

Which is an established risk factor for post-operative Crohn's disease recurrence:

- A. Cannabis exposure
- B. HLA-DQA1*05 allele
- C. Smoking cessation
- D. Prior intestinal resection





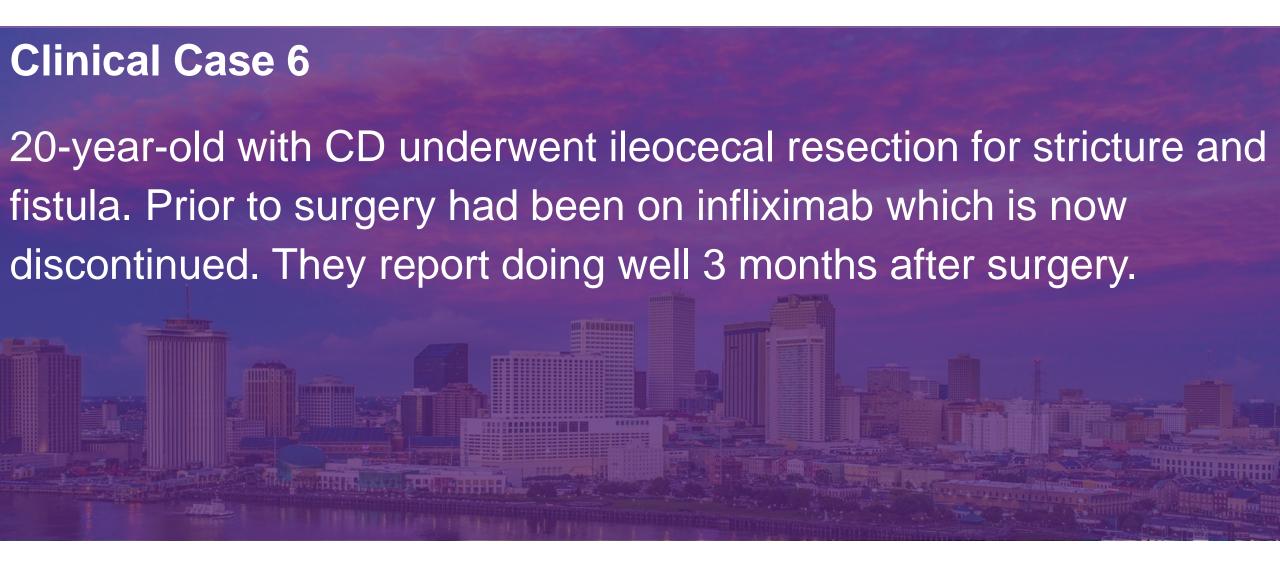
Which is NOT recommended after ileocecal resection for Crohn's disease:

- A. Checking Vitamin B12 levels
- B. Serial stool calprotectin
- C. Initiation of probiotics
- D. Colonoscopy 6-12 months after surgery regardless of symptoms





Present clinical case for session 6:





Postoperative Disease Management in IBD

Gary R. Lichtenstein, MD

Professor of Medicine
University of Pennsylvania School of Medicine
Director, Center for Inflammatory Bowel Diseases
University of Pennsylvania Health System
Philadelphia, Pennsylvania





Disclosures

Grants/Research Support: Celgene, Bristol Meyers Squibb, UCB, Takeda, Janssen Ortho Biotech, Celgene

Consultant: AbbVie, Allergan, American Gastroenterological Association, American Regent, Bristol Meyers Squibb, Celgene, Eli Lilly (Consultant and DSMB), Endo Pharmaceuticals, Ferring, Gilead, Janssen OrthoBiotech, MedEd Consultants, Merck, Morphic Therapeutics, Pfizer Pharmaceuticals, Prometheus Laboratories, Inc., Romark, Sandoz, Salix Pharmaceuticals / Valeant, Sandoz, Shire Pharmaceuticals, Takeda, UCB, Virgo (stock options)

Honorarium Recipient: Chemed (CME), IMEDEX (CME), Ironwood (CME), American Regent (CME programs), Merck (CME Program), University of Kentucky (CME), Vindico (CME),

Editorial Board Involvement: Gastroenterology and Hepatology (Gastro-Hep Communications)- Executive Editor, American College of Gastroenterology (Associate Editor – American Journal of Gastroenterology).

