures being more successful than peptic, anastomotic, or achalasia strictures.[41] In addition, length of the stricture also played a role, with shorter strictures being at lower risk of having a stricture reoccur.[42]

SEPSs

SEPSs are the other stent type used for this indication. The Polyflex stent (Boston Scientific, Natick, MA) is the only SEPS currently available. It is a silicone device with an encapsulated monofilament braid made of polyester. During the last 5 years, 8 studies have reported on more than 150 patients treated with a Polyflex stent for (refractory) benign esophageal strictures (Table 2).[48-56] Indications for stent placement in these series included anastomotic strictures, followed by peptic strictures, caustic strictures, postradiation strictures, and some other causes.

The initial studies with Polyflex stents showed promising results, with relief of dysphagia in as many as 80% of patients.[48-50] However, more recent studies have shown less favorable results, with high stent migration rates and recurrent strictures after stent removal reported in as many as 90% of patients.[55,56] An advantage of Polyflex stents is that they are easily removable. In addition, hyperplastic tissue overgrowth is unusual after Polyflex stent

TABLE 2. Reported results of self-expanding plastic stents for benign esophageal stricture. Dysphagia improvement is defined according to the dysphagia scoring system developed by Atkinson et al[74]*

Author	Patients (n)	Stricture	Previous therapy	Dysphagia improvement	Stenting time	Complications (%)	Long-team effect (%)
Broto et al[48]	10	Caustic (n = 9)	Caustic: 9 dilations	Unknown	Success (n = 5): 20 days-4 mo	3/10 (30): Migration	5/10 (50): No recurrent stricture
		Atresia (n = 1)	Atresia 1 dilation		Restricture (n = 5): 20-133 days	4/10 (40): Esophagitis	
Repici et al[49]	15	Caustic (n = 5)	9.5 (mean) dilations	3 → 1	6 wks	1/15 (7): Migration	12/15 (80): No recurrent stricture
		Anastomotic (n = 4)					
		Postradiation (n = 4)					
		Peptic (n = 2)					
Evrard et al[50]	21	Hyperplastic after previous SEMS (n = 5)	6 (med.)/year dilations	2 → ?	2 wks-18 months	11/21 (57): Migration	17/21 (81): No recurrent stricture
		Anastomotic (n = 4)					
		Fistula leak (n = 4)					
		Postradiation (n = 3)					
		Caustic (n = 3)					
		Peptic (n = 2)					
Karbowski et al[51]	14	Anastomotic (n = 5)	Unknown	Unknown	52 (14-256) days	7/14 (50): Migration	No improvement
		Peptic (n = 4)				7/14 (7): Severe pain	
		Postradiation (n = 2)				7/14 (7): Fistula	
		Caustic (n = 1)					
		Autoimmune (n = 1)					
		Post-Nissen (n = 1)					
Garcia-Cano[52]	4	Peptic (n = 3)	Unknown	Unknown	4 months-5 y	4/4 (100): Migration	2/4 (50): No recurrent stricture
		Anastomotic (n = 1)					
Barthel et al[53]	8	Anastomotic (n = 8)	≥ 3 dilations	3 → 1	83 (14–295) days	11/13 (85): Migration	1/8 (12): No recurrent stricture

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TABLE 2 (*Continued*)

