Pouchitis

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Outlines

Background

- Ulcerative colitis
- FAP
- Why are Pouches created?
- Types of Pouches
- IPAA complication

Pouchitis

- Definition, Epidemiology
- Pathogenesis
- Risk factors
- Spectrum & Clinical Picture
- Classification
- Disease Activity
- Diagnosis
- Treatment and Prevention
- AGA guidelines
- Pouch Failure
- Common Mistakes & Message
- References

Ulcerative Colitis (UC)

- **Definition:**
  - A chronic inflammatory condition characterized by relapsing and remitting episodes of inflammation limited to **mucosal layer** of the **colon.**
  - 20%-30% of patient with advanced UC will require **surgical resection**.

Indications for Surgery in UC

Emergency Surgery:

1. Colonic perforation (toxic megacolon)
2. Life-threatening GIT haemorrhage

Urgent Surgery: (2 days)

Acute fulminant colitis refractory to medical treatment.

Elective Surgery:

1. Patient with persistent symptoms
2. Cancer risk and long-standing disease

Familial Adenomatous Polyposis Coli (FAP)

- Characterized by the presence of multiple colorectal **adenomatous polyps** (typically **> 100** for Classic FAP and **10-99** for attenuated FAP)
- **Prevalence:** 1 in 8000-18000 in USA
- **Colorectal cancer** occurs in nearly **100%** of patients if untreated.
- Surgery is indicated to **prevent** malignancy

Surgical Treatment for UC and FAP

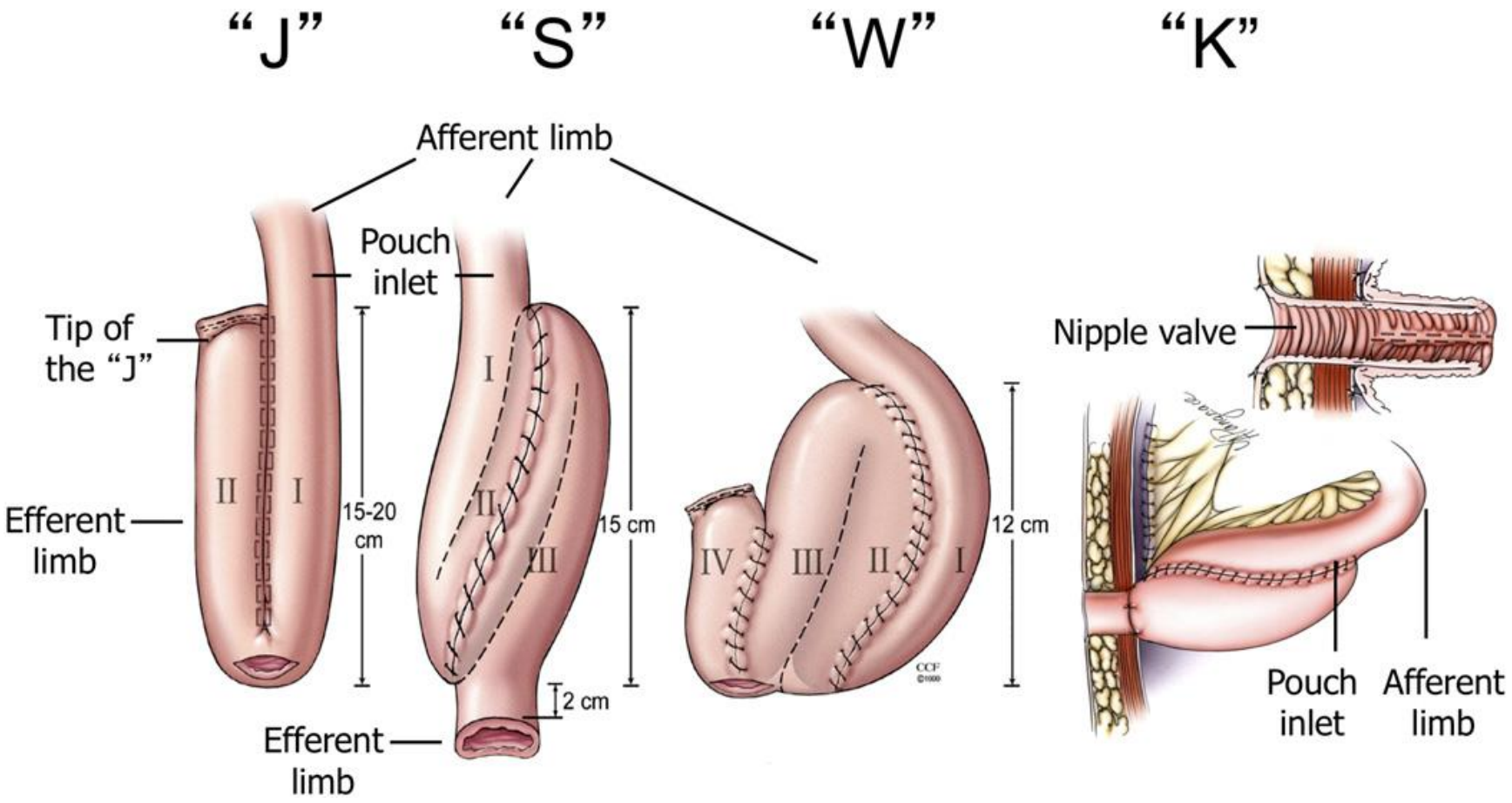
Restorative procto-colectomy with ileal pouch anal anastomosis (IPAA):

- Performed oftenly for patients with **UC and FAP** who require surgical treatment.

