Microscopic colitis, Colonic ischeamia, Diversion colitis

The other colopathies

Shaun-Ray Temmers

Outline

- Microscopic Colitis
- Diversion Colitis
- Colon ischaemia
  - Acute ischaemia not chronic mesenteric ischaemia

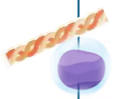
What is microscopic colitis(MC)

Type of inflammatory bowel disease that involves chronic inflammation on a smaller scale than Crohn's disease and ulcerative colitis, its not visible to the naked eye ∴ histology is essential

Three types

Collagenous colitis (CC) – Excess collagen, little lymphocyte

Lymphocytic colitis (LC) – Excess lymphocytes, little collagen



Microscopic colitis incomplete (MCi) – Excess of collagen & lymphocytes, but not enough

Just how rare is MC?

- Polled incidence 11.4 cases per 100000[1]
- Frequency 12.8%
- Higher in elderly (>60years)[2]
  - ➢CC 64.5 years
  - ➢LC 62.2 years

  - ➢Last decade however ~25% of patients younger than 45 years[3]
  - ➢Case reports of MC in children

MC should be considered in any person with chronic watery diarrhoea
Bristol Stool scale, type 7

1. Miehlke S et al; UEGJ 2020
2. Weimers P et al; JCC 2020
3. Munch A et al; UEGE 2021

Risk factors for MC

Smoking

- Up to 40%
- CC >LC
- Current > Former OR 2.9 vs 1.6
- ?cessation

Gender

- Female > Male, OR 2.52

Drugs

- Proton pump inhibitors (PPI)
- Non-steroidal anti-inflammatories
- Selective serotonin uptake inhibitors
- Exposure Continuous 4-12months
- Not causal rather trigger

1. Mielhke et al; UEGJ 2020

Are there any association?

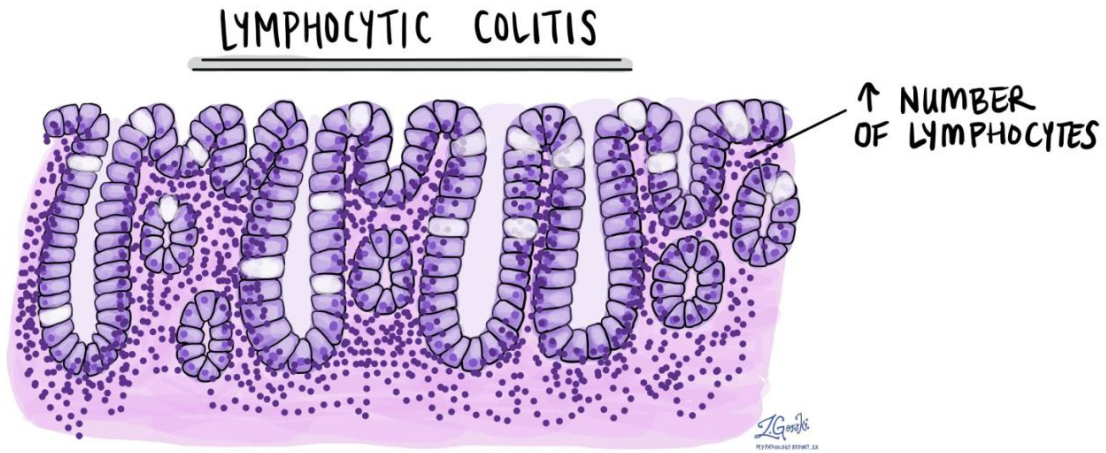
- 30-40% of MC patient have concomitant autoimmune disease
- No autoantibody has been identified
- HLA-DQ3,1; HLA-DR3-DQ2 haplotype

- Coeliacs disease 2%-20%
- Autoimmune thyroid disease 10%-20%
- Sjögren's disease
- Diabetes Mellitus

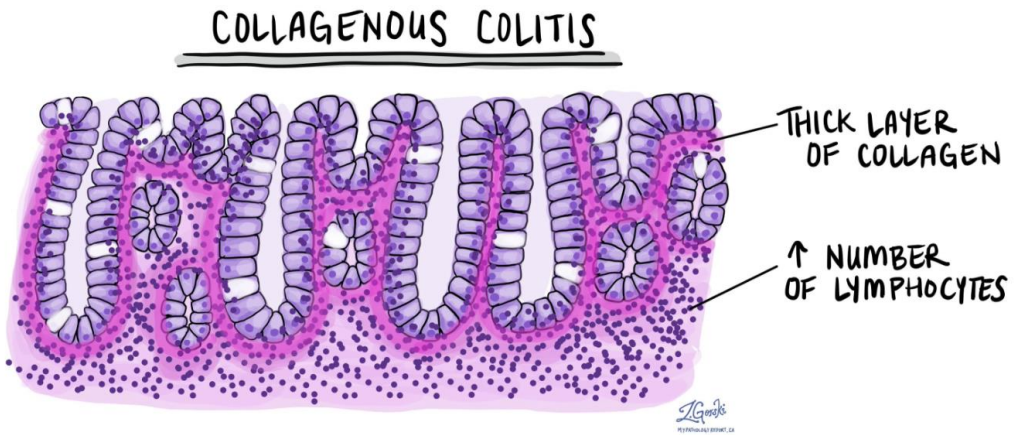
- Conversely no association with autoimmune hepatitis as seen in IBD

1. Bohr et al; Clinical and experimental gastroenterology 2014
2. Mielhke et al; UEGJ 2020

Histological criteria



↑ IEL ≥ 20 per 100 surface epithelial cells, ↑ inflammatory infiltrate in LP & thickened collagenous band <10mm



Thickened subepithelial collagenous band > 10mm with ↑ intraepithelial lymphocytes (IEL) in the lamina propria

Relationship between IBS and MC

- 44% of patients with MC fulfilled criteria for IBS: LC > CC[1]
- 9% IBS-D, had MC[2]

Clinical history	Irritable bowel syndrome (IBS)	Microscopic colitis
First occurrence of disease	< 50 years	>50years
Stool consistency	Soft, variable or hard	Watery/soft
Stool Frequency	Vary from day to day	High and more consistent
Nocturnal diarrhoea	Very unlikely	possible
Feeling of incomplete bowel evacuation	Common	No
Feeling of fullness/bloating	Common	Rare
Accompanying autoimmune disease	Rare	Common

1. Guagnozzi et al; APT 2016
2. Kamp EJ et al; CGH 2016
3. Munch et al; UEGE 2021

What defines quality of life when setting a treatment target?

- Chronic diarrhoea is ≥ 3 defecations/day for ≥ 4 weeks
- MC = watery diarrhoea (Bristol type 7) ∴ consistency better marker of activity

