IBD : dysplasia and activity scoring

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Overview

- Increased risk of developing intestinal (CRC+++) and extra-intestinal malignancies in IBD
- Role of chronic inflammation in the development of neoplasia (« field defect »)
- Advances in endoscopic technology (video endoscope, high definition and chromoendoscopy)
- Dysplasia, a pre-neoplastic lesion; non-conventional types of dysplasia
- Distinct clinicopathologic and molecular features that can assist in their risk stratification
- The emerging role of histologic disease activity assessment in UC (and CD)

Increased risk of developing intestinal and extra-intestinal malignancies in patients with IBD

Table 1. Background risk of cancer in patients with IBD.[1–8]

Tumour	SIR in IBD	Incidence in background population	5-year Survival
Small bowel adenocarcinoma in CD	18.7–46	0.3–0.5	±40%
Colorectal cancer in IBD	1.7–8.6	0.5–0.8	64%
Cholangiocarcinoma [* IBD with PSC]	2–160*	0.08	8%[4]
Gastric cancer in CD	2.8	0.3–1[5]	31%[6]
Leukaemia in UC [** adult age]	2	0.015	24%**–67%[7]
Urinary tract cancer in CD	2	0.5	77%[8]

Annese V. JCC 2020

+ Extra-intestinal malignancies (consequence of an underlying inflammatory state and immunosuppressive therapies)

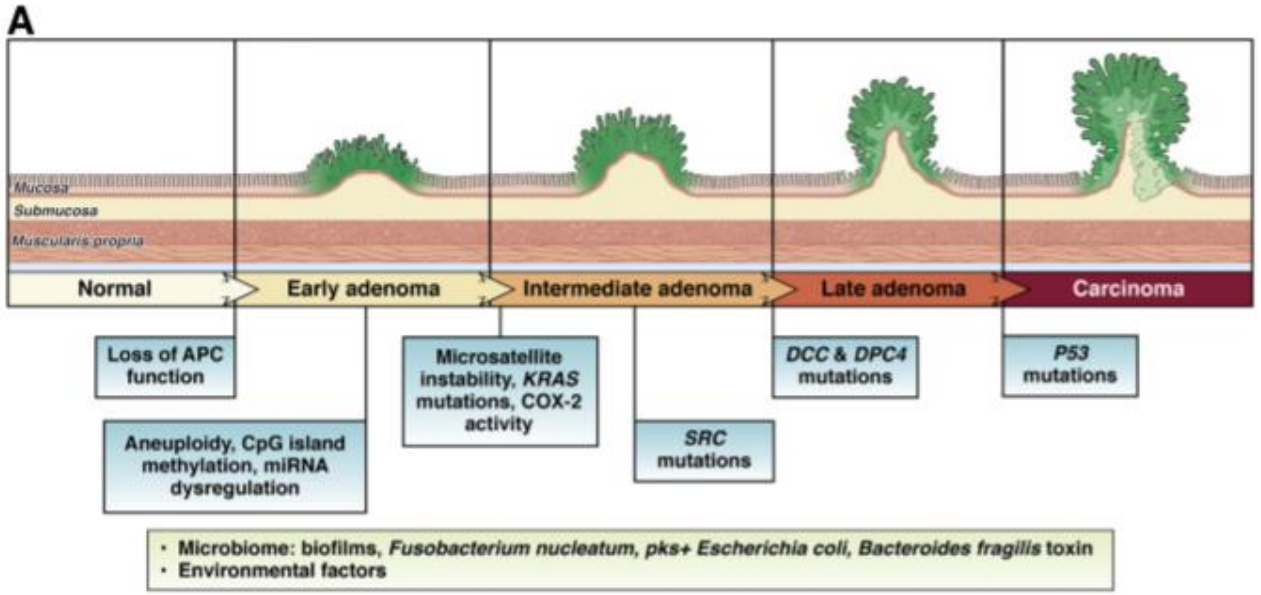
Risk factors for CRC in patients with IBD