Author	Patients (n)	Stricture	Previous therapy	Dysphagia improvement	Stenting time	Complications (%)	Long-team effect (%)
						1/13 (8): Nausea vomitting	
Pennathur et al[54]	17	Esophageal:	Unknown	Unknown	Unknown	14/17 (82): Migration	Esophageal: 2/9(22): no recurrent stricture
		Postradiation (n = 2)			Unknown	1/17 (6): Severe pain	Anastomotic: No improvement
		Peptic (n = 6)					
		Other (n = 1)					
		Gastric conduit (n = 3)					
		Anastomotic (n = 5)					
Holm et al[55]	33	Benign esophageal (n = 8)	Unknown	Unknown	53 (1-131) days	53/83 (64) Proc: Migration	5/83 (6) Proc no recurrent stricture
		Anastomotic (n = 11)				23 (28) Proc: Chest pain, dysphagia, etc	
		Fistula/leak (n = 9)				8 (10) Proc: Nausea/ vomitting	
		Postradiation (n = 5)				8 (10) Proc: Other	
						15 Proc: (18): Hyperplastic tissue overgrowth	
Dua et al[56]	40	Anastomotic (n = 12) (+ 4 fistula)	12 (mean) dilations	3 → 0.6	4 wks	8/38 (22): Migration	12/38 (32): No recurrent stricture
		Caustic (n = 8)				4/36 (11): Severe chest pain	
		Postradiation (n = 7)				3/36 (8): Bleeding	
		Pill-induced (n = 4)				2/36 (6): Perforation	
		Posttrauma (n = 3) (+ 3 fistula)				2/36 (6): Reflux	
		Peptic (n-2)				2/36 (6): Inability to remove the stent	
		Others (n = 4) (+ 1 fistula)				1/36 (3): Fistula	

PROC, Procedures.
*Please see Table 3.

placement for benign esophageal strictures, because it was not reported in 7 of the 8 published series.[48-54,56] This is probably because of the nonmetal material used, the fully covered design, and the relatively low radial force at the stent ends. On the other hand, migration rates were high after Polyflex stent placement, occurring in almost

TABLE 3. Dysphagia scoring system[74]

Score	Definition
0	Able to eat normal diet
1	Unable to swallow certain solids
2	Able to swallow semisolid foods
3	Able to swallow liquids only
4	Unable to swallow liquids

Adapted from Atkinson et al[74]

half of patients in 7 series,[48-54,56] and in almost two-thirds of procedures in the remaining series.[55] This high migration rate is likely the result of the fully covered stent design, the smooth outer surface of the stent, and the insufficient anchoring support provided by the stricture. Risk factors for migration were demonstrated to be location (more often in distal and proximal esophageal strictures compared with mid-esophageal strictures),[52,56] and etiology (more often in peptic strictures, followed by anastomotic strictures, fistulas/leaks, and postradiation strictures) of the stricture.[56] Major complications were seen in less than 10% of patients and consisted of perforations, fistulas, bleeding, reflux esophagitis, and pain.

Polyflex stents were removed in all patients, after stenting times varying between 4 weeks and 18 months. Long-term improvement of dysphagia was seen, however, in only 39% of patients,[48-54,56] whereas in one series this was even less with only 5 of 83 patients (6%), with interventions resulting in long-term success.[55]

In summary, the results on stent placement for refractory benign esophageal strictures suggest that various pathologic processes result in different clinical scenarios of dysphagia, with some of them requiring a single stent for a few weeks, although others need prolonged and/or repeat stenting. For example, the initial inflammatory reaction in peptic and caustic strictures may be severe, but will ultimately resolve, and a satisfactory outcome is achieved after stricture management. By contrast, in transmural (ischemic) insults to the esophagus, such as in postoperative anastomotic and postradiation strictures, resolution of the stricture takes more time, necessitating a prolonged dilation and/or stenting time. It should be remembered that placing a stent (either SEMS or SEPS) for a benign esophageal stricture is a temporary maneuver that allows the inflammatory reaction to resolve with time, and with resolution of the stricture as a final stage.[57] In addition, the only fully covered SEMS currently available in the United States is the Alimaxx-E stent (Merit Medical Systems, South Jordan, Utah). A number of failures have occurred with this stent,[58] and both this stent and other (partially covered) SEMSs are not approved by the U.S. Food and Drug Administration for therapy of benign strictures. Moreover, the only SEPS available, the Polyflex stent, is also not approved by the U.S. Food and Drug Administration for this indication. Therefore, it is recommended that SEMSs or SEPSs for benign esophageal strictures should only be used in approved clinical trials or in patients who have given informed consent to use a stent for this indication.

