

# How Reliable Is Endoscopic Scoring of Postoperative Recurrence in Crohn Disease?

## A Systematic Review and Meta-Analysis

Eline M. L. van der Does de Willebois, MD,\* Vittoria Bellato, MD,† Marjolijn Duijvestein, MD, PhD,‡ Susan van Dieren, MD, PhD,\* Silvio Danese, MD, PhD,† Pierpaolo Sileri, MD, PhD,† Christianne J. Buskens, MD, PhD,\*§ Andrea Vignali, MD, PhD,† and Willem A. Bemelman, MD, PhD\*†§

**Objective:** Guidelines advise to perform endoscopic surveillance following ileocolic resection (ICR) in Crohn disease (CD) for timely diagnosis of recurrence. This study aims to assess the variation in endoscopic recurrence (ER) rates in patients after ICR for CD using the most commonly used classification systems, the Rutgeerts score (RS) and modified Rutgeerts score (mRS) classifications.

**Methods:** A systematic literature search using MEDLINE, Embase, and the Cochrane Library was performed. Randomized controlled trials and cohort studies describing ER < 12 months after an ICR for CD were included. Animal studies, reviews, case reports (<30 included patients), pediatric studies, and letters were excluded. The Newcastle–Ottawa Quality Assessment Scale and Cochrane Collaboration’s tool were used to assess risk of bias. Main outcome was the range of ER rates within 12 months postoperatively, defined as RS ≥ i2 and/or mRS ≥ i2b. A proportional meta-analysis was performed. The final search was performed on January 4, 2022. The study was registered at PROSPERO, CRD42022363208.

**Results:** Seventy-six studies comprising 7751 patients were included. The weighted mean of ER rates in all included studies was 44.0% (95% confidence interval, 43.56–44.43). The overall range was 5.0% to 93.0% [interquartile range (IQR), 29.2–59.0]. The weighted means for RS and mRS were 44.0% and 41.1%, respectively. The variation in ER rates for RS and mRS were 5.0% to 93.0% (IQR, 29.0–59.5) and 19.8% to 62.9% (IQR, 37.3–46.5), respectively. Within studies reporting both RS and mRS, the weighted means for ER were 61.3% and 40.6%, respectively.

**Conclusions:** This study demonstrates a major variation in ER rates after ICR for CD, suggesting a high likelihood of inadequate diagnosis of disease recurrence, with potentially impact on quality of life and health care consumption. Therefore, there is an important need to improve endoscopic scoring of recurrent disease.

**Keywords:** Crohn disease, ileocolic resection, postoperative endoscopic recurrence, (modified) Rutgeerts score

\*From the Department of Surgery, Amsterdam UMC, Location University of Amsterdam, Amsterdam, The Netherlands; †Coloproctology and Inflammatory Bowel Disease Unit, HSR, Milan, Italy; ‡Department of Gastroenterology, Radboud UMC, Nijmegen, The Netherlands; and §Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam, The Netherlands.

The data that support the findings of this study are available from E.M.L.D.W., upon reasonable request.

Disclosures: W.A.B. has received research funding from VIFOR and is a consultant for Braun. M.D. has received speaking and teaching honoraria from Galapagos, Bristol Myers Squibb, and Takeda. She was also member of the advisory committee of Bristol Myers Squibb, Abbvie, and Janssen. C.J.B. has received an unrestricted grant from Boehringer Ingelheim and Roche. She also received consultancy fees and/or speaker’s honoraria from AbbVie, Tillotts, Takeda, and Janssen. The other authors declare that they have nothing to disclose.

**SDC** Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal’s Web site ([www.annalsofsurgery.com](http://www.annalsofsurgery.com)).

Reprints: Willem A. Bemelman, MD, PhD, Department of Surgery, Amsterdam University Medical Centre, Location AMC, PO Box 22660, 1100DD, Amsterdam, The Netherlands. Email: [w.a.bemelman@amsterdamumc.nl](mailto:w.a.bemelman@amsterdamumc.nl).

Copyright © 2024 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Annals of Surgery Open (2024) 1:e397

Received: 5 September 2023; Accepted 12 February 2024

Published online 18 March 2024

DOI: 10.1097/AS9.0000000000000397

## INTRODUCTION

The main localization of enteral Crohn disease (CD) is the terminal ileum. A laparoscopic ileocolic resection (ICR) is indicated in both complicated disease and as an alternative for patients with uncomplicated disease not responding to immune modulators.<sup>1–3</sup> Unfortunately, surgery is not curative, and the majority of the patients develop recurrent disease.<sup>4,5</sup> According to guidelines (ie, European Crohn’s and Colitis Organisation), patients should be assessed by endoscopy at 6 to 12 months postoperatively to diagnose endoscopic recurrence (ER). In case of ER, therapeutic medical therapy is (re)initiated; and if prescribed prophylactically, optimized in order to prevent long-term complicated disease.<sup>3</sup> The guidelines recommend the use of the Rutgeerts classification to assess recurrence severity. Lesions in the category i2–i4 are considered ER.<sup>4,6,7</sup> The classification was modified to discriminate pure anastomotic lesions, which are considered more likely due to postoperative changes (i2a), from the presence of more than 5 aphthous lesions in the neo-terminal ileum, with or without anastomotic lesions (i2b).<sup>8,9</sup> Despite this modification, the reproducibility of the classification is disputed.<sup>10–12</sup> Moreover, the mRS is (yet) not advised in European Crohn’s and Colitis Organisation guidelines.

Adequate endoscopic scoring is important, as it is used to tailor medical therapy and to monitor its effect. Especially in this asymptomatic patient group, where endoscopy is used as postoperative surveillance, a reliable scoring system is of utmost importance. After all, improper diagnosis of recurrent disease results in unnecessary prescribing of medical therapy. This potentially impairs quality of life and increases health care consumption. Moreover, the Rutgeerts classification is used as a

primary outcome in clinical trials. However, the Rutgeerts score was initially neither designed nor validated for this purpose.

For these reasons, the objectives of this study are to assess the variation in ER rates in patients after ICR for CD, using the most common classification systems, the Rutgeerts and/or modified Rutgeerts classifications, and to assess the variation and the difference in ER rates when comparing the original Rutgeerts with the modified Rutgeerts classifications.

## METHODS

The study protocol was prospectively registered at PROSPERO (registration number: CRD42022363208), and the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidance was followed throughout the process.<sup>13</sup> The final search was performed on January 4, 2022.

### Search Strategy

MEDLINE (PubMed), Embase (Ovid), and the Cochrane Library were searched systematically with the assistance of a clinical librarian.

Medical subject headings and free-text terms used included 'Crohn's Disease', 'ileocolic resection', 'ileocecal resection', 'ileo-caecal resection', 'modified Rutgeerts score', 'Rutgeerts score', 'anastomotic ulcer'. There were no restrictions considering the publication date or language in the initial search, and no other methodological filters were applied. Further details of the search terms are provided in Supplemental Table 2, see <http://links.lww.com/AOSO/A297>.