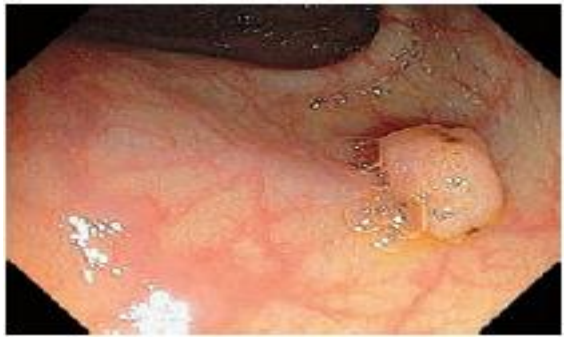
Table 1. Risk Factors for Colorectal Cancer in Patients with Inflammatory Bowel Disease.

Risk factors established in the general population
Increasing age*
Male sex*
History of colorectal cancer in first-degree relatives*
Increased body-mass index†
Low level of physical activity†
Cigarette smoking†
High consumption of red meat†
Consumption of alcohol†
Risk factors specific to patients with inflammatory bowel disease
Coexisting primary sclerosing cholangitis
Increasing cumulative extent of colonic inflammatory lesions‡
Increasing duration of inflammatory bowel disease§
Active chronic endoscopically assessed inflammation
Active chronic histologically assessed inflammation
Anatomical abnormalities
Foreshortened colon
Strictures
Pseudopolyps
Personal history of flat dysplasia

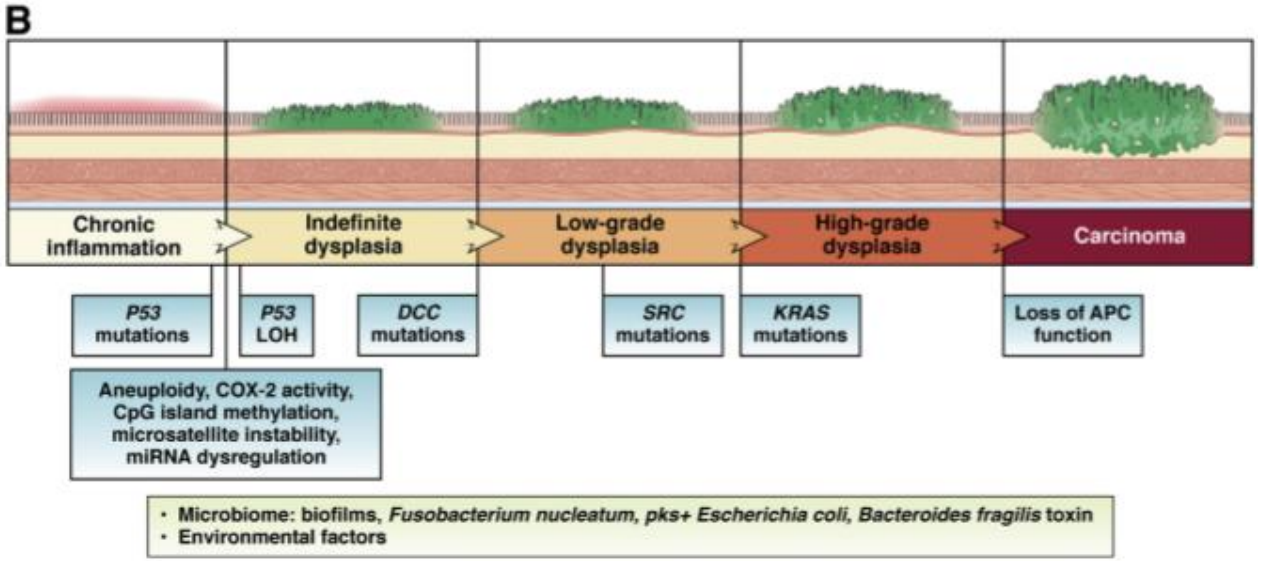
Beaugerie et al, NEJM 2015

Pathogenesis of colitis-associated CRC





85% CIN
15% MSI



Shah et al., Gastroenterology 2021

Morphologic and molecular characterization and classification of dysplastic lesions

Dysplasia (or intra-epithelial neoplasia), a pre-neoplastic lesion in IBD

Dysplasia: «Unequivocal neoplasia of the epithelium confined to the basement membrane, without invasion into the lamina propria» (Riddell, Inflammatory Bowel Disease-Dysplasia Morphology Study group, 1983).