Other Financial Material Support: SLACK, Inc. (book royalty), Janssen OrthoBiotech (IBD Fellowship Funding), Pfizer (IBD Fellowship Funding), Professional Communications, Inc. (textbook editor honorarium), Takeda (grant), Up To Date (Author), Springer Science and Media (Editor Honorarium), Takeda (IBD Fellowship Funding)

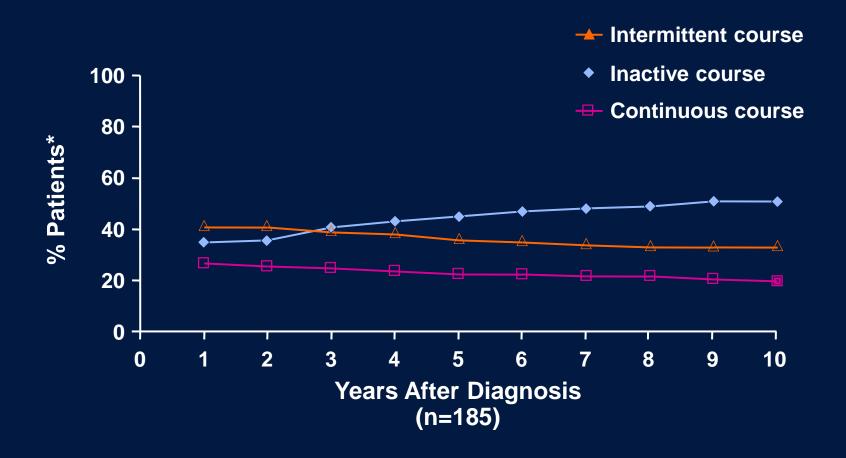


Crohn's Disease

Natural History of Disease

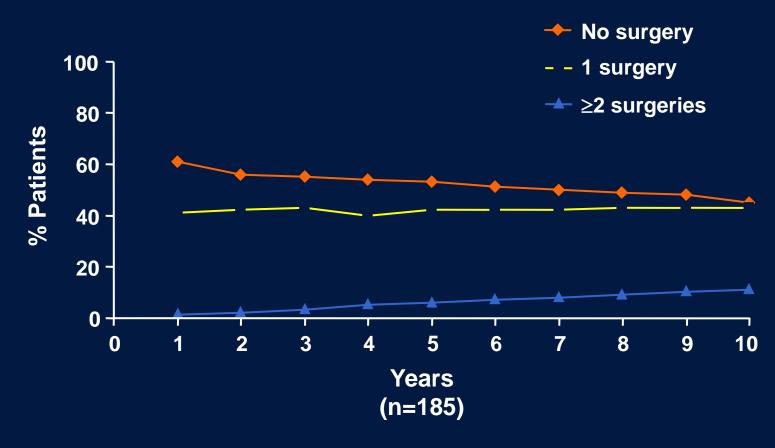


Course of CD After Diagnosis





Cumulative Probabilityof Surgery After Diagnosis of CD





Rates of Postoperative Recurrence

Endoscopic

- 70% at 6 months ¹
- -73% ² to > 90% at 1 year ³ *

Clinical

- 20%-35% after 1 year ^{2,4}
- 34%-86% after 3 years ^{2,4}

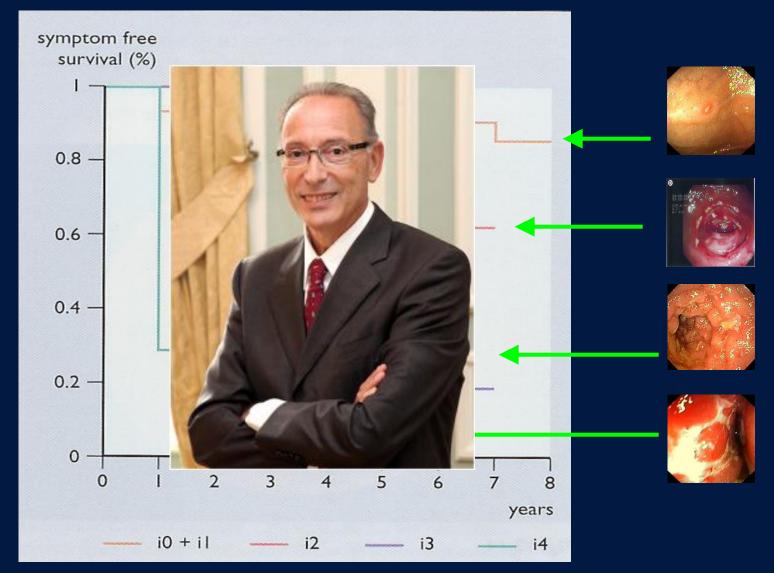
Surgical

- 25% after 5 years ^{2,4}
- 35% after 10 years ^{2,4}
 - 1- Rutgeerts P et al. Lancet. 1991; 338: 771-774
 - 2- Rutgeerts, P, et al Gastroenterology. 1990; 99: 956-963
 - 3- Olaison P et al. Gut. 1992; 33: 331-335
 - 4- Swoger J, et al. Gastroenterol Clin North Am. 2012; 41: 303-314



^{*-(}approximately 50% having 'severe' recurrence (Rutgeerts score ≥ 2)

Actuarial Analysis of Symptomatic Recurrence in Patients Stratified According to Severity of Endoscopic Lesions



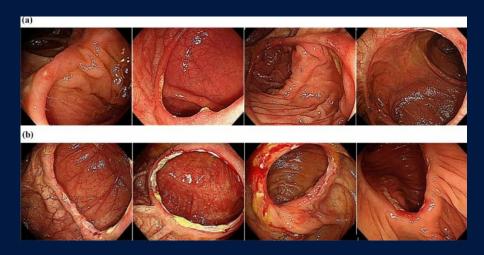


Endoscopic Recurrence Score

- io: no lesions
- i1: ≤ 5 aphthous lesions
- i2: > 5 aphthous lesions with normal intervening mucosa
- i3: diffuse aphthous ileitis with diffusely inflamed mucosa
- i4: diffuse inflammation with large ulcers, nodules, and/or narrowing



Modified Rutgeerts Score



Digestive Diseases and Sciences (2021) 66:3132–3140 https://doi.org/10.1007/s10620-020-06599-3

ORIGINAL ARTICLE



The Clinical Significance of Anastomotic Ulcers After Ileocolic Resection to Predict Postoperative Recurrence of Crohn's Disease