INCISIONAL THERAPY

Strictures at the esophagogastric anastomosis after esophageal resection have been reported in as many as 30% of patients. Postoperative complications, such as anastomotic leakage, fistula formation, or ischemia of the proximal gastric tube, contribute to anastomotic stricture formation.[6,59,60] The success rate of dilation therapy of anastomotic strictures ranges from 70% to 90%, with up to 40% of patients requiring more than 3 dilation sessions to achieve an adequate result.[7,59-61] An alternative treatment option for refractory benign anastomotic strictures is the use of incisional therapy, which was first effectively reported in the treatment of Schatzki's ring.[62,63] A small series using incisional therapy by means of electrocautery combined with balloon dilation,[64] electrocautery combined with argon plasma coagulation,[65,66] or electrocautery alone (Fig. 2)[67-69] for benign esophageal strictures had a report of favorable results. Hordijk et al[68] treated 20 patients with an anastomotic stricture refractory to a mean of 8 dilations with needle-knife electrocautery. A single electrocautery treatment was effective in 12 patients with a short stricture (<10 mm). Patients with longer strictures (≥ 10 mm) required a mean of 3 electrocautery procedures; however, this was still not successful in 2 patients (25%). The same authors also performed a randomized trial in 62 patients with a primary anastomotic stricture after esophageal resection and with varying grades of dysphagia.[70] Patients were randomized between Savary-Gilliard dilation and electrocautery incision. Clinical success was defined as the percentage of patients requiring a maximum of 5 dilations in 6 months. No difference in clinical success rate was observed between incisional therapy and dilation therapy (80.6% vs 67.7%; $P = .26$). In addition, no complications were observed.

In summary, incisional therapy can be considered in patients with a refractory Schatzki's ring and a refractory anastomotic stricture, particularly in those with a relatively short length stricture; however, more studies are needed to confirm these findings.

MANAGEMENT OF REFRACTORY BENIGN ESOPHAGEAL STRICTURES

Step 1

The first step in managing a benign esophageal stricture is balloon or Savary-Gilliard dilation, preferably to 16 mm or to 18 mm (Fig. 1). The recommendation to

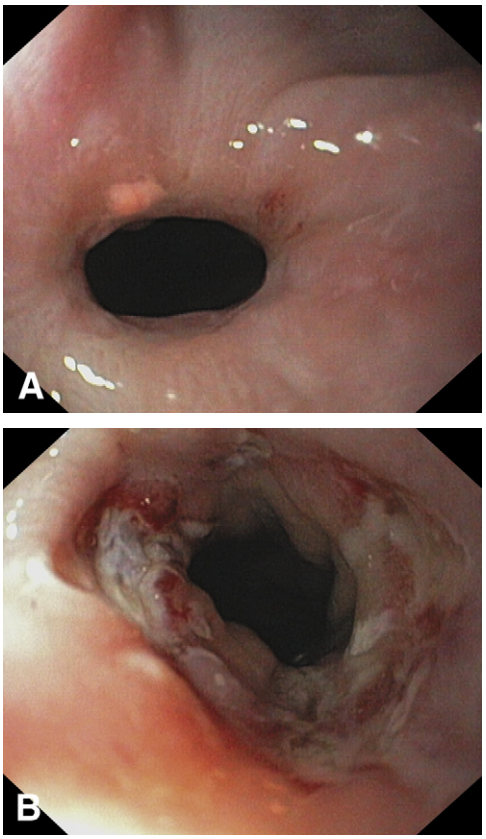

Figure 2. Anastomotic stricture after esophageal resection with gastric tube interposition (**A**) treated with incisional therapy by means of electrocautery (**B**).

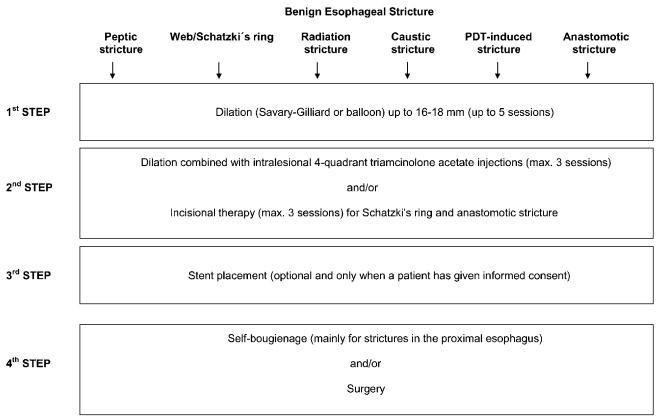

Figure 3. Treatment algorithm of benign esophageal strictures. PDT, photodynamic therapy.