No molecular markers routinely used to stratify IBD patients into groups at low or high risk for developing colorectal neoplasia.

Dysplasia : best marker for the increased risk of CRC in IBD (Goldman, Cancer 1996)

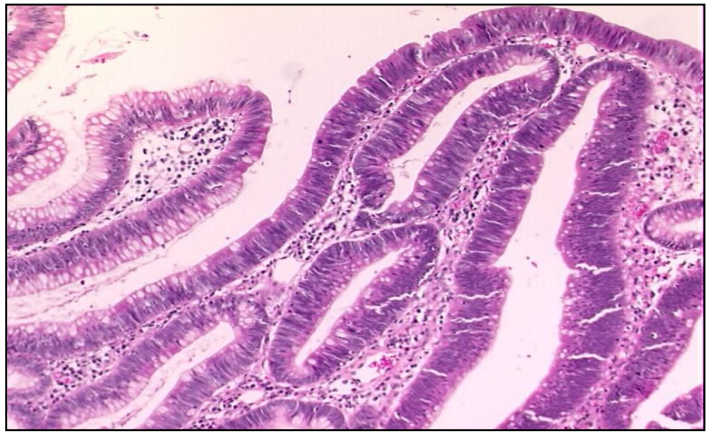
Dysplasia in IBD

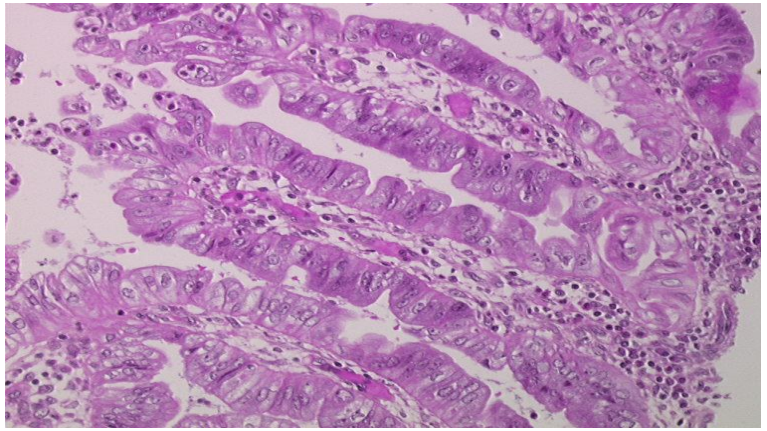
(i) Intestinal (or conventional) dysplasia

