

A global consensus on the definitions, diagnosis and management of fibrostenosing small bowel Crohn's disease in clinical practice

A list of authors and their affiliations appears at the end of the paper

Abstract

Fibrostenosis of the small bowel is common in patients with Crohn's disease. No consensus recommendations on definition, diagnosis and management in clinical practice are currently available. In this Consensus Statement, we present a clinical practice RAND/UCLA appropriateness study on the definition, diagnosis and clinical management of fibrostenosing Crohn's disease. It was conducted by a panel of 28 global experts and one patient representative. Following a systematic literature review, 526 candidate items grouped into 136 questions were generated and subsequently evaluated for appropriateness. Strictures are best defined as wall thickening, luminal narrowing and prestenotic dilation. Cross-sectional imaging is required for accurate diagnosis of fibrostenosing Crohn's disease, and it is recommended before making treatment decisions. It should also assess the degree of inflammation in the bowel wall. Multiple options for medical anti-inflammatory, endoscopic and surgical therapies were suggested, including follow-up strategies following therapy. This Consensus Statement supports clinical practice through providing guidance on definitions, diagnosis and therapeutic management of patients with fibrostenosing small bowel Crohn's disease.

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Consensus statement

Introduction

Crohn's disease is a chronic progressive disease of the gastrointestinal tract¹. It is estimated that >50% of patients with Crohn's disease develop clinically apparent fibrostenosing lesions in their lifetime², most frequently in the terminal ileum³. Before treatment selection, early and accurate detection and characterization of fibrostenosing lesions is vital. The diagnostic yield of clinical assessment is hampered by limited sensitivity and specificity of symptoms for the presence and characteristics of fibrostenosing lesions. Furthermore, no rigorous approach to patient-reported outcomes for fibrostenosis is available. The accuracy of cross-sectional imaging techniques including intestinal ultrasonography (IUS), CT and MRI is high for detection of stenosis, but is not accurate enough for distinguishing fibrosis from inflammation⁴. There are substantial limitations of data interpretation owing to heterogeneity in definitions and approaches. Although only a limited number of controlled studies are available, it seems that anti-inflammatory therapy does not provide long-term treatment benefit in patients with fibrostenosing Crohn's disease⁵. Hence, endoscopic interventions and surgery are the main long-term therapeutic approaches for fibrostenosing Crohn's disease^{6,7}. However, endoscopic and surgical interventions to treat fibrostenosing Crohn's disease strictures are not standardized^{7,8}. Despite substantial advances in our understanding of intestinal fibrogenesis⁹, no anti-fibrotic drugs specifically for intestinal fibrostenosis are currently available^{10,11}.

Given that the current overall level of evidence to support clinical decisions in patients with fibrostenosing Crohn's disease is inadequate, providing all available evidence to expert panels and utilizing consensus methodology to generate recommendations that can be implemented in clinical practice is a reasonable proposition. Following multiple systematic reviews^{4,5,7,12,13}, we assembled a global, multidisciplinary panel of 28 experts and one patient representative and conducted a two-round appropriateness study using modified RAND/UCLA methodology¹⁴. We generated statements to guide definitions, diagnosis and clinical management of patients with fibrostenosing Crohn's disease of the distal small bowel, with the aim of standardizing routine clinical practice.

Methods

Systematic literature review

Multiple systematic reviews covering topics related to fibrostenosis have been performed^{4,5,7,12,13,15–17}. These systematic reviews formed the basis of this project (Supplementary Box 1).

Consensus process

A total of 28 experienced gastroenterologists, interventional endoscopists, abdominal radiologists, histopathologists and colorectal surgeons from North America, Asia and Europe were chosen to participate. In addition, a patient representative, located in North America, was included. Panellists were selected based on publication record, international reputation in diagnosis or treatment of stricturing Crohn's disease, and experience in the development and validation of evaluative scoring systems, and also taking into consideration diversity in gender and regional distribution. After reviewing a list of eligible experts, the final group of participants was selected by D.B. and F.R. This project was hosted under the umbrella of the Stenosis Therapy and Anti-Fibrotic Research (STAR) Consortium, a global investigator group with the mission to develop a pathway to testing anti-stricture therapies in Crohn's disease^{4,12,15}. An abstract reporting the results of the Consensus Statement was presented at the European Crohn's and Colitis Organisation (ECCO) congress in 2023 (ref. 18).

All panellists received the results of the previous systematic reviews^{4,5,7,12,13,15–17}. The evidence base of these systematic reviews were used to inform the generation of statements upon which panellists voted for this Consensus Statement. The distributed literature list can be found in Supplementary Box 1.

A modified RAND/UCLA appropriateness methodology was used to assess the face validity of items identified in the systematic reviews. RAND/UCLA appropriateness methodology employs a modified Delphi panel approach to combine the best available evidence with the experience of relevant experts without requiring consensus^{14,19}. This process is widely accepted, iterative and evidence-based^{20,21}, and the group of authors has substantial experience in conceiving and executing this methodology^{13–15,17}. After reviewing the proposed items during an initial online meeting by all panellists, additional items were introduced into the final item list. The final item list was circulated among all participants, and each statement was individually rated for appropriateness using an online voting system (SurveyMonkey). Following the RAND methodology, the results of the first voting round were statistically analysed and subsequently discussed during a moderated web conference with all panellists. The videoconference was recorded and distributed to the panellists for additional review as needed. Finally, a second voting round was conducted for those items for which agreement was not reached, for items that were categorized as 'uncertain' in the first voting round, and for new or modified items that were introduced after the videoconference call. The final item list can be found in Supplementary Table 1.

Given the interdisciplinary nature of the panel, it was left to the judgement of the participants to not vote on items outside their area of expertise (for example, endoscopic management for a pathologist, or surgical management for a radiologist). To promote patient-centred care, a patient representative was also asked to comment on the items before each voting round and offer feedback. The representative was selected based on personal experience with fibrostenosing Crohn's disease, national reputation for patient advocacy and role as patient adviser of the STAR Consortium.

The authors note that the terms 'stenosis', 'stricture' and 'fibrostenosis' are used interchangeably in the literature and describe the same pathophysiological and clinical process. A stricture or stenosis in the small bowel of patients with Crohn's disease represents the coexistence of inflammation, fibrosis and muscularis propria hyperplasia, among other processes. To reflect its histopathological composition most appropriately, the term fibrostenosis combines fibrosis and inflammation or muscle thickness causing the clinical correlate of stenosis. Although 'stenosis', 'fibrostenosis' and 'stricture' are used interchangeably in the literature, we decided to use the term fibrostenosis throughout the manuscript. This term encompasses the possibility of the coexistence of inflammatory, fibrotic and muscular components²².

Statistical analysis

To assess the level of appropriateness, the medians (30%, 70%) of ratings were calculated. Each survey item was classified as inappropriate, uncertain or appropriate based on the median panel rating and degree of panel disagreement (median 1 to 3 without disagreement considered inappropriate; median 4 to 6 or any median with disagreement considered uncertain; median 7 to 9 without disagreement considered appropriate). To determine the levels of disagreement, the interpercentile range adjusted for symmetry (IPRAS) for each question was calculated²³. If the interpercentile range was greater than IPRAS,

Box 1

Consensus statements on definitions and diagnosis of fibrostenosing Crohn's disease

Statement 1: Symptoms indicative of the presence of fibrostenosing Crohn's disease are cramping, dietary restrictions or changes, vomiting and abdominal pain after eating.

Statement 2: Symptoms are not required to diagnose fibrostenosing Crohn's disease.

Statement 3: In clinical practice, fibrostenosing Crohn's disease cannot be accurately diagnosed by clinical symptoms, physical examination, laboratory investigations, kidney, ureter, bladder plain radiography or endoscopic mucosal biopsies.

