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**Short- and long-term efficacy of endoscopic balloon dilation in Crohn’s disease structures**

**de’Angelis N** *et al*. Endoscopic dilation in Crohn’s Disease Structures

Nicola de’Angelis, Maria Clotilde Carra, Osvaldo Borrelli, Barbara Bizzarri, Francesca Vincenzi, Fabiola Fornaroli, Giuseppina De Caro, Gian Luigi de’Angelis

**Nicola de’Angelis,** Department of Digestive Surgery, Hopital Henri Mondor - University Paris Est, 51 avenue du Maréchal de Lattre de Tassigny, 94010 Creteil, France

**Maria Clotilde Carra, Barbara Bizzarri, Francesca Vincenzi, Fabiola Fornaroli, Giuseppina De Caro, Gian Luigi de’Angelis**, Gastroenterology and Operative Endoscopy Unit, University Hospital of Parma, 43121 Parma, Italy

**Osvaldo Borrelli,** Department of Gastroenterology, Great Ormond Street Hospital and UCL, London WC1N 3JH, United Kingdom

**Author contributions:** de’Angelis N contributed to the study design, data analysis, data collection, data interpretation, manuscript revision, and the final approval of the submitted version; Carra MC contributed to data analysis, data interpretation, manuscript drafting, manuscript revision, and final approval of the submitted version;Borrelli O contributed to study design, data interpretation, manuscript revision, and final approval of the submitted version;Bizzarri B, Vincenzi F, De Caro G, and Fornaroli F coordinated and provided data collection; de’Angelis GL contributed to the study design and data interpretation, and he also performed the clinical procedures and gave his final approval of the submitted version. All authors gave their approval to the present manuscript for publication.

**Correspondence to:** **Dr. Nicola** **de’Angelis**, Department of Digestive Surgery, Hopital Henri Mondor - University Paris Est, 51 avenue du Maréchal de Lattre de Tassigny, 94010 Creteil, France. nic.deangelis@yahoo.it

**Telephone:** +33-1-49812348 **Fax:** +33-1-49812432

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**Abstract**

**AIM:** To evaluate short- and long-term efficacy of endoscopic balloon dilation in a consecutive patients cohort with symptomatic Crohn’s Disease (CD)-related structures.

**METHODS**: Twenty-six CD patients (11 men; median age 36.8 year, range 11-65) with 27 symptomatic structures underwent endoscopic balloon dilation (EBD). Both naive and post-operative structures, of any length and diameter, with or without associated fistula were included. After a clinical and radiological assessment, EBD was performed with a Microvasive Rigiflex through the scope balloon system. The procedure was considered successful if no symptoms reoccurred in the following 6 mo. The long-term clinical outcome was to avoid surgery.

**RESULTS**: The mean follow-up time was 40.7 ± 5.7 mo (range 10-94 mo). In this period, forty-six EBD were performed with a technical success of 100%. No procedure-related complicationwas reported. Surgery was avoided in 92.6% of the patients during the entire follow-up. Two patients, both presenting ileo-coecal structures associated with fistula, failed to respond to the treatment and underwent surgical structure resection. Of the 24 patients who did not undergo surgery, 11 patients received 1 EBD, and 13 required further dilations over time for the treatment of relapsing structures (7 patients underwent 2 dilations, 5 patients 3 dilations, and 1 patient 4 dilations). Overall, the EBD success rate after the first dilation was 81.5%. No difference was observed between the EBD success rate for naïve (*n =* 12) and post-operative (*n =* 15) CD related structures (*P >* 0.05).

**CONCLUSION**: EBD appears to be a safe and effective procedure in the therapeutic management of CD-related structures of any origin and dimension in order to prevent surgery.

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**Key words:** Endoscopic Balloon Dilation; Crohn’s Disease; Structures; Endoscopy; Gastrointestinal Surgery

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**INTRODUCTION**

In the last two decades, the medical therapy for Crohn’s Disease (CD) has remarkably improved and the introduction of biological therapies has dramatically changed the therapeutic approach in both adults and children[[1](#_ENREF_1),[2](#_ENREF_2)]. However, CD still displays an unpredictable clinical course with high incidence of recurrence frequently leading to complications such as structures, fistulas and abscesses[[3](#_ENREF_3)]. At the time of diagnosis, intestinal structures may occur throughout the gastrointestinal tract in about 5% of patients, whereas up to one third of the patients develop an intestinal structure within 10 year of disease activity, with majority of them occurring at the terminal ileum, ileo-colonic, and colonic level[[2](#_ENREF_2),[4](#_ENREF_4),[5](#_ENREF_5)].

CD-related structure is defined as a constant luminal narrowing, which can remain clinically silent or manifest with prestenotic dilatation and obstructive symptoms, such as abdominal bloating, distention, and pain. As the result of the continuous healing response to the chronic inflammation within the intestinal walls, the intestinal structure induces a progressive narrowing of the lumen and an increased pressure gradient around the structure, which might ultimately result into the development of internal fistula proximately to the obstruction[[6](#_ENREF_6)]. Structure-associated fistulas contribute to increase the disease severity and worsen the clinical management.

CD structures generally show a poor response to medical therapies, and surgical bowel resection or surgical stricturoplasty are often required[[5](#_ENREF_5),[7](#_ENREF_7),[8](#_ENREF_8)]. In patients with CD, intestinal surgery is needed for as many as 80% of CD patients, and a permanent stoma is required in more than 10% of CD patients[[3](#_ENREF_3)]. However, high rate of relapse (defined by recurrence of clinical symptoms) is also observed after surgical resection: 40% at 4 year after bowel resection[[9](#_ENREF_9), [10](#_ENREF_10)], and 50% at 10 to 15 year after ileo-coecal resection[[11](#_ENREF_11),[12](#_ENREF_12)]. Stricturoplasty has also been associated with a risk of structure relapse in 34% of the cases at 7.5 year[[13](#_ENREF_13)]. This implies that up to one third of CD patients will undergo more than one surgery in their life course[[14-16](#_ENREF_14)]. Patients with an early onset disease have an increased risk of surgical relapse and need of repeated resections, which in turn may result in a short bowel syndrome[[13](#_ENREF_13),[17-20](#_ENREF_17)].

