Acute Severe Ulcerative colitis

Dr MY Sungay
Gastroenterology Fellow
Tygerberg Hospital
University of Stellenbosch
Supervisor: Dr N Seabi

Photo by Stefan Els

Introduction

Epidemiology

- Incidence of IBD in Western countries have Increase and plateaued
- Similar trend has been noted in Asia, North Africa and South America
- Exponential increase in IBD over the past 70 years in SA
- Apart from South Africa, IBD in sub-Saharan Africa is considered uncommon
- Affects all Ethnic groups with UC more prevalent in black African groups
- Paucity of data in Sub Saharan Africa

G Watermeyer et al 2020

Introduction

Ulcerative colitis

- Peak Incidence between age 15-45
- Left-sided colitis is the most common location
- Disease extension occurs in 10–30%
- Most patients have a mild-moderate course
- Most active at diagnosis there after varying degrees of activity
- Cumulative risk of relapse is 70–80% at 10 years

M Fumery et al 2017
P Hindryckx et al 2016

Introduction

Acute severe Ulcerative colitis

- **25%** of UC patients will have at **least 1 ASUC episode**
- More than a quarter of ASUC events occur at index presentation of UC
- Each episode risk complications :
- Bowel perforation, haemorrhage , thromboembolic events, electrolyte disturbance, colectomy rate of 13%
- Mortality is around 1% - risk factors include: colectomy , age 50, delay in management/surgery

G Watermeyer et al 2020

Acute Severe Ulcerative colitis

- Little is known about ASUC pathogenesis:
- Dysregulated systemic immune response to commensal pathogens in genetically predisposed individuals
- Highlights the intricate interplay between genetic susceptibility and immune dysfunction

Acute Severe Ulcerative colitis

- ASUC is a distinctive Ulcerative colitis flare presentation characterised by:
- 1) Systemic inflammation
- 2) Bloody Diarrhoea

- Sidney Truelove and Leslie Witts identified that systemic inflammation to be a major driver of complications and mortality in UC.
- Most applicable in extensive colitis, limitations with limited colitis
- The Truelove and Witts criteria has never been validated in clinical practice

P Riviera et al,2024

Truelove and Witts

Modified Truelove and Witt's criteria for classification of severity of ulcerative colitis

	Mild	Moderate	Severe
Bloody stools per day	< 4	4 to 6	> 6
Pulse	< 90 bpm	≤ 90 bpm	> 90 bpm
Temperature	< 37.5 °C	≤ 37.8 °C	> 37.8 °C
Hemoglobin	> 11.5 gm/dL	≥ 10.5 gm/dL	< 10.5 gm/dL
ESR	< 20 mm/h	≤ 30 mm/h	> 30 mm/h
CRP	Normal	≤ 30 mg/dL	> 30 mg/dL

Kedia S et al,2014

	Moderate	Severe
	4 to 6	> 6
pm	≤ 90 bpm	> 90 bpm
°C	≤ 37.8 ºC	> 37.8 °C
gm/dL	≥ 10.5 gm/dL	< 10.5 gm/dL
m/h	≤ 30 mm/h	> 30 mm/h
l	≤ 30 mg/dL	> 30 mg/dL

n of severity of ulcerative colitis

For ASUC you need:

1) >6 bloody stools /day

2) Any one of the other criteria of systemic toxicity

Kedia S et al 2014

Oxford criteria

Oxford Criteria	
Complete Responders	< 3 stools/day
Incomplete Responders	3-8 stools/day and CRP <45
Non responders	>8 stool/day or 3-8 stools/day and CRP>45

Poor Prognostic Factors

Poor Prognostic Factors in Ulcerative colitis disease severity
Younger than 40 at diagnosis
Extensive colitis
Severe endoscopic disease (Mayo endoscopic subscore 3, UCEIS>7)
Hospitalised for colitis
Elevated CRP
Low serum albumin
The greater the number of prognostic factors the worse the prognosis as measured by the likelihood of colectomy

D Rubin et al 2025

Severity factors

Severity factors of acute severe ulcerative colitis (ASUC)	
Factor	Effect
NSAIDs intake	Frequent and early clinical relapse of quiescent diseases
Clostridioides difficile	In hospitalized patients for IBD, the mortality rate is 4 times higher in the Clostridoides difficile group
CMV	In steroid-refractory patients, 50% of colectomy in patients with CMV reactivation versus 15% in patients without CMV.
Toxic megacolon	Small bowel distension is associated with steroids failure (odds ratio of 3.55 in patients who failed steroid therapy)
Venous thromboembolism	Age and comorbidity excess mortality of 2.1 compared with non-IBD patients. Associated with longer length of hospital stay.
Time to colectomy	Duration of in-hospitalization treatment associated with higher postoperative complications (OR 1.12, p-value 0.044)