Statement 4: In clinical practice, fibrostenosing Crohn's disease can be accurately diagnosed by CT, MRI, intestinal ultrasonography (IUS), endoscopy, intraoperative assessment by the surgeon and full-thickness histopathology.

Statement 5: CT, MRI, IUS or endoscopy are required for the diagnosis of fibrostenosing Crohn's disease.

Statement 6: Fibrostenosing Crohn's disease on CT, MRI or IUS is best defined by luminal narrowing, prestricture dilation and wall thickness.

Statement 7: The inability to pass an adult or paediatric colonoscope is required to diagnose fibrostenosing Crohn's disease.

Statement 8: Cross-sectional imaging using CT, MRI or IUS, as well as endoscopy and mucosal biopsies, may assist in identifying active inflammation in fibrostenosing Crohn's disease.

Statement 9: Currently, no cross-sectional imaging modality is able to accurately determine the degree of fibrosis in fibrostenosing Crohn's disease.

Listed are core statements by the consensus group to define or diagnose naive and anastomotic fibrostenosing Crohn's disease. Detailed information about the quantitative voting results on each candidate item is provided in Supplementary Table 1.

disagreement among the panellists' answers was recorded. Due to different expertise of panellists, some questions were not answered by all 28 panellists, which led to an uneven number of panellists. Analyses were performed using R (version 3.6.2; Vienna, Austria).

Results

Survey development

Voting Round 1 consisted of 474 items. After analysis and the moderated teleconference, 95 items were revised and 52 newly added, leading to a final list of 526 items grouped into 136 questions. The final items and results can be found in Supplementary Table 1.

In clinical practice, the majority of patients with fibrostenosing Crohn's disease have clinical symptoms²⁴, while up to 20% remain asymptomatic²⁵. In addition to cross-sectional imaging, endoscopic evaluation of fibrostenosing Crohn's disease can be helpful but might be limited by superficial biopsy samples. Cross-sectional imaging techniques including CT, MRI and IUS are used to assess for the presence and characteristics of fibrostenosing Crohn's disease²⁶. These diagnostic modalities seem to be helpful as they provide a full-thickness evaluation of the bowel wall and potentially of associated complications. However, a systematic review identified a substantial heterogeneity in definitions used in clinical studies⁴. Furthermore, conventional CT, MRI and IUS-based diagnostic approaches do not enable accurate differentiation between predominant inflammatory and fibrotic strictures^{27–29}.

Survey results

Definitions and diagnosis of naive and anastomotic fibrostenosing Crohn's disease. The panel agreed that naive and anastomotic fibrostenosis in patients with Crohn's disease can occur at any time during the disease course, and that fibrostenosing and internal penetrating disease phenotypes can commonly coexist in the same patient.

We felt that diagnostic criteria for naive and anastomotic fibrostenosis are identical (Box 1). Abdominal CT without luminal contrast, CT enterography (CTE), IUS, abdominal MRI without luminal contrast and magnetic resonance enterography (MRE) as well as endoscopy, intraoperative assessment by the surgeon and full-thickness histopathology were considered appropriate for diagnosis of fibrostenosis. MRE achieved the highest score, followed by CTE. Clinical symptoms, physical examination, laboratory investigations, endoscopic mucosal biopsies and abdominal plain radiography were considered inappropriate for diagnosis of fibrostenosis.

Given that multiple imaging techniques, endoscopy, intraoperative assessment by the surgeon and full-thickness histopathology were all considered appropriate for diagnosis of fibrostenosis, we then explored which modalities are required for the diagnosis of fibrostenosing Crohn's disease. The panel considered CTE, endoscopy, IUS or MRE (but not full-thickness histopathology) to be required for the diagnosis of fibrostenosing Crohn's disease (Fig. 1a; Supplementary Table 1), with MRE and CTE gaining the highest scores.

We voted that the presence of the following cross-sectional imaging features on CT or MRI (with use of enteric contrast medium, MRE) or IUS (without enteric contrast medium) best defines naive or anastomotic fibrostenosing Crohn's disease: the combination of "luminal narrowing, prestricture dilation and wall thickness" (highest appropriateness score), the combination of "prestricture dilation and luminal narrowing", the combination of "prestricture dilation and wall thickness" or "prestricture dilation" alone. Notably, exactly the same items or combination of items were considered optimal to diagnose fibrostenosing Crohn's disease on cross-sectional imaging (Fig. 1b, Supplementary Table 1).

For endoscopic definition of fibrostenosing Crohn's disease, the inability to pass an adult or paediatric colonoscope with a reasonable amount of pressure was considered appropriate. Visual luminal

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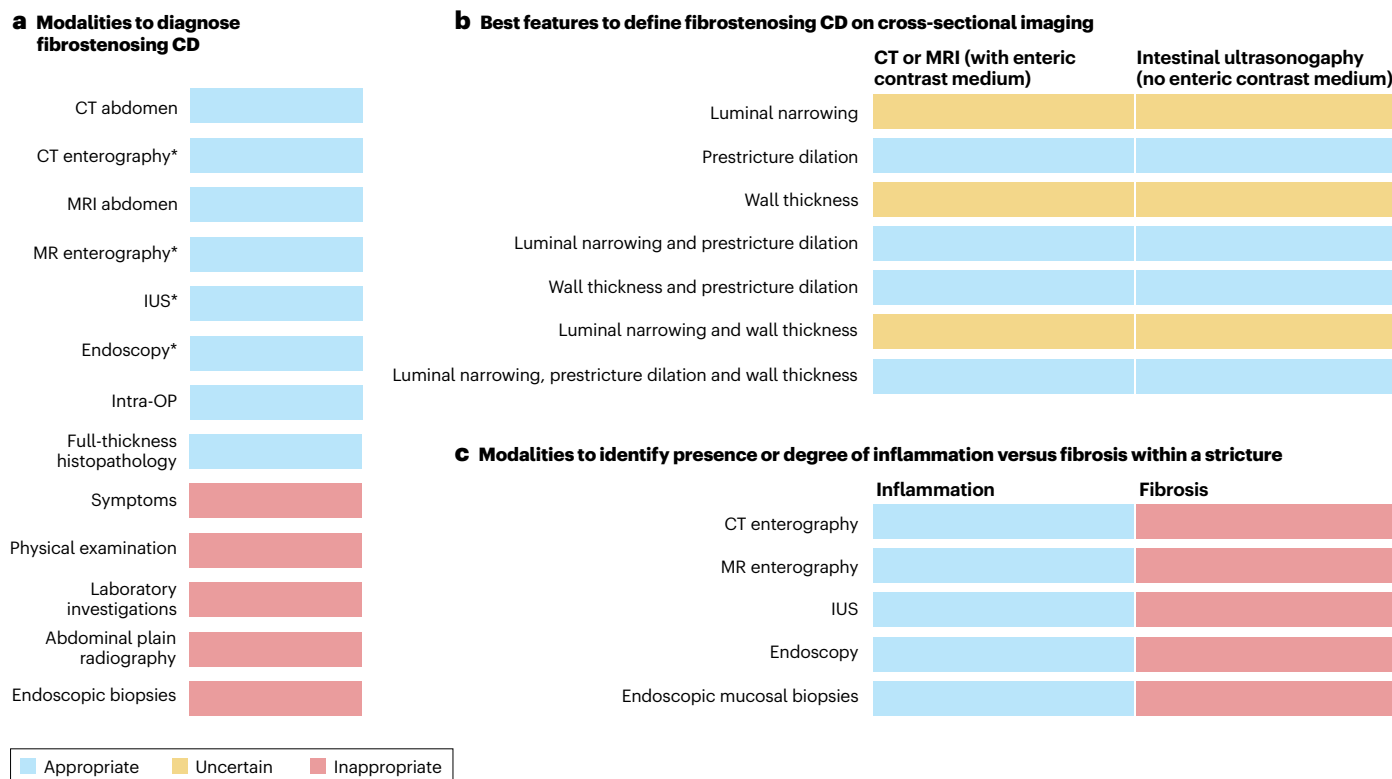