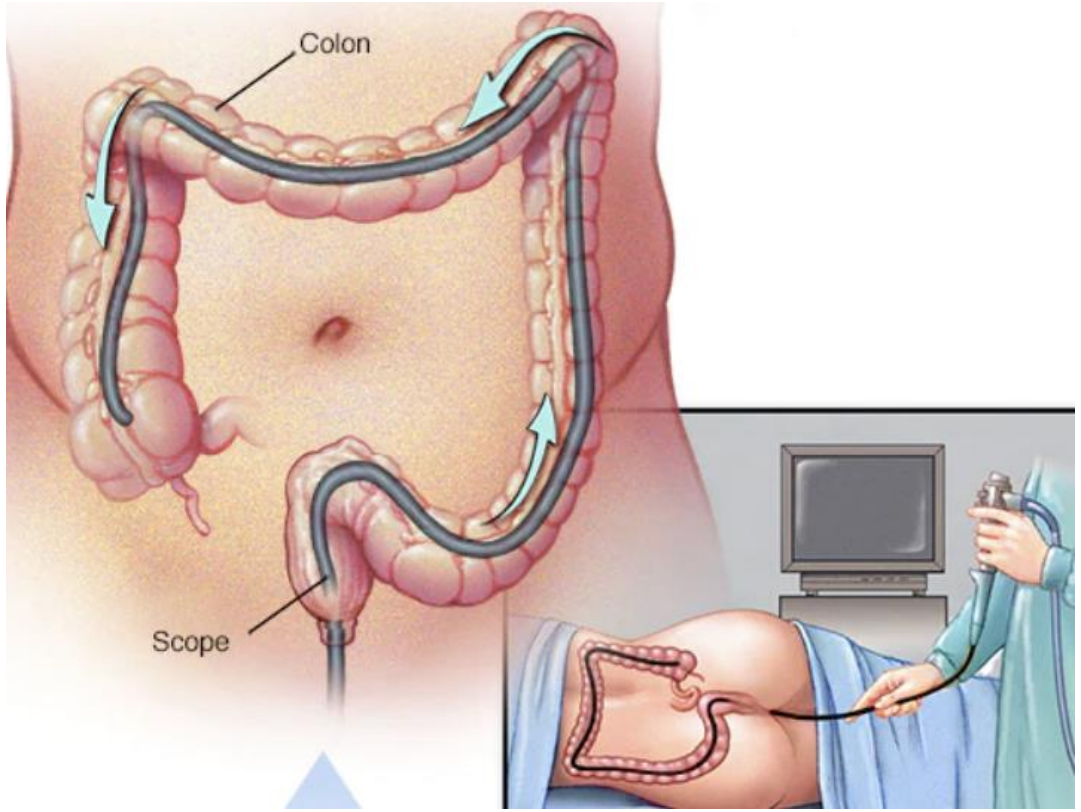
Hjortswang criteria

	Stools per day		Watery stools per day
Clinical remission	<3	And	<1
Clinical activity	≥3	Or	≥1

1. Hjortsawng et al; IBD 2009

Role of colonoscopy

- Often normal
- Some non-specific findings has been reported
- Biopsy – ideally for right and left colon



1. Mielhlke S et al; Gastroenterology 2007

Budesonide

- 6-8 weeks, 9mg/day
  - 81% clinical response compare to 36% - RR 2.98[1]
  - Histological response 78% - RR 2.68
  - Gastrointestinal quality of life index(GIQLI) – significant improvement
  - Results similar efficacy for LC & CC

- Maintenance 6mg/day
  - 68% maintained clinical response RR 3.30, 6 months[2]

- Budesonide, synthetic 95% metabolized by first past effect ∴ little to no systemic absorption
- Expensive est. cost ~ R1450/28days

1. Mielhlke S et al; Gastroenterology 2007
2. Kafil TS et al; CDSR 2017

Other adjuncts

Bile acid binders

- Bile acid diarrhoea coexist with MC
- CR in MC when treated with cholestyramine

Loperamide

- Efficacy extrapolated from data on effects on chronic diarrhoea
- Recommendation for mild disease
- Several cohorts with loperamide as adjunct showed improvement in MC

1. Mielhke et al; UEGJ 2020

Nutrition & Foods

- Many recommendation for elimination on “proinflammatory foods”
  - ➢Based on observational studies in IBD
  - ➢Gluten free only if dual diagnosis of coeliacs disease
  - ➢**B**anana **R**ice **A**pplesauce **T**oast diet for non-responders[1,2]
  - ➢Probiotics some improvement[3] – No recommendation
    - ➢ Lactobicillus acidophillus; Bifidobacterium animalis
  - ➢Boswellia serrata extract[4] – mix results

1. Fasil R et al; IJG 1994
2. Schiller LR et al; Lancet 2000
3. Wildt S et al; IBD 2006
4. Madish A et al; IJCD 2007

Is Faecal calprotectin useful in MC?

- FC can indicate active inflammation in bowel
  - ➢ Mainly released by neutrophils – cells are not involved in MC pathogen
- Signal that FC was ↑ compare to organic or IBS[1]
  - ➢ Predictive value was low
- Wildt[2] et al showed that 50% of patient with active MC had a FC >100mcg/L

Table 1 Results of faecal calprotectin and lactoferrin measurements in patients with active and quiescent collagenous colitis and healthy controls

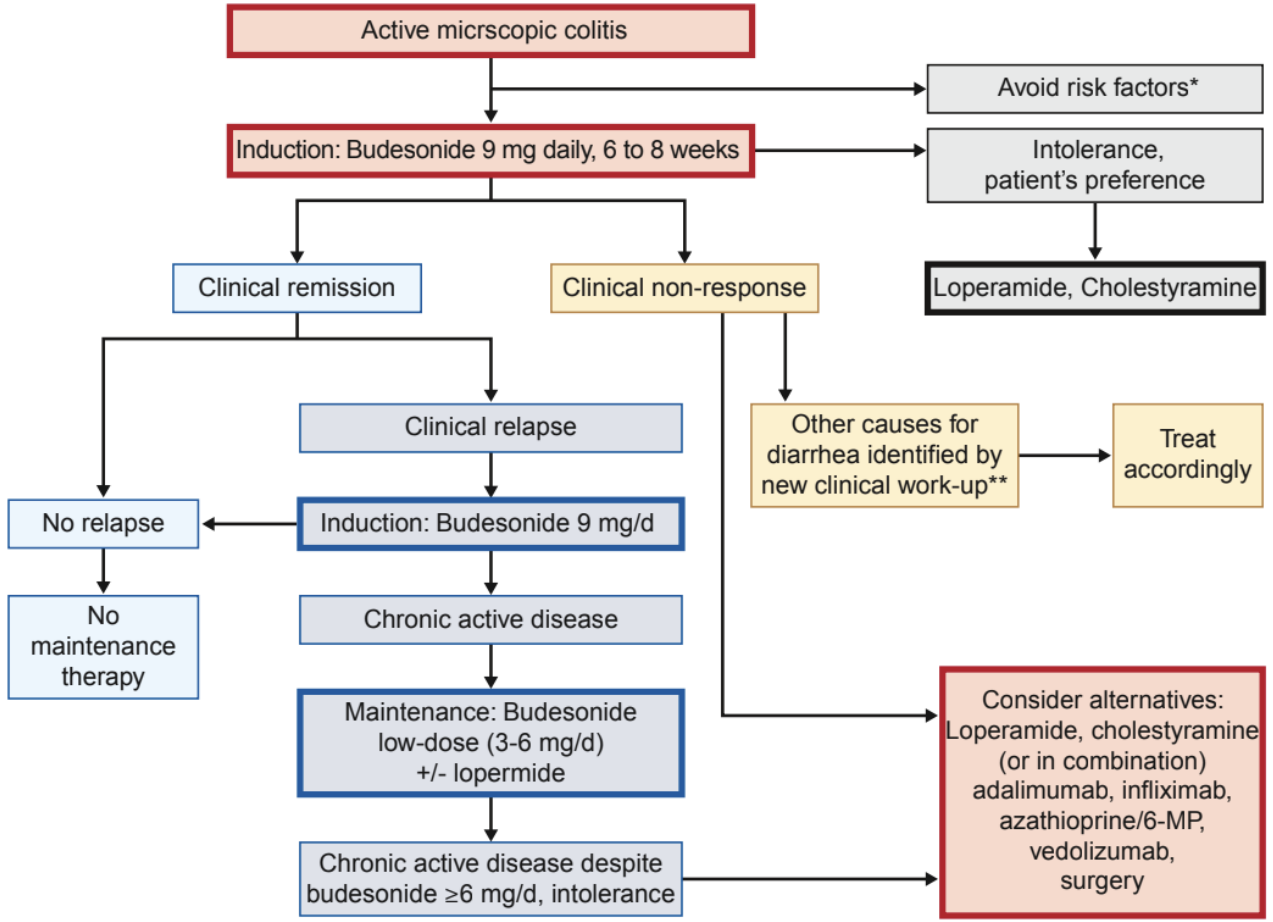
	Active disease, $n=21$	Remission, $n=12$	Controls, $n=13$
Bowel frequency/day	5 (3–13)	1 (1–2)	1 (0–2)
Bristol scale; score	6.5 (5–7)	3.5 (1.5–4)	NA
Faecal calprotectin (μg/g)	80 (6.25–1899)[a,b]	26 (6.25–340)[c]	6.25 (6.25–99)
Faecal lactoferrin; no. positive tests	1	0	NA

Medians and ranges.
[a]Active disease versus remission, $P=0.025$ (Wilcoxon).
[b]Active disease versus controls, $P=0.002$ (Mann–Whitney).
[c]Remission versus controls, $P=0.035$ (Mann–Whitney).
NA, not applicable/analysed.

