Diverticular diseases including SCAD

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Definition

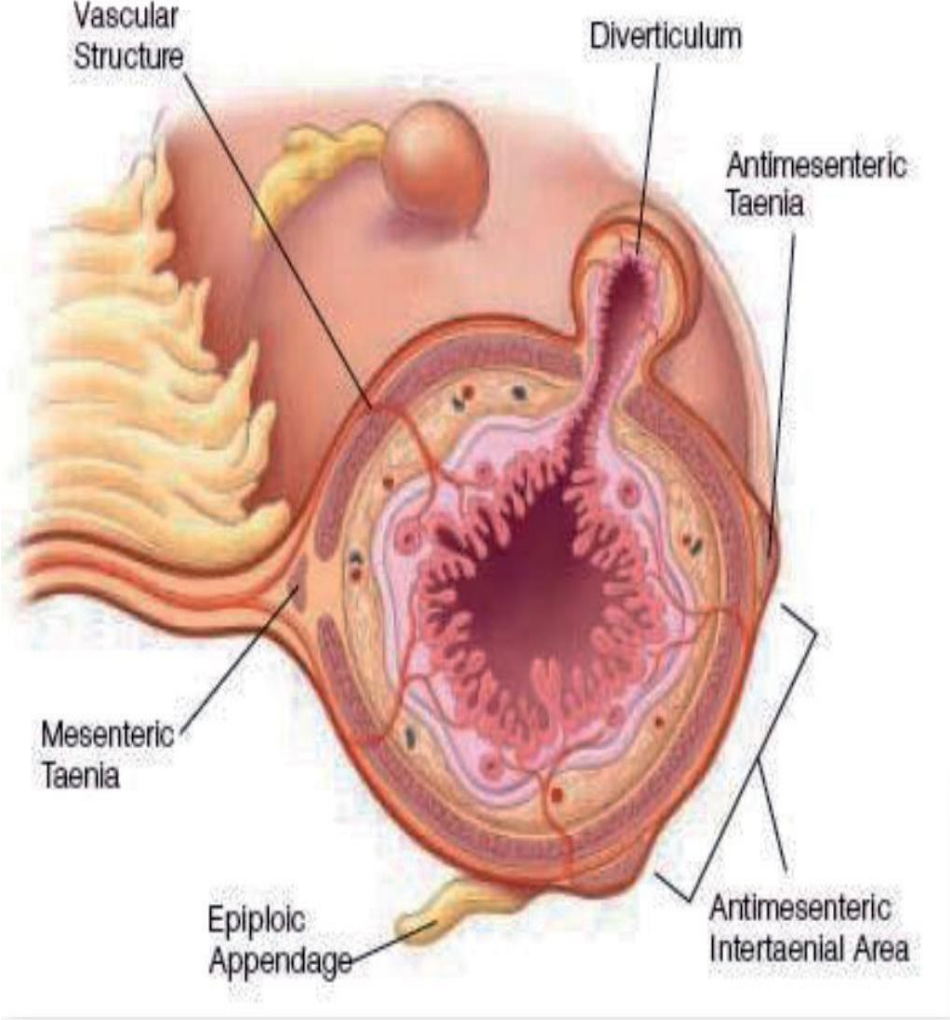
- A diverticulum is a sac-like protrusion of the colonic wall.
- Diverticular disease is defined as clinically significant and symptomatic because of:
  - bleeding
  - diverticulitis
  - segmental colitis associated with diverticula, or
  - symptomatic, uncomplicated diverticular disease.

Pathophysiology

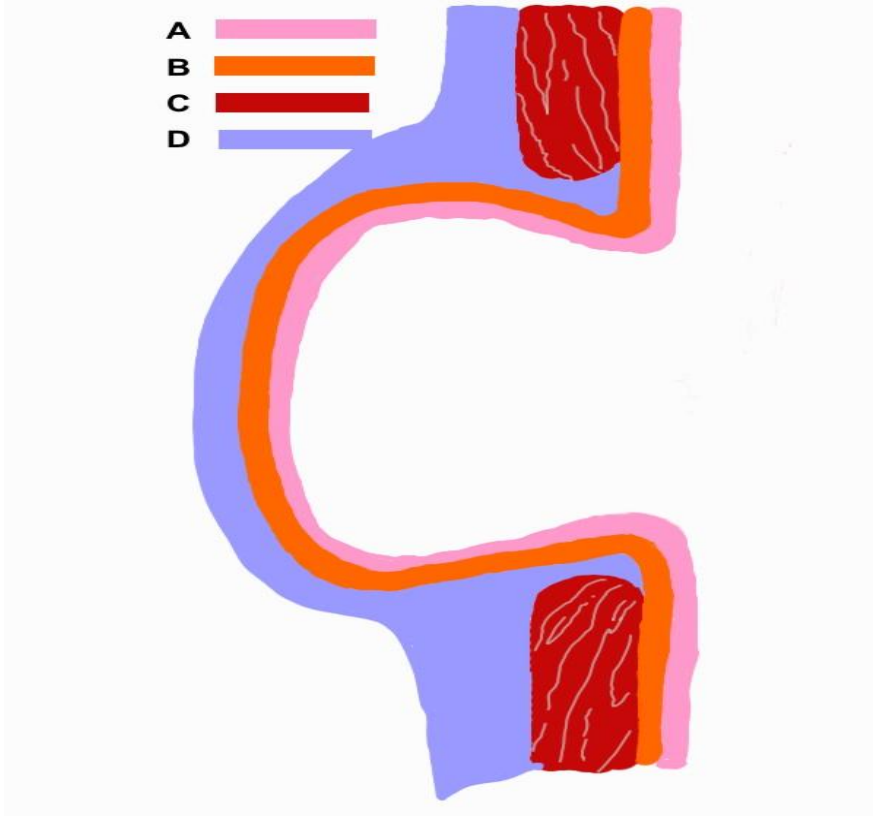
Develop at

- well-defined points of weakness
- which correspond to where the vasa recta penetrate the circular muscle layer of the colon

Typically: A diverticulum is a "false" or pulsion diverticulum, in which mucosa and submucosa herniate through the muscle layer, covered only by serosa.



False diverticulum
a- mucosa, b- submucosa, c muscular layer, d-serosa



Pathophysiology

Abnormal colonic motility and exaggerated segmentation contractions in which segmental muscular contractions separate

The neural basis for the abnormal motility observed in patients with diverticulosis remains unclear

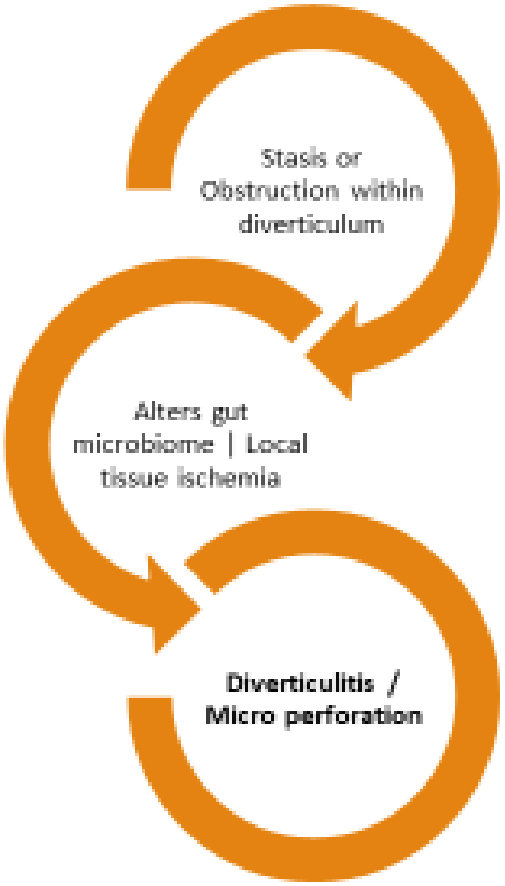
Site of Higher Tension- Sigmoid colon

Sigmoid colon has the smallest diameter equally the segment with the highest-pressure during segmentation hence higher risk for diverticular as in Laplace law

pressure (P) is proportional to wall tension (T) and inversely proportional to bowel radius (R), where k is a conversion factor ($P = kT \div R$).

Barbaro MF. Int J Mol Sci 20??