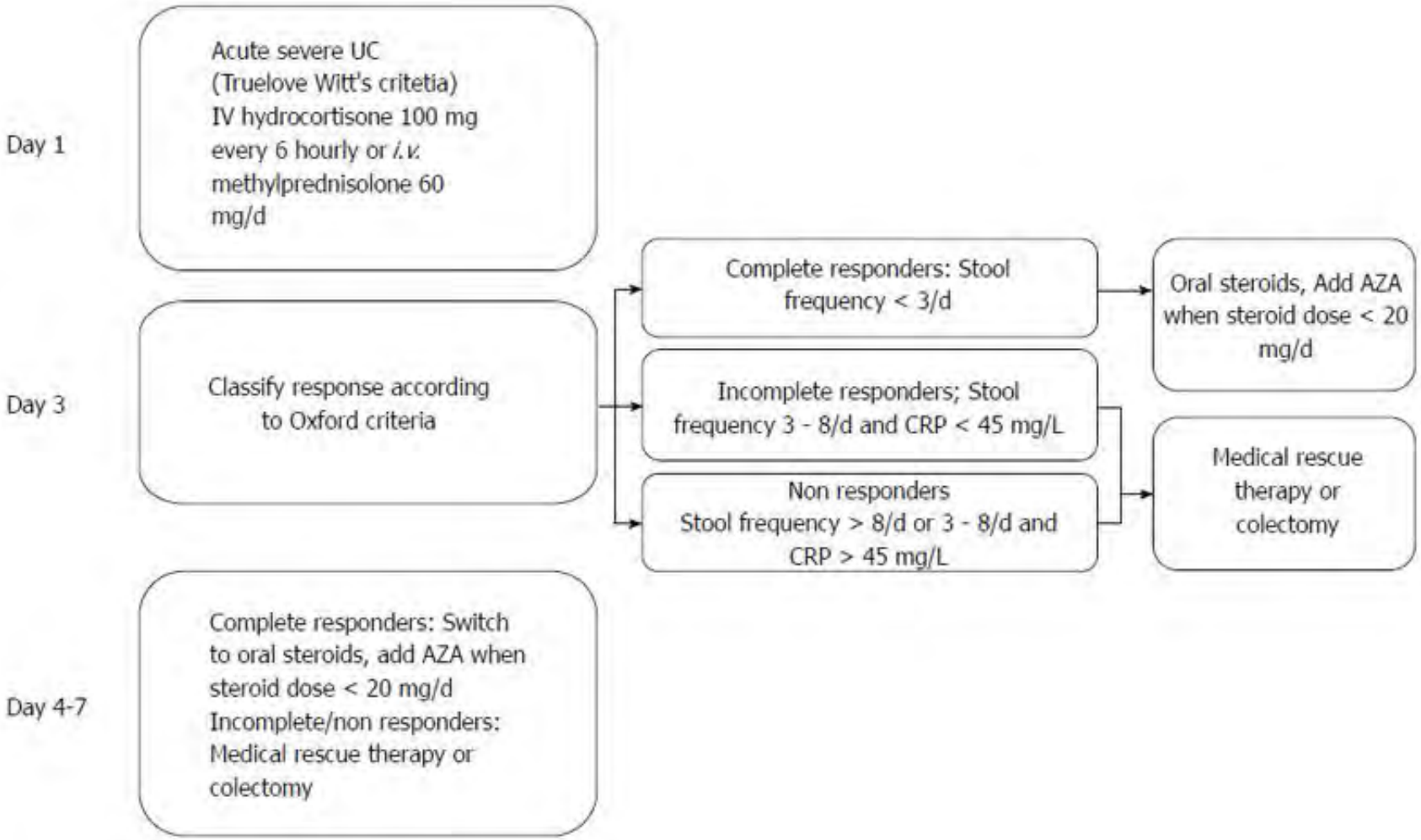
L Calmejane et al 2023

Differential diagnosis

Category	Condition
Infectious Colitis	Clostridioides difficile (C. diff)
	Bacterial Pathogens (Campylobacter, Salmonella, Shigella, E. coli O157:H7)
	Viral Pathogens (Cytomegalovirus)
	Parasitic Pathogens (Entamoeba histolytica), Schistosomiasis
Ischemic Colitis	Ischemic Colitis
Other Inflammatory Bowel Disease	Crohn's Disease
Medication-Induced	Medication-Induced Colitis (e.g., **NSAIDs**, immune checkpoint inhibitors)
Other Conditions	Diverticular Colitis
	Microscopic Colitis
	Colorectal Cancer

General principles of management of ASUC

- Swift diagnosis to decrease colectomy rates
- Identify triggering factors
- Identify worsening factors
- Assess endoscopic severity
- Imaging for abscess or perforation
- Manage thromboembolism risk
- Mitigate surgery associated morbidity and mortality
- Optimize nutritional status



Kedia S et al 2014

Management of ASUC

- Day 1

-Baseline investigations: FBC, U&E,CMP, CRP,ESR

- Stool MCS and C diff
- Chest and Abdominal Xray's –(Toxic megacolon)/ CT Abdomen
- Veno thromboembolism prophylaxis – Enoxaparin
- Endoscopic assessment- disease extent and rule out CMV colitis (within 72hrs preferably within 24 hours)
- Withhold 5- ASA – paradoxically worsens diarrhoea
- Early surgical consult- daily review
- No place for routine antibiotics in ASUC management