- Jin Yong Kim¹ · Sang Hyoung Park¹ · Jae Cheol Park¹ · Soomin Noh¹ · Jung Su Lee¹ · Jeongseok Kim¹ Nam Seok Ham¹ · Eun Hye Oh¹ · Sung Wook Hwang¹ · Dong-Hoon Yang¹ · Byong Duk Ye¹ · Jeong-Sik Byeon¹ · Seung-Jae Myung¹ · Jong Lyul Lee² · Yong Sik Yoon² · Chang Sik Yu² · Suk-Kyun Yang¹

Received: 5 April 2020 / Accepted: 1 September 2020 / Published online: 14 September 2020 © Springer Science+Business Media, LLC, part of Springer Nature 2020

Background The Rutgeerts score is used to predict postoperative recurrence in CD patients after ileocolic resection and is primarily based on endoscopic findings at the neoterminal ileum. However, the optimal assessment of anastomotic ulcers (AUs) remains subject to debate.

Aims We aimed to investigate the association between anastomotic ulcers (AUs) and endoscopic recurrence in postoperative

Methods This single-center retrospective study, conducted between 2000 and 2016, evaluated postoperative CD patients with endoscopic remission at the first ileocolonoscopy within 1 year after ileocolic resection and those who underwent subsequent ileocolonoscopic follow-up. The study outcome was the clinical significance of AUs in predicting endoscopic recurrence. Results Among 116 patients who were in endoscopic remission defined as the RS of i0 to i1 at the index postoperative

ileocolonoscopy, 84.5% (98/116) underwent subsequent ileocolonoscopies. During the median 30.0 months (interquartile range, 21.3-53.3) of follow-up after the first ileocolonoscopy, 56.1% (55/98) of patients showed endoscopic recurrence. Furthermore, 65.8% (48/73) with AUs and 75.5% (40/53) with major AUs, defined as either an ulcer occupying > 1/4 of the circumference, > 3 ulcers confined to an astomotic ring, or any ulcers extending to the ileocolonic mucosa, showed endoscopic recurrence. On multivariable analysis, AUs (adjusted hazard ratio [aHR], 4.33; 95% confidence interval [CI], 1.87-10.0; P < 0.001) and major AUs (aHR, 3.64; 95% CI, 1.95–79; P < 0.001) were associated with endoscopic recurrence.