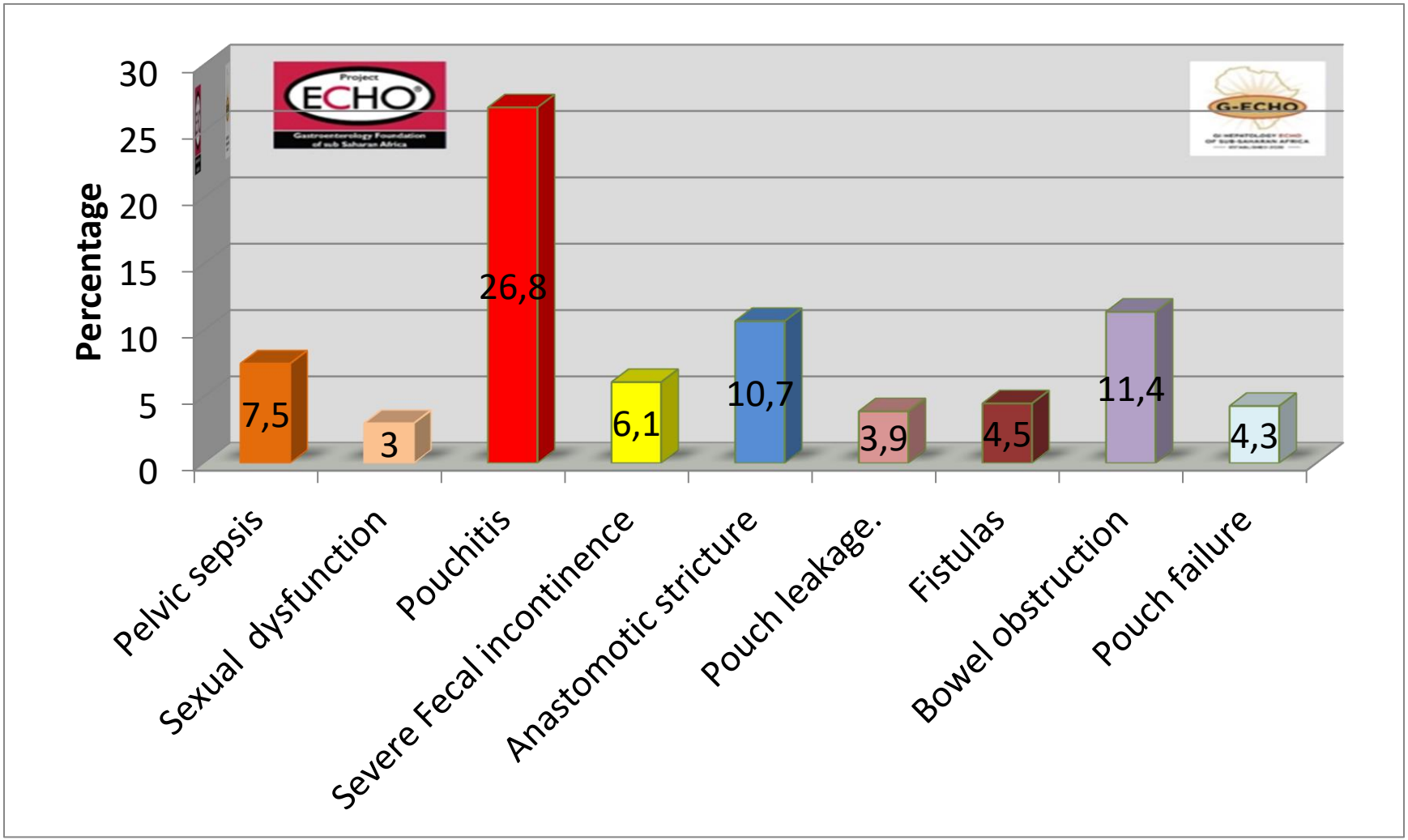
Why Are Pouches Created ?

- **To restore** intestinal **transit** and **evacuation** function → Bowel movements 4-6 day time and 1-2 at night.
- **Pouch maturation is required for optimal functioning** (colonic metaplasia) → flattening of the villi, hypertrophy of the crypts and increase in size.

Types of Pouches



IPAA Late Complications



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Pouchitis

Definition

Pouchitis is an **idiopathic**, **nonspecific** acute inflammation of the pouch.

Typically presents with increased **stool frequency** (> 7 motions per day) and **urgency.**

Epidemiology

- **Incidence: 20% - 50%**

  More frequently among patients who have undergone total colectomy with an IPAA for **UC** than those with **FAP**.

- **Age:**

  At **any** age.

Pathogenesis

- **Idiopathic pouchitis:**
  - Aetiology unclear
  - Hypothesized to result from an abnormal immune response to altered luminal/mucosal bacteria in genetically susceptible hosts
- **Secondary Pouchitis:**
  - Infectious: C diff, CMV
  - Inflammatory: Crohn's disease of the pouch
  - Autoimmune: IgG4-disease
  - Ischaemic
  - Drug: related NSAIDs

Risk Factors

Pre-operative

- UC (extensive colitis, extra-intestinal manifestations, younger age)
- Co-existing autoimmune disorder
- Drugs: Glucocorticoids, TNF
- Hematologic disorders
- Previous surgeries
- Obesity (BMI > 30)
- Life style (Dietary & smoking)

Post-operative

- Postoperative weight gain
- Faecal stasis
- Pouch configuration (J-shaped vs others)
- Drugs: NSAID
- PSC
- Reflux

Spectrum of Pouchitis

- **Many** patients with ileal pouches have some degree of **(Chronic)** endoscopical and / or histological inflammation
- Pouchitis represents a disease **spectrum** with a range of presentations that may evolve over time

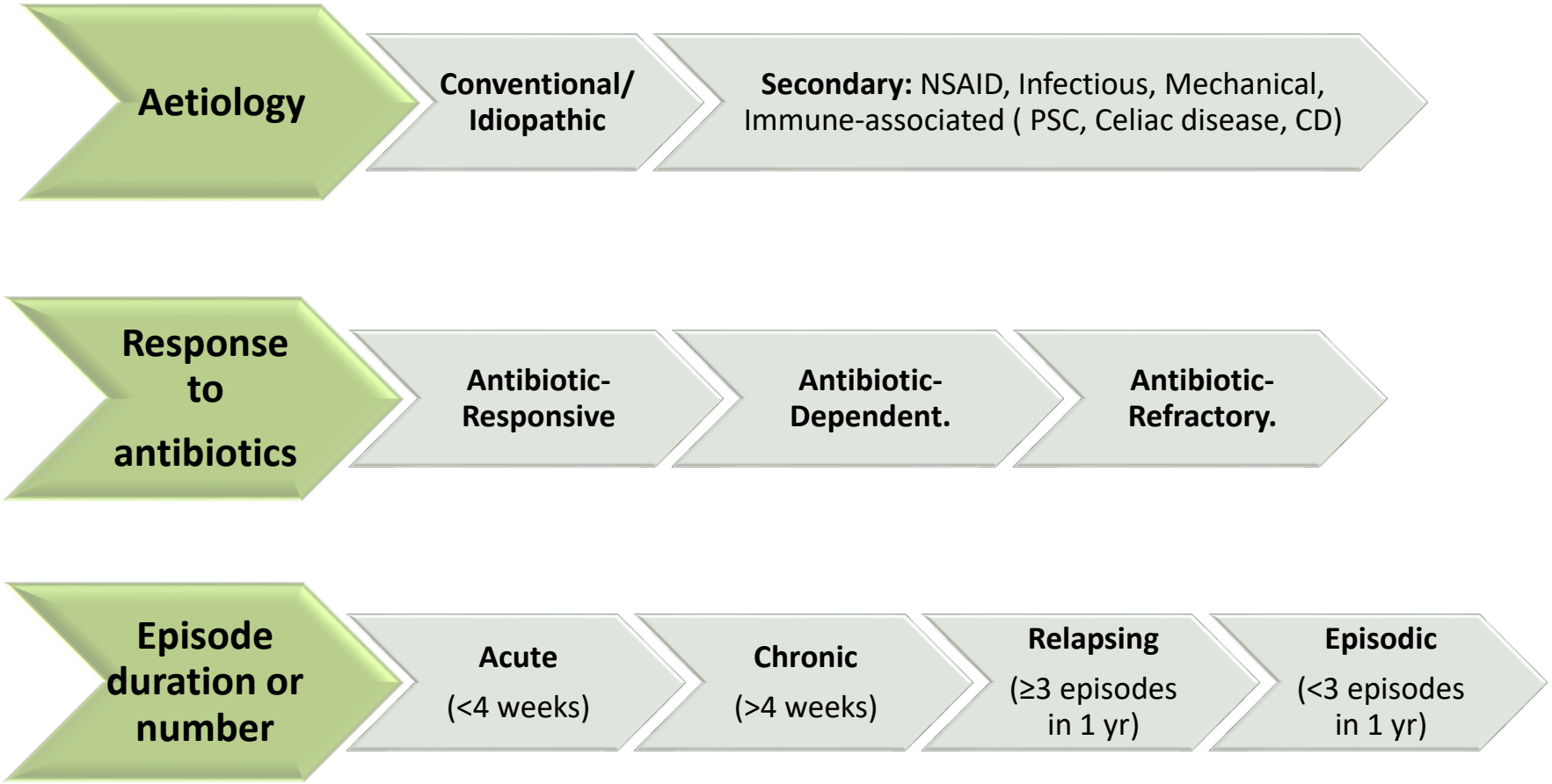
Clinical Pictures

- Pouchitis has variety of clinical **phenotypes**:
  - Acute or chronic disease
  - With or without relapsing pattern
- Patient presentation:
  - Stool frequency (>7 motion per day).
  - Urgency
  - Hematochezia
  - Pelvic pain and incontinence
  - Abdominal cramping