Endoscopic through the scope balloon dilation (EBD) is a minimally invasive technique that can reduce or delay the need of surgery in patients with CD-related structures[[21](#_ENREF_21),[22](#_ENREF_22)]. With the new generation of double or single endoscopic balloon enteroscopy, this procedure can be performed at almost any level of the gastrointestinal tract. Moreover, the EBD in CD structures appears to be a safe technique with a low complication rate (0 to 10%)[[22-24](#_ENREF_22)]. It has been shown that the technical success rate of the endoscopic balloon dilation is 95%[[25-27](#_ENREF_25)], with up to 47% of CD patients showing a long-term global benefit, i.e. a surgery-free period at 3 year follow-up[[22](#_ENREF_22),[24](#_ENREF_24)].

In this prospective study, we aimed to assess the effectiveness and safety of the EBD in a cohort of consecutive CD patients with symptomatic intestinal structures.

**MATERIALS AND METHODS**

***Study Cohort***

Twenty-six consecutive CD patients (11 males, 15 females), presenting 27 symptomatic structures (one patient was treated for two structures), and complaining up to two intestinal symptomatic obstructive episodes as suspected by plain abdominal X-rays or contrast study in the preceding 6 mo, were prospectively enrolled into the trial between March 2004 and March 2011. Diagnosis of Crohn’s Disease in both adult and children was based on widely agreed endoscopic and histological criteria[[28](#_ENREF_28),[29](#_ENREF_29)], and disease classification was done according to the Montreal criteria for adults and Paris criteria for children[[30](#_ENREF_30),[31](#_ENREF_31)]. A detailed personal and family history was obtained from each patient. The clinical assessment of the patients was performed through the Pediatric Crohn’s Disease Activity Index (PCDAI) in children, and through the Crohn’s Disease Activity Index (CDAI) in adult[[32](#_ENREF_32),[33](#_ENREF_33)]. A PCDAI ≤ 10 and a CDAI ≤ 150 indicate inactive disease.

Prior to the endoscopic procedure, all patients underwent radiological assessment by abdominal ultrasound with eco-color doppler of mesenteric and the ileo-coecal region, and magnetic resonance imaging with contrast enhancement to confirm the suspected structure and to investigate the presence of concomitant fistula or abscess. No exclusion criterion was applied in the selection of structures to be treated with EBD. Naïve and post-surgical structures, structures associated with fistula or abscess, and structure of any length and diameter were included in the study. In all patients surgery was considered for treatment.

***Endoscopic balloon dilation technique***

Before the endoscopic procedure, all patients underwent the following tests and medications: standard laboratory blood tests including coagulation tests; mechanical intestinal bowel preparation (approximately 36 h before); and liquid diet (starting at least 12 h before).

The endoscopic dilations were performed under unconscious sedation, obtained by administering IV midazolam +/- meperidine or propofol, under constant monitoring of the vital parameters. All procedures were performed by the same endoscopist (GL de’A), and lasted approximately 1 h. The EBD was carried out using Olympus PCF 140 (Olympus, Germany) and Olympus Ileoscopy single balloon SIF 180 (Olympus Germany) (according to the structures site).

The EBD was carried out with a hydrostatic Microvasive Rigiflex through the scope balloon system (Microvasive Endoscopic, Boston Scientific Corporation®, Natick, Massachusetts, United States), with a diameter of 15-18 mm. The correct insertion and positioning of the balloon was checked by fluoroscopic control. After reaching the optimal placement through the structure, the balloon was gradually inflated with water and gastrografin up to 15 mm of diameter, held for 90 s and then deflated. A second inflation up to 18 mm diameter for 90 s was always performed. In case of resilient structures, the process of inflation was repeated up to 6 times in the same session, reaching progressively larger balloon diameters. Once the balloon dilation was accomplished, a combination of metilprednisolone (40 mg) diluted in 5 ml of normal salin solution were injected intra-lesionally with Olympus single use injector 0, 5 mm (Olympus, Japan). The ultimate step of the procedure consisted in examining the proximal bowel (30 cm above the structure) in order to detect others possible lesions that were undetected by the pre-procedural assessing imaging.

In combination with underlying treatment, after EBD each patient was treated by administering prednisolone with a dosing scheme determined by body weight: 1.5 mg/kg daily (maximum allowed dose 60 mg daily) for 2 wk, followed by a 4 wk tapering course.

***Clinical Outcomes***

The technical success of the procedure was defined as the passage of the endoscope through the structure, reaching a diameter of approximately 15 mm. Procedure-related complications were defined as intestinal perforation, and active bleeding requiring surgery or blood transfusions. The long-term clinical success was defined as surgery was avoided all long the follow-up period by obtaining symptom relief with repeated EBD procedures. The short-term clinical success was defined as 6 mo symptom-free period after the EBD. The need of re-dilation was determined based on clinical and imaging criteria in association with persistence or reoccurrence of obstructive symptoms. Surgery was reserved for structures that did not respond to the medical and the endoscopic therapy.