### Study Selection

All studies describing primary ileocecal or ileocolic resection in patients with CD with ER rates were included. ER was defined as Rutgeerts score (RS)  $\geq 2$  or modified Rutgeerts score (mRS)  $\geq 2b$  at 6 to 12 months postoperatively.

Studies not reporting primary ICR or ER defined as RS or mRS within 12 months after surgery were excluded. Animal studies, reviews, case reports, and letters were excluded. Other exclusion criteria were patients aged less than 18 years and less than 30 patients included in the study. In case of overlapping study cohorts, the original study or, if postoperative endoscopic recurrence (POR) was not reported, the study with the most included patients was included.

Two reviewers (E.M.L.D.W., V.B.) separately screened the titles and abstracts of the retrieved articles and independently assessed the full text of the remaining articles. Disagreements concerning the selection were resolved by joint discussion and, when necessary, the opinion of a third researcher (W.A.B.) was obtained. Studies without a retrievable English full text were excluded.

### Outcomes

The primary outcome was the overall variation in ER rates and the interquartile range (IQR) (to correct for outliers) of ER rates defined as RS  $\geq 2$  or mRS  $\geq 2b$  within 1 year after ICR.

Secondary outcomes were (1) the overall range (and IQR) of ER rates defined as RS  $\geq 2$  within 1 year after surgery; (2) the overall range (and IQR) of ER rates defined as mRS  $\geq 2b$  within 1 year after surgery; (3) the overall range (and IQR) of ER according to subcategories (i0, i1, i2a, i2b, i3, and i4); and (4) the difference in ER rates, presented as weighted means, comparing RS and mRS in studies reporting mRS.

### Risk of Bias Assessment

Risk of bias was assessed by 2 reviewers (E.M.L.D.W., V.B.) separately. The methodological quality of cohort studies was assessed

by the Newcastle–Ottawa Quality Assessment Scale. In 3 different domains (selection, comparability, and outcome), stars were assigned, with a total maximum of 9 stars. In the outcome domain, a minimum follow-up period of 12 months and a maximum proportion of 5% of subjects lost to follow-up were considered acceptable. Studies were rated as good, fair, or poor depending on the number of stars, following the Agency for Healthcare Research and Quality standard.<sup>14</sup> For randomized controlled trials, the Cochrane Collaboration's tool for assessing risk of bias was used.<sup>15</sup> This tool focuses on selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias, rated as low, high, or unclear risk (Supplemental Tables 3 and 4, see <http://links.lww.com/AOSO/A297>). Three of the randomized controlled trials were considered high risk. In 2 studies, the primary reason was the lack of blinding of endoscopists to the treatment. In the third study, 56% of patients withdrew before the primary outcome assessment.

### Data Extraction and Statistical Analysis

Study and patient characteristics collected included first author, year of publication, number of patients, design, single- versus multicenter, and ER rates within 12 months. The ER rates were extracted directly from the results or calculated by subtracting number of recurrences from the recurrence rates. Within the group of patients with ER defined as  $\geq 2b$ , the ER rates according to the Rutgeerts score ( $\geq 2$ ) for each study individually were calculated manually. Studies reporting mRS were divided into subcategories in order to calculate the range of ER according to subcategories. The per protocol analysis was selected if both the intention to treat and per protocol analysis were available.

Data analysis was done using IBM SPSS Statistics Data Editor, version 28. Weighted mean differences of the percentage of POR with 95% confidence intervals (CIs) were computed and reported including the total range and IQR. A histogram was computed to show the distribution of the percentages reported by the included studies, weighted by the number of patients evaluated. A meta-analysis with forest plot was not preferable due to the large number of included studies.

## RESULTS

### Included Studies

The initial literature search identified 966 studies in PubMed, in Embase, and from the Cochrane Library, after removal of duplicates 618 studies remained. Subsequently, titles and abstracts were screened. Eventually, 222 potentially eligible publications were assessed based on full text, of which 76 studies met the inclusion criteria and were included in this review and meta-analysis (Fig. 1), including 11 randomized controlled trials<sup>16–26</sup> and 65 cohort studies.<sup>4,7,27–89</sup>

### Primary Outcome Endoscopic Recurrence

In total, 76 studies including 7751 patients investigated ER defined by RS  $\geq 2$ , mRS  $\geq 2b$ , or both, within 1 year after primary ICR for CD (Supplemental Table 1, see <http://links.lww.com/AOSO/A297>). A pooled analysis showed a weighted mean of the ER rates of 43.99% (95% CI, 43.56–44.43). The overall range of reported ER was 5.0% to 93.0% (IQR, 29.2–59.0). A histogram shows the distribution of the ER percentages weighted by number of patients as reported in the included studies (Fig. 2).

### Secondary Outcomes

#### Range of ER Rates Defined as RS $\geq 2$

Of the 76 included studies, 64 studies including 6562 patients investigated ER according to RS ( $\geq 2$ ). The weighted mean of

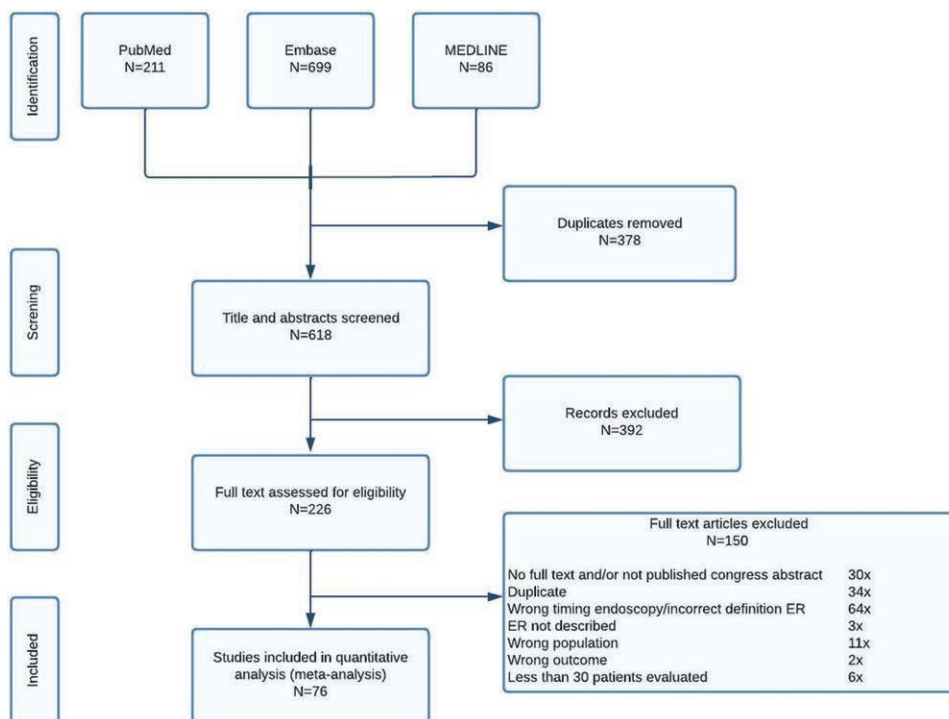


FIGURE 1. PRISMA flowchart.

