Management of Fibro-Stenosing Crohn's Disease

Subjects: Gastroenterology & Hepatology

Contributor: Virginia Solitano , Arianna Dal Buono , Roberto Gabbiadini , Marek Wozny , Alessandro Repici , Antonino Spinelli , Stefania Vetrano , Alessandro Armuzzi

Fibro-stenosing Crohn's disease (CD) is a common disease presentation that leads to impaired quality of life and often requires endoscopic treatments or surgery. Managing the treatment of individuals with fibro-stenosing CD is challenging and requires a multidisciplinary team comprising a gastroenterologist, a colorectal surgeon, and a radiologist to evaluate the appropriate strategy. The optimal therapeutic approach changes according to the features of the stenosis (i.e., location, length, angulation), the presence of any associated complications (i.e., fistula, abscess, dysplasia), and the patient's preference.

fibrosis stricture IBD

1. Introduction

Fibrosis represents a major challenge in the management of Crohn's disease (CD) [1]. Around 50% of CD patients will develop fibrotic strictures or penetrating lesions, and up to 75% will eventually need surgery [2]. Nevertheless, it is common for patients to experience post-operative recurrence of fibrosis, especially at the ileocolonic anastomotic site, which might lead to the onset of re-stricturing disease and necessitate further surgeries [3].

The mechanism underlying the development and progression of fibrosis in inflammatory bowel disease (IBD) is still unclear, but growing evidence suggests that chronic intestinal inflammation, causing repetitive unphysiological healing of injured tissue, represents the main driver [4]. However, fibrotic changes persist once inflammatory stimuli are eliminated, and suppression of inflammation does not necessarily have an effect on intestinal fibrosis [4]. Multi-modal single-cell approaches are revealing a deeper understanding of the role of distinct cell populations [5].

Furthermore, a lack of accepted clinical trial endpoints and treatment targets for fibro-stenosis, as well as the extreme heterogeneity in disease definitions, diagnostic techniques, and study design, led an international study group to develop a framework for trial design and endpoints to help researchers and regulators in the development of new drugs [6].

2. Medical Therapy

CD patients with fibro-stenosing lesions are currently treated with the best available medical therapies, given that specific anti-fibrotic therapies are only available within clinical trials. The evidence for the effectiveness of medical

treatments in fibrosis-predominant lesions remains very limited. The available data on corticosteroids have shown their efficacy in reducing obstructive symptoms in almost 100% of patients; however, this method has high recurrence rates (around 50%) and often requires surgery [7]. It is worth noting, in experimental mice models of CD, a one-week treatment with prednisolone administered via enemas resulted in anti-fibrotic effects at histological assessment [8]. Such anti-fibrotic effects of steroids were mediated by TRPA1 channel activation concomitant with an anti-TGF-β action [8].

In the past, the efficacy of anti-tumor necrosis factor (TNF) agents in fibro-stenosing CD has produced conflicting results. Previous studies have reported high clinical response after infliximab in CD patients with strictures [9][10]. However, concerns were raised about anti-TNFs promotion of fibrosis through extremely rapid tissue healing and scarring [10][11]. Subsequently, robust evidence confuted these concerns: neither progression in strictures' severity nor new occurrence of strictures were repeatedly observed [12][13][14], and possible mechanisms mediated by anti-TNFs able to prevent fibrosis have been suggested [15]. In the multi-center, prospective CREOLE study, adalimumab treatment was successful in approximately 60% of CD patients with strictures and obstructive symptoms after 6 months of treatment, and 30% of the patients continued to be in clinical remission after a median follow-up time of 4 years (still on adalimumab, without any endoscopic or surgical treatment) [14]. Over the 4-year study period, slightly more than 50% of the included patients remained free of surgery after commencing adalimumab [14]. Finally, the STRIDENT trial, which included CD patients with evidence of stricturing disease and associated chronic or subacute intestinal obstruction, showed high rates of clinical and radiological response (assessed on BUS and MRE) in both adalimumab arms (intensive vs. standard treatment) [16].

