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Endoscopic balloon dilatation of Crohn's-associated intestinal strictures: High patient satisfaction and long-term efficacy

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Abstract

Introduction: Stricture formation is a common long-term complication of Crohn's disease. Endoscopic balloon dilatation offers a bowel-sparing treatment option, but long-term outcome and its association with patient-, stricture-, and procedure-related factors is only poorly understood. Patient satisfaction with endoscopic balloon dilatation is largely unknown.

Methods: We performed a retrospective review of all endoscopic balloon dilatation for Crohn's disease-related strictures between January 2005 and January 2013. Long-term outcome, complication rates and predictive factors were evaluated. Patient satisfaction was assessed using a questionnaire and telephone interviews.

Results: A total of 118 balloon dilatations were performed for 69 strictures in 46 patients. One patient was excluded from further analysis due to malignancy. Median time from diagnosis of Crohn's disease to symptomatic stricture formation was 19 years. Technical success, defined as passage of the endoscope after dilatation, was reportedly obtained in 95 of 106 procedures (89.6%). Two perforations occurred, one of which could be managed conservatively. No episodes of severe bleeding were recorded (procedure-related complication rate: 2/118; 1.7%). During a median follow-up of 4.8 years (range 0.4–8.7), 55.6% (25/45) of patients were able to avoid surgery. Of the patients, 35.6% (16/45) did not need any further intervention, 40.0% (18/45) underwent more than one dilatation, and 24.4% (11/45) were operated after the first dilatation. The percentage of patients who were satisfied with the procedure and would again opt for balloon dilation as first line therapy was 83.3% (35/42). None of the risk factors examined in this study correlated with the necessity for subsequent surgery.

Discussion: Endoscopic balloon dilatation is a safe and effective first line therapy for Crohn's disease-related strictures. No technical, stenosis-, or patient-related factor reliably predicted sustained dilatation success. Patient satisfaction was high.

Keywords

Endoscopic balloon dilatation, Crohn's disease, stricture

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Introduction

Crohn's disease is a chronic inflammatory bowel disease which can affect any part of the intestine. Stricture formation is one of the most frequent complications of Crohn's disease. About one third of all patients suffering from Crohn's disease develop a stricture within 10 years after diagnosis.[1] Strictures are defined as a constant luminal narrowing which is often accompanied by prestenotic dilatation. Primary (de novo) or anastomotic strictures are differentiated. Stricture formation is caused by transmural inflammation which results in tissue remodeling with hypertrophia and hyperplasia of mesenchymal cells. The most frequent localization is in the terminal ileum or at ileocolonic anastomosis. Clinical symptoms of obstruction include abdominal cramps, nausea, vomiting and weight-loss. To date, there is no specific antifibrotic medication available.

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Only inflammatory strictures may respond to anti-inflammatory therapy. Therefore, fibrotic strictures are a frequent indication for surgery. Repeat resections are often necessary due to a high recurrence rate and comprise the risk of developing a short bowel syndrome.[2]

Stricturoplasty and endoscopic balloon dilatation (EBD) offer bowel-sparing therapeutic alternatives. Outcomes of EBD have been published before, but only a few studies have analyzed the long-term outcome with a follow-up longer than three years.[3–8] At present there is little evidence about factors impacting on the outcome. Only few recommendations on "best practice" are available.[9] Patient adherence with treatment strategies is essential in chronic diseases such as Crohn's disease, but patient satisfaction with EBD to the best of our knowledge has not been investigated previously.

Patients and methods

Patients and outcome parameters

We performed a retrospective review of all patients who underwent EBD for Crohn's associated strictures of the upper, mid, and lower GI-tract between January 2005 and January 2013 at our tertiary center. Firstly, all patients who had an EBD for any indication between January 2005 and January 2013 at the University Hospital Tuebingen were identified from our database by the OPS (operation and procedure) code. Secondly we performed a manual chart analysis to identify all patients suffering from Crohn's disease. Indications for EBD included obstructive symptoms and presence of a stricture that could not be passed with a standard colonoscope.

