GI Alliance

Advancing GI Patient Care 2021

SATURDAY, JULY 24, 2021

Accredited by:

RMCHCS
Rehoboth McKinley Christian Health Care Services

This program is supported by an educational grant from
AbbVie, Janssen Biotech, Inc., Mallinckrodt Pharmaceuticals and Pfizer Inc.

Common Complications in IBD

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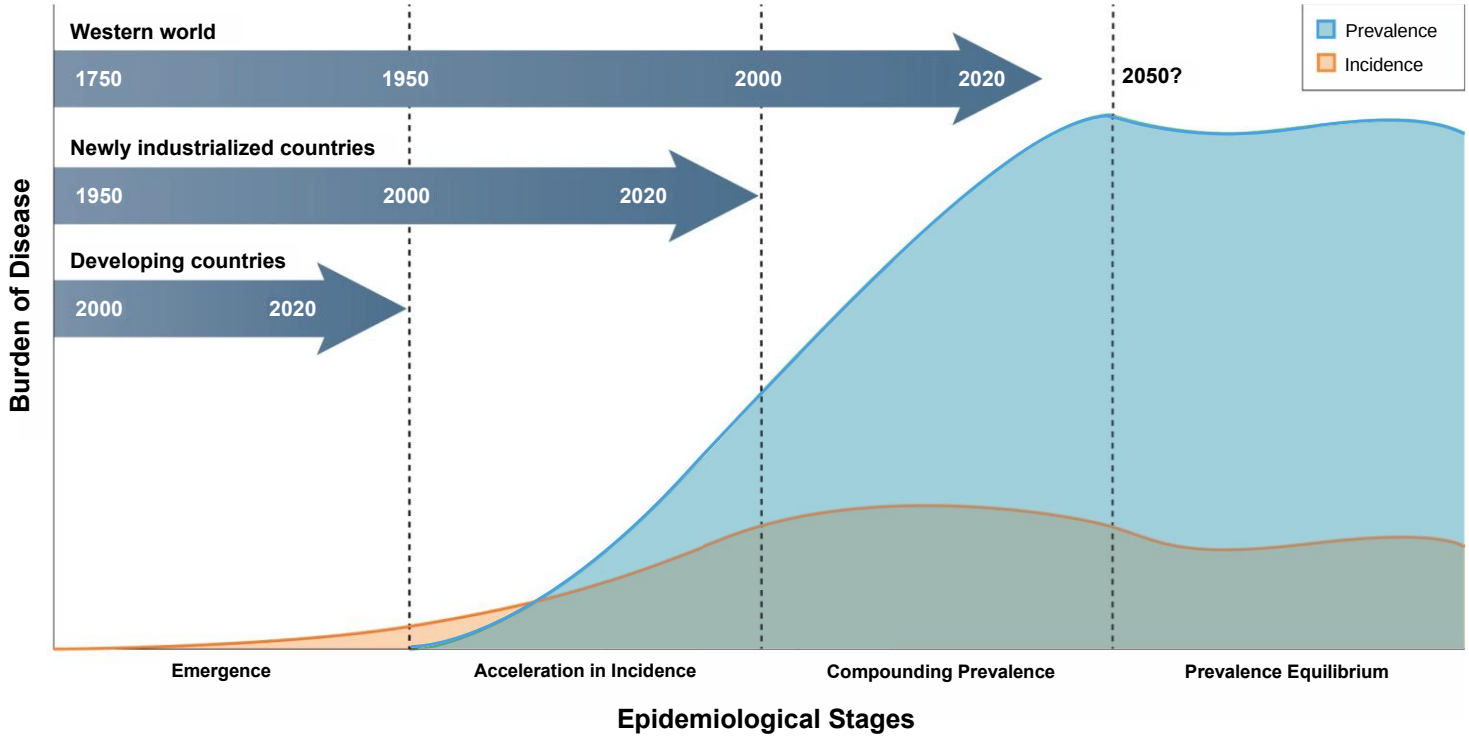
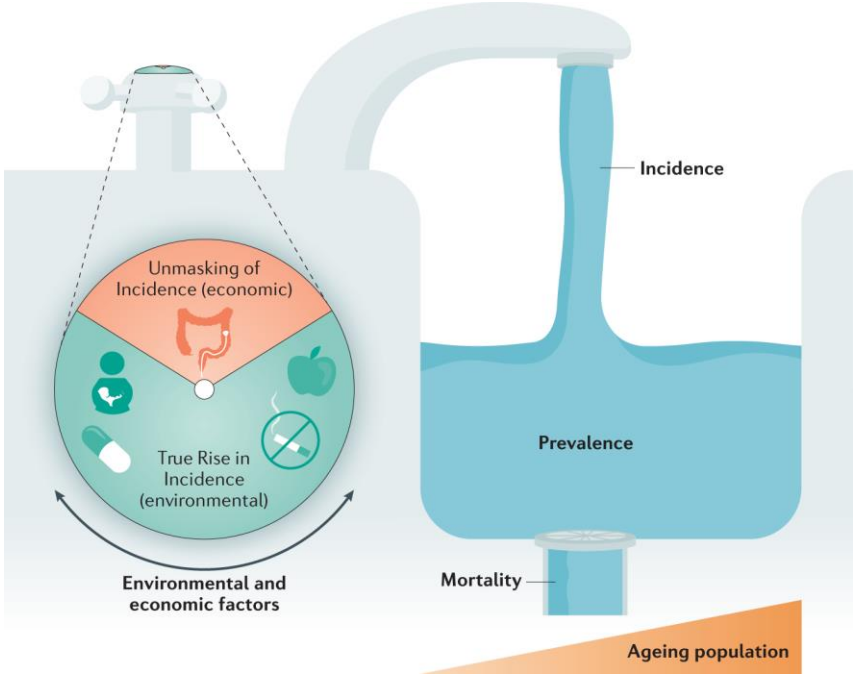
Disclosures

J. Casey Chapman, MD

- **Speaker/Advisor:** Abbvie, Pfizer, Bristol Meyers Squibb, Janssen, Medtronic, Takeda



Kaplan GG, Windsor JW. *Nat Rev Gastroenterol Hepatol*. 2021; 18: 56–66.



Kaplan GG, Windsor JW. *Nat Rev Gastroenterol Hepatol*. 2021; 18: 56–66.

CASE STUDY:

- 24 y/o gentleman with history of ileal CD, three ED visits and two hospitalizations for abdominal pain, nausea and vomiting. He is on biologic anti-TNF therapy with optimal drug levels and no antibody formation. He has had NO prior surgeries.

Labs:

Hemoglobin: 9.2	Ferritin: 39
CRP 8.6	TIBC: 300
Platelets: 552	Transferrin sat: 14%
Albumin: 3.2	

Prognosticators of Low Versus High-Risk Crohn's Disease

Low Risk

- Low Inflammatory Burden
  - Aphthous/small ulcers
  - Limited anatomic involvement
  - Nml CRP, nml albumin
- No Structural Damage
  - No fistula, abscess/stricture
  - No prior CD surgery
- No/little symptoms on QOL

High Risk

- High inflammatory Burden
  - Large/deep ulcers
  - UGI disease
  - Elevated CRP, low albumin ☑
- Structural damage
  - Stricturing, penetrating disease
  - Intestinal resection
  - Perianal disease/rectal disease
- High symptom burden/reduced QOL
- Age <30 ☑
- Smoker ☑

Others?