Still, a certain heterogeneity in the characteristics of the lesions analyzed in the above-mentioned studies might bias clear conclusions on the effectiveness of both steroids and anti-TNFs in fibrosis-predominant strictures.

3. Endoscopic Therapy

No medical therapy that prevents or reverses fibrosis is currently available in clinical practice and these patients are generally managed with endoscopic balloon dilation (EBD) or surgery [17][18].

EBD is a cost-effective, minimally invasive procedure for handling symptomatic short CD strictures [17][18][19][20]. The procedure ameliorates obstructive symptoms and can be repeated if the stricture re-occurs, improving the long-term prognosis of subjects with CD [21]. Furthermore, EBD may also have an important role as a bridge-to-surgery therapy, allowing the improvement of the patient's nutritional status [22]. EBD should be avoided in stenosis associated with problems such as fistula, abscess, or underlying dysplasia; however, it can be used in naive or anastomotic, straight (non-angulated) strictures that are less than 5 cm in length [20][23][24]. Generally, the most used device for EBD is a through the scope (TTS) radial expanding balloon dilator which pneumatically dilates the stricture [20]. Graded dilation up to the largest size (18–20 mm) in a stepwise mode is recommended to obtain maximum efficacy [24]. Indeed, in the study by Reutmann et al., patients who failed to achieve a maximum dilation of 14 mm or more had an increased risk of surgery (hazard ratio [HR] 2.88; 95% CI 1.10–7.53), while those reaching a dilation of 16–18 mm displayed a longer interval between EBDs (mean 240 ± 136.7 days vs. 456 ±

357.3 days) [25]. Overall, EBD exhibited optimal rates of immediate technical success, typically defined as the possibility to pass the stenosis with the endoscope after the procedure (technical success of 89.1% with clinical efficacy of 80.8%) [26]. Regarding long-term outcomes, Bettenworth et al. observed that re-dilation for ileal and anastomotic strictures was needed in 36.5%, 51.8%, and 73.5% of cases at 6, 12, and 24 months, respectively; while 17.5%, 30.1%, and 42.9% of patients required surgery at 6, 12, and 24 months, respectively [26]. The length of the stricture was a predictor of surgery-free interval (≤5 cm stricture was associated with a longer surgery-free survival time, HR 2.5; 95% CI 1.4–4.4) [26].

Conversely, although EBD can also be attempted in colonic stenosis, surgical intervention should be considered in these cases due to the increased risk of malignancy and because stricture biopsy may not rule out the presence of dysplasia [23][27].

EBD has low rates of adverse events (i.e., perforation, bleeding, abscess, or dilation-related need for surgery) which are estimated to be 2.8–4% [26][28]. Unlike long-term outcomes, stricture length does not seem to be associated with the risk of bleeding or perforation. However, the use of systemic steroids may be positively associated with post-EBD perforation while fibrotic stricture has a potential protective role [29].

Other endoscopic techniques have been proposed for CD-related strictures. Endoscopic stricturotomy is an emergent technique in which a needle knife or an insulated-tip knife is used for radial, circumferential, or horizontal incisions of a stenotic bowel tract to progressively widen the bowel lumen [24][30][31]. Although data are limited, this technique exhibits high immediate technical success rates [32], with excellent rates of reported clinical and endoscopic improvement [33]. A lower risk of perforation has been reported (0% vs. 2.4%, albeit p not significant), but the higher risk of bleeding compared to EBD (14% vs. 0%, $p < 0.001$) has raised some concerns [33]. Thus, the role of endoscopic stricturotomy in the treatment of CD strictures has yet to be defined and more studies are needed to understand the real efficacy and safety of this technique.

Similarly, some reports have described the use of stents as an alternative treatment for CD-related strictures with high rates of improvement or resolution of symptoms [34][35][36].

In a recent multi-center randomized trial, individuals with CD-related strictures, which were treated with EBD, more often avoided a new therapeutic intervention at one year compared to those treated with fully covered self-expandable metal stents (FCSEMS) (80% vs. 51% respectively; OR 3.9; 95% CI 1.4–10.6) [37]. It is noteworthy that success rates were around 65% for both procedures when the length of the stricture was >3 cm, hence FCSEMS may have a role in the treatment of longer strictures [37]. More research is required to determine SEMSs proper place in the endoscopic management of CD strictures; for now, EBD is still the preferred technique.