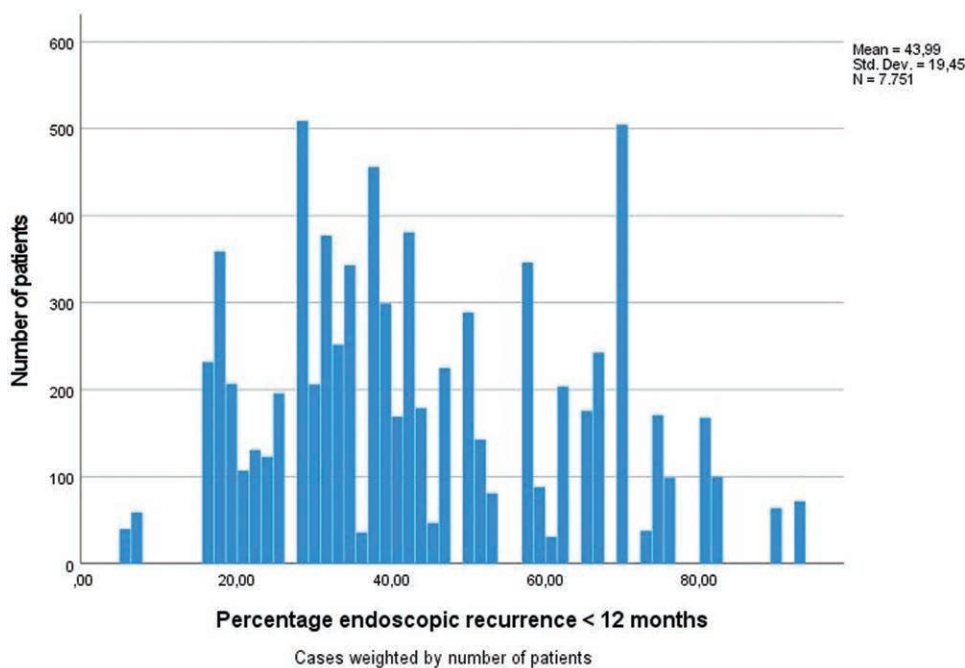


FIGURE 2. Histogram of distribution reported ER percentages weighted by number of patients in included studies, defined as either RS ≥ 2 or mRS ≥ i2b.

the ER rates was 44.02% (95% CI, 43.53–44.51). The overall range was 5.0% to 93% (IQR, 29.0–59.5) (Fig. 3).

**Range of ER Rates Defined as RS ≥ i2b**

Seventeen studies, including 2083 patients, investigated ER rates according to mRS (≥i2b). The weighted mean of the ER rates for this group was 41.06% (95% CI, 40.60–41.52). The overall range was 19.8% to 62.9% (IQR, 37.3–46.5) (Fig. 4).

**Range of ER According to Subcategories (i0, i1, i2a, i2b, i3, and i4)**

Within 17 studies reporting mRS (Table 1), the weighted mean and range of ER were evaluated per subcategory: 9 studies reported the percentages for all categories, 1 study reported i2a and i2b, and 1 other study only reported the percentage for i2b. A minimum of 1209 patients was evaluated for each category and weighted means were calculated (Table 2).

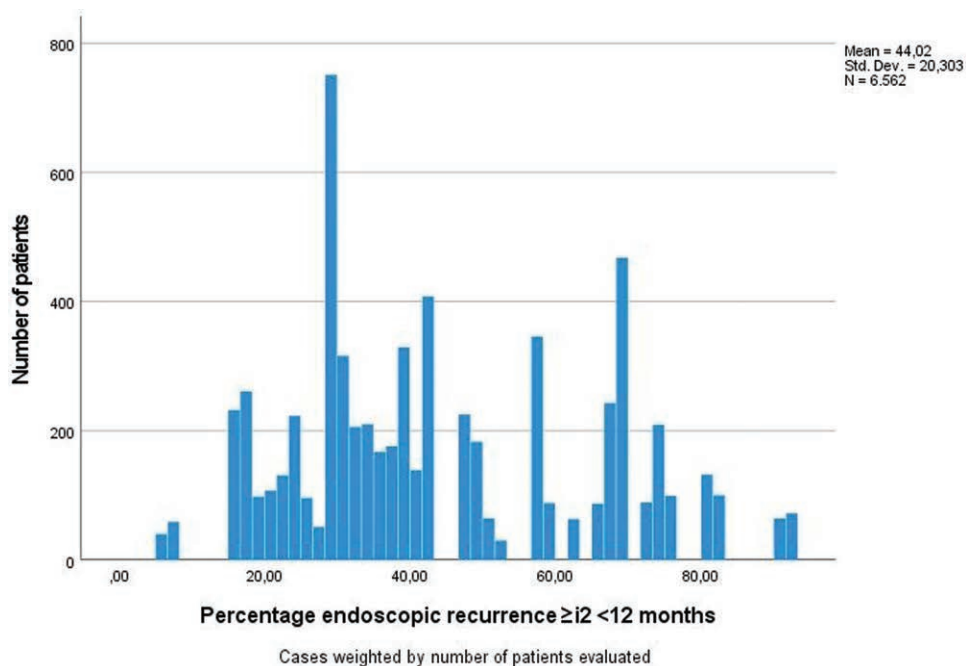


FIGURE 3. Histogram of distribution reported ER percentages weighted by number of patients in included studies according to the RS classification.

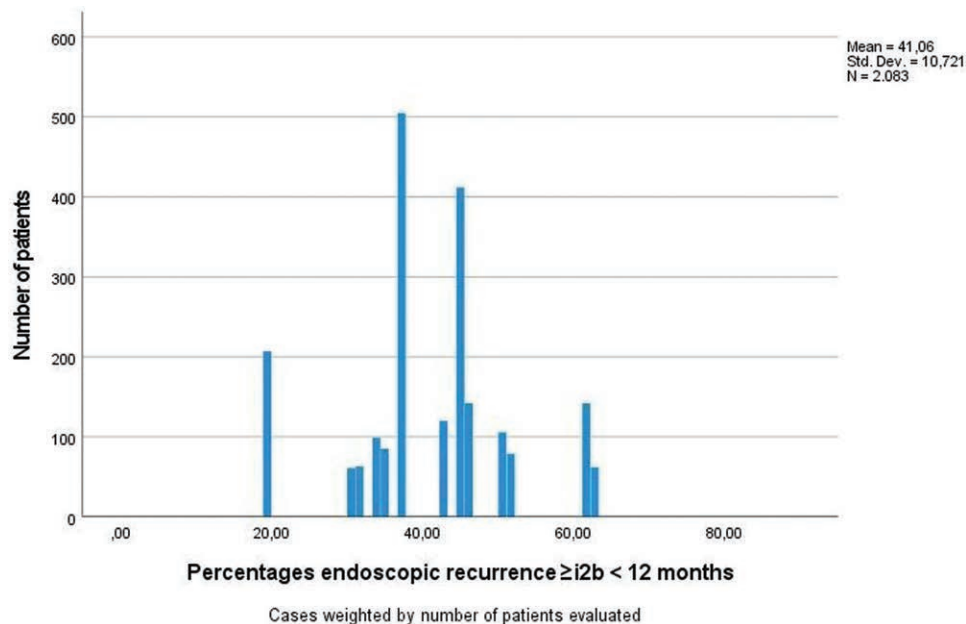


Figure 4. Histogram of distribution reported ER percentages weighted by number of patients in included studies according to the mRS classification.

