ADVANCING GI PATIENT CARE 2022

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When Is Surgery Indicated for IBD?

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Disclosures

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- Consultant: AbbVie
- Consultant: BMS
- Consultant: Janssen
- Consultant: Pfizer
- Consultant: Takeda

Objectives

- Surgery in Ulcerative Colitis
- Surgery in Crohn's Disease
- Peri-Operative Optimization

Ulcerative Colitis

Indications for Surgery

ULCERATIVE COLITIS

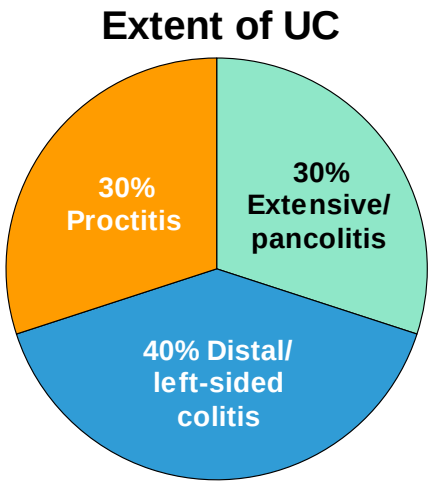
- Perforation
- Hemorrhage
- Cancer
- High Grade Dysplasia
- Fulminant Colitis /Toxic Megacolon
- Acute Severe Ulcerative Colitis

Call Colorectal Surgery knowledgeable in IBD!

UC Severity Classification

Truelove & Witts

Severity	Characteristics
Mild	• <4 stools daily, with or without blood • No systemic signs of toxicity • Normal ESR
Moderate	• >4 stools daily, usually with bleeding • Minimal signs of toxicity
Severe	• >6 bloody stools daily • Signs of systemic toxicity (eg, fever, tachycardia, anemia, elevated ESR)
Fulminant	• >10 bowel movements daily • Continuous bleeding • Signs of systemic toxicity • Abdominal tenderness and distension • Need for blood transfusion • Colonic dilation on X-ray films (i.e. transverse dilatation>6cm)

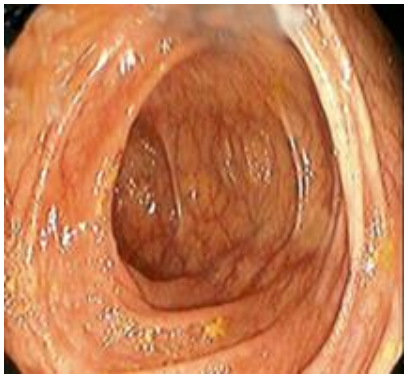


ESR=erythrocyte sedimentation rate.

Kornbluth A et al. *Am J Gastroenterol.* 2010.

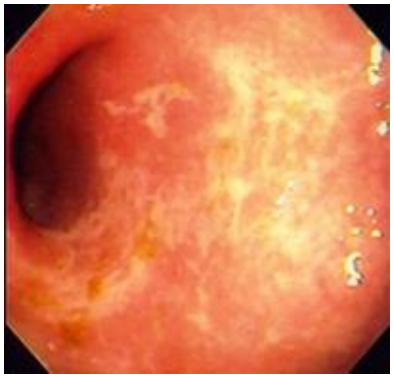
Endoscopic Severity of UC

Mayo Score >10



NORMAL

Vascular markings present

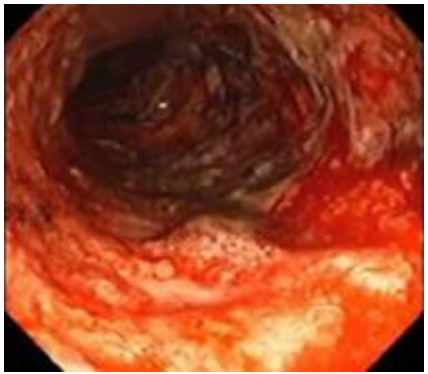


MILD

Diminished vascular markings, mild erythema, granularity, and friability

MODERATE

Marked erythema, absent vascular markings, contact friability, no ulcers



SEVERE

Spontaneous bleeding, ulcers

Stool Frequency
Rectal Bleeding
Physicians Global Assessment
Endoscopic score

Acute Severe UC Management:

Timing of Surgery

ASUC Algorithm
Day 0

Initial Workup

- Abdominal exam
- CBC, CMP, ESR, CRP
- GI panel, C difficile
- TB, Hep B, Mg, cholesterol (pre-biologic assessment)
- AXR/ CT

Initial Treatment

- IV steroids 40-60mg
- IVFs
- Electrolyte supplementation
- Thromboprophylaxis
- Enteral nutrition support
- Stop antidiarrheals/ anticholinergics

Follow-Up:

- Assess for clinical& lab improvement
- Consider flex sig/ colonoscopy
- Consider cross-sectional imaging
- Treat infectious colitis
- **Consult colorectal surgery**

ASUC Algorithm
Day 3

Re-assess

- Abdominal exam
- Clinical status
- Stool frequency
- Labs (hgb, albumin, CRP)
- Reconsider AXR/ CT

Treatment

IMPROVED:

- Transition to oral steroids
- Maintenance Medication discussion

- **WORSENED:**
- IFX 5 vs. 10mg/kg (low albumin, severe)
- Cyclosporine 2 vs. 5mg/kg IV
- **Consider Surgery!**

Follow-Up:

- Consider adding thiopurine
- Consider flex sig/ colonoscopy
- Consider cross-sectional imaging

ASUC Algorithm
Day 3-7

Re-assess

- Abdominal exam
- Clinical status
- Stool frequency
- Labs (hgb, albumin, CRP)
- Nutrition
- Imaging

Treatment

IMPROVED:
- Continue IFX, add thiopurine
- OR Transition cyclosporine to 5mg/kg oral
- Taper corticosteroids

WORSENED:
- Accelerated IFX dosing
- Tofacitinib 30mg/d (divided)
- Flex sig/ colon to rule out CMV
- **Surgery**

Infectious Complications

- Consider surgery in **CMV colitis** if noted on biopsies – high rate of colectomy requirement
- Refractory/ Recurrent **C difficile infection** despite FMT, fidoxamycin, long term vancomycin in setting of active UC.

Crohn’s Disease

Indications for Surgery

Crohn's Disease

- Perforation
- Hemorrhage
- Cancer / High Grade Dysplasia
- Fibrotic obstructing stricture
- Intractable disease
- Delayed growth (pediatrics)
- Perianal complications
- Complex fistulae and abscesses

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Perianal Fistulizing Disease

Fistula Classification:
AGA

Simple fistula

- Low (superficial or low intersphincteric or low trans-sphincteric origin of the fistula tract)
- Single external opening
- No pain or fluctuation to suggest perianal abscess
- No evidence of a rectovaginal fistula
- No evidence of anorectal stricture

Complex fistula

- High (high intersphincteric or high trans-sphincteric or extrasphincteric or suprasphincteric origin of the fistula tract)
- Multiple external openings
- Presence of pain or fluctuation to suggest a perianal abscess
- Rectovaginal fistula
- Anorectal stricture

Earlier/ Urgent Colorectal Surgery Referral

Panes J et al. *Nature Reviews: Gastroenterology & Hepatology.* 2017; 14: 652-664.

Medication	Evidence
Aminosalicylates:	No benefit! (Systematic reviews and meta-analyses)
Corticosteroids:	**No benefit! May worsen fistula discharge & need for surgery**
Antibiotics:	Metronidazole & ciprofloxacin most used- scarce evidence Reduces fistula drainage, Does NOT heal → Recurs if discontinued **Therefore: Use as adjunctive treatment for fistulas.**
Thiopurines:	(No prospective studies)
Tacrolimus:	(1 RCT) 0.2 mg/kg/d x 10 wks, fistula closure) 43% vs. 8% (*P* = 0.004).
Cyclosporine:	(Observational studies) Rapid improvements 50–80% but high relapse rates after D/C
Methotrexate:	**(**2 uncontrolled case series)"Might be effective in fistulizing Crohn's disease"
Infliximab	**= MOST EVIDENCE** Complete drainage of all fistula tracts (36% IFX v 19% PBO *P* = 0.009).
Adalimumab & Certolizumab	Post-hoc analyses : benefit/ mixed results
Concomitant use of immunosuppressants + anti-TNF therapy	Controversial, mixed data