4. Surgical Therapy

Symptomatic CD strictures that are not manageable with EBD should be referred for surgery, namely surgical resection or strictureplasty [23][30][38]. Early surgical resection, shortly after diagnosis, should be the preferred

strategy for localized ileocecal fibro-stenosing CD [39]. Indeed, many studies showed that early surgery may prolong clinical remission and reduce the need for subsequent biologic therapy, or the risk of further surgery compared to late surgery (surgery performed during the disease) [40][41][42].

Interestingly, Li et al. observed that patients with ileocolonic anastomotic stricture, which underwent salvage surgery after one or more EBDs, were associated with increased rates of stoma formation (p = 0.030) and surgical-site infection (p = 0.025), compared with individuals who underwent immediate surgery [43]. Furthermore, early surgery may also be considered the best therapeutic option over EBD for primary CD ileocolic strictures. In a retrospective study conducted by Lan et al., surgical resection of primary CD ileocolic strictures was associated with a reduced need for secondary surgery and a longer surgery-free time interval compared to individuals managed with EBD (11.1 ± 0.6 vs. 5.4 ± 0.6 years; $p < 0.001$) [44].

Strictureplasty is a validated and safe surgical choice for the management of CD strictures and is an alternative to bowel resection [45][46]. This surgical technique is recommended for multiple fibrotic strictures or previous extensive resections, thus protecting against small bowel loss [18]. However, strictureplasty is not always technically feasible, and it is not recommended in the colon, in cases of penetrating or actively diseased terminal ileum.

The Heineke-Mikulicz and Finney strictureplasties are the most common techniques used for short (<10 cm) and medium length (10–20 cm) strictures of the small bowel, respectively; while the "non-conventional" Michelassi side-to-side isoperistaltic strictureplasty, with or without mid-stricture resection, is suggested for long strictured tracts (>20 cm) and is less commonly performed [23][47]. Interestingly, recurrence rates are low and the quality-of-life post-strictureplasty is comparable with surgical resection [48]. In a meta-analysis conducted by Yamamoto et al., (1112 individuals and 3259 stricturoplasties included) the recurrence rate at 5 years was 28% [49]. Adverse events of this surgical intervention have been described in 4% to 18% of individuals and comprise surgical site infection, obstruction, stricture-site hemorrhage, sepsis, perforation, and early reoperation [38][46][49][50][51][52]. It is important to note that low albumin, weight loss, older age, preoperative steroid therapy, and the presence of abscess or fistula at the moment of strictureplasty increase the risk of intra-abdominal septic adverse events [38]. Therefore, optimization of nutritional status is a crucial measure for the best management of these patients [23].

References

1. Rieder, F.; Fiocchi, C.; Rogler, G. Mechanisms, Management, and Treatment of Fibrosis in Patients with Inflammatory Bowel Diseases. Gastroenterology 2017, 152, 340–350.e6.
2. Yoo, J.H.; Holubar, S.; Rieder, F. Fibrostenotic Strictures in Crohn's Disease. Intest. Res. 2020, 18, 379–401.
3. 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.