Characterization

- **Different classifications exist which assist in guiding treatment:**
  - Aetiology
  - Response to antibiotics
  - Frequency of relapses

Classifications of Pouchitis



Disease Activity

- Active inflammation
- Disease in remission

Pouchitis Disease Activity Index (PDAI):

- Scoring systems for assessing disease activity:
- Used in research studies and less in clinical practice

Criteria	Score
Clinical	
Stool frequency	
Usual postoperative stool frequency	0
1–2 stools/day > postoperative usual	1
3 or more stools/day > postoperative usual	2
Rectal bleeding	
None or rare	0
Present daily	1
Fecal urgency or abdominal cramps	
None	0
Occasional	1
Usual	2
Fever (temperature >37.8 °C)	
Absent	0
Present	1
Endoscopic inflammation	
Edema	1

Acute pouchitis as PDAI score of ≥7 points.

Diagnosis

Based on:

- **Correct clinical context** (increased stool frequency, urgency)
- **Endoscopic** (mucosal erythema, ulceration, friability)
- **Histological** (active inflammation)

Diagnosis

- **History:**
  - Good focused history
- **Physical examination:**
  - Good clinical examination

Peri-anal Inspection and DRE

(fistula, fissure, dermatitis)

Diagnosis

Endoscopy and Biopsy:

- Endoscopic Visualization:
  - **Mucosal Changes** (diffuse):

    Erythema, friability, granularity, exudates, erosions, and / or ulceration typically distributed throughout the pouch body
  - **Shape:**

    Configuration, size and distensibility of the pouch body
- Biopsies:
  - Pouch body and afferent limb
  - **Avoid** biopsies from the suture-line

Pouchitis
Endoscopic Picture and Reporting

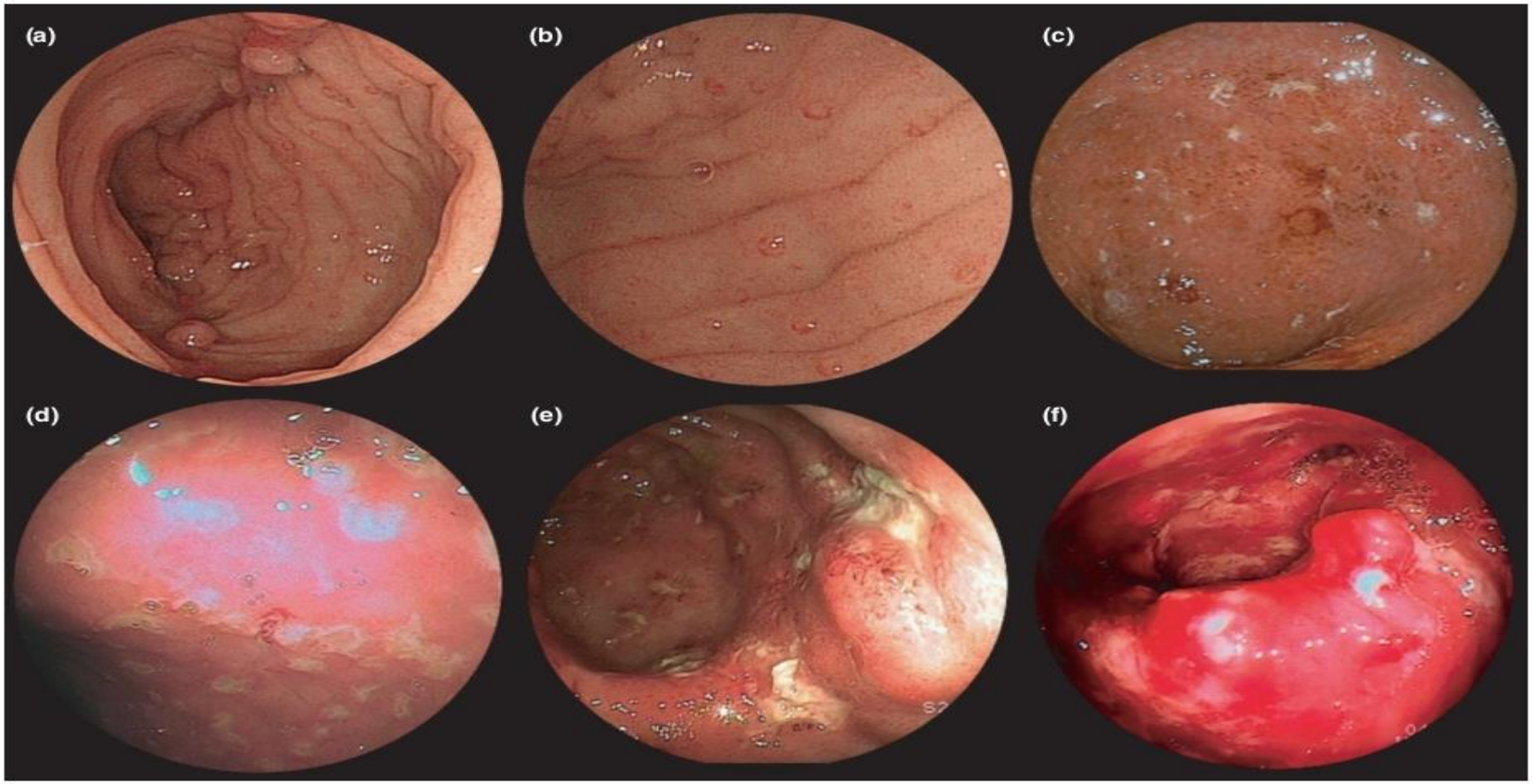


Figure 1 Typical endoscopic appearance of pouchitis. (a,b) Endoscopic appearance of mild pouchitis. (a) Loss of vascularity and (b) mild redness are relatively frequently observed in patients without pouchitis. Therefore, these findings are not diagnostic of pouchitis if patients exhibit no symptoms. (c,d) Endoscopic appearance of moderate pouchitis includes aphthoid lesions, erosions, shallow ulcers, and mucous exudates. (e,f) Endoscopic appearance of severe pouchitis includes (e) multiple deep ulcers and (f) spontaneous bleeding.