1. Mielhke et al; UEGJ 2020
2. Wildt et al; EJGH 2007

Proposed management strategies

- >90% of patient will have some response to budesonide/prednisone
- Consider adjuncts e.g Loperamide and bile acid binders
- Once relapse occurs, maintenance therapy is indicated
- Response based on CR, not recommended to check histology
- Those that have failed response to consider alternatives on individualized basis

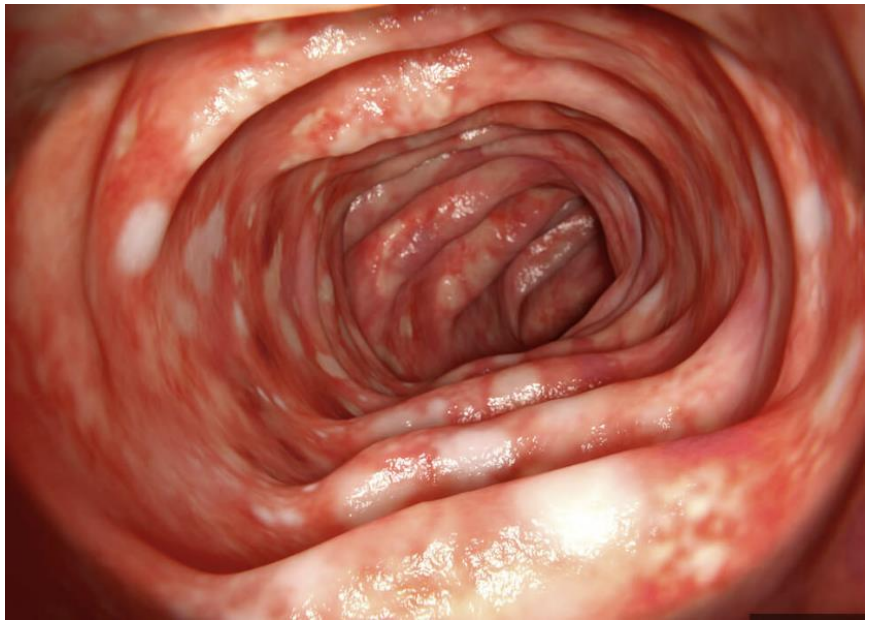


1. Mielhke et al; UEGJ 2020


Microscopic
Colitis
Condensed
Version
By
Wayne Persky

Diversion Colitis (DC)

Inflammation of mucosa in de-functioned segment of colon after colostomy or ileostomy



Definition

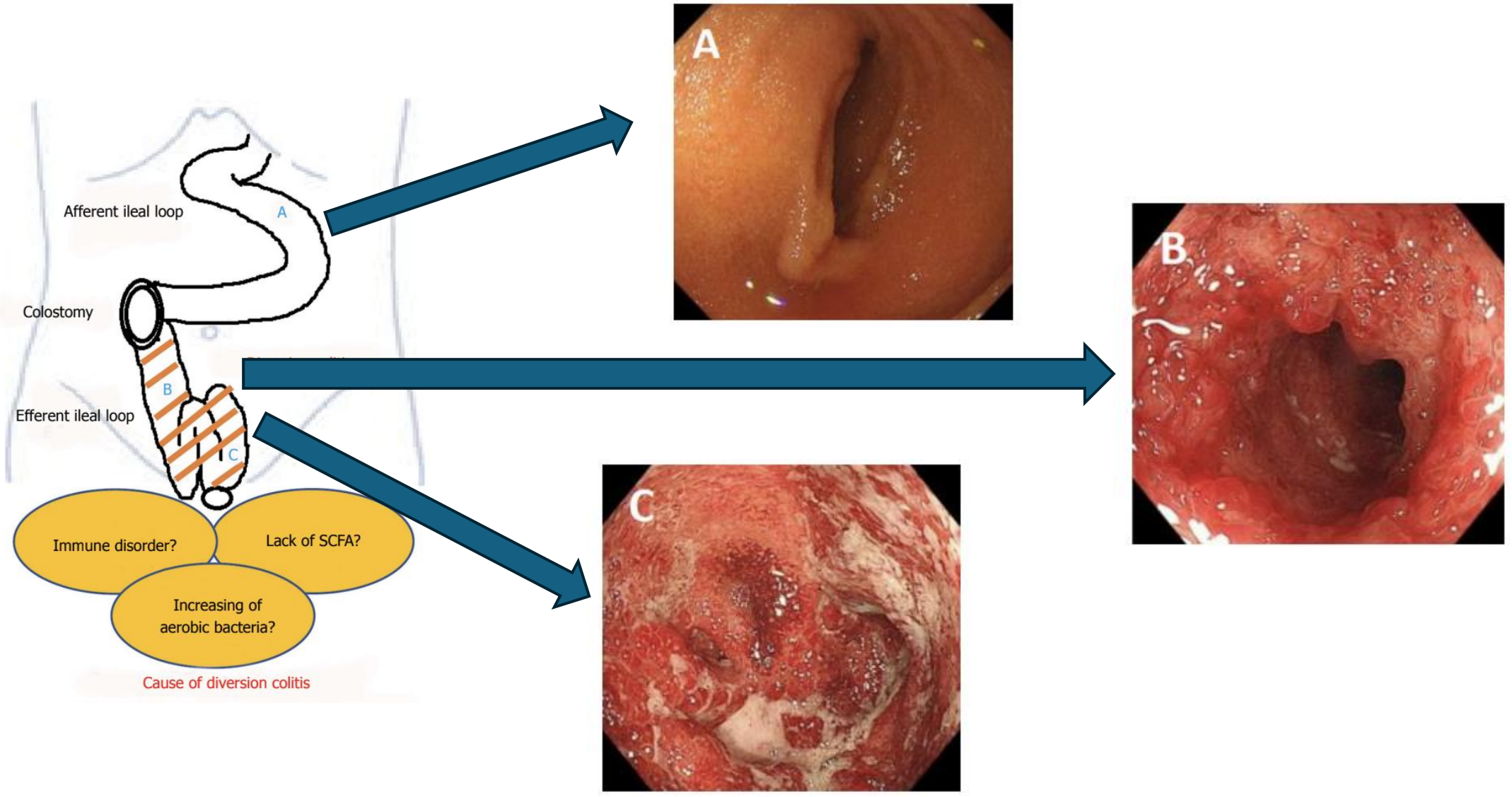
- First coined in 1981 by Glotzer in a series of 10 patients
- Asymptomatic
- 33% will have symptoms; ~87% in inflammatory bowel disease (IBD)
  - Lower abdominal discomfort
  - Pelvic/anorectal pain
  - Tenesmus & mucous discharge
  - Rectal bleeding
  - Fever

= 40%

- No pathognomic features
- Incidence ~100% with onset ranging from 4 weeks – 3 years
- Symptoms resolves once faecal stream is restored in 100% of cases

1. Kabir SI et al; IJS 2012
2. Dal Buono et al; UEGJ July 2021

Endoscopic appearance by segment



Appearance

Macroscopic:
Entire de-functioned colon or segments

Diffuse granularity
Mucous plugs
Erythema
Blurring of vascular pattern (90%)
Mucosal friability (80%)
Oedema (60%)
Aphthous ulceration
Bleeding