4. Rimola, J.; Capozzi, N. Differentiation of Fibrotic and Inflammatory Component of Crohn’s Disease-Associated Strictures. Intest. Res. 2020, 18, 144–150.
5. Henderson, N.C.; Rieder, F.; Wynn, T.A. Fibrosis: From Mechanisms to Medicines. Nature 2020, 587, 555–566.
6. Rieder, F.; Bettenworth, D.; Ma, C.; Parker, C.E.; Williamson, L.A.; Nelson, S.A.; van Assche, G.; di Sabatino, A.; Bouhnik, Y.; Stidham, R.W.; et al. An Expert Consensus to Standardise Definitions, Diagnosis and Treatment Targets for Anti-Fibrotic Stricture Therapies in Crohn’s Disease. Aliment. Pharmacol. Ther. 2018, 48, 347–357.
7. Yaffe, B.H.; Korelitz, B.I. Prognosis for Nonoperative Management of Small-Bowel Obstruction in Crohn’s Disease. J. Clin. Gastroenterol. 1983, 5, 211–216.
8. Kurahara, L.H.; Hiraishi, K.; Hu, Y.; Koga, K.; Onitsuka, M.; Doi, M.; Aoyagi, K.; Takedatsu, H.; Kojima, D.; Fujihara, Y.; et al. Activation of Myofibroblast TRPA1 by Steroids and Pirfenidone Ameliorates Fibrosis in Experimental Crohn’s Disease. Cell. Mol. Gastroenterol. Hepatol. 2017, 5, 299–318.
9. Pelletier, A.L.; Kalisazan, B.; Wienckiewicz, J.; Bouarioua, N.; SoulÉ, J.C. Infliximab Treatment for Symptomatic Crohn’s Disease Strictures. Aliment. Pharmacol. Ther. 2009, 29, 279–285.
10. Lu, C.; Baraty, B.; Lee Robertson, H.; Filyk, A.; Shen, H.; Fung, T.; Novak, K.; Ma, C.; Panaccione, R.; Achkar, J.P.; et al. Systematic Review: Medical Therapy for Fibrostenosing Crohn’s Disease. Aliment. Pharmacol. Ther. 2020, 51, 1233–1246.
11. D’Alessio, S.; Ungaro, F.; Noviello, D.; Lovisa, S.; Peyrin-Biroulet, L.; Danese, S. Revisiting Fibrosis in Inflammatory Bowel Disease: The Gut Thickens. Nat. Rev. Gastroenterol. Hepatol. 2022, 19, 169–184.
12. Pallotta, N.; Barberani, F.; Hassan, N.A.; Guagnozzi, D.; Vincoli, G.; Corazziari, E. Effect of Infliximab on Small Bowel Stenoses in Patients with Crohn’s Disease. World J. Gastroenterol. 2008, 14, 1885–1890.
13. Hanauer, S.B.; Feagan, B.G.; Lichtenstein, G.R.; Mayer, L.F.; Schreiber, S.; Colombel, J.F.; Rachmilewitz, D.; Wolf, D.C.; Olson, A.; Bao, W.; et al. Maintenance Infliximab for Crohn’s Disease: The ACCENT I Randomised Trial. Lancet 2002, 359, 1541–1549.
14. Bouhnik, Y.; Carbonnel, F.; Laharie, D.; Stefanescu, C.; Hébuterne, X.; Abitbol, V.; Nachury, M.; Brixi, H.; Bourreille, A.; Picon, L.; et al. Efficacy of Adalimumab in Patients with Crohn’s Disease and Symptomatic Small Bowel Stricture: A Multicentre, Prospective, Observational Cohort (CREOLE) Study. Gut 2018, 67, 53–60.
15. di Sabatino, A.; Ciccocioppo, R.; Benazzato, L.; Sturniolo, G.C.; Corazza, G.R. Infliximab Downregulates Basic Fibroblast Growth Factor and Vascular Endothelial Growth Factor in Crohn’s Disease Patients. Aliment. Pharmacol. Ther. 2004, 19, 1019–1024.