Feurestein et al. *Gastroenterol*. 2020; 158 (5): 1450-1461.

Anemia in IBD

- Most common nutrient deficiency in IBD
- Significant morbidity and poorly recognized
- Mean prevalence of IDA in severe IBD is 45% (Note: Rule rather than the exception in severe IBD?)

Prediction of severity?
Prediction of cost?

de la Morena F, Gisbert JP. *Esp Enferm Dig*. 2008; 100: 285-293.

Factors That Predict High Health Care Utilization and Costs for Patients With Inflammatory Bowel Diseases

Table 3. Sensitivity Analysis of the Unified Model Predicting High Charges at Different Cutoffs										
	***β*-coefficient value, *P* value**									
Variable	**50%tile (>$12,000)**		**60%tile (>$15,000)**		**75%tile (>$30,000)**		**90%tile (<$78,000)**		**95%tile (>$127,000)**	
Psychiatric Illness	0.31	.07	0.28	.11	**0.37**	**.04**	0.46	.06	0.64	.06
Minimal Hgb Level (per g/dL)	**–0.13**	**<.01**	**–0.15**	**<.01**	**–0.17**	**<.01**	**–0.18**	**<.01**	**–0.16**	**.03**
On Corticosteroids	**0.36**	**.02**	**0.37**	**.01**	**0.58**	**<.01**	**0.66**	**<.01**	**0.90**	**.02**
On Narcotics	**0.54**	**<.01**	**0.70**	**<.01**	**0.58**	**<.01**	0.42	.13	–0.26	.51
IBD-related Hospitalization	0.15	.10	0.12	.19	**0.289**	**<.01**	**0.26**	**.01**	**0.47**	**<.01**
AuROC (Validation Data Set)	**0.705**		**0.709**		**0.744**		**0.788**		**0.749**	
NOTE. Boldface indicated statistically significant values (P < .05). %tile, percentile										

# of outpatient visits inversely affected ED visits, hospitalization and total charges.

Limsrivilai et al. *Clinical Gastroenterology and Hepatology*. 2017; 15: 385-392.

Anemia in IBD: Clinical Decision Support Tool

Probability of bad outcomes in the upcoming year

In the last year:

Use of corticosteroids:

No

Use of narcotics:

No

Presence of psychiatric illness (depressive disorders, anxiety disorders, bipolar disorder:

No

Minimal hemoglobin value in the past year in g/dL:

9

Number of IBD-related hospitalization in the past year:

0

The probability of IBD-related hospitalization (%)

12.26

The probability of emergency department visit (%)

15.78

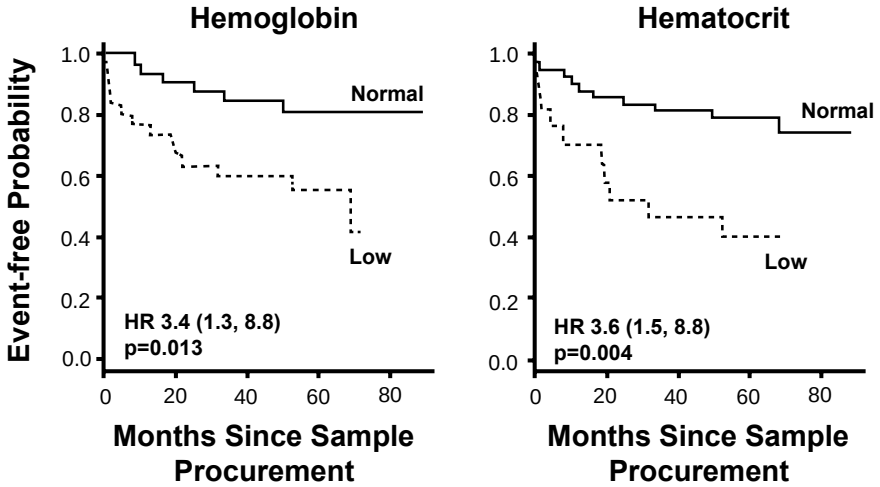
The probability of high total charges (>$30,000) (%)

17.31

https://www.pathology.med.umich.edu/shiny/.

Anemia in IBD: Cost and Morbidity

- Substantial impact on quality of life
  - QoL in anemic IBD patients may be as low as in anemic patients with advanced cancer.
  - Equally as impactful to QoL as abdominal pain and diarrhea.
  - Predictor of outcome.



*Predictor of fistula, stenosis or surgery

Gasche C et al. *Gut*. 2004; 53: 1190-1197; Leitgeb C et al. *Cancer*. 1994; 73: 2535-254;
Rieder F et al. *PLoS One*. 2014; 9: e104706.

Anemia in IBD: Discordant Clinical Questions

Definitions

1. Nml Hg low serum iron
2. Low Hg with microcytosis
3. Low serum iron and increased TIBC
4. Iron sat <10 %
5. High transferrin with low ferritin
6. Low iron, low saturation and low ferritin
7. Acute inflammation and high TIBC

Clinical Recognition

Recognition

- Uncertainty in defining anemia in patients with IBD
- Lack of awareness on non-anemic iron deficiency
- Perception of anemia is secondary to importance of IBD activity

Treatment

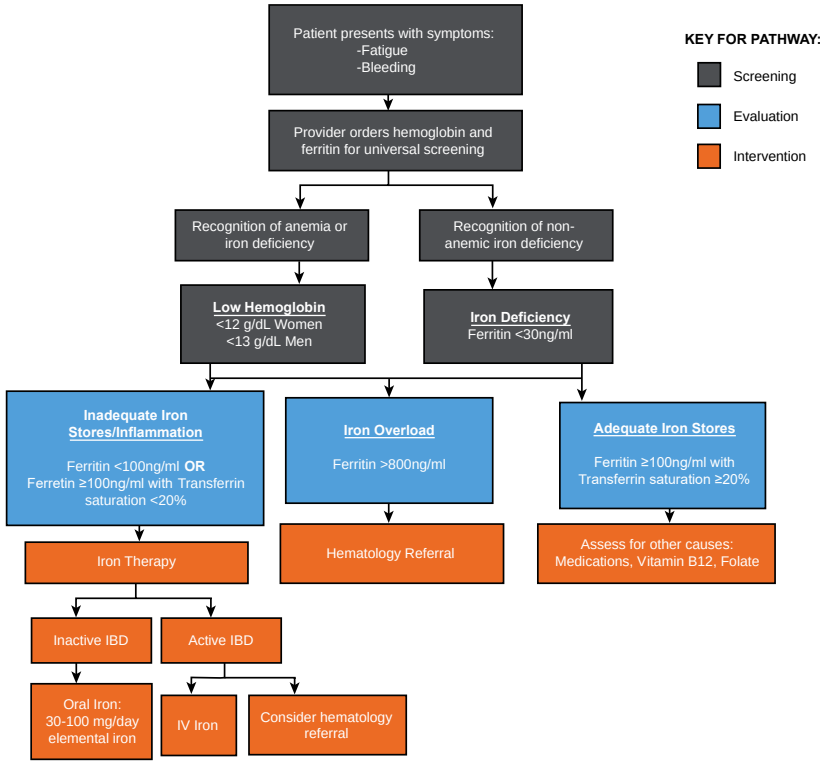
- Variations in thresholds
- Variations in decision of oral v. parenteral iron
- Lack of comfort with parenteral iron

Follow Up

- Timing and monitoring

Hau et al. *Inflamm Bowel Dis*. 2017; 23: 35-43.