Chronic Constipation → Increased intraluminal pressure → Colonic mucosal hypertrophy → Mucosal & Submucosal herniation @ entry points of penetrating vessels → Diverticulosis



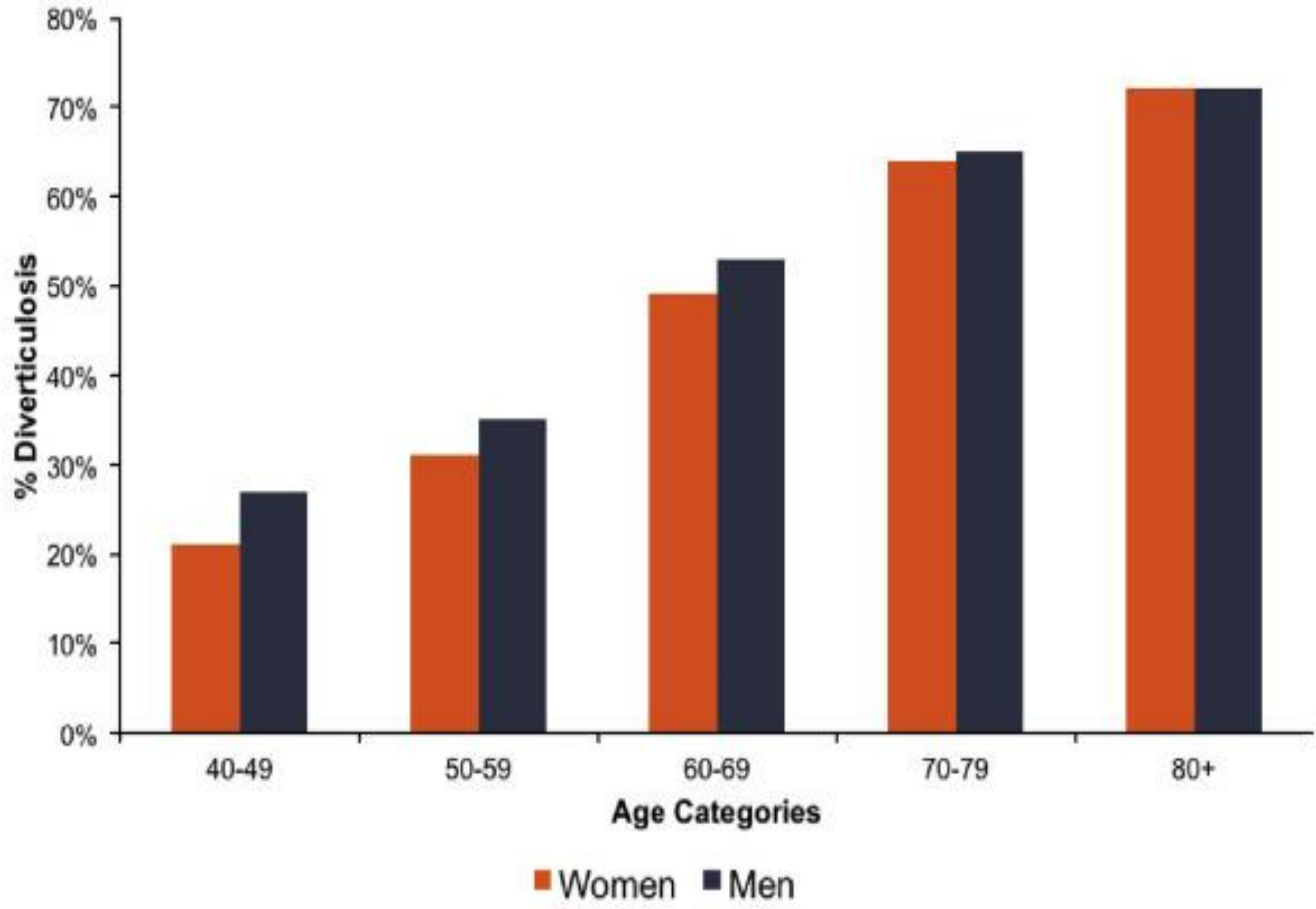
- Usually diverticulosis may develop through out entire colon
- More in sigmoid colon / Left side because that's where stool is formed commonly
- Diverticulosis (presence of diverticula without inflammation) usually asymptomatic
- But there may be significant overlap b/w IBS-C and diverticulosis ∴ Pain/Constipation (SUDD)

- **Two most common complications** of diverticulosis are:
  - Bleeding (usually from non inflamed diverticula)
    - Abrupt
    - Can be Severe or` massive
    - May be cyclic & difficult to locate
    - D/D to consider: AVM (commonly on Rt. Colon)
  - Diverticulitis (Bleeding & Chronic anemia are not a/w diverticulitis)
    - Clinical triad of acute diverticulitis

    - Chronic diverticulitis presents with Fibrostenotic stricture (LBO) or Fistula to Bladder/Vagina/SB & Skin.

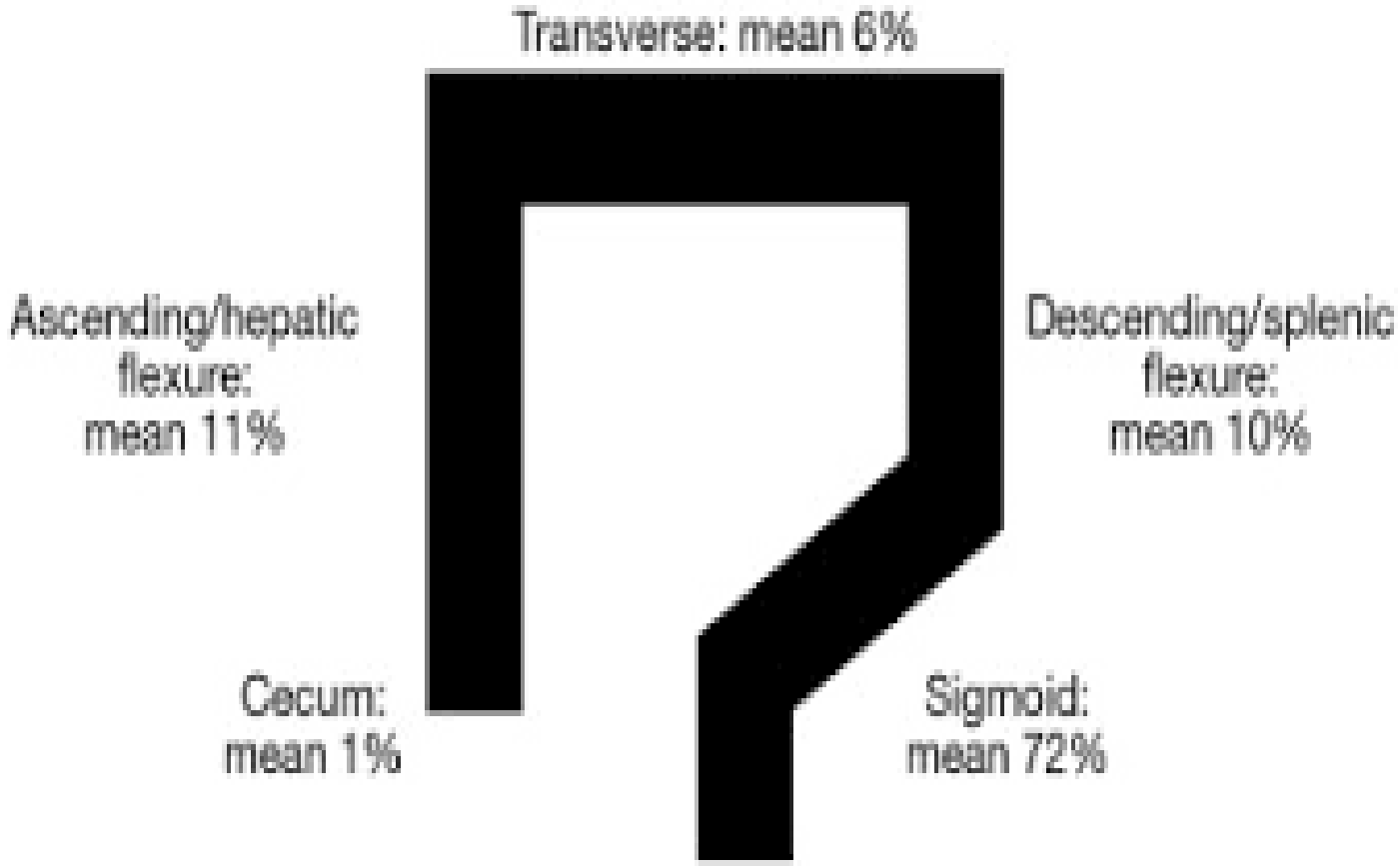
Prevalence

- Prevalence by age
- • Age 40: 5%
- • Age 60: 30% •
- Age 80: 65%
- Prevalence by sex:
- • Age < 50: more common in males
- • Age 50–70: slight preponderance in women
- • Age > 70: more common in women 1



Young-Fadok TM, Roberts PL, Spencer MP, Wolff BG. Colonic diverticular disease. Curr Prob Surg 2000;37:457-514 (PMID: 10932672)

Distribution of diverticular disease



WGO Practice Guidelines Diverticular disease 2007

Local prevalence

SAMJ RESEARCH

An investigation of diverticular disease among black patients undergoing colonoscopy at Dr George Mukhari Academic Hospital, Pretoria, South Africa

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Background. Diverticular disease was previously thought to be non-existent in the black African population. Studies over the past four decades, however, have shown a steady increase in the prevalence of the disease.