Gomollon F et al. *J. Crohns Colitis*. 11, 3–25 (2017); Lennard-Jones J. E. *Gut*. 24, 177–181 (1983);
Panes J et al. *Nature Reviews: Gastro & Hep.* 2017; 14: 652-664; Sandborn WJ et al. *Gastroenterology.* 125, 380–388 (2003);
Pearson DC et al. *Ann. Intern. Med*. 123, 132–142 (1995); Dejaco C et al. *Aliment. Pharmacol. Ther*. 18, 1113–1120 (2003);
Mahadevan U et al. *Aliment. Pharmacol. Ther*. 18, 1003–1008 (2003); Schroder O et al. *Aliment. Pharmacol. Ther*. 19, 295–301 (2004).

Perianal Fistula
Medical Management

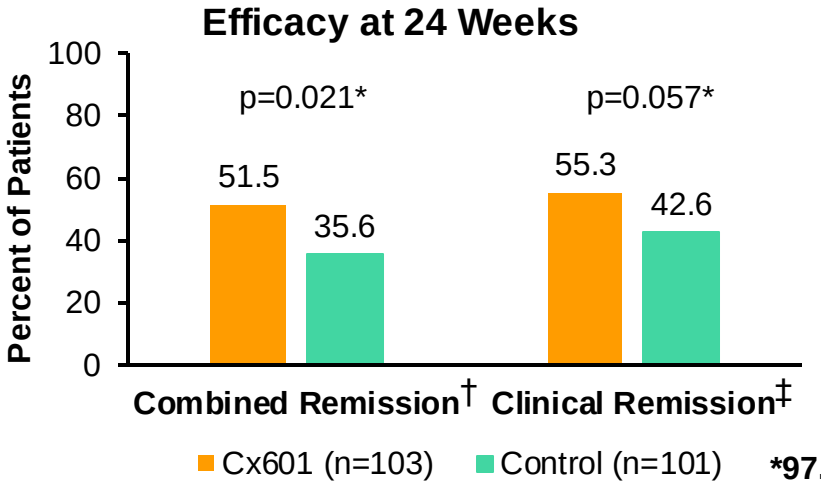
Best Evidence	Consider: Limited/ Mixed Results	No Benefit/ AVOID
Infliximab: Induction & Maintenance: Complete drainage cessation - all fistulas **36% IFX vs 19% PBO *P* = 0.009**	**Ustekinumab:** (Subgroup RCT Analysis Perianal fistula resolution) **Week 44: 85.5% vs Placebo 44.4%** **Vedolizumab** (Subgroup RCT analysis – Perianal fistula closure) **Week 52: VDZ 41.2% v 11% PBO (*P* = 0.03)** **Adalimumab & Certolizumab:** Post-hoc analyses **Possible benefit/ mixed results**	**Corticosteroids: No benefit!** May *worsen* fistula discharge & increase surgery requirements.
Antibiotics: *(adjunct treatment)* Metronidazole & ciprofloxacin mostly used- Reduces fistula drainage but NOT healing → Recurs if discontinued	**Thiopurines:** RCT subanalysis benefit **Tacrolimus**: 1 RCT: 0.2mg/kg/d x 10 wks **Cyclosporine:** (observational): rapid improvement (50-80%) *high relapse* **Methotrexate:** (2 uncontrolled series)	**Aminosalicylates: No benefit!** (Systematic reviews and meta-analyses)
Hyperbaric oxygen (adjunct treatment) Drainage cessation 33–71%	**Concomitant immunosuppressants + anti-TNF**: Controversial data	**Thalidomide:** (small studies) Dose reduction needed, High adverse events