Anemia in IBD: Proposed Treatment

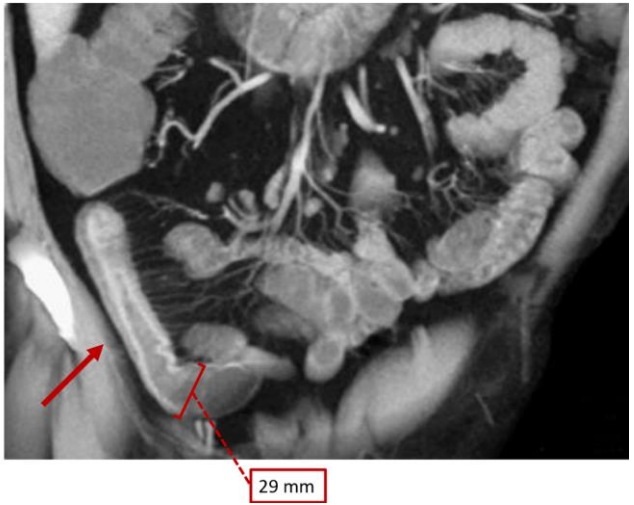


Hau et al. *Inflamm Bowel Dis*. 2017; 23: 35-43.

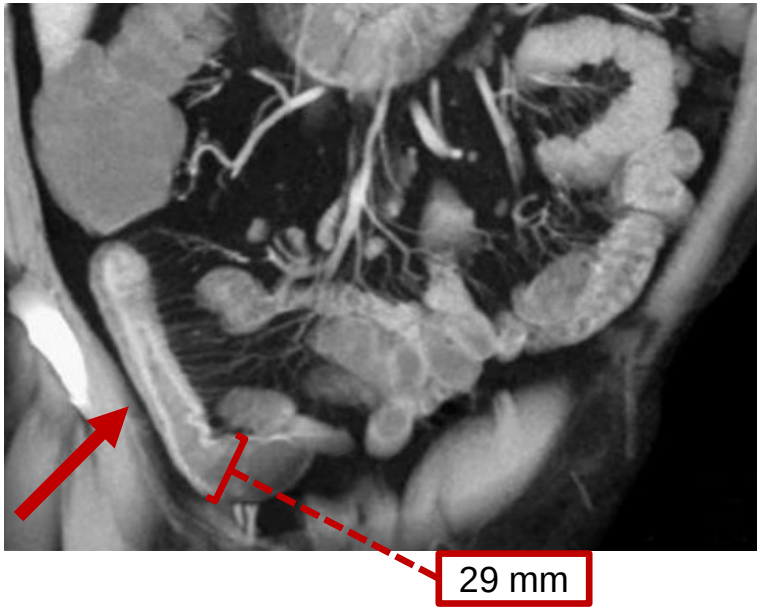
Back to the Case Study:

- 24 y/o gentleman with history of ileal CD, three ED visits and two hospitalizations for abdominal pain, nausea and vomiting. He is on biologic anti-TNF therapy with optimal drug levels and no antibody formation. He has had NO prior surgeries.

Imaging: CT: 11 cm of ileal inflammation with mural hyperenhancement. Proximal dilation segment up to 29 mm to max diameter. Wall thickness at 9 mm at maximum thickness.



CT: 11 cm of ileal inflammation with mural hyperenhancement. Proximal dilation segment up to 29 mm to max diameter. Wall thickness at 9 mm at maximum thickness.



Half of patients require surgery within the first 10 years of diagnosis.

CT and MR are the best methods to assess for structuring disease.

http://rad.desk.nl/en/p5289d9a1932db/crohns-disease.html.

Risk Stratification for Surgery in Stricturing Ileal Crohn's Disease: The BACARDI Risk Model

- Difficult to predict need and timing of surgery
- 1803 XSI on 957 patients
- All charts were reviewed for demographic, biochemical, imaging, genetic and endoscopic factors.
- Ileal Stricturing CD (IS-CD) was diagnosed in 235 patients and 161 required surgery (61%).
- Five factors remains significantly associated with the need for surgery.

Bossuyt et al. *J Crohns and Colitis.* 2018; 12 (1): 32-38; Masselli et al. *Abdom Imaging*. 2013. 38, 249-259.

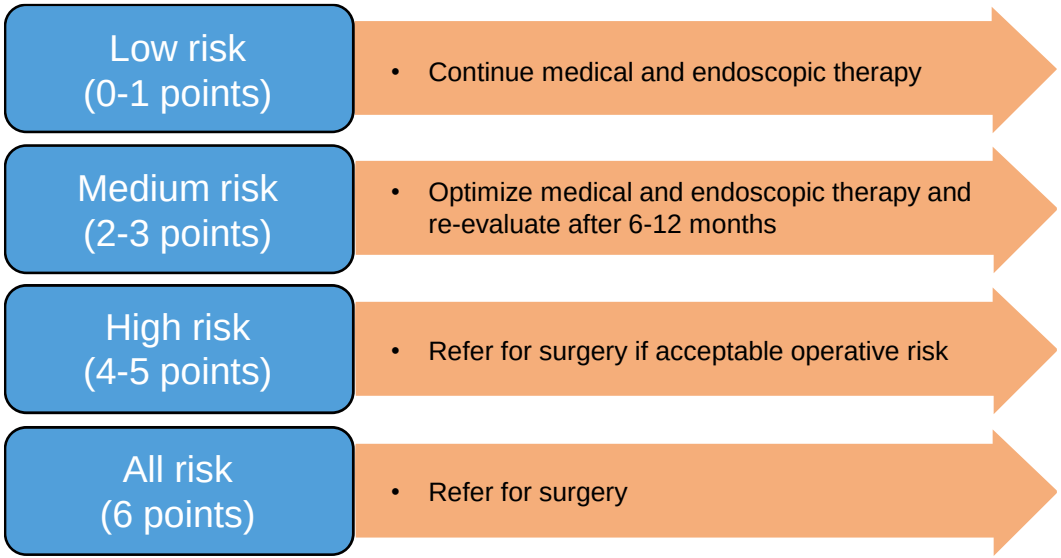
BACARDI Risk Model

- **B**3 Montreal class, **A**nti-TNF exposure, ***CAR****D15/NOD2* mutation, **D**ilation of the prestenotic segment, and Inflammation [CRP > 11 mg/L] at diagnosis of stricturing CD.