Fig. 1 | Diagnosis, definitions and differentiation of fibrostenosing Crohn's disease in clinical practice. **a**, Modalities that were considered appropriate (blue) or inappropriate (red) by the panel to diagnose fibrostenosis. **b**, Best features to define fibrostenosing Crohn's disease (CD) on cross-sectional imaging. Each survey item was classified as inappropriate (red), uncertain (yellow) or appropriate (blue) based on the median panel rating and degree of panel disagreement (median 1 to 3 without disagreement considered inappropriate; median 4 to 6 or any median with disagreement considered uncertain; median 7 to 9 without disagreement considered appropriate; the results of the individual appropriateness voting on the best features and their

combinations for naive and anastomotic fibrostenosing CD are provided in Supplementary Table 1). **c**, Modalities to differentiate inflammation from fibrosis in fibrostenosing CD. While several diagnostic modalities were considered appropriate (blue) for identifying active inflammation, no cross-sectional imaging modality is currently available to accurately determine the degree of fibrosis (red) in fibrostenosing CD (results of the individual appropriateness voting on modalities to differentiate inflammation from fibrosis in fibrostenosing CD are provided in Supplementary Table 1). IUS, intestinal ultrasonography; MR, magnetic resonance; OP, operative. *Any of these required for diagnosis of fibrostenosing CD.

narrowing was considered uncertain to endoscopically define naive fibrostenosis but appropriate to define anastomotic fibrostenosis. We recommend that the inability to pass an adult or paediatric colonoscope or cross-sectional imaging features, but not symptoms, are required to diagnose fibrostenosing Crohn's disease.

Symptoms considered to be indicative of fibrostenosing Crohn's disease were abdominal distension (only in naive fibrostenosis), cramping, dietary restrictions or changes, vomiting, abdominal pain after eating and the duration of postprandial abdominal pain.

Fibrostenosis commonly comprises a mix of inflammation and fibrosis in varying degrees in symptomatic and asymptomatic fibrostenosis. We voted that CT, IUS, MRI as well as endoscopy and endoscopic mucosal biopsy samples can help identify the inflammatory component within fibrostenosis, with cross-sectional imaging and endoscopy achieving the highest scores. However, currently no cross-sectional imaging modality, endoscopy or endoscopic biopsies or biomarkers were found to be appropriate to accurately determine the presence or degree of fibrosis (Fig. 1c; Supplementary Table 1).

Importantly, we recommend that cross-sectional imaging is required before any treatment decision in naive and anastomotic Crohn's disease fibrostenosis.

Therapy. Given the commonly coexisting inflammatory and fibrostenosing components in patients with stricturing Crohn's disease, initial therapeutic approaches usually aim to reduce the inflammation within fibrostenosing Crohn's disease. However, the published evidence on the therapeutic efficacy of advanced treatment options is still limited, in particular regarding newer biologicals such as ustekinumab and vedolizumab as well as small molecules⁵. Owing to the superior efficacy of combined therapies in purely inflammatory Crohn's disease³⁰, one might speculate as to whether combination therapies might similarly increase the therapeutic efficacy in patients with fibrostenosing Crohn's disease. In addition, balancing clinical treatment decisions between medical and interventional (endoscopic or surgical) approaches can be challenging and is not sufficiently studied in clinical trials so far. Although endoscopic balloon dilation is an established treatment option in selected patients with fibrostenosing Crohn's

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disease, a substantial heterogeneity in terms of practical performance parameters has been reported⁸. Research gaps include knowledge of the optimal balloon diameter and duration of insufflation, timing of follow-up evaluations and concomitant therapies such as intralesional injection, stricturotomy and stent placement.

Finally, deciding between different surgical procedures might depend on individual characteristics of fibrostenosing lesions as well as on patient-related factors. Importantly, surgical techniques were modified over time, aiming to reduce postoperative Crohn's disease recurrence rates, for instance by performing the Kono-S anastomosis³¹. Likewise, this gives rise to the question of whether a preferred surgical intervention in patients with fibrostenosing Crohn's disease exists and what potential contraindications might exist.

General approach. Although we were unable to come to a conclusion as to whether naive and anastomotic fibrostenosing Crohn's disease should be treated with identical therapeutic approaches, the panel considered hospitalization and treatment by a multidisciplinary team to be appropriate in patients with both naive and anastomotic Crohn's disease with confirmed intestinal obstruction.

Factors that were considered appropriate to determine the further management plan for an individual patient were length and location of fibrostenosis, concomitant inflammation, accompanying features such as abscess, phlegmon and dysplasia, remaining bowel length (in case of previous surgery) and number of fibrostenosing intestinal segments.

We agreed to evaluate the presence of active inflammation in the fibrostenosis before any intervention. For patients with naive or anastomotic fibrostenosing Crohn's disease with a confirmed active inflammatory component, the panel considered anti-inflammatory therapy to be appropriate. We were uncertain whether anti-inflammatory therapy should be considered irrespective of the presence of a discernible inflammatory component.

Medical, endoscopic and surgical therapy for naive and anastomotic fibrostenosing Crohn's disease. Next, we voted on medical treatment options for patients with fibrostenosing Crohn's disease (Box 2). The panel agreed that currently no drug with a proven specific anti-fibrotic effect is available. Hence, medical anti-inflammatory therapies were considered for treatment of fibrostenosis in clinical practice, given that fibrosis and inflammation often coexist in fibrostenosing lesions. We evaluated various clinical scenarios depending on whether the patient had had previous anti-TNF therapy, a naive or anastomotic fibrostenosis as well as symptomatic or asymptomatic fibrostenosis presentation (Fig. 2; Supplementary Table 1). In addition, we queried the role of endoscopic intervention and surgery for each scenario.

In bio-naive patients with naive symptomatic fibrostenosing Crohn's disease, corticosteroids, ustekinumab, anti-TNF agents and immunomodulator plus anti-TNF agent were considered appropriate, with the latter two reaching the highest scores. 5-Aminosalicylic acid (5-ASA), thiopurines, methotrexate and calcineurin inhibitors were

Box 2

Consensus statements on medical treatment of fibrostenosing Crohn's disease

Statement 1: Cross-sectional imaging is required prior to making any treatment decision in naive or anastomotic fibrostenosing Crohn's disease.

Statement 2: Patients with Crohn's disease with a naive or anastomotic fibrostenosing disease phenotype should undergo evaluation to assess for the presence of active inflammation prior to any intervention.

Statement 3: No drug with proven specific intestinal anti-fibrotic effect is available.

Statement 4: Patients with confirmed intestinal obstruction due to naive or anastomotic fibrostenosing Crohn's disease should be hospitalized and treated by a multidisciplinary team.

Statement 5: Anti-inflammatory medical therapy should only be considered if an active inflammatory component was confirmed in a patient with naive or anastomotic fibrostenosing Crohn's disease.

Statement 6: Bio-naive patients with symptomatic naive fibrostenosing Crohn's disease can be treated with corticosteroids, anti-TNF agents with or without immunomodulators, ustekinumab, endoscopic balloon dilation or surgery.

Statement 7: Bio-naive patients with symptomatic anastomotic fibrostenosing Crohn's disease can be treated with corticosteroids, anti-TNF agents with or without immunomodulators, ustekinumab

with or without immunomodulators, endoscopic balloon dilation or surgery.

Statement 8: Bio-naive patients with asymptomatic naive fibrostenosing Crohn's disease can be treated with anti-TNF agents with or without immunomodulators or ustekinumab.

Statement 9: Bio-naive patients with asymptomatic anastomotic fibrostenosing Crohn's disease can be treated with anti-TNF agents with or without immunomodulators or ustekinumab.

Statement 10: In patients with anti-TNF treatment failure, symptomatic naive fibrostenosing Crohn's disease should be treated with ustekinumab, endoscopic balloon dilation or surgery.