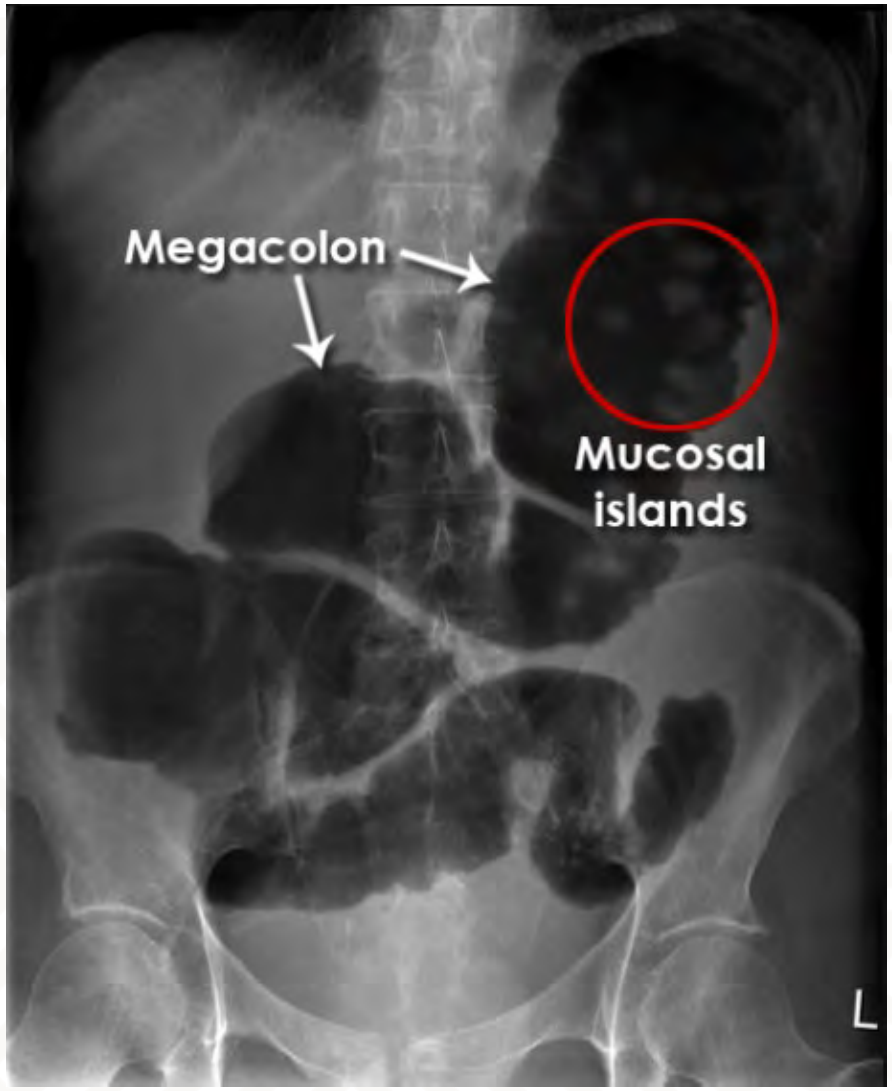
Day 1

- Other test to consider- Tb QuantiFERON, Hep B, screening for VTE
- IVI Corticosteriods- **Hydrocortisone 100mg 6-8 hourly** for 3-5 days
- Monitor response – symptoms
- Avoid NSAIDS, opioids and drugs with anticholinergic side effects- Specifically morphine, tramadol and loperamide

Imaging

- Xrays
- Erect Chest – free air under diaphragm
- Abdominal Xray
  - Loss haustra, thumbprinting, lead piping
  - Look for features of megacolon
  - 3-6-9 rule
- Ultrasound
- CT scan

Imaging



Endoscopy

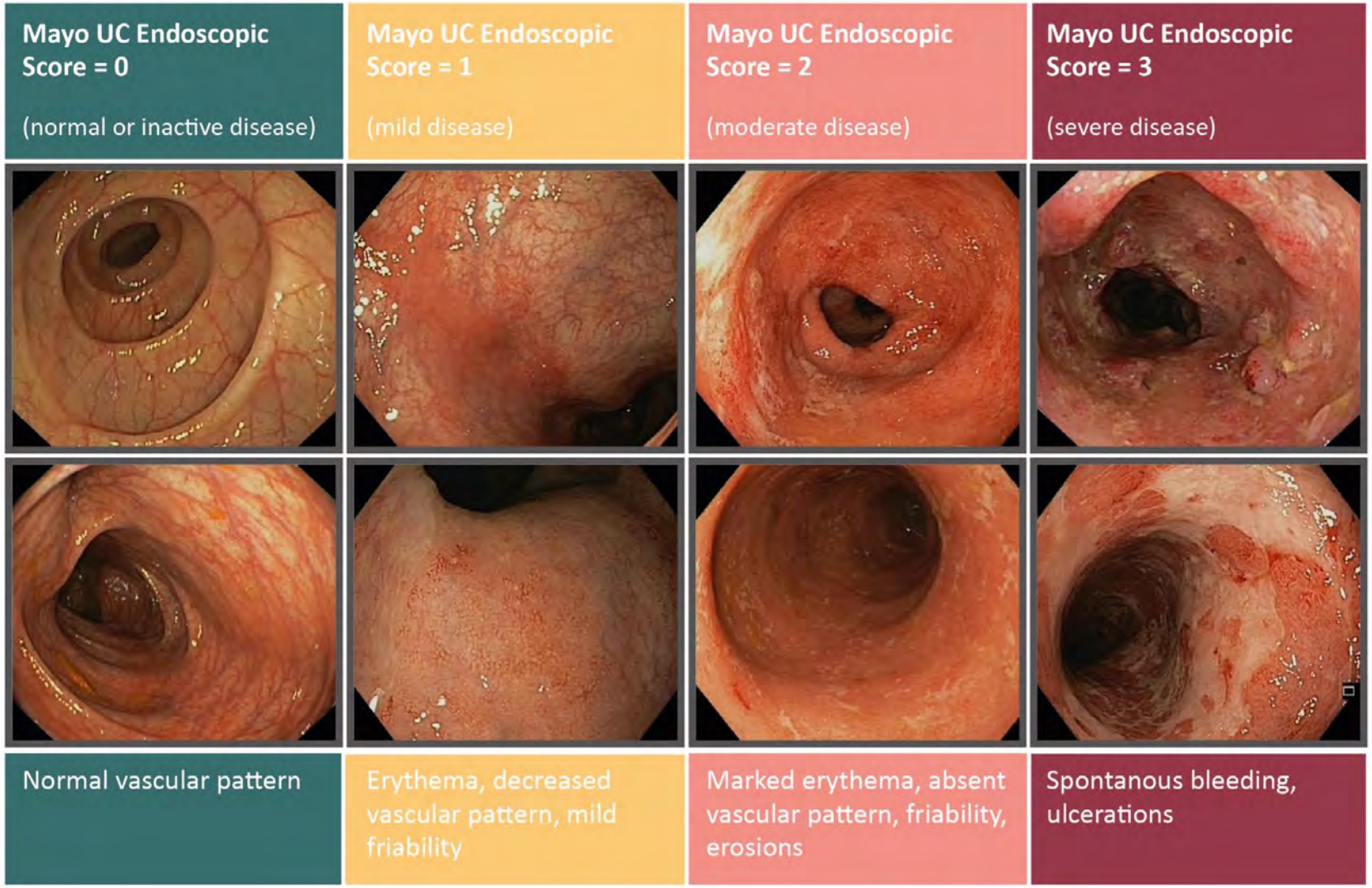
- The goals of endoscopic evaluation:

1. Confirm diagnosis(diagnostic uncertainty)
2. Establish severity of inflammation
3. Obtain biopsies for CMV colitis

Full **colonoscopy** is associated with high rates of **colonic dilation and perforation**

Flexible sigmoidoscopy with minimal insufflation is sufficient

Mayo Endoscopic Score



Mayo Score

Parameter	Clinical evaluation	Score
1. Stool frequency	normal number of stools	0
(per day)	1-2 more than normal	1
	3-4 more than normal	2
	≥ 5 more than normal	3
2. Rectal bleeding	none	0
	streaks of blood with stool in in less than half of the cases	1
	obvious blood with stools in most cases	2
	blood alone passes	3
3. Endoscopic findings	normal mucosa or inactive disease	0
	mild activity (erythema, decreased vascular pattern,	
	mild friability)	1
	moderate activity (marked erythema,	
	lack of vascular pattern, friability, erosions)	2
	severe activity (spontaneous bleeding, large ulcerations)	3
4. Physician's global assessment	normal	0
	mild disease	1
	moderate disease	2
	severe disease	3

Mayo Score

Score	Decoding
0 to 2	remission(provided that no subscore for each single parameter is greater than 1)
3 to 5	mild activity
6 to 10	moderate activity
> 10	severe activity

Montreal classification : extent and severity

Extent	Anatomy
E1	Ulcerative proctitis; involvement limited to rectum (rectosigmoid junction)
E2	Left sided ulcerative colitis
E3	Extensive ulcerative colitis

Severity	Definition
S0	Ulcerative colitis in clinical remission; no symptoms of UC
S1	Mild UC ≤ 4 bloody stools daily, lack of fever, pulse <90 bpm, haemoglobin >105g/L, ESR < 30mm/hr
S2	Moderate ulcerative colitis: > 4-5 stools daily but with minimal signs of systemic toxicity
S3	Severe ulcerative colitis: ≥ 6 bloody stools daily, pulse > 90 bpm, temperatures > 37.5°C, haemoglobin < 105 g/L, ESR > 30 mm/hr

Ulcerative Colitis Endoscopic Index of severity - UCEIS

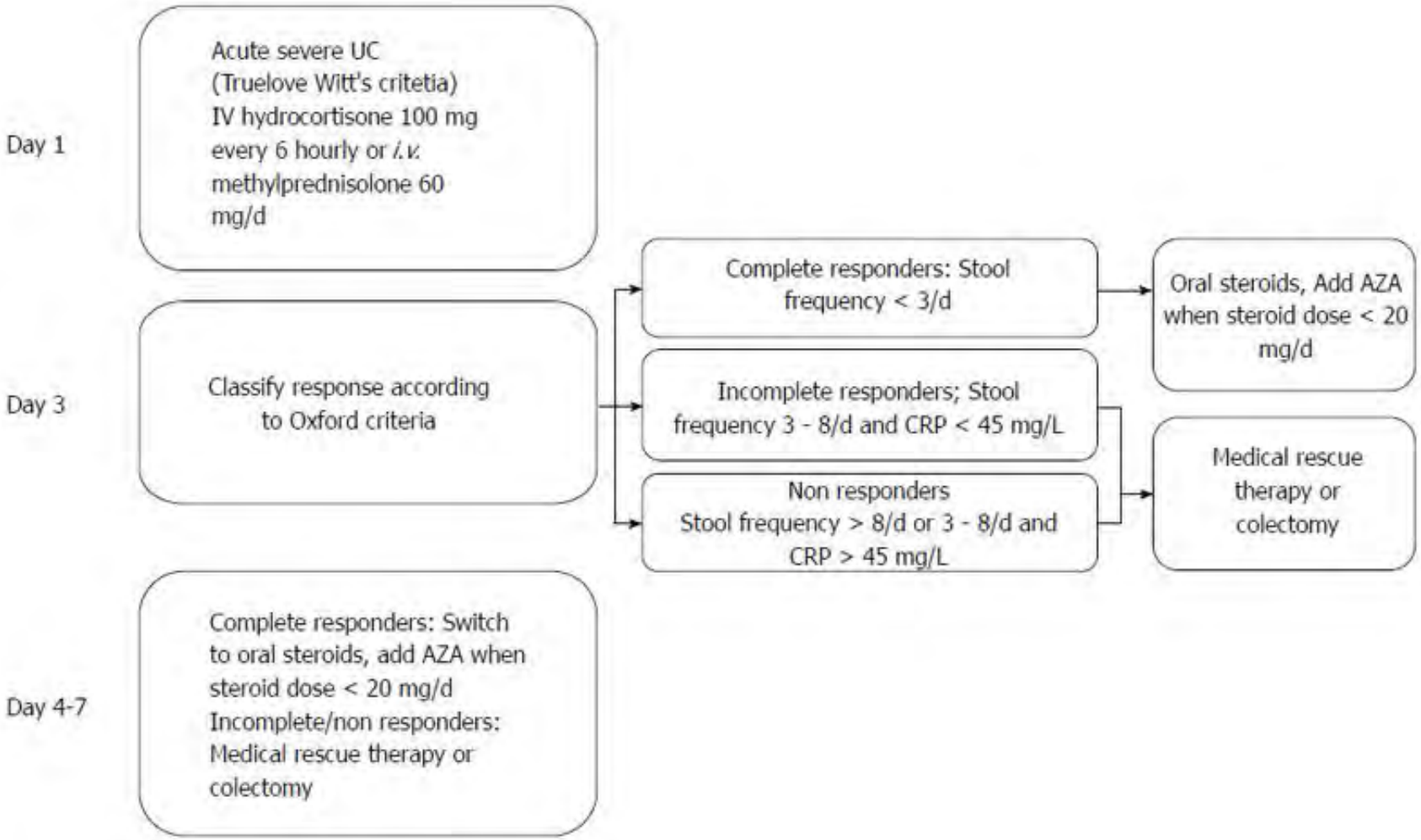
Variable	Scores			
	0	1	2	3
Vascular pattern	Normal	Patchy obliteration	Complete loss of vascular pattern	
Bleeding	None	Mucosal	Luminal, mild	Luminal, severe
Erosions & ulcers	None	Erosions	Superficial ulcers	Deep ulcers