	Hazard Ratio	Confidence Interval	*p*-Value*	
CRP >11mg/L at diagnosis structuring CD	1.53	1.05–2.24	0.026	1 point
Previous/current anti-TNF therapy	1.44	1.00–2.06	0.048	1 point
Associate Montreal B3 phenotype	1.58	1.06–2.36	0.023	1 point
Heterozygous mutation *NOD2* snp rs2066844	1.51	1.02–2.23	0.038	1 point
Prestenotic dilation	2.05	1.22–3.45	0.007	2 points

J Crohns Colitis. 2018; 12 (1): 32-38.

BACARDI Risk Model

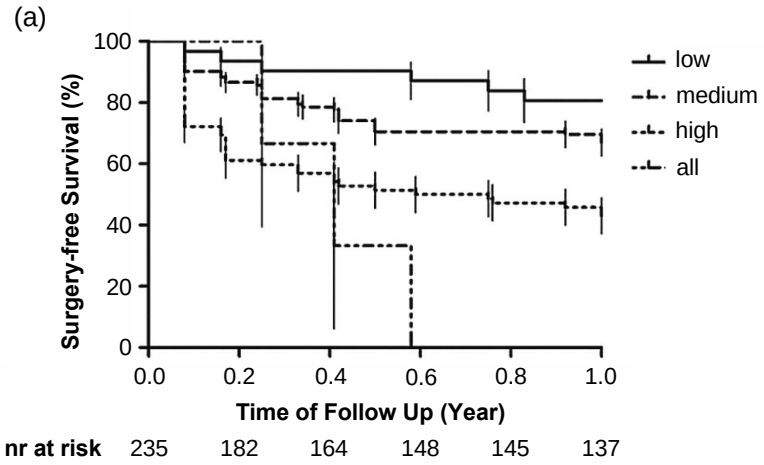


J Crohns Colitis. 2018; 12 (1): 32-38.

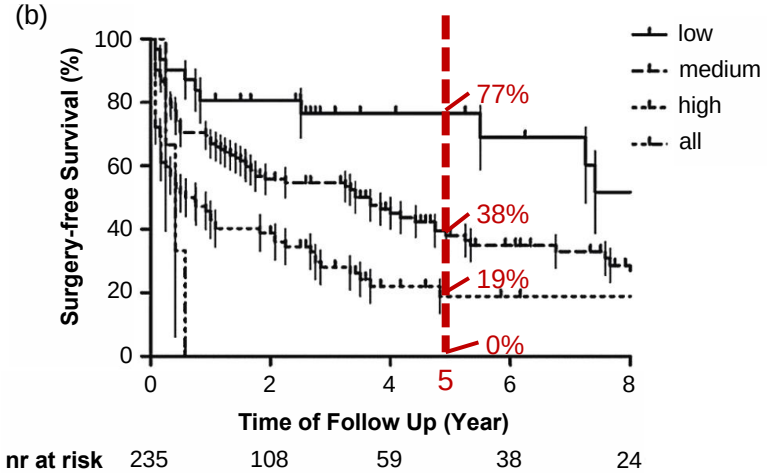
BACARDI Risk Model

- Estimates of the surgery-free survival time for Crohn's disease [CD] patients with structuring on XSI

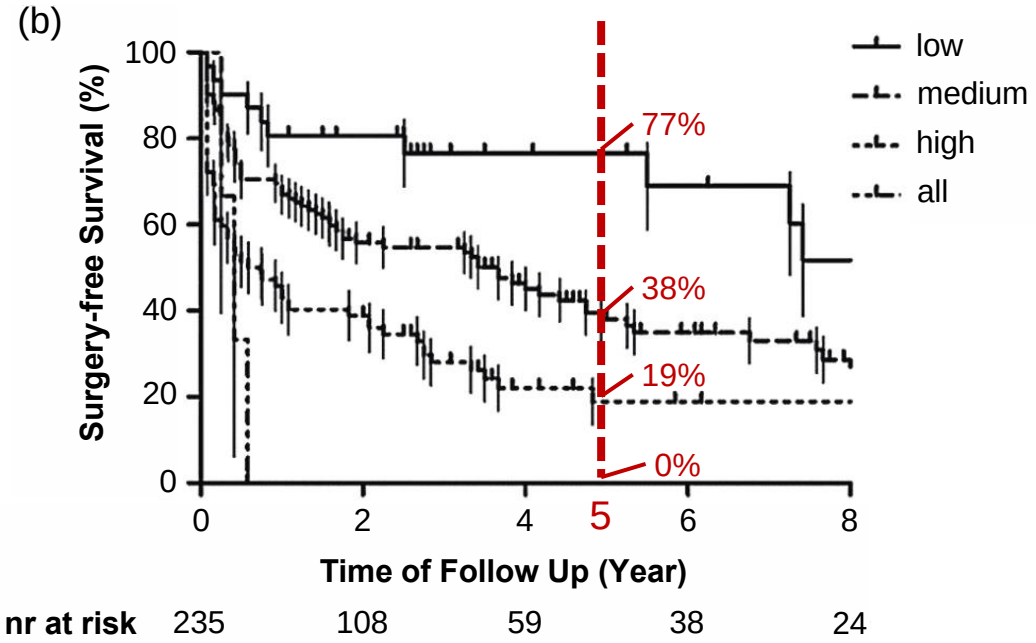
One year



Eight years



J Crohns Colitis. 2018; 12 (1): 32-38.


(b)
Surgery-free Survival (%)
100
80
60
40
20
0
0
2
4
5
6
8
Time of Follow Up (Year)
77%
38%
19%
0%
low
medium
high
all
nr at risk
235
108
59
38
24

Efficacy of Adalimumab in Patients With Crohn's Disease and Symptomatic Small Bowel Stricture: A Multicentre, Prospective, Observational Cohort (CREOLE) Study

OBJECTIVE: Aim to identify factors predicting successful treatment of symptomatic small bowel strictures (SBSS).

METHODS: Patients underwent MRE then received standard dose adalimumab.

- Success defined as continuation 24 weeks without:

  1. CS after 8 weeks 2. Endoscopic dilation 3. Bowel Resection

- Secondary endpoint: Success after week 24 without dilation or surgery

Bouhnik Y et al. *Gut*. 2018; 67 (1): 53-60.