**ER Rates for mRS Versus RS**

Of 11 studies who reported the recurrence percentages for mRS and RS (reported or calculated), including 1497 patients, the difference in ER rates was calculated for  $\geq i2$  versus  $\geq i2b$ .<sup>19,21,27,34,35,39,44,45,51,59,64</sup> In studies reporting ER defined as  $\geq i2$ , the weighted mean was 61.32% (95% CI, 60.61–62.03). The overall range was 39.1% to 84.7% (IQR, 47.0–69.6). In those reporting POR defined as  $\geq i2b$ , the weighted mean of ER was 40.60% (95% CI, 40.01–41.18). The overall range was 19.8% to 62.0% (IQR, 34.0–46.5).

Data on the use of medication within the 2 different groups could not be determined, as this was either not reported or not reported unambiguously in all included studies. Therefore, no reliable analysis could be performed.

**DISCUSSION**

This systematic review and meta-analysis, consisting of 76 articles, showed a wide range of ER rates according to both the RS and mRS within 1 year after ICR for CD (ranging from 5% to 93%). Moreover, data from this study suggest that scoring ER according to the original RS could even lead to a 20% increase in diagnosis of disease recurrence compared to using the mRS.

Earlier studies showed that the interobserver agreement and reproducibility of the original Rutgeerts were suboptimal. Recently, studies have suggested an update of the postoperative ER score.<sup>10,90,91</sup> The agreement on the distinction between lesions classified as  $< i2$  versus  $> i2$  was low.<sup>8,11,92,93</sup> The original Rutgeerts considers  $< 5$  lesions in the terminal ileum, an  $i1$ .

**TABLE 1.**  
**Studies Reporting mRS**

Author	Year	Patients (n)	Endoscopic Recurrence <1 yr (%)
Djelouah et al <sup>59</sup>	2021	40	37.5
Lopez-Sanroman et al <sup>21</sup>	2017	61	31.1
Buisson et al <sup>64</sup>	2021	63	44.4
Lemmens et al <sup>45</sup>	2017	74	50.0
Primas et al <sup>35</sup>	2021	79	51.9
Lopes et al <sup>44</sup>	2016	99	76.0
Ollech et al <sup>39</sup>	2019	207	19.8
Joustra et al <sup>51</sup>	2022	142	67.6
de Bruyn et al <sup>19</sup>	2021	142	62.0
Auzolle et al <sup>27</sup>	2018	225	47.0
Riviere et al <sup>34</sup>	2021	365	69.6
Cerrillo et al <sup>62</sup>	2019	32	50.0
Bachour et al <sup>72</sup>	2022	240	37.5
Bislenghi et al <sup>70</sup>	2021	47	44.7
Bommelaer et al <sup>16</sup>	2020	62	62.9
De Cruz et al <sup>61</sup>	2022	85	35.3
Machiels et al <sup>43</sup>	2020	120	43.0

**TABLE 2.**  
**Weighted Mean and Range of POR Rates According to Subcategory**

mRS	Patients Evaluated (n)	Weighted Mean (95% CI)	Range
i0	1209	23.61% (22.94–24.29)	8.5%–45.9% (IQR, 19.0–27.5)
i1	1209	11.88% (11.58–12.17)	4.2%–22.0% (IQR, 10.0–14.9)
i2a	1449	22.20% (21.85–22.55)	11.4%–42.0% (IQR, 19.3–25.0)
i2b	1481	20.86% (20.54–21.18)	10%–34.3% (IQR, 16.5–24.0)
i3	1209	9.16% (8.94–9.37)	3.5%–15.0% (IQR, 4.8–12.0)
i4	1209	10.04% (9.77–10.32)	2.9%–22.8% (IQR, 9.0–12.7)

One explanation for the large variation in ER rates might be that patients with <5 lesions in the neo-terminal ileum in combination with lesions at the anastomosis were not considered i1, but interpreted and therefore overscored as i2. The same might be the case in scoring according to the mRS, where the variation in ER rates in subcategories i2a and i2b is up to 30%. A combination of anastomotic ulcerations with <5 neo-terminal ileum lesions might be overscored as i2b instead of i2a.

The weighted means for subcategories i2a and i2b were doubled compared to subcategories i1, i3, and i4: 20% versus 10%, respectively, with a wider range for i2a and i2b compared to the others. This may suggest that the definitions for subcategories i1, i3, and i4 are less prone to interobserver variability in comparison with the i2 subcategories i2a and i2b.

It can be debated whether the discrimination between i2a and i2b is clinically significant.<sup>39,53,90,94</sup> A recent individual patient data meta-analysis concluded that the probability of both surgical and clinical recurrence is not different in patients with i2a compared with patients with i2b.<sup>12</sup> This could be explained by the fact that the variance in scoring of i2a and i2b was large because of inadequate scoring. Not surprisingly, the postoperative course was not affected by type i2 (i2a or i2b).

The other subcategory that showed a wide variation was subcategory i4, both in RS and mRS. Large ulcers with diffuse mucosal inflammation in between, as well as an unpassable stricture, are classified as i4. In the case of an anastomotic stricture, it may have been caused by a sealed anastomotic leak healed stricture formation or stricture, as seen in stapled anastomoses. If these strictures do not show inflammation in the terminal ileum, they should theoretically be scored as i0.

Finally, this study even showed some variation in category i0. This could be due to the differences in pre- and postoperative treatment and monitoring strategies in the included studies in

this review. What could be seen as the main limitation of this review is the heterogeneity observed in the included studies, which may hinder an objective comparison of study results. This diversity is a natural consequence of including studies over several years, during which there were changes in both endoscopic scoring (RS vs mRS) and shifts in practice patterns (such as initiation of medical therapy based on risk factors and variations in the timing of colonoscopies). In addition, information on the type of anastomosis was often not reported. Subanalyses were not performed to examine the impact of postoperative treatment and monitoring, as these aspects were often inadequately reported.