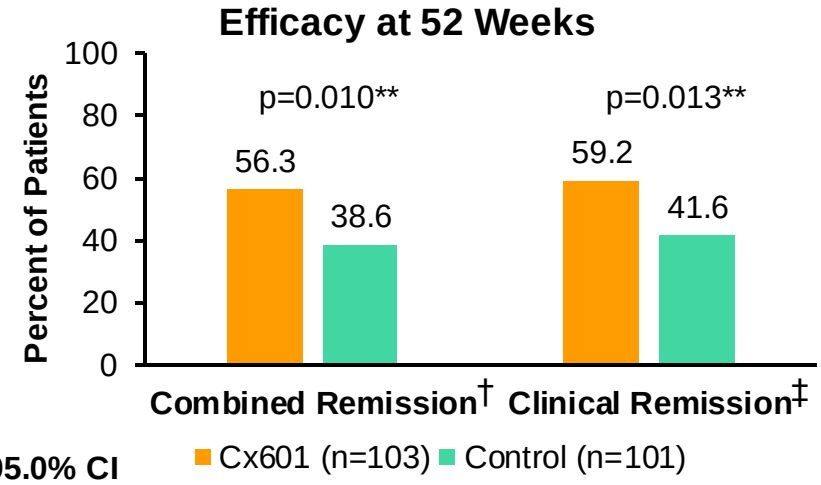
Panes J et al. *Nature Reviews: Gastro & Hep.* 2017; 14: 652-664; Dejaco C et al. *Aliment. Pharmacol. Ther*. 18, 1113–1120 (2003); Sands B. E. et al. *N. Engl. J. Med*. 350, 876–885 (2004); Lennard-Jones, J. E. *Gut.* 24, 177–181 (1983); Sands BE et al. Abstract at DDW May 2017; Lavy A et al. *J. Clin. Gastroenterol.* 19, 202–205 (1994); Sandborn WJ et al. *Gastroenterology.* 125, 380–388 (2003); Mahadevan U et al. *Aliment. Pharmacol. Ther*. 18, 1003–1008 (2003); Bouguen G et al. *Clin. Gastroenterol. Hepatol*. 11, 975–981.e1-4 (2013); Sandborn WJ et al. *NEJM.* 369, 711–721 (2013); Colombel JF et al. *Dis Colon Rectum.* 38, 609–614 (1995); Pearson DC et al. *Ann. Intern. Med.* 123, 132–142 (1995); Schroder O et al. *Aliment. Pharmacol. Ther*. 19, 295–301 (2004); Gomollon F et al. *J. Crohns Colitis.* 11, 3–25 (2017); Ehrenpreis ED et al. *Gastroenterol*. 117,1271–1277 (1999); Weisz G et al. *J. Clin. Immunol*. 17, 154–159 (1997).

Stem Cell Injection: Fistulizing CD (212 Patients)

Allogeneic Adipose-Derived Mesenchymal Stem Cells for Complex Perianal Fistulas: Phase III RCT

