Review Article

Refractory benign esophageal strictures

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Abstract Refractory benign esophageal stricture (RBES) is a frequently encountered problem worldwide. These strictures arise from various causes such as corrosive injury, radiation therapy, peptic origin, ablative therapy, and after surgery. Most strictures can be treated successfully with endoscopic dilatation using bougies or balloons, with only a few complications. Those patients who fail after serial dilatation with bougies or balloons will come to the category of refractory strictures. Dilatation combined with intralesional steroid injections can be considered for peptic strictures, whereas incisional therapy has been demonstrated to be effective for short anastomotic strictures. When these therapeutic options do not resolve the stenosis, stent placement should be considered. Self-bougienage can be proposed to a selected group of patients with a proximal stenosis. Most of the patients of RBES respond to above-mentioned treatment and occasional patient may require surgery as the final treatment option. This review aims to provide a comprehensive approach toward endoscopic management of RBESs based on current literature and personal experience.

Key words

Biodegradable stent, dilatation, dysphagia, incisional therapy, refractory benign esophageal strictures, self-expandable metal stent, self-expandable plastic stent

Introduction

Refractory benign esophageal stricture (RBES) is a frequently encountered problem, which negatively affects patient's quality of life and has significant complications such as malnutrition, weight loss, and aspiration pneumonia.^[1] Typical benign esophageal strictures are characterized by a cicatricial, anatomic narrowing of the esophagus, which define as either simple or complex strictures. Simple strictures are short (<2 cm) focal, straight, and can be traversed with an adult endoscope prior to dilatation and are mostly caused by Schatzki rings, esophageal webs, or peptic injury. In contrast, complex strictures are long (>2 cm), irregular, angulated, or difficult to traverse with an endoscope and mainly caused by

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surgery, radiotherapy, or corrosive injury.^[2] Peptic strictures are common in Western countries and usually respond to few sessions of dilatation. Corrosive strictures are common in developing countries and require repeated sessions of endoscopic dilatation.[3-5]

Refractory esophageal strictures are the ones which require more than five sessions of dilatation at 2 weeks interval to achieve a diameter of 14 mm in the absence of endoscopic evidence of inflammation. Inability to maintain the satisfactory esophageal lumen for 4 weeks after achieving a 14 mm diameter is a recurrent stricture.^[6]

The extent of fibrosis of the esophageal wall is an important determinant of stricture severity, maximum wall thickness of 9 mm, or more require a higher number of dilatation sessions than those with <9 mm on computed tomography scan [Figure 1].^[7] Endoscopic ultrasonography gives more detailed examination of the full thickness of the esophageal

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wall, the maximum wall thickness has been found to be greater in patients with corrosive and postradiation strictures as compared to patients with peptic strictures. Those patients with involvement of muscularis propria require more sessions of dilatation as compared to patients having involvement of mucosa and submucosa [Figure 2].^[8]

Serial endoscopic dilatation with bougies or balloons has been the standard treatment for esophageal strictures. In patients with benign simple strictures, dilatation gives good relief in 85–93% of cases.^[9] Dilatation appears less effective in those with radiation- or corrosive-induced complex strictures. The recurrence rate reaches to 30–40% during long-term follow-up, especially in complex strictures.^[3]

Those patients who fail after serial dilatation with bougies or balloons will come to the category of refractory strictures. Adding local steroid injection followed by dilatation is found to decrease the number and frequency of dilatation in peptic strictures [Table 1].^[10,11] Intralesional steroid injection followed by dilatation has been found to be useful in patients with corrosive strictures in nonrandomized trial,^[13,14] but its usefulness could not be proved in a randomized controlled trial [Table 2].^[15] Similarly, adding local steroid injection to dilatation did not result in clinical benefit in patients of anastomotic strictures.^[12] Incisional therapy can be performed for short strictures (<1 cm) using needle knife or tip of the polypectomy snare. It has been found to be useful and safe in short anastomotic strictures, the results are comparable to dilatation.^[16]



Figure 1: Computed tomography Images of esophageal wall thickness in benign esophageal stricture reproduced from Lahoti *et al.*^[7] (a) Normal esophageal wall (arrow). (b) Mid increase in esophageal wall thickness (arrow). (c) Marked increase in esophageal wall thickness note the esophageal lumen (long arrow) and the outer limit of thickened esophageal wall (short arrow)

Self-expandable stents work on the principle of persistent dilatation till the inflammation subsides. The advantage is avoiding repeated sessions of dilatations. Uncovered self-expandable metal stents (SEMS) have a high complication rate (up to 80%) due to hyperplasic tissue in growth; therefore, fully covered SEMS (FCSEMS) are preferable but studies with FCSEMS showed high migration rate with lower clinical success [Table 3].^[17-22]

To overcome the problem of hyperplastic tissue reaction, self-expandable plastic stents (SEPS) were introduced. A meta-analysis concluded SEPS to be technically successful in 98% with 50% clinical success and 9% major complications.^[23] Another review showed similar technical and clinical success but stent migration in one-third of patients [Table 4].^[24.36]

Biodegradable stents (BD) are the alternative to SEPS, they are either Polydioxanone BD stent or Poly-L-lactic acid BD stent. Their degradation occurs by hydrolysis, which starts after 4–5 weeks and dissolves over a period of 2–3 months. Limitations of BD stents are low radial force contributing to early stricture recurrence and their high cost. Sequential BD stent placement is an effective alternative to avoid the burden of frequent dilatation.

The technical success rate of BD stents in various studies ranges from 85 to 100% with median 96% and clinical success rate



Figure 2: Endoscopic ultrasonography images of benign esophageal stricture reproduced from Rana *et al.*⁽⁸⁾ (a) Endoscopic ultrasonography in a patient with peptic stricture showing the involvement of the mucosa and submucosa. Muscularis propria is seen as hypoechoic layer (arrows). (b) Endoscopic ultrasonography in a patient with corrosive stricture showing involvement of the muscularis propria of esophagus with thickened esophageal wall. (c) Endoscopic ultrasonography in a patient with postradiation stricture showing involvement of all the layers of esophagus with thickened esophageal wall

Table 1: Results of steroid injection therapy in peptic and anastomotic esophageal strictures							
Author	Year	Type of study	Number of patients	Type of stricture	Results		
Dunne <i>et al</i> . ^[11]	1999	Prospective randomized (steroid group and control group)	42	Peptic	Decreased dilation frequency in steroid group from 6 to 2 at 1 year		
Ramage et al.[10]	2005	Prospective double blind randomized (steroid group and shame group)	30	Peptic	Decreased frequency of repeat dilation 13% in steroid group versus 60% in shame group		
Hirdes et al.[12]	2013	Double-blind trial	60	Anastomotic	Did not result in clinical benefit		

Table 2: Results of steroid injection therapy in corrosive esophageal strictures						
Author	Year	Type of study	Number of patients	Results Median periodic dilation index decreased significantly from 1.67 to 0.32		
Kochhar <i>et al.</i> ^[13]	1999	Nonrandomized	70			
Kochhar and Makharia ^[14]	a ^[14] 2002 Nonrandomized		29	Median periodic dilation index decreased from 1.24 to 0.53		
Camargo <i>et al.</i> ^[15] 2003 Randomized (Group A - dilation with steroid Group B - dilation with saline solution injection)		14	No statistically difference in dilation frequency and dysphagia between the two groups			

Author	Year	Study design	Number of patients	Duration of stent placement (days)	Early stent migration (%) ^a	Clinical success n (%) ^b	
Song et al.[17]	2000	Prospective	25	56	12	12 (48)	
Eloubeidi and Lopes ^[18]	2009	Prospective	7	46	36	2 (29)	
Kim <i>et al.</i> ^[19]	2009	Prospective	55	60	25.4	17 (31)	
Bakken et al.[20]	2010	Retrospective	7	67	50	2 (29)	
Eloubeidi et al.[21]	2011	Retrospective	10	-	37	2 (21)	
Hirdes et al.[22]	2012	Prospective	15	86	33.3	0 (0)	

Early stent migration was defined as the occurrence of stent migration within 4 weeks from stent placement. Clinical success was defined as clinical remission without the need for further endoscopic dilation or surgery after stent removal or migration

Table 4: Results of self-expandable plastic stents in refractory benign esophageal strictures								
Authors	Years	Study design	Number of patients	Technical success ^a	Early stent migration ^b	Reintervention	Clinical success°	
Broto et al.[25]	2003	Retrospective	10	10 (100)	2 (20)	6 (50)	5 (50)	
Evrard et al.[26]	2004	Prospective	17	17 (100)	5 (29)	5 (29)	13 (76)	
Repici et al.[27]	2004	Prospective	15	15 (100)	1 (7)	1 (7)	12 (80)	
Triester et al.[28]	2006	Retrospective	5	5 (100)	2 (40)	2 (40)	0 (0)	
Barthel et al.[29]	2008	Retrospective	8	8 (100)	-	4 (50)	1 (13)	
Dua <i>et al</i> . ^[30]	2008	Retrospective	40	38 (95)	-	23 (58)	12 (30)	
Martin et al.[31]	2008	Retrospective	18	18 (100)	1 (6)	2 (11)	17 (94)	
García-Cano ^[32]	2008	Retrospective	4	4 (100)	3 (75)	4 (100)	2 (50)	
Karbowski <i>et al.</i> [33]	2008	Retrospective	12	12 (100)	5 (42)	-	5 (42)	
Oh <i>et al</i> . ^[34]	2010	Prospective	13	13 (100)	4 (31)	-	3 (23)	
van Boeckel <i>et al</i> .[35]	2011	Prospective	20	19 (95)	5 (25)	-	6 (30)	
Canena et al.[36]	2012	Prospective	10	10 (100)	6 (60)	9 (90)	1 (10)	
Total			172	169	39 (31)	56 (44)	77 (45)	

Reproduced from Ham and Kim.^[24] Values are presented as number (%). ^aTechnical success was defined as the correct positioning of the stent within the stricture, ^bEarly stent migration was defined as the occurrence of stent migration within 4 weeks from stent placement, ^cClinical success was defined as clinical remission without the need for further endoscopic dilation or surgery after stent removal or migration

ranges from 25 to 100% with median 47% [Table 5].^[24,35-43] A study comparing SEPS and BD stents showed clinical relief of dysphagia in 30% and 33% patients, respectively, of patients with RBES.^[35] A prospective multicenter study compared temporary placement of three different SEPS (FCSEMS, SEPS, BD) for the treatment of RBES. These stents were placed for 12 weeks. Short-term benefit was comparable for all three stents at 8–9 weeks, long-term benefit could be achieved with BD and FCSEMS but not with SEPS.^[36] The technical success was 100% among all 3 stents long-term clinical success was higher with FCSEMS (40%) than BD stents (30%) and least with SEPS (10%). The migration rates of SEPS, FCSEMS, and BD were 18%, 9%, and 6%, respectively.

The cost of BD stent is an important issue, especially in developing countries. Cost of FCSEMS and SEPS are 1000\$

(USD) and 400\$ (USD), respectively, whereas the cost of BD stent is around 900£ (pound).

The duration of stent placement in RBES is till the inflammation subsides. Strictures longer than 5 cm may require longer duration of stenting. The duration of stent placement ranges from 12 to 16 weeks. The other factors such as the etiology of stricture and severity of inflammation also affect the outcome of stent placement.

Summary

All patients of RBESs except anastomotic stricture after the failure of conventional dilatation treatment should be subjected to three sessions of dilatation with intralesional four quadrant triamcinolone injections. Incisional therapy (maximum three

Table 5: Result of biodegradable stents in benign esophageal strictures									
Authors	Year	Study design	Stent type	Number of patient	Technical success ^a	Early stent migration ^b	Tissue hyperplasia	Clinical success°	
Tanaka <i>et al.</i> [38]	2006	Retrospective	PLLA	2	2 (100)	2 (100)	0 (0)	2 (100)	
Saito et al.[39]	2007	Prospective	PLLA	13	13 (100)	10 (77)	0 (0)	13 (100)	
Saito et al.[40]	2008	Prospective	PLLA	2	2 (100)	0 (0)	0 (0)	2 (100)	
Repici et al.[37]	2010	Retrospective	ELLA	21	21 (100)	2 (10)	1 (5)	9 (43)	
van Boeckel et al.[35]	2011	Retrospective	ELLA	18	16 (85)	4 (22)	2 (11)	6 (33)	
van Hooft <i>et al</i> .[41]	2011		ELLA	10	10 (100)	0 (0)	2 (20)	6 (60)	
Canena <i>et al</i> .[36]	2012	Retrospective	ELLA	10	10 (100)	2 (20)	3 (30)	3 (30)	
Hirdes et al.[42]	2012	Retrospective	ELLA	28	26 (93)	3 (11)	-	7 (25)	
Karakan <i>et al</i> . ^[43]	2013	Retrospective	ELLA	7	7 (100)	0 (0)	3 (43)	4 (57)	
Total				111	107 (96)	23 (21)	11 (13)	52 (47)	

Reproduced from Ham and Kim.^[24] ^aTechnical success was defined as the correct positioning of the stent within the stricture, ^bEarly stent migration was defined as the occurrence of stent migration within 4 weeks from stent placement, ^cClinical success was defined as clinical remission without the need for further endoscopic dilation or surgery after stent removal or migration. PLLA=Poly-L-lactic acid



Figure 3: Algorithm for management of refractory benign esophageal strictures (original) FCSEMS: Fully covered self-expandable metallic stents; BD: Biodegradable stents SEPS: Self-expandable plastic stents

sessions) is recommended for short (<1 cm) anastomotic strictures. Temporary placement of fully covered metallic stent should be tried if the above treatment fails and BD stent may be an option in these cases. Occasional patients with proximal esophageal refractory strictures may do self-bougienage when all these above treatment options fail. Most of the patients of RBES respond to above-mentioned treatment and occasional patient may require surgery as the final treatment option. An algorithm for the management of RBES is given in Figure 3.

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Conflicts of interest

There are no conflicts of interest.

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