Patient-, stricture-, and procedure-related characteristics were analyzed. Patient characteristics included age, sex, disease duration, previous surgery, medication, and smoking habits. Stricture characteristics included stricture quality (de novo vs. anastomotic), length, number and location (Table 1). Presence of inflammation was graded by post-hoc blinded assessment of endoscopic pictures by an experienced endoscopist (MG), and acute inflammation assumed in the presence of an erosion or ulcer in inflamed/reddened mucosa, mucosal edema, aphthous lesions, whereas chronic inflammation defined as chronic erosion or ulcer in non-inflamed/non-reddened mucosa or an ulcer clearly located on the fibrotic ring of an anastomosis/in scar tissue. Procedure-related parameters included balloon diameter, technical success and complications. Technical success was defined by the ability to pass the stricture with the endoscope after dilatation. Complications were defined as perforation or bleeding requiring blood transfusion and were assessed from the endoscopy report and the clinical follow-up.

Table 1. Patient characteristics

Patient characteristics: 46 patients/69 strictures	
Number of dilatations	118
% female/% male	41/59
Mean age (range)	48 (27–83)
Disease duration (median)	222 (1–419) months
Median follow up	4.8 years
% previous surgery	61
% anastomotic vs. de novo	38 vs. 62
% smokers	36
% disease location (n/total no. of stenoses)	
Ileocolonic	39 (27/69)
Ileum	27 (19/69)
Colon	22 (15/69)
Duodenum	4 (3/69)
Jejunum	4 (3/69)
Rectum	2 (1/69)
Ileorectal	2 (1/69)
% medical therapy at first dilatation (n/total no. of pts)	
No medical therapy	15 (7/46)
5-ASA	2 (1/46)
Corticosteroids	35 (16/46)
Anti-metabolites	41 (19/46)
Anti-TNF	7 (3/46)
% multiple (>1) medical therapy at first dilatation	28 (13/46)
% inflammation	
Not active	40 (18/45)
Acute	38 (17/45)
Chronic	22 (10/45)

All patients were treated as inpatients (for at least one night), so all complications within 24 h were documented. Additionally, the patient questionnaire specifically asked for complications after hospital discharge.

Patient questionnaire

Patients were contacted by questionnaire or telephone to assess satisfaction with EBD and to document additional interventions at other hospitals. We specifically asked for further dilatations or surgery at another hospital or for any complication. We also registered information about medication and smoking habits at the time of first dilatation. We specifically asked whether patients were satisfied with the procedure and if they would opt again for balloon dilatation.

Endoscopic balloon dilatation procedure

EBD dilatation was carried out under conscious sedation with propofol. In some cases, midazolam or

buscopan were administered i.v. in addition, if needed. Dilatation was performed using Microvasive Rigiflex Through The Scope Balloon (TTS, Boston Scientific Microvasive, MA, USA) or Cook Balloon (Cook Endoscopy, Winston-Salem, NC, USA). Diameters ranged from 10 mm to 20 mm with dilatation pressure according to the manufacturer's instructions. Choice of balloon size and duration of inflation (usually 1 min) was at the discretion of the endoscopist. Cross sectional imaging and histological stricture assessment was not part of the routine preintervention workup, no routine periinterventional antimicrobial therapy was administered.

Statistics

For evaluation of technical success, all dilatation procedures were assessed (i.e. $n = 118$ corresponds to 100%); for evaluation of clinical success, all patients were assessed ($n = 45$). Statistical analyses were performed by using SPSS (IBM SPSS Statistics, Version 20). Kaplan-Meier analysis was performed for periods free of surgery and free of intervention (re-dilatation or surgery). Two sided Fisher's exact test was performed to evaluate whether the need for surgery was higher for patients with anti-inflammatory medication, endoscopically active inflammation or tobacco use. After performing a Bonferroni correction, a p-value ≤ 0.0166 was considered significant.