Statement 11: In patients with anti-TNF treatment failure, symptomatic anastomotic fibrostenosing Crohn's disease should be treated with corticosteroids, ustekinumab with or without immunomodulator, endoscopic balloon dilation or surgery.

Statement 12: In patients with anti-TNF treatment failure, asymptomatic naive or anastomotic fibrostenosing Crohn's disease should be treated with ustekinumab or endoscopic balloon dilation.

Listed are core statements by the consensus group to treat naive or anastomotic fibrostenosing Crohn's disease. Detailed information about the quantitative results of the voting process is provided in Supplementary Table 1.

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a Patients with naive fibrostenosing CD					<div> <div>Appropriate</div> <div>Uncertain</div> <div>Inappropriate</div> </div>
	Bio-naïve and symptomatic	Bio-naïve and asymptomatic	Anti-TNF-experienced and symptomatic	Anti-TNF-experienced and asymptomatic	
5-ASA	1.0 (1.0, 1.0)	1.0 (1.0, 2.0)	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	
Corticosteroids	7.5 (6.8, 8.0)	2.0 (1.7, 4.0)	5.0 (2.2, 7.0)	3.0 (1.0, 4.3)	
Thiopurines	2.0 (2.0, 3.0)	3.0 (2.0, 4.0)	2.5 (2.0, 6.0)	2.5 (2.0, 5.0)	
Anti-TNF agents	8.0 (6.6, 8.0)	7.5 (7.0, 9.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	
Immunomodulators and anti-TNF agent	7.5 (5.0, 8.0)	8.0 (5.7, 8.3)	3.0 (2.0, 4.3)	3.5 (2.0, 5.0)	
Vedolizumab	4.0 (3.7, 6.0)	5.0 (4.0, 6.3)	3.0 (2.0, 5.0)	3.0 (2.0, 5.0)	
Immunomodulator and vedolizumab	4.0 (3.7, 6.0)	5.0 (4.0, 6.3)	4.0 (3.0, 5.0)	4.0 (2.0, 5.0)	
Ustekinumab	6.5 (6.0, 7.9)	6.5 (5.0, 8.0)	7.0 (6.0, 8.0)	7.0 (5.3, 8.0)	
Immunomodulator and ustekinumab	5.0 (4.0, 6.3)	5.5 (4.0, 7.0)	6.0 (3.7, 8.0)	5.5 (4.0, 8.0)	
Methotrexate	2.0 (2.0, 3.0)	3.0 (2.7, 4.0)	3.0 (2.0, 5.0)	3.0 (1.0, 3.3)	
Calcineurin inhibitors	2.0 (1.3, 4.0)	2.0 (2.3)	2.0 (1.3, 2.0)	2.0 (1.0, 2.0)	
Endoscopic balloon dilation	8.0 (7.7, 8.3)	5.5 (4.0, 7.0)	8.0 (7.7, 9.0)	7.0 (5.4, 8.0)	
Surgery	7.0 (7.0, 8.0)	4.5 (3.7, 6.0)	8.0 (8.0, 9.0)	0.0 (0.0, 0.0)	

b Patients with anastomotic fibrostenosing CD					<div> <div>Appropriate</div> <div>Uncertain</div> <div>Inappropriate</div> </div>
	Bio-naïve and symptomatic	Bio-naïve and asymptomatic	Anti-TNF-experienced and symptomatic	Anti-TNF-experienced and asymptomatic	
5-ASA	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	
Corticosteroids	8.0 (6.3, 9.0)	2.5 (1.0, 5.0)	7.0 (4.3, 8.7)	2.0 (1.0, 5.0)	
Thiopurines	3.0 (2.0, 4.0)	3.0 (2.0, 4.7)	2.5 (2.0, 4.7)	3.0 (2.0, 5.0)	
Anti-TNF agents	8.0 (6.6, 9.0)	7.5 (6.0, 8.7)	2.0 (1.3, 3.7)	3.0 (1.0, 4.0)	
Immunomodulators and anti-TNF agent	8.0 (5.7, 8.0)	7.0 (5.7, 8.0)	3.5 (1.7, 5.0)	3.0 (1.7, 4.0)	
Vedolizumab	5.0 (3.7, 6.0)	5.0 (3.7, 6.3)	4.0 (1.7, 5.3)	3.0 (2.0, 5.3)	
Immunomodulator and vedolizumab	5.0 (3.0, 6.0)	5.0 (3.0, 6.3)	3.5 (2.0, 5.3)	3.5 (1.7, 5.3)	
Ustekinumab	7.0 (6.0, 8.0)	7.0 (5.0, 8.0)	7.0 (5.3, 8.0)	7.0 (5.0, 8.0)	
Immunomodulator and ustekinumab	6.5 (4.4, 7.3)	5.5 (4.4, 7.0)	6.5 (4.1, 8.0)	7.0 (3.7, 8.0)	
Methotrexate	3.0 (2.0, 4.7)	2.5 (2.0, 5.0)	3.0 (1.0, 3.0)	3.0 (2.0, 5.0)	
Calcineurin inhibitors	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	
Endoscopic balloon dilation	8.0 (8.0, 9.0)	6.0 (5.0, 8.0)	8.0 (8.0, 9.0)	7.0 (5.7, 8.0)	
Surgery	8.0 (8.0, 8.0)	4.0 (2.0, 5.3)	8.0 (8.0, 8.0)	5.0 (2.7, 5.3)	

Fig. 2 | Rating of appropriateness of medical treatment options for fibrostenosing Crohn's disease. Patients with naive (part **a**) and anastomotic (part **b**) fibrostenosing Crohn's disease (CD). The level of appropriateness is reflected by the medians (30%, 70%) of the ratings. Each survey item was classified as inappropriate (red), uncertain (yellow) or appropriate (blue) based on the median panel rating and degree of panel disagreement (median 1 to 3

without disagreement considered inappropriate; median 4 to 6 or any median with disagreement considered uncertain; median 7 to 9 without disagreement considered appropriate; the results of the individual appropriateness voting on medical treatment options for fibrostenosing CD are provided in Supplementary Table 1). 5-ASA, 5-aminosalicylic acid. Adapted with permission from ref. 18, ECCO.

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considered inappropriate. We were uncertain about vedolizumab, immunomodulator plus vedolizumab and immunomodulator plus ustekinumab. Endoscopic balloon dilation and surgery were also considered appropriate.

In bio-naïve patients with naïve asymptomatic fibrostenosing Crohn's disease, ustekinumab, anti-TNF agents and immunomodulator plus anti-TNF agent were considered appropriate. 5-ASA, corticosteroids, thiopurines, methotrexate and calcineurin inhibitors were considered inappropriate. We were uncertain about vedolizumab, vedolizumab plus immunomodulator, ustekinumab plus immunomodulator, endoscopic balloon dilation and surgery in this treatment scenario.

In patients with naïve symptomatic fibrostenosing Crohn's disease and anti-TNF failure, ustekinumab, endoscopic balloon dilation and surgery were considered appropriate. 5-ASA, thiopurines, anti-TNF agents, anti-TNF agent plus immunomodulator, vedolizumab, methotrexate and calcineurin inhibitors were considered inappropriate. We were unable to come to a conclusion regarding corticosteroids, immunomodulator plus vedolizumab and immunomodulator plus ustekinumab.

In patients with naïve asymptomatic fibrostenosing Crohn's disease and anti-TNF failure, ustekinumab and endoscopic balloon dilation were considered appropriate. 5-ASA, corticosteroids, thiopurines, anti-TNF agents, vedolizumab, methotrexate and calcineurin inhibitors were considered inappropriate. We were uncertain about immunomodulator plus anti-TNF agent, immunomodulator plus vedolizumab, immunomodulator plus ustekinumab and surgery.