.

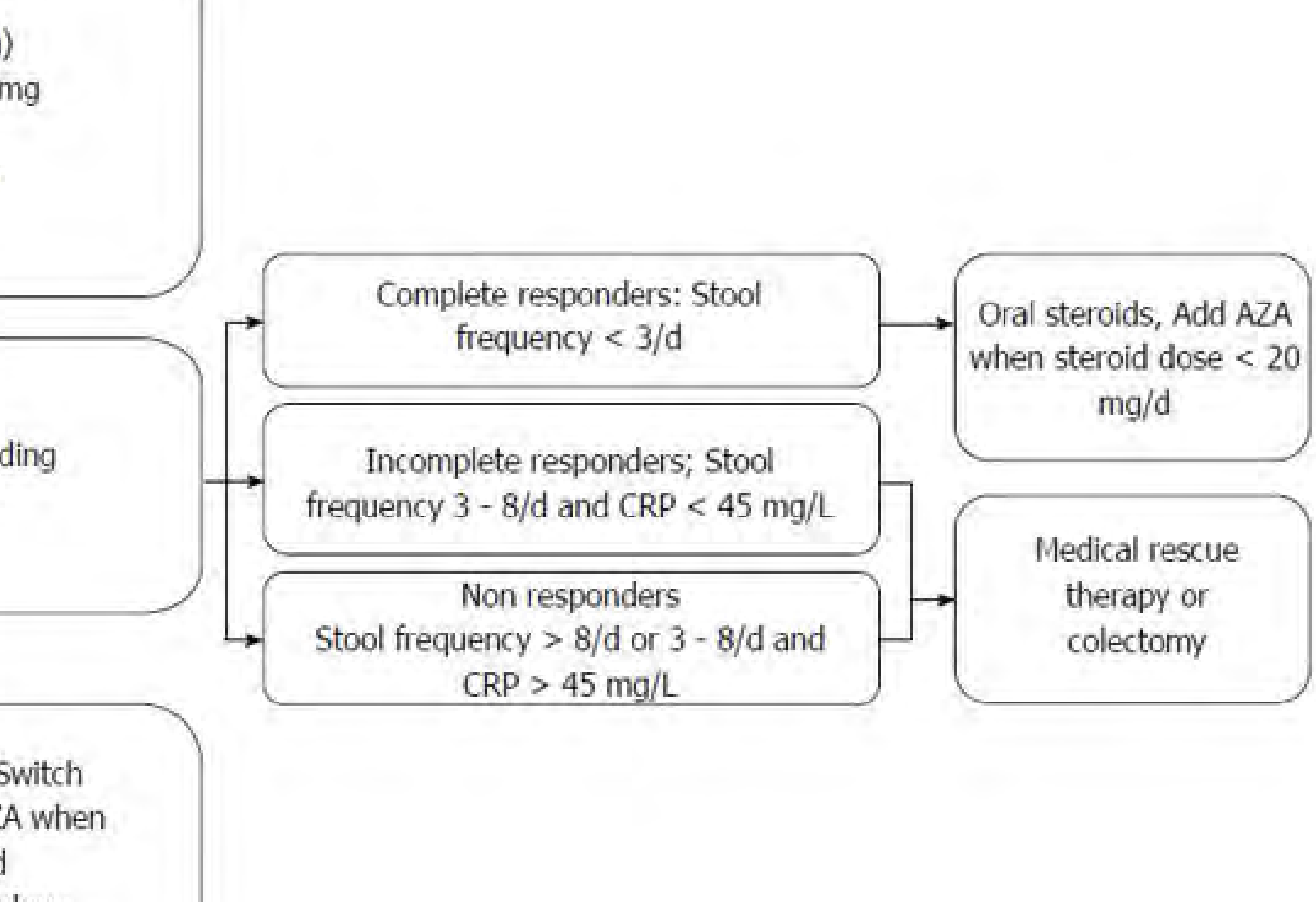
- Day 2 and 3
- Daily symptom review- Stool count/ rectal bleeding/any pain or tenderness
- NB! abdominal pain in ASUC is a marker of instability
- Perform daily abdominal X Rays – guided by symptoms
- Surgical consult early

Day 3 – Decision Day!!