Conclusions AUs are associated with a significantly high risk of endoscopic recurrence in postoperative CD patients who are in endoscopic remission.

Modified Rutgeerts score

:0

i0	No lesions in the distal ileum
i1	\leq 5 aphthous lesions in the distal ileum
i2a	Lesions confined to the ileocolonic anastomosis (including anastomotic stenosis)

> 5 aphthous ulcers or large lesions, with normal mucosa in-between, in the neo-terminal ileum

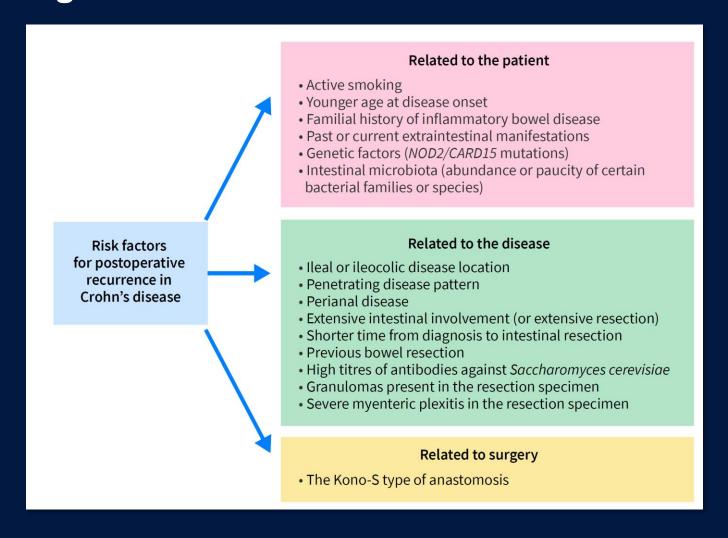
(with or without anastomotic lesions)

Diffuse aphthous ileitis with diffusely inflamed mucosa

Large ulcers with diffuse mucosal inflammation or nodules or stenosis in the neo-terminal ileum



Risk Factors for Postop Endoscopic and Clinical Recurrence of Crohn's Disease After Surgical Resection





Diagnostic Accuracy of Fecal Calprotectin Postoperatively in Crohn's Disease

FC threshold	FC 50 µg/g	FC 100 μg/g	FC 150 μg/g	FC 200 µg/g		
Included studies	7	9	6	6		
Total patients	528	588	340	284		
Sensitivity (95% CI)	90% (83–96%) /² = 73%	81% (71–91%) <i>I</i> ² = 83.1%	70% (59–81%) / ² = 51.8%	55% (43–69%) / ² = 49.7%		
Specificity (95% CI)	36% (25–47%) /² = 66.6%	57% (48–64%) <i>I</i> ² = 38.2%	69% (61–77%) <i>I</i> ² = 24.9%	71% (62–79%) <i>I</i> ² = 48.7%		
DOR (95% CI)	5.72 (2.41–13.73) $I^2 = 0\%$	6.35 (2.93–13.04) $I^2 = 8.4\%$	5.92 (2.61–12.17) $I^2 = 55.4\%$	$3.32 (1.50-7.14)$ $I^2 = 32.1\%$		
Positive LR (95% CI)	1.41 (1.18–1.72) /² = 30.1%	1.88 (1.52–2.28) $I^2 = 0\%$	2.35 [1.60–3.39] $I^2 = 44.9\%$	1.96 (1.28–3.00) $I^2 = 17.1\%$		
Negative LR (95% CI)	$0.29 (0.11-0.51)$ $I^2 = 0\%$	$0.33 (0.16-0.54)$ $I^2 = 58.8\%$	$0.43 (0.26-0.63)$ $I^2 = 60.2\%$	$0.63 (0.40-0.86)$ $I^2 = 42.7\%$		
Rho	0.87	0.68	0.10	0.23		
CI, confidence interval; DOR, diagnostic odds ratio; FC, fecal calprotectin; LR, likelihood ratio; Rho, Spearman's correlation coefficient.						