In bio-naïve patients with anastomotic symptomatic fibrostenosing Crohn's disease, corticosteroids, ustekinumab, anti-TNF agents, immunomodulator plus anti-TNF agent and immunomodulator plus ustekinumab were considered appropriate, with the latter two reaching the highest scores. 5-ASA, thiopurines, methotrexate and calcineurin inhibitors were considered inappropriate. We were uncertain about thiopurines, vedolizumab and vedolizumab plus immunomodulator. Endoscopic balloon dilation and surgery were also considered appropriate.

In bio-naïve patients with anastomotic asymptomatic fibrostenosing Crohn's disease, ustekinumab, anti-TNF agents and immunomodulator plus anti-TNF agent were considered appropriate. 5-ASA, corticosteroids, thiopurines, methotrexate and calcineurin inhibitors were considered inappropriate. We were uncertain about vedolizumab, vedolizumab plus immunomodulator, ustekinumab plus immunomodulator, endoscopic balloon dilation and surgery in this treatment scenario.

In patients with anastomotic symptomatic fibrostenosing Crohn's disease and anti-TNF failure, corticosteroids, ustekinumab, immunomodulator plus ustekinumab, endoscopic balloon dilation and surgery were considered appropriate. 5-ASA, thiopurines, methotrexate, calcineurin inhibitors and anti-TNF agents were considered inappropriate. We were uncertain about vedolizumab, immunomodulator plus vedolizumab and immunomodulator plus anti-TNF agent.

In patients with anastomotic asymptomatic fibrostenosing Crohn's disease and anti-TNF failure, ustekinumab and endoscopic balloon dilation were considered appropriate. 5-ASA, corticosteroids, thiopurines, methotrexate, anti-TNF agents, immunomodulator plus anti-TNF agent, vedolizumab and calcineurin inhibitors were considered inappropriate. We were uncertain about immunomodulator plus vedolizumab, immunomodulator plus ustekinumab and surgery (Fig. 2b; Supplementary Table 1).

Interventional endoscopic therapy for fibrostenosing Crohn's disease. We considered it appropriate that cross-sectional imaging (MRI, CT or IUS) should be performed in patients with naïve and anastomotic fibrostenosing Crohn's disease before any endoscopic intervention.

For short (<5 cm) naïve or anastomotic fibrostenosis, endoscopic balloon dilation and intestinal resection were considered appropriate (Box 3). Strictureplasty was considered appropriate for naïve, but uncertain for anastomotic fibrostenosis. Endoscopic stricturotomy was voted uncertain for both naïve and anastomotic fibrostenosis. For the maximum length of naïve or anastomotic fibrostenosing Crohn's disease that should be treated by endoscopic dilation, 5 cm was considered to be appropriate and fibrostenosing Crohn's disease of >5 cm should not be treated by endoscopic dilation or endoscopic stricturotomy, according to the panel. Strictureplasty and intestinal resection were both considered appropriate treatment approaches for long (>5 cm) fibrostenosing Crohn's disease.

We recommend endoscopic dilation using antegrade deployment of the balloon (not passing the fibrostenosis first but pushing the deflated balloon through the fibrostenosing lumen in an antegrade fashion before inflation) as the preferred technical approach. A recommended time of balloon insufflation during endoscopic dilation of 60–90 s was considered appropriate. The diameter of the luminal orifice of the fibrostenosis was considered appropriate to influence the choice of the initial balloon diameter for dilation. The severity of mucosal inflammatory alteration within the fibrostenosis was voted appropriate for naïve, but uncertain for anastomotic, fibrostenosis to influence the choice of the initial balloon diameter for dilation. A maximum of three steps for graduated dilation was considered appropriate during one procedure. At the end of dilation therapy, we recommend that 15–18 mm is the most adequate maximum balloon diameter (which might include several procedures in the same patient).

After clinically successful dilation therapy, the panel was uncertain about a predetermined time frame for re-dilation based on the endoscopic or cross-sectional imaging appearance of the fibrostenosis. Instead, we recommend determining the timing of re-dilation on the basis of clinical symptoms or the endoscopic appearance of the fibrostenosis and cross-sectional imaging appearance of the fibrostenosis at the time of dilation, with clinical symptoms and cross-sectional appearance of the stricture considered to be the most appropriate factors. We considered it inappropriate that after clinically successful dilation therapy only those patients with recurrent obstructive symptoms should receive another dilation therapy. Medical anti-inflammatory therapy should be escalated after dilation if active inflammation is visible within the fibrostenosis at the time of dilation.

We recommend that endoscopic dilation therapy of fibrostenosing Crohn's disease is contraindicated in the presence of deep ulcers, malignant alterations within the fibrostenosis or associated penetrating complications. The presence of mucosal erythema, erosions, superficial ulcers within the fibrostenosis or significant prestenotic dilation, however, was not seen as a contraindication to dilation. We determined that in appropriate patients, endoscopic balloon dilation has a high technical success rate, a favourable short-term clinical efficacy, and an acceptable complication rate. We were uncertain about the favourable long-term clinical efficacy in naïve fibrostenosis, but considered that dilation of anastomotic fibrostenosis has a high long-term clinical efficacy (Box 4, Supplementary Table 1).

Fluoroscopic guidance is suggested for patients with complex fibrostenosis or angulated, long or multiple fibrostenoses who undergo endoscopic interventions. Serial dilation of recurrent

Box 3

Consensus statements on endoscopic treatment of fibrostenosing Crohn's disease

Statement 1: Cross-sectional imaging (CT, MRI or intestinal ultrasonography) should be performed before any endoscopic intervention in a patient with naive or anastomotic fibrostenosing Crohn's disease.

Statement 2: A reasonable treatment approach for short (<5 cm) naive fibrostenosing Crohn's disease is endoscopic balloon dilation, strictureplasty and intestinal resection.

Statement 3: A reasonable treatment approach for short (<5 cm) anastomotic fibrostenosing Crohn's disease is endoscopic balloon dilation and intestinal resection.

Statement 4: A reasonable treatment approach for long (>5 cm) naive fibrostenosing Crohn's disease is strictureplasty and intestinal resection.

Statement 5: Endoscopic dilation therapy in naive or anastomotic fibrostenosing Crohn's disease is contraindicated in the presence of deep ulcers within the stricture, associated penetrating complications or malignant alterations associated with the stricture.

Statement 6: Naive or anastomotic fibrostenosing Crohn's disease longer than 5 cm should not be treated by endoscopic dilation therapy.

Statement 7: For patients with naive or anastomotic fibrostenosing Crohn's disease, endoscopic dilation using antegrade deployment of the through-the-scope balloon (not passing the stricture first, but pushing the deflated balloon through the stricture lumen in an antegrade fashion prior to inflation) is the preferred technical approach.

Statement 8: The recommended time of balloon insufflation during endoscopic dilation of naive or anastomotic fibrostenosing Crohn's disease is 60–90 s.

Statement 9: The most adequate maximum balloon diameter at the end of the endoscopic dilation therapy of naive or anastomotic fibrostenosing Crohn's disease is 15–18 mm.

Statement 10: The recommended maximum number of steps for graduated dilation during one sitting for naive or anastomotic fibrostenosing Crohn's disease is three.

Statement 11: After successful endoscopic dilation therapy of naive fibrostenosing Crohn's disease, the time to re-assessment should

be determined by clinical symptoms, endoscopic appearance of the stricture and cross-sectional imaging appearance of the stricture.

Statement 12: After successful endoscopic dilation therapy of anastomotic fibrostenosing Crohn's disease, the time to re-assessment should be determined by clinical symptoms and cross-sectional imaging appearance of the stricture.

Statement 14: In patients with naive or anastomotic fibrostenosing Crohn's disease, medical anti-inflammatory therapy should be escalated after dilation if active inflammation is visible within the stricture at the time of dilation.

