Indeterminate Colitis – How to Approach?

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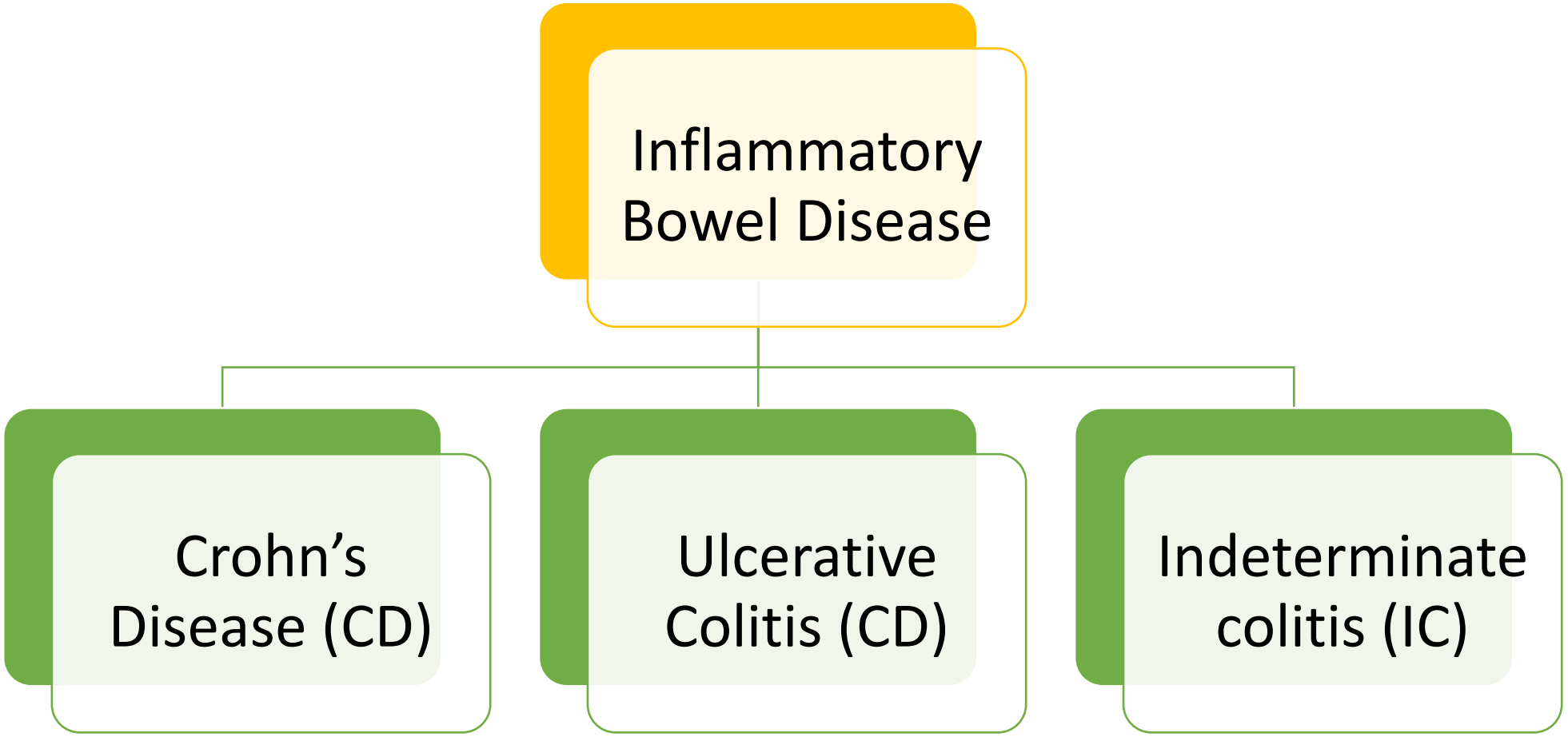
Objectives

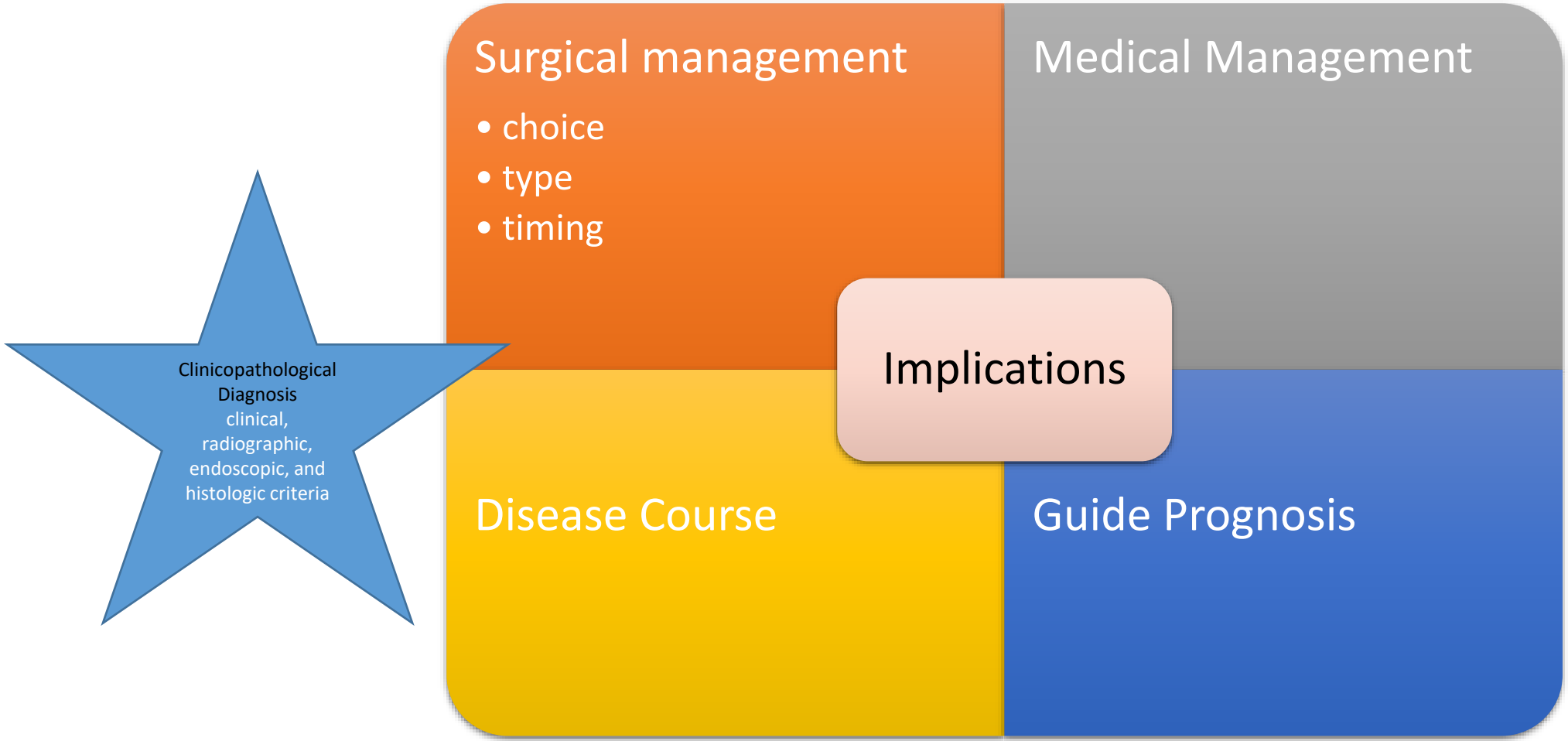
- Define IBD subtypes
- Define IBD-U/indeterminate colitis (IC)
- Discuss the management of indeterminate colitis

Diagnosing IBD Subtype

Subtypes of IBD



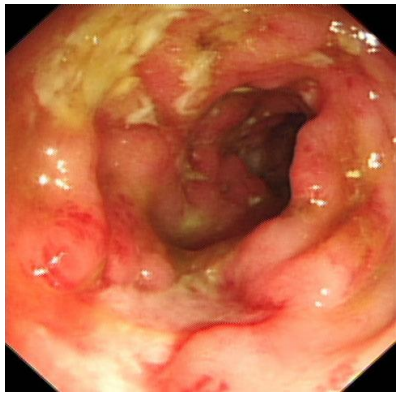
Why is defining IBD subtype important?