Objective. To report on the profile and current prevalence of diverticular disease in the black South African (SA) population at Dr George Mukhari Academic Hospital, Pretoria, SA.

Methods. A retrospective descriptive study was performed in black SA patients who were diagnosed with diverticular disease by colonoscopy between 1 January and 31 December 2015.

Results. Of 348 patients who had undergone colonoscopies and who were eligible for inclusion in this study, 47 were diagnosed with diverticular disease – a prevalence of 13.50% (95% confidence interval 10.30 - 17.50). The greatest number of patients diagnosed were in their 7th and 8th decades, with an age range of 46 - 86 (mean 67) years. There was a female predominance of 57.45%. Lower gastrointestinal bleeding was the most common (65.96%) indication for colonoscopy. The left colon was most commonly involved (72.34%), followed by the right colon (55.31%). A substantial number of patients had pancolonic involvement (27.65%).

Conclusion. This retrospective study suggests that there has been a considerable increase in the prevalence of diverticular disease among black South Africans, possibly owing to changes in dietary habits and socioeconomic status.

S Afr Med J 2017;107(2):137-139. DOI:10.7196/SAMJ.2017.v107i2.12007

Table 2. Summary of age data

Age data	All cases	Male	Female
Number (*n*)	42	18	24
Age (years), mean	67.40	68.90	66.25
SD	9.60	9.15	9.96

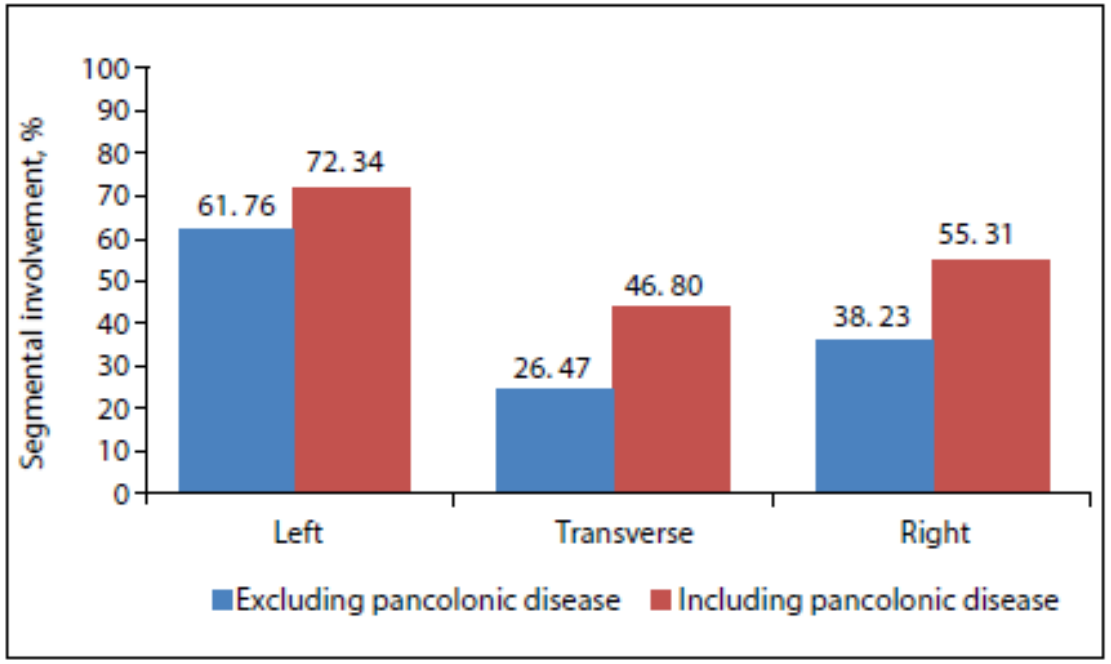


Fig. 1. Comparison of segmental involvement with and without pancolonic

Table 3. Summary of pattern of involvement

Segment	*n* (%)	Male	Female
Left side only	13 (27.65)	5	8
Left side and transverse	5 (10.64)	2	3
Transverse only	3 (6.38)	2	1
Right side only	9 (19.14)	4	5
Right and left sides	3 (6.38)	1	2
Right side and transverse	1 (2.13)	1	0
Pancolonic	13 (27.65)	5	8
Total	47 (100)	20	27

Risk factors-Genetics

- Genetics also play a central role in determining the risk of diverticulitis.
- Genome-wide association studies (GWAS) have identified over 30 susceptibility loci for diverticular disease.
- Of these, four have stronger effects for diverticulitis than diverticulosis or non-specific diverticular disease including PHGR1, FAM155A, CALCB and S100A10. Genes implicated in diverticular disease are important for immunity, cell adhesion, connective tissue integrity, membrane transport, and smooth muscle function

Risk factors for development of diverticulosis

- Age
- Alcohol use
- Low fiber diet
- NSAIDS Opioids Steroids
- Obesity (BMI >30kg/m^2
- Sedentary lifestyle
- Smoking

- Western lifestyle = low fiber increased red meat
- Prevalence in Africa a low 4%, probably due to a low-fat diet while in Asia its prevalence is between 8 and 25%
- Predominantly right-colon involvement (70–74%) in Africa and Asia