Statement 15: In appropriate patients with naive fibrostenosing Crohn's disease, endoscopic balloon dilation has a high technical success rate, a favourable short-term clinical efficacy and an acceptable complication rate.

Statement 16: In appropriate patients with anastomotic fibrostenosing Crohn's disease, endoscopic balloon dilation has a high technical success rate, a favourable long-term clinical efficacy and an acceptable complication rate.

Statement 17: Serial dilation of recurrent naive or anastomotic fibrostenosing Crohn's disease is efficacious and feasible.

Statement 18: The choice between surgery and repeated dilation in patients with naive or anastomotic fibrostenosing Crohn's disease should be made based on technical feasibility, symptom-free interval, patient preferences, remaining bowel length, length of fibrostenosing Crohn's disease, presence of inflammation at the site of the stricture and the location within the gastrointestinal tract.

Statement 19: In routine clinical practice, it is not recommended to treat naive or anastomotic fibrostenosing Crohn's disease with bare metal stents, anchored stents, removable stents, biodegradable stents or cutting techniques (for example, needle knife).

Listed are core statements by the consensus group for endoscopic treatment of naive and anastomotic fibrostenosing Crohn's disease. Detailed information about the quantitative results of the voting process is provided in Supplementary Table 1.

fibrostenosing Crohn's disease is efficacious and feasible. We recommend that after prior dilation, the choice between surgery and repeated endoscopic dilation should be made based on technical feasibility, symptom-free interval, patient preferences, remaining bowel length, length of fibrostenosing Crohn's disease, presence of inflammation at the site of the fibrostenosis, location within the gastrointestinal tract and concomitant features such as dysplasia, malignancy or internal penetrating disease. In case of successful endoscopic dilation therapy, we do not recommend injection of corticosteroids or anti-TNF agents intralesionally. It was also considered inappropriate to place a stent or use cutting techniques, such as with a needle knife.

Surgical therapy of naive and anastomotic fibrostenosing Crohn's disease. We felt that strictureplasty should be the preferred option if fibrostenosing Crohn's disease is not accessible to endoscopy for anastomotic fibrostenosis, but considered this to be uncertain for naive fibrostenosis (Box 5). Moreover, we do not recommend strictureplasty as the preferred treatment option for naive and anastomotic fibrostenosing Crohn's disease with associated internal penetrating disease, abscesses, phlegmon, dysplasia or malignancy. The decision to perform strictureplasty in patients with naive and anastomotic fibrostenosing Crohn's disease should be based on the length of fibrostenosis, presence of multiple fibrostenoses, history of intestinal resection and length of remaining bowel. Likewise, the decision for type of

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strictureplasty (for example, Heineke–Mikulicz, Finney, isoperistaltic) in patients with fibrostenosing Crohn's disease should be based on these four features.

We recommend that intestinal resection should be the preferred option for naive and anastomotic fibrostenosing Crohn's disease with associated abscesses, phlegmon, internal penetrating disease, dysplasia, malignancy and for long-segment fibrostenosis. In contrast, intestinal resection was voted inappropriate in patients with fibrostenosing Crohn's disease and limited length of the remaining bowel. The panel was uncertain whether Kono-S anastomosis should be regarded as the preferred option in case of intestinal resection for both naive and anastomotic fibrostenosing Crohn's disease.

We considered the laparoscopic approach to be preferable to open surgery due to superior recovery, better cosmesis, fewer adhesions and incisional hernias, and similar surgical recurrence rates. After successful surgical fibrostenosis resection, we recommend a structured follow-up strategy, which should include evaluation of obstructive symptoms, endoscopic evaluation, and cross-sectional imaging. Finally, we recommend that after successful surgical resection of fibrostenosing Crohn's disease, the choice of anti-inflammatory therapy after surgery should depend on a thorough risk factor assessment.

Discussion

This global Consensus Statement, based on RAND/UCLA methodology, determined definitions, diagnosis and management of fibrostenosing Crohn's disease for use in clinical practice. Cross-sectional imaging including MRI and CT with or without enteric contrast medium or IUS (without contrast medium) was considered appropriate to diagnose naive and anastomotic fibrostenosing Crohn's disease, whereas clinical symptoms, physical examination and laboratory testing were not considered appropriate. The combination of the imaging features luminal narrowing, wall thickening and prestricture dilation, or the presence of prestenotic dilation with either luminal narrowing or wall thickness, were considered to be optimal to define fibrostenosis. In case of signs of active inflammation, anti-inflammatory therapy is the next step in management. The panel devised detailed recommendations for the type of anti-inflammatory therapy depending on prior anti-TNF exposure, naive or anastomotic fibrostenosis and the presence or absence of symptoms. Regarding interventional therapy, panellists deemed endoscopic balloon dilation to be appropriate for fibrostenosing Crohn's disease no longer than 5 cm, whereas strictureplasty and intestinal resection were both considered reasonable treatment approaches for long (>5 cm) fibrostenosing Crohn's disease.

According to the CONSTRUCT definitions¹⁷, clinical symptoms such as acute abdominal distension, cramping, dietary restrictions, nausea, vomiting, abdominal pain and postprandial abdominal pain can be indicative of fibrostenosing Crohn's disease. However, clinical symptoms are not strongly correlated with the presence of small bowel fibrostenosing Crohn's disease on cross-sectional imaging and can vary in their severity. Therefore, clinical symptoms were considered inappropriate for diagnosis of fibrostenosis by the panel. In clinical practice, the degree of symptoms should be carefully evaluated by an interdisciplinary care team followed by shared decision-making with the patient to decide on hospitalization and the treatment approach.

Cross-sectional imaging techniques such as CT, IUS and MRI are valuable modalities to assess fibrostenosing Crohn's disease given their ability to enable a full-thickness evaluation of the bowel wall and their potential to detect associated complications²². In contrast, the sensitivity of small-bowel follow-through for detection of extra-enteric

complications in fibrostenosing Crohn's disease is substantially lower³², and its use was widely replaced by CT, IUS or MRI. Its use might be reserved for assessing the temporal dynamics of contrast medium passage through a known stenosis with no extra-enteric complications. Commonly applied imaging features to assess fibrostenosing Crohn's disease are luminal narrowing, wall thickening and prestricture dilation. These three features are equally assessed on MRI, CT and IUS. However, there is substantial heterogeneity in published studies regarding the need for one, two or all three features to be present to define fibrostenosing Crohn's disease on cross-sectional imaging⁴. This Consensus Statement confirms that luminal narrowing, wall thickening and prestricture dilation are the three crucial imaging features for detection of fibrostenosing Crohn's disease. Additionally, the highest score of appropriateness for fibrostenosis definition was reached for the combination of all three features. This is important as one can assume that the specificity for fibrostenosis is higher if all three features are present than if each feature is individually present or a combination of two features is present. This might reflect the observation that wall thickness or luminal narrowing can also occur due to active inflammation only³³. This is consistent with the definitions devised by the CONSTRUCT study group for clinical trials in fibrostenosing Crohn's disease¹⁷. For definitions useable in clinical practice, the panel also considered prestenotic dilation with luminal narrowing or wall thickening as an appropriate definition. Although conclusive evidence is missing, the presence of prestenotic dilation was considered by the expert panellists to be a more severe degree of fibrostenosis. Patients with fibrostenosing Crohn's disease with associated small bowel dilation have a shorter time to surgical resection than those without associated small bowel dilation³⁴.