***Statistical Analyses***

Data were analyzed by using SPSS (IBM SPSS Statistics, Version 17.0.0 for Macintosh, Chicago, IL, United States). Kaplan-Meier analysis was performed for periods free of surgery and free of endoscopic re-dilation. Regression statistics were used to relate the clinical and demographic variables to the main outcome (i.e., need of surgery). P value ≤ 0.05 was considered significant. Data are expressed as median and range, or mean ± SEM, unless otherwise stated.

***Ethical Considerations***

The work carried out was in accordance with the principles laid down in the Declaration of Helsinki for biomedical research involving humans. All adult patients included in the study gave their consent for the use of their clinical data. For children, written consent was obtained from both parents and those older than 12 year signed a statement of assent.

**RESULTS**

The patients’ demographic and clinical characteristics, and the structures characteristics are summarized in Tables 1 and 2 respectively. Forty-six EBD were performed for 27 symptomatic structures occurred in the 26 CD patients. Of these, 15 patients had post-surgical structures and 11 had naïve structures.

The technical success of the endoscopic procedure was achieved in all patients without any endoscopic related complication (Figure 1).

The mean follow-up time of the cohort was 40.7 ± 5.7 mo (range 10-94 mo). All patients survived during the follow-up period. Of the 26 CD patients that were treated with EBD, only two failed to respond to the treatment and underwent elective surgical laparoscopic structure resection. Both patients requiring surgery presented ileo-coecal structures associated with fistula. The overall long-term clinical success rate was 92.6% (24/26 patients remained free of surgery) (Figure 2A).

Of the 24 patients who did not undergo surgery all long the follow-up period, 11 patients received only 1 EBD, and 13 required further dilations over time for the treatment of relapsing structures (7 patients underwent 2 dilations, 5 patients 3 dilations, and 1 patient 4 dilations). The mean time free of re-dilation between the first and the second EBD was 21.2 ± 5 mo. The cumulative percentages of patients free of re-dilation over the entire follow-up period are shown in Figure 2B.

Throughout the study population, the short-term clinical success rate was 81.5% (2 patients required surgery; 3 patients did not have symptom-free 6 mo) after the first EBD. After the second EBD, the clinical success rate was 92.3% (12/13 patients); after the third EBD, the clinical success rate was 83.3% (5/6 patients). Only one patient underwent a fourth EBD showing a clinical success. The subgroup analysis dividing the study population into two groups based on the nature of the structure, i.e. naïve *vs* post-operative, showed no statistical difference between groups in term of clinical success after repeated EBD. Indeed, after the first dilation, short-term clinical success was obtained in 93.3% of the post-operative structures and 66.7% of the naïve structures [Not sufficient (NS)]; after the second EBD, success was obtained in 100% of the post-operative structures and in 80% of the naïve ones (NS); after the third EBD, success was observed in 100% of the post-operative structures and 66.7% of the naïve structures (NS). The cumulative percentages of patients free of re-dilation over the entire follow-up period for both naïve and post-operative structure are shown in Figure 2C.

Of the variables evaluated, the presence of structure-associated fistula and the structure location at the ileo-coecal level resulted significant predictive factors on the long-term negative clinical outcome, i.e., the need of surgery (both *P* = 0.002). In fact, the 2 structures that required surgery after the first EBD due to the failure of the endoscopic procedure (i.e., persistency of subocclusion symptoms) were sited at the ileo-coecal level and were associated with fistula. On the contrary, the sex and age of the patient, the nature of the structures (naïve *vs* post-surgical), the severity of CD activity, the dimension of the structures (lengths and diameters), and the medical therapy did not influence the long- term clinical outcomes (Table 3).

**DISCUSSION**

The present study describes the clinical follow-up of a cohort of 26 CD patients presenting with symptomatic structures and treated with EBD. The EBD appeared to be a safe technique that prevented the need of surgery in 92.6% of the patients during our follow-up period. The endoscopic treatment associated with the medical therapy influenced the natural history of the disease and thus it can be considered an effective strategy in the management of symptomatic structures in CD patients.

EBD has become more and more used in the treatment of CD structures since it demonstrated to be a safe and minimally invasive technique, while conserving the intestinal length. At the same time, the medical therapy is largely applied to manage the clinical course of this inflammatory disease and to control its clinical evolution. A combined medical and endoscopic therapy has shown to be effective in the treatment of CD-related structures[[22](#_ENREF_22),[34](#_ENREF_34)]. However, standardized clinical guidelines and protocols are missing.

Our cohort study presents some points of strength and novelty. In fact, to describe the effectiveness of EBD and its influence of the natural history of the disease, we decided to recruit in the study consecutive CD patients without any structure related exclusion criterion. Conversely to the other studies[[21](#_ENREF_21),[22](#_ENREF_22),[34](#_ENREF_34),[35](#_ENREF_35)], we considered structures of any nature and lengths (up to 12 cm), with and without associated fistula. The objective was to analyze a population that is the most often seen in the everyday clinical practice compared to the highly selected cohorts of patients that are usually described in the literature. Our results demonstrated that the EBD can be effectively used also in CD related structures longer than 4 cm in order to avoid or postpone surgery. The lengths of the structure did not appear to be a contraindication for performing EBD as a first line treatment in contrast to previous studies[[24](#_ENREF_24), [34](#_ENREF_34)]. The EBD overall long-term success rate in our study is higher than the values of Hassan et al.[[34](#_ENREF_34)] in a recent systematic review, which reported a cumulative mean success rate of 67% (ranging from 41% to 100%) over an average follow–up time very close to one in the present study. In order to avoid surgery, EBD was repeated -up up to 4 times during the follow with a high short-term clinical success rate after each procedure and a technical success rate of 100% with no procedure-associated complication. This result may be also related to the high-volume endoscopy center in which EBD were performed.

