

Review

Endoscopic Management of Crohn's Disease Strictures

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Abstract

Crohn's disease is a chronic inflammatory condition of the gastrointestinal tract which can result in luminal stenosis and up to 90% of patients requiring surgery during their lifetime. Medical management aims to reduce the inflammatory burden to prevent the development of inflammatory strictures, progression to fibro-stenosis and subsequent obstructive symptoms. Endoscopic balloon dilatation (EBD) is a well-established, safe technique in the management of short strictures to prevent patients having multiple surgical resections. In this review the evidence and safety of EBD for colonic and small bowel strictures will be discussed as well as adjuvant techniques (including endoscopic stenting and endoscopic intralesional therapy), current trials and new evidence on the medical management of stricturing disease.

Keywords

Endoscopic; Crohn's disease



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1. Introduction

Crohn's disease is a chronic inflammatory condition of the gastrointestinal tract and is characterised by transmural inflammation of intestinal tissue with a natural tendency to affect the distal small intestine and proximal large bowel [1]. This can result in stenosis of the small and large bowel with up to 90% of patients with Crohn's disease requiring surgery during their lifetime [2-4].

Approximately 30% of patients diagnosed with Crohn's disease are observed to develop intestinal strictures within 10 years of disease diagnosis [5]. These strictures can be inflammatory, fibrotic or mixed [6]. The likelihood of development tends to be exacerbated by well identified poor prognostic factors such as diagnosis under 40 years of age, the presence of peri-anal disease, the early use of corticosteroids in treatment [7] and smoking [8]. All of these risk factors are predictors of disabling disease.

Medical management using immunomodulator and biologic agents aims to reduce the inflammatory burden in Crohn's disease to prevent the development of inflammatory strictures and progression to fibro-stenosis. Despite this a high proportion of patients will require surgery and up to 50% of these patients will require subsequent operations [9-11]. Recurrent bowel resections lead to an increased risk of short bowel syndrome, potential need for parenteral nutrition and reduced quality of life in patients living with Crohn's disease. Therefore bowel-conserving strategies such as strictureplasty and endoscopic balloon dilatation are better used in managing these patients.

In order to write this narrative review a literature search was performed to assess all relevant meta analysis and journal articles found in PubMed using the following key words: "Crohn's disease", "Crohn's" and "stricture" or "endoscopic dilatation" or "balloon dilatation".

2. Balloon Dilatation for Crohn's Strictures

Endoscopic balloon dilatation is a well-established treatment modality and involves the use of a through-the-scope balloon catheter to pneumatically dilate a stricture under direct visualisation. This can be aided through the assistance of wire guidance or fluoroscopy in more complex cases. Benign colonic and ileocolonic anastomotic strictures can be easily treated using a balloon dilator through an adult colonoscope, however small bowel dilatation can also be performed using push enteroscopy (duodenal or proximal strictures) or balloon assisted enteroscopy (for mid or distal small bowel strictures) with either an antegrade or retrograde approach.

There is a large body of evidence which reports good results for endoscopic dilatation of fibrotic native, anastomotic colonic and small bowel strictures (see Table 1 and 2) and its use is recommended by The European Crohn's and Colitis Organisation (ECCO) and the British Society of Gastroenterology (BSG) for the management of colonic and small bowel strictures under 4cm, based on the systematic review by Hassan et al [12, 13]. This review in 2007 demonstrated that the only predictor of surgery-free follow-up at multivariate analysis was a short stricture where stricture length is usually <4cm.

More recently regarding the efficacy of colonic dilatation in Crohn's disease strictures, a meta-analysis of 25 studies involving over 1,000 patients and 2,664 dilatations demonstrated the proportion of patients who required further dilatation at 1, 2 and 5 years of follow up was 31.6%,

25.9% and 1.7% respectively. The resulting cumulative proportion of patients requiring further dilatation over 5 years was 80.6% [14].

Much fewer studies with smaller numbers of patients have been performed in relation to small bowel strictures. Hirari et al [15] demonstrated a short term success rate of 80% in 65 patients with small bowel Crohn's disease strictures. Complications were observed in six of the 65 patients (which included bleeding, perforation and pancreatitis) and seventeen patients (26.2%) ultimately underwent surgery during the observation period of the study. Cumulative surgery-free rate after initial dilatation was 79% at 2 years and 73% at 3 years. However the re-dilatation rate was high; in 52 of the successful cases the cumulative dilatation-free rate after initial balloon dilatation was 64% at 2 years and 47% at 3 years.

De novo strictures have better technical success when dilated than anastomotic strictures. This was highlighted in a literature review by Bettenworth et al [16] analysing over 3000 dilatation procedures. However the review concluded that there was no long term difference between outcomes in dilatation of de novo vs anastomotic strictures. Other factors that were highlighted in this review included that there was no association with symptom recurrence and predictive factors for repeat dilatations. Also for every 1cm increase in stricture length there is an increased hazard for surgery and strictures less than 5cm are associated with higher surgery free outcome with or without correction for stricture location and type of stricture. In terms of complications the stricture location, type, length, disease activity, balloon calibre, length and pressure were not associated with increased risk of complications. Major complications were defined as perforations, bleeding, intra-abdominal abscesses or fistulas. No study seems to suggest that severe inflammation is a risk factor for perforation when a stricture is dilated, although care should be taken and that recurrence is more likely as demonstrated by Hoffman et al [17]. In regards to balloon diameter it was further demonstrated by Bettenworth that the calibre of dilation was associated with significantly higher rates of technical success, but did not result in increased rates of clinical efficacy and reduced need for redilatation or surgery, and that complication rates stayed the same independent of balloon diameter.