The endoscopic definition of fibrostenosing Crohn's disease (inability to pass an adult or paediatric colonoscope with reasonable amount of pressure applied) would also apply if in exceptional cases an enteroscope were required to access the terminal ileum. This Consensus Statement is intended for the practising clinician and hence

Box 4

Technical parameters for endoscopic balloon dilation

Suggested performance parameters, monitoring strategies and contraindications of endoscopic balloon dilation for small bowel fibrostenosing Crohn's disease:

- Cross-sectional imaging prior to intervention
- Maximal stricture length 5 cm
- Luminal diameter influences initial balloon size
- Balloon insufflation time 60–90 s
- Maximum of three steps for graduated dilation
- 15–18 mm is adequate luminal diameter at end of dilation therapy
- Time to re-assessment after dilation: symptoms, endoscopic appearance, imaging appearance
- Contraindications to dilation: deep ulcers, malignant alterations, associated penetrating complications
- Escalation of anti-inflammatory therapy after dilation in case of active inflammation

Box 5

Consensus statements on surgical treatment of fibrostenosing Crohn's disease

Statement 1: Strictureplasty should be the generally preferred option for anastomotic fibrostenosing Crohn's disease with lack of accessibility via endoscope.

Statement 2: The decision to perform strictureplasty in patients with naive or anastomotic fibrostenosing Crohn's disease should be based on the length of stricture, the presence of multiple strictures, the history of intestinal resection and the length of the remaining bowel.

Statement 3: The decision for type of strictureplasty (Heineke–Mikulicz, Finney, isoperistaltic, etc.) in patients with naive or anastomotic fibrostenosing Crohn's disease should be based on the length of stricture, the presence of multiple strictures, the history of intestinal resection and the length of the remaining bowel.

Statement 4: Intestinal resection should be the generally preferred option for naive fibrostenosing Crohn's disease with associated abscesses, phlegmon, internal penetrating disease, dysplasia, malignancy and long-segment fibrostenosing Crohn's disease.

Statement 5: Intestinal resection should be the generally preferred option for anastomotic fibrostenosing Crohn's disease with associated abscesses, phlegmon, internal penetrating disease,

dysplasia, malignancy, lack of accessibility via endoscope and long-segment fibrostenosing Crohn's disease.

Statement 5: The laparoscopic approach in naive or anastomotic fibrostenosing Crohn's disease is preferable because of superior recovery, better cosmesis, fewer adhesions and incisional hernias, and similar surgical recurrence rates.

Statement 6: After successful surgical stricture resection of naive or anastomotic fibrostenosing Crohn's disease a structured follow-up strategy should include evaluation of obstructive symptoms, endoscopic evaluation and cross-sectional imaging of stricture recurrence.

Statement 7: After successful surgical stricture resection of naive or anastomotic fibrostenosing Crohn's disease the choice of anti-inflammatory therapy after surgery should depend on a thorough risk factor assessment.

Listed are core statements by the consensus group for surgical treatment of naive and anastomotic fibrostenosing Crohn's disease. Detailed information about the quantitative results of the voting process is provided in Supplementary Table 1.

strictures outside the reach of an ileocolonoscopy, requiring an enteroscopy to reach them, were not discussed.

From a clinical point of view, quantification of the fibrotic component in fibrostenosing Crohn's disease would be desirable to guide a treatment decision for or against medical therapy. Fibrostenosis with a high grade of fibrosis can be suitable for interventional therapy, whereas low grades of fibrosis might be treated with anti-inflammatory therapy. However, the panel stated that there is currently no cross-sectional imaging modality that can accurately determine the degree of fibrosis in fibrostenosing Crohn's disease. Novel imaging techniques are fast emerging. Future advances such as magnetization transfer MRI³⁵, diffusion-weighted MRI³⁶ and elastography³⁷ might help overcome this limitation. Nevertheless, any positive finding using these new imaging techniques would need external validation, which to date has not been successfully performed for any of the tested approaches.

One of the most challenging questions of interdisciplinary care of patients with fibrostenosing Crohn's disease is the choice between medical, endoscopic and surgical treatment. Complicating this challenge is the fact that no randomized controlled trials (RCTs) have been performed comparing medical with non-medical therapy or endoscopy with surgery in the fibrostenosis setting, and given the complexities of such trials, high-level evidence might never be generated. In addition, the number of prospective studies of medical therapy of patients with fibrostenosing Crohn's disease is small⁵. The panel considered it appropriate that an anti-inflammatory medical therapy should only be considered if an active inflammatory component was confirmed in a patient with fibrostenosing Crohn's disease. Inflammation is probably present in almost all patients with advanced fibrostenosis, given the

strong correlation between the transmural degree of inflammation and fibrosis in this situation^{38,39}. Anti-TNF therapy in bio-naive patients is the most likely first choice. Its efficacy is supported by the prospective single-arm CREOLE trial⁴⁰. More recently, the efficacy of anti-TNF therapy in fibrostenosis was confirmed in the STRIDENT trial, an open-label prospective RCT, which additionally pointed to the possibility that intensified anti-TNF agent dosing might result in a greater reduction in fibrostenosis-associated inflammation⁴¹. We added the combination of ustekinumab plus immunomodulator to the list of queried medications, because this option might be considered in clinical practice to enhance the efficacy of ustekinumab and is at times used by practising providers in patients who have developed anti-drug antibodies to a previous biologic^{42,43}. Data on novel biologics, such as vedolizumab and ustekinumab, for fibrostenosis, although only available in an abstract³⁸, suggest potential efficacy in this population, but the level of evidence is restricted to studies with a retrospective observational design⁴⁴. Therefore, there is no high-level evidence for the efficacy of second-line biologic therapies in bio-experienced patients with fibrostenosing Crohn's disease. It has to be noted that the choice of therapy in fibrostenosing Crohn's disease should be influenced by additional factors such as comorbidities, extra-intestinal manifestations and regional availability of medications, among others.

Owing to the limited supporting literature, the expert opinion of the panel can aid in decision making in clinical practice (Fig. 2; Supplementary Table 1). Notably, biologic therapy was considered more appropriate in symptomatic than in asymptomatic fibrostenosis, whereas medical therapy options were not considered to be different when assessing naive versus anastomotic fibrostenosis. Furthermore,

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no specific sequences were queried but medical options were presented as equal choices for each of the scenarios. The decision to commence or adjust anti-inflammatory medical therapy should also be influenced by the individual patient disease history and might be considered to maintain remission in patients without evidence of ongoing inflammation.

Notably, endoscopic dilation and surgery were considered appropriate alternative options to medical therapy for most clinical scenarios. This is supported by a large body of observational evidence indicating balloon dilation to be a safe option, with high short-term and long-term efficacy in short (<5 cm) fibrostenosing Crohn's disease accessible to endoscopy⁷. The expert panel provided detailed technical guidance on, for example, graded dilation and dilation times. The recommendation that antegrade dilation is preferred over retrograde dilation, if feasible, might reflect the fact that many strictures cannot be transversed initially. We did not query the distinction between initially passable and non-passable strictures when considering the dilation approach, and a detailed evaluation of this selective scenario might be performed at a later stage. This might also explain the discrepancy with a previous consensus on endoscopic management of fibrostenosing Crohn's disease⁴⁵. Regarding novel techniques such as the use of a needle knife and cutting techniques, future controlled studies with prespecified end points and follow-up evaluations might help identify the appropriate indications for these approaches. The optimal follow-up strategy after successful endoscopic balloon dilation to date is unclear. Hence, an important recommendation of this Consensus Statement is that follow-up should be individualized based on the re-occurrence of obstructive symptoms and the endoscopic and imaging appearance of the fibrostenosis at the time of dilation. Nevertheless, more data are needed to determine the appropriate structure of follow-up examinations.