perform at least 5 dilations to the maximum diameter before deciding to switch to an alternative treatment is usually attempted, although this treatment is not based on evidence. In our experience, this treatment management is recommended to be performed in dilation frequencies of once per week or even twice per week. This is also not evidence-based; however, the stricture has often returned to its predilation diameter with longer periods between dilation sessions, making it more difficult to reach the maximum diameter. Caustic, postradiation, postphotodynamic therapy, and anastomotic strictures are most frequently labeled as refractory.

Step 2

Before Step 2 is considered, it is important to emphasize that the treatment plan should always be discussed with the patient, because in some refractory benign esophageal strictures, many endoscopy sessions are indicated (Fig. 3). The patients' cooperation is important and they should know what treatment options are available and what to expect. Some patients may not be not willing to undergo a multitude of endoscopy sessions, and would prefer to have a stent placed or even opt for a surgical solution, after only one or two dilations.

After maximum dilation, the next step in the management of a refractory benign esophageal stricture is to combine dilation with intralesional steroid injections (Fig. 1). Because there is no treatment schedule that has been shown to be optimal in this case, it is recommended to perform at least 4 quadrant injections of 0.5 mL triamcinolone acetate (40 mg/mL) into the lesion.[30] At our institution, we use lower concentrations of triamcinolone acetate (20 mg/mL) for intralesional injection, and we also inject another 4 aliquots of 0.5 mL at the proximal margin of the stricture. However, there is no evidence substantiating our protocol. We suggest limiting dilation combined with intralesional steroid injection to a maximum of 3 sessions; in our experience, more treatment sessions are rarely effective.

In refractory Schatski's rings and anastomotic strictures, unsuccessful dilation can also be followed by incisional therapy with electrocautery. Again, we suggest performing a maximum of 3 treatment sessions, mainly because of a lack of further effect with more than three. Moreover, previous data, although performed in a small series, have shown no complications when a maximum of 3 sessions were performed.[68] We incise the stricture in 4 quadrants and we also coagulate the bridging (fibrous) tissue in between the incisions to establish a maximum wide luminal diameter.

Step 3

Stent placement is a treatment option to consider when an adequate luminal diameter has not been established with previous treatment modalities or when the stricture still recurs within a short time interval (Fig. 1). The preferred stent choice is a Polyflex stent for patients with a longer stricture in the mid-esophagus (>2 to 4 cm), such as those strictures that have occurred after caustic injuries or radiation therapy. In patients with an anastomotic stricture in the proximal esophagus or with a stricture in the distal esophagus, for example a peptic

stricture, a more flexible partially covered stent is recommended because the risk of migration is lower with this stent type (unpublished results).

It is not clear how long a stent should be left in the esophagus. Factors that influence stenting time include the underlying cause, the time since the injury to the esophagus occurred, and the stricture length. In the literature, no clear guidelines have been proposed. The following protocol for stent placement in refractory benign esophageal strictures is followed at our own institution[46]:

(1) Strictures that are caused by ischemic injury, present within <6 to 12 months after the injury, and/or are longer than 5 cm are stented for at least 8 to 16 weeks.
(2) In all other cases, stents are inserted for a shorter period, usually 4 to 8 weeks.
(3) When symptoms recur after stent removal, then a second stent is placed.
(4) When partially covered SEMSs are used, endoscopy should be performed at 4-week intervals to visualize whether embedding of the uncovered stent part in the esophageal mucosa has occurred. If this is the case, stent removal is performed, and another stent is placed, preferably a fully covered stent.
(5) Because fully covered SEMSs and Polyflex stents also carry a risk of hyperplastic tissue overgrowth, periodic endoscopy at 6-week intervals is recommended.