Chicago Classification of Pouchitis

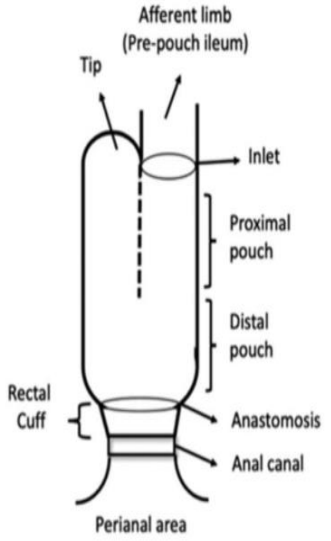
It is a new novel **classification system** based on the pattern of inflammation observed in pouches and evaluated the **contributing factors** and **prognosis** of each endoscopic **phenotype**

Akiyama et al (2022)

Chicago Classification of Pouchitis

A New Endoscopic Phenotype Classification for J Pouch Outcomes in IBD
The Chicago Classification

N = 426 pts
1,359 pouchoscopies



7 phenotypes

- Normal
- Afferent limb involvement
- Inlet involvement
- Diffuse inflammation
- Focal inflammation
- Cuffitis
- Pouch with fistulas

Log-rank test
Inlet stenosis, diffuse inflammation, and cuffitis significantly increased the risk of pouch excision.

Cox proportional hazards model
Diffuse inflammation was independently associated with pouch excision (HR 2.69; 95% CI 1.34-5.41).

Clinical Gastroenterology and Hepatology

ORIGINAL ARTICLE

Risk Factors and Quality of Life in Patients with Diffuse Pouchitis After Ileal Pouch Anal Anastomosis According to the Chicago Classification for J Pouch: a Retrospective Multicenter Cohort Study in China

Weimin Xu[1,4] · Yaosheng Wang[1,4] · Zhebin Hua[1,4] · Hang Hu[2,4] · Wenhao Chen[2,4] · Zerong Cai[3,4] · Long Cui[1,4] · Xiaojian Wu[3,4] · Lei Lian[3,4] · Zhao Ding[2,4] · Peng Du[1,4]

Received: 19 September 2022 / Accepted: 2 December 2022 / Published online: 3 January 2023

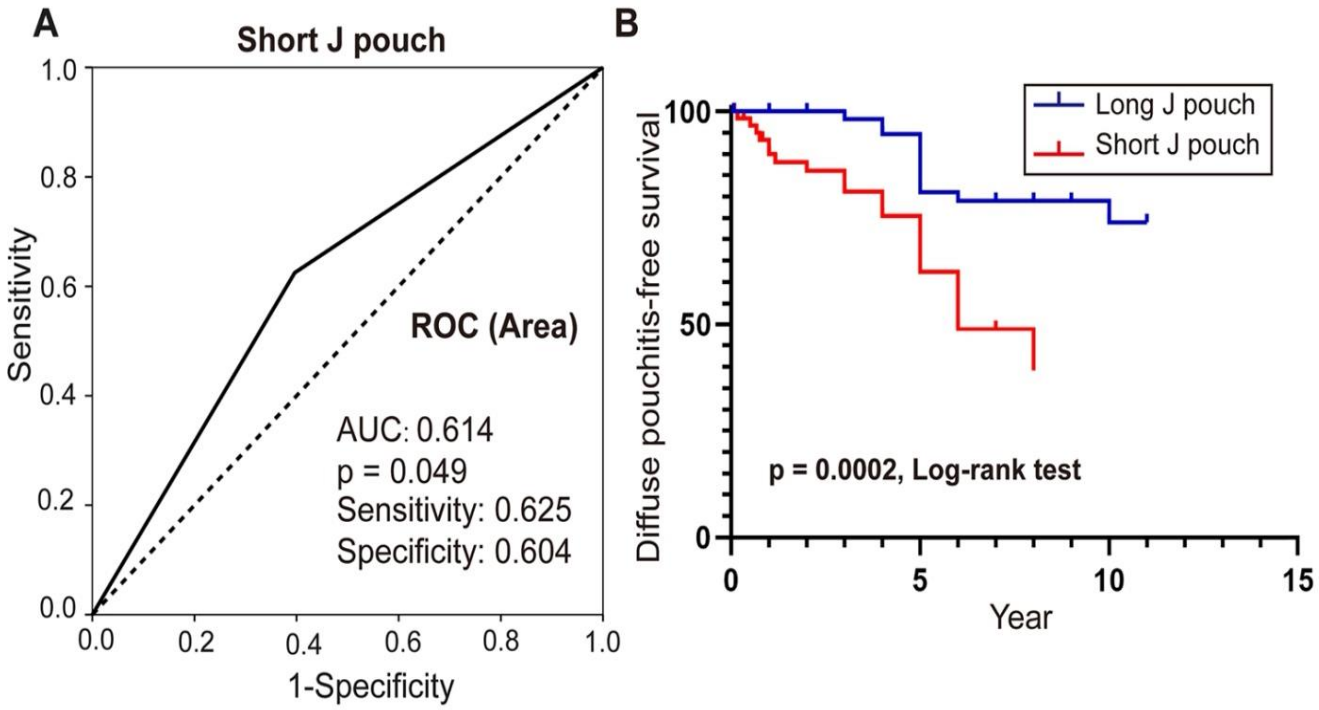
Results Altogether, 143 patients with a median follow-up time of 5.0 years (interquartile range: 2.0–8.0) were enrolled. Among them, 41 patients (28.7%) developed pouchitis and 32 patients (78%) had diffuse inflammation of the pouch. Patients with diffuse pouchitis had a higher pouchitis disease activity index and more seriously impaired improvement of long-term quality of life than those with pouch phenotypes. A short J pouch, recurrent UC, and preoperative high white blood cell count were independent risk factors for diffuse pouchitis. Furthermore, a short J pouch could effectively predict the occurrence of diffuse pouchitis with an area under the receiver-operating characteristic curve of 0.614, a sensitivity of 62.5%, and a specificity of 60.4% ($p = 0.049$) and significantly decreased the overall diffuse pouchitis-free survival compared to a long J pouch ($p = 0.0002$).

Conclusion Diffuse pouchitis is a common phenotype of pouchitis that seriously impairs long-term prognosis. For colorectal surgeons, decision-making regarding pouch construction with an appropriate length should be considered to prevent the development of diffuse pouchitis.

Keywords Diffuse Pouchitis · Ileal Pouch–anal Anastomosis · Ulcerative Colitis · Long-term Quality of Life · Pouch Length

Predictive Value of Pouch Length

Fig. 4 Predictive value of pouch length for diffuse pouchitis. **A** ROC analysis indicated short J pouch had a significant AUC of 0.614 with a sensitivity of 62.5% and specificity of 60.4%. **B** Kaplan–Meier method with the log-rank test performed to analyze the overall diffuse pouchitis-free survival in patients with short and long J pouch



Diagnosis

- **Histology:**
  - Characterized by **acute inflammation** (neutrophil infiltration, crypt abscess, and mucosal ulceration)

+/-

  - Background of **chronic changes** (villous atrophy, crypt distortion, hyperplasia, pyloric gland metaplasia and chronic inflammatory cell infiltration