Creole Results:

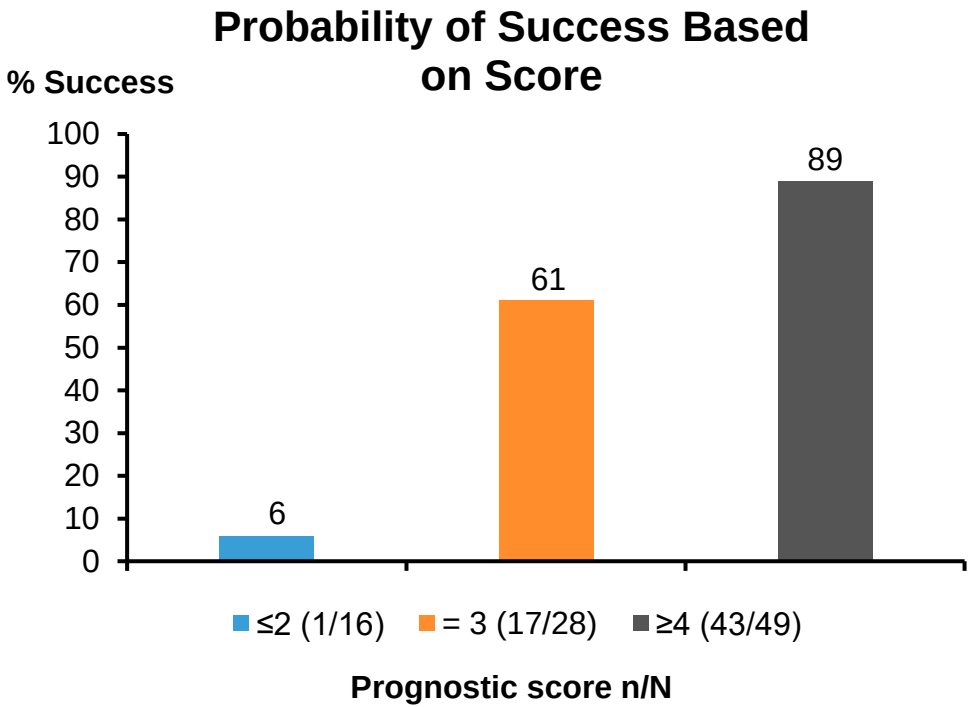
64% reached week 24 and success was associated with:

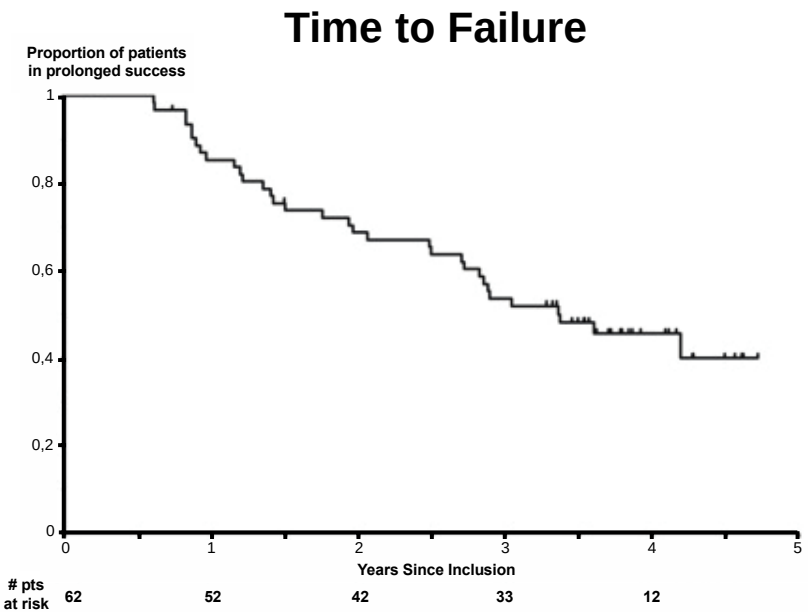
Table 4. Estimated and final coefficients of the clinic-radiological prognostic score to be applied to the independent factors associated with a high rate of success (n=93)

Factor/Group with a high rate of success	Coefficient estimate±SE	OR of success estimate (95% CI)	p Value	Points, n
Immunosuppressive treatment/yes	1.23±0.62	3.42 (1.01–11.57)	0.040	1
Crohn's disease obstructive score />4	1.25±0.65	3.48 (0.97–12.46)	0.046	1
Duration obstructive symptoms (weeks)/<5	1.79±0.81	6.00 (1.23–29.17)	0.016	1
Length of stricture <12 cm	1.80±0.67	6.04 (1.61–22.67)	0.0042	1
Maximal small bowel diameter proximal to stricture(s) (mm)/(18-29)	1.99±0.68	7.32 (1.92–27.85)	0.0013	1
Enhancement on delayed T1-weighted sequence/marked	1.78±0.66	5.92 (1.63–21.50)	0.0034	1
Fistula/no	1.55±0.76	4.72 (1.05 to 21.11)	0.035	1

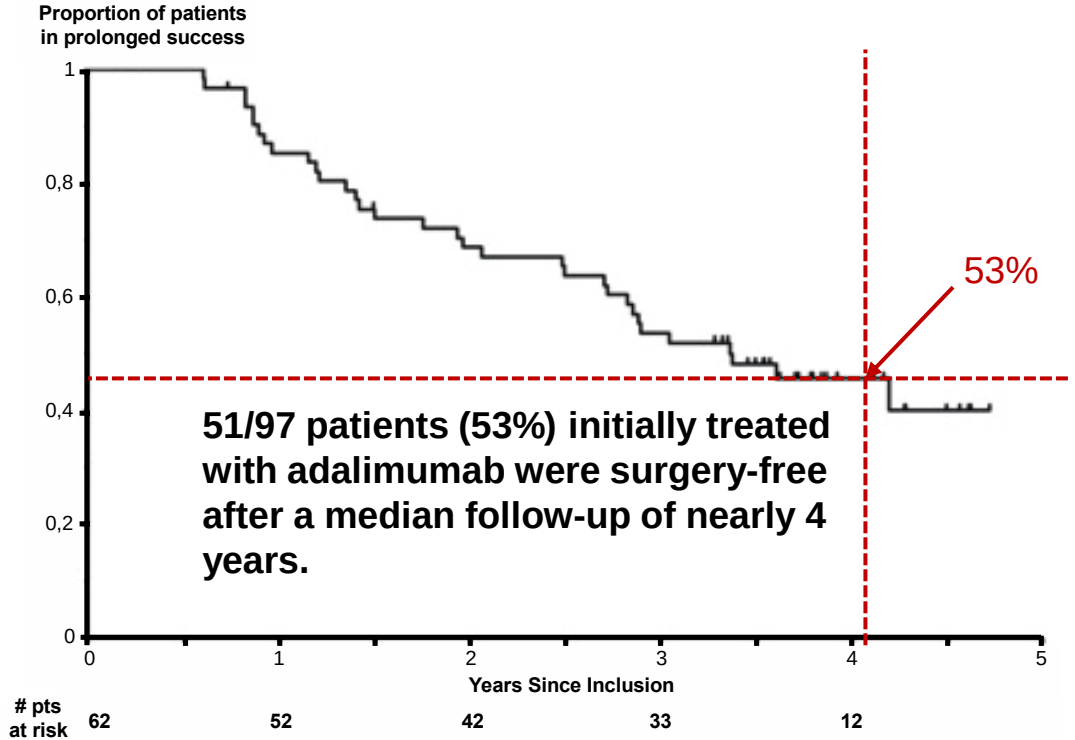
Bouhnik Y et al. *Gut*. 2018; 67 (1): 53-60.