Ethical considerations

The study was approved by the local ethics' committee (Ref. no. 196/2013BO2).

Results

Patients

Between January 2005 and January 2013, 118 balloon dilatations were performed for 69 strictures (26 anastomotic and 43 primary inflammatory strictures) in 46 patients. Patient characteristics are summarized in Table 1. Ten patients had more than one (2–8) stricture. Median follow-up was 57.5 months (range 5–104 months), mean follow-up was 52.9 months (+–SD 28.6 months).

Of the patients, 33 returned the questionnaire by mail, and 10 patients were interviewed by telephone. For one patient who suffered from dementia at follow-up, his wife was able to sufficiently respond on his behalf. Two patients were lost to personal follow up but included in the evaluation of clinical success; for one patient, clinical documentation was available for 44 months after dilatation. Another patient passed away due to causes unrelated to Crohn's disease and dilatation but the database offered detailed information for 27 months after first dilatation. One patient was operated for an anal canal carcinoma, and the sigmoid stricture was resected at the same time. He was excluded from the study. Thus, follow up for evaluation of patient satisfaction was available for 95.6% (43/45), for clinical success for 100% (45/45) of patients.

Technical success

Of the interventions, 89.6% (95/106) were technically successful – that is, the endoscope could be navigated across the stenosis after EBD. In 12 cases the outcome was not documented. The overall need for surgery in the subsequent course of disease was nearly equal in the patient-group with technically successful and without technically successful dilatations (41% vs. 44%).

Clinical success: Long-term efficacy

During a median follow-up of 4.8 years (range 0.4–8.7), 25 of 45 patients (25/45; 55.6%) remained free of stricture-related surgical interventions (Figure 1). Of the patients, 16/45 (35.6%) did not need any further intervention, and 11/45 (24.4%) underwent surgery after the first dilatation (after a median time of nine months) due to failure of sustained relief ($n = 6$), fistula (2), stricture length (1), technical failure (1) or perforation (1). Median surgery-free and intervention-free survival

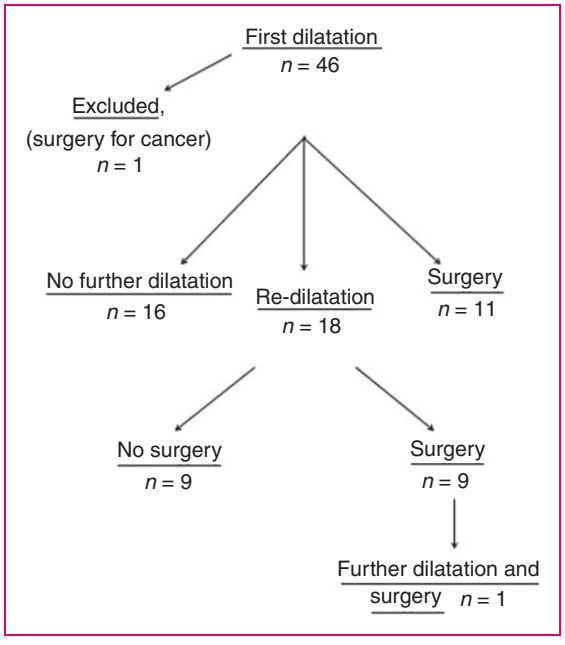

Figure 1. Long-term follow-up.