Evaluation of Postoperative Recurrence in Crohn's Disease

CLINICAL REVIEW ARTICLE

Capsule Endoscopy, Magnetic Resonance Enterography, and Small Bowel Ultrasound for Evaluation of Postoperative Recurrence in Crohn's Disease: Systematic Review and Meta-Analysis

Diana E. Yuna, MD,* Ofir Har-Noy, MD,† Yuen Sau Tham, MD,* Shomron Ben-Horin, MD,† Rami Eliakim, MD,† Anastasios Koulaouzidis, DM,* and Uri Kopylov, MD†

Background: Anastomotic recurrence is frequent in patients with Crohn's disease (CD) following ileocecal resection. The degree of endoscopic recurrence, quantified by the Rutgeerts score (RS), is correlated with the risk of clinical and surgical recurrence. Noninvasive modalities such as capsule endoscopy (CE), magnetic resonance enterography (MRE), and intestinal ultrasound (US) may yield similar information without the need for ileocolonoscopy (IC). The aim of our meta-analysis was to evaluate the accuracy of those modalities for detection of endoscopic recurrence in postoperative CD patients.

Methods: We performed a systematic literature search for studies comparing the accuracy of CE, MRE, and US with IC for detection of postoperative recurrence in CD. We calculated pooled diagnostic sensitivity, specificity, diagnostic odds ratio (DOR), and area under the curve (AUC) for each comparison

Results: A total of 135 studies were retrieved: 14 studies were eligible for analysis. For CE, the pooled sensitivity was 100% (95% CI, 91%–100%). specificity was 69% (95% CI, 52%-83%), DOR was 30.8 (95% CI, 6.9-138), and AUC was 0.94. MRE had pooled sensitivity of 97% (95% CI. 89%-100%), specificity of 84% (95% CI, 62%-96%), DOR of 129.5 (95% CI, 16.4-1024.7), and AUC of 0.98. US had pooled sensitivity of 89% (95% CI, 85%–92%), specificity of 86% (95% CI, 78%–93%), DOR of 42.3 (95% CI, 18.6–96.0), and AUC 0.93.

Conclusions: CE, MRE, and US provide accurate assessment of postoperative endoscopic recurrence in CD. These modalities should gain wider use for detection of postoperative recurrence; the prognostic value of those diagnostic findings merits evaluation in further prospective studies.

Key Words: capsule endoscopy, Crohn's disease, magnetic resonance enterography, meta-analysis, postoperative recurrence, small bowel ultrasound, systematic review

Tp to one-third of Crohn's disease (CD) patients will Up to one-third of Crouns underso (CE) Find undergo surgery at least once during the course of their disease.1 As surgery is not curative in CD, disease recurrence

Received for publication August 8, 2017; Editorial Decision September 12, 2017. 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.ibdjournal.org).

From the *Centre for Liver and Digestive Disorders, The Royal Infirmary of Edinburgh, Edinburgh, United Kingdom; †Department of Gastroenterology, Sheba Medical Center, Ramat-Gan, and Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel

Author contributions: U.K. and A.K. conceived the study and oversaw the process as a whole. O.H., U.K., and Y.S.T. performed the database searches. O.H., U.K., and D.Y. extracted the data, and Y.S.T. performed quality analyses of the included studies, D.Y. conducted the statistical analyses, U.K. drafted the manuscript for submission, S.B.H., A.K., R.E., and S.O. reviewed the manuscript and provided invaluable scientific input. All authors reviewed and approved the final manuscript.

The authors have no conflicts of interest to declare

Inflamm Bowel Dis . Volume 24, Number 1, January 2018

Address correspondence to: Uri Kopylov, MD, Department of Gastroenterology, Sheba Medical Center, 1 Emek HaEla St, Ramat Gan, Israel (ukopylov@gmail.com).