When stent placement is not successful and the stricture still persists, consideration to continue stenting may be the treatment plan, depending on the time to the occurrence of hyperplastic tissue ingrowth and overgrowth in a particular patient, with replacement of the stent at timeframes determined by this interval. As discussed, it is likely that the inflammatory reaction underlying the stricture will finally subside and the luminal diameter achieved at that time will remain, allowing the patient to eat a diet that is almost normal.

Step 4

An alternative treatment option is to teach the patient self-bougienage using Maloney dilators[71] (Fig. 1). This is not a commonly performed practice, but self-bougienage is safe and effective when patients have sufficiently learned the technique, and this can be useful in selected patients who are not afraid of performing the procedure. In our experience, self-bougienage is most successful when there is a favorable anatomy (eg, proximal strictures of caustic or anastomotic origin without significant diverticula formation).

Finally, there is a subgroup of patients in whom all efforts to dilate a refractory benign esophageal stricture are not successful. Alternatively, there are also patients who are not able to tolerate stent placement, or who just do not have enough patience to let the stricture resolve. In these patients, performing a surgical procedure can be considered, which often means that an esophageal resection is performed, or when an esophagogastric anastomosis is strictured, then a colonic interposition can be performed (Fig. 3).

CONCLUSION

Various factors determine the severity and persistence of benign esophageal strictures. Similarly, these factors also determine the long-term effectiveness of the currently available dilation procedures. It is recommended to treat esophageal strictures in a structured way by using the treatment algorithm as suggested in Figure 3. It should be stressed that no data are available to demonstrate that this treatment algorithm is indeed cost-effective. Furthermore, it is important to explain to patients the underlying mechanism(s) of stricture formation, to discuss pros and cons of the various treatment modalities, as suggested in Figure 1, and to convince patients that patience is required to achieve an optimal treatment result. When considering electrocautery or stenting, we suggest this should be performed in expert centers with experience in this modality. Although the results in this review are promising, further developments are obviously needed. There is limited evidence that biodegradable stents might be promising.[72,73] More information is currently needed on the safety of the material used. Moreover, it would be of great clinical value to have a selection of biodegradable stents available with variable durations of mechanical expansion force depending on the stricture that is treated. Finally, before biodegradable stents can be recommended, long-term clinical results of biodegradable stents in patients with refractory benign esophageal strictures are needed.

REFERENCES

1. Lew RJ, Kochman ML. A review of endoscopic methods of esophageal dilatation. J Clin Gastroenterol 2002;35:117-26.
2. Ferguson DD. Evaluation and management of benign esophageal strictures. Dis Esophagus 2005;18:359-64.
3. AGA. Technical review on treatment of patients with dysphagia caused by benign disorders of the distal esophagus. Gastroenterology 1999;117:233-54.
4. Shah JN. Benign refractory esophageal strictures: widening the endoscopist's role. Gastrointest Endosc 2006;63:164-7.
5. Spiess AE, Kahrilas PJ. Treating achalasia: from whalebone to laparoscope. JAMA 1998;280:638-42.
6. Siersema PD. Treatment options for esophageal strictures. Nat Clin Pract Gastroenterol Hepatol 2008;5:142-52.
7. Pereira-Lima JC, Ramires RP, Zamin I Jr, et al. Endoscopic dilation of benign esophageal strictures: report on 1043 procedures. Am J Gastroenterol 1999;94:1497-501.
8. Kochman ML, McClave SA, Boyce HW. The refractory and the recurrent esophageal stricture: a definition. Gastrointest Endosc 2005;62:474-5.
9. Scolapio JS, Pasha TM, Gostout CJ, et al. A randomized prospective study comparing rigid to balloon dilators for benign esophageal strictures and rings. Gastrointest Endosc 1999;50:13-7.
10. Abele JE. The physics of esophageal dilatation. Hepatogastroenterology 1992;39:486.