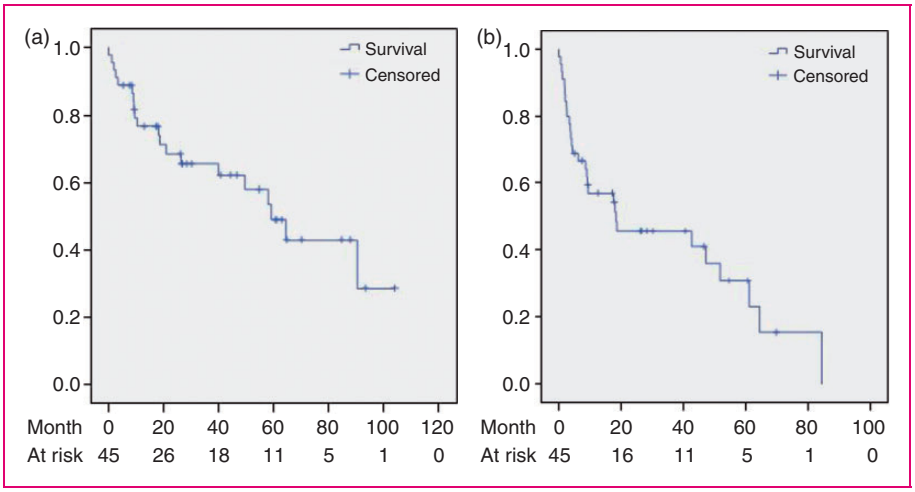

Figure 2. Kaplan-Meyer analysis of (a) surgery-free survival (months), (b) dilatation- and surgery-free survival (months).

were 59.1 and 18.3 months, respectively (Kaplan-Meier analysis, Figure 2).

Influence of inflammation, medication and smoking

Endoscopic images from the first EBD were scored as "acute inflammation" in 17 of 45 patients (37.8%), as "chronic inflammation" in 10/45 (22.2%), and as "no inflammation" in 18/45 (40.0%). There was no significant influence of inflammation on the need of surgical intervention ($p = 0.76$). We noted a trend towards higher surgery rates in patients with anti-inflammatory medication at time of first dilatation (51% vs. 0%). However, this result did not meet the predefined level of significance ($p = 0.027$). Smoking habits did not significantly influence the need for subsequent surgery (smokers 44% vs. non-smokers 46%). A trend towards a lower surgery rate in shorter stenoses was noted, however data on the total length of the stenosis were only available from 23 endoscopic procedures and nine cross sectional imaging reports (32/68 stenoses, 47.1%).

Complications

Two perforations were documented, corresponding to a procedure-related rate of 1.7% (2/118) and a patient-related complication rate of 4.6% (2/45). Both perforations were noticed during endoscopy. In one case perforation occurred during dilatation with an 18 mm balloon diameter at a primary inflammatory stricture in the rectum. The mucosa was graded as "acutely inflamed". The patient underwent emergency surgery and received a temporary stoma for four months. The second perforation occurred at an ileorectal, non-inflamed anastomosis which was dilated up to 20 mm. It was the third dilatation procedure for this patient. He was treated conservatively with intravenous antibiotics, and later underwent seven more dilatations. No severe bleedings were recorded.

Patient satisfaction

Feedback on satisfaction with the intervention was available for 42 of 45 patients (93.3%). In total, 35/42 (83.3%) were satisfied with the procedure – that is, they would opt for EBD as first line treatment again if they were in the same situation. Of the satisfied patients, 34% subsequently underwent surgery. One of two patients with perforation noted overall satisfaction with EBD. The most frequent reasons for dissatisfaction were failure of clinical relief and the feeling that surgery would be required despite previous endoscopic interventions.

Discussion

Stricture formation is a common complication of long-standing Crohn's disease that seems to be only insufficiently modified even by modern anti-TNF-therapy.[10] Current approaches to the patient with stenosis include anti-inflammatory therapy, endoscopic balloon dilation, stricturoplasty and resection.