> © 2017 Crohn's & Colitis Foundation. Published by Oxford University Press, All rights reserved. For permissions, please e-mail: journals.permissions@oup.com doi: 10.1093/ibd/izx027 Published online 19 December 2017

is inevitable.2 Inflammatory lesions at the anastomotic site appear in 70%-90% of the patients within a year of surgery.2-The severity of these lesions is associated with the risk of symptomatic disease recurrence.5 Rutgeerts score (RS) is an endoscopic score that was designed to evaluate the severity of anastomotic inflammation and to predict future clinical relapse.2 Ileocolonoscopy is considered the reference standard for assessment of endoscopic recurrence and is recommended within the first 6-12 months following surgery.6 Several modalities are available for small bowel (SB) assessment, for example, capsule endoscopy (CE), magnetic resonance (MR) enterography (with several different techniques and protocols available such as MR enteroclysis and diffusion-weighted enterography), and SB ultrasound (including SB contrast-enhanced ultrasound [SICUS] and contrast-enhanced US [CEUS]).

The overall diagnostic yield (DY) of these modalities has been considered comparable⁷; nevertheless, each modality has its relative advantages and limitations. Although considered the reference standard, ileocolonoscopy is invasive and associated with procedural risks and often significant patient discomfort. Noninvasive and endoscopic techniques may be able to provide an accurate and safe alternative to ileocolonoscopy

Capsule Endoscopy

- Sensitivity was 100% (95% CI, 91%–100%),
- Specificity was 69% (95% CI, 52%–83%),
- DOR was 30.8 (95% CI, 6.9–138), and
- AUC was 0.94.

MRI Enterography

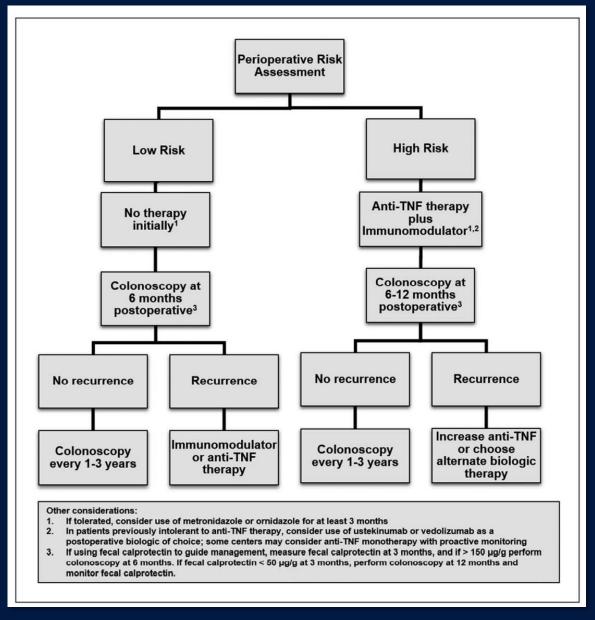
- Sensitivity of 97% (95% CI, 89%–100%),
- Specificity of 84% (95% CI, 62%–96%),
- DOR of 129.5 (95% CI, 16.4–1024.7),
- AUC of 0.98.

Ultrasonography

- Sensitivity of 89% (95% CI, 85%–92%),
- Specificity of 86% (95% CI, 78%–93%),
- DOR of 42.3 (95% CI, 18.6–96.0), and
- AUC 0.93.
- DOR Diagnostic Odds Ratio
- AUC Area Under the Curve



Crohn's Disease Postoperative Management Algorithm



Crohn's Disease Postoperative Management Algorithm

Decision / Indication For Surgery

- Review prior CD therapies, failure reasons
- Discuss natural history of postop CD
- Perform preop Risk Factor Assessment to determine postop medical therapy
- High risk: continue biologic therapy if already on¹ or obtain labs, insurance approval for new starts
- Smoking: Refer or prescribe cessation
- · Optimize nutrition
- Wean steroids (if elective, able)

Click B et al.
Practical
Gastroenterol
March 2021; 13- 25



Surgery

- Follow for postoperative complications
- DVT prophylaxis



2 - 4 weeks postop

- Review operative note: anastomosis details, ileostomy,² surgical pathology; update Risk Factor Assessment, prophylaxis plan
- Review Start/continue biologic if no contraindication per surgeon
- Consider fecal calprotectin
- Stress smoking cessation