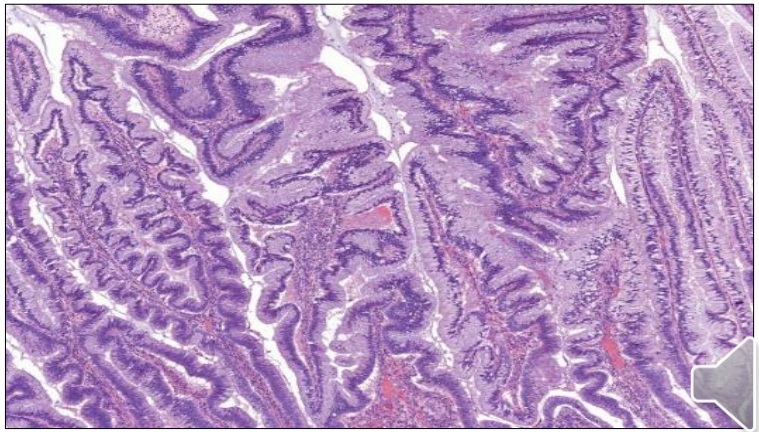
(ii) Hypermucinous/villous dysplasia

(iii) Serrated dysplasia

From WHO Classification of Tumours of the Digestive System, 2010

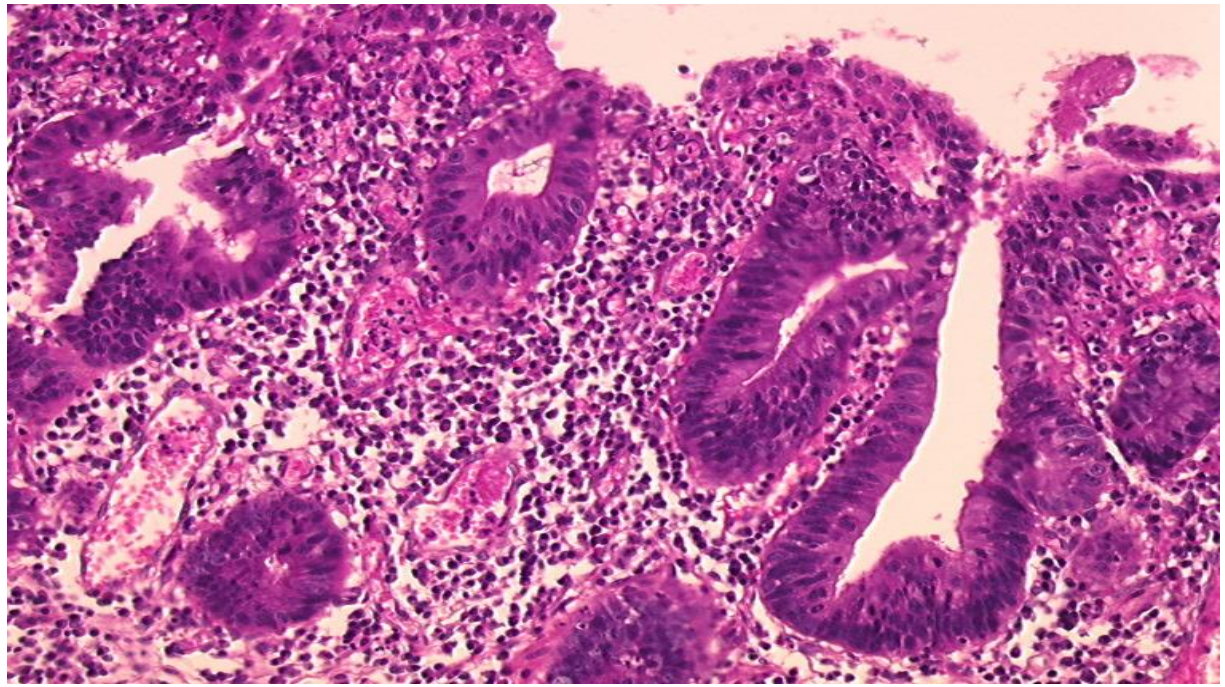






Different types of dysplasia

Low grade



High grade

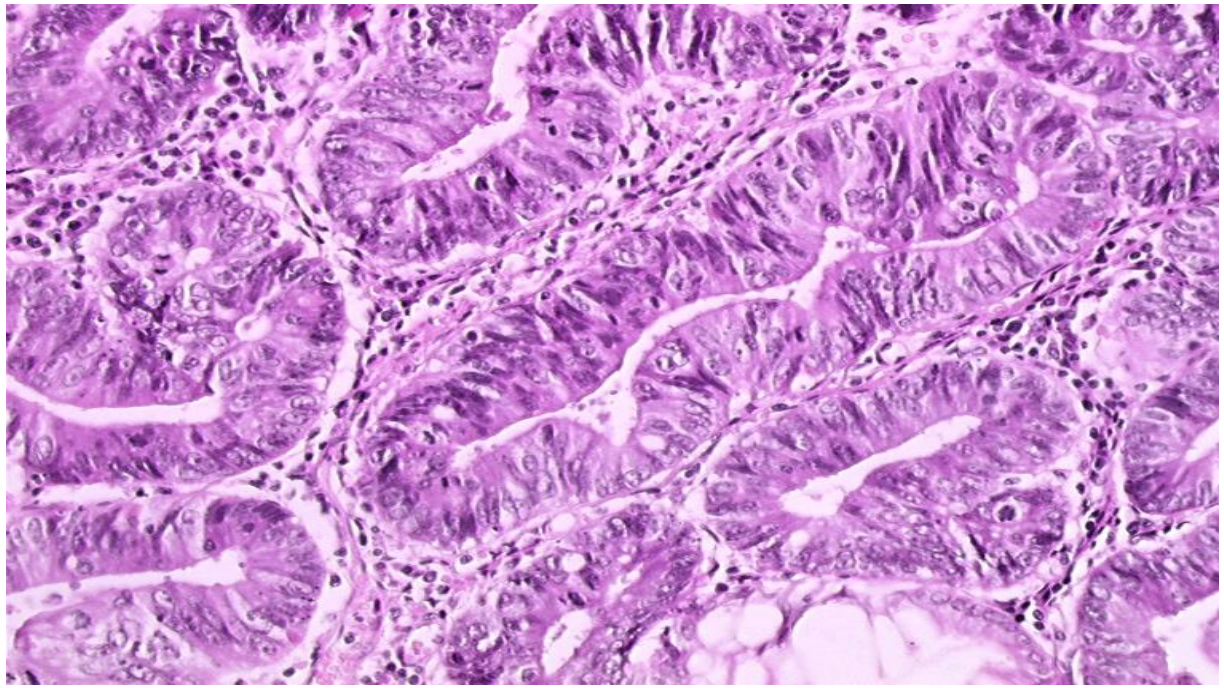


Table 1 Vienna classification of gastrointestinal epithelial neoplasia

Category 1	Negative for neoplasia/dysplasia
Category 2	Indefinite for neoplasia/dysplasia
Category 3	Non-invasive low grade neoplasia (low grade adenoma/dysplasia)
Category 4	Non-invasive high grade neoplasia
	4.1 High grade adenoma/dysplasia
	4.2 Non-invasive carcinoma (carcinoma in situ)*
	4.3 Suspicion of invasive carcinoma
Category 5	Invasive neoplasia
	5.1 Intramucosal carcinoma†
	5.2 Submucosal carcinoma or beyond

*Non-invasive indicates absence of evident invasion.
†Intramucosal indicates invasion into the lamina propria or muscularis mucosae.