Mimickers of IBD

Infection	Bacterial (Cdiff, mycobacterial) Viral Parasitic Fungal
Localized inflammation	Diverticular colitis Appendicitis Mucosal prolapse Endometriosis
Iatrogenic	Chemicals (bowel prep) Drugs (NSAID, abx, chemo) Medical interventions (radiation, pouch surgery, diversion)
Rare	Ischemic colitis Bechet's disease GVHD CVID Lymphoma Sarcoidosis Vasculitis

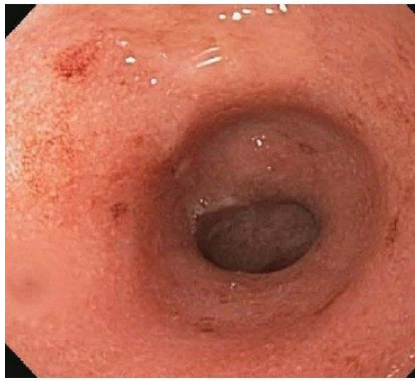
Diagnosis of Crohn's Disease



- Clinical Features[1]
  - Inflammation: Transmural, ulceration, and skip lesions
  - Complications: fistulas, abscesses, malignancies, and strictures
  - EIM – MSS (spondyloarthritis), ophthalmologic (uveitis, episcleritis, or iritis), dermatologic (erythema nodosum, pyoderma gangrenosum), neurologic (peripheral neuropathy), and renal (calcium oxalate and uric acid stones, bladder fistulas and hydronephrosis)
- Endoscopic Features
  - Rectal sparing, skip lesions, deep ulcerations
  - Terminal ileal involvement
- Histopathology
  - Chronic inflammation
    - architectural distortion with crypt disarray, crypt branching, crypt shortening, basal lymphoplasmacytosis, and Paneth cell metaplasia
  - In early stages or in a flare, acute inflammation
    - inflammatory infiltrate including neutrophils after which cryptitis and crypt abscesses
  - Granulomas only found in 20–30% of biopsies[2]

[1]Abraham C, Cho JH. Inflammatory bowel disease. N Engl J Med. 2009;361:2066–78.
[2]Ramzan NN, Leighton JA, Heigh RI, et al. Clinical significance of granuloma in crohn's disease. Inflamm Bowel Dis. 2002;8:168–73
[3]Shivashankar, et al. Inflamm Bowel Dis • Volume 24, Number 11, November 2018

Diagnosis of Ulcerative Colitis



- Clinical Features[1]
  - Inflammation: Confined to the mucosa and is continuous, extending proximally from the rectum and affecting colon only
  - Complications: colorectal cancer, excessive bleeding, and toxic megacolon
  - EIM – similar to Crohn's but in addition PSC more common in UC
- Endoscopic Features
  - Rectum and extends proximally
  - +/- backwash ileitis, cecal patch
  - Superficial inflammation
- Histopathology[3]
  - Chronic inflammation
    - architectural distortion with crypt disarray, crypt branching, crypt shortening, basal lymphoplasmacytosis, and Paneth cell metaplasia
  - In early stages or in a flare, acute inflammation
    - inflammatory infiltrate including neutrophils after which cryptitis and crypt abscesses

[1]Abraham C, Cho JH. Inflammatory bowel disease. N Engl J Med. 2009;361:2066–78.
[2]Chachu KA, Osterman MT. How to diagnose and treat IBD mimics in the refractory IBD patient who does not have IBD. Inflamm Bowel Dis. 2016;22:1262–74
[3]Bhaijee F, Arnold C, Lam-Himlin D, et al. Infectious mimics of inflammatory bowel disease. Diagnostic Histopathology. 2015;21:267–75.
[4]Shivashankar, et al. Inflamm Bowel Dis • Volume 24, Number 11, November 2018

Diagnosis of Indeterminate Colitis (IC) (aka IBDU)

- IBD with no definitive features of CD or UC (5-15%)[1,2,3,4] with inadequate clinical data or histopathological examination showing features of CD and UC[1]
  - 1978, pathologist Price used IC to describe colectomy specimens in which no specific features for CD or UC seen (10-15% of pts)
  - 1979, Kent et al used IC when evaluation rendered a diagnosis of UC or Crohn's indefinite
  - 2004 Burakoff thought IC was a separate entity
  - 2009, Geboes, et al used the term inflammatory bowel disease unclassified (IBDU) and the surgeons used the term indeterminate colitis for the same condition.
- Has not changed much in 30 years despite newer diagnostic modalities[5]
- Diagnosed in 9%- 20% of colectomy specimens
- IC higher (up to 29%) in children

[1]Magro, F et al. J Crohn's Colitis 2017, 11, 649-70.
[2]Chachu KA, Osterman MT. Inflamm Bowel Dis. 2016;22:1262–74
3Peyrin-Biroulet, L et al. Am J Gastroenterol 2015, 110, 1324-1338
4Feuerstin, JD et al. Mayo Clin Proc 2014, 89, 1553-1563.
[5]Mahdi, B. Journal of Gastroenterology and Hepatology Research 2012; 1(10): 241-246
[6]Harbord, M et al. J Crohn's Colitis 2017, 11, 769-784
[7]Geboes, K et al. Inflamm Bowel Dis 2008; 14(6): 850-857
[8]Emad, Mansoor FJ-D, et al. Am J Gastroenterol 2019; 114(p):S1594
[9]Giundi, M et al. Indeterminate Colitis. J Clin Pathol 2004;57:1233–1244
[10]Price AB. J Clin Path 1978;31: 567-77
[11]Mahdi, B. Journal of Gastroenterology and Hepatology Research 2012; 1(10): 241-246

Pediatric Clinical Presentation

Table 1
Differences in clinical presentations between ulcerative colitis, Crohn's disease, and indeterminate colitis. Histologic features for indeterminate colitis are according to the ESPGHAN revised porto criteria for the diagnosis of inflammatory bowel disease in children and adolescents[39].

Presentation	Ulcerative colitis[6–8]	Crohn's disease[6–9]	Indeterminate colitis[6–8,22]
Pediatric IBD (%)	24–32	59–73	3–13
Clinical features			
Abdominal pain	Common	Common	Common
Rectal bleeding	Common	Occasionally	Variable
Diarrhea	Common	Common	Common
Anemia	Common	Occasionally	Variable
Weight loss/growth failure	Infrequent	Common	Variable
Disease extent	Limited to colon, spreads proximally from the rectum in a continuous fashion	Rectal sparing, anywhere from mouth to anus	Variable
Perianal involvement	Infrequent	Common	Variable
Stenosis	Infrequent	Common	Variable
Abscess	Infrequent	Common	Variable
Fistula	Infrequent	Common	Variable
Endoscopic features	• Diffuse continuous inflammation from rectum extending proximally • "Sandpaper" appearance of mucosa • Friable mucosa • Small superficial ulcers • Gastritis may be present	• Patchy inflammation with aphthous or linear ulcers • Active ileitis • Fissures, fistulization and strictures • Cobblestoning • Gastritis may be present	Variable
Histologic features	• Crypt abscesses • Crypt architectural distortion • Inflammation limited to mucosa • Periappendiceal inflammation alone with distal colitis is frequently seen	• Granulomas • Crypt architectural distortion • Transmural inflammation • Colitis with granulomatous inflammation of esophagus, stomach, or duodenum • Absolute rectal sparing	• UC features with absence of severe colitis but transmural inflammation present • UC features with significant growth delay • UC features with presence of ileitis atypical for backwash or discontinuous inflammation • Pancolitis with anal fissures or anal tags • UC features with macroscopic and microscopic rectal sparing • Reverse gradient of mucosal inflammation

Morphological Features in IC (overlap of UC and CD)

UC -continuous mucosocentric pathology with rectum bearing brunt of disease and variable proximal extension, ulcerative appendicitis
CD - fibro-stricturing or inflammatory pathology and associated with deep fissures and fistulation

Macroscopic	
1	Colitis
2	Extensive Ulceration
3	Involvement of Tx and Right colon (more severe than distal colon)
4	Involvement of >50% of mucosal surface
5	Usually diffuse disease, but may show rectal sparing
6	Toxic dilation may be present

Microscopic	
1	Extensive ulceration with a sharp transition to normal adjacent mucosa
2	Transmural lymphoid inflammation with an absence of lymphoid aggregates
3	Absence of well-defined, epithelioid granulomas distant form crypts
4	Multiple squat V-shaped ulcers, lacking surrounding inflammation
5	Scanty deep penetrating slit-like fissures

Mahdi, B. Journal of Gastroenterology and Hepatology Research 2012; 1(10): 241-246

Diagnosis of Indeterminate Colitis (IC)

- It is still debated whether indeterminate colitis represents:
  - a problem of classification
  - a distinct clinical entity from ulcerative colitis and Crohn's disease
  - incomplete evaluation or early/incomplete disease expression at time of evaluation

[1]Magro, F et al. J Crohn's Colitis 2017, 11, 649-70.
[2]Chachu KA, Osterman MT. Inflamm Bowel Dis. 2016;22:1262–74
3Peyrin-Biroulet, L et al. Am J Gastroenterol 2015, 110, 1324-1338
4Feuerstin, JD et al. Mayo Clin Proc 2014, 89, 1553-1563.
[5]Mahdi, B. Journal of Gastroenterology and Hepatology Research 2012; 1(10): 241-246
[6]Harbord, M et al. J Crohn's Colitis 2017, 11, 769-784
[7]Geboes, K et al. Inflamm Bowel Dis 2008; 14(6): 850-857
[8]Emad, Mansoor FJ-D, et al. Am J Gastroenterol 2019; 114(p):S1594