Microscopic:
Inconsistent and often similar features seen in IBD

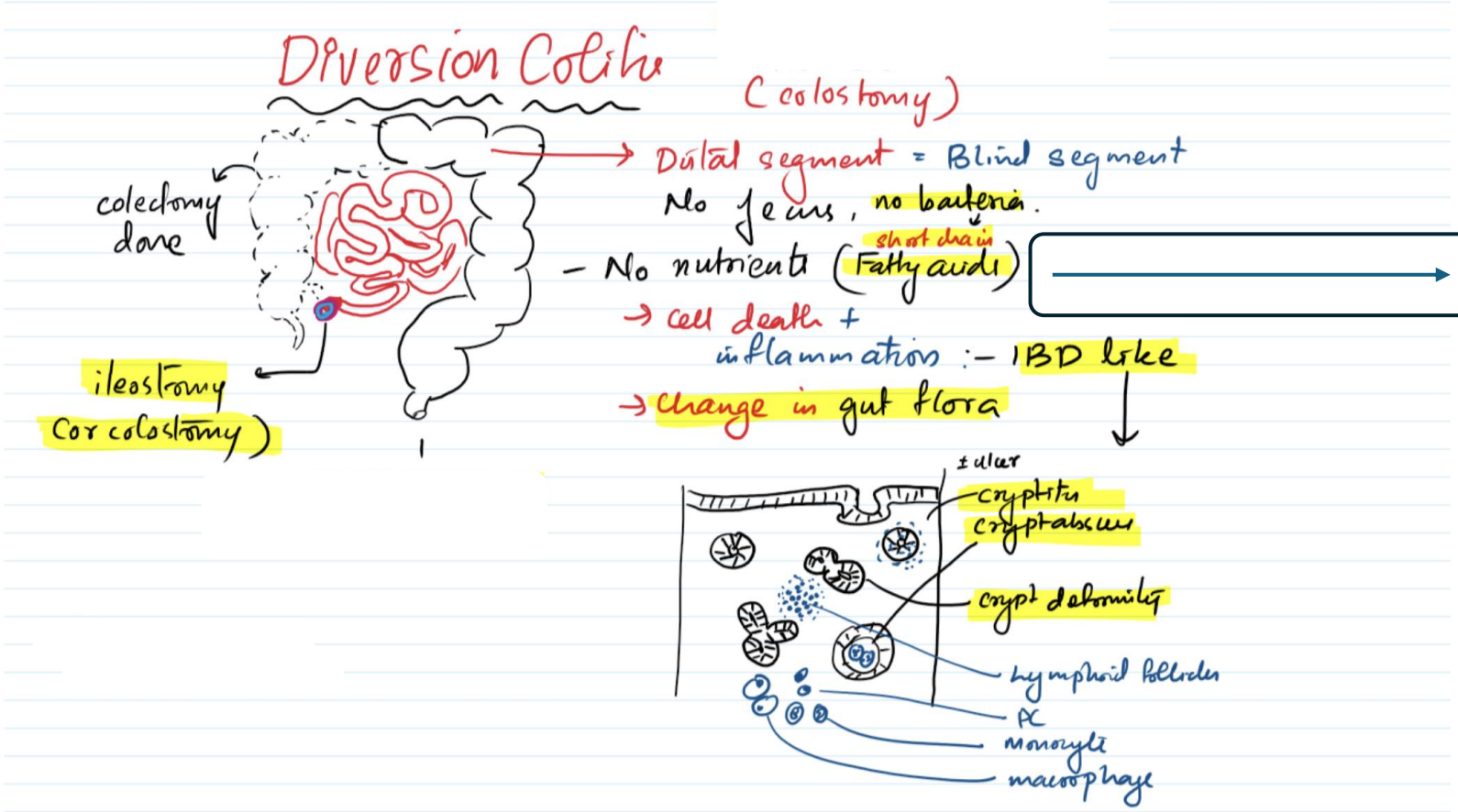
Follicular hyperplasia
Superficial coagulative necrosis

*Can often mimic CD:

- Crohn rosary = Lymphoid aggregates on outer border of muscularis propria

1. Kabir SI et al; IJS 2012
2. Dal Buono et al; UEGJ July 2021

Why does this occur?



↓ SCFA
↑ Arteriolar resistance
↓ Nitric oxide (NO)
(-) vasodilatation
= ischeamia

Management strategies & staging

Szczepkowski[1] staging was based on 145 consecutive patient with de-functioned colostomies of any cause

	Group 1	Group 2	Group 3
Description	No clinical, morphological or endoscopic evidence of colitis	Mild or moderate signs of DC	Severe DC
Management	Conservative options: Choice of enema slurries as needed or f/u	Trail of topical slurries with aim to restore faecal stream	Restoration of feacal stream

1. Ma CK et al; Human pathology 1990

Formulation of short chain fatty acids (SCFA)

Reference study	SCFA Formulation	Intervention	Outcome
Harig[1]	Na-acetate 60mM Na- propionate 30mM Na-n-butyrate 40mM NaCl 22mM	60ml BD for 2-4 weeks	Endoscopic response and microscopic resolution
Guillemot F[2]	As above	60ml BD for 14 days	Endoscopic & histologic response
Neut C[3]	Acetate 60mmol/L Propionate 30mmol/L N-butyrate 40mm0l/L	60ml BD for 14 days	No significant changes in flora
Schauber J[4]	Na-acetate 60mM Na- propionate 30mM Na-n-butyrate 40mM	60ml BD for 3 weeks	No difference compared to saline
Luceri[5]	Sodium Butyrate 2g/30ml	BD for 30 days	Reduction in endoscopic grading score
Zundler S[6]	100ml of coconut oil	Daily continuously for 6 months	Clinical remission, histologic & endo improvement 6-8 weeks

Dal Buono et al; UEGJ July 2021

Surgery

- Re-anastomosis of diverted segment to mainstream.
  - ➢Sutured/stapled

- Most effective method for eliminating symptoms and signs

Major side effects/complications				
Bleeding	Infection	Anastomotic leaks	Stricture	Aneasthetic risk

1. Kabir SI et al; IJS 2012
2. Dal Buono et al; UEGJ July 2021

Other strategies with varying success

5-ASA Enemas[1]

- Effect postulated on DNA repair and anti-inflammatory properties
- 4g daily dose for 4-5 weeks
- Occasional acute intolerance(abdominal cramps, diarrhoea)

Fiber irrigation[2]

- 11 patients 5% fibers for 7 days
- Endoscopic improvement in mucosa
- Probable role in peri-operative setting

Dextrose spray[3]