Complementary Work up

Diagnosis

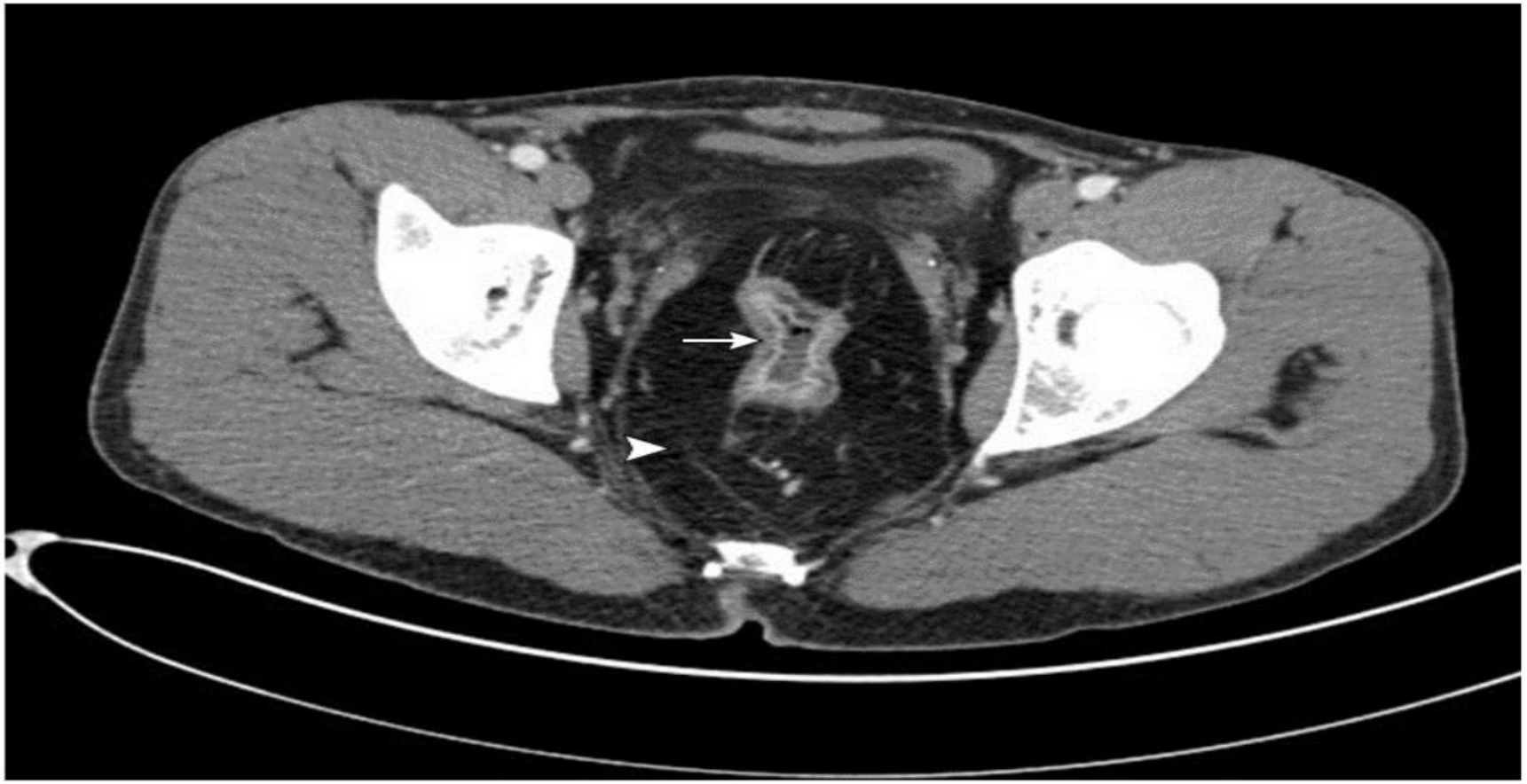
- **Laboratory findings:**
  - FBC (IDA)
  - Electrolytes abnormalities
  - CRP
  - Vitamin D deficiency
  - LFT & IgG4
  - Stool studies (faecal calprotectin, lactoferrin, C. difficile, Stool culture)
  - Basic metabolic panel

Diagnosis

- **Imaging:**
  - Abdominal CT
  - Pouchogram with water-soluble contrast
  - MRI

  Only needed for patients with symptoms suggestive **other pouch disorders** (anastomotic stricture or pouch prolapse)

Pelvic-CT for Acute Pouchitis



This computed tomography of the pelvis was performed in a patient with acute pouchitis. The pouch wall appears thickened with mucosal hyperenhancement (arrow). There is a large accumulation of peripouch fat (arrowhead).

Differential Diagnosis

Infectious pouchitis:	Bacteria - Fungal - Viruses
Ischemic pouchitis:	Characterized by asymmetric inflammation and ulceration of the pouch
Pouch prolapse:	Mucosal edema, erythema, and a distorted pouch inlet area
Cuffitis:	Circumferential inflammation of the rectal cuff with histological findings consistent with UC
Crohn disease (CD) of the pouch:	Similar to luminal CD. +/- Granuloma on biopsy
Irritable pouch syndrome of the pouch:	Normal endoscopic and histologic examination
Autoimmune associated pouchitis	
NSAID associated pouchitis	

Treatment And Prevention

Preprinted Copy

AGA Guidelines

2024

Treatment Goals and Targets

The recommended target is

- Resolution of symptoms

- Resolution of endoscopic and/or histologic inflammation

  (**not recommended)**

- Treatment of asymptomatic patient

  (**not recommended)**

Treatment of Pouchitis

- **General Measures:**
  - Rehydration
  - Correct electrolytes imbalance
  - Correct vitamins deficiencies

Treatment of Acute Pouchitis

AGA suggests using **antibiotics** for treatment of **infrequent episodes** of acute pouchitis.

- ✓ **Ciprofloxacin** (500 mg orally twice daily for 2ws) **OR** **Metronidazole** (500 mg orally twice daily for 2ws)
- ✓ Combination
- ✓ Oral **Vancomycin** (125 mg orally twice daily).

Outcome of Antibiotics Treatment

Most of the patients **respond** to antibiotics initially, but

- **Episodic Pouchitis** (50% - 90%)
- **Chronic Pouchitis** (30%)
  - Chronic **antibiotic-dependent** pouchitis
  - Chronic **antibiotic-refractory** pouchitis
- **Crohn's-like disease** of the pouch

Episodic (Intermittent) Pouchitis

- Isolated and infrequent episodes of typical pouchitis symptoms that resolve with therapy (most commonly, antibiotics)

  OR

- Spontaneous recovery followed by **extended periods of normal pouch function** (typically months to years)

Chronic Antibiotic-Dependent Pouchitis

- Recurrent episodes of pouchitis that responds to antibiotic therapy but **relapses shortly after stopping antibiotics** (typically within days to weeks)
- Usually requires recurrent or continuous antibiotic therapy or other advanced therapies to achieve symptom control

Chronic Antibiotic-Refractory Pouchitis

Pouchitis **not responding** to **≥ 4** weeks of antibiotic therapy.

Crohn's-Like Disease of the Pouch

- Definition is based on the most common and accepted diagnostic criteria, which include:
  - Presence of Peri-anal or other **fistula** that developed at least 12 months after the final stage of IPAA surgery
  - **Stricture** of the pouch body or pre-pouch ileum
  - Presence of pre-pouch **ileitis**.

Treatment of Chronic Antibiotic-Dependent Pouchitis

AGA suggests using **chronic antibiotic** therapy to treat chronic antibiotic-dependent pouchitis.