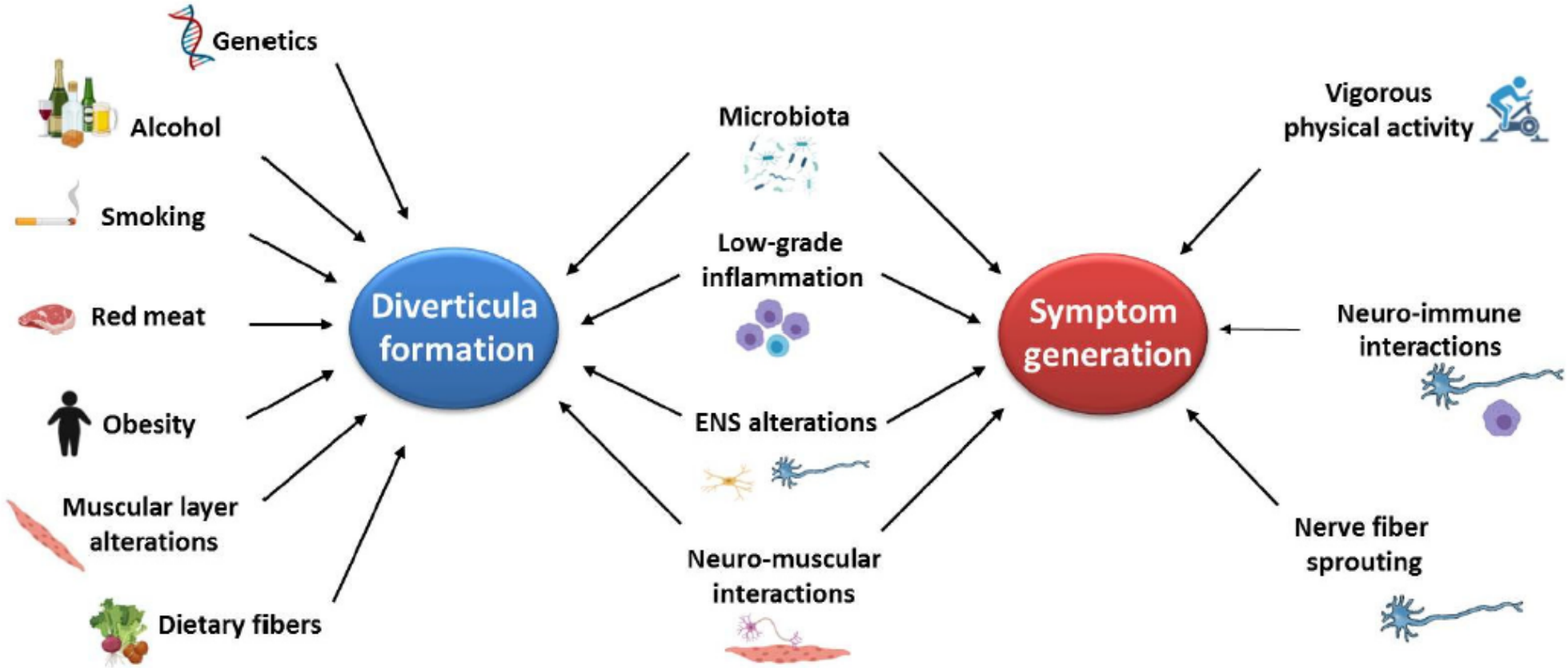
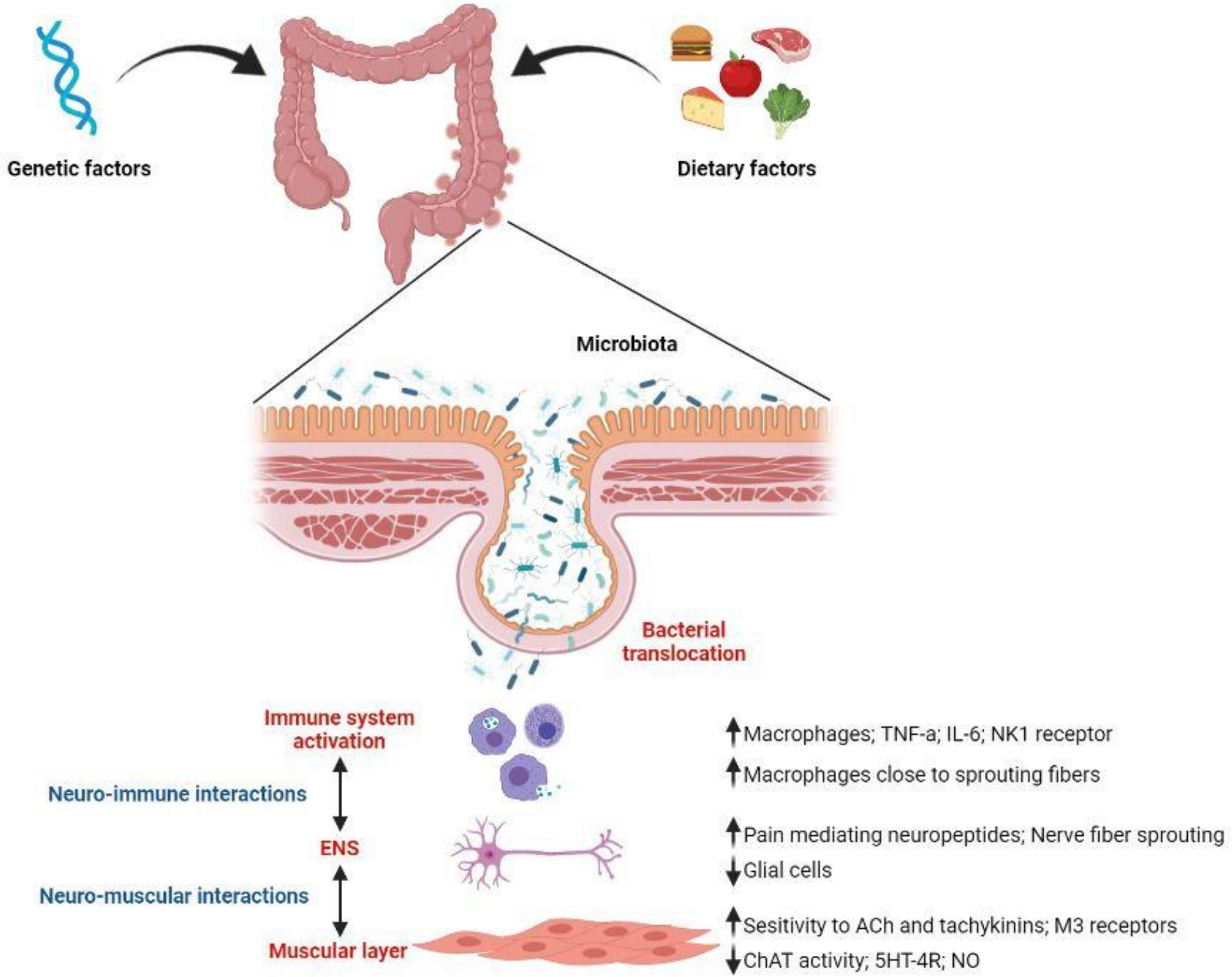


Figure 1. Factors involved in diverticula formation and/or in symptom generation. On the basis of the available data, the figure shows which factors are likely involved in diverticula formation (i.e., in the pathophysiology of diverticulosis and SUDD) and/or in symptom generation (i.e., in the pathophysiology of SUDD).


Genetic factors
Dietary factors
Microbiota
Bacterial translocation
Immune system activation
Neuro-immune interactions
ENS
Neuro-muscular interactions
Muscular layer
Macrophages; TNF-a; IL-6; NK1 receptor
Macrophages close to sprouting fibers
Pain mediating neuropeptides; Nerve fiber sprouting
Glial cells
Sesitivity to ACh and tachykinins; M3 receptors
ChAT activity; 5HT-4R; NO