Based on these findings and in accordance with other studies[[22](#_ENREF_22),[24](#_ENREF_24),[34](#_ENREF_34),[35](#_ENREF_35)], EBD appeared to be a safe procedure with a very low complication rate when an endoscopist experienced in the management of bowel structure performs it. In our study, we showed that EBD is safe and feasible even in a non-selected sample of CD patients. Moreover, the safety of the procedure may be related to the diameters of the endoscopic balloon used. In our study the 18 mm balloon was the largest applied, for not more than 90 s inflations and no more than 6 dilations per session. If prudency is respected in the selection of balloon dimensions, number of dilations, and progressive inflations, the intra-operative complications may be minimized[[22](#_ENREF_22),[23](#_ENREF_23),[36](#_ENREF_36)]. The procedural safety is essential in consideration of the need of frequent re-dilations over time in the same patient in order to obtain and maintain symptomatic relief.

EBD can be considered a valuable and safe alternative of surgical resection, but EBD and surgery must not be seen as mutually exclusive solutions for CD structures. Rather EBD may be a complementary procedure that should be considered in both adult and pediatric patients in order to reach a symptom-free condition with a low risk associated.

As previously reported, we found that the structure location at the ileo-coecal level appeared to be a significant negative predictor on the long-term clinical outcome, i.e., the need of surgery[[24](#_ENREF_24)]. In our study, also the presence of fistula was associated with the occurrence of surgery. Notwithstanding, three patients with fistulizing phenotype (2 located at the colo-rectal anastomosis and 1 in the sigma), showed good clinical short and long-term outcomes after EBD, suggesting that the analysis results may represent a type II error and that larger groups could provide different results. Studies on EBD in CD patients presenting structure associated with fistula are scarce in the literature, since the majority of the previously published case series considered the presence of fistula as a patient’s exclusion criterion[[21](#_ENREF_21),[27](#_ENREF_27),[35](#_ENREF_35),[37](#_ENREF_37)]. Although the paucity of data, in a similar clinical scenario the EBD should not be excluded *a priori*. Furthermore, it could be used, together with the medical therapy, as an option to bridge the patient to surgery in better performance conditions (e.g., nutrition, inflammatory status), shifting from an emergency to an elective surgery. It is noteworthy that in patients with an adequate nutrition status in which the intestinal obstructive condition has been endoscopically managed (even if suboptimally), the response to surgery and the post-surgical complication rate (e.g., anastomotic leakage) are generally improved[[38](#_ENREF_38),[39](#_ENREF_39)]. The other examined variables seem to not affect the clinical outcomes. However, we were not able to detect which variables are associated with clinical success after only one EBD, and which can predict the need of further dilations. These aspects should be studied in a larger sample of patients.

In our cohort, both naïve and post-surgical structures responded to the EBD treatment, without significant difference on the clinical outcomes as seen by other authors[[24](#_ENREF_24),[25](#_ENREF_25)]. Thus, EBD can be considered a valuable strategy in the management of both naïve and post-surgical CD related structures. In parallel, EBD resulted equally effective in adult and pediatric CD patients. It must be emphasized that the endoscopic management of CD structures is cardinal in pediatrics because of the long life expectancy of these patients, who would more probably develop a short bowel syndrome if repeated surgical resections are performed. Moreover, many clinical concerns are related to the malnutrition and subsequent failure to thrive that will follow the obstructive condition in children if this is not immediately managed[[40](#_ENREF_40)].

Interestingly, all our patients were still medically both before and after the endoscopic treatment, mainly with azathioprine and/or biological therapy. Factors determining the development of structures are not fully understood, but chronic and trans-mural inflammation probably plays a major role[[41-43](#_ENREF_41)]. Although the lack of data in the literature, azathioprine has been shown to reverse the inflammatory changes at the anastomotic site and to maintaining remission in CD patients[[44](#_ENREF_44),[45](#_ENREF_45)]. Conversely, because of reports of complete obstruction after infliximab in patients with or without initial structures, its use has been contra-indicated in stenotic forms of CD[[46](#_ENREF_46)]. Theoretically, the rapid tissue healing induced by infliximab administration may result in marked architectural changes in the intestinal wall, which may lead to wall stricturing. However, structures do not occur without inflammation, and chronic inflammation *per se* may lead to structures. In fact, a long-term inflammatory process sustained by increased cytokine production leads to an excess of fibrotic response. On the other hand, substantial thickening of the mesenchymal layers is observed during mucosal repair. The control of chronic inflammation to prevent fibrosis and stenosis seems more important than the risk of fibrosis induced by treatment, thus justifying infliximab infusions[[41](#_ENREF_41)]. However, the role of biological therapy in case of CD structures remains controversial[[47](#_ENREF_47),[48](#_ENREF_48)]. In our cohort, we were not able to define the role and support of the two medical therapies on the clinical outcomes evaluated. With this objective, multicenter, randomized, controlled, blind clinical trials should be performed. The use of EBD is supported not only by the clinical risk/benefit ratio, but also by the costs associated to this procedure. In Italy, the entire EBD procedure (pre-endoscopy exams; hospitalization; medications; balloon dilation kit) is comprised between 1000 and 1200 Euros (reimbursed by the National Health System).

In conclusion, the EBD is not just an attractive treatment option in the management of CD-related structures. The available literature provides quite enough evidence to support its use. However, clinical guidelines, especially on the combined medical and endoscopical therapy, are still lacking. Time has come to investigate EBD clinical benefits and success in large clinical studies in order to define and standardize the protocol of use.

**COMMENTS**

***Background***

Crohn’s Disease (CD)-related structures are scarcely responsive to medical therapy and thus they are mainly treated surgically. Recently,endoscopic balloon dilation has been increasingly used in the treatment of CD-related structures.