Obstruction in a patient with Crohn's disease is largely considered a failure of medical treatment, the panel supported intensifying medical therapy after dilation. Only one retrospective observational study has addressed this question in patients with anastomotic Crohn's disease fibrostenosis⁴⁶, suggesting that escalation of patients to anti-TNF combination therapy delays the time to re-dilation. In general, balloon-assisted enteroscopy can be used to diagnose and treat fibrostenosing Crohn's disease of the small bowel with comparable efficacy and safety rates to endoscopic dilation therapy of the distal small bowel¹⁶. However, stricture locations other than the distal small intestine were not evaluated in this Consensus Statement, which was designed for the practising gastroenterologist. If fibrostenosing Crohn's disease is endoscopically not accessible and therapy is warranted, then medical treatment or surgical intervention should be attempted. In 2020, a Delphi-based consensus statement on endoscopic treatment for Crohn's disease strictures was published⁴⁵. The recommendations covered various practical aspects of endoscopic procedures to treat fibrostenosing Crohn's disease, including the management of procedure-associated adverse events, and the outcomes were largely comparable to our panel's opinion. However, the previous consensus statement did not provide guidance regarding the definition and performance of cross-sectional imaging or the choice of medical therapy and surgical procedures, but instead remained focused on endoscopy alone⁴⁵.

Surgical intervention has long been considered an option in patients with Crohn's disease in whom all other therapeutic approaches have failed. This paradigm is changing in luminal disease, with early surgical resection increasingly being considered a possible treatment⁴⁷. This also held true for this RAND/UCLA panel, for which surgery was

considered appropriate next to medical therapy and endoscopic intervention for all scenarios in which fibrostenosis was symptomatic, even in anti-TNF-naïve scenarios. Strictureplasty as a bowel-preserving therapy choice was considered appropriate in the absence of penetrating complications or dysplasia/malignancy. Notably, bowel preservation is key in Crohn's disease, and the potential risk of short bowel syndrome should be considered when treatment decisions are made. Deciding between endoscopic balloon dilation therapy or surgery should also be influenced by the experience of the endoscopist or surgeon.

Conclusions

Taken together, in the absence of prospective RCTs for the management of fibrostenosing Crohn's disease in clinical practice, this Consensus Statement provides clear recommendations on definitions, diagnosis, treatment and long-term management of affected patients based on all available evidence as well as expert opinion. To continue progress in the field of fibrostenosing Crohn's disease, multiple obstacles need to be overcome. There is a need for trials that use novel biologics and other advanced therapies, as well as comparative trials of existing medical therapies, in patients with existing fibrostenosis. Although considered challenging, RCTs comparing medical with surgical approaches could be paradigm-changing. The development of tools that accurately measure fibrostenosis to assess improvement or determine prognosis is critical. For this purpose, the STAR Consortium^{4,11,15} is developing patient-reported outcome tools, as well as an index programme for IUS, CT and MR. The ultimate goal remains the development of selective anti-fibrotic therapies for patients with fibrostenosing Crohn's disease.

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Author contributions

The authors contributed equally to all aspects of the article.

Competing interests

D.B. is on the advisory board or consultant for AbbVie, Amgen, Arena, Atheneum, BNG Service GmbH, Bristol Myers Squibb, CED-Service GmbH, Celltrion, DGVS, Diaplan, Doctorflif, Else Kröner-Fresenius Foundation, Falk Foundation, Galapagos, Guidepoint, Impulze, Ferring, Janssen Cilag, Lilly, Medical Tribune, Med Today, MedTriX, MSD, Mylan, Onkowsissen, Pharmacosmos, Pfizer, Roche, Sandoz, Takeda, Tetrameros, Thieme, Tillotts Pharma, UCB Biopharma, Viatrix and Vifor Pharma. I.D. has served as a speaker, consultant and advisory board member for Takeda, Janssen, AbbVie, Pfizer, Ferring, Roche/Genentech, Celgene/BMS, Falk Pharma, Rafa Laboratories, Neopharm, Nestle, Arena, Gilead, MSD, DSM, Celltrion, Sublimity, Sandoz, Abbott and Athos Therapeutics. R.F. has served as central reader for Alimentiv, received speaker's fees from Janssen Pharmaceuticals and consulting fee from Decibio. M.E.B. receives no direct support. Cleveland Clinic receives support for him from Siemens Healthineers in the form of salary, software and hardware for the investigation of reduced exposure in CT enterography. S.A.T. is a research consultant to Robarts. J.P. received financial support for research from AbbVie and Pfizer; consultancy fees/honorarium from AbbVie, Arena, Athos, Atomwise, Boehringer Ingelheim, Celgene, Celltrion, Ferring, Galapagos, Genentech/Roche, GlaxoSmithKline, Janssen, Mirum, Morphic, Nestlé, Origo, Pandion, Pfizer, Progenity, Protagonist, Revolo, Robarts, Takeda, Theravance and Wasserman; reports payment for lectures including service on speaker's bureau from Abbott, Ferring, Janssen, Pfizer and Takeda; and reports payment for development of educational presentations from Abbott, Janssen, Pfizer, Roche and Takeda. J.R. is on the advisory board or consultant for Alimentiv, Boehringer Ingelheim, Janssen, Origo, Takeda and TiGenix; and received research grants from AbbVie and Genentech. W.B. served as speaker for Johnson & Johnson, Braun and Takeda; and obtained research grants from Braun, VIFOR and Medtronic. A.d'H. has served as speaker for Johnson & Johnson and Takeda. A.D. has received research support or acted as a principal investigator for AbbVie, Arena, Dr. Falk Pharma, Celgene, Gilead, Janssen and Takeda; has acted as a consultant or AbbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Dr. Falk Pharma, Ferring, Fresenius Kabi, Celltrion, Janssen, Lilly, MSD, Pfizer, Pharmacosmos, Roche, Takeda, Tillotts and Vifor; and has participated in speaker's bureaus for AbbVie, Amgen, Falk Foundation, Ferring, Janssen, Lilly, Med Today, Med Update, MSD, Pfizer, Roche, Streamed-up, Takeda, Tillotts and Vifor. W.J.S. reports consulting fees from Abbvie, Abivax, Alfasigma, Alimentiv, Beigene, Biora (Progenity), Celltrion, Forbion, Genentech, Gossamer Biosciences, Index Pharmaceuticals, Prometheus Biosciences, Protagonist Therapeutics, Shoreline Biosciences, Vedanta Biosciences, Ventyx Biosciences and Zealand Pharma; stock or stock options from BeiGene, Gossamer Bio, Biora (Progenity), Prometheus Biosciences, Prometheus Laboratories, Shoreline Biosciences, Ventyx Biosciences, Vimalan Biosciences, Vivreon Gastrosciences; and is an employee at Shoreline Biosciences and Ventyx Biosciences (spouse: Iveric Bio (consultant, stock options); Biora (Progenity) (stock); Prometheus Biosciences (employee, stock, stock options); Prometheus Laboratories (stock, stock options); Ventyx Biosciences (stock, stock options); and Vimalan Biosciences (stock)). S.C.N. served as a speaker for AbbVie, Janssen, Tillotts, Menarini, Ferring, Takeda and Pfizer; and received research funding from Olympus, Janssen and Ferring. C.L. has received consulting fees from AbbVie, Janssen, Takeda, Fresenius Kabi, Ferring, Eli Lilly; speaker's fees from AbbVie, Janssen and Fresenius Kabi. D.H.B. is a consultant for Medtronic and Janssen; and receives research support from Medtronic and Takeda. G.R. is a consultant for Abbott, AbbVie, Augurix, Boehringer, Calypso, FALK, Ferring, Fisher, Genentech, Essex/MSD, Novartis, Pfizer, Phadia, Roche, Takeda, Tillots, UCB, Vifor, Vital Solutions and Zeller; received speaker's honoraria from AstraZeneca, Abbott, AbbVie, FALK, MSD, Phadia, Tillots, UCB and Vifor; and received educational grants and research grants from Abbott, AbbVie, Ardeypharm, Augurix, Calypso, Essex/MSD, FALK, Flamentara, Novartis, Roche, Takeda, Tillots, UCB and Zeller. B.V. Received research support from AbbVie, Biora Therapeutics, Pfizer, Sossei Heptares and Takeda; speaker's fees from Abbvie, Biogen, Bristol Myers Squibb, Celltrion, Chiesi, Falk, Ferring,

Consensus statement

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