CREOLE Results:





Bouhnik Y et al. *Gut*. 2018; 67 (1): 53-60.



Bouhnik Y et al. *Gut*. 2018; 67 (1): 53-60.

Post Operative Recurrence

Rutgeert's Score

Endoscopic Score	Definition
i0	No lesions
i1	≤5 aphthous lesions
i2	>5 aphthous lesions with normal mucosa between the lesions or skip areas of larger lesions or lesions confined to the ileocolonic anastomosis
i3	Diffuse aphthous ileitis with diffusely inflamed mucosa
i4	Diffuse inflammation with already larger ulcers, nodules and/or narrowing

- **i0** (no inflammation) or **i1** considered 'low-risk' patients , 80-85% will remain asymptomatic (on no Crohn's disease medications) for 3 years after ileocolonic resection.
- **i3** (diffuse aphthous ileitis) or **i4** (diffuse inflammation with already larger ulcers, nodules and/or narrowing), only 10% are likely to remain asymptomatic for the 3 years following their resection.

Hashash J. *Expert Rev Gastroenterol Hepatol*. 2012; 6 (5): 637-648.

Types of Anastomosis

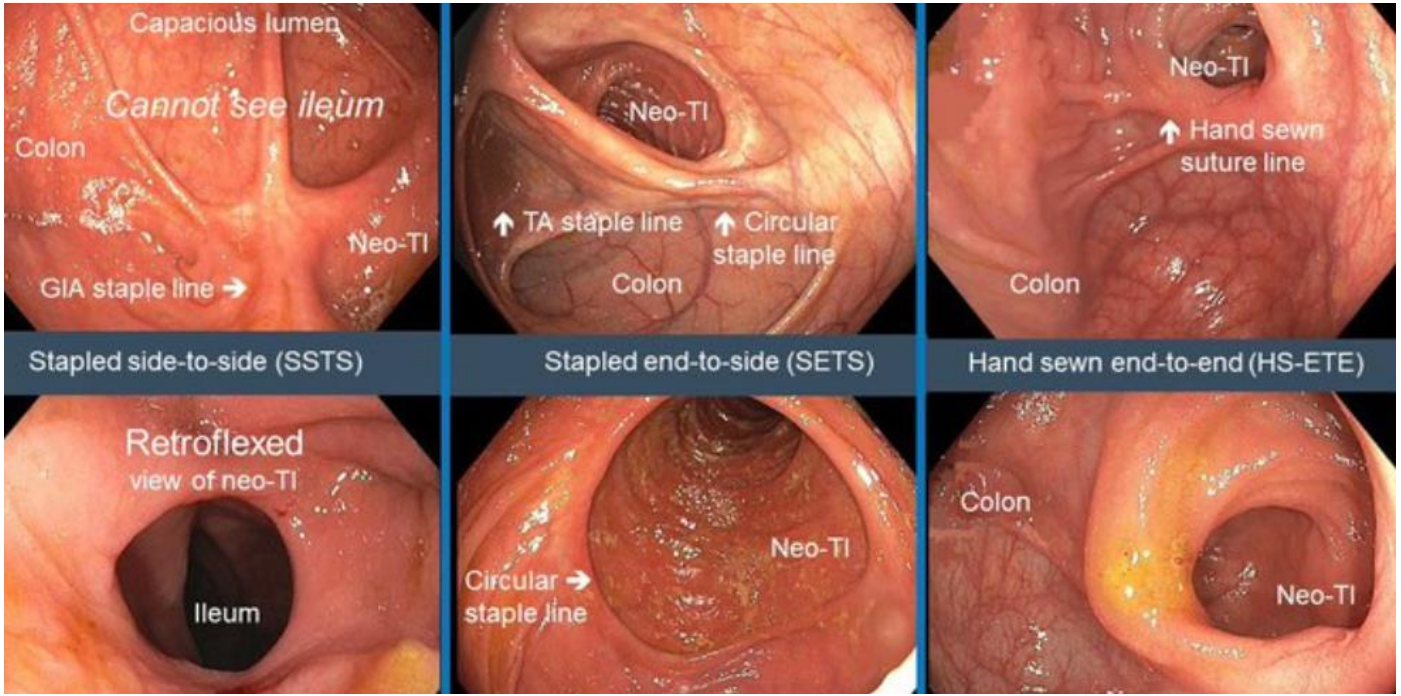


Photo courtesy Dr. JP Achkar

A New Antimesenteric Functional End-to-End Handsewn Anastomosis: Surgical Prevention of Anastomotic Recurrence in Crohn's Disease

BACKGROUND: Recurrence of Crohn's disease usually occurs at anastomotic sites.

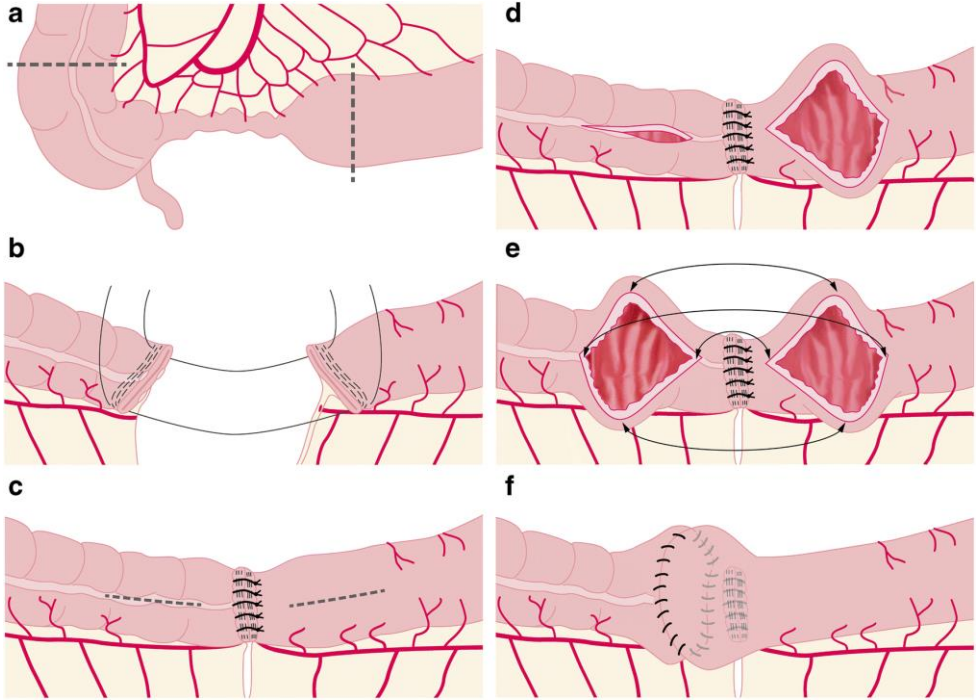
OBJECTIVE: A new anastomosis technique (Kono-S anastomosis) designed to minimize anastomotic restenosis was compared with conventional anastomoses.