***Innovations and breakthroughs***

The present study evaluated the efficacy of endoscopic balloon dilation in CD-related structures of any length (up to 12 cm), both naïve and post-operative, with or without associated fistula, and in both adult and pediatric patients. Structures located in both upper and lower gastrointestinal were successfully treated using gastroscope, colonscope or ileoscope according to the structure site. Our results confirmed that over a mean follow-up period of 40.7 mo multiple endoscopic balloon dilations were safe and effective to manage CD-related structures.

***Applications***

The present study supports endoscopic balloon dilation as a valuable option in the treatment of symptomatic CD patients. Moreover, endoscopic balloon dilation demonstrated as a safe technique, which can be repeated over time in order to avoid surgery, since it can be performed successfully also in relapsing patients who were previously endoscopically dilated. The associated complications are very rare (none in this study).

***Terminology***

Endoscopic balloon dilation is an operative endoscopy procedure used to dilate intestinal structures in unconscious patients. The dilation is carried out with a hydrostatic through the scope balloon system, which, once inserted and positioned through the structure, is gradually inflated with water, held for 90 s and then deflated to obtain structure dilation.

***Peer review***

de’Angelis and colleagues report an interesting series of endoscopic balloon dilation of structures in CD. The inclusion of both naive and postoperative structures with or without associated fistula reflects the usual clinical scenario in CD structures. Although the number of the cases included in the study is not so large, the conclusions are well presented and discussed. I agree with the authors that until clinical guidelines are available endoscopic balloon dilation would be a treatment option before surgery in this kind of patients.

**REFERENCES**

1 **Hanauer SB**, Dassopoulos T. Evolving treatment strategies for inflammatory bowel disease. *Annu Rev Med* 2001; **52**: 299-318 [PMID: 11160781 DOI: 10.1146/annurev.med.52.1.299]

2 **Louis E**, Collard A, Oger AF, Degroote E, Aboul Nasr El Yafi FA, Belaiche J. Behaviour of Crohn's disease according to the Vienna classification: changing pattern over the course of the disease. *Gut* 2001; **49**: 777-782 [PMID: 11709511]

3 **Cosnes J**, Gower-Rousseau C, Seksik P, Cortot A. Epidemiology and natural history of inflammatory bowel diseases. *Gastroenterology* 2011; **140**: 1785-1794 [PMID: 21530745 DOI: S0016-5085(11)00164-8]

4 **Wibmer AG**, Kroesen AJ, Gröne J, Buhr HJ, Ritz JP. Comparison of structureplasty and endoscopic balloon dilatation for stricturing Crohn's disease--review of the literature. *Int J Colorectal Dis* 2010; **25**: 1149-1157 [PMID: 20628881 DOI: 10.1007/s00384-010-1010-x]

5 **Cosnes J**, Cattan S, Blain A, Beaugerie L, Carbonnel F, Parc R, Gendre JP. Long-term evolution of disease behavior of Crohn's disease. *Inflamm Bowel Dis* 2002; **8**: 244-250 [PMID: 12131607]

6 **Van Assche G**, Geboes K, Rutgeerts P. Medical therapy for Crohn's disease structures. *Inflamm Bowel Dis* 2004; **10**: 55-60 [PMID: 15058528]

7 **Travis SP**, Stange EF, Lémann M, Oresland T, Chowers Y, Forbes A, D'Haens G, Kitis G, Cortot A, Prantera C, Marteau P, Colombel JF, Gionchetti P, Bouhnik Y, Tiret E, Kroesen J, Starlinger M, Mortensen NJ. European evidence based consensus on the diagnosis and management of Crohn's disease: current management. *Gut* 2006; **55 Suppl 1**: i16-i35 [PMID: 16481629 DOI: 10.1136/gut.2005.081950b]

8 **Coelho J**, Soyer P, Pautrat K, Boudiaf M, Vahedi K, Reignier S, Valleur P, Marteau P. [Management of ileal stenosis in patients with Crohn's disease]. *Gastroenterol Clin Biol* 2009; **33**: F75-F81 [PMID: 19733458 DOI: 10.1016/j.gcb.2009.07.024]

9 **Rutgeerts P**, Geboes K, Vantrappen G, Kerremans R, Coenegrachts JL, Coremans G. Natural history of recurrent Crohn's disease at the ileocolonic anastomosis after curative surgery. *Gut* 1984; **25**: 665-672 [PMID: 6735250]

10 **Rutgeerts P**, Geboes K, Vantrappen G, Beyls J, Kerremans R, Hiele M. Predictability of the postoperative course of Crohn's disease. *Gastroenterology* 1990; **99**: 956-963 [PMID: 2394349]

11 **Sampietro GM**, Cristaldi M, Porretta T, Montecamozzo G, Danelli P, Taschieri AM. Early perioperative results and surgical recurrence after structureplasty and miniresection for complicated Crohn's disease. *Dig Surg* 2000; **17**: 261-267 [PMID: 10867460]

12 **Shore G**, Gonzalez QH, Bondora A, Vickers SM. Laparoscopic vs conventional ileocolectomy for primary Crohn disease. *Arch Surg* 2003; **138**: 76-79 [PMID: 12511156]

13 **Dietz DW**, Laureti S, Strong SA, Hull TL, Church J, Remzi FH, Lavery IC, Fazio VW. Safety and longterm efficacy of structureplasty in 314 patients with obstructing small bowel Crohn's disease. *J Am Coll Surg* 2001; **192**: 330-37; discussion 330-37; [PMID: 11245375]

14 **Bernell O**, Lapidus A, Hellers G. Risk factors for surgery and postoperative recurrence in Crohn's disease. *Ann Surg* 2000; **231**: 38-45 [PMID: 10636100]