Consider:

- Endoscopic evaluation
- Lowest effective dose of antibiotics:

  (Ciprofloxacin 500mg / day or 250mg BID)

  - Intermittent gap periods **(one week/month)**

    OR

  - Cyclical use **(every 1-2 weeks).**

Treatment of Chronic Antibiotic-Dependent Pouchitis

AGA suggests using **immuno-suppressive** therapies to treat recurrent Pouchitis.

(Can be used in lieu of chronic antibiotic therapy)

Treatment of Chronic Antibiotic-Refractory Pouchitis

AGA suggests using:

- Advanced **immunosuppressive** therapies
- **Corticosteroids:**
  - Controlled ileal-release budesonide
  - Short duration (<8-12 weeks)
  - Consideration of steroid-sparing therapies for long-term use
- Suggests **against** the use of **mesalamine**.

Vedolizumab for Treatment of Chronic Pouchitis

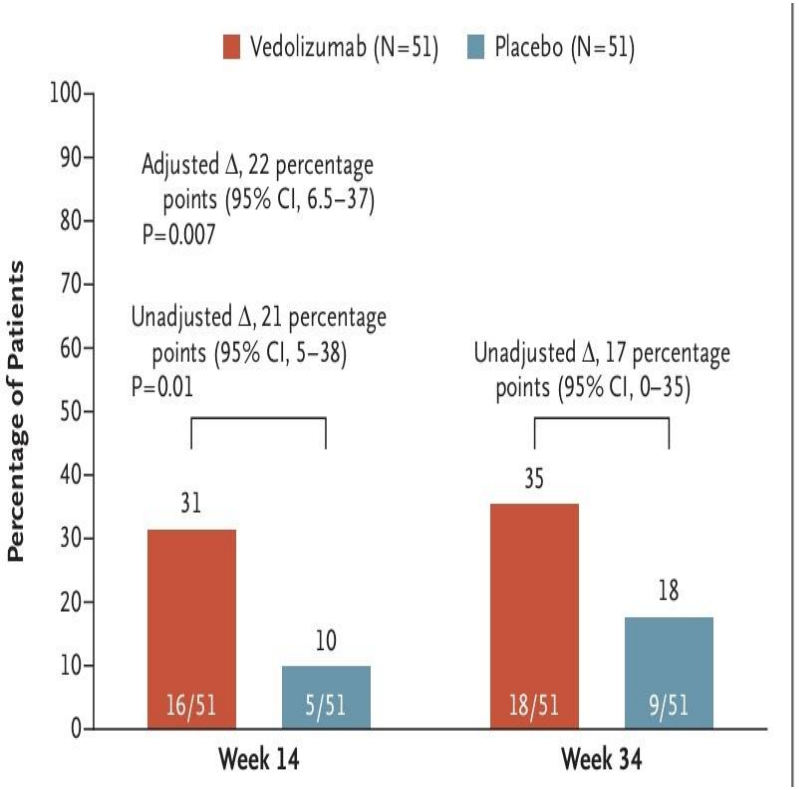
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Vedolizumab for the Treatment of Chronic Pouchitis

S. Travis, M.S. Silverberg, S. Danese, P. Gionchetti, M. Löwenberg, V. Jairath, B.G. Feagan, B. Bressler, M. Ferrante, A. Hart, D. Lindner, A. Escher, S. Jones, and B. Shen, for the EARNEST Study Group*

Vedolizumab for Treatment of Chronic Pouchitis



RESULTS

Among the 102 patients who underwent randomization, the incidence of mPDAI-defined remission at week 14 was 31% (16 of 51 patients) with vedolizumab and 10% (5 of 51 patients) with placebo (difference, 21 percentage points; 95% confidence interval [CI], 5 to 38; P=0.01). Differences in favor of vedolizumab over placebo were also seen with respect to mPDAI-defined remission at week 34 (difference, 17 percentage points; 95% CI, 0 to 35), mPDAI-defined response at week 14 (difference, 30 percentage points; 95% CI, 8 to 48) and at week 34 (difference, 22 percentage points; 95% CI, 2 to 40), and PDAI-defined remission at week 14 (difference, 25 percentage points; 95% CI, 8 to 41) and at week 34 (difference, 19 percentage points; 95% CI, 2 to 37). Serious adverse events occurred in 3 of 51 patients (6%) in the vedolizumab group and in 4 of 51 patients (8%) in the placebo group.

CONCLUSIONS

Treatment with vedolizumab was more effective than placebo in inducing remission in patients who had chronic pouchitis after undergoing IPAA for ulcerative colitis. (Funded by Takeda; EARNEST ClinicalTrials.gov number, NCT02790138; EudraCT number, 2015-003472-78.)

Good outcome of treatment of pouchitis

Primary Prevention

Antibiotics:

AGA suggests **against** using **antibiotics** for the primary prevention of Pouchitis