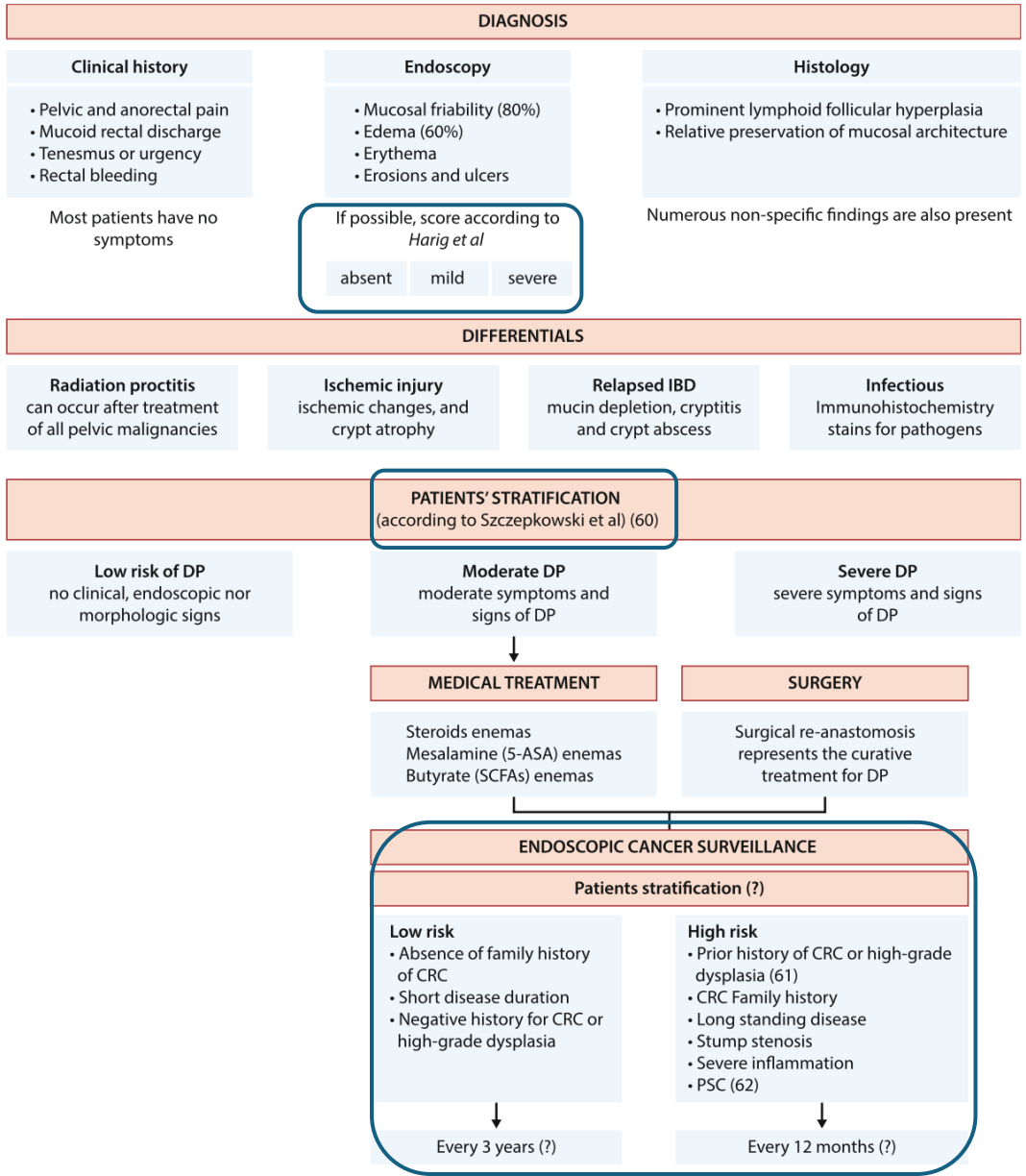
- Single patient with IBD(UC)
- Endoscopic irrigation with 50% dextrose
- 2 weeks post spray, normal pouch with no bleeding or friability
- Postulated hypertonic dextrose works via sclerosant effect
- Low cost and relatively safe

Autologous faecal transplant[4]

- Faeces collected from colostomy bag; filtered and diluted
- 3 times within 4 weeks
- All symptoms dramatically improved within 5 days
- Colonoscopy at 28days – no signs of inflammation in stamp

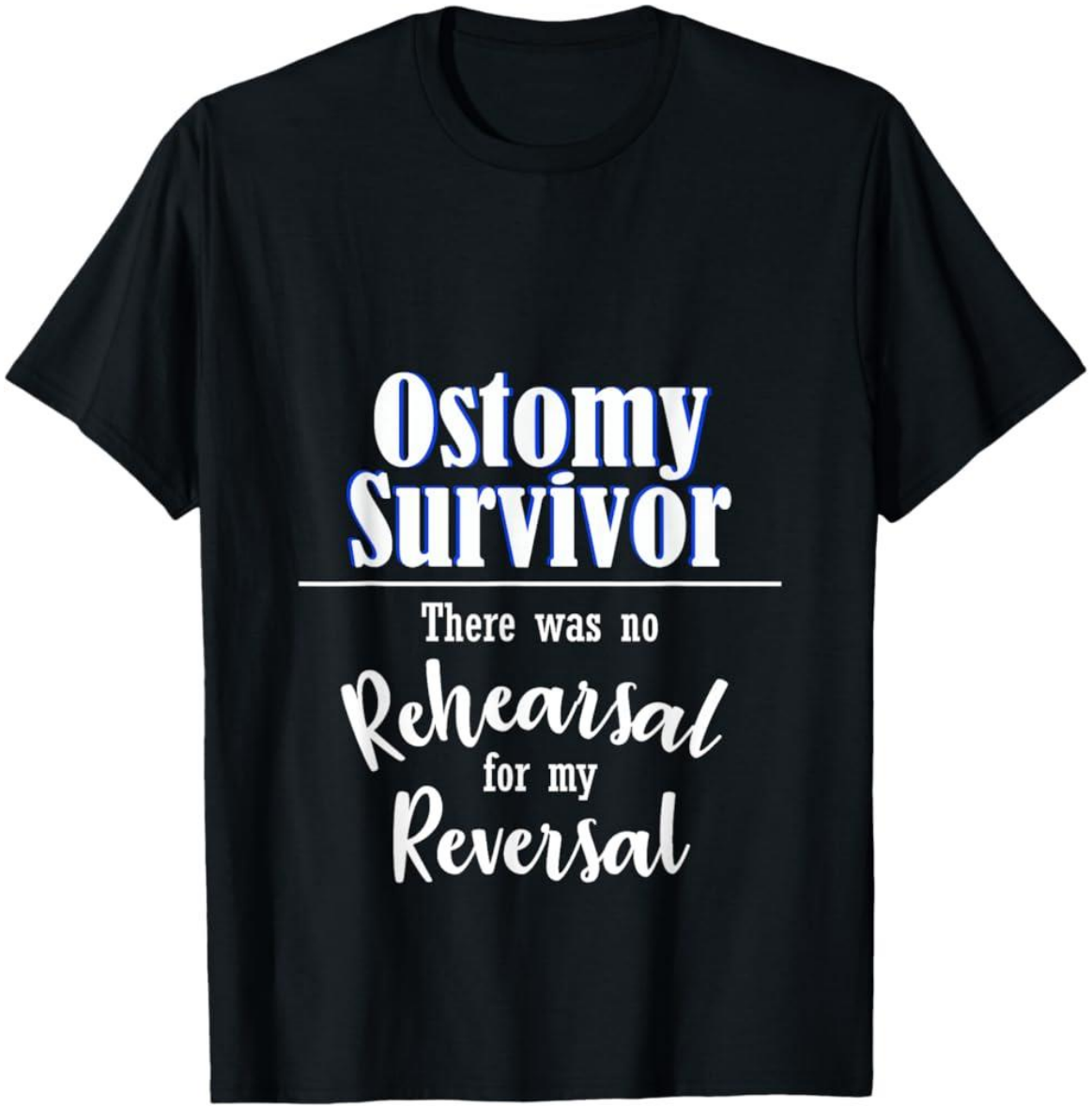
1. Tominaga K et al; WJG 2018
2. de Oliveira-Neto et al; Nutrition 2004
3. Nyabanga CT et al; ACG Case Rep J 2017
4. Gundling F et al; Tech Coloproctol 2015

Diagnostic algorithm for DC



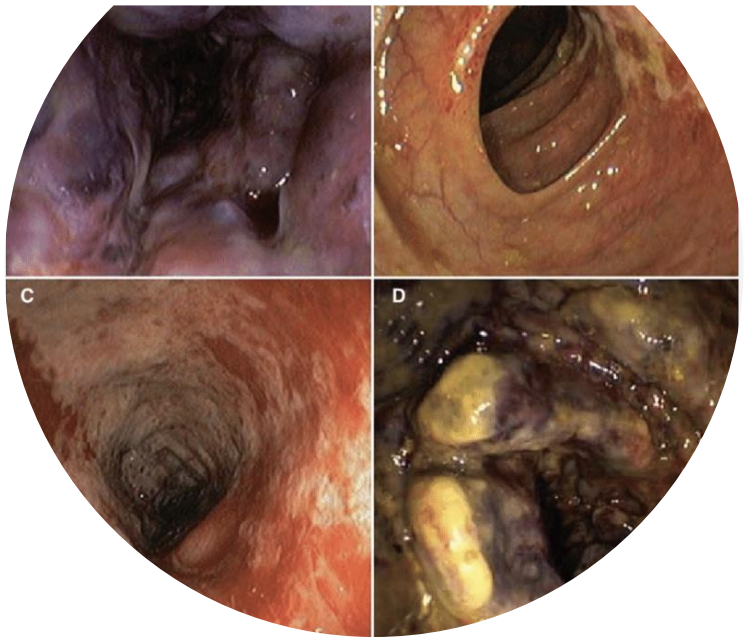
- Grading/scoring disease extend essential for risk stratification and management
- Consider other aetiologies
- Re-anastomosis, reverses pathology but not always possible
- Endoscopic surveillance strategy should be established