11. Cox JG, Winter RK, Maslin SC, et al. Balloon or bougie for dilatation of benign oesophageal strictures? An interim report of a randomized controlled trial. Gut 1988;29:1741-7.
12. Yamamoto H, Hughes RW Jr, Schroeder KW, et al. Treatment of benign esophageal strictures by Eden-Puestow or balloon dilators: a comparison between randomized and prospective nonrandomized trials. Mayo Clin Proc 1992;67:228-36.
13. Saeed ZA, Winchester CB, Ferro PS, et al. Prospective randomized comparison of polyvinyl bougies and through-the-scope balloons for dilation of peptic strictures of the esophagus. Gastrointest Endosc 1995;41:189-95.
14. Mandelstam P, Sugawa C, Silvis SE, et al. Complications associated with esophagogastroduodenoscopy and with esophageal dilation. Gastrointest Endosc 1976;23:16-9.
15. Hernandez LJ, Jacobson JW, Harris MS. Comparison among perforation rates of Maloney, balloon and Savary dilation of esophageal strictures. Gastrointest Endosc 2000;51:460-2.
16. Tucker LE. The importance of fluoroscopic guidance for Maloney dilation. Am J Gastroenterol 1992;87:1709-11.
17. Kadakia SC, Parker A, Carrougher JG, et al. Esophageal dilation with polyvinyl bougies, using a marked guidewire without the aid of fluoroscopy: an update. Am J Gastroenterol 1993;88:1381-6.
18. Wang YG, Tio TL, Soehendra N. Endoscopic dilation of esophageal stricture without fluoroscopy is safe and effective. World J Gastroenterol 2002;8:766-8.
19. Polese L, Angriman I, Bonello E, et al. Endoscopic dilation of benign esophageal strictures in a surgical unit: a report on 95 cases. Surg Laparosc Endosc Percutan Tech 2007;17:477-81.
20. Bueno R, Swanson SJ, Jaklitsch MT, et al. Combined antegrade and retrograde dilation: a new endoscopic technique in the management of complex esophageal obstruction. Gastrointest Endosc 2001;54:368-72.
21. Mukherjee K, Cash MP, Burkey BB, et al. Antegrade and retrograde endoscopy for treatment of esophageal stricture. Am Surg 2008;74: 686-7.
22. Maple JT, Petersen BT, Baron TH, et al. Endoscopic management of radiation-induced complete upper esophageal obstruction with an antegrade-retrograde rendezvous technique. Gastrointest Endosc 2006; 64:822-8.
23. Baumgart DC, Veltzke-Schlieker W, Wiedenmann B, et al. Successful recanalization of a completely obliterated esophageal stricture by using an endoscopic rendezvous maneuver. Gastrointest Endosc 2005;61: 473-5.
24. Lew RJ, Shah JN, Chalian A, et al. Technique of endoscopic retrograde puncture and dilatation of total esophageal stenosis in patients with radiation induced strictures. Head Neck 2004;26:179-82.
25. Ketchum LD, Smith J, Robinson DW, et al. The treatment of hypertrophic scar, keloid and scar contracture by triamcinolone acetonide. Plast Reconstr Surg 1966;38:209-18.
26. Griffith BH. The treatment of keloids with triamcinolone acetonide. Plast Reconstr Surg 1966;38:202-8.
27. Holder TM, Ashcraft KW, Leape L. The treatment of patients with esophageal strictures by local steroid injections. J Pediatr Surg 1969; 4:646-53.
28. Kochhar R, Ray JD, Sriram PV, et al. Intralesional steroids augment the effects of endoscopic dilation in corrosive esophageal strictures. Gastrointest Endosc 1999;49:509-13.
29. Kochhar R, Makharia GK. Usefulness of intralesional triamcinolone in treatment of benign esophageal strictures. Gastrointest Endosc 2002;56:829-34.
30. Altintas E, Kacar S, Tunc B, et al. Intralesional steroid injection in benign esophageal strictures resistant to bougie dilation. J Gastroenterol Hepatol 2004;19:1388-91.
31. Ramage JI Jr, Rumalla A, Baron TH, et al. A prospective, randomized, double-blind, placebo-controlled trial of endoscopic steroid injection therapy for recalcitrant esophageal peptic strictures. Am J Gastroenterol 2005;100:2419-25.
32. Homs MY, Siersema PD. Stents in the GI tract. Expert Rev Med Devices 2007;4:741-52.