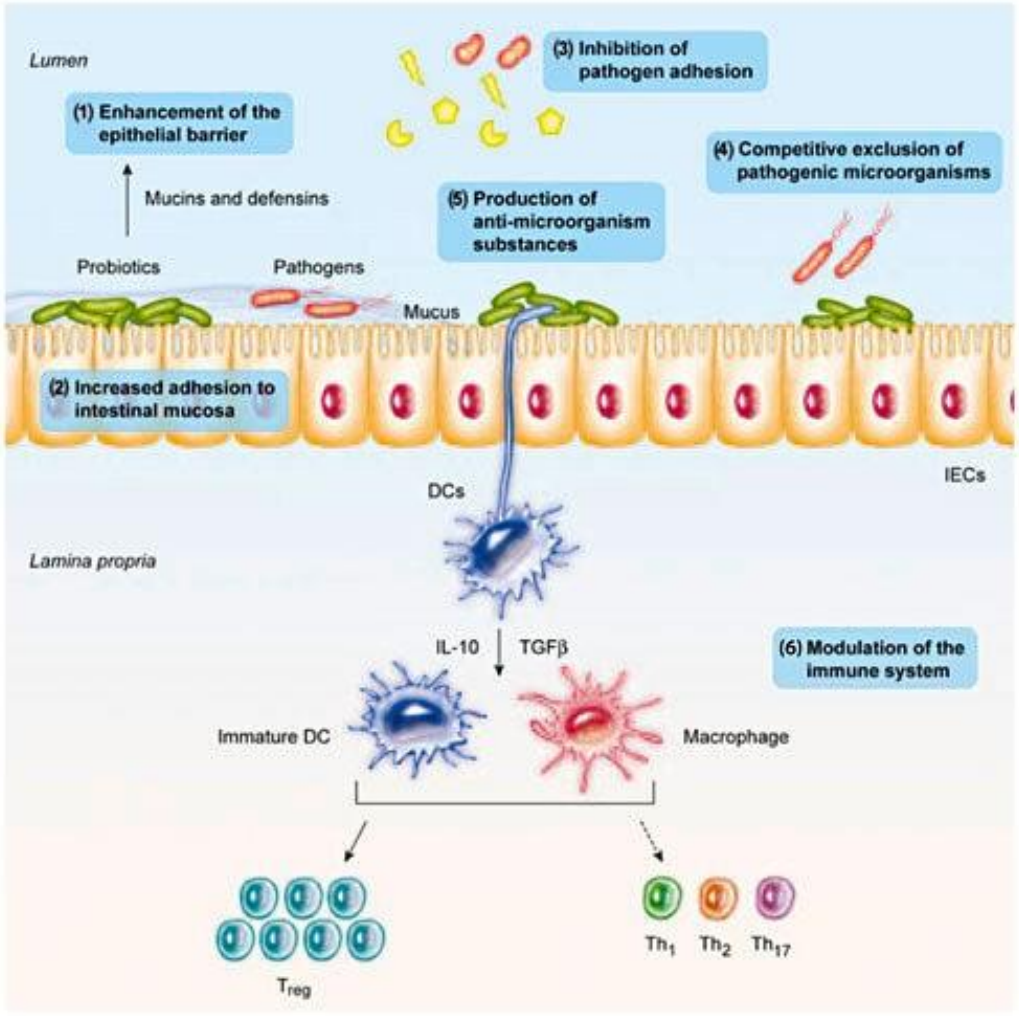
Treatment And Prevention

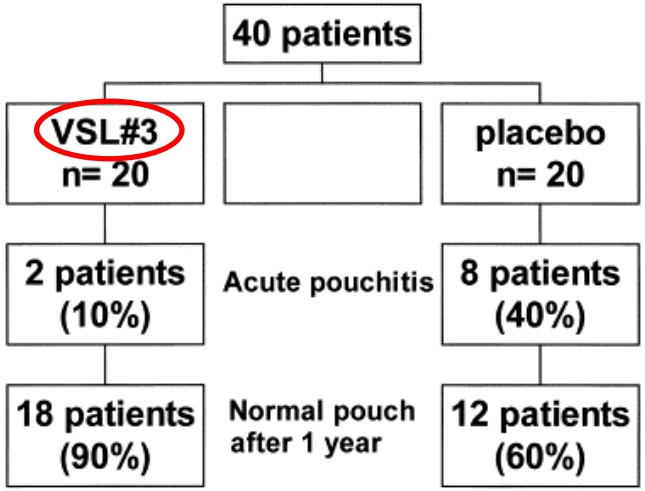
Probiotics:

- AGA makes **no recommendation** in favor of, or against, the use of probiotics for **primary prevention** or **treatment** of pouchitis

- AGA suggests **using probiotics** for preventing recurrent pouchitis

Probiotics





Prophylaxis of pouchitis onset with probiotic therapy: a **double-blind, placebo-controlled trial**

Treatment Crohn's-like Pouchitis

AGA suggests:

- Using **corticosteroids:** Preferred
  - Controlled ileal-release budesonide
  - Short duration (<8 weeks)
  - Steroid-sparing therapies for long-term use
  - Endoscopic evaluation of the pouch to confirm Crohn's- like disease
- Using advanced **immunosuppressive** therapies

Treatment of Cuffitis

AGA suggests:

- Using **topical therapies**
  - (Mesalamine and Corticosteroid) as first line treatment
- Using **Immunosuppressive** therapies for refractory cuffitis

What do other guidelines say?

- **ECCO** guidelines (2017) recommendation **consistent** with **AGA** for treatment of **acute pouchitis** principles

- **ECCO** guidelines **did not** explicitly provide recommendations on:
  - **Primary** or **secondary prevention** of pouchitis
  - Role of chronic or alternative **antibiotic** therapy
  - Role of **immunosuppressive** medications.
  - The management of **Crohn's-like disease** of the pouch

Future Directions

- **Standardization** of disease entities
- **Natural history** and **risk factors** for inflammatory disorders of the pouch
- Improving **clinical trial design** in pouchitis

Pouch Failure

Meta-Analysis

Prevalence of 'pouch failure' of the ileoanal pouch in ulcerative colitis: a systematic review and meta-analysis

Zaid Alsafi et al. Int J Colorectal Dis. 2022 Feb.

Conclusion

This systematic review and meta-analysis of patients with UC who underwent IPAA demonstrates an overall prevalence of pouch failure of 6%. Despite the intricacies of the subject matter, the question of pouch failure is an important one to address, with these data being particularly important for counselling patients considering the procedure. Importantly, for those patients with UC being considered for a pouch, their disease course has often resulted in both physical and psychological morbidity and hence providing accurate expectations is vital.

Treatment of Pouch Failure

- Permanent diversion.
- Removal of the pouch.

Management Common Mistakes

1. Assuming all pouch dysfunction is primary idiopathic pouchitis **without excluding** alternative diagnoses
2. Missing **pelvic sepsis** as a cause of pouchitis
3. Not systematically assessing and reporting all pouch **regions endoscopically**
4. Failing to appreciate the impact of symptoms on **quality of life**

5. Not recognising the presence of **cuffitis**
6. Labelling the diagnosis as Crohn's disease when the features may be due to **another aetiology**
7. Commencing **biologics** without fully reassessing the diagnosis and patient needs
8. Failing to **reassess** patients regularly when they are taking long-term antibiotic treatment
9. Failing to optimise **diet** and **fluid** intake
10. Managing patients with pouch dysfunction outside a **specialist centre**

My Message

The Endoscopic Pictures of Pouchitis

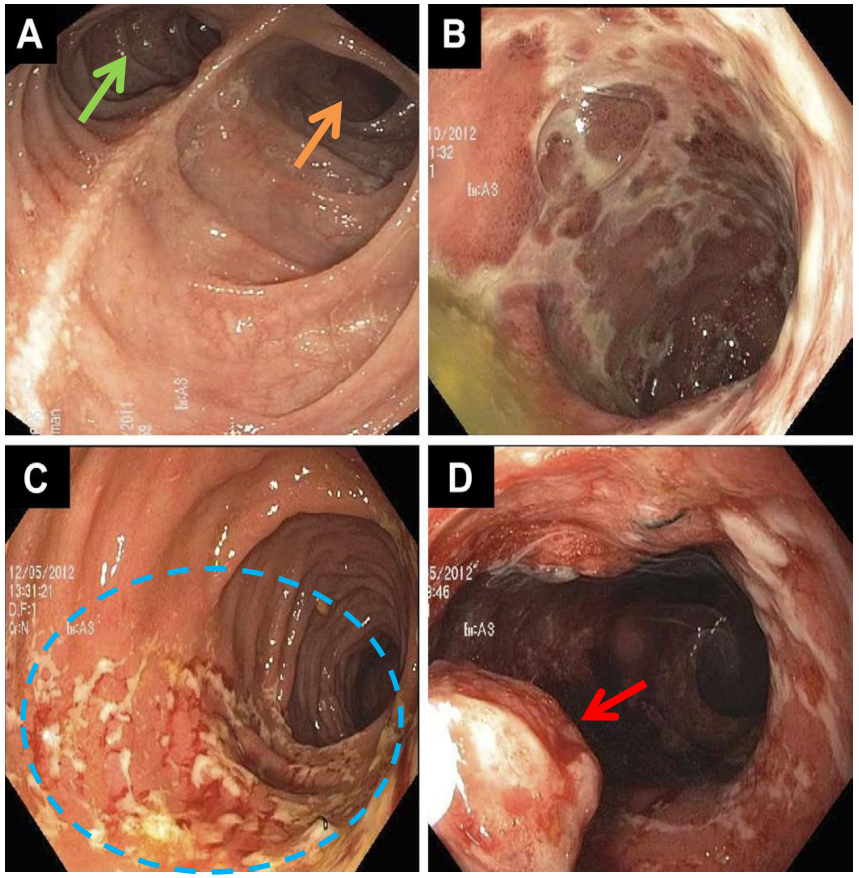
Pouchitis
Various Etiologies on Endoscopy

A. *Normal pouch* with an owls' eye configuration, reflecting a widely opened pouch inlet and the tip of a J.

B. Chronic pouchitis with ulcers and a stiff pouch.

C. *Pouchitis* with an ischemic pattern, with inflammation at the afferent limb side, and normal mucosa at the efferent limb side of the J pouch, with sharp demarcation of inflammation and non inflamed parts along the suture line.