We retrospectively analyzed 118 balloon dilatations for 69 strictures in 46 patients from our center. In our cohort, we had a very high clinical follow-up of 100% over almost five years and a personal feedback from 96% of patients. Remarkably, clinical evidence of stricture formation occurred 19 years (median) after initial diagnosis. This long period may indicate that population-based influences of modern anti-inflammatory therapy may only be seen with delay or that such

therapy may actually postpone the first advent of clinically relevant stenosis. However, the retrospective nature of our trial does not provide a definite answer to this important question. In prior studies, most of the strictures were at an anastomotic site, for example 84%.[6] In contrast, we found a high percentage (62%) of de novo-stenoses.

In our cohort, stenosis-, patient- and procedure-related parameters were analyzed and correlated with surgical intervention as a well-defined surrogate of long-term outcome. Of the patients, 56% remained free of stricture-related surgical interventions, and 36% did not need any further intervention, including follow-up balloon dilatation. This is in the range previously reported: Hassan et al. reported 58% surgery-free survival in a meta-analysis,[11] and Morini et al. reported 53% surgery-free outcome within a follow-up of 59 months.[4] Even better long term results with a surgery-free outcome of 73% to 92% were reported by Dear and Hunter, Stienecker et al., Thienpont et al., de'Angelis et al.,[3,5,6,12] however with a higher rate of anastomotic strictures, shorter length or patients with only a low disease activity.

Our current technical success rate of 90% is comparable with previously reported rates (45–97%),[13] but was not predictive of long term surgery-free survival. Balloon size, although not formally correlated, did also fail to impact on long term success, supporting the notion that is followed in our department that balloon diameter should be estimated by the experienced endoscopist during the procedure rather than by preset criteria. Stenosis-associated factor did not significantly influence long term results, although a trend towards better outcome in shorter strictures was noted. While this may be due to the number of stenoses analyzed, it is in keeping with previously reported results.[6] The same holds true for most patient-related factors including smoking and systemic markers of inflammation. However, we found a trend towards a negative impact of the need for anti-inflammatory drugs, probably indicating ongoing active disease in these patients. We cannot exclude that patients with suspected high inflammatory activity within the stricture were not sent for evaluation of EBD a priori, and the retrospective design and observation over many years does not allow a clear allocation of treatment effect to a single therapeutic agent. On the other hand, our data indicate that EBD could also be used to bridge the time until medical therapy is fully effective on inflammatory strictures. In most patients, the indication for surgery following EBD was failure of clinical relief. While this is considered a failure of conventional therapy in many trials (if only for statistical reasons), we rather see surgery as an important adjunct in a step-up approach towards strictures. Since the difficulty of surgical stricture therapy is not substantially different after EBD, surgery could potentially be postponed until the inflammatory burden and nutritional status of acutely ill patients is optimized. In a minority of patients, fistula formation (three of four at the anastomotic site) was the (post-hoc) reason for surgery. While usually we would not perform dilatation in patients with fistulas in the area of dilatation, this may also represent a long term complication of dilatation (micro-perforation), but more likely an under-diagnosis at the time of dilatation or the natural course of the disease.

Our rate of 1.7% for severe complications is in the lower range of previously reported procedure-related complication rates. All were noted during endoscopy. In one stenosis, malignant disease was suspected during endoscopy and confirmed by histopathology. This illustrates that a high level of suspicion should always be maintained.

Our study was the first to include patient satisfaction in the analysis of results of EBD. Of note, patient satisfaction rates were higher than the long term efficacy of dilatation. This indicates that even delay of surgery or only intermittent, rapid reduction of symptom load is highly appreciated by the patients. The responses by patients who were not satisfied with EBD illustrate that the possibility of long-term failure of EBD, though evident to most physicians, must be (more) frankly discussed with the patients.

In summary, our long-term retrospective analysis shows a good efficacy of EBD over almost five years. It adds to the current notion that no technical, stenosis-, or patient-related factor reliably predicts sustained dilatation success. Patient satisfaction was high, much higher than the long term effectiveness. Taken together, these results indicate that EBD, if technically feasible, is a favorable, safe and preferred first line intervention in Crohn's disease related strictures.

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