Challenges in Diagnosing UC or CD

- Broad spectrum of pathology seen in UC and CD and not conforming to traditional findings[5]
- Interobserver variability or bias among physicians, pathologists/institutions[3,4]
  - Lack of consistency and clarity among pathologists regarding definition[7]
  - Failure to incorporate major diagnostic features for UC and CD[8]
- Changes in the mucosa of UC can evolve with time with variation in extent of involvement and lack of endoscopic-histologic correlation
  - IBD in: the fulminant or refractory phase, chronic phase, early stages
  - Backwash ileitis
  - Effect on treatment on the histology
- Insufficient endoscopic specimens[8]

1Peyrin-Biroulet, L et al. Am J Gastroenterol 2015, 110, 1324-1338
2Feuerstin, JD et al. Mayo Clin Proc 2014, 89, 1553-1563.
3Berg, DR et al. Inflamm Bowel Dis 2019, 25, 1896-1905.
4Rocchi, A et al. Can J Gastroenterol 2012, 26, 811-817.
5Guindi, M et al. J Clin Pathol 2004; 557(12):q1233-1244.
6Zaool, C et al. Dig Dis 2012, 30 (Suppl3) 67-72.
7Gumaste, V et al. Gut 1992, 33, 938-941.
8Torres, J et al. Inflamm Bowel Dis 2012, 18, 1356-1363.

Distinguishing between CD and UC using Serological Markers

Blood based markers	Significance
Antineutrophil cytoplasmic antibodies (pANCA)	Increased in UC (+ in 55-64%), resistant to treatment left sided disease and early surgery
Anti-Saccharomyces cerevisiae Antibodies (ASCA)	Differentiate CD from UC with reported 55% sensitivity, 93% specificity
Anti-Outer Membrane Protein C (Anti-Omp C)	In CD 55% seroreactive, complicated CD, may be helpful in ASCA negative CD (5-15%)
Anti-I2 antibody (I2)	Reportedly + 30% to 50% CD vs 2% to 10% UC; correlate positively with strictures, internal perforations, and small-bowel surgery risk
Antibodies to Flagellin (flagellin CBir1)	CD > UC, small-bowel, internal-penetrating, and fibro-stenosing disease features

Soubieres, A et al. Inflamm Bowel Dis 2016;22:2016–2022

ASCA+/pANCA- predicts CD in 80% and ASCA-/pANCA+ predicts UC in 63.6% in IC

- Since 1996, 97 patients with IC from 3 centers (Leuven, Lille, and Vienna) followed and analyzed for pANCA and ASCA
- ASCA+/pANCA- correlated with CD in 8 of 10 patients
- ASCA-/pANCA+ correlated with UC in 7 of 11 patients
- Remaining 4 cases became CD, clinically behaving as UC-like CD
- 47 of 97 [48.5%]) negative for ASCA and pANCA
- 40 remain diagnosed with IC to date of publication
- Only 7 seronegative cases (14.9%) became CD or UC compared with 48% (24 of 50) of seropositive patients ($P < 0.001$)

Table 3. Results of ASCA and pANCA in the Study Population

	n (%)	CD (%)	UC (%)	IC (%)
ASCA+/pANCA−	26 (26.8)	8 (30.8)	2 (7.7)	16 (61.5)
ASCA−/pANCA+	20 (20.6)	4 (20)	7 (35)	9 (45)
ASCA+/pANCA+	4 (4.1)	2 (50)	1 (25)	1 (25)
ASCA−/pANCA−	47 (48.5)	3 (6.4)	4 (8.5)	40 (85.1)
Total	97 (100)	17 (17.5)	14 (14.4)	66 (68.1)

Table 4. Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value of the Combination of ASCA and pANCA

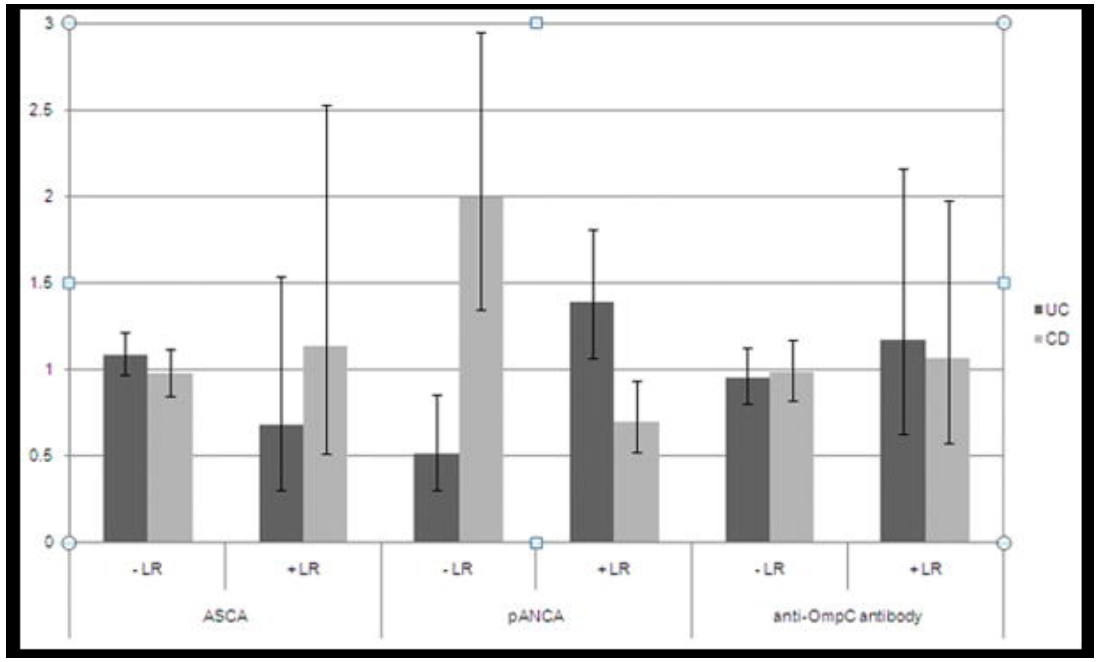
	Diagnosis	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
ASCA+/pANCA−	CD	8/12 (66.7)	7/9 (77.8)	8/10 (80)	7/11 (63.6)
ASCA−/pANCA+	UC	7/9 (77.8)	8/12 (66.7)	7/11 (63.6)	8/10 (80)

PPV, positive predictive value; NPV, negative predictive value.

Joossens S, et al. The value of serologic markers in indeterminate colitis: a prospective follow-up study. Gastroenterology. 2002;122(5):1242–1247.

pANCA, ASCA, and anti-OmpC, of limited utility in predicting IC subsequent disease phenotype

- Observational Study
- 117 pts IC who underwent IBD serology, 1 year follow up
- 1 yr after testing, 58 (50%) IC diagnosed with UC, 49 (42%) with CD, and 10 (9%) remained IC
- Sensitivity/specificity:
  - Positive pANCA for a subsequent diagnosis of UC was 78%/44%
    - + ANCA likelihood ratio (LR) of 1.4 for UC dx at 1 yr in IC pts
  - Positive ASCA and anti-OmpC for subsequent diagnosis of CD was 18%/84% and 27%/75%
    - Neither markers associated with a subsequent diagnosis of CD in IC



Sura SP et al. J Clin Gastroenterol. 2014;48(4):351–355

Disease Course

Influence of Phenotype at Diagnosis and of Other Potential Prognostic Factors on the Course of Inflammatory Bowel Disease

Table 3. Prevalence of medication (% of patients) at different time points

Crohn's disease	t=1 year (*N*=466)	t=3 years (*N*=435)	t=5 years (*N*=337)	t=7 years (*N*=249)	t=9 years (*N*=185)	t=11 years (*N*=122)
No medication	19.7	26.2	32.6	34.5	31.9	37.7
Sulfazalazine	4.3	3.2	3.9	4.4	3.8	4.1
5-ASA	68.2	63.0	57.9	59.0	60.0	54.1
Steroids	33.5	28.3	22.8	24.5	22.2	30.3
Immunosuppressive	12.0	20.7	23.4	20.5	23.2	29.5
Infliximab	1.5	2.8	1.2	2.8	4.9	5.7
Ulcerative colitis	**t=1 year (*N*=588)**	**t=3 years (*N*=511)**	**t=5 years (*N*=402)**	**t=7 years (*N*=303)**	**t=9 years (*N*=204)**	**t=11 years (*N*=121)**
No medication	26.4	32.7	32.3	36.0	39.2	38.8
Sulfazalazine	5.4	6.1	6.0	6.6	8.3	4.1
5-ASA	73.3	67.9	64.7	61.7	61.8	59.5
Steroids	19.9	16.4	17.9	16.2	16.7	11.6
Immunosuppressive	5.4	8.0	11.7	13.2	12.3	11.6
Indeterminate colitis	**t=1 year (*N*=77)**	**t=3 years (*N*=71)**	**t=5 years (*N*=55)**	**t=7 years (*N*=45)**	**t=9 years (*N*=34)**	**t=11 years (*N*=20)**
No medication	27.3	26.8	32.7	22.2	29.4	35.0
Sulfazalazine	6.5	5.6	9.1	6.7	5.9	10.0
5-ASA	67.5	66.2	63.6	64.4	58.8	40.0
Steroids	19.5	18.3	16.4	17.8	17.6	30.0
Immunosuppressive	9.1	12.7	20.0	35.6	35.6	30.0