RESULTS: The median endoscopic recurrence score in group S was significantly lower than that in group C (2.6 vs 3.4; P = .008).

- This study was limited by its historical retrospective nature

Kono et al. *Disease of the Colon & Rectum*. 2011; 54 (5): 586-592.

Kono-S Technique



a. Mesentery of the IC region to be excised is divided at the mesenteric wall of the bowel.

b. Intestine transected with staple cutter at 90 degree to mesentery.

c. Staple lines sutured together.

d. Longitudinal enterotomies 1 cm from staple column

e. Anastomosis then created transversely in a hand-sewn fashion

Horisberger K et al. *Archives of Surgery*. 2021; 406: 1173-1180.

Surgical Prevention of Anastomotic Recurrence by Excluding Mesentery in Crohn's Disease: The SuPREMe-CD Study – A Randomized Clinical Trial

BACKGROUND: Antimesenteric functional end to end, hand-sewn ileocolic anastomosis(Kono-S) has shown significant reduction in endoscopic recurrence rate in Crohn's disease(CD).

OBJECTIVE: Provide Randomized Control Data comparing Kono-S anastomosis and stapled ileocolic side-to-side anastomosis.

Luglio et al. *Annals of Surgery*. 2020; 272 (2): 210-217.

Surgical Prevention of Anastomotic Recurrence by Excluding Mesentery in Crohn's Disease: The SuPREMe-CD Study – A Randomized Clinical Trial

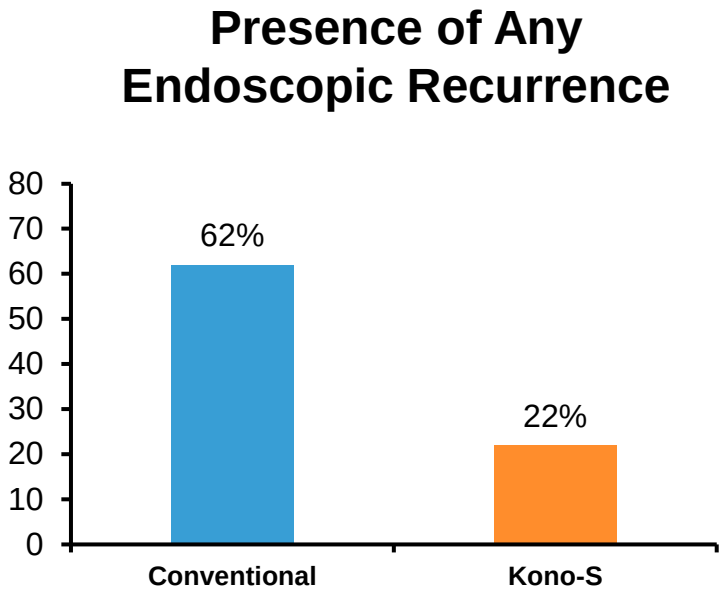
METHODS: Randomized controlled trial enrolling to undergo either Kono -S group or the Conventional Group

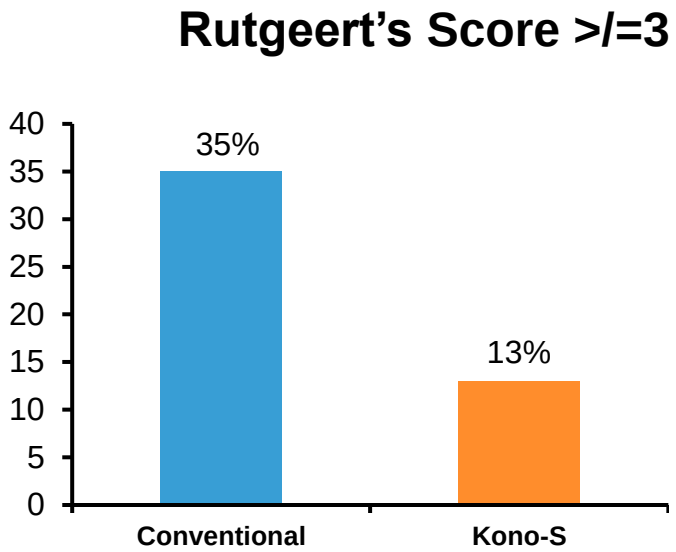
- Primary endpoint: Endoscopic Recurrence(ER)(Rutgeert's score >/= i2 after 6 months
- Secondary endpoints: Clinical Recurrence(CR) after 12 and 24 months, ER after 18 months and surgical recurrence(SR) after 24 months

Luglio et al. *Annals of Surgery*. 2020; 272 (2): 210-217.

Post-Op ENDOSCOPIC Recurrence

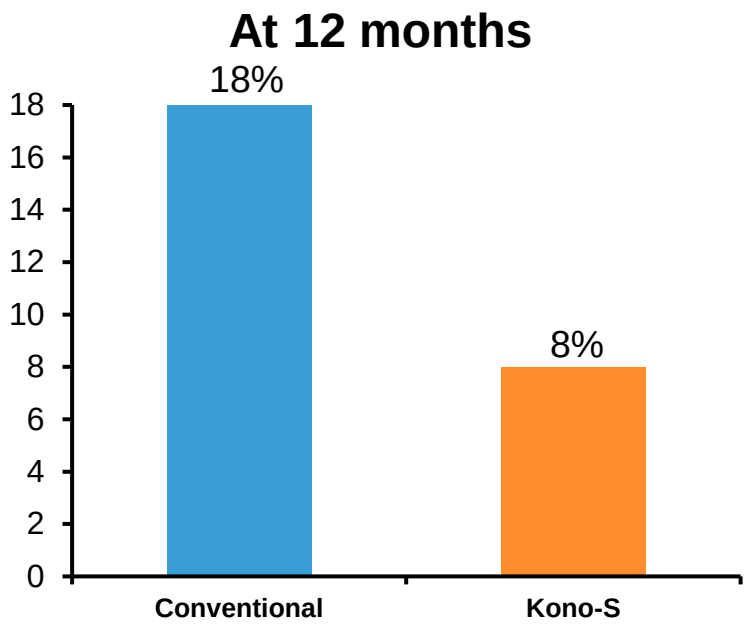
At 6 Months

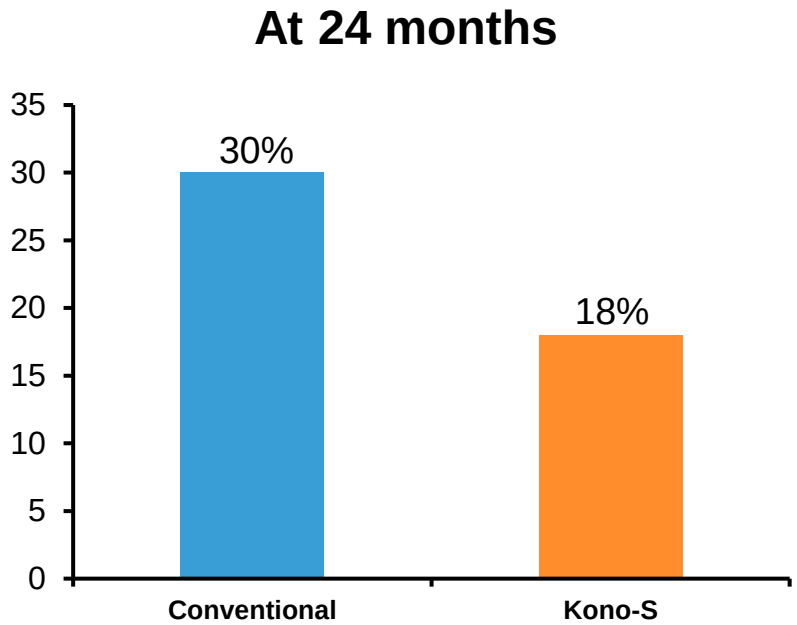




Luglio et al. *Annals of Surgery*. 2020; 272 (2): 210-217.