33. Verschuur EM, Repici A, Kuipers EJ, et al. New design esophageal stents for the palliation of dysphagia from esophageal or gastric cardia aancer: a randomized trial. Am J Gastroenterol 2008;103:304-12.
34. Siersema PD. Stenting for benign esophageal strictures. Endoscopy 2009 (in press).
35. Cwikiel W, Willén R, Stridbeck H, et al. Self-expanding stent in the treatment of benign esophageal strictures: experimental study in pigs and presentation of clinical cases. Radiology 1993;187:667-71.
36. Tan BS, Kennedy C, Morgan R, et al. Using uncovered metallic endoprostheses to treat recurrent benign esophageal strictures. AJR Am J Roentgenol 1997;169:1281-4.
37. Song HY, Park SI, Jung HY, et al. Benign and malignant esophageal strictures: treatment with a polyurethane-covered retrievable expandable metallic stent. Radiology 1997;203:747-52.
38. Song HY, Jung HY, Park SI, et al. Covered retrievable expandable nitinol stents in patients with benign esophageal strictures: initial experience. Radiology 2000;217:551-7.
39. Lee JG, Hsu R, Leung JW. Are self-expanding metal mesh stents useful in the treatment of benign esophageal stenoses and fistulas? An experience of four cases. Am J Gastroenterol 2000;95:1920-5.
40. Mukherjee S, Kaplan DS, Parasher G, et al. Expandable metal stents in achalasia–is there a role? Am J Gastroenterol 2000;95:2185-8.
41. Fiorini A, Fleischer D, Valero J, et al. Self-expandable metal coil stents in the treatment of benign esophageal strictures refractory to conventional therapy: a case series. Gastrointest Endosc 2000;52:259-62.
42. Song HY, Jung HY, Park SI, et al. Covered retrievable expandable nitinol stents in patients with benign esophageal strictures: initial experience. Radiology 2000;217:551-7.
43. De Palma GD, Iovino P, Masone S, et al. Self-expanding metal stents for endoscopic treatment of esophageal achalasia unresponsive to conventional treatments. Long-term results in eight patients. Endoscopy 2001;33:1027-30.
44. Wadhwa RP, Kozarek RA, France RE, et al. Use of self-expandable metallic stents in benign GI diseases. Gastrointest Endosc 2003;58:207-12.
45. Cheng YS, Li MH, Chen WX, et al. Temporary partially-covered metal stent insertion in benign esophageal stricture. World J Gastroenterol 2003;9:2359-61.
46. Siersema PD, Hirdes MM. What is the optimal duration of stent placement for refractory, benign esophageal strictures? Nat Clin Pract Gastroenterol Hepatol 2009;6:146-7.
47. Evrard S, Le Moine O, Lazaraki G, et al. Self-expanding plastic stents for benign esophageal lesions. Gastrointest Endosc 2004;60:894-900.
48. Broto J, Asensio M, Vernet JM. Results of a new technique in the treatment of severe esophageal stenosis in children: poliflex stents. J Pediatr Gastroenterol Nutr 2003;37:203-6.
49. Repici A, Conio M, De Angelis C, et al. Temporary placement of an expandable polyester silicone-covered stent for treatment of refractory benign esophageal strictures. Gastrointest Endosc 2004;60: 513-9.
50. Evrard S, Le Moine O, Lazaraki G, et al. Self-expanding plastic stents for benign esophageal lesions. Gastrointest Endosc 2004;60:894-900.
51. Karbowski M, Schembre D, Kozarek R, et al. Polyflex self-expanding, removable plastic stents: assessment of treatment efficacy and safety in a variety of benign and malignant conditions of the esophagus. Surg Endosc 2008;22:1326-33.
52. García-Cano J. Dilation of benign strictures in the esophagus and colon with the Polyflex stent: a case series study. Dig Dis Sci 2008;53: 341-6.
53. Barthel JS, Kelley ST, Klapman JB. Management of persistent gastroesophageal anastomotic strictures with removable self-expandable polyester silicon-covered (Polyflex) stents: an alternative to serial dilation. Gastrointest Endosc 2008;67:546-52.
54. Pennathur A, Chang AC, McGrath KM, et al. Polyflex expandable stents in the treatment of esophageal disease: initial experience. Ann Thorac Surg 2008;85:1968-72.