IC numbers small for calculations

Table 4. Disease severity parameters during the disease course according to phenotype at diagnosis

Crohn's disease	*N*	Cumulative % in the course of disease: % Operated (resective)	% Steroid use	% Immunosuppressive	Recurrence per 100 p-y mean (s.d.)
Overall	476	43	73	44	41 (98)
Age at diagnosis					
<40 years	340	44	76	47	46 (113)
≥40 years	136	43	65[a]	36[b]	29 (35)[c]
Disease location at diagnosis					
Terminal ileum	147	59[d]	67	31[h]	33 (37)[j]
Colon	128	23	73	49	39 (36)
Ileocolonic	149	49[e]	76	52	51 (164)
Upper GI	25	52[f]	96[g]	60	51 (57)
Unknown	27	15	59	33	34 (60)
Disease behavior at diagnosis					
Inflammatory	361	35	74	46	43 (109)
Stricturing	66	76[i]	73	35	37 (45)
Penetrating	36	56	61	44	35 (52)
Stricturing and penetrating	13	85[k]	69	38	39 (69)
Ulcerative colitis		**Cumulative % in the course of disease**			
	N	**% Operated (resective)**	**% Steroid use**	**% Immunosuppressive**	**Recurrence per 100 p-y mean (s.d.)**
Overall	630	11	57	20	35 (49)
Disease location at diagnosis					
Proctitis	240	10	52	17	39 (59)
Distal colitis	273	9	59	23	35 (41)
Extensive colitis	83	20[l]	73[m]	24	31 (44)
Unknown	34	3	47	9	19 (27)
Indeterminate colitis		**Cumulative % in the course of disease**			
	N	**% Operated (resective)**	**% Steroid use**	**% Immunosuppressive**	**Recurrence per 100 p-y mean (s.d.)**
Overall	81	14	62	36	34 (42)
Disease location at diagnosis					
Proctitis	10	30	80	40	62 (82)
Distal colitis	37	16	59	38	35 (32)
Extensive colitis	22	5	68	45	26 (33)
Unknown	12	8	42	8	23 (23)

p-y, patient-years.
[a]$P<0.05$. [b]$P<0.05$. [c]$P<0.0005$. [d]$P<0.0001$ terminal ileum vs. colonic localization. [e]$P<0.0001$ ileocolonic vs. colonic localization. [f]$P<0.005$ upper GI versus colonic localization. [g]$P<0.05$ upper GI vs. terminal ileum, colon, ileo-colonic, and unknown. [h]$P<0.05$ terminal ileum vs. colonic and ileo-colonic localization. [i]$P<0.05$ terminal ileum vs. colonic localization. [j]$P<0.0001$ inflammatory vs. stricturing. [k]$P<0.001$ inflammatory vs. stricturing and penetrating. [l]$P<0.05$ pancolitis vs. left sided colitis. [m]$P<0.05$ extensive colitis vs. proctitis and unknown.

Romberg-Camps et al. Am J Gastroenterol 2009; 104:371–383

Indeterminate Colitis (IC) Course

- 80% of IC patients eventually acquired a diagnosis of UC or CD within 8 years of diagnosis
  - 50/1113 IBD patients (4.6%) with IC
  - At follow up, 37/50 (72.5%) had diagnosis of CD or UC
  - Diagnosis of CD if pts presented with fever, segmental endoscopic lesions, EIM and in smokers
  - Diagnosis of UC in pts who had not undergone appendectomy before diagnosis

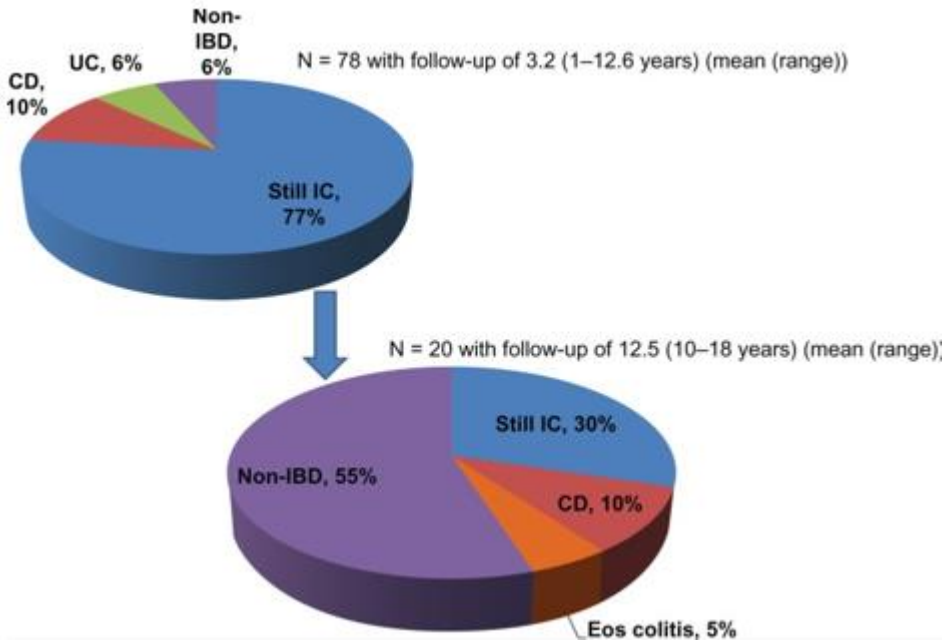
Meucci, G et al. Eur J Gastroenterol Hepatol 1999; 11 (8):909-913

- In a population-based study, IBDU incidence decreased significantly between 1988 and 2014, probably because of better diagnosis performances allowing CD and UC identification
  - 6% (1988–1996) → 2% (2006–2014) ($p < 0.0001$)

Mayer, P et al. Journal of Crohn's and Colitis, Volume 13, Issue Supplement_1, March 2019, S494–S495

IC Course In Pediatric Population

- Retrospective study on 420 children with IBD 1986-2003
- 22% (78) IC, mean age at dx 9.2 ± 4 years, mean follow-up period 4.1 ± 2 yrs
- Follow up period 10-18 years
- 2011 of the 20/60 IBD-U
  - CD 2 (10%), IBDU 6 (30%), Resolution 11 (55%)



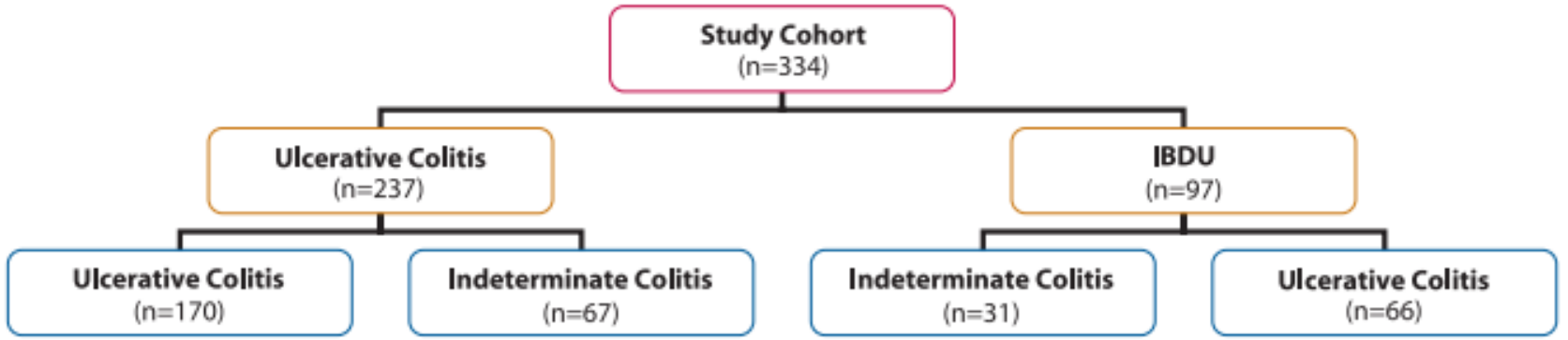
Malaty, HM et al. Clin Exp Gastroenterol 2013 Jul 23;6:115-21

Changes in IBD subtype over time

- 2002-2014 International Classification of Diseases coding in pts with ≥2 IBD diagnostic listings in national patient register evaluated
- 18% changed diagnosis (17% of adults, 29% of children) in median follow-up of 3.8 years
- 97% with CD or UC stayed the same
- 67% with IBDU followed by another IBDU
- Prior to change: CD 29%, UC 62%, IBDU 10%
- At end: CD 31%, UC 58%, IBDU 11%
- IBDU more common in children (12% → 18%)

Everhov, AH et al. Scand J Gastroenterol 2019 Jan; 54(1):55-63.