There is minimal data on dilatations for Crohn's strictures in the upper Gastrointestinal (GI) tract. Bettenworth et al [18] recently performed a multi-centred meta-analysis in 94 patients with Crohn's disease who underwent balloon dilatation for upper GI strictures associated with the disease. The conclusion of this study was that balloon dilatation is an effective alternative to surgery with a high rate of short-term technical (100%) and clinical success (87%), moderate long-term efficacy (median follow up of 23 months) and an acceptable rate of complications - 2.9% of all procedures.

A study by Li et al [19] compared the perioperative outcomes of patients who had surgery for failure of endoscopic balloon dilatation with those outcomes in patients who underwent resection first for ileocolonic anastomotic stricture caused by recurrent Crohn's disease. This study showed that patients requiring salvage surgery after failure of endoscopic balloon dilatation for ileocolonic anastomotic stricture have an increased incidence of stoma diversion and postoperative surgical site infection compared with those having early surgical intervention.

Therefore what can we do to improve the management of fibro-stenotic Crohn's disease and improve the efficacy of balloon dilatation in order to reduce the need for surgery?

There are currently no anti-fibrotic therapies licensed for the management of Crohn's disease and no specific diagnostic tests to predict susceptibility to the more debilitating stricturing or penetrating phenotypes of the disease [20].

3. Intralesional Injection for Crohn's Disease Strictures

The use of intralesional steroid injection (through the use of Triamcinolone in the management of benign peptic, corrosive, anastomotic or post-radiotherapy fibrotic strictures [21]) has not currently been shown to be beneficial in adult Crohn's strictures [16] however was previously beneficial in paediatric Crohn's strictures [22]. ECCO's position on this is that the evidence is retrospective and uncontrolled, therefore it is not recommended [23]. Conversely a prospective randomised control trial with 13 patients with Crohn's disease was terminated early after reporting that triamcinolone injection led to an earlier need for re-dilatation and worse outcome when compared with placebo [24].

In small case reports and series there has been some benefit seen in the endoscopic injection of intralesional anti TNF therapy with an improvement in stricture appearance and symptoms [25, 26]. Larger trials are currently ongoing in regards to this treatment modality and may show benefit for this in the future [27].

4. Stents for Crohn's Disease Strictures

Endoscopic metallic stent insertion has been trialled in small numbers in patients with Crohn's (some with and without stent removal). The technical success rate was reported to be high (up to 100%), but has complications: migration, surgery to remove, perforation and obstruction [28]. Different authors have differing opinions on the duration of how long these should be left in for. A review by Loras et al [29] in 2016 included 16 studies for this indication. Most of these are small series of fewer than 10 patients with a wide variety of different stents (partially, fully covered and uncovered self expanding metal stents). The review demonstrated a high clinical success – up to 80%. The authors felt that a safe duration for removal was a mean time of 4 weeks. However, Attar et al [30] demonstrated that removal after 1 week was more appropriate in order to prevent complications. Furthermore, one study group did not feel that stent migration should be considered an adverse outcome, provided the patient did not develop obstruction. Attar et al suggested that more evidence is required and further work on the design of anti-migration stents might reduce the risk of distal migration and impaction. More evidence is clearly required to demonstrate the efficacy endoscopic stenting and its short term and long term benefits. This will hopefully be answered by a large multicentred randomised controlled trial that is currently recruiting in Spain, aiming to assess the efficacy of balloon dilatation versus self-expanding metallic stent placement for endoscopic treatment of stenosis in Crohn's Disease [31].

Biodegradable stents have also been trialled. In one study undertaken in 6 patients initial technical success was again high (83%), however only 1 patient had clinical benefit whilst the others clinically failed due to stent overgrowth, migration and stent collapse [32].

Currently the intra-luminal use of injection corticosteroids, anti-TNF agents or the use of luminal stents are not recommended by ECCO [23].

5. Escalation of Medical Therapy and Balloon Dilatation for Crohn's Disease Strictures

There has been some recent promising data that has come from Ding et al [33] in the medical management of Crohn's strictures. The escalation of patients to combination medical therapy in Crohn's anastomotic strictures with active inflammation at the site of the anastomosis was found to decrease the need for repeat dilatation and surgery. In further subgroup analysis escalation to anti-TNF therapy was the only medication found to be significantly associated with a decreased risk of repeat dilatation. One of the limitations of this study was that in each case the degree of luminal narrowing caused by inflammation versus fibrosis was unknown and escalation of medical treatment would have been biased towards those with active inflammation.