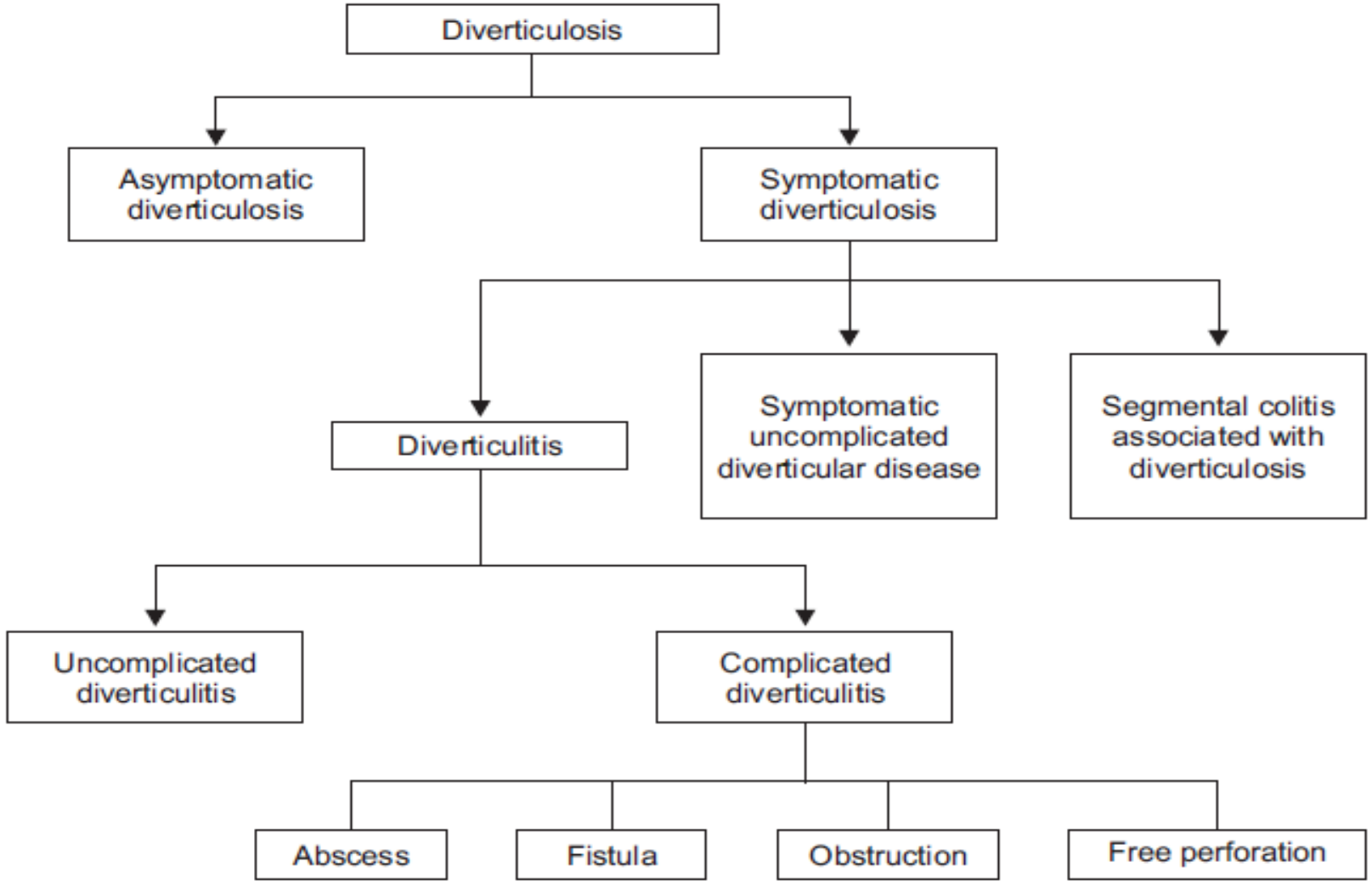
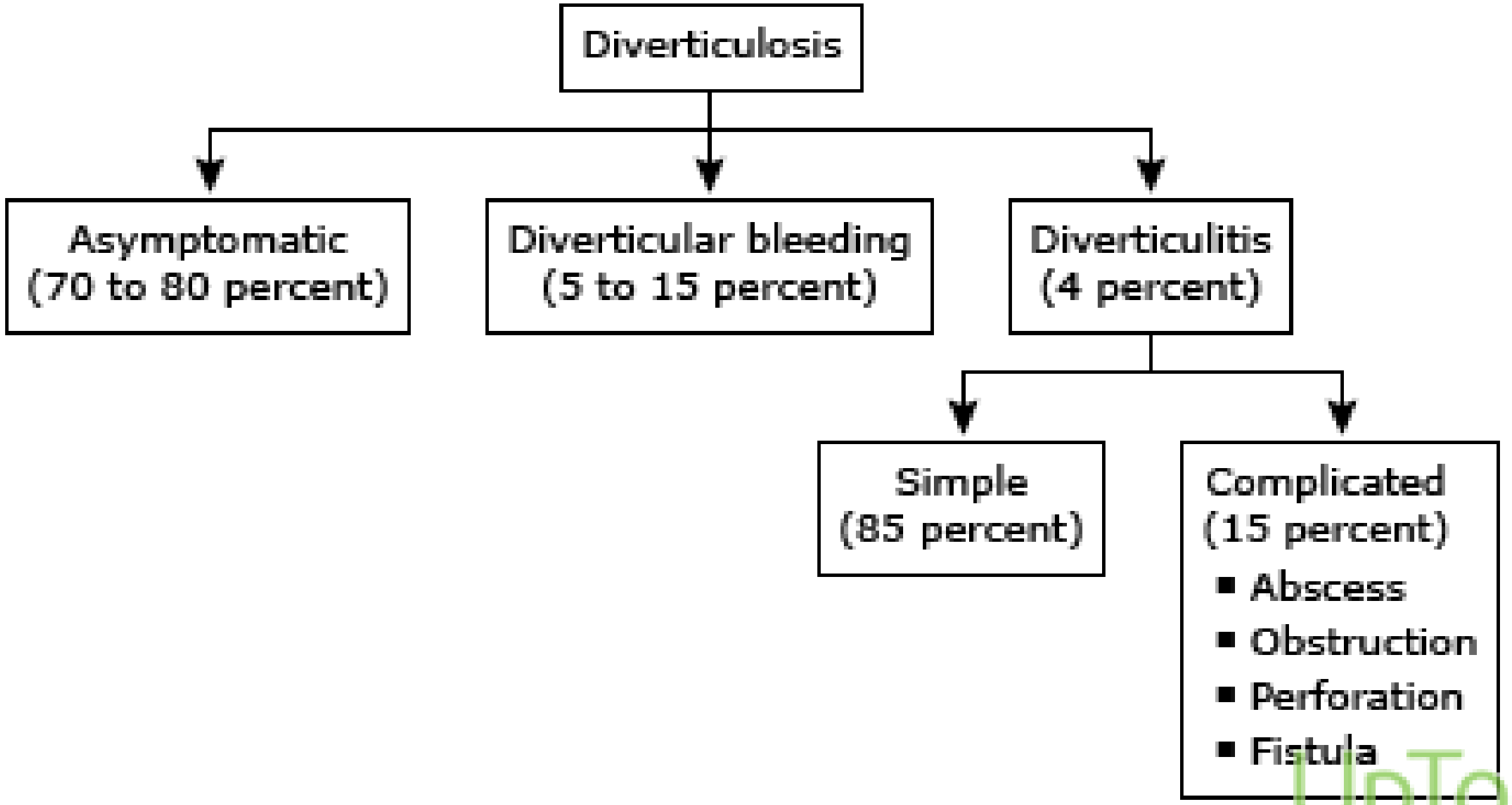


Fig. 1. Classification of diverticular disease.

Natural history of diverticulosis



Natural history of diverticular disease

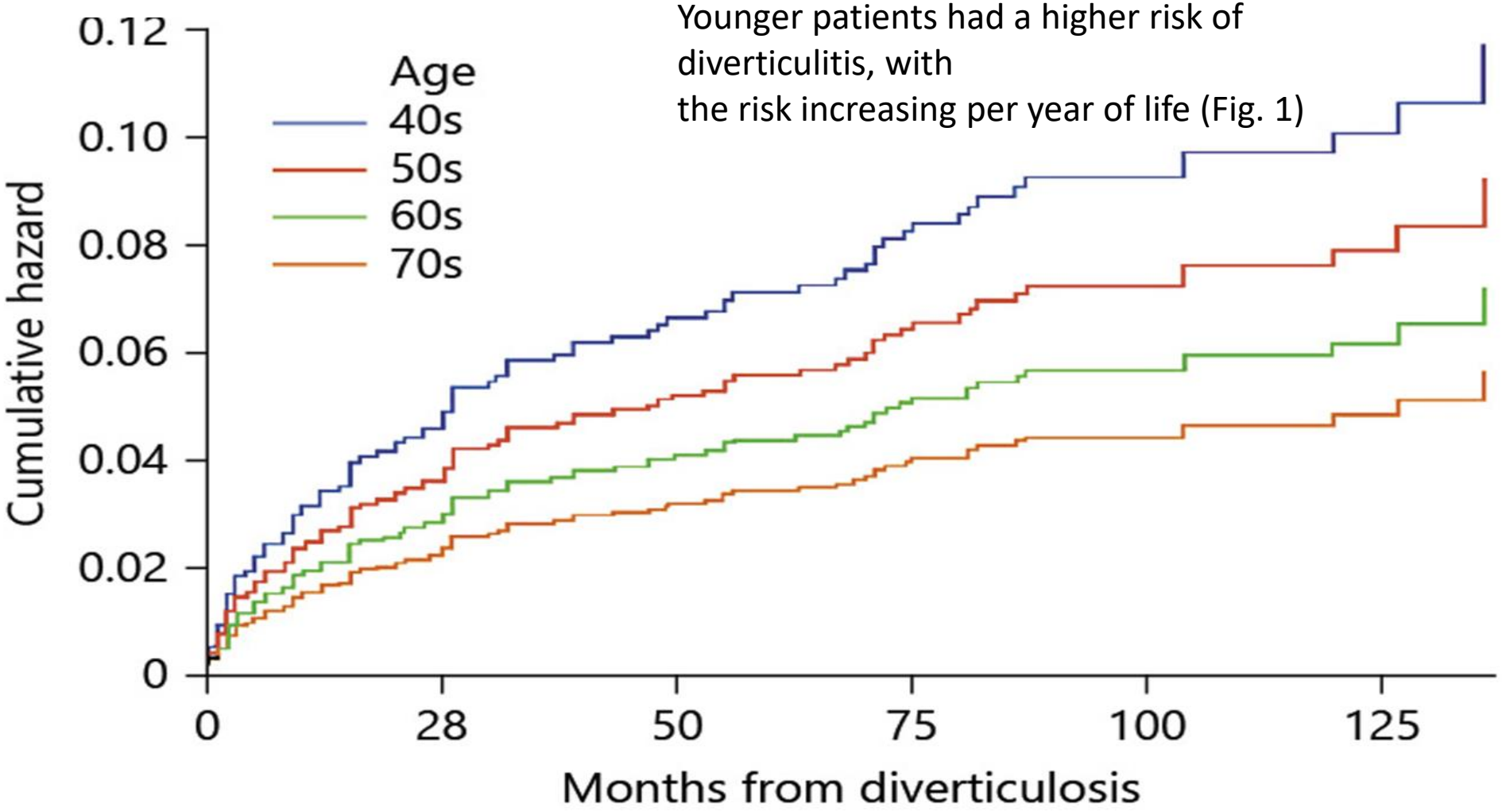
Study	Year	Type of study	Patients, *n*	Duration of follow-up, years	Clinical endpoint and incidence	Mean time to event, years	Limitations and strengths
Shahedi et al. [23]	2013	Retrospective	2,222	15	Acute diverticulitis 1.5–6.0/1,000 patient-years	7.1	No information on diverticular bleeding 97% males Baseline colonoscopy: all indications Large number of patients Rigorously defined endpoint
Niikura et al. [24]	2015	Retrospective	1,514	10	Diverticular bleeding 0.46/1,000 patient-years	4.2[a]	No information on diverticulitis Baseline colonoscopy: all indications Large number of patients Diverticular bleeding in 35 patients: definitive in 7, presumptive in 28
Shayto et al. [25]	2016	Retrospective	144	10	Acute diverticulitis and diverticular bleeding 5.9/1,000 patient-years	5.1	Small number of patients Average-risk CRC screening population: true asymptomatic population Ascertained both complications Well-defined, prospectively enrolled cohort

[a] Median time to event.