- Day 3 decision made on steroid responsive or not- based on the **Oxford criteria**
- If steroid responsive then continue IVI for 3 to 5 additional days before switching to oral prednisone
- Consider steroid sparing therapy



Kedia S et al 2014


mg
ding
Switch
ZA when
d
Complete responders: Stool frequency < 3/d
Incomplete responders; Stool frequency 3 - 8/d and CRP < 45 mg/L
Non responders
Stool frequency > 8/d or 3 - 8/d and CRP > 45 mg/L
Oral steroids, Add AZA when steroid dose < 20 mg/d
Medical rescue therapy or colectomy

Maintenance therapy in steroid responders

- Start Oral Prednisone 1 mg/kg – 60mg
- Consider steroid sparing therapy
- The optimal long-term maintenance therapy for immunomodulator(IMM)-naïve patient remains unclear
- A multicenter retrospective study in Italy showed there is no difference in three regimens- aminosalisalytes/ IMM/ IFX – IMM Naïve patients
- Based on – Cases to case, previous exposures and depth of response to steroids

S Admin et al 2022
L Calmejane et al 2023

ASUC-IVI Steroid non responders

- Risk stratification is essential in ASUC management
- Helps determine need for early rescue therapy
- Guides timely decision for colectomy
- Critical step to improve outcomes and reduce complications

Prognostic scores for steroid failure

Prognostic scores of corticosteroid failure in chronological order		
Composite criteria	Factors	Steroids failure
Oxford criteria	>8 stools or 3 to 8 stools per day and CRP >45mg/L on day 3	Colectomy rate 85% if one criterion is present
Lindgren et al	Body temperature >37.4°C, number of bowel movements, persistence of bloody stools, elevated CRP on day 3, Score: Stool frequency/day +0.14 x CRP	72% of colectomy when score ≥8
Ho et al	Mean stool number on first 3 days, albumin <30g/L on admission, colonic dilatation >5.5 cm on Xray	85% of steroids failure when score ≥4
Gibson et al	3 stools per day and CRP/albumin ratio on day 3	Relative risk of steroids failure of 3.9 (95% CI 2.1–7.2)
Adams et al	Albumin <25 g/L, CRP ≥100 mg/L, UCEIS ≥4 or ≥7 on admission	84% of steroids failure when score ≥3

L Calmejane et al 2023

Digestive Diseases and Sciences (2025) 70:2414–2425
https://doi.org/10.1007/s10620-025-08982-4

ORIGINAL ARTICLE

Evaluation of Acute Severe Ulcerative Colitis Predictors for Steroid Therapy Refractoriness

Alaa Abdelmeguid[1,2] · Amany Ahmed El Banna[1] · Wafaa Elsheikh[1] · Ahmed Ismail Ellakany[1] · Shaji Sebastian[2]

- Lower albumin and oral steroids prior to admission for ASUC are predictors of IVI steroid failure

Rescue medical management for steroid non responders

- Steroid non responders –which can be up to a third of patients
- Medical rescue therapy:

1) Infliximab
2) Cyclosporin
3) Tacrolimus
4) Tofacitinib

Infliximab Rescue therapy

Infliximab (IFX) TNF inhibitors increasingly preferred over calcineurin inhibitors (CsA) due to:

- Better side-effect profile
- Availability for maintenance therapy

- Induction Dosage: 5mg/kg at 0,2,6 weeks
- Efficacy reports:
  - Short-term response rates vary widely: 0–100%
  - Long-term colectomy-free rates: 41–81% after rescue therapy for ASUC
  - IFX and CsA have comparable short- and long-term outcomes
  - IFX often preferred in practice

H Nakase 2023

Patients not responding to Infliximab Rescue therapy

- High TNF burden is implicated in IFX failure.
- Proteolytic degradation of anti-TNF is associated with increased drug clearance.
- Fecal losses from increased gut permeability are associated with severe inflammation.
- To overcome these factors and achieve successful induction of remission, accelerating IFX dosing is considered for patients with ASUC
- However overall data from retrospective studies does not show superiority for accelerated IFX dosing- perhaps in a select group of patients with low albumin

H Nakase 2023

Cyclosporin

- In the past was the primary treatment for ASUC
- Bridge to AZA
- Recent Studies – Efficacy of Csa as bridge to Vedo/Ustekinamab
- Dose: 2mg/kg/day
- Drug Level monitoring, requires high care with cardiac and electrolyte monitoring
- Side Effects include nephrotoxicity, BP, seizures,anaphylaxis, sepsis
- Remission Achieved with Csa then Maintenance therapy with thiopurine/ vedolizumab

L Calmejane et al March 2023

Tacrolimus

- Calcineurin inhibitor with good oral bioavailability.
- Oral: Initial dose 0.1–0.15 mg/kg/day IV: Initial dose 0.015 mg/kg/day
- Target trough level: 10–15 ng/mL during induction until complete remission.
- side effects: Similar to cyclosporine (CsA).
- **Treatment outcomes:**
  - Short-term efficacy in refractory UC: ~70%.
  - Long-term colectomy-free rate: >50% (1–2 years).
- **Prognosis:** Effective for induction; long-term outcomes remain suboptimal.

H Nakase 2023

Tofacitinib- Emerging therapy for ASUC

- Oral, rapid-acting pan–JAK inhibitor approved for UC.
- Potential benefit due to fast onset of action.