16. Schulberg, J.D.; Wright, E.K.; Holt, B.A.; Hamilton, A.L.; Sutherland, T.R.; Ross, A.L.; Vogrin, S.; Miller, A.M.; Connell, W.C.; Lust, M.; et al. Intensive Drug Therapy versus Standard Drug Therapy for Symptomatic Intestinal Crohn’s Disease Strictures (STRIDENT): An Open-Label, Single-Centre, Randomised Controlled Trial. Lancet Gastroenterol. Hepatol. 2022, 7, 318–331.
17. Rodríguez-Lago, I.; Gisbert, J.P. The Role of Immunomodulators and Biologics in the Medical Management of Stricturing Crohn’s Disease. J. Crohn’s Colitis 2020, 14, 557–566.
18. Adamina, M.; Bonovas, S.; Raine, T.; Spinelli, A.; Warusavitarne, J.; Armuzzi, A.; Bachmann, O.; Bager, P.; Biancone, L.; Bokemeyer, B.; et al. ECCO Guidelines on Therapeutics in Crohn’s Disease: Surgical Treatment. J. Crohn’s Colitis 2020, 14, 155–168.
19. Lee, K.E.; Lim, F.; Faye, A.S.; Shen, B.; Hur, C. Endoscopic Balloon Dilation Is Cost-Effective for Crohn’s Disease Strictures. Dig. Dis. Sci. 2022, 67, 5462–5471.
20. Sivasailam, B.; Lane, B.F.; Cross, R.K. Endoscopic Balloon Dilation of Strictures: Techniques, Short- and Long-Term Outcomes, and Complications. Gastrointest. Endosc. Clin. 2022, 32, 675–686.
21. Yamamoto, H.; Yano, T.; Araki, A.; Esaki, M.; Ohtsuka, K.; Ohmiya, N.; Oka, S.; Nakase, H.; Bamba, S.; Hirai, F.; et al. Guidelines for Endoscopic Balloon Dilation in Treating Crohn’s Disease-Associated Small Intestinal Strictures (Supplement to the Clinical Practice Guidelines for Enteroscopy). Dig. Endosc. 2022, 34, 1278–1296.
22. Ma, C.; Jairath, V.; Click, B.; Hirota, S.A.; Lu, C.; Parker, C.E.; Rieder, F.; Stenosis Therapy and Anti-Fibrotic Research (STAR) Consortium. Targeting Anti-Fibrotic Pathways in Crohn’s Disease—The Final Frontier? Best. Pract. Res. Clin. Gastroenterol. 2019, 38–39, 101603.
23. El Ouali, S.; Click, B.; Holubar, S.D.; Rieder, F. Natural History, Diagnosis and Treatment Approach to Fibrostenosing Crohn’s Disease. United Eur. Gastroenterol. J. 2020, 8, 263–270.
24. Shen, B.; Kochhar, G.; Navaneethan, U.; Farraye, F.A.; Schwartz, D.A.; Iacucci, M.; Bernstein, C.N.; Dryden, G.; Cross, R.; Bruining, D.H.; et al. Practical Guidelines on Endoscopic Treatment for Crohn’s Disease Strictures: A Consensus Statement from the Global Interventional Inflammatory Bowel Disease Group. Lancet Gastroenterol. Hepatol. 2020, 5, 393–405.
25. Reutemann, B.A.; Turkeltaub, J.A.; Al-Hawary, M.; Waljee, A.K.; Higgins, P.D.R.; Stidham, R.W. Endoscopic Balloon Dilation Size and Avoidance of Surgery in Stricturing Crohn’s Disease. Inflamm. Bowel Dis. 2017, 23, 1803–1809.
26. Bettenworth, D.; Gustavsson, A.; Atreja, A.; Lopez, R.; Tysk, C.; Van Assche, G.; Rieder, F. A Pooled Analysis of Efficacy, Safety, and Long-Term Outcome of Endoscopic Balloon Dilation Therapy for Patients with Stricturing Crohn’s Disease. Inflamm. Bowel Dis. 2017, 23, 133–142.
27. Fumery, M.; de Chambrun, G.P.; Stefanescu, C.; Buisson, A.; Bressenot, A.; Beaugerie, L.; Amiot, A.; Altwegg, R.; Savoye, G.; Abitbol, V.; et al. Detection of Dysplasia or Cancer in 3.5% of Patients

With Inflammatory Bowel Disease and Colonic Strictures. Clin. Gastroenterol. Hepatol. 2015, 13, 1770–1775.