Diagnosis Change after IPAA



Before surgery: UC (71%) , IBDU (29 %)

After surgery: UC 71%, IBDU 29%

Murrell, et al. Dis Colon Rectum 2009 May;52(5):872-8

Treatment of IC

Medical treatment of IC

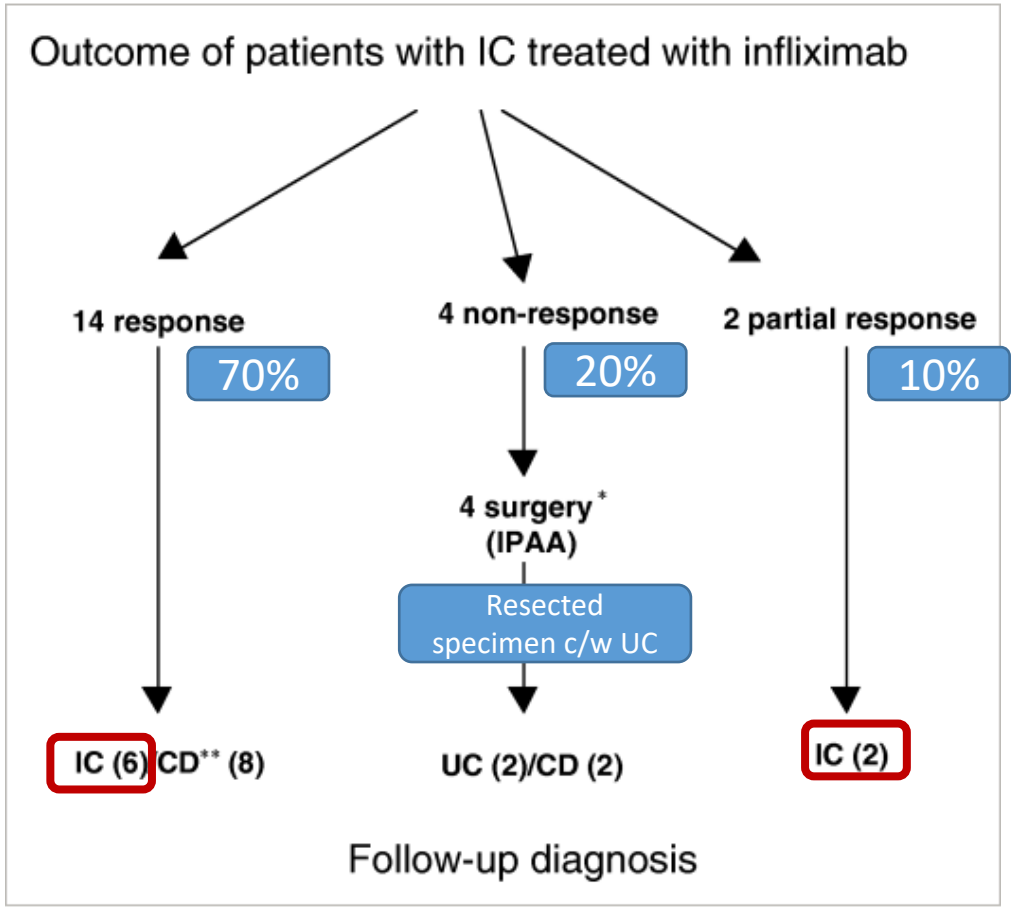
- Randomized controlled trials have included patients with a well-characterized type of IBD (CD or UC)
- Insufficient evidence on specific management in IC due to lack of large randomized prospective treatment trials in IC
  - 5ASA
  - Corticosteroids
  - Thiopurines
  - Vedolizumab
  - Ustekinumab
  - Small molecules (eg tofactinib)
- IC is treated similarly to UC or CD patients based on clinical disease severity and extent and severity of endoscopic and histologic findings

Refractory IC

- Infliximab
- Total proctocolectomy and ileal pouch-anal anastomosis

IFX in IC

- 20 patients, steroid resistant or dependent colitis
- Severe medically refractory colitis
  - Failed 5ASA, 14 refractory to thiopurines, 3 failed cyclosporine
- All patients initially received infliximab, 5mg/kg, intravenously and, in some patients, the dose was subsequently increased to 10mg/kg



Papadakis KA, et al. Infliximab in the treatment of medically refractory indeterminate colitis. Aliment Pharmacol Ther. 2003;18(7):741–747. doi:10.1046/j.1365-2036.2003.01739

IFX in IC

- 24 patients steroid refractory or dependent disease, failed induction with tacrolimus – included were 18 UC, 6 IC
- 6 of 24 tacrolimus resistant patients (17%) achieved clinical remission after infusion, 4 achieved clinical remission after IFX infusion, additional had initial response but needed colectomy and 14/24 (58%) had no response and needed colectomy

Herrlinger KR, Barthel DN, Schmidt KJ, et al. Infliximab as rescue medication for patients with severe ulcerative/indeterminate colitis refractory to tacrolimus. Aliment Pharmacol Ther. 2010;31 (9):1036–1041.

TPC and IPAA in IC

- IC natural history tends to overlap with UC more than CD
  - Pouch complications
    - IC >UC have complications including pouch failure with IPAA[1,2,3,4,5]
  - Pouch failure
    - Several studies - similar pouch failure rates between IC and UC[6,7,8]
- Crohn's disease
  - 15% of pts with IC undergoing TPC and IPAA reclassified as CD on long term follow up[1]

1Yu CS, Pemberton JH, Larson D. Ileal pouch-anal anastomosis in patients with indeterminate colitis: long-term results. Dis Colon Rectum. 2000;43(11):1487–1496. doi:10.1007/BF02236726
2Guindi M, Riddell RH. Indeterminate colitis. J Clin Pathol. 2004;57 (12):1233–1244. 3McIntyre PB, Pemberton JH, Wolff BG, Dozois RR, Beart RW Jr. Indeterminate colitis. Long-term outcome in patients after ileal pouch-anal anastomosis. Dis Colon Rectum. 1995;38(1):51–54. 4. Atkinson KG, Owen DA, Wankling G. Restorative proctocolectomy and indeterminate colitis. Am J Surg. 1994;167(5):516–518.
5Koltun WA, Schoetz DJ Jr, Roberts PL, Murray JJ, Coller JA, Veidenheimer MC. Indeterminate colitis predisposes to perineal complications after ileal pouch-anal anastomosis. Dis Colon Rectum. 1991;34(10):857–860.
6Brown CJ, MacLean AR, Cohen Z, Macrae HM, O'Connir B, McLeod RS. Crohn's disease and indeterminate colitis and the ileal pouch-anal anastomosis: outcomes and patterns of failure. Dis Colon Rectum. 2005;48(8):1542–1549.
7Pishori T, Dinnewitzer A, Zmora O, et al. Outcome of patients with indeterminate colitis undergoing a double-stapled ileal pouch-anal anastomosis. Dis Colon Rectum. 2004;47(5):717–721.
8Dayton MT, Larsen KR, Christiansen DD. Similar functional results and complications after ileal pouch-anal anastomosis in patients with indeterminate vs ulcerative colitis. Arch Surg. 2002;137(6):690–694; discussion 694–695.

Using pathology to definitively diagnose IC and prognosis of pouch success/failure

- 175 pts who underwent restorative proctocolectomy Nov 1984 to Dec 1992
- Pathology reviewed by two pathologists
  - UC - 158 pts, IC 16 pts
  - Pouch success rate: UC 95% and IC 81%
    - Removal of pouch – UC 8/158 and IC 3/16
    - IC – 8/16 have satisfactory pouch function and 5/16 have some ongoing problems

TABLE I

Patient Data

	Ulcerative Colitis	Indeterminate Colitis
Age range (y)	19–59	20–50
Average age (y)	34	32.6
Sex distribution (M:F) (%)	62:38	50:50
Type of pouch		
S pouch	83	12
J pouch	75	4

TABLE II

Complications

	Ulcerative Colitis(%)	Indeterminate Colitis(%)
Fistulae	1	25
Anastomotic leaks	6	0
Small bowel obstruction	7	6
Pelvic infection	1	25
Fistulae associated with pouch	1.25	25
Perforation/torsion pouch	0.6	0
Pelvic infection/no fistulae	5.7	6.25

Atkinson KG, et al. Restorative proctocolectomy and indeterminate colitis. Am J Surg. 1994;167(5):516–518.