D. *A* large pouch inflammatory polyp resulting from chronic mucosal inflammation.

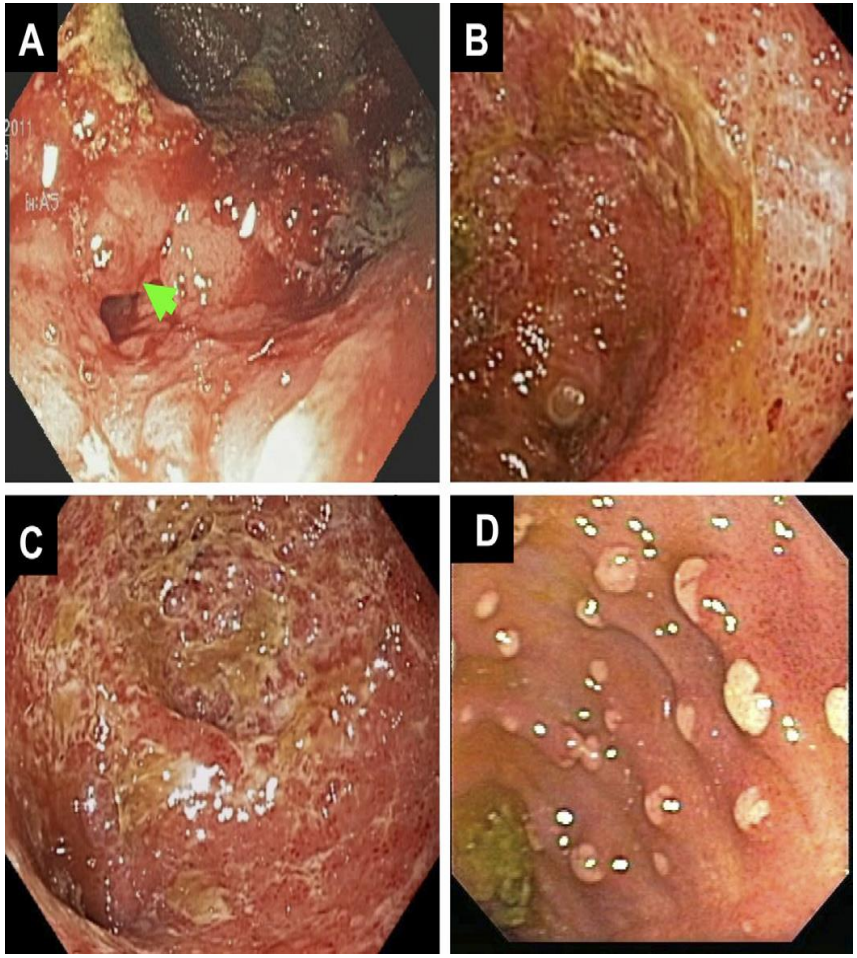


Pouchitis
Various Etiologies on Endoscopy

A. *Chronic pouchitis with concurrent distal pouch sinus (arrow).*

B. *& C. Diffuse pouchitis and enteritis with a similar mucosa pattern in a patient with PSC.*

D. *Chronic pouchitis with C.difficile infection.*



References

1. Barnes EL, et al. AGA Clinical Practice Guideline on the Management of Pouchitis and Inflammatory Pouch Disorders, AGA Preprinted guidelines, 2024. https://aga-fileuploader-bucket.s3.us-east-2.amazonaws.com/Aga-Files/AGA%20Guidelines%20-%20Pouchitis%20-%20Manuscript%20FINAL.pdf
2. Cesano S, Jones GR, Jenkinson PW, et al. Vedolizumab for the treatment of chronic pouchitis: The Edinburgh experience. Journal of Crohn's and Colitis 2019;13(Supplement 1):S341.
3. Darrell S. Pardi, Geert D'Haens, Bo Shen, Simon Campbell, Paolo Gionchetti, Clinical Guidelines for the Management of Pouchitis, *Inflammatory Bowel Diseases*, Volume 15, Issue 9, 1 September 2009, Pages 1424–1431, https://doi.org/10.1002/ibd.21039
4. Harbord M, Eliakim R, Bettenworth D, Karmiris K, Katsanos K, Kopylov U, Kucharzik T, Molnár T, Raine T, Sebastian S, de Sousa HT, Dignass A, Carbonnel F; European Crohn's and Colitis Organisation [ECCO]. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 2: Current Management. J Crohns Colitis. 2017 Jul 1;11(7):769-784. doi: 10.1093/ecco-jcc/jjx009. Erratum in: J Crohns Colitis. 2017 Dec 4;11(12):1512. Erratum in: J Crohns Colitis. 2022 Aug 16;: PMID: 28513805.

References

5. Barnes EL, Kochar B, Jessup HR, et al. The Incidence and Definition of Crohn's Disease of the Pouch: A Systematic Review and Meta-analysis. Inflamm Bowel Dis 2019;25:1474-1480.
6. Barnes EL, Allin KH, Iversen AT, et al. Increasing Incidence of Pouchitis Between 1996 and 2018: A Population-Based Danish Cohort Study. Clin Gastroenterol Hepatol 2023;21:192-199 e7.
7. Lightner AL, Mathis KL, Dozois EJ, et al. Results at Up to 30 Years After Ileal PouchAnal Anastomosis for Chronic Ulcerative Colitis. Inflamm Bowel Dis 2017;23:781-790.
8. Quinn KP, Raffals LE. An Update on the Medical Management of Inflammatory Pouch Complications. Am J Gastroenterol 2020;115:1439-1450.
9. Gionchetti P, Rizzello F, Helwig U, et al. Prophylaxis of pouchitis onset with probiotic therapy: a double-blind, placebo-controlled trial. Gastroenterology 2003;124:1202-9.
10. Akiyama S, Ollech JE, Rai V, Glick LR, Yi Y, Traboulsi C, Runde J, Cohen RD, Skowron KB, Hurst RD, Umanskiy K, Shogan BD, Hyman NH, Rubin MA, Dalal SR, Sakuraba A, Pekow J, Chang EB, Rubin DT. Endoscopic Phenotype of the J Pouch in Patients With Inflammatory Bowel Disease: A New Classification for Pouch Outcomes. Clin Gastroenterol Hepatol. 2022 Feb;20(2):293-302.e9. doi: 10.1016/j.cgh.2021.02.010. Epub 2021 Feb 5. PMID: 33549868; PMCID: PMC8339185.

THANK YOU