Dal Buono et al; UEGJ July 2021


Ostomy
Survivor
There was no
Rehearsal
for my
Reversal

Colon ischaemia (CI)

Reduced intestinal blood flow (Small vessel occlusion or Hypoperfusion) → Injury to colon mucosa →results in transmural ischaemia



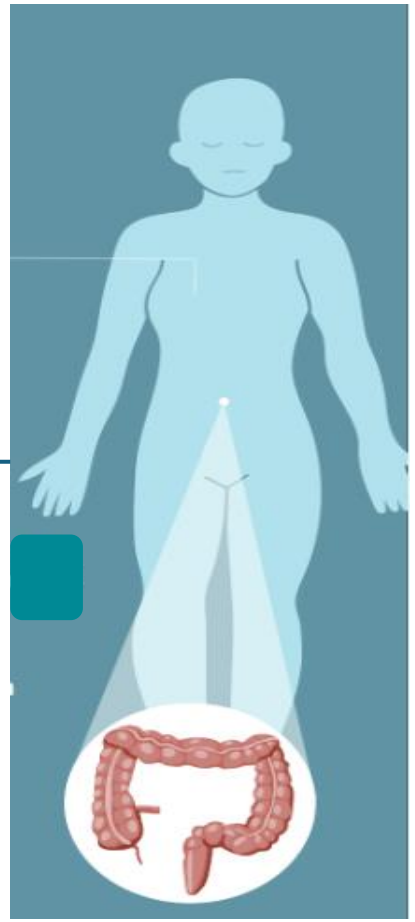
Incidence

- Annual incidence rate 17.7 per 100000
- ↑ 49 years and older
- Females > men; up to 76% of reported cases female
- Mortality 4-12%
- Isolated right sided colitis (IRCI) carriers a higher mortality risk

Brandt l et al; ACG Clinial guideline AmJG 2015

Clinical features

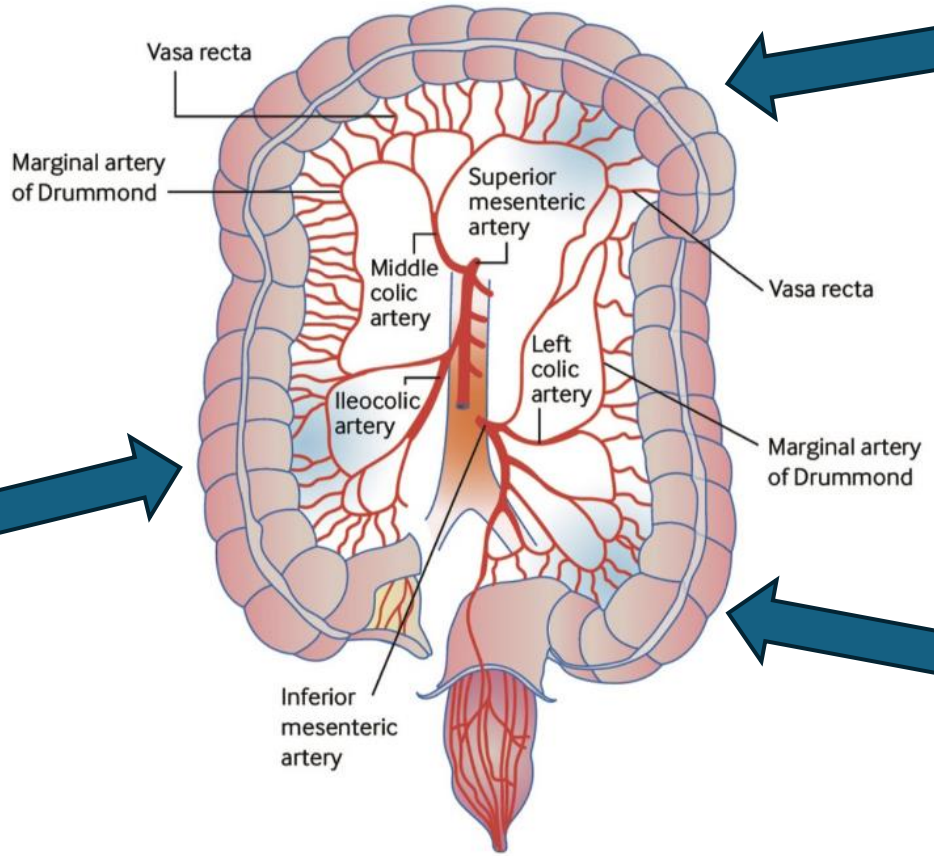
- Abdominal pain (87%)
- Rectal bleeding (84%)
- Diarrheoa (56%)
- Melaena infrequently present
- Rectal bleeding > left sided & absent in IRCI



1. Hung A et al; Frontline Gastroenterology 2021
2. Brandt L et al; ACG Clinical guideline AmJG 2015

Watershed areas of Colon

Griffith's point



>50% marginal artery undeveloped

Sudeck's point

1. Hung A et et al; Frontline gastroenterology 2021

Risk factors

- Co-morbid cardiovascular disease and diabetes mellitus
- Irritable bowel syndrome and constipation
- Chronic kidney disease
- History of thrombophilia or suspected
- Abdominal surgery

Drugs or medications
Immunomodulator
Constipation inducing drugs
Illicit drug use

1. Hung A et al; Frontline Gastroenterology 2021

Features associated with severe CI and failure of conservative management

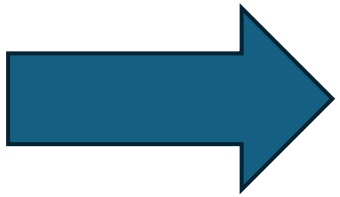
Patient factors	Clinical features	Laboratory test	Cross-sectional imaging
Male gender	Peritoneal signs evident	Anaemia	Free intraperitoneal fluid
Pre-existing renal dysfunction	Absence of rectal bleeding	Leukocytosis	Disease localized to or involving right colon (IRCI)
History of atrial fibrillation	Tachycardia	Hyponatreamia Thrombocytopeania Elevated CRP Elevated serum lactate	

1. Hung A et al; Frontline Gastroenterology 2021

Ischaemic Colitis Mortality Risk (ICMR) score

Risk factors

- Preoperative lactate >2.5
- Acute kidney injury
- Pre/intraoperative catecholamine use
- Low output heart failure <20% on echocardiogram
- Subtotal or total colectomy



Scale	
0	10.5%
1	28.9%
2	37.1%
3	50.0%
4	76.7%
5	100%

- Age >75
- Multiple organ failure
- ASA status >4
- Intraoperative blood loss > 500ml

1. Hung A et al; Frontline Gastroenterology 2021
2. Reissfelder C et al; Surgery April 2011

Indication for surgery

Acute

- Peritoneal signs
- Massive bleeding
- Fulminant colitis with or with toxic megacolon
- Portal venous gas/pneumatosis intestinalis
- Deteriorating clinical condition