15 **Michelassi F**, Balestracci T, Chappell R, Block GE. Primary and recurrent Crohn's disease. Experience with 1379 patients. *Ann Surg* 1991; **214**: 230-28; discussion 230-28; [PMID: 1929605]

16 **Renna S**, Cammà C, Modesto I, Cabibbo G, Scimeca D, Civitavecchia G, Mocciaro F, Orlando A, Enea M, Cottone M. Meta-analysis of the placebo rates of clinical relapse and severe endoscopic recurrence in postoperative Crohn's disease. *Gastroenterology* 2008; **135**: 1500-1509 [PMID: 18823987 DOI: 10.1053/j.gastro.2008.07.066]

17 **Post S**, Herfarth C, Böhm E, Timmermanns G, Schumacher H, Schürmann G, Golling M. The impact of disease pattern, surgical management, and individual surgeons on the risk for relaparotomy for recurrent Crohn's disease. *Ann Surg* 1996; **223**: 253-260 [PMID: 8604905]

18 **Ryan WR**, Allan RN, Yamamoto T, Keighley MR. Crohn's disease patients who quit smoking have a reduced risk of reoperation for recurrence. *Am J Surg* 2004; **187**: 219-225 [PMID: 14769308 DOI: 10.1016/j.amjsurg.2003.11.007]

19 **Scarpa M**, Angriman I, Barollo M, Polese L, Ruffolo C, Bertin M, Pagano D, D'Amico DF. Risk factors for recurrence of stenosis in Crohn's disease. *Acta Biomed* 2003; **74 Suppl 2**: 80-83 [PMID: 15055041]

20 **Krupnick AS**, Morris JB. The long-term results of resection and multiple resections in Crohn's disease. *Semin Gastrointest Dis* 2000; **11**: 41-51 [PMID: 10706228]

21 **Stienecker K**, Gleichmann D, Neumayer U, Glaser HJ, Tonus C. Long-term results of endoscopic balloon dilatation of lower gastrointestinal tract structures in Crohn's disease: a prospective study. *World J Gastroenterol* 2009; **15**: 2623-2627 [PMID: 19496192]

22 **Scimeca D**, Mocciaro F, Cottone M, Montalbano LM, D'Amico G, Olivo M, Orlando R, Orlando A. Efficacy and safety of endoscopic balloon dilation of symptomatic intestinal Crohn's disease structures. *Dig Liver Dis* 2011; **43**: 121-125 [PMID: 20561831 DOI: 10.1016/j.dld.2010.05.001]

23 **Couckuyt H**, Gevers AM, Coremans G, Hiele M, Rutgeerts P. Efficacy and safety of hydrostatic balloon dilatation of ileocolonic Crohn's structures: a prospective longterm analysis. *Gut* 1995; **36**: 577-580 [PMID: 7737567]

24 **Mueller T**, Rieder B, Bechtner G, Pfeiffer A. The response of Crohn's structures to endoscopic balloon dilation. *Aliment Pharmacol Ther* 2010; **31**: 634-639 [PMID: 20047581 DOI: 10.1111/j.1365-2036.2009.04225.x]

25 **Blomberg B**, Rolny P, Järnerot G. Endoscopic treatment of anastomotic structures in Crohn's disease. *Endoscopy* 1991; **23**: 195-198 [PMID: 1915133 DOI: 10.1055/s-2007-1010654]

26 **Dear KL**, Hunter JO. Colonoscopic hydrostatic balloon dilatation of Crohn's structures. *J Clin Gastroenterol* 2001; **33**: 315-318 [PMID: 11588547]

27 **Thomas-Gibson S**, Brooker JC, Hayward CM, Shah SG, Williams CB, Saunders BP. Colonoscopic balloon dilation of Crohn's structures: a review of long-term outcomes. *Eur J Gastroenterol Hepatol* 2003; **15**: 485-488 [PMID: 12702904 DOI: 10.1097/01.meg.0000059110.41030.bc]

28 **Bousvaros A**, Antonioli DA, Colletti RB, Dubinsky MC, Glickman JN, Gold BD, Griffiths AM, Jevon GP, Higuchi LM, Hyams JS, Kirschner BS, Kugathasan S, Baldassano RN, Russo PA. Differentiating ulcerative colitis from Crohn disease in children and young adults: report of a working group of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the Crohn's and Colitis Foundation of America. *J Pediatr Gastroenterol Nutr* 2007; **44**: 653-674 [PMID: 17460505 DOI: 10.1097/MPG.0b013e31805563f3]

29 **Van Assche G**, Dignass A, Reinisch W, van der Woude CJ, Sturm A, De Vos M, Guslandi M, Oldenburg B, Dotan I, Marteau P, Ardizzone A, Baumgart DC, D'Haens G, Gionchetti P, Portela F, Vucelic B, Söderholm J, Escher J, Koletzko S, Kolho KL, Lukas M, Mottet C, Tilg H, Vermeire S, Carbonnel F, Cole A, Novacek G, Reinshagen M, Tsianos E, Herrlinger K, Oldenburg B, Bouhnik Y, Kiesslich R, Stange E, Travis S, Lindsay J. The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: Special situations. *J Crohns Colitis* 2010; **4**: 63-101 [PMID: 21122490 DOI: 10.1016/j.crohns.2009.09.009]

30 **Levine A**, Griffiths A, Markowitz J, Wilson DC, Turner D, Russell RK, Fell J, Ruemmele FM, Walters T, Sherlock M, Dubinsky M, Hyams JS. Pediatric modification of the Montreal classification for inflammatory bowel disease: the Paris classification. *Inflamm Bowel Dis* 2011; **17**: 1314-1321 [PMID: 21560194 DOI: 10.1002/ibd.21493]