This study also demonstrated that the more severe the disease activity at initial endoscopy (Rutgeerts i4) the greater risk of future surgical resection. When active inflammation is present escalation of therapy to include at least an anti-TNF is necessary to augment the natural history of Crohn's disease and improve clinical outcomes.

The only other study which demonstrates data similar to this is Honzawa et al [34]. In this study the mean number of dilatation procedures was significantly lower in patients commenced on immunomodulator therapy pre-dilatation vs. post dilatation. Of note there was no significant difference in the intervals between dilatations in each group.

6. Conclusion

Crohn's disease strictures are unfortunately common and patients frequently require intervention such as repeated dilatations and surgical resection which can be debilitating for patients. Medical therapies are moving towards earlier and effective treatment to reduce bowel inflammation and therefore complications such as strictures and fistulas which commonly require surgical intervention. When patients require surgery for Crohn's disease anastomotic disease recurrence is common and earlier treatment post operatively may reduce inflammation and thereby stricturing disease [35].

In Crohn's disease strictures less than 5cm in length endoscopic balloon dilatation is less invasive than surgery, is safer and shows good short and long term results. Although it may not be able to prevent surgery in all patients, it has been shown to delay its need [16]. New evidence that escalation of therapy in those with active inflammation at the site of an anastomosis to include combination therapy with an immunomodulator and anti-TNF shows a reduction in the need for repeat dilatation and reduces the number of patients requiring surgery. Now that there is some evidence for this hopefully this treatment method can be applied in the future in order to better manage these patients. The total number of dilatations that a patient requires will ultimately depend on their clinical response and disease status [16]. In the near future however there may be more therapeutic options with evidence from upcoming randomised control trials available to us to manage these patients [27, 31]. This will hopefully reduce long term disability that can be associated with Crohn's disease [36].

Table 1 Colonic large bowel dilatation.

Reference	Authors	Published year	No. of patients	Anastomotic Strictures (%)	Maximum balloon calibre (mm)	Technical Success (%)	Clinical efficacy* (%)	Major Complications (%) **
[37]	Blomberg et al	1991	27	100	25	100	67	0
[38]	Breysem et al	1992	18	78	18	89	50	0
[39]	Couckuyt et al	1995	55	67	20	85	62	8
[40]	Ramboer et al	1995	13	69	18	100	100	0
[41]	Matsui et al	2000	55	43	20	86	78	2
[42]	Dear et al	2001	22	95	18	100	73	0
[43]	Morini et al	2003	43	67	18	79	43	0
[44]	Thomas-Gibson et al	2003	59	90	18	73	41	3
[45]	Ajlouni et al	2006	37	37	20	90	87	3
[46]	Ferlitsch et al	2006	46	59	20	85	66	4
[17]	Hoffmann et al	2008	25	57	20	100	52	16
[47]	Mueller et al	2010	55	23	18	95	76	2
[48]	Thienpont et al	2010	138	84	18	97	76	3
[49]	Scimeca et al	2011	37	90	20	84	89	0
[50]	Gustavsson et al	2012	178	80	25	89	64	11
[51]	De'Angelis et al	2013	26	52	18	100	93	2
[34]	Honzawa et al	2013	25	21	20	88	62	12
[52]	Nanda et al	2013	31	100	18	100	45	0
[53]	Atreja et al	2014	128	48	20	83	67	3
[54]	Bhalme et al	2014	79	61	20	98	77	0
[55]	Hagel et al	2014	77	57	20	55	65	10
[33]	Ding et al	2016	54	100	20	89	82	2

Table 2 Small bowel dilatation.

References	Author	Year	No. of patients	Maximum balloon calibre	Technical Success (%)	Clinical efficacy* (%)	Major Complications (%) **
[56]	Despott et al	2009	22	20	73	73	9
[57]	Hirai et al	2010	25	18	72	72	0
[58]	Gill et al	2014	10	16.5	100	80	20
[15]	Hirai et al	2014	65	20	80	80	2

* Clinical efficacy - resolution of obstructive symptoms after dilation with the avoidance of surgery or additional intervention.

** Complications were defined as perforations, bleeding, intra-abdominal abscesses or fistulas.

Author Contributions

Oliver Reed wrote the manuscript with input and guidance from Patrick B Allen, Grant Caddy, John Eccles and Tony CK Tham.

Competing Interests

The authors have declared that no competing interests exist.

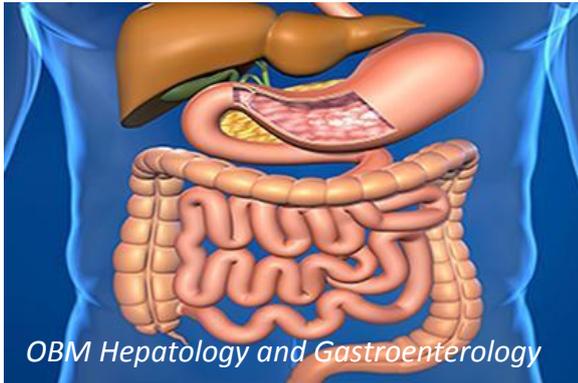
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