6 months postop

- Check fecal calprotectin
- Colonoscopy: Rutgeerts' scoring:
 - ≥i2b: Start, dose optimize, or change biologic and repeat colonoscopy in 6 mo
 - i0-i2a: Monitor with q3-6 mo fecal calprotectin and repeat colonoscopy in 1 yr
- Consider enterography (CT or MR) if history of proximal small bowel CD, or unable to intubate neo-TI during colonoscopy
- Monitor for Vitamin B12 deficiency, bile acid diarrhea
- Smoking cessation



3 months postop

- Consider fecal calprotectin: if >150, consider early colonoscopy
- Ensure biologic started/continued
- Consider proactive therapeutic drug monitoring
- · Smoking cessation



Systematic Review and Network Meta-Analysis of Medical Therapies to Prevent Recurrence of Post-Operative Crohn's Disease

Efficacy of Therapy on Postoperative Endoscopic Crohn's Disease Recurrence

League table showing the efficacy of treatments for prevention of endoscopic recurrence of Crohn's disease at 12 months post-operation, defined as a Rutgeerts score of ≥i2.

Anti-TNF-α							
0.42 [0.10; 1.74]	Anti-TNF-α and						
	5-ASA						
0.32 [0.09; 1.10]	0.76 [0.26; 2.19]	Anti-TNF-α and					
		5-Nitroimidazole					
0.22 [0.07; 0.72]	0.53 [0.20; 1.41]	0.70 [0.46; 1.08]	Thiopurine and				
			5-Nitroimidazole				
0.15 [0.05; 0.49]	0.37 [0.14; 0.95]	0.49 [0.29; 0.82]	0.70 [0.52; 0.93]	5-Nitroimidazole			
0.15 [0.05; 0.46]	0.36 [0.14; 0.90]	0.47 [0.27; 0.83]	0.67 [0.47; 0.96]	0.97 [0.74; 1.26]	Thiopurine		
0.14 [0.04; 0.43]	0.33 [0.14; 0.78]	0.43 [0.24; 0.79]	0.62 [0.40; 0.95]	0.88 [0.62; 1.26]	0.91 [0.70; 1.19]	5-ASA	
0.13 [0.04; 0.39]	0.30 [0.12; 0.75]	0.40 [0.23; 0.69]	0.56 [0.40; 0.80]	0.81 [0.64; 1.03]	0.84 [0.74; 0.94]	0.92 [0.70; 1.20]	Placebo

Note: Combined direct and indirect evidence. The treatments are shown in relative ranking of efficacy. The treatment in the top-left position is considered 'best', and shaded boxes represent statistically significant comparisons. The comparisons should be read from left to right.



BDHorizons

Systematic Review and Network Meta-Analysis of Medical Therapies to Prevent Recurrence of Post-Operative Crohn's Disease

Efficacy of Therapy on Postoperative Clinical Crohn's Disease Recurrence

League table showing the efficacy of treatments for prevention of clinical recurrence of Crohn's disease at 12 months post-operation.

Anti-TNF-α and 5-Nitroimidazole							
0.41 [0.15; 1.15]	Thiopurine and						
	5-Nitroimidazole						
0.22 [0.02; 2.20]	0.52 [0.06; 4.20]	Anti-TNF-α					
0.18 [0.03; 1.06]	0.44 [0.10; 1.84]	0.84 [0.19; 3.84]	5-Nitroimidazole				
0.09 [0.01; 1.26]	0.21 [0.02; 2.47]	0.41 [0.05; 3.16]	0.49 [0.07; 3.54]	Anti-TNF-α and			
				_5-ASA			
0.06 [0.01; 0.42]	0.14 [0.03; 0.76]	0.27 [0.08; 0.89]	0.32 [0.13; 0.80]	0.65 [0.11; 3.78]	Placebo		
0.05 [0.01; 0.41]	0.13 [0.02; 0.75]	0.24 [0.08; 0.76]	0.29 [0.10; 0.84]	0.59 [0.10; 3.34]	0.90 [0.52; 1.58]	Thiopurine	
0.05 [0.01; 0.37]	0.11 [0.02; 0.68]	0.22 [0.07; 0.71]	0.26 [0.09; 0.75]	0.53 [0.10; 2.84]	0.82 [0.48; 1.41]	0.91 [0.56; 1.46]	5-ASA

Note: Combined direct and indirect evidence. The treatments are shown in relative ranking of efficacy. The treatment in the top-left position is considered 'best' and shaded boxes represent statistically significant comparisons. The comparisons should be read from left to right. Clinical recurrence was defined as per the individual study criteria.