Extension of inflammation into MP predicts pouch-related complications in UC or IC

- 1992 and 2011, 142 patients (132 with UC and 10 with IC)
- Median follow-up of 36 (3-149) months
  - 51 (35.9%) pouch related complication
    - Pouchitis, pouch-cutaneous fistula, pouch failure, stricture
- Presence of extension of the inflammation into the muscularis propria of the resected specimen was associated with an increased risk of pouch-related complications (P = 0.01)
- Presence of submucosal edema was also a significant risk factor (P = 0.03)

Pouch Prognosis

IC predisposes to IPAA to perineal complications and high chance of reservoir loss

- Retrospective study
- 288 patients who underwent IPAA, 235 patients (82 percent) had a diagnosis of chronic ulcerative colitis, 18 patients (6 percent) had indeterminate colitis, 6 patients (2 percent) had Crohn's disease, and 29 patients (10 percent) had familial polyposis
- All complications occurred at least 6 months after closure of the stoma and required operative therapy
  - Complications in 50% (9/18) IC pts vs 3% (8/235) UC ($P < 0.001$)
  - Risk of eventual ileostomy because of perineal complications in UC 0.4% vs IC 28% ($P < 0.001$)

Koltun WA, et al. Indeterminate colitis predisposes to perineal complications after ileal pouch-anal anastomosis. Dis Colon Rectum. 1991;34(10):857–860. doi:10.1007/BF02049696

Function similar yet more failure IC vs UC

- 71 IC with IPAA, 56 month mean follow up vs 1,232 chronic UC with IPAA followed 60 month mean follow up
- Functional results - Frequency of daily BM: no difference in IC vs UC
- Pouchitis – 33% (same for IC and UC)
- Pouch failure rate IC (19%) > UC (8%), P = 0.03

McIntyre PB, et al. Indeterminate colitis. Long-term outcome in patients after ileal pouch-anal anastomosis. Dis Colon Rectum. 1995;38(1):51–54.

Higher complication rate but similar pouch failure IC vs UC

- 1,270 pts 1982 and 2001, TPC Mt Sinai: 1,135 UC, 36 CD, 21 IC, 78 another dx
- Pouch complications: CD (64%), IC (43%) vs UC (22%), $p < 0.05$
- Pouch excision/defunctioning: CD (56%) vs IC (10%), UC (6%), $p < 0.01$

Brown CJ, et al. Crohn's disease and indeterminate colitis and the ileal pouch-anal anastomosis: outcomes and patterns of failure. Dis Colon Rectum. 2005;48(8):1542–1549.

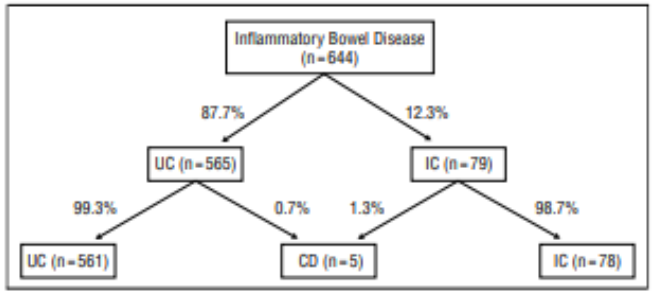
Pouch complications slightly higher IC vs UC

- Retrospective study in IC vs UC with IPAA
- July 1, 1982, and July 1, 2001, 723 pts underwent IPAA, 644 for colonic IBD
- 79 (12.3%) IC, 565 (87.7%) UC
- 98% 1 yr f/u, 89% long term f/u 78.5 months
- IC vs UC
  - cuff abscess (1.3% vs 1.6%), J-pouch leak (5.1% vs 2.3%), intra-abdominal abscess (0% vs 1.1%), stricture (7.6% vs 4.8%), and fistula (2.5% vs 1.6%)
  - small bowel obstruction (6.3% vs 5.5%), pouchitis (34.2% vs 25.0%), eventual diagnosis of Crohn disease (1.3% vs 0.7%), redo IPAA (1.3% vs 0.9%), and eventual pouch loss (2.5% vs 1.2%)
  - no differences in pouch function
  - pathologists classified IC into 3 groups: IC but favor UC (group 1), IC but favor Crohn (group 2), and IC (group 3)
    - Most postoperative complications occurred in group 1 patients, but the only pouch loss occurred in those in group 2

Table 1. Complications After Ileal Pouch–Anal Anastomosis (IPAA)*

Complication	Indeterminate Colitis (n = 79)	Ulcerative Colitis (n = 565)	*P* Value
Cuff abscess	1 (1.3)	9 (1.6)	.82
J-pouch leak	4 (5.1)	13 (2.3)	.15
Intra-abdominal abscess	0	6 (1.1)	.36
Stricture	6 (7.6)	27 (4.8)	.29
Pouch fistula	2 (2.5)	9 (1.6)	.55
Surgical small bowel obstruction	5 (6.3)	31 (5.5)	.76
Pouchitis	27 (34.2)	141 (25.0)	.15
Crohn diagnosis	1 (1.3)	4 (0.7)	.36
Redo IPAA	1 (1.3)	5 (0.9)	.87
Pouch loss	2 (2.5)	7 (1.2)	.36

*Data are given as number (percentage) unless otherwise indicated.

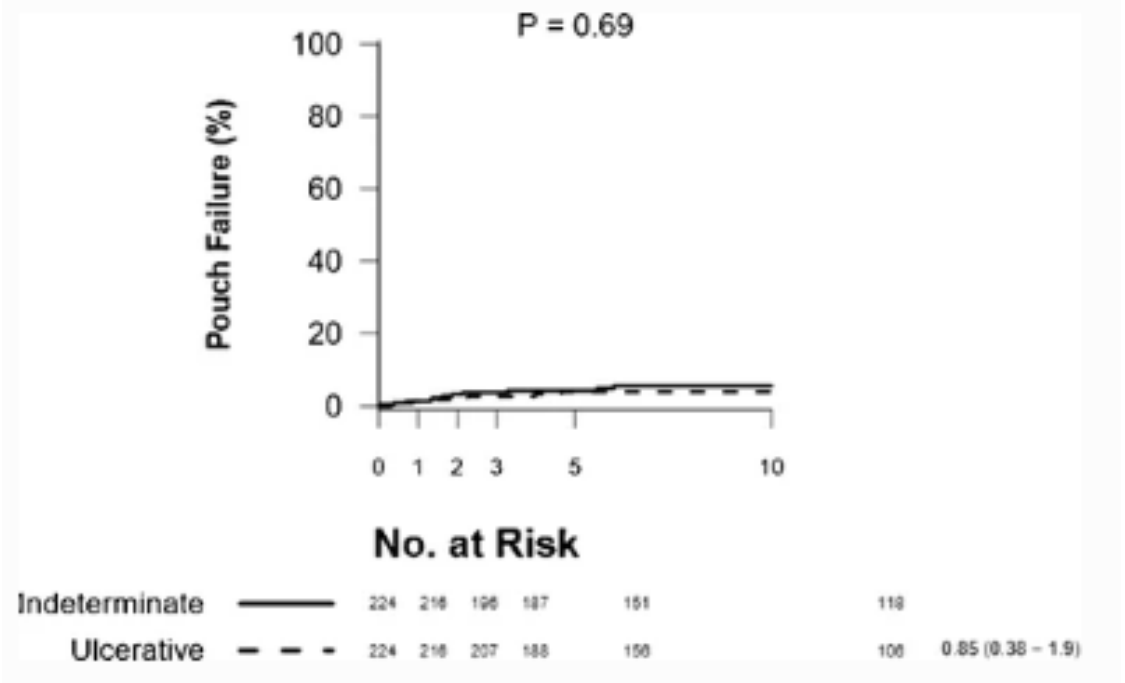


Long-term follow-up demonstrates the eventual diagnosis of the 644 patients who originally underwent ileal pouch–anal anastomosis. While 0.7% of patients (4/565) with ulcerative colitis (UC) eventually developed Crohn disease (CD), 1.3% of patients (1/79) with indeterminate colitis (IC) went on to develop CD.

Dayton MT, Larsen KR, Christiansen DD. Similar functional results and complications after ileal pouch-anal anastomosis in patients with indeterminate vs ulcerative colitis. Arch Surg. 2002;137(6):690–694;

IC more fistula and IPAA CD but pouch function and survival rates similar c/w UC

- Case matched analysis (matched age, gender, date of surgery, type of anastomosis, diverting loop ileostomy)
- IPAA for IC or UC 1985-2014
- 448, age 36.8 yrs, male 52.7 %
- IC with more fistula (IC 15.6 %, UC 8.0 %, p = 0.01) and IPAA CD (IC 6.7 %, UC 2.7 %, p = 0.04) c/w UC
- IC and UC comparable morbidity, functional outcomes, quality of life scores and pouch failure rates



Jackson, KL et al. J Gastrointest surg 2017 Jan;21(1):56-61

Meta-analysis of 17 studies

- 1057 IC, 6511 UC
- IC mean pouch failure rate 7.5%
- IC mean pouch complication rate 67%
- Pouch failure, pouchitis, anastomotic leak, stricture, small bowel obstruction (IC and UC similar)
- Complications IC > UC after IPAA (odds ratio [OR]: 2.6, p <0.001):
  - pouch fistula [OR:4.98, p <0.001]
  - pelvic sepsis [OR:3.98, p =0.002]
  - pelvic or cuff abscess [OR: 4.5, p <0.001]
  - perineal complications [OR: 5.13, p <0.001]
  - ultimate diagnosis of CD [OR: 2.57, p <0.001]

Table 3. Outcomes of pouch surgery in patients with indeterminate colitis.