Rustom LB. Inflamm Intest Dis 2018

Fig. 1. Kaplan-Meier curves stratified by the decade of life at the time of initial diverticulosis detection and the risk of diverticulitis. Reprinted with permission from Shahedi et al. [23].

Younger patients had a higher risk of diverticulitis, with
the risk increasing per year of life (Fig. 1)



Diverticulitis

- Common
- In US: 1.9m outpatient visit
  208 000 inpatients
- Incidence: 180/100000/year

- Diverticulitis is the inflammation of diverticula and may be acute or chronic.
- Acute diverticulitis (AD) can be uncomplicated or complicated.
- Uncomplicated AD refers to diverticular inflammation without complications,

  While

- complicated AD indicates diverticulitis associated with complications (bleeding, abscess, perforation, peritonitis, fistula, obstruction)

DIVERTICULITIS

Diverticulitis — The underlying cause of diverticulitis is micro- or macroscopic perforation of a diverticulum.

Mechanisms- previously thought to be due to obstruction of the diverticula It (eg, by fecaliths). However, such obstruction is now thought to be rare

The primary process is thought to be erosion of the diverticular wall by increased intraluminal pressure or inspissated food particles.

Inflammation and focal necrosis ensue, resulting in perforation

The inflammation is frequently mild, and a small perforation is walled off by pericolic fat and mesentery.

This may lead to a localized abscess or, if adjacent organs are involved, a fistula or obstruction

. Poor containment of the inflamed diverticulum or abscess results in free perforation and peritonitis.

cont

- Simple diverticulitis: 75% of cases
- Complicated diverticulitis: 25% of cases (abscess, fistula, or perforation)

- Diagnosis.
- The majority of patients have left lower quadrant pain.
- An element of rebound tenderness implies some degree of peritoneal involvement.
- Fever and leukocytosis are other important but nonspecific findings.

Presentation

- Elevated WBC and/or CRP
- Clinical suspicion of diverticulitis alone is correct in only 40–65% of patients.
- Contrasted CT scan of the abdomen and (sensitivity/specificity 95%)
- USS is an alternative but is operator dependent
- MRI very sensitive but poor specificity
- Xray- useful for assessing complications

Imaging

- CT should be considered to confirm the diagnosis of diverticulitis in patients without a prior imaging-confirmed diagnosis and to evaluate for potential complications in patients with severe presentations.
- Imaging should also be considered in those who fail to improve with therapy,
- Immunocompromised,
- or who have multiple recurrences and are contemplating prophylactic surgery in order to confirm the diagnosis and location(s) of disease.

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AGA Clinical Practice Update on Medical Management of Colonic Diverticulitis: Expert Review

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Risk of progression of uncomplicated to complicated diverticulitis

- Among patients with acute uncomplicated diverticulitis, the risk of progression to complicated diverticulitis is 5%.

.

Risk factors

- Baseline ASA score III or IV,
- duration of symptoms longer than 5 days prior to presentation,
- presence of vomiting, CRP >140 mg/L, and baseline white blood cell count > 15 × 109 cells per liter.
- The presence of a fluid collection or longer segment of inflammation on baseline CT (86 mm versus 65mm).
- Therefore, patients with one of these factors should be considered high risk and treated with a course of antibiotics.

cont

- When antibiotic treatment is necessary, the regimen usually includes broad spectrum agents with gram-negative and anaerobic coverage.

- In the outpatient setting, treatment of mild uncomplicated diverticulitis either a combination of an oral fluoroquinolone and metronidazole
- or monotherapy with oral amoxicillin-clavulanate.
- The duration of treatment is usually 4–7 days but can be longer. Up to 10-14days in more severe cases or immunosuppressed

Guide

- Immunocompromised patients are more likely to present with severe or complicated disease.
- For these patients there should be a low threshold for cross sectional imaging, antibiotic treatment, and consultation with a colorectal surgeon.
- Corticosteroid use is a risk factor for diverticulitis and may contribute to complications including perforation and death.

Guide on preventive measures

- To reduce the risk of recurrence, patients with a history of diverticulitis should consume a high-quality diet,
- achieve or maintain a normal BMI
- routinely be physically active, and not smoke.
- Avoid indiscriminate use of NSAID <2x/week, except for aspirin
- Patients with a history of diverticulitis should not be treated with 5-aminosalicylic acid, probiotics, or rifaximin to prevent recurrent diverticulitis. No data to support

The role of colonoscopy

- After an acute episode of diverticulitis colonoscopy should be delayed by 6–8 weeks or until symptoms resolution. Colonoscopy if alarming symptoms are present.

- Alarm symptoms include change in stool caliber, iron deficiency anemia, blood in stool, weight loss, and abdominal pain.

There is evidence for increase chances of Cancer among those with complicated AD vs Mild Diverticulitis

AGA guideline on role of surgery

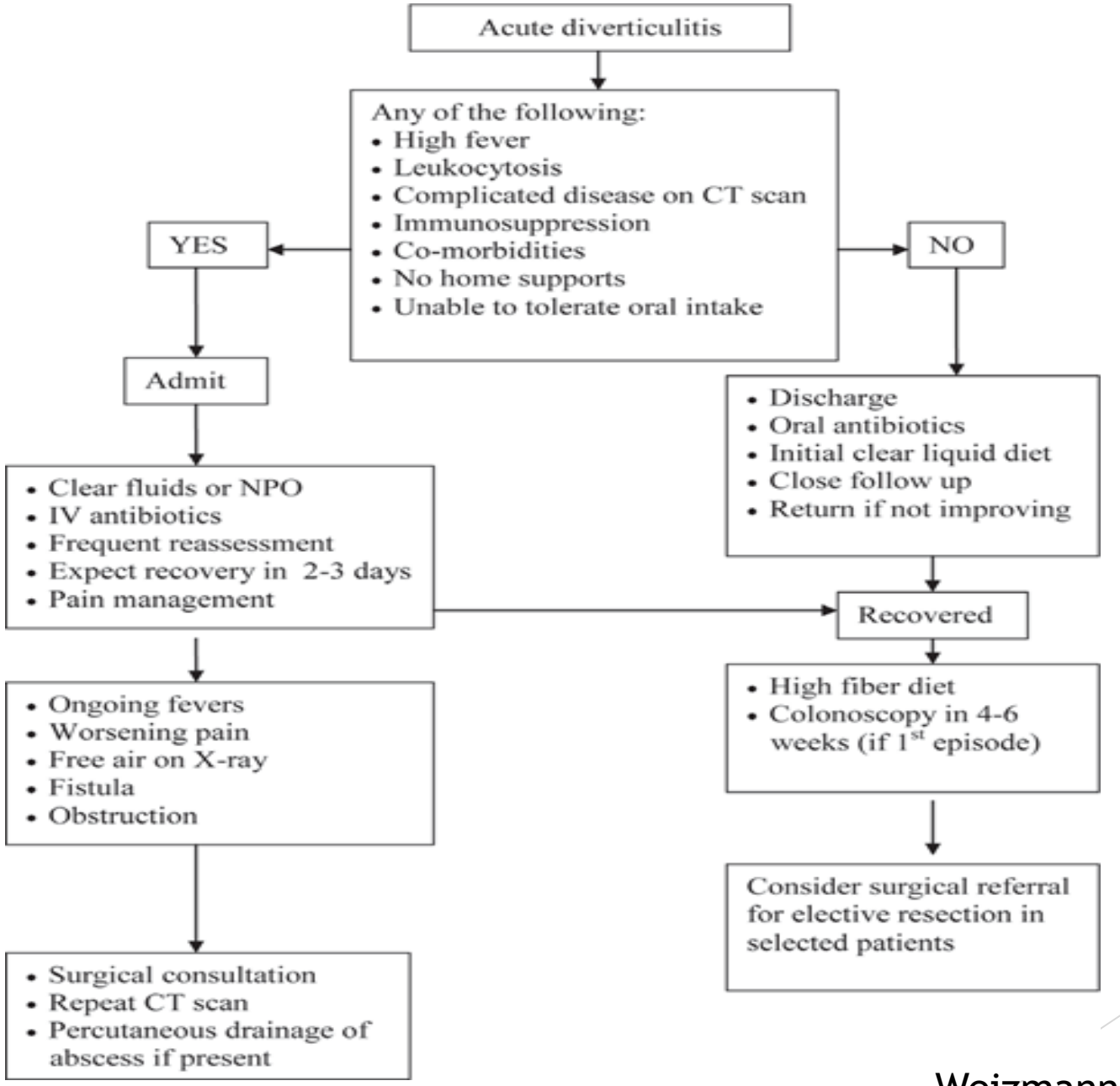
Patients with a history of complicated diverticulitis successfully managed without surgery are at increased risk of recurrence and complicated recurrence.