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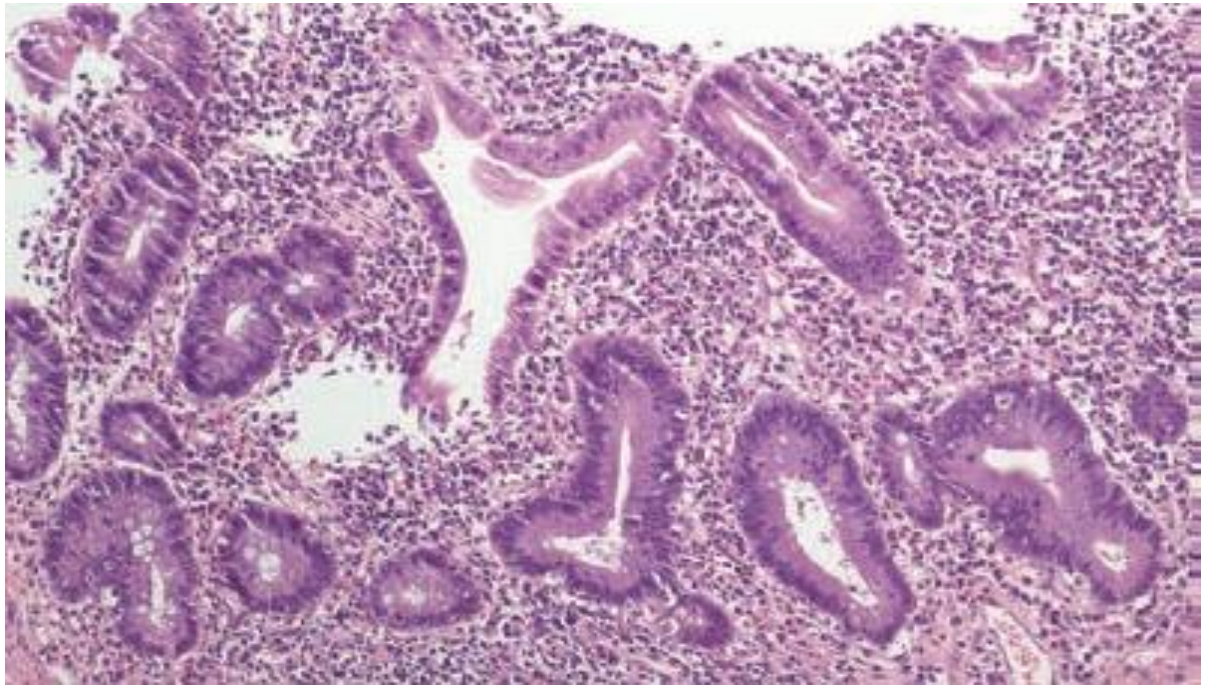
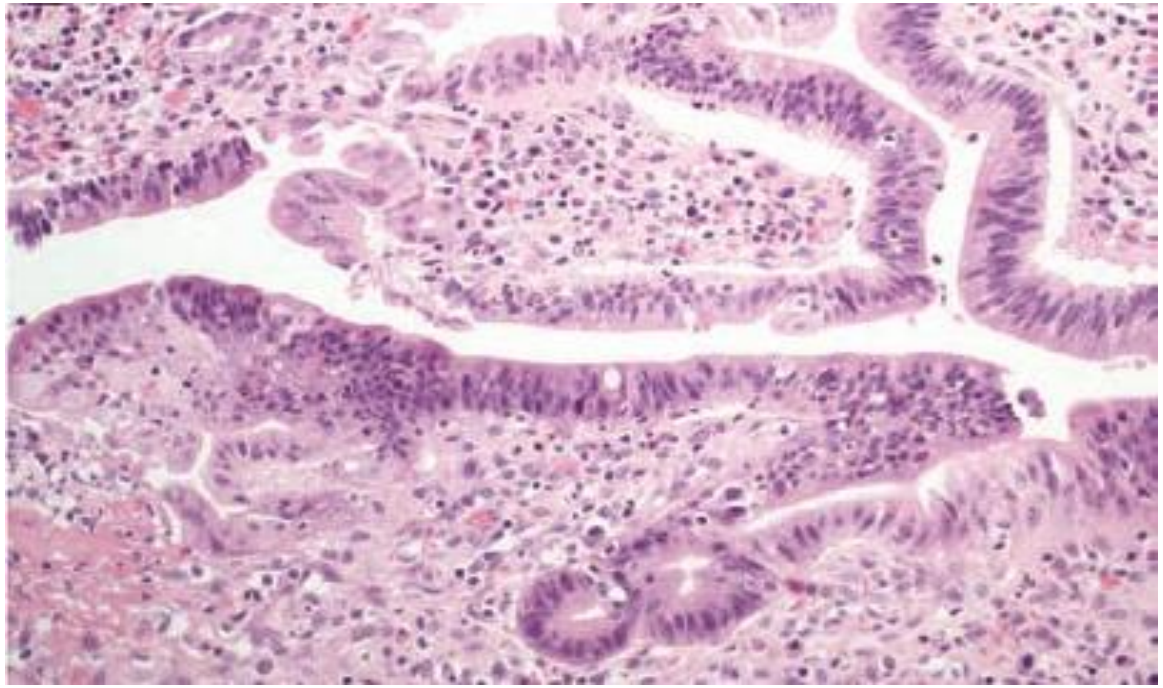
« Indefinite for dysplasia »