Study First author, date	Failure	Total complications	Pouchitis	Leak	Fistula	Perineal complications	Stricture	Crohn's disease
Netz, 2018	9	41	32	0	0	0	9	0
Jackson, 2017	13	90	NA	7	35	0	0	15
Murrell, 2009	7	41	27	0	0	0	0	14
Brown, 2005	2	22	9	2	4	0	3	0
Hui, 2005	0	16	13	0	0	0	0	3
Tekkis, 2005	3	35	3	5	5	0	6	0
Pishori, 2004	0	6	0	0	1	0	0	0
Gramlich, 2003	4	37	0	4	4	8	0	11
Alexander, 2003	1	8	5	0	3	0	0	0
Rudolph, 2002	0	32	21	1	4	0	0	0
Delaney, 2002	4	37	0	4	4	8	0	11
Dayton, 2002	2	46	27	4	2	0	6	1
Yu, 2000	19	93	34	0	20	0	13	0
Marcello, 1997	6	33	12	0	0	21	0	0
McIntyre, 1995	13	37	22	0	0	0	0	0
Atkinson, 1994	3	13	0	0	4	0	0	0
Koltun, 1991	5	26	0	8	8	9	0	0
Total	91	613	205	35	94	46	37	55

Table 4. Comparison between characteristics and outcomes of patients with indeterminate colitis, ulcerative colitis, and Crohn's disease.

Variable	Indeterminate colitis	Ulcerative colitis	Crohn's disease
Number	1057	6511	105
Mean age in years	33	34	32.4
Male %	51.3	49.6	40.7
Pouch failure %	8.6	6.7	55.2
Incontinence %	22.1	12.5	NA
Complications %	58	49.1	83.8
Pouchitis %	19.4	24.4	11.4
Leak %	3.3	2.7	7.6
Stricture %	3.5	4.9	16.2
Fistula %	8.9	2.7	26.7
Pelvic sepsis %	4.2	2.5	3.8
Pelvic/cuff abscess %	4.8	1.4	11.4
Perineal complications %	4.3	1.9	23.8
Bowel obstruction %	4.2	7.4	9.5
Crohn's disease %	5.2	0.67	----

NA, not available.

Emile SH, Gilshtein H, Wexner SD. Outcome of ileal pouch-anal anastomosis in patients with indeterminate colitis: a systematic review and meta-analysis. J Crohns Colitis. 2020;14(7):1010–1020.

Outcome of IPAA in UC similar to IC

- Retrospective study, IPAA, August 1988 to January 2000
- 303 patients included, 40 months mean duration follow up
- 56 (18.1%) preop dx IC → Post-op dx: IC 13 (4.3%), UC 285 (9%), and CD 5 (1.6%)
- Complications: 37.7% UC, 60% CD, and 30.7% IC
- Postoperative hemorrhage, abscess, and fistula: UC 2.4%, 6.3%, and 3.9% and IC 0%, 15.3%, and 7.7%
- Small-bowel obstruction UC 8.5%, CD 20%, IC 7.7%
- Pouchitis: UC 4.6%, IC 0
- None of the patients with indeterminate colitis had a postoperative diagnosis of Crohn's disease during the follow-up period
- Functional outcome comparable in all three patient groups.

Pishori T, et al. Outcome of patients with indeterminate colitis undergoing a double-stapled ileal pouch-anal anastomosis. Dis Colon Rectum. 2004;47(5):717–721

No difference in pouch UC, IBDU or IC

- Prospective study: UC vs IBD-U/IC undergoing TPC + IPAA
- N=334 patients
- Prior to surgery: 237 (71 %) UC, IBD-U 97 (29%)
- After surgery: 236 (71%) UC, IC 98 (29%)
- After a median follow-up after stoma closure of 26 months median follow up after stoma closure:
  - Acute pouchitis: 53 patients (16 percent)
  - Chronic pouchitis: 37 patients (11 percent)
  - De novo Crohn's: 40 patients (12 percent)
  - No significant difference in the incidence of acute pouchitis, chronic pouchitis, or de novo Crohn's disease between UC, IBD-U or IC

TABLE 3. Association between type of colitis and pouchitis/Crohn's disease

Diagnosis	*n*	*Median follow-up (months)*	*Acute pouchitis*	*Chronic pouchitis*	*Crohn's Disease*
Preoperative					
Ulcerative colitis	237	27	39 (16)	26 (11)	24 (10)
IBDU	97	26	14 (14)	11 (11)	16 (16)
Postoperative					
Ulcerative colitis	236	29	39 (17)	24 (10)	26 (11)
IC	98	25	14 (14)	13 (13)	14 (14)

IBDU = inflammatory bowel disease-unclassified; IC = indeterminate colitis. Values in parentheses denote percentage.

TABLE 4. Association between type of colitis and reasons for *de novo* Crohn's disease

Diagnosis	*n*	*De novo Crohn's Disease*	*Afferent ileal limb inflammation*	*New perianal disease*
Preoperative				
Ulcerative colitis	237	24	18 (75)	6 (25)
IBDU	97	16	12 (75)	4 (25)
Postoperative				
Ulcerative colitis	236	26	19 (73)	7 (27)
IC	98	14	11 (79)	3 (21)

IBDU = inflammatory bowel disease-unclassified; IC = indeterminate colitis. Values in parentheses denote percentage of patients developing Crohn's disease.

Murrell, et al. Dis Colon Rectum 2009 May;52(5):872-8

Pouch function and failure IC similar to UC

- Patients with IC fare better than those with CD
- 5-10% of pts with colitis have endoscopic, radiologic and histologic findings from colectomy that are indeterminate with mixed features of UC and CD
- IC more likely to develop CD pouch
- IC pouch function similar to UC
  - # BM, FI, nighttime seepage
- Pouch failure similar to UC

Table 3. Indeterminate Colitis and Pouch Retention

Study	Year	N	Follow-Up (yrs)	Pouch Retention (%)
Brown et al[15]	2005	21	NS	90.0
Fazio et al[95]	1995	75	1.5	98.1
Gramlich et al[102]	2003	115	3.4	96.6
Jackson et al[92]	2017	224	10.2	94.2
Pezim et al[103]	1989	25	3.2	92.0
Lightner et al[8]	2017	76	30.0	90.0
Rudolph et al[100]	2002	35	NS	100.0
Pishori et al[104]	2004	13	4.0	100.0
Fazio et al[18]	2013	63	7.0	95.2
Delaney et al[105]	2002	115	3.4	98.3
Tekkis et al[97]	2005	26	1.8	89.5
Yu et al[106]	2000	82	10.0	73.0
Marcello et al[107]	1997	53	NS	75.0

NS, not specified.

Chang, S et al. Gastroenterology & Hepatology Volume 13, Issue 8 August 2017

Overall conditional IC/UC pouch survival improves over time with post-op anastomotic leak + abscess

- Retrospective study at CCF 1986-2016
- 3468 pts UC or IC who underwent IPAA
- 10-year pouch survival rate: 0.94 (95% CI, 0.93-0.95)
- Post- op: After 1 year the conditional pouch survival increased to 0.95 (95% CI, 0.94-0.96), after 3 years to 0.97 (95% CI, 0.96-0.98), and after 5 years to 0.98 (95% CI, 0.98-0.99)
- Anastomotic leak: 122 patients (3.5%) with the 10-year IPAA survival in patients with leak was 0.85 (95% CI, 0.77-0.93). In this group, after 1 year of pouch survival, the conditional pouch survival increased to 0.89 (95% CI, 0.82-0.96) and after 3 years to 0.98 (95% CI, 0.94-1.00)
- Postop abscess similar to anastomotic leak

Years already survived	*Survival probability (95% CI)*	*Survival probability (95% CI)*	*Standardized difference*
	Anastomotic leak (N = 122)	**No anastomotic leak (N = 3346)**	
0	0.85 (0.77–0.93)	0.95 (0.94-0.96)	0.44
1	0.89 (0.82–0.96)	0.95 (0.95-0.96)	0.27
3	0.98 (0.94–1.00)	0.97 (0.96-0.98)	0.06
5	0.98 (0.94–1.00)	0.98 (0.98-0.99)	0.00
10	1.00 (1.00–1.00)	1.00 (1.00–1.00)	NA
	Abscess (N = 188)	**No abscess (N = 3280)**	
0	0.83 (0.76–0.90)	0.95 (0.94–0.96)	0.52
1	0.87 (0.80–0.93)	0.96 (0.95–0.97)	0.43
3	0.97 (0.94–1.00)	0.97 (0.96–0.98)	0.00
5	0.99 (0.96–1.00)	0.98 (0.98–0.99)	0.07
10	1.00 (1.00–1.00)	1.00 (1.00–1.00)	NA
	Fistula (N = 87)	**No fistula (N = 3381)**	
0	0.89 (0.82-0.96)	0.95 (0.94–0.96)	0.27
1	0.91 (0.84-0.97)	0.95 (0.94–0.96)	0.18
3	0.96 (0.91–1.00)	0.97 (0.96–0.98)	0.06
5	0.97 (0.93–1.00)	0.98 (0.98–0.99)	0.07
10	1.00 (1.00–1.00)	1.00 (1.00–1.00)	NA

NA = not applicable.