Safety Concerns

- Reported risks: thromboembolic events (VTE) and cancer.
- Data primarily from rheumatoid arthritis patients >50 years with cardiovascular risk factors.
- Reassuring safety data in IBD populations

L Calmejane et al 2023

Tofacitinib- Emerging therapy for UC

Clinical Position

- Promising therapy for ASUC, especially for young patients without CV risk factors.
- Aggressive strategies proposed:
  - IV steroids + tofacitinib 10 mg thrice daily from admission (promising retrospective data)
- The Triumph study - Prospective open labeled interventional trial
  - Tofacitinib is effective rescue therapy, RCT are required to compare
- Filgotinib & Upadacitinib: quick onset, potential ASUC options; no current ASUC recommendation yet.

L Calmejane et al 2023
N Nurala et al 2025

Other factors to consider in non responders

- **C- Diff Positive-** treat : Vancomycin 125mg PO QID 10-14days/ fidaxomicin 200mg QID 10-14day(EXPENSIVE)
- **CMV Infection:**
- If patients have steroid-refractory UC, Immunohistochemistry and mucosal PCR for CMV should be checked
- If patients respond to IFX, cyclosporin, or tacrolimus and CMV tests positive: No need for treatment
- If non responder and CMV + then treat for CMV-Ganciclovir 5mg/kg 3-5days then oral valganciclovir 900mg BD
- If severe systemic CMV- stop immunosuppressive therapy

Sequential therapy

- Benefit outweighs risk
- Done at expert IBD centre
- Conflicting data leads to not recommend second line salvage therapy as it delays colectomy

L Calmejane et al 2023

Nutrition

- Debate -enteral or IV nutrition is the better management option for ASUC
- No difference in colectomy rates or mortality were observed between patients with ASUC receiving IV steroids on bowel rest with parenteral nutrition and those with oral diet

H Nakase 2023

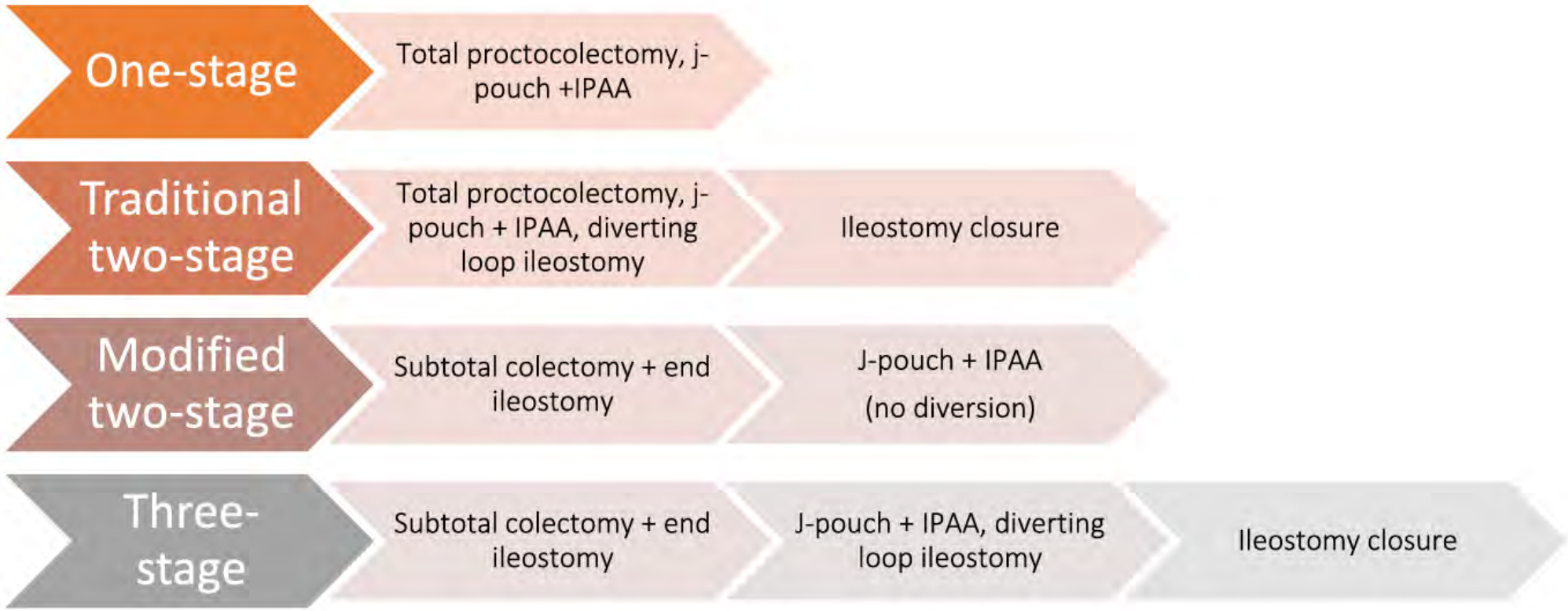
Indication for colectomy

- Patients that don’t respond to rescue therapy
- Intestinal perforation
- Massive hemorrhage
- Toxic dilation with impending perforation
- Long standing colitis with intractability