Biopsies « probably negative » and « probably positive » for dysplasia

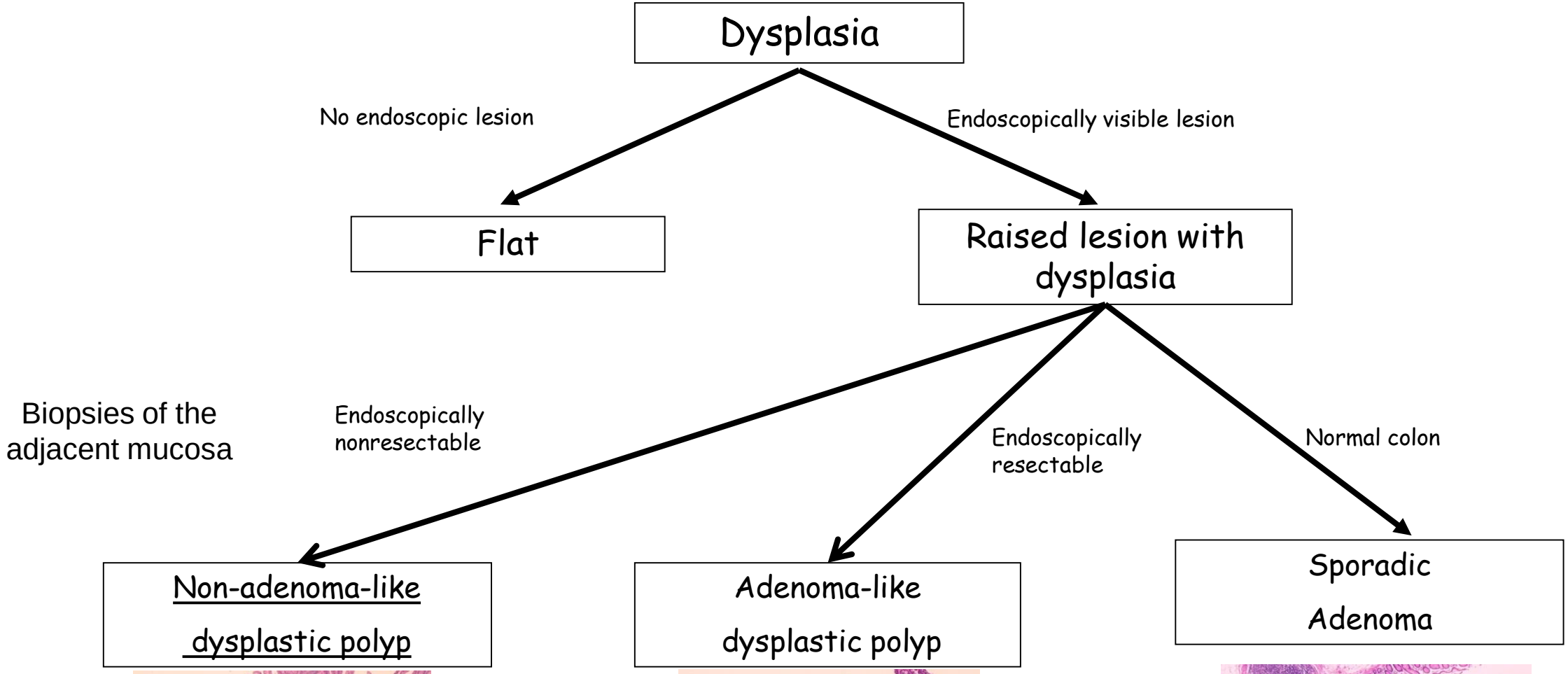
Another series of biopsies, after an increased anti-inflammatory treatment

It is important to distinguish low-grade and high-grade dysplasia

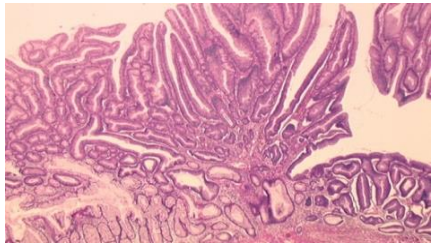
- Consequences for the management of patients
- Important inter and intra-observer variability (poor agreement for low-grade and indefinite for dysplasia)
- Confirmation of dysplasia by an independent GI pathologist is recommended (ECCO-ESP statement 17).

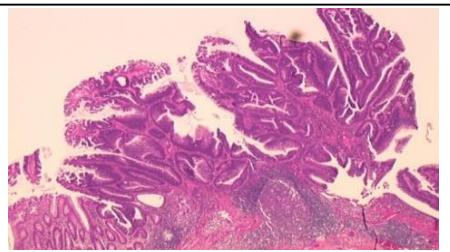
Macroscopic classification of dysplