Chapter 16
Endoscopic Therapy of Intestinal Strictures: What Is State of the Art?

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Abstract Symptomatic intestinal strictures develop in more than one third of patients with Crohn's disease during their lifetime. Strictures can be inflammatory, fibrotic or mixed. Fibrosis occurs as a result of excessive deposition of extracellular matrix protein. It can lead to severe symptoms affecting patients' quality of life. As a result, patients will often need to undergo surgery to improve their symptoms. Endoscopic balloon dilatation appears to be a safe and effective alternative therapeutic procedure to replace or postpone surgery. It is less invasive and can be performed during a regular colonoscopy. Non-complex strictures that are ≤5 cm can be dilated endoscopically. Up to 80% of patients will have immediate relief of symptoms and it can prevent surgery in up to 70% of patients after a 3-year follow up. Serious complications are rare and occur in less than 3% of procedures.

Keywords Endoscopic balloon dilatation · Stricture · Crohn's disease

16.1 Introduction

The natural history and phenotype of Crohn's disease (CD) is highly variable [1]. Even though most patients will present with purely uncomplicated inflammation, approximately 70% will develop either strictures or fistulae within 10 years of disease [2–5]. Whereas the location of disease remains stable over time, changes in disease behavior may occur. Approximately 30–50% of patients with fibrostenotic disease present as such and many others will develop a stricture over the course of their life [2, 3, 5, 6]. Intestinal strictures will occur in at least one-third of CD patients and can be fibrotic, inflammatory or mixed leading to luminal narrowing resulting in symptomatic obstruction, pre-stenotic fistulizing disease and potentially

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harbor malignant lesions. It is currently one of the main indications for surgical treatment of CD [7, 8]. In fact, 75% of affected individuals will undergo surgery in their lifetime [2]. Disease recurrence at the site of anastomosis is common which may lead to recurrence of luminal strictures [9].

The development of fibrosis is caused by excessive deposition of extracellular matrix protein produced by activated myofibroblasts as a consequence of chronic uncontrolled localized inflammation [10, 11]. Given the transmural nature of CD, all bowel layers are involved by fibrosis and will present features of histomorphological thickening. Despite recent advances in the understanding of the pathophysiology of CD, the exact mechanism responsible for luminal fibrosis remains to be elucidated. In addition, the incidence of intestinal strictures has not changed over time despite the introduction of novel therapeutic options [12–16]. Although biologics and immunosuppressants may delay the onset of complicated disease, they have not been shown to prevent it. Currently, specific anti-fibrotic therapy is not commercially available [17].

Significant bowel strictures will often lead to a varying degree of severity of obstructive symptoms that negatively impact on patients' quality of life [8]. As a result, patients will often need to undergo repeated surgical resections of the affected segments which exposes them to the risk of immediate and long term postoperative complications such as short bowel syndrome, loss of gut functionality, and high risk of stricture recurrence (up to 50%) [8, 18]. In light of this information, endoscopic balloon dilatation (EBD) has emerged as an attractive alternative therapeutic procedure [19]. Given that most strictures are located in the colon or ileum [3], they are accessible by using through-the-scope colonoscope or balloon-assisted enteroscope [20–22]. To improve outcomes of EBD, injection of medical therapy has been attempted.

In this chapter, we will describe the data on endoscopic balloon dilation as well as presenting the short and long term outcomes and complications associated with it. In addition, we will provide a practical description on how to perform the procedure.

16.2 Efficacy of Endoscopic Balloon Dilatation

In the absence of medical therapy targeted at treating intestinal fibrosis and with the failure of medical therapy to relieve obstructive symptoms, endoscopic balloon dilatation is a very good alternative to conserve bowel length. EBD has become an accepted modality for the treatment of bowel strictures in patients with CD. It is mainly applicable in short strictures (≤5 cm) and in locations that easily accessible by endoscopy [23]. The most common location tends to be at the ileocolonic anastomosis in a patient who underwent bowel resection [17, 19, 24]. EBD can also be performed anywhere in the colon using a colonoscope, in the upper GI tract using a gastroscope or in the small intestine when reachable with an enteroscope.

Most of the published data on outcomes of EBD is observational with its inherent limitations. However, the data clearly confirm the role of EBD with excellent short

term efficacy and moderate long term efficacy for EBD in the management of CD strictures. The immediate success rate is generally very high ranging between 71% and 100% [23, 24]. In a recent pooled analysis of 33 retrospective studies including 1463 CD patients treated with 3213 EBD procedures, the immediate intra-procedure success rate was 89% [23]. The median stricture length was 2 cm and the treated lesions were mainly post-operative strictures. More recently, the Cleveland Clinic group also showed that in their cohort of patients with post-operative anastomotic strictures, the immediate success rate was 91.3% [25]. Although the technical success is important, it needs to translate into a clinical symptomatic improvement. In the same pooled analysis, 80.8% of patients had relief of clinical symptoms or clinical efficacy [23]. Long term clinical efficacy defined as being free of surgery with a median follow up period of 40.1 months was achieved in 69.2% of patients. However, at 24 months, 73.5% of patients required repeat dilatation. Interestingly, the technical success for dilating a post-operative stricture was lower than that of native strictures (odds ratio (OR) = 2.3, $P < 0.001$) but the long-term outcomes were similar [23]. This finding is contradictory to common experience as most endoscopists find it technically easier to dilate a post-operative stenosis provided the anastomosis is not too angulated. On the other hand, these findings were not corroborated in the Cleveland Clinic cohort where the success rate was much lower with 52% of patients requiring surgery over the follow up period post EBD [25].

Factors that have been associated with favorable short term dilatation outcomes include greater maximal dilatation diameter (OR = 1.4, $P < 0.001$), 'de novo' or native strictures (OR = 2.3, $P < 0.001$, not confirmed), technically successful dilatation, stricture ≤5 cm, and absence of ulcers in the stricture [26–28]. Clinical efficacy was neither associated with location of stricture nor was it dependent on the type of stricture (native vs post-operative). In addition, no factors were identified as a predictor of long term outcomes or of the need for repeat dilatation [17]. Neither CRP, endoscopic disease activity, or medical treatment after dilation influenced the subsequent disease course [29]. As for factors predicting need for surgery, every increase by 1 cm in stricture length resulted in an increased risk for surgery by 8% ($P < 0.005$). A stricture length of ≤5 cm was associated with a surgery-free outcome (hazard ratio (HR) = 2.5, 95% confidence interval (CI) = 1.4–4.4). Strictures located in the duodenum compared with those located in the jejunum/ileum or colon were associated with a nearly 5 times increased hazard for shorter time to surgery (HR 4.7, $P < 0.038$; HR 5.6, $P < 0.03$, respectively). None of the other investigated factors was linked to need for earlier surgery [17].

16.3 Safety of Endoscopic Therapy

In general, EBD is considered as a safe procedure. However, when mechanically dilating the bowel, perforation is a valid concern. In the above mentioned systematic review, major complications defined as hospitalization, bleeding or perforation was observed in 2.7% of procedures [17]. In the Cleveland clinic cohort, the perforation

rate was only 1.1% which is very reassuring when compared to postoperative complications which occurred in 8.8% of patients and consisted mainly of intra-abdominal abscesses and enterocutaneous fistula [25]. No death related to EBD has ever been recorded and none of the factors evaluated in the systematic review was associated with a higher risk of complications. Although it is a rare occurrence, small bowel adenocarcinoma could be fatal if overlooked [30]. Therefore, it is recommended to take biopsies of the stricture prior to EBD, particularly when it is irregular or displays other features suspicious of malignancy. There has been no evidence to suggest that mucosal biopsy prior to EBD increases the risk of perforation. It noteworthy to mention that EBD is contraindicated in a stenosis associated with an abscess, a phlegmon, fistula, high-grade dysplasia or malignancy [31].

16.4 Concomitant Injection of Pharmacological Agents

The use of intra-lesion injection of steroids has been shown to be effective in the management of several types of gastrointestinal strictures such as peptic, post-radiotherapy, and corrosive strictures but is still controversial in CD-associated strictures [32–35]. Most of these studies have used triamcinolone as it is considered an appropriate agent given its long local effect which can last up to 3–4 weeks [36]. Much of the data available on the use of steroids in the management of CD-related strictures is retrospective and uncontrolled. In a systematic review, the use of steroids injection in addition to EBD did not show an additive effect [23]. However, in a small randomized controlled trial of 29 pediatric CD patients, combination of EBD and intra-lesional triamcinolone was shown to reduce the time to re-dilatation and surgery when compared to the placebo group [37]. On the contrary, a small prospective study including 13 adult patients was terminated prematurely when initial results showed that patients who received steroid injection required earlier re-dilatation compared to placebo [38]. However, this study was limited to longstanding post-operative strictures and the methodology might harbor significant biases. Meanwhile, intra-lesional injection of anti-tumor necrosis factor alpha was only assessed in small, uncontrolled cases reports and series but the preliminary results are promising [39, 40]. Immunization to biologics is of course a concern when local injection is performed.

16.5 How to Perform an EBD

Commonly, EBD is performed using the through-the-scope balloons (TTS) and pneumatic dilatation is applied to the stricture. However, the available reports are very heterogeneous with respect to the balloon size used, inflation time, endpoints achieved, and follow-up intervals.

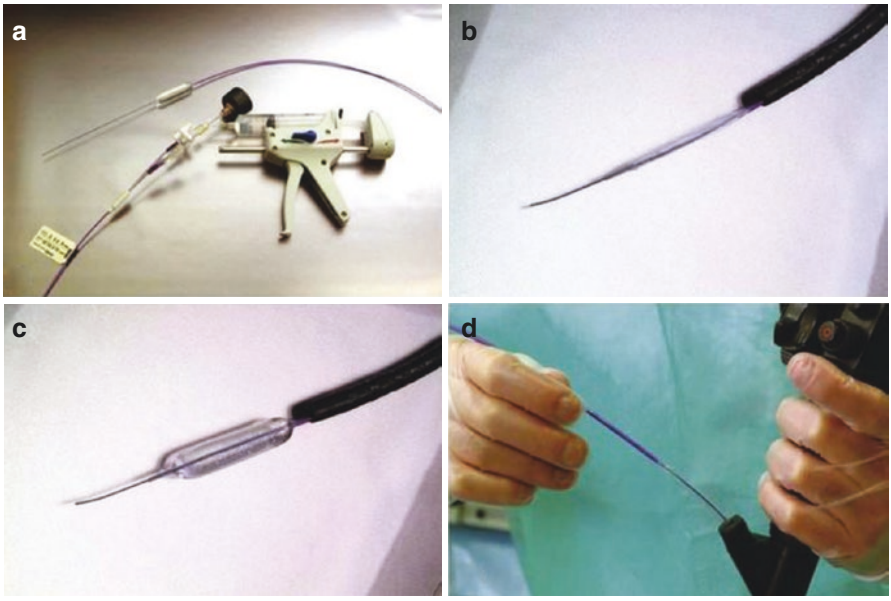

Fig. 16.1 Balloon dilation. Syringe gun, manometer and balloon (**a**). Through the scope (TTS) balloon (**b**), and following inflation (**c**). TTS balloon is inserted into the operating channel (**d**)

Radially expanding balloon dilators are available commercially in several calibers and lengths (Fig. 16.1). Balloon dilators are made of low-compliance inflatable thermoplastic polymers which will allow to have a reproducible and uniform expansion of the balloon to its desired maximal size. Dilator diameter is measured in millimeters or French (Size in millimeters can be converted to French at a ratio of 1:3, e.g. 10 mm = 30 F). The balloons usually range in size from 6 to 20 mm diameter. Most balloons allow for sequential expansion and they are marked as single-use. The balloon is expanded by pressure injection of liquid, mainly water but in some instances with radiopaque contrast, by using a handle accessory device. The hydraulic pressure of the balloon is monitored manometrically to gauge the radial expansion force [41].

Before attempting to perform a dilatation, it is very important to know the length and complexity of the stricture. If this information can be obtained during the endoscopy i.e. the stenosis is very short, can easily see through it and the length can be estimated than no other investigation is required. If this is not the case, further imaging with either a CT enterography or MR enterography is required to gather all the required information for a safe procedure. This is preferably done prior to dilation. In some centers, luminal contrast assisted radioscopy is performed during the procedure using the balloon catheter to inject contrast fluid. As discussed earlier, strictures $\leq$5 cm without any of the mentioned contraindications is amenable for dilatation.

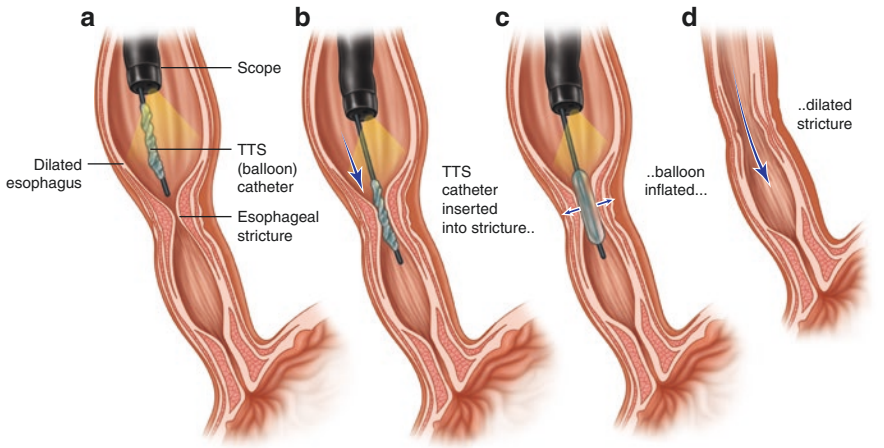

Fig. 16.2 Balloon dilatation. Through the scope (TTS) balloon inserted into the endoscopic lumen (**a**). TTS balloon passed through the stricture (**b**). Insufflation of balloon to dilate stricture (**c**). Dilated stricture (**d**)

Once the endoscope is passed to the stenosis site, initial selection of the dilator size is based on an estimation of the diameter of the stenosis (Fig. 16.2). The balloon is then passed through the scope accessory channel with or without a guidewire which allows direct visualization during the procedure. If a guidewire is used, it should be first advanced through the stenosis and the balloon is advanced over the wire. The balloon is placed across the obstruction and inflated under direct vision and the guidewire is retracted. If the guidewire is not used, the balloon is directly advanced through the stricture and placed across. The balloon is then inflated with a pressure or volume-controlled handles to the desired pressure, representing the chosen balloon diameter. After removal of the balloon, the dilated stricture is usually examined endoscopically [41]. A three-step inflation is preferred as it is considered to induce more controlled dilation. The diameter of the balloon will increase with every step of increased pressure. The diameter corresponding with every step is clearly depicted on the balloon catheter. Most centers dilate to a maximum of 18–20 mm. Repeated dilation, with intermittent deflation, during the same procedure can be employed if the first dilation is judged to be suboptimal.

16.6 Conclusion

In non-complex strictures that are ≤5 cm in length, endoscopic balloon dilatation is a safe and effective alternative procedure to surgery. The short-term outcomes are excellent and it can prevent or delay surgery in most patients.

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