Since the primary outcome of this study was the presentation of variations in ER rates, perioperative management is less relevant. A separate analysis was performed focusing only on studies presenting the mRS, which also showed a substantial variation. The only endpoint related to any aspect of performance, specifically the comparison of the 2 scoring systems, was performed within the same population, reducing heterogeneity. These studies were all conducted in the same time frame.

In the statistical analyses, the CI is narrow due to the large number of included studies. The “poor performance” of ER classification shown by this meta-analysis is not reflected in the CI, but it is reflected in the wide range and the relatively large variation in IQR.

Interpretation of the ER and classification according to the mRS are clearly not easy. Considering the clinical impact of recurrence on patients’ quality of life and health care consumption, there seems to be an unmet need to improve the diagnosis of ER. Gastroenterologist should be trained in the correct assessment of anastomoses. Standard operating procedures for videotaping the anastomosis are important to allow central reading by an expert panel to reduce the unacceptable variation in recurrence rates.<sup>95</sup>

Another explanation for the variation could be due to a wound healing phenomenon. Dziki et al described in 1991 that stapled anastomoses (serosa-serosa adaptation) heal differently compared to handsewn anastomoses (mucosa-mucosa adaptation). The inverted staple line heal with linear ulcers on the staple line due to ischemia and secondary wound healing.<sup>96</sup> Recently, we demonstrated that both patients with stapled anastomoses after resection for colorectal cancer and for CD show these ulcerations at 6 months after surgery.<sup>97</sup> These ulcerations might influence endoscopic scoring of recurrence and might lead to overscoring. In fact, when handsewn and Kono-S anastomoses are compared with stapled anastomoses, this normal wound healing phenomenon of the stapled anastomosis may even interfere with the diagnosis disease recurrence when assessing ER.<sup>22</sup> Therefore, the distinction between handsewn and stapled anastomoses holds significant relevance. Unfortunately, only in 25 of 76 papers included in this review, the type of anastomosis was reported. As a result, in this study a potential impact of the configuration of the anastomosis on outcomes could not be calculated.

The message of this meta-analysis is of great significance to the surgical society. The optimal anastomosis after ileocecal resection for CD is currently a frequently debated and studied topic. There are many studies nowadays investigating the role of the type of anastomosis on disease recurrence after resection; and ER is in most studies the primary endpoint. Luglio et al,<sup>22</sup> for example, demonstrated (in the SUPREME trial) a significant reduction in postoperative ER for patients who underwent Kono-S anastomosis compared to a conventional anastomosis. This systematic review shows a huge variation in ER rates, confounding the results of these studies. It is of utmost importance for surgeons performing these studies to realize that endoscopic scoring is inherently subject to a huge variation in ER rates, as demonstrated in this meta-analysis.

In conclusion, this study demonstrates a major variation in ER rates after ICR for CD. This indicates a high likelihood of

inadequate diagnosis of disease recurrence, with major implications for quality of life of the patient and health care consumption. The wider range of recurrence when using the RS compared to the mRS, as well as the higher weighted mean in the RS, suggests that there is an unmet need to improve endoscopic scoring of recurrent disease using training programs and central reading. Since the greatest variation and overscoring were observed when using the original Rutgeerts classification, consideration may be given to using the modified Rutgeerts score (contrary to what the current guidelines recommend). Moreover, since the type of anastomotic healing of stapled anastomoses might influence the discrimination of i2a from i2b and the diagnosis i4, it should be considered to neglect pure anastomotic lesions or pure anastomotic stricturing to avoid overdiagnosis of recurrent CD, with all its consequences.

## ACKNOWLEDGMENTS

The authors thank F. S. van Etten-Jamaludin (clinical librarian) for assisting with the literature search.

E.M.L.D.W., V.B., and W.A.B. wrote the study protocol. E.M.L.D.W. and V.B. collected the data. E.M.L.D.W., V.B., and W.A.B. drafted the article. E.M.L.D.W. performed statistical analyses. S.D. (senior epidemiologist) revised the statistical analysis. M.D., S.D., C.J.B., P.S., A.V., and W.A.B. interpreted data and critically revised the article for important intellectual content. All authors agreed with the final version of the article.