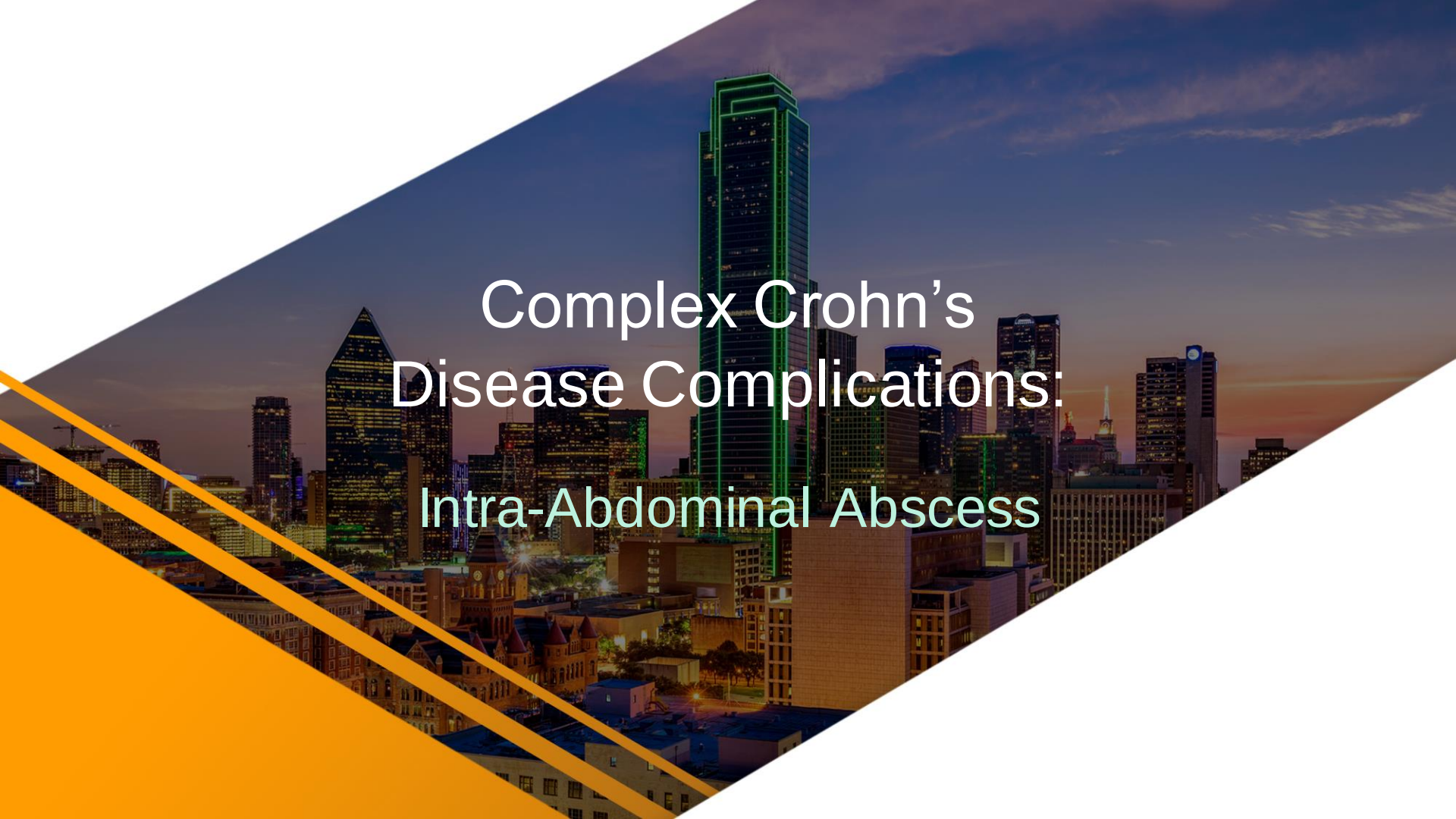
- Minimal to no luminal CD but complex active perianal fistulas
- Randomized to single injection of stem cells to all tracts + Std of Care or PBO + SOC
- More stem cell treated patients had no relapse at wk 52 (75% vs. 55.9%)
- AEs were similar (20.4% vs. 26.5%): mostly anal abscess & proctalgia





***97.5% CI; **95.0% CI**

Panes J et al. *Gastroenterology*. 2018 Apr;154:1334-1342.e4; Panes J et al. *Lancet*. 2016 Sep;388(10051):1281-90.



Complex Crohn's Disease Complications:

Intra-Abdominal Abscess

Initiate Multidisciplinary Care

Radiology
- Order appropriate imaging & review imaging with radiology & colorectal surgery
- IR placement of drains

Colorectal Surgery
- **Elective** > Urgent > Emergent Surgery
- Ostomy training & follow-up

Infectious disease
- IV antibiotics, PICC line, long term

Dietician
- Enteral nutrition
- Need for TPN

Case Manager
- Discharge planning

If no expertise, transfer patient to a center with expertise

Intra-Abdominal Abscess

Diet & Nutrition

- Initiate TPN early.
- Monitor after oral intake: If worsening abscess → NPO

Close Monitoring:

- Serial abdominal exams
- Repeat imaging

Labs

- Optimize Nutrition
  - ❑ iron panel, B12, folate, zinc, Mg, vitamin D
- Monitor for improvement in leukocytosis

Thromboembolism Prophylaxis!

Medical Therapy:

- IV Antibiotics
- Initiate biologic soon after ID clearance.
- AVOID Steroids!

Employ pain management strategies

Prevent/Manage Complications

Perioperative IBD Management: **Nutrition**

WHAT TO OPTIMIZE

Pre-operative Albumin
<21 g/l: increases morbidity 10% → 65%; mortality <1%→ 28% (vs >45 g/l)
<25 g/l: increases post-op intra-abdominal sepsis after ileo-colonic resection
<30 g/l: increases all complications (postop sepsis & prolonged inpatient stay)

Pre-operative Anemia: Hb <13 g/l (M) <12 g/l(F):

- Increases postop intra-abdominal sepsis s/p ileocolonic resection
- Pre-op correction improves postoperative outcomes (intestinal obstruction, hemorrhage, pulmonary edema, intra-abdominal abscess, anastomotic leak, post-op perforation, pneumonia, wound infection)
- pRBC transfusion post-op:
  - Increases mortality
  - Increases morbidity (nosocomial infection, multiorgan dysfunction syndrome, ARDS)
  - Increases surgical and endoscopic Crohn's disease recurrence

Barnes et al. *Clin Gastro and Hep.* 2020;18(6): 1356-66; Patel KV. *Nature Reviews | Gastro & Hep*. 2016; 13: 707-719.