While some guidelines recommended interval elective resection, there is a growing literature suggesting a more conservative and personalized approach to these patients.

In an observational study, long-term rates of emergency surgery and/or death were low (5%) among patients after an episode of complicated diverticulitis successfully managed without surgery.

Elective resection was not associated with reduced rates of emergency surgery or death.

Immunocompromised patients should be prioritized, the aim is to prevent recurrent and more complicated diverticulitis



Weizmann AV. Can J Gastroenterol 2011

Fistulas

- Among patients with diverticulitis, only a few will develop complications as fistula .
- most common etiology for colo-vesical fistula is a diverticular disease (40–80%) .
- CVF in cancer (19%),
- Occur also in Crohn’s disease, radiotherapy, or iatrogenic.
- Open surgery management has been the standard treatment for these fistulas. More recently, laparoscopic surgery has shown to be an alternative; conversion rates up to 46.9%.

Abscess following acute diverticulitis

In general, intra-abdominal abscesses are formed by:

- — Anastomosis leakage: 35%
- — Diverticular disease: 23%
- Limited spread of the perforation forms a phlegmon, while further (but still localized) progression creates an abscess

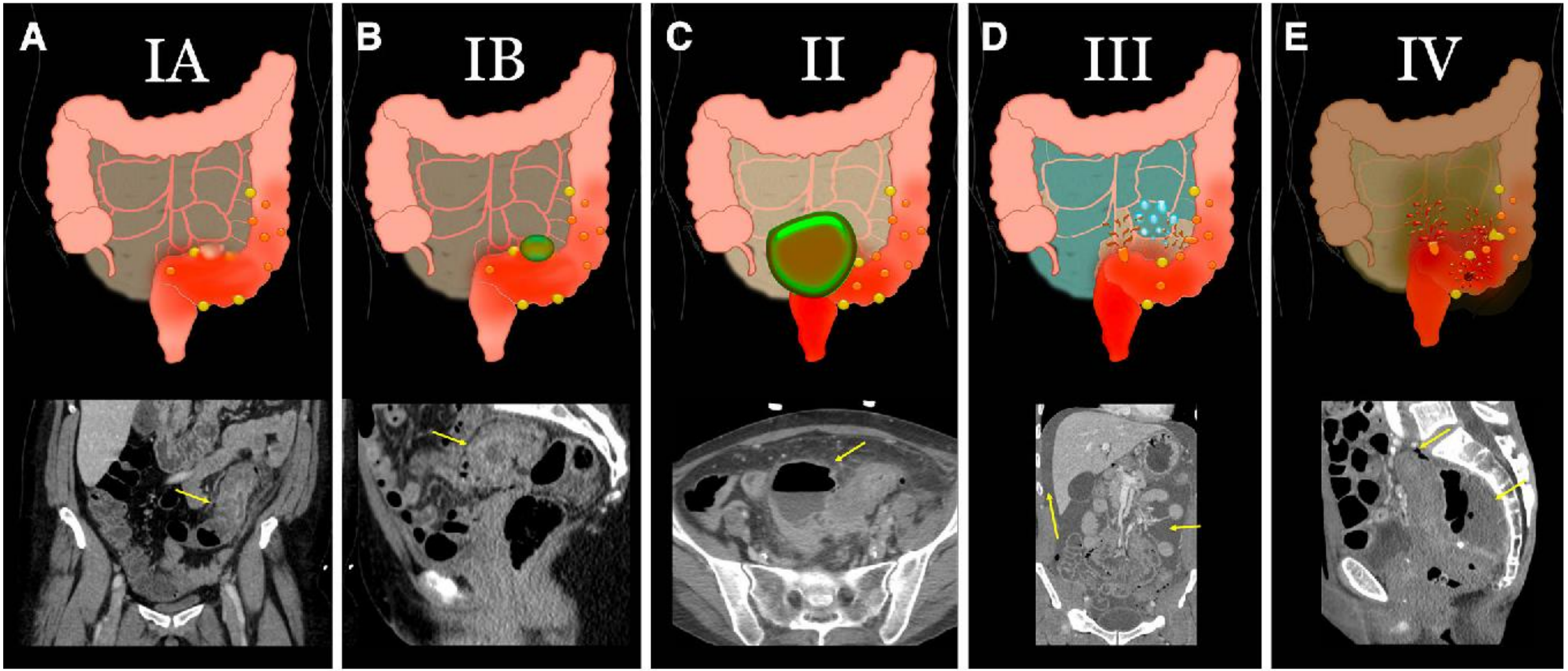
cont

- — Small pericolic abscess: 90% will respond to antibiotics and conservative management alone.
- — Percutaneous abscess drainage (PAD) is the treatment of choice for small, simple, well-defined collections. A group at the University of Minnesota published an overall success rate for PAD of 76%.
- — 100% of simple unilocular abscesses resolved with PAD and antibiotic therapy.
- Factors limiting success -multilocular collection, abscesses associated with enteric fistulas, and abscesses containing solid or semisolid material

Tabel I. Hinchey's classification of acute diverticulitis and CT findings [56]

0	Colonic wall thickening	Diverticula ± colonic wall thickening
Ia	Confined pericolic inflammation - phlegmon	Colonic wall thickening with pericolic soft tissue changes
Ib	Confined pericolic abscess	Ia changes + pericolic or mesocolic abscess
II	Pelvic, distant intra-abdominal or retroperitoneal abcess	Ia changes + distant abscess (generally deep in the pelvis or interloop regions)
III	Generalized purulent peritonitis	Free gas associated with localized or generalized ascites and possible peritoneal wall thickening
IV	Fecal peritonitis, Fistula colo-vesical/vaginal/enteric/ cutaneous, Obstruction Large and/or small bowel	Same findings as III

J Gastrointestin Liver Dis, December 2018 Vol. 27 No 4: 449-457


A
IA
B
IB
C
II
D
III
E
IV

Significant of this classification

Guidelines recommend that antibiotic treatment can be used selectively, rather than routinely, immunocompetent patients with acute

uncomplicated diverticulitis (Hinchey Ia)

Hinchey Ib/II diverticulitis

Smaller (<3 cm) paracolic abscesses are treated with antibiotics that cover Gram negative and anaerobic bacteria with or without Perc drain

Acute diverticulitis with purulent or feculent

contamination of the peritoneal cavity is almost always managed with surgery and antibiotics. Hinchey III & IV

Diverticular bleed

- Among patients with diverticulosis, the risk of bleeding is approximately 0.5 per 1000 person-years
- Risk factors for bleeding included
- age ≥70 years and
- bilateral diverticulosis
- obesity also appears to increase the risk of diverticulitis and colonic diverticular bleeding.

Pathogenesis

- Due to segmental weakness of the penetrating vasa recta at the point of herniation.
- There is because the penetrating vessel responsible for the wall weakness at the point of herniation becomes draped over the dome of the diverticulum, separated from the bowel lumen only by mucosa, ➡ rupture of these vessels
- 50-90% of diverticular bleed occur in the right colon.? Wider neck and dome, ?thinner wall

cont

- 75% diverticular bleeds will stop spontaneously
- There is increased risk of rebleeding

- Mgt
- Resuscitation, Endoscopic therapy, CT angiography and coiling if these fails then surgery.