31 **Satsangi J**, Silverberg MS, Vermeire S, Colombel JF. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. *Gut* 2006; **55**: 749-753 [PMID: 16698746 DOI: 10.1136/gut.2005.082909]

32 **Hyams JS**, Ferry GD, Mandel FS, Gryboski JD, Kibort PM, Kirschner BS, Griffiths AM, Katz AJ, Grand RJ, Boyle JT. Development and validation of a pediatric Crohn's disease activity index. *J Pediatr Gastroenterol Nutr* 1991; **12**: 439-447 [PMID: 1678008]

33 **Friedman S**. General principles of medical therapy of inflammatory bowel disease. *Gastroenterol Clin North Am* 2004; **33**: 191-208, viii [PMID: 15177534 DOI: 10.1016/j.gtc.2004.02.003]

34 **Hassan C**, Zullo A, De Francesco V, Ierardi E, Giustini M, Pitidis A, Taggi F, Winn S, Morini S. Systematic review: Endoscopic dilatation in Crohn's disease. *Aliment Pharmacol Ther* 2007; **26**: 1457-1464 [PMID: 17903236 DOI: 10.1111/j.1365-2036.2007.03532.x]

35 **Di Nardo G**, Oliva S, Passariello M, Pallotta N, Civitelli F, Frediani S, Gualdi G, Gandullia P, Mallardo S, Cucchiara S. Intralesional steroid injection after endoscopic balloon dilation in pediatric Crohn's disease with structure: a prospective, randomized, double-blind, controlled trial. *Gastrointest Endosc* 2010; **72**: 1201-1208 [PMID: 20951986 DOI: 10.1016/j.gie.2010.08.003]

36 **Foster EN**, Quiros JA, Prindiville TP. Long-term follow-up of the endoscopic treatment of structures in pediatric and adult patients with inflammatory bowel disease. *J Clin Gastroenterol* 2008; **42**: 880-885 [PMID: 18645528 DOI: 10.1097/MCG.0b013e3181354440]

37 **Erkelens GW**, van Deventer SJ. Endoscopic treatment of structures in Crohn's disease. *Best Pract Res Clin Gastroenterol* 2004; **18**: 201-207 [PMID: 15123092 DOI: 10.1016/j.bpg.2003.08.003]

38 **Yamamoto T**, Allan RN, Keighley MR. Risk factors for intra-abdominal sepsis after surgery in Crohn's disease. *Dis Colon Rectum* 2000; **43**: 1141-1145 [PMID: 10950014]

39 **Iesalnieks I**, Kilger A, Glass H, Müller-Wille R, Klebl F, Ott C, Strauch U, Piso P, Schlitt HJ, Agha A. Intraabdominal septic complications following bowel resection for Crohn's disease: detrimental influence on long-term outcome. *Int J Colorectal Dis* 2008; **23**: 1167-1174 [PMID: 18690466 DOI: 10.1007/s00384-008-0534-9]

40 **Grossman AB**, Baldassano RN. Specific considerations in the treatment of pediatric inflammatory bowel disease. *Expert Rev Gastroenterol Hepatol* 2008; **2**: 105-124 [PMID: 19072374 DOI: 10.1586/17474124.2.1.105]

41 **Pelletier AL**, Kalisazan B, Wienckiewicz J, Bouarioua N, Soulé JC. Infliximab treatment for symptomatic Crohn's disease structures. *Aliment Pharmacol Ther* 2009; **29**: 279-285 [PMID: 19035967 DOI: APT3887]

42 **Brenmoehl J**, Falk W, Göke M, Schölmerich J, Rogler G. Inflammation modulates fibronectin isoform expression in colonic lamina propria fibroblasts (CLPF). *Int J Colorectal Dis* 2008; **23**: 947-955 [PMID: 18633626 DOI: 10.1007/s00384-008-0523-z]

43 **Quinn PG**, Binion DG, Connors PJ. The role of endoscopy in inflammatory bowel disease. *Med Clin North Am* 1994; **78**: 1331-1352 [PMID: 7967913]

44 **D'Haens G**, Geboes K, Ponette E, Penninckx F, Rutgeerts P. Healing of severe recurrent ileitis with azathioprine therapy in patients with Crohn's disease. *Gastroenterology* 1997; **112**: 1475-1481 [PMID: 9136824]

45 **Riello L**, Talbotec C, Garnier-Lengliné H, Pigneur B, Svahn J, Canioni D, Goulet O, Schmitz J, Ruemmele FM. Tolerance and efficacy of azathioprine in pediatric Crohn's disease. *Inflamm Bowel Dis* 2011; **17**: 2138-2143 [PMID: 21910176 DOI: 10.1002/ibd.21612]

46 **Louis E**, Boverie J, Dewit O, Baert F, De Vos M, D'Haens G. Treatment of small bowel subocclusive Crohn's disease with infliximab: an open pilot study. *Acta Gastroenterol Belg* ; **70**: 15-19 [PMID: 17619533]

47 **Samimi R**, Flasar MH, Kavic S, Tracy K, Cross RK. Outcome of medical treatment of stricturing and penetrating Crohn's disease: a retrospective study. *Inflamm Bowel Dis* 2010; **16**: 1187-1194 [PMID: 19902541 DOI: 10.1002/ibd.21160]

48 **Lichtenstein GR**, Olson A, Travers S, Diamond RH, Chen DM, Pritchard ML, Feagan BG, Cohen RD, Salzberg BA, Hanauer SB, Sandborn WJ. Factors associated with the development of intestinal structures or obstructions in patients with Crohn's disease. *Am J Gastroenterol* 2006; **101**: 1030-1038 [PMID: 16606351 DOI: AJG463]

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**Figure Legends:**

**Figure 1 Images of Crohn’s Disease-related structure in one patient**

A: Direct visualization of the ileal structure; B: Inflation of the endoscopic balloon under fluoroscopic control; C:Direct visualization of the bowel site after the endoscopic balloon dilation.