## REFERENCES

- Stevens TW, Haasnoot ML, D'Haens GR, et al; LIR!C study group. Laparoscopic ileocaecal resection versus infliximab for terminal ileitis in Crohn's disease: retrospective long-term follow-up of the LIR!C trial. *Lancet Gastroenterol Hepatol.* 2020;5:900–907.
- Ponsioen CY, de Groof EJ, Eshuis EJ, et al; LIR!C study group. Laparoscopic ileocaecal resection versus infliximab for terminal ileitis in Crohn's disease: a randomised controlled, open-label, multicentre trial. *Lancet Gastroenterol Hepatol.* 2017;2:785–792.
- Gionchetti P, Dignass A, Danese S, et al; ECCO. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: part 2: surgical management and special situations. *J Crohns Colitis.* 2017;11:135–149.
- Rutgeerts P, Geboes K, Vantrappen G, et al. Predictability of the postoperative course of Crohn's disease. *Gastroenterology.* 1990;99:956–963.
- Buisson A, Chevaux JB, Allen PB, et al. Review article: the natural history of postoperative Crohn's disease recurrence. *Aliment Pharmacol Ther.* 2012;35:625–633.
- Sturm A, Maaser C, Calabrese E, et al; European Crohn's and Colitis Organisation [ECCO] and the European Society of Gastrointestinal and Abdominal Radiology [ESGAR]. ECCO-ESGAR Guideline for Diagnostic Assessment in IBD Part 2: IBD scores and general principles and technical aspects. *J Crohns Colitis.* 2019;13:273–284.
- Olaisson G, Smedh K, Sjodahl R. Natural course of Crohn's disease after ileocolic resection: endoscopically visualised ileal ulcers preceding symptoms. *Gut.* 1992;33:331–335.
- Ma C, Gecse KB, Duijvestein M, et al. Reliability of endoscopic evaluation of postoperative recurrent Crohn's disease. *Clin Gastroenterol Hepatol.* 2020;18:2139–2141.e2.
- Gecse KB, Lowenberg M, Bossuyt P, et al. Agreement among experts in the endoscopic evaluation of postoperative recurrence in Crohn's disease using the Rutgeerts score. *Sa1198. Gastroenterology.* 2014;146:S227.
- Riviere P, Bislenghi G, Vermeire S, et al. Postoperative Crohn's disease recurrence: time to adapt endoscopic recurrence scores to the leading surgical techniques. *Clin Gastroenterol Hepatol.* 2022;20:1201–1204.
- Marteau P, Laharie D, Colombel JF, et al; GETAID. Interobserver variation study of the Rutgeerts score to assess endoscopic recurrence after surgery for Crohn's disease. *J Crohns Colitis.* 2016;10:1001–1005.
- Riviere P, Pekow J, Hammoudi N, et al. Comparison of the risk of Crohn's disease postoperative recurrence between modified Rutgeerts score i2a and i2b categories: an individual patient data meta-analysis. *J Crohns Colitis.* 2022;17:269–276.
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Int J Surg.* 2021;88:105906.
- Penson DFKS, Jules A. *Newcastle–Ottawa Quality Assessment Form for Cohort.* 2012. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK115843/bin/appe-fm3.pdf>. Accessed January, 2022.
- Higgins JP, Altman DG, Gotzsche PC, et al; Cochrane Bias Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ.* 2011;343:d5928.
- Bommelaer G, Laharie D, Nancey S, et al; POPCUR study group. Oral curcumin no more effective than placebo in preventing recurrence of Crohn's disease after surgery in a randomized controlled trial. *Clin Gastroenterol Hepatol.* 2020;18:1553–1560.e1.
- Caprilli R, Cottone M, Tonelli F, et al. Two mesalazine regimens in the prevention of the post-operative recurrence of Crohn's disease: a pragmatic, double-blind, randomized controlled trial. *Aliment Pharmacol Ther.* 2003;17:517–523.
- Caprilli R, Corrao G, Taddei G, et al. Prognostic factors for postoperative recurrence of Crohn's disease. *Dis Colon Rectum.* 1996;39:335–341.
- de Bruyn JR, Bossuyt P, Ferrante M, et al; Dutch-Belgian The Effect of Vitamin D3 to Prevent Postoperative Relapse of Crohn's Disease: A Placebo-controlled Randomized Trial Study Group. High-dose vitamin D does not prevent postoperative recurrence of Crohn's disease in a randomized placebo-controlled trial. *Clin Gastroenterol Hepatol.* 2021;19:1573–1582.e5.
- Hanauer SB, Korelitz BI, Rutgeerts P, et al. Postoperative maintenance of Crohn's disease remission with 6-mercaptopurine, mesalamine, or placebo: a 2-year trial. *Gastroenterology.* 2004;127:723–729.
- Lopez-Sanroman A, Vera-Mendoza I, Domenech E, et al; Spanish GETECCU group [APPRECIATE study]. Adalimumab vs azathioprine in the prevention of postoperative Crohn's disease recurrence: a GETECCU randomised trial. *J Crohns Colitis.* 2017;11:1293–1301.
- Luglio G, Rispo A, Imperatore N, et al. Surgical prevention of anastomotic recurrence by excluding mesentery in Crohn's disease: the SuPREME-CD study - a randomized clinical trial. *Ann Surg.* 2020;272:210–217.
- Mañosa M, Cabré E, Bernal I, et al. Addition of metronidazole to azathioprine for the prevention of postoperative recurrence of Crohn's disease: a randomized, double-blind, placebo-controlled trial. *Inflamm Bowel Dis.* 2013;19:1889–1895.
- McLeod RS, Wolff BG, Ross S, et al. Recurrence of Crohn's disease after ileocolic resection is not affected by anastomotic type: results of a multicenter, randomized, controlled trial. *Dis Colon Rectum.* 2009;52:919–927.
- Rutgeerts P, Van Assche G, Vermeire S, et al. Ornidazole for prophylaxis of postoperative Crohn's disease recurrence: a randomized, double-blind, placebo-controlled trial. *Gastroenterology.* 2005;128:856–861.
- Satsangi J, Kennedy NA, Mowat C, et al. A randomised, double-blind, parallel-group trial to assess mercaptopurine versus placebo to prevent or delay recurrence of Crohn's disease following surgical resection (TOPPIC). *EME.* 2017;4:1–57.
- Auzolle C, Nancey S, Tran-Minh ML, et al; REMIND Study Group Investigators. Male gender, active smoking and previous intestinal resection are risk factors for post-operative endoscopic recurrence in Crohn's disease: results from a prospective cohort study. *Aliment Pharmacol Ther.* 2018;48:924–932.
- de Barcelos IF, Kotze PG, Spinelli A, et al. Factors affecting the incidence of early endoscopic recurrence after ileocolonic resection for Crohn's disease: a multicentre observational study. *Colorectal Dis.* 2017;19:O39–O45.
- Yamamoto T, Bamba T, Umegae S, et al. The impact of early endoscopic lesions on the clinical course of patients following ileocolonic resection for Crohn's disease: a 5-year prospective cohort study. *United European Gastroenterol J.* 2013;1:294–298.
- Walsh M, Nayeri S, Ji J, et al. A role for CXCR3 ligands as biomarkers of post-operative Crohn's disease recurrence. *J Crohns Colitis.* 2022;16:900–910.
- Veyre F, Boschetti G, Meunier C, et al. Low levels of fecal calprotectin 3 months after surgery predict subsequent endoscopic postoperative remission in Crohn's disease. *Dig Dis Sci.* 2021;66:4429–4435.
- Tang S, Liu W, Qi W, et al. Real-world experience with AGA guidelines in the management of Crohn's disease following ileocolonic resection: a retrospective cohort study. *Gastroenterol Res Pract.* 2020;2020:8618574.
- Shen W, Li Y, Cao L, et al. Decreased expression of prox1 is associated with postoperative recurrence in Crohn's disease. *J Crohns Colitis.* 2018;12:1210–1218.