Perioperative IBD Management: **Nutrition**

HOW TO OPTIMIZE

SCREEN:
for malnutrition
IDENTIFY:
high-risk patients

- albumin < 30 g/L,
- weight loss > 10–15% in 6 months, or
- BMI < 18.5

Initiate TPN or EEN:
(Decreases inflammatory burden, infectious and non-infectious complications)

- Enteral nutrition preferred if patient can maintain energy & protein requirements
- Parenteral nutrition if reduced ability to absorb enteral nutrition
- **If Malnutrition:** Delay IBD-related surgery until intensive artificial feeding initiated.
- Weak evidence to support the use of intravenous albumin
- **Stricture:** TPN / NPO/ low residual diet to reduce prestenotic dilation

POST-OP:
Initiate early enteral nutrition!
(within 24 hrs of surgery associated with improved outcomes)

Barnes et al. *Clin Gastro and Hep.* 2020;18(6): 1356-66; Grass F et al. *Nutrients*. 2017 Jun; 9(6):E562; Braga M et al. *Clin Nutr*. 2009; 28: 378–86; Herbert G et al. *Cochrane Database Syst Rev.* 2018;10:CD004080.

Thromboembolism

Risk: 1.4% of thromboembolic events for CD surgery; **3.3%** for UC.

Risks factors:

- Bleeding disorders, emergency surgery, anemia, steroid use, malnutrition
- Active inflammation, pre-op/ prolonged hospitalization, thrombocytosis, reduced mobility
- Specific operations (stoma [OR 1.95] ; J-pouch [OR 2.66] creation)
- **Laparoscopy protective (OR, 0.75 (95% CI, 0.67–0.83); *p* < 0.001).**

Postoperative:

- Mean time to VTE in Crohn's: 10.8 days
- Increased risk for up to 6 weeks after discharge

THEREFORE

Pre-Op: Prophylaxis with unfractionated or low-molecular-weight heparin

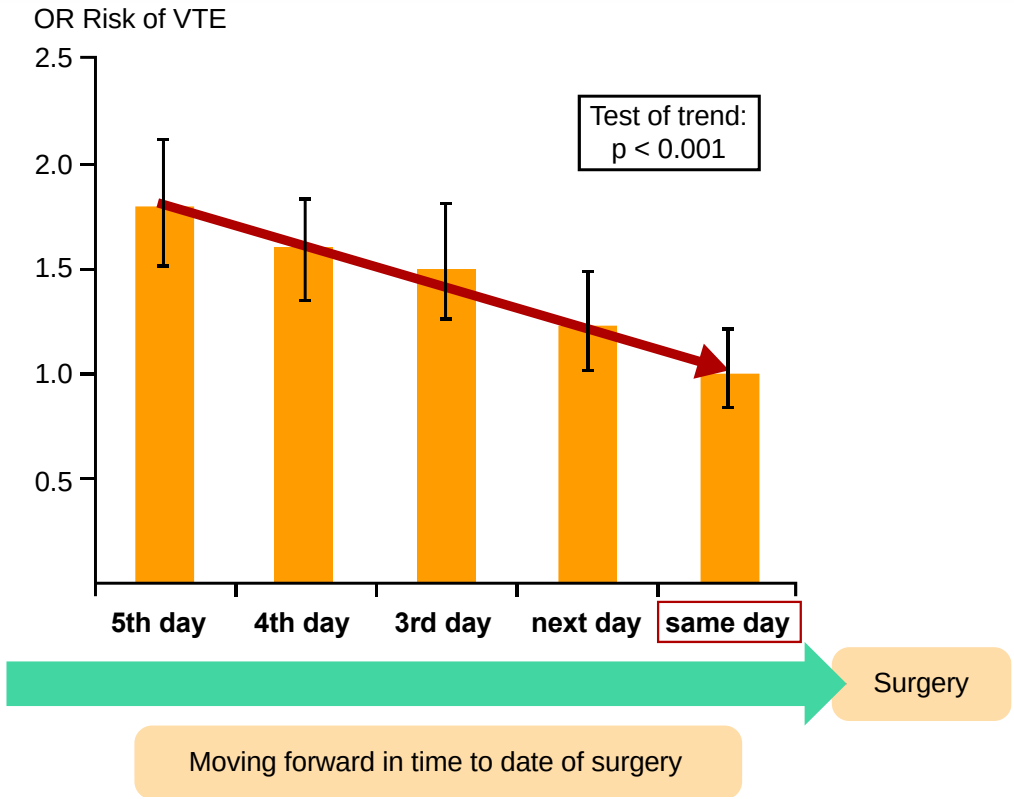
Post-Op: Compression stockings & early mobilization/ ambulation; Consider continued post-discharge prophylaxis in high risk patients.