Feinberg, A et al. Dis Colo and Rectum July 2020 – Vol 64 (7): 927-933

Crohn’s Disease Dx post IPAA

CD subsequent diagnosis (in both UC and IC) with poor long-term outcome

- Mean age of chronic UC higher (34 vs. 31; $P < 0.01$)
- At 10 years, pts with IC > chronic UC:
  - pelvic sepsis (17% IC vs. 7% chronic UC $p < 0.001$)
  - pouch fistula (31 vs 9 percent; $p < 0.001$)
  - pouch failure (27 vs. 11 percent, $p < 0.001$)
- During follow up, dx changed to CD: 15% IC, 2% chronic UC, $p < 0.001$
- When the outcomes of these patients newly diagnosed with CD separated, rate of complications for remaining IC pts = chronic UC pts
- Functional outcomes comparable among all three groups

Yu CS, et al. Ileal pouch-anal anastomosis in patients with indeterminate colitis: long-term results. Dis Colon Rectum. 2000;43(11):1487–1496.

CD Diagnosis after IPAA

TABLE 5. Recent studies of ileal pouch-anal anastomosis in indeterminate colitis

Author (ref)	*Year*	*Study design*	*Time of IC diagnosis*	*Clinical end point definition*		*Long-term outcome (IC vs. UC)*
				Pouchitis	*CD*	
Marcello *et al.*[10]	1997	R	Preop/ postop	C, E	Clinical, radiographic, endoscopic, or pathologic	Increased risk of CD
Yu *et al.*[11]	2000	R	Postop	Not stated	Symptoms "suggestive" of CD	No difference in pouchitis Increased risk of CD
Dayton *et al.*[14]	2002	P	Postop	Clinical	Not stated	No difference
Delaney *et al.*[12]	2002	R	Postop	Not stated	Pouchitis "suggestive" of CD; CD antibody profile	Increased risk of CD
Alexander *et al.*[15]	2003	R	Postop	C	Clinical, radiographic, or histologic criteria	No difference
Shen *et al.*[13]	2006	P	Postop	C, E	Afferent limb inflammation, perianal disease	Increased risk of CD
Melmed *et al.*[16]	2008	P	Postop	C, E	Afferent limb inflammation, perianal disease	No difference

IC = indeterminate colitis; CD = Crohn's disease; R = retrospective; P = prospective; C = clinical; E = endoscopic; IBDU = inflammatory bowel disease-unclassified.

Murrell, et al. Dis Colon Rectum 2009 May;52(5):872-8

Crohn's disease after TPC and IPAA for UC

- Retrospective study
- Montreal Canada, 301 pts 1985-2014
- Cumulative incidence of Crohn's disease was 7.5% at 5 years postoperatively and gradually increased to 17.7% at 10 yrs and 33.0% at 20 years
- Predictive risk factors for CD:
  - current tobacco smoking at surgery (HR 3.56 (95% CI, 1.54-8.22))
  - suspicion of indeterminate colitis (HR 3.50 (95% CI, 1.69-7.24))*
  - presence of mouth ulcers before surgery (HR 2.16 (95% CI, 1.03-4.53))
  - age at diagnosis of ulcerative colitis (HR 0.94 (95% CI, 0.90-0.97))*

  *remained statistically significant on multivariant analysis
- Removal of the pouch in 16% with CD

TABLE 2. Univariate analysis of clinical factors and change of diagnosis to CD postoperatively

Clinical factors	*UC diagnosis maintained*	*CD diagnosed postoperatively*	*HR (95% CI)*	*p value*
Age at diagnosis of UC, y	30.4	24.2	0.94 (0.90–0.97)	<0.001
Duration of UC before surgery, y	7.5	6.4	0.99 (0.94–1.04)	0.76
Female sex, n (%)	112 (42.5)	13 (34.2)	0.63 (0.32–1.24)	0.18
Current smoker at time of surgery, n (%)	18 (7.1)	7 (20.6)	3.56 (1.54–8.22)	0.003
Former smoker, n (%)	81 (32.1)	7 (20.6)	0.49 (0.21–1.14)	0.097
Never smoker, n (%)	153 (60.7)	20 (58.8)	1.00 (0.50–1.99)	0.99
Suspicion of indeterminate colitis, n (%)	23 (8.7)	10 (26.3)	3.50 (1.69–7.24)	<0.001
Mouth ulcers before surgery, n (%)	21 (11.9)	10 (28.6)	2.16 (1.03–4.53)	0.041

CD = Crohn's disease; UC = ulcerative colitis.

Hercun J et al. Dis Colon Rectum. 2021 Feb 1; 64(2):217-224.

Long-term pouch function in IC good if no CD

- 56% pts, mean follow up 14 ± 7 yrs
- Behavior developed: 39% Crohn's disease-like, 61% non-Crohn disease-like
- Pouchitis - both groups (57%)
- Crohn disease-like patients required more:
  - anti-inflammatory/immunomodulatory medications (95% vs 18%, P < .001)
  - dilatations for afferent-limb strictures (41% vs 0%, P < .001)
  - pouch reoperations (32% vs 6%, P = .02)
- Pouch excision or diversion in 8
  - 7 Crohn disease-like behavior

Table 2
Long-term outcomes following IPAA for indeterminate colitis.

Outcome		Total patients $n = 56$ (%)		Non-CD-like behavior $n = 34$ (%)		CD-like behavior $n = 22$ (%)		*P* value
Average follow-up after initial colectomy, y (±SD)		14	(±7)	14	(±7)	15	(±8)	.60
Pouch complications								
Pouchitis, recurrent/chronic	Yes	32	(57)	19	(56)	13	(59)	.968
	No	24	(43)	15	(44)	9	(41)	
Afferent limb stricture (requiring dilatation)	Yes	9	(16)	0	(0)	9	(41)	<.001
	No	47	(84)	34	(100)	13	(59)	
Pouch reoperation (revision or excision)	Yes	9	(16)	2	(6)	7	(32)	.022
	No	47	(84)	32	(94)	15	(68)	
Long-term requirement for anti-inflammatory/immunomodulatory medications after IPAA, $n = 54$*								
Any medication	Yes	26	(48)	6	(18)	20	(95)	<.001
	No	28	(52)	27	(82)	1	(5)	
5-ASA	Yes	4	(7)	2	(6)	2	(10)	.638
	No	50	(93)	31	(94)	19	(90)	
Steroids	Yes	7	(13)	3	(9)	4	(19)	.408
	No	47	(87)	30	(91)	17	(81)	
Antimetabolite	Yes	5	(9)	1	(3)	4	(19)	.069
	No	49	(91)	32	(97)	17	(81)	
Anti-TNF-α therapy	Yes	18	(33)	0	(0)	18	(86)	<.001
	No	36	(67)	33	(100)	3	(14)	
Anti-integrin therapy	Yes	1	(2)	0	(0)	1	(5)	.389
	No	53	(98)	33	(100)	20	(95)	
Physician assessment at last clinic appointment†								
J-pouch in continuity: good function		32	(57)	23	(68)	9	(41)	.009
J-pouch in continuity: bad function		16	(29)	10	(29)	6	(27)	(.741‡)
Diverted: stoma		8	(14)	1	(3)	7	(32)	

SD, standard deviation.
* Data on 2 patients not available from medical record.
† As assessed by physician in accordance with pouch function and subjective QOL.
‡ *P* after excluding patients in discontinuation.

Netz U, et al. Long-term outcomes following ileal pouch-anal anastomosis in patients with indeterminate colitis. Surgery. 2018;163(3):535–541

Conclusions

- IBDU/IC is a diagnosis of IBD where the exact diagnosis of CD or UC cannot be determined (5-15%)
- Because of a paucity of data for medications in IC, treatment is based on disease location and severity (usually treated as if UC)
- There is data on refractory indeterminate colitis for which infliximab and total proctocolectomy with ileoanal pouch anastomosis can be used successfully
- If a patient undergoes IPAA, re-evaluation of colectomy specimen to re-evaluate diagnosis can be helpful to determine prognosis for the pouch and CD development