34. Riviere P, Vermeire S, Irls-Depe M, et al. Rates of postoperative recurrence of Crohn's disease and effects of immunosuppressive and biologic therapies. *Clin Gastroenterol Hepatol.* 2021;19:713–720.e1.
35. Primas C, Hopf G, Reinisch S, et al. Role of fecal calprotectin in predicting endoscopic recurrence in postoperative Crohn's disease. *Scand J Gastroenterol.* 2021;56:1169–1174.
36. Poredska K, Kunovsky L, Marek F, et al. The influence of microscopic inflammation at resection margins on early postoperative endoscopic recurrence after ileocaecal resection for Crohn's disease. *J Crohns Colitis.* 2020;14:361–368.
37. Paredes JM, Ripolles T, Cortes X, et al. Contrast-enhanced ultrasonography: usefulness in the assessment of postoperative recurrence of Crohn's disease. *J Crohns Colitis.* 2013;7:192–201.
38. Onali S, Calabrese E, Petruzzello C, et al. Post-operative recurrence of Crohn's disease: a prospective study at 5 years. *Dig Liver Dis.* 2016;48:489–494.
39. Ollech JE, Aharoni-Golan M, Weisshof R, et al. Differential risk of disease progression between isolated anastomotic ulcers and mild ileal recurrence after ileocolonic resection in patients with Crohn's disease. *Gastrointest Endosc.* 2019;90:269–275.
40. Nakao S, Itabashi M, Yamamoto T, et al. Predictive value of myenteric and submucosal plexitis for postoperative Crohn's disease recurrence. *J Anus Rectum Colon.* 2017;1:56–64.
41. Monteiro S, Curdia Goncalves T, Boal Carvalho P, et al. Updating predictors of endoscopic recurrence after ileocolic resection for Crohn disease. *Turk J Gastroenterol.* 2017;28:260–265.
42. Maggiori L, Brouquet A, Zerbib P, et al; GETAID Chirurgie group. Penetrating Crohn disease is not associated with a higher risk of recurrence after surgery: a prospective nationwide cohort conducted by the GETAID Chirurgie group. *Ann Surg.* 2019;270:827–834.
43. Machiels K, Pozuelo Del Rio M, Martinez-De la Torre A, et al. Early postoperative endoscopic recurrence in Crohn's disease is characterised by distinct microbiota recolonisation. *J Crohns Colitis.* 2020;14:1535–1546.
44. Lopes S, Andrade P, Afonso J, et al. Correlation between calprotectin and modified Rutgeerts score. *Inflamm Bowel Dis.* 2016;22:2173–2181.
45. Lemmens B, de Buck van Overstraeten A, Arijis I, et al. Submucosal plexitis as a predictive factor for postoperative endoscopic recurrence in patients with Crohn's disease undergoing a resection with ileocolonic anastomosis: results from a prospective single-centre study. *J Crohns Colitis.* 2017;11:212–220.
46. Lasson A, Strid H, Ohman L, et al. Fecal calprotectin one year after ileocaecal resection for Crohn's disease—a comparison with findings at ileocolonoscopy. *J Crohns Colitis.* 2014;8:789–795.
47. Laffin MR, Perry T, Park H, et al. Endospore forming bacteria may be associated with maintenance of surgically-induced remission in Crohn's disease. *Sci Rep.* 2018;8:9734.
48. Kotze PG, Spinelli A, da Silva RN, et al. Conventional versus biological therapy for prevention of postoperative endoscopic recurrence in patients with Crohn's disease: an international, multicenter, and observational study. *Intest Res.* 2015;13:259–265.
49. Kono T, Ashida T, Ebisawa Y, et al. A new antimesenteric functional end-to-end handsewn anastomosis: surgical prevention of anastomotic recurrence in Crohn's disease. *Dis Colon Rectum.* 2011;54:586–592.
50. Keshтели AH, Tso R, Dieleman LA, et al. A distinctive urinary metabolic fingerprint is linked with endoscopic postoperative disease recurrence in Crohn's disease patients. *Inflamm Bowel Dis.* 2018;24:861–870.
51. Joustra V, Duijvestein M, Mookhoek A, et al. Natural history and risk stratification of recurrent Crohn's disease after ileocolonic resection: a multicenter retrospective cohort study. *Inflamm Bowel Dis.* 2022;28:1–8.
52. Huang ZC, Yang QF, Tang J, et al. Thiopurines are superior to mesalazine for preventing postoperative recurrence in patients with Crohn's disease and two or more risk factors. *J Dig Dis.* 2021;22:590–596.
53. Hirten RP, Ungaro RC, Castaneda D, et al. Anastomotic ulcers after ileocolic resection for Crohn's disease are common and predict recurrence. *Inflamm Bowel Dis.* 2020;26:1050–1058.
54. Han ZM, Qiao WG, Ai XY, et al. Impact of capsule endoscopy on prevention of postoperative recurrence of Crohn's disease. *Gastrointest Endosc.* 2018;87:1489–1498.
55. Glick LR, Sossenheimer PH, Ollech JE, et al. Low-dose metronidazole is associated with a decreased rate of endoscopic recurrence of Crohn's disease after ileal resection: a retrospective cohort study. *J Crohns Colitis.* 2019;13:1158–1162.
56. Fortinsky KJ, Kevans D, Qiang J, et al. Rates and predictors of endoscopic and clinical recurrence after primary ileocolic resection for Crohn's disease. *Dig Dis Sci.* 2017;62:188–196.
57. Domenech E, Manosa M, Bernal I, et al. Impact of azathioprine on the prevention of postoperative Crohn's disease recurrence: results of a prospective, observational, long-term follow-up study. *Inflamm Bowel Dis.* 2008;14:508–513.
58. Domenech E, Garcia V, Iborra M, et al. Incidence and management of recurrence in patients with Crohn's disease who have undergone intestinal resection: the Practicrohn Study. *Inflamm Bowel Dis.* 2017;23:1840–1846.
59. Djelouah M, Marical V, Kanagaratnam L, et al. Diagnosis of postoperative recurrence of Crohn disease with MR-enterography: value of diffusion-weighted imaging. *Diagn Interv Imaging.* 2021;102:743–751.
60. De Cruz P, Kamm MA, Hamilton AL, et al. Efficacy of thiopurines and adalimumab in preventing Crohn's disease recurrence in high-risk patients - a POCER study analysis. *Aliment Pharmacol Ther.* 2015;42:867–879.
61. De Cruz P, Hamilton AL, Burrell KJ, et al. Endoscopic prediction of Crohn's disease postoperative recurrence. *Inflamm Bowel Dis.* 2022;28:680–688.
62. Cerrillo E, Moret I, Iborra M, et al. A nomogram combining fecal calprotectin levels and plasma cytokine profiles for individual prediction of postoperative Crohn's disease recurrence. *Inflamm Bowel Dis.* 2019;25:1681–1691.
63. Calabrese E, Petruzzello C, Onali S, et al. Severity of postoperative recurrence in Crohn's disease: correlation between endoscopic and sonographic findings. *Inflamm Bowel Dis.* 2009;15:1635–1642.
64. Buisson A, Nancey S, Manlay L, et al; USTEK Post-Op study group. Ustekinumab is more effective than azathioprine to prevent endoscopic postoperative recurrence in Crohn's disease. *United European Gastroenterol J.* 2021;9:552–560.
65. Buisson A, Cannon L, Umanskiy K, et al. Factors associated with anti-tumor necrosis factor effectiveness to prevent postoperative recurrence in Crohn's disease. *Intest Res.* 2022;20:303–312.
66. Bourreille A, Jarry M, D'Halluin PN, et al. Wireless capsule endoscopy versus ileocolonoscopy for the diagnosis of postoperative recurrence of Crohn's disease: a prospective study. *Gut.* 2006;55:978–983.
67. Boschetti G, Nancey S, Moussata D, et al. Enrichment of circulating and mucosal cytotoxic CD8+ T cells is associated with postoperative endoscopic recurrence in patients with Crohn's disease. *J Crohns Colitis.* 2016;10:338–345.
68. Boschetti G, Laidet M, Moussata D, et al. Levels of fecal calprotectin are associated with the severity of postoperative endoscopic recurrence in asymptomatic patients with Crohn's disease. *Am J Gastroenterol.* 2015;110:865–872.
69. Bobanga ID, Bai S, Swanson MA, et al. Factors influencing disease recurrence after ileocolic resection in adult and pediatric onset Crohn's disease. *Am J Surg.* 2014;208:591–596.
70. Bislinghi G, Fieuids S, Wolthuis A, et al. Positioning strictureplasty in the treatment of extensive Crohn's disease ileitis: a comparative study with ileocecal resection. *Int J Colorectal Dis.* 2021;36:791–799.
71. Bellingher J, Munoz-Bongrand N, Pariente B, et al. Endoscopic and clinical recurrences after laparoscopic or open ileocolic resection in Crohn's disease. *J Laparoendosc Adv Surg Tech A.* 2014;24:617–622.
72. Bachour SP, Shah RS, Lyu R, et al. Mild neoterminal ileal post-operative recurrence of Crohn's disease conveys higher risk for severe endoscopic disease progression than isolated anastomotic lesions. *Aliment Pharmacol Ther.* 2022;55:1139–1150.
73. Siva SS, Dachman A, Baad M, et al. Visceral adipose tissue volume does not predict post-operative disease recurrence after ileocectomy in patients with Crohn's disease. *Am J Gastroenterol.* 2016;111:S320.
74. Walters TD, Steinhart AH, Bernstein CN, et al. Validating Crohn's disease activity indices for use in assessing postoperative recurrence. *Inflamm Bowel Dis.* 2011;17:1547–1556.
75. Nakamura TI, Shah RS, Chauhan K, et al. Tumor necrosis factor antagonists are superior to anti-integrin and anti-IL-12/23 therapies for preventing postoperative recurrence in adult Crohn's disease patients requiring postoperative therapy. *Gastroenterology.* 2020;158:S924.
76. Mocchiari F, Giunta M, Di Mitri R, et al. Surgical recurrence in Crohn's disease patients with severe post-operative endoscopic recurrence: risk difference between purely anastomotic lesions and lesions limited to the neoterminal ileum. *J Crohns Colitis.* 2019;13:S147–S148.
77. Kasalicky M, Duricova D, Lukas M, et al. Risk of short-term endoscopic recurrence of Crohn's disease after ileo-colonic resection: results from a single, tertiary IBD center. *Gastroenterology.* 2014;1:S230.
78. Suzuki Y, Kotze PG, Spinelli A, et al. Retrospective comparison of the efficacy of anti-TNF agents in isolation or combined with azathioprine in prevention of early postoperative endoscopic recurrence in Crohn's disease from the MULTIPER database. *J Crohns Colitis.* 2014;8:S216.