Subacute

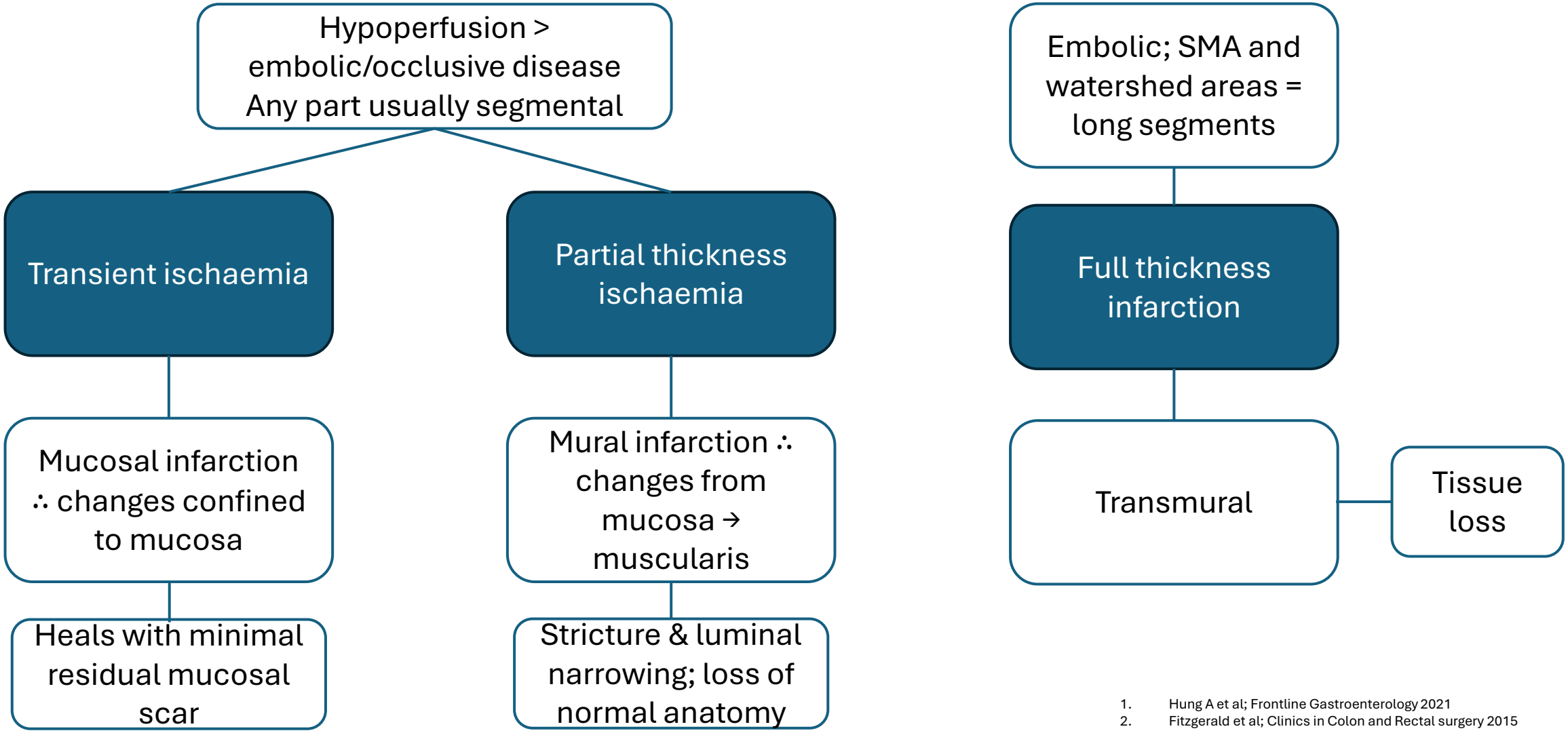
- Segmental colitis that fails to respond to Rx within 2-4 weeks or a protein-losing enteropathy
- Recurrent sepsis, despite apparent healing

Chronic

- Symptomatic stricture
- Symptomatic segmental colitis

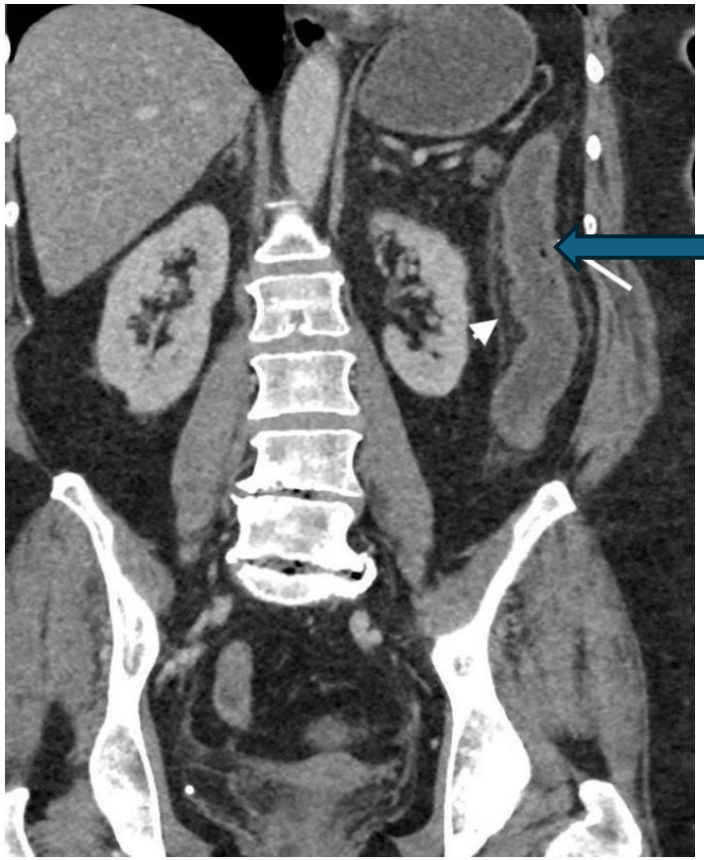
Brandt l et al; ACG Clinial guideline AmJG 2015

Phases of ischaemia

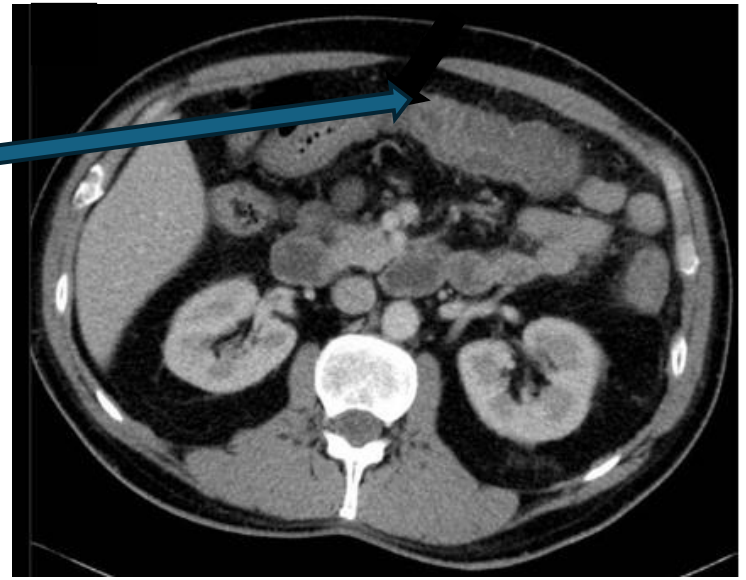


1. Hung A et al; Frontline Gastroenterology 2021
2. Fitzgerald et al; Clinics in Colon and Rectal surgery 2015
3. Brandt L et al; ACG Clinical guideline AmJG 2015

Severity of CI: Computer topography with IV & oral contrast



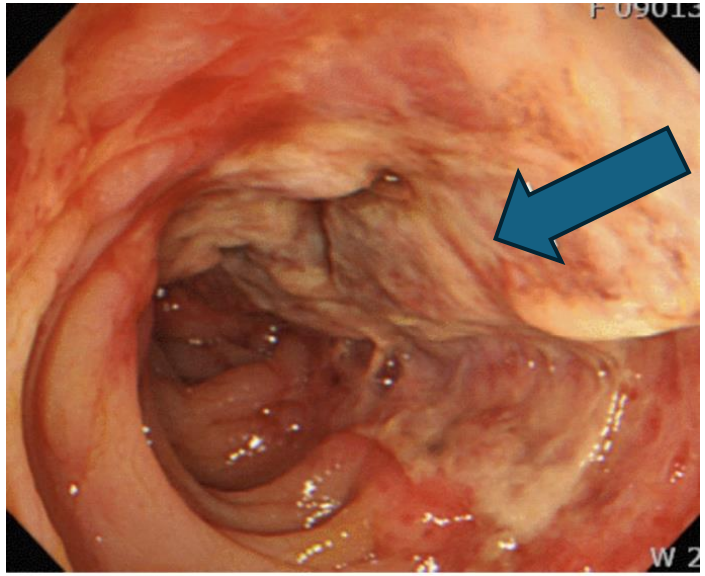
- Sharp cutoff in mid-distal transverse colon
- Featureless/peri colic oedema