H Nakase 2023

Surgical management of ASUC

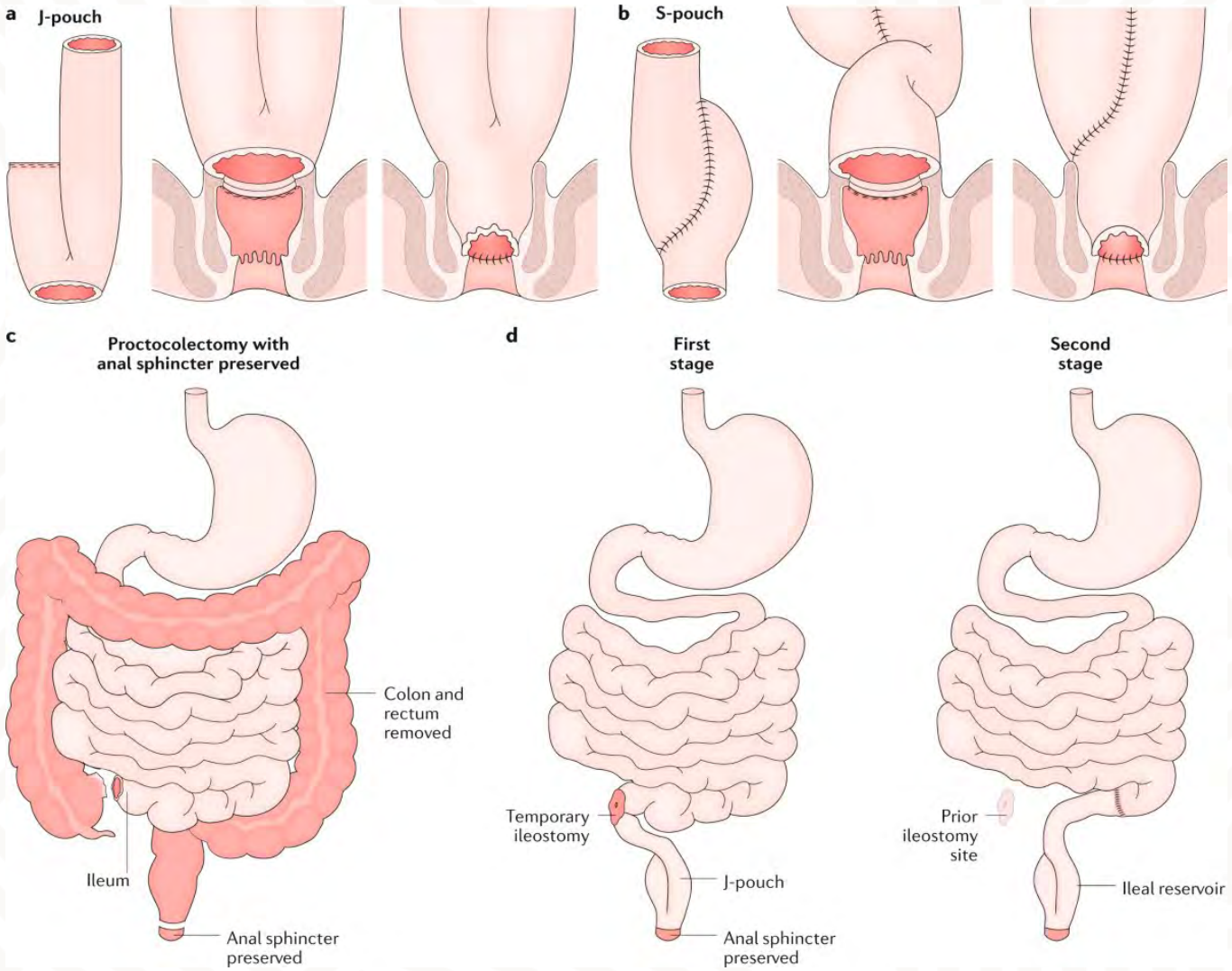
E. Clement et al.



Surgical management

- After total proctocolectomy for medically refractory UC, IPAA is the procedure of choice, but permanent end ileostomy is also a reasonable option for some patients
- IPAA may be performed as a two or three stage procedure.
- IPAA may be constructed using either a stapled or a handsewn technique, with comparable functional outcomes.
- UC patients with mild rectal disease may undergo ileo-rectal anastomosis.

A Spinelli et al 2022


a J-pouch
b S-pouch
c
Proctocolectomy with anal sphincter preserved
Colon and rectum removed
Ileum
Anal sphincter preserved
d
First stage
Temporary ileostomy
J-pouch
Anal sphincter preserved
Second stage
Prior ileostomy site
Ileal reservoir

Predictors of Poor surgical outcomes

- Increased age
- Low albumin
- Multiple comorbidities
- Prolonged steroid use
- Infections
- infliximab was not associated an increased risk of 30-day post-operative complications

A li et al 2023

Updated management of acute severe ulcerative colitis: from steroids to novel medical strategies

General principles at admission

- Stool cultures (**C. Difficile**)
- Blood samples (Hb, CRP, albumin, TB, pre-biologic work-up)
- Abdominal CT-scan
- Endoscopic assessment (CMV identification)
- Thromboprophylaxis
- No systematic use of antibiotics
- Consider enteral nutrition

Always consider surgery

First line

IV corticosteroids
0.8-1 mg/kg

Daily assessment (Lichtiger, clinical evaluation) and close monitoring

Evaluation at day 3-5

Always consider surgery

Second line

1. Anti-TNF naive
Infliximab or ciclosporin

2. Anti-TNF exposed
IV ciclosporin 2 mg/kg as a bridge to
- Vedolizumab
- Ustekinumab

Tofacitinib or other JAK inhibitor?

Always consider surgery

Third line

Colectomy is recommended

A third line may be considered selected patients in expert centers

1. Infliximab -> Ciclosporin

2. Ciclosporin -> Infliximab

3. Tofacitinib

Project ECHO
Gastroenterology Foundation of sub Saharan Africa

G-ECHO
GI HEPATOLOGY ECHO OF SUB-SAHARAN AFRICA
ESTABLISHED 2020

Stellenbosch UNIVERSITY
IYUNIVESITHI
UNIVERSITEIT

forward together
sonke siya phambili
saam vorentoe

Thank you
Enkosi
Dankie

Photo by Stefan Els

Medicine and Health Sciences | EyeNzululwazi ngezoNyango neMpilo | Geneeskunde en Gesondheidswetenskappe