Locating the source of bleeding

- The source of bleeding is not identified in up to 30–40% of cases.
- Selective angiography: — The minimum rate needed is 1.0–1.3 mL/min.
- Radioisotope scanning: — Bleeding can be detected at rates as low as 0.1 mL/min. — takes a short time to complete the study; repeated for up to 24–36 hours.
- The accuracy of bleeding studies varies widely, from 24% to 91%.
- Colonoscopy is best reserved for self-limited bleeding

WGO, 2007 WGO Practice Guidelines Diverticular disease

SCAD

- Segmental colitis associated with diverticulosis (SCAD) is a chronic inflammatory change. It occurs between colonic diverticula,
- limited to the sigmoid and left colon,
- Diverticular ostium not commonly affected
- Rectum and right colon are spared
- The inflammation of the colonic mucosa may resemble other inflammatory bowel diseases (IBD). It appears to be a self-limited inflammatory process.

Terminology

- Several terms have been used
- crescentic fold disease,
- colitis associated with diverticular disease,
- Diverticular colitis, diverticular-associated colitis (DAC),
- Segmental colitis associated with diverticulosis (SCAD), this being the most currently accepted.

Cont.

- In one prospective study of 6230 colonoscopies performed for evaluation of gastrointestinal symptoms,
- the overall prevalence of SCAD and the prevalence in individuals with diverticulosis were 1.5 and 11 percent, respectively.
- The prevalence of SCAD is higher in men with a mean age of 64 years at diagnosis.
- However, SCAD has also been reported in younger patients.

Pathogenesis

- The exact pathogenic mechanism is not known, but it appears to be multifactorial pathogenesis.
- Several hypotheses have been raised, including
- mucosal prolapse leading to mucosal ischemia,
- fecal stasis within diverticula, and consequent dysbiosis that can trigger an immune response, and high exposure to intraluminal antigens and toxins.

Clinical condition

- The clinical picture associated with SCAD is variable, with studies citing complaints of diarrhea,
- rectal bleeding (only or with other changes),
- abdominal pain, and tenesmus .
- Fever and weight loss are rare .
- More than a third of patients have at least two associated symptoms at diagnosis.

Type	Pattern	Endoscopic appearance	Histological appearance
A	Crescentic fold	Swollen red patches as of 0.5 to 1.5 cm in diameter.	Without architectural changes in the crypts. Neutrophil and lymphocyte infiltrate are limited to crypt epithelium.
B	Mild to moderate UC-like	Diffuse loss of vascular pattern, mucosal edema and hyperemia, and diffuse erosions.	Active inflammation with architectural changes in the crypt, crypt abscesses, and goblet cell depletion. Chronic changes of the lamina propria.
C	Crohn's colitis-like	Isolated aphthous ulcers.	Highest variability. Transmural inflammation with microfissures. Lymphoid follicles and non-specific infiltrates.
D	Severe UC-like	As type B but more severe with diffuse ulceration and reduced caliber of the lumen.	Crypt architectural changes, diffuse cryptitis, crypt abscesses, and goblet cell depletion. Chronic changes of the lamina propria.

Table 1.
SCAD classification (endoscopic and histological appearance).

cont

- The clinical picture can be very similar to that of mild inflammatory bowel disease.
- Occasionally, the patient may be asymptomatic.
- Symptoms may vary according to the subtype of SCAD presented, with diarrhea being more common in type A
- and rectal bleeding and abdominal pain in types C and D.
- Type B presents with more than one symptom 39% of the time, with diarrhea and rectal bleeding being the main ones.

. Diagnosis

- The diagnosis of SCAD must initially be performed excluding other pathologies that cause intestinal inflammation, among these differential diagnoses
- Ischemic colitis,
- colitis induced by anti-inflammatory drugs,
- infectious colitis (mainly cytomegalovirus and Clostridium difficile), and IBD.
- Colonoscopy is the mainstay for the diagnosis of SCAD.

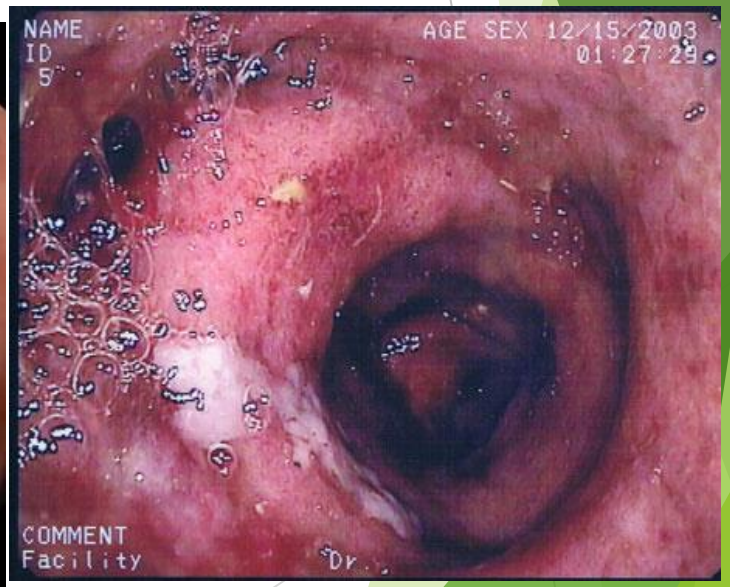
cont

- It is indicated to perform biopsies of affected areas and normal areas to accurately locate inflammatory changes.
- It is also suggested to perform a rectal biopsy (whose result should be negative) to strengthen the diagnosis.
- The pathologist must be informed about the clinical suspicion for better elucidation of the case.

Figure- Endoscopic appearances of inflammation in association with diverticula. (a) Inflammation affects only the diverticulum . (a)This is diverticulitis. (b). Inflammation affects only inter-diverticular mucosa, with sparing of the diverticulum. This is segmental colitis associated with diverticulosis (SCAD).) (c) Inflammation affects the entire colonic mucosa. This is ulcerative colitis in a patient with diverticulosis

UC

Diverticulitis vs SCAD



Treatment

- **Treatment**
- Since SCAD can resemble inflammatory diseases. It could be treated following the precepts of mild forms of IBD.
- It is considered more benign than other IBD, some resolve spontaneously.
- Types A and C SCAD seem to show a milder evolution,
- while types B and D have a high propensity to relapse, being highly indicated a more aggressive clinical and endoscopic follow-up and treatment for these two types.

- The standard treatment for SCAD is still not well defined, and it is possible to use a high fiber diet, use antibiotics (e.g., ciprofloxacin 500 mg twice a day associated with metronidazole 500 mg three times a day for 7 days) and
- Aminosalicylates (mesalamine 2.4 to 3.2 g per day) in cases of unsatisfactory response to antibiotics or recurrent symptoms,
- which can be continued for 7 to 10 days
- Steroids are used in severe third-line cases.

- Recent studies have demonstrated the possibility of combining beclomethasone dipropionate (BDP) (for 4 weeks) and the probiotic VSL#3 (for 15 days in a row) for the treatment of mild-to-moderate acute conditions, with the vast majority of patients reaching remission in week4 .
- In patients' refractory to conventional therapy for SCAD, infliximab and adalimumab could be good therapeutic options .

Table 2 Treatment algorithm for segmental colitis associated with diverticulosis

	Treatment	Duration
1st line*		
Step 1	Ciprofloxacin 500 mg b.i.d. + Metronidazole 400 mg t.i.d.	7 days
Step 2	Mesalazine 2.4-3.2 g/day**	4 weeks
Maintenance	Mesalazine 1.6 g/day	
2nd line		
Step 1	BDP 10 mg/day+VSL#3 2.5 g/day for 15 consecutive days	4 weeks
Step 2	BDP 5 mg/day+VSL#3 2.5 g/day for 15 consecutive days	4 weeks
Maintenance	Mesalazine 1.6 g daily+VSL#3 2.5 g daily 15 days/month	
3rd line***		
Step 1	Prednisolone 1 mg/kg/day	10 days
Step 2	Surgery if steroid-refractory or steroid-dependant	

*Together with a high-fiber diet
**Step 1 and Step 2 together if recurrent symptoms or incomplete response
***Reconsider diagnosis and look for evidence of IBD
BDP, beclomethasone dipropionate; IBD, inflammatory bowel disease; SCAD, segmental colitis associated with diverticulosis

INVITED REVIEW

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Segmental colitis associated with diverticulosis: is it the coexistence of colonic diverticulosis and inflammatory bowel disease?

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