Wallaert JB et al. *Dis Colon Rectum*. 2012 Nov; 55(11): 1138–44; Van Assche G et al. *J Crohns Colitis*. 2013; 7: 1–33; Chu TP et al. *Aliment Pharmacol Ther*. 2018 Nov; 48(10): 1099–108; Bryant R. V. et al. *J. Crohns Colitis* **8**, 166–171 (2014); Gustafsson UO et al. *World J Surg*. 2013 Feb; 37(2): 259–84; Greaves SW & Holubar SD. *Dis Colon.* 2015 58:782-791.

VTE Risk Factors:
Pre-op Hospitalization

Study of > 242,670 patients undergoing colorectal surgery:

Pre-surgical length of stay increased risk of VTE!



Greaves SW & Holubar SD. *Dis Colon Rectum.* Volume 58: 8 (2015) 782-791.

Perioperative IBD Management: Medications

Perioperative IBD Management: **Corticosteroids**

Corticosteroids → Multiple postoperative complications:

- **Superficial surgical site infections**
- **Deep space infections**
- **Anastomotic leakage (even in low dose <20mg/d prednisone)**

Topical corticosteroids (budesonide):

- **Likely OK (no significant systemic absorption)**
- **Limited studies**

Limiting corticosteroid exposure perioperatively
Reduce intraoperative stress dose
Rapidly taper when possible
If high dose, consider diverting surgery *no increased complications.

Lightner AL. *Dis Colon Rectum.* 2018;61:428–431; Ziv Y et al. *Dis Colon Rectum.* 1996;39(5):504-508.

Perioperative IBD Management: **Medications**

Immunomodulators (AZA/ 6MP/ MTX): no risk of adverse postoperative outcomes.
Small Molecules: limited data
Biologics

- **Prior data controversial; (indication bias – severe IBD, corticosteroid use)**
- **Recent studies: Favorable safety profile of vedolizumab, ustekinumab, antiTNFs.**

PUCCINI TRIAL: Prospective 955 patients cohort undergoing intra-abdominal surgery
Anti-TNF exposure in the 12 weeks preceding surgery/ Detectable levels of antiTNFs
No association with increased risk of any infection or surgical site infection

THEREFORE:

- **Do not delay surgery on these medications .**
- **A diverting ileostomy is not required for an intestinal CD resection in the setting of preoperative biologic exposure.**
- **Delaying surgery in severe cases may increase risk of complications, including mortality.**

Colombel JF et al. *Am J Gastroenterol.* 2004;99:878–883; Aberra FN et al. *Gastroenterology.* 2003;125:320–327;
Novello M et al. *J Crohns Colitis.* 2020;14:185–191; Lightner AL et al. *J Crohns Colitis.* 2018;12:402–407;
Novello M et al. *Int J Colorectal Dis.* 2019;34:451–457; Cohen BL et al. *Gastroenterology.* 2019;156:S-80.

Conclusion

- **Refer to surgery for absolute indications for both UC and CD**
- **Consult colorectal surgery (preferably with IBD expertise) early for severe disease**
- **Provide multidisciplinary care for complex disease management**
- **Optimize patient prior to surgery to reduce complications**