55. Holm AN, de la Mora Levy JG, Gostout CJ, et al. Self-expanding plastic stents in treatment of benign esophageal conditions. Gastrointest Endosc 2008;67:20-5.
56. Dua KS, Vleggaar FP, Santharam R, et al. Removable self-expanding plastic esophageal stent as a continuous, non-permanent dilator in treating refractory benign esophageal strictures: a prospective two-center study. Am J Gastroenterol 2008;103:2988-94.
57. Kochman ML. Removable endoprothetics in the management of esophageal pathology: all strictures and fistulae are not created equal…. Gastrointest Endosoc 2008;67:26-7.
58. Berman KH, Rex DK. Alveolus AliMAXX-E esophageasl stent disintegration and breakage. Gastrointest Endosc 2009;69:980-1.
59. Honkoop P, Siersema PD, Tilanus HW, et al. Benign anastomotic strictures after transhiatal esophagectomy and cervical esophagostomy: risk factors and management. J Thorac Cardiovasc Surg 1996;11: 1141-8.
60. Johansson J, Zilling T, Stael von Holstein C, et al. Anastomotic diameters and strictures following esophagectomy and total gastrectomy in 256 patients. World J Surg 2000;24:78-85.
61. Ikeya T, Ohwada S, Ogawa T, et al. Endoscopic balloon dilation for benign esophageal anastomotic stricture: factors influencing its effectiveness. Hepatogastroenterology 1999;46:959-66.
62. Burdick JS, Venu RP, Hogan WJ. Cutting the defiant lower esophageal ring. Gastrointest Endosc 1993;39:616-9.
63. DiSario JA, Pedersen PJ, Bichis-Canoutas C, et al. Incision of recurrent distal esophageal (Schatzki) ring after dilation. Gastrointest Endosc 2002;56:244-8.
64. Hagiwara A, Togawa T, Yamasaki J, et al. Endoscopic incision and balloon dilatation for cicatricial anastomotic strictures. Hepatogastroenterology 1999;46:997-9.
65. Schubert D, Kuhn R, Lippert H, et al. Endoscopic treatment of benign gastrointestinal anastomotic strictures using argon plasma coagulation in combination with diathermy. Surg Endosc 2003;17: 1579-82.
66. Pross M, Manger T, Lippert H. Combination of diathermia and argon plasma coagulation in treatment of cicatricial esophageal stenoses. Zentralbl Chir 1998;123:1145-7.
67. Brandimarte G, Tursi A. Endoscopic treatment of benign anastomotic esophageal stenosis with electrocautery. Endoscopy 2002;34:399-401.
68. Hordijk ML, Siersema PD, Tilanus HW, et al. Electrocautery therapy for refractory anastomotic strictures of the esophagus. Gastrointest Endosc 2006;63:157-63.
69. Simmons DT, Baron TH. Electroincision of refractory esophagogastric anastomotic strictures. Dis Esophagus 2006;19:410-4.
70. Hordijk ML, van Hooft JE, Hansen BE, et al. A randomized comparison of electrocautery incision with Savary bougienage for relief of anastomotic gastroesophageal strictures. Gastrointest Endosc 2009:70:849-55.
71. Bapat RD, Bakhshi GD, Kantharia CV, et al. Self-bougienage: long-term relief of corrosive esophageal stricture. Indian J Gastroenterol 2001;20:180-2.
72. Freeman ML. Bioabsorbable stents for gastrointestinal endoscopy. Tech Gastrointest Endosc 2001;3:120-5.
73. Saito Y, Tanaka T, Andoh A, et al. Usefulness of biodegradable stents constructed of poly-l-lactic acid monofilaments in patients with benign esophageal stenosis. World J Gastroenterol 2007;13:3977-80.
74. Atkinson M, Ferguson R, Ogylvie AC. Management of malignant dysphagia by intibation at endoscopy. J Roy Soc Med 1979;27:894-7.

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Department of Gastroenterology & Hepatology, University Medical Center Utrecht, The Netherlands.

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