**Figure 2** **Kaplan Meier curve for interval free of surgery.** A: Kaplan Meier curve for interval free of surgery after endoscopic balloon dilation or re-dilation; B. Kaplan Meier curve for interval free of re-dilation during the follow-up period; C: Kaplan Meier curve for the interval free of re-dilation over the follow-up period for patients with naïve (in green) and post-operative (in blue) structures.

**Table 1** **Clinical characteristics of the study cohort**

|  |  |
| --- | --- |
| **Clinical characteristics of the study cohort (*n =* 26)** |  |
| Gender distribution (*n*):   * Male * Female | 11  15 |
| Pediatric/Adult patients distribution (*n*):   * Pediatric * Adult | 3  23 |
| CD indexes of activity (mean ± SE):   * PCDAI (*n =* 3) * CDAI (*n =* 23) | 38 ± 7.2  365 ± 75 |
| Ongoing Medical Therapy (*n*):   * Azathioprine * Azathioprine + Infliximab | 20  6 |
| Mean age at the time of the CD diagnosis [mean ± SE (range)] | 22.9 ± 2.8  (2-50 yr) |
| Mean age at the time of the occurrence of the first structure  [mean ± SE (range)] | 36.8 ± 3.6  (11-65 yr) |

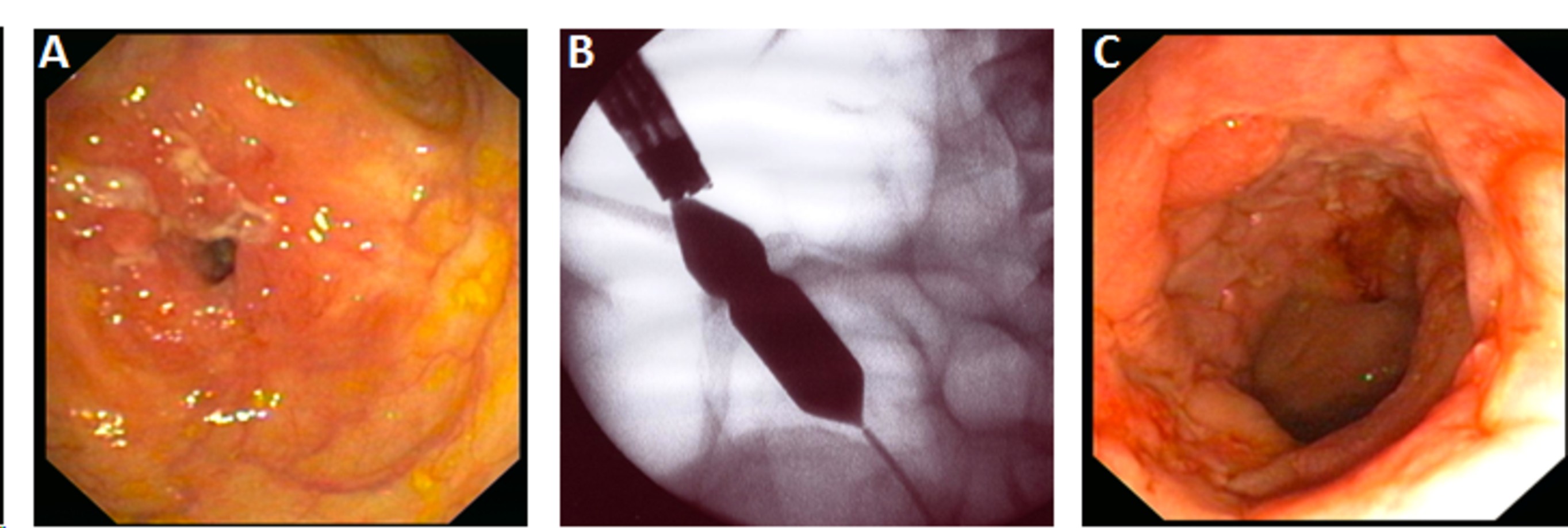
**Table 2 Clinical characteristics of Crohn’s Disease-related structures**

|  |  |
| --- | --- |
| Structures characteristics (*n =* 27) |  |
| Nature of the structure (*n*):   * Naïve * Post-surgical | 12  15 |
| Location of the Structure (*n*):   * Upper Gastrointestinal * Small intestine * Ileo-colonic * Colonic | 1  2  14  10 |
| Mean length (cm) [mean ± SE (range)]   * ≤ 4 cm (*n*) * > 4 cm (*n*) | 4.6 ± 0.4 (2-12)  15  12 |
| Mean diameter (mm) [mean ± SE (range)]   * ≤ 5 mm (*n*) * > 5 mm (*n*) | 2.5 ± 0.2 (1-6)  26  1 |
| Structure associated fistula (*n*):   * yes * no | 5  22 |

**Table 3 Analyses of the influence of the clinical variables on the occurrence of surgery**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **No Surgery (*n*)** | **Surgery (*n*)** | ***P* value** |
| Male sex | 10 | 1 | NS |
| Adult patients | 21 | 2 | NS |
| Naïve structures | 10 | 2 | NS |
| Moderate disease activity | 12 | 2 | NS |
| Structures length > 4 cm | 11 | 1 | NS |
| Structures diameters ≤ 5 mm | 24 | 2 | NS |
| Structures with fistula | 3 | 2 | **0.002** |
| Structures at the ileo-coecal level | 3 | 2 | **0.002** |
| Pharmacological therapy (Azathioprine) | 18 | 2 | NS |

NS: Not significant.



**Figure 1**

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**Figure 2A**

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**Figure 2B**

****

**Figure 2C**