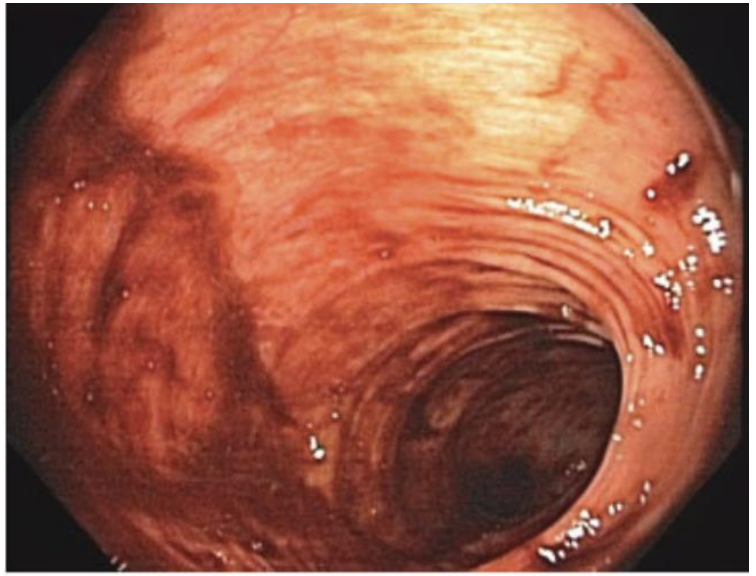
Type 1: Inflammation limited to mucosa
Type 2: Extends to muscularis layer
Type 3: Transmural inflammation

1. Hung A et al; Frontline Gastroenterology 2021
2. Fitzgerald et al; Clinics in Colon and Rectal surgery 2015

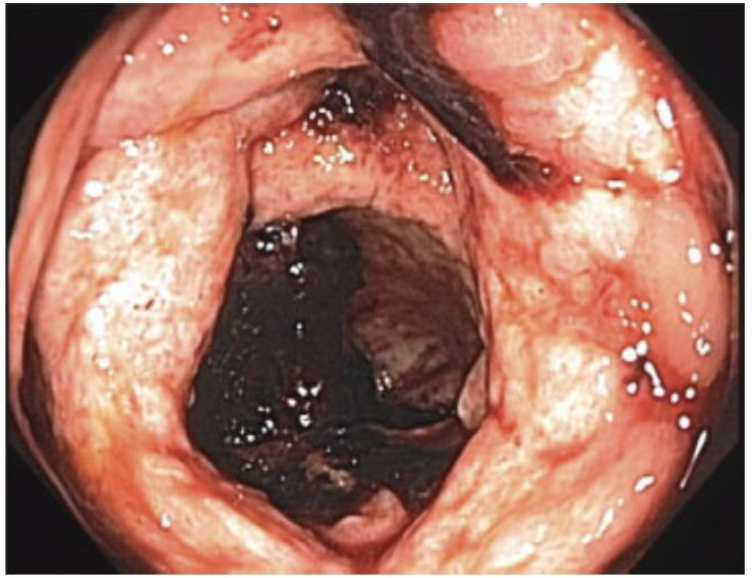
Severity of CI: Endoscopy



Single stripe sign sign: Longitudinal strip/ulceration or inflamed segment of colon



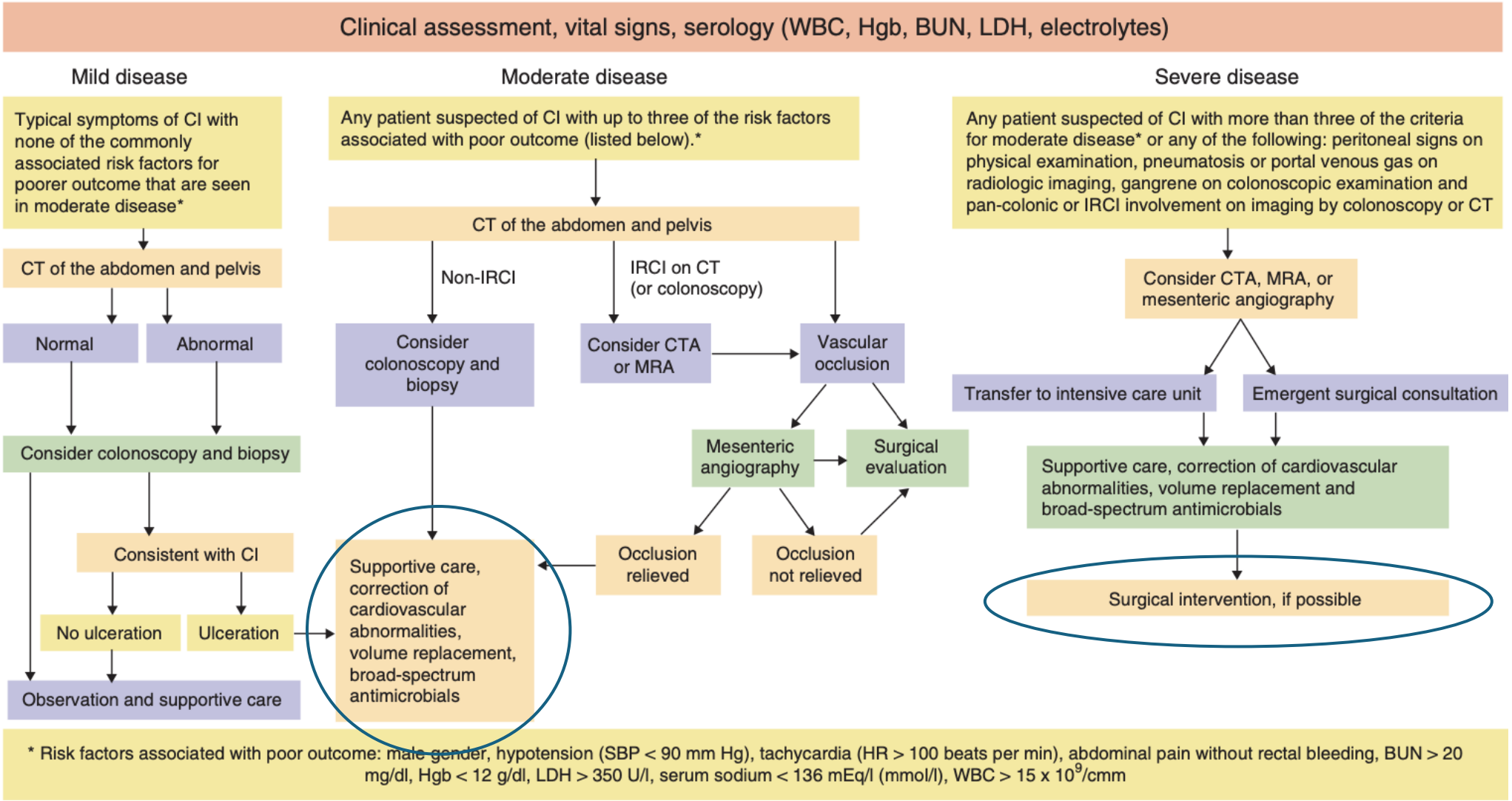
Erythema, mucosal bleeding and intraluminal blood



Ulceration, erosions and intraluminal clots

1. Hung A et al; Frontline Gastroenterology 2021
2. Fitzgerald et al; Clinics in Colon and Rectal surgery 2015

Management



Brandt l et al; ACG Clinial guideline AmJG 2015

Summary

MC

- Not at rare as previously thought
- Watery diarrhoea defines quality of life
- Highly responsive to topical budesonide
- Steroid-refractory MC exist and rescue options should be sought
- No CRC risk, but adequate f/u should be offered

DC

- Asymptomatic in 2/5 patients
- SCFA slurries effective if able to obtain it
- Surgery often cures the problem, bloating and pain may persist afterwards
- Carriers CRC risk

CI

- Disease of elderly, can occur in young
- High mortality if not recognised and treated early
- Role for conservative therapy
- Heal with stricture formation, f/u important