Conclusions: "In network meta-analysis, anti-TNF-α therapies alone, or in combination, appear to be the best medications for preventing endoscopic post-operative recurrence of CD."



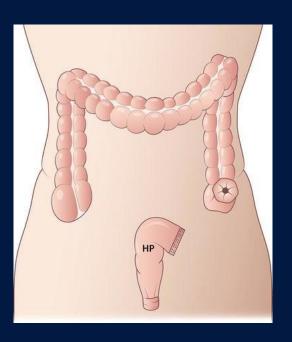
Indications for Surgical Therapy in Ulcerative Colitis

Emergency situations

- Fulminant disease activity unresponsive to maximal medical therapy
- Toxic megacolon
- Perforation
- Hemorrhage

Elective situations

- Disease activity refractory to medical therapy
- Complications related to adverse effects of chronic medical therapy
- Intestinal dysplasia or mass lesion
- Cancer
- Chronic disease
- Growth retardation in children



Management After Colectomy Hartmann's Pouch

Active Symptoms

- Mucous in the stool or BRBPR
 - Diversion colitis
 - Active UC in remaining colon
 - Infection- C diff, etc.
- Abdominal Pain
 - Consider cross sectional imaging ? Crohn's disease
- Growth retardation in children

Surveillance

- Endoscopic every 1-2 years for dysplasia carcinoma detection
- If considering IPAA or anastomosis in the future- consider cross sectional imaging (CTE or MRE) and endoscopic study

Laboratory Assessment

Check CBC, CMP, vitamin D at least once annually if no biologics; more frequently if using biologic therapy



Conclusion



- The majority of patients with Crohn's disease will require an intestinal resection at some point in their lifetime.
- Postoperative management of these patients remains a challenge.
- It is important to identify high-risk patients who exhibit risk factors for recurrence and to aggressively treat these patients to prevent or ameliorate recurrence of their Crohn's disease.
- All patients regardless of their risk should have an ileocolonoscopy 6-12 months postoperatively (6 months postoperative if low-risk and on no therapy) to initiate or adjust medications in cases of endoscopic recurrence (ileal score ≥i2).
- Even if asymptomatic, if endoscopic recurrence is present of adequate significance, therapy should be initiated or optimized.
- An algorithm for approaching postoperative Crohn's disease patients has been shared.
- Surveillance and routine lab assessment in patients with UC s/p partial colectomy and Hartman's pouch is appropriate

University of Pennsylvania Multidisciplinary IBD Center



Perelman Center for Advanced Medicine



The Pavilion

Gary R. Lichtenstein, MD Director

James D. Lewis, MD, MSCE

Associate Director, Director, GI, Penn Presbyterian

Faten Aberra, MD, MSCE

Clinical Practice Director

Shivali Berera, MD

Meena Bewtra, MD, MPH

Anna Buchner, MD, PhD

Nabeel Khan, MD

Director, GI, VA Medical Center

Helen Lee, MD

Neil Nandi, MD

Farzana Rashid MD

Akriti Saxena, MD

Robert Stein, MD

Director, GI, Radnor

CS Tse, MD

Alexandra Weiss, MD

Gary D. Wu, MD

Director, Molecular Biology Core



Presbyterian- Penn Medicine University City



Penn Medicine at Radnor





Which is an established risk factor for post-operative Crohn's disease recurrence:

- A. Cannabis exposure
- B. HLA-DQA1*05 allele
- C. Smoking cessation
- D. Prior intestinal resection





Which is an established risk factor for post-operative Crohn's disease recurrence:

- A. Cannabis exposure
- B. HLA-DQA1*05 allele
- C. Smoking cessation
- D. Prior intestinal resection





Which is NOT recommended after ileocecal resection for Crohn's disease:

- A. Checking Vitamin B12 levels
- B. Serial Stool calprotectin
- C. Initiation of probiotics
- D. Colonoscopy 6-12 months after surgery regardless of symptoms





Which is NOT recommended after ileocecal resection for Crohn's disease:

- A. Checking Vitamin B12 levels
- B. Serial Stool calprotectin
- C. Initiation of probiotics
- D. Colonoscopy 6-12 months after surgery regardless of symptoms