28. Navaneethan, U.; Lourdusamy, V.; Njei, B.; Shen, B. Endoscopic Balloon Dilation in the Management of Strictures in Crohn’s Disease: A Systematic Review and Meta-Analysis of Non-Randomized Trials. Surg. Endosc. 2016, 30, 5434–5443.
29. Winder, O.; Fliss-Isakov, N.; Winder, G.; Scapa, E.; Yanai, H.; Barnes, S.; Dekel, R.; Dotan, I.; Maharshak, N. Clinical Outcomes of Endoscopic Balloon Dilatation of Intestinal Strictures in Patients with Crohn’s Disease. Medicine 2019, 98, e16864.
30. Fousekis, F.S.; Mitselos, I.V.; Tepelenis, K.; Pappas-Gogos, G.; Katsanos, K.H.; Lianos, G.D.; Frattini, F.; Vlachos, K.; Christodoulou, D.K. Medical, Endoscopic and Surgical Management of Stricturing Crohn’s Disease: Current Clinical Practice. J. Clin. Med. 2022, 11, 2366.
31. Navaneethan, U.; Lourdusamy, D. Endoscopic Stricturotomy and Strictureplasty. Gastrointest. Endosc. Clin. 2022, 32, 687–697.
32. Lan, N.; Shen, B. Endoscopic Stricturotomy with Needle Knife in the Treatment of Strictures from Inflammatory Bowel Disease. Inflamm. Bowel Dis. 2017, 23, 502–513.
33. Lan, N.; Shen, B. Endoscopic Stricturotomy Versus Balloon Dilation in the Treatment of Anastomotic Strictures in Crohn’s Disease. Inflamm. Bowel Dis. 2018, 24, 897–907.
34. Das, R.; Singh, R.; Din, S.; Lund, J.; Krishnamoorthy, R.; Hearing, S.; Norton, B.; Williams, J.; Fraser, C.; Goddard, A.; et al. Therapeutic Resolution of Focal, Predominantly Anastomotic Crohn’s Disease Strictures Using Removable Stents: Outcomes from a Single-Center Case Series in the United Kingdom. Gastrointest. Endosc. 2020, 92, 344–352.
35. Attar, A.; Branche, J.; Coron, E.; Privat, J.; Caillo, L.; Chevaux, J.B.; Vuitton, L.; Amiot, A.; Belkhodja, H.; Dray, X.; et al. An Anti-Migration Self-Expandable and Removable Metal Stent for Crohn’s Disease Strictures: A Nationwide Study From GETAID and SFED. J. Crohn’s Colitis 2021, 15, 521–528.
36. Giri, S.; Gopan, A.; Sundaram, S.; Kale, A. Efficacy and Safety of Endoscopic Stenting for Crohn’s Disease Related Strictures: A Systematic Review and Meta-Analysis. Korean J. Gastroenterol. 2022, 80, 177–185.
37. Loras, C.; Andújar, X.; Gornals, J.B.; Sanchiz, V.; Brullet, E.; Sicilia, B.; Martín-Arranz, M.D.; Naranjo, A.; Barrio, J.; Dueñas, C.; et al. (GETECCU) Self-Expandable Metal Stents versus Endoscopic Balloon Dilation for the Treatment of Strictures in Crohn’s Disease (ProtDilat Study): An Open-Label, Multicentre, Randomised Trial. Lancet Gastroenterol. Hepatol. 2022, 7, 332–341.
38. Lightner, A.L.M.; Vogel, J.D.M.; Carmichael, J.C.M.; Keller, D.S.M.; Shah, S.A.M.; Mahadevan, U.M.; Kane, S.V.M.; Paquette, I.M.M.; Steele, S.R.M.; Feingold, D.L.M. The American Society of

Colon and Rectal Surgeons Clinical Practice Guidelines for the Surgical Management of Crohn’s Disease. Dis. Colon. Rectum 2020, 63, 1028–1052.