Post-Op CLINICAL Recurrence





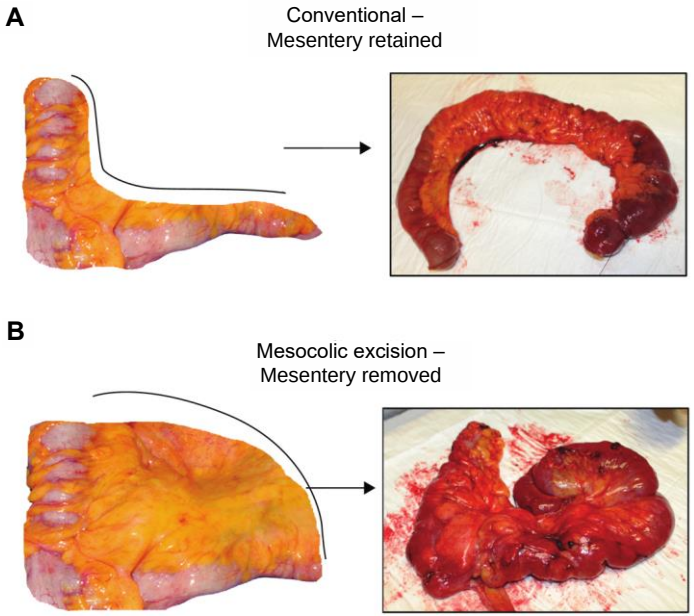
Luglio et al. *Annals of Surgery*. 2020; 272 (2): 210-217.

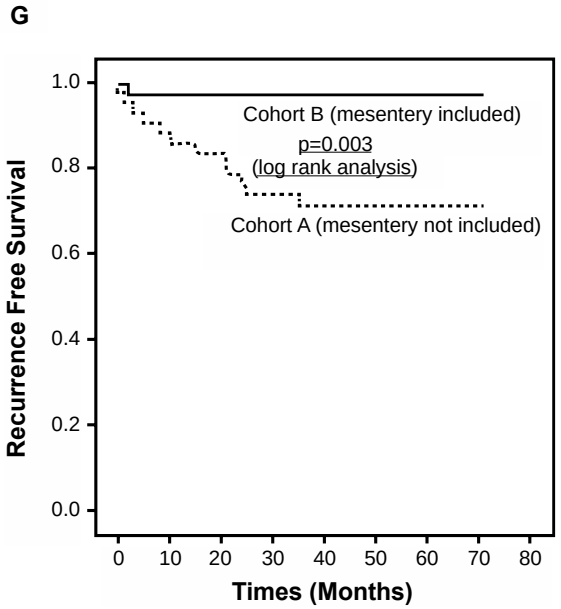
Kono-S Anastomosis in Crohn's Disease

Outcome	Kono-S	(% on Postop ant-TNF)	End-End	(% on Post op anti-TNF)
More Surgery	3	49	24	44
"Median Rutgeerts"	2.6	42	3.4	16
Re-Operation	3	42	26	16
Stenosis	0	42	15	16

Shimada N et al. *Journal of Gastrointestinal Surgery*. 2019; 23: 312-3199;
Kono T et al. *J Gastrointest Surg*. 2016; 20 (4): 783-90; Kono T et al. *Dis colon Rectum*. 2011; 54 (5): 586-92.

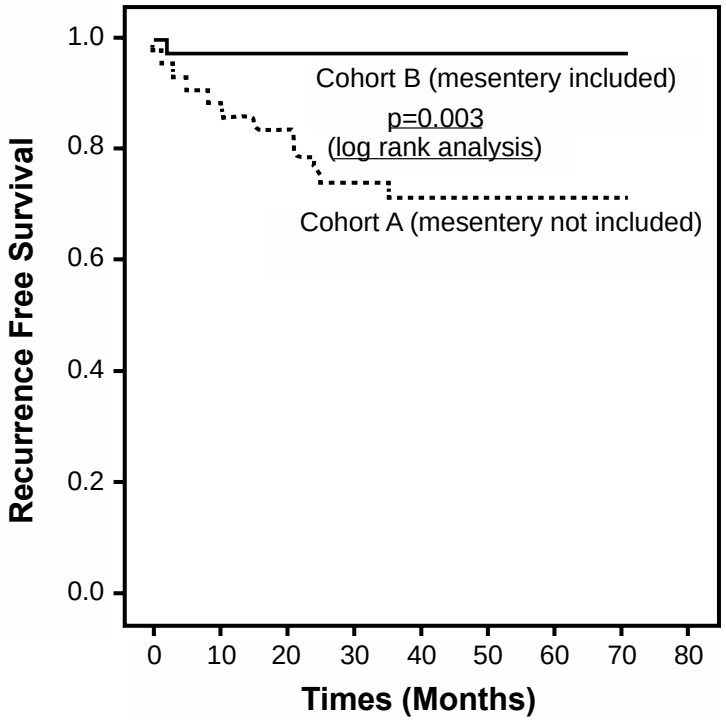
Inclusion of the Mesentery in Ileocolic Resection for Crohn's Disease Is Associated With Reduced Surgical Recurrence





Coffey et al. *J Crohns Colitis*. 2018; 12(10): 1139–1150.

G


1.0
0.8
0.6
0.4
0.2
0.0
Recurrence Free Survival
Cohort B (mesentery included)
p=0.003
(log rank analysis)
Cohort A (mesentery not included)
0
10
20
30
40
50
60
70
80
Times (Months)

In Summary…

- Two of the most common complications in IBD are iron deficiency anemia and fibrostenotic Crohn's disease.
- IDA needs to be clearly defined and screened for as is affects cost and quality of life.
  - Assess for fatigue and bleeding as screening mechanism along with low Hg
  - Consider oral iron for those without active inflammation.
- Consider surgery in those patients with stricture:
  - >12cm
  - Prestenotic dilation 18-29mm
  - B3 Montreal classification
- Consider a discussion with your surgeon regarding new modalities of surgical intervention including Kono-S and mesenteric resection.