79. Zagherian KN, Melmed GY, Dubinsky M, et al. Medical prophylaxis after ileocolic resection for Crohn's disease-no need to rush. *Gastroenterology*. 2014;146:S454.
80. Echarrri A, Gallego JC, Ollero V, et al. Magnetic resonance enterography for the diagnosis and grading of postsurgical recurrence of Crohn's disease. *J Crohns Colitis*. 2012;6:S70.
81. Machiels K, Vanhove W, Sabino J, et al. Intestinal microbial signature predicts postoperative Crohn's disease recurrence following ileocaecal resection with ileocolonic anastomosis. *J Crohns Colitis*. 2015;1:S438-S459.
82. Sooben S, Thin L, Picardo S, et al. A high CRP before surgery and early medical prophylaxis predict postoperative endoscopic Crohn's disease recurrence. *J Crohns Colitis*. 2018;12:S465-S466.
83. Camargo M, Brandstetter S, Aiello A, Stocchi L, Hull T, et al. Handsewn anastomosis after ileocolic resection for Crohn's disease: a lost art? *Gastroenterology*. 2019;156:S58-S59.
84. Lavelle A, Keegan D, Byrne K, et al. Grading post-operative recurrence in Crohn's disease: a comparison between MRE and ileocolonoscopy. *J Crohns Colitis*. 2017;11:S210.
85. Golovey R, Hoffman S, Scapa E, et al. Faecal protease activity as a predictor marker of disease recurrence in patients with Crohn's disease following ileocectomy. *J Crohns Colitis*. 2019;13:S089-S090.
86. Papamichael K, Archavlis E, Kyriakos N, et al. Faecal calprotectin but not serum CRP predicts post-operative endoscopic recurrence of Crohn's disease. *J Crohns Colitis*. 2012;1:S169.
87. Viazis N, Varitimias L, Galanopoulos M, et al. The diagnostic yield of small bowel capsule endoscopy in postsurgical Crohn's disease. *J Crohns Colitis*. 2016;10:S211.
88. Savarino E, Bodini G, Dulbecco P, et al. Adalimumab is more effective than azathioprine and mesalamine at preventing postoperative recurrence of Crohn's disease: a randomized controlled trial. *Am J Gastroenterol*. 2013;108:1731-1742.
89. Noben M, De Buck Van Overstraeten A, Lockton S, et al. Active smoking, and pre-operative anti-flagellin Fla2 and pANCA antibodies may predict postoperative Crohn's disease recurrence: results from a prospective mono-centric trial. *J Crohns Colitis*. 2014;8:S39-S40.
90. Hammoudi N, Auzolle C, Tran Minh ML, et al. Postoperative endoscopic recurrence on the neoterminal ileum but not on the anastomosis is mainly driving long-term outcomes in Crohn's disease. *Am J Gastroenterol*. 2020;115:1084-1093.
91. Hanzel J, Jairath V, De Cruz P, et al. Recommendations for standardizing clinical trial design and endoscopic assessment in postoperative Crohn's disease. *Inflamm Bowel Dis*. 2021;28:1321-1331.
92. Daperno M, Comberlato M, Bossa F, et al. Inter-observer agreement in endoscopic scoring systems: preliminary report of an ongoing study from the Italian Group for Inflammatory Bowel Disease (IG-IBD). *Dig Liver Dis*. 2014;46:969-973.
93. Fernandes SR, Pinto J, Marques da Costa P, et al; Gedii. Disagreement among gastroenterologists using the Mayo and Rutgeerts endoscopic scores. *Inflamm Bowel Dis*. 2018;24:254-260.
94. Bayart P, Duveau N, Nachury M, et al. Ileal or anastomotic location of lesions does not impact rate of postoperative recurrence in Crohn's disease patients classified i2 on the Rutgeerts score. *Dig Dis Sci*. 2016;61:2986-2992.
95. Daperno M, Comberlato M, Bossa F, et al; IGIBDendo Group. Training programs on endoscopic scoring systems for inflammatory bowel disease lead to a significant increase in interobserver agreement among community gastroenterologists. *J Crohns Colitis*. 2017;11:556-561.
96. Dziki AJ, Duncan MD, Harmon JW, et al. Advantages of handsewn over stapled bowel anastomosis. *Dis Colon Rectum*. 1991;34:442-448.
97. van der Does de Willebois EML, Duijvestein M, Wasmann KA, et al. Endoscopic recurrence or anastomotic wound healing phenomenon after ileocolic resection for Crohn's disease: the challenges of accurate endoscopic scoring. *J Crohns Colitis*. 2022;17:693-699.