39. Rieder, F.; Latella, G.; Magro, F.; Yuksel, E.S.; Higgins, P.D.; Di Sabatino, A.; de Bruyn, J.R.; Rimola, J.; Brito, J.; Bettenworth, D.; et al. European Crohn’s and Colitis Organisation Topical Review on Prediction, Diagnosis and Management of Fibrostenosing Crohn’s Disease. J. Crohn’s Colitis 2016, 10, 873–885.
40. Aratari, A.; Papi, C.; Leandro, G.; Viscido, A.; Capurso, L.; Caprilli, R. Early versus Late Surgery for Ileo-Caecal Crohn’s Disease. Aliment. Pharmacol. Ther. 2007, 26, 1303–1312.
41. Latella, G.; Cocco, A.; Angelucci, E.; Viscido, A.; Bacci, S.; Necozione, S.; Caprilli, R. Clinical Course of Crohn’s Disease First Diagnosed at Surgery for Acute Abdomen. Dig. Liver Dis. 2009, 41, 269–276.
42. Golovics, P.A.; Lakatos, L.; Nagy, A.; Pandur, T.; Szita, I.; Balogh, M.; Molnar, C.; Komaromi, E.; Lovasz, B.D.; Mandel, M.; et al. Is Early Limited Surgery Associated with a More Benign Disease Course in Crohn’s Disease? World J. Gastroenterol. 2013, 19, 7701–7710.
43. Li, Y.; Stocchi, L.; Shen, B.; Liu, X.; Remzi, F.H. Salvage Surgery after Failure of Endoscopic Balloon Dilatation versus Surgery First for Ileocolonic Anastomotic Stricture Due to Recurrent Crohn’s Disease. Br. J. Surg. 2015, 102, 1418–1425.
44. Lan, N.; Stocchi, L.; Ashburn, J.H.; Hull, T.L.; Steele, S.R.; Delaney, C.P.; Shen, B. Outcomes of Endoscopic Balloon Dilation vs Surgical Resection for Primary Ileocolic Strictures in Patients With Crohn’s Disease. Clin. Gastroenterol. Hepatol. 2018, 16, 1260–1267.
45. Ozuner, G.; Fazio, V.W.; Lavery, I.C.; Milsom, J.W.; Strong, S.A. Reoperative Rates for Crohn’s Disease Following Strictureplasty. Long-Term Analysis. Dis. Colon. Rectum 1996, 39, 1199–1203.
46. Bellolio, F.; Cohen, Z.; Macrae, H.M.; O’connor, B.I.; Victor, J.C.; Huang, H.; McLeod, R.S. Strictureplasty in Selected Crohn’s Disease Patients Results in Acceptable Long-Term Outcome. Dis. Colon. Rectum 2012, 55, 864–869.
47. Strong, S.A. Strictureplasty in complex Crohn’s disease: Beyond the basics. Clin. Colon Rectal Surg. 2019, 32, 243–248.
48. Broering, D.; Eisenberger, C.; Koch, A.; Bloechle, C.; Knoefel, W.; Dürig, M.; Raedler, A.; Izbicki, J. Strictureplasty for Large Bowel Stenosis in Crohn’s Disease: Quality of Life after Surgical Therapy. Int. J. Color. Dis. 2001, 16, 81–87.
49. Yamamoto, T.; Fazio, V.W.; Tekkis, P.P. Safety and Efficacy of Strictureplasty for Crohn’s Disease: A Systematic Review and Meta-Analysis. Dis. Colon. Rectum 2007, 50, 1968–1986.
50. Campbell, L.; Ambe, R.; Weaver, J.; Marcus, S.M.; Cagir, B. Comparison of Conventional and Nonconventional Strictureplasties in Crohn’s Disease: A Systematic Review and Meta-Analysis.

Dis. Colon. Rectum 2012, 55, 714–726.

51. Dietz, D.W.; Laureti, S.; A Strong, S.; Hull, T.L.; Church, J.; Remzi, F.H.; Lavery, I.C.; Fazio, V.W. Safety and Longterm Efficacy of Strictureplasty in 314 Patients with Obstructing Small Bowel Crohn’s Disease. J. Am. Coll. Surg. 2001, 192, 330–337.
52. Geltzeiler, C.B.; Hart, K.D.; Lu, K.C.; DeVeney, K.E.; Herzig, D.O.; Tsikitis, V.L. Trends in the Surgical Management of Crohn’s Disease. J. Gastrointest. Surg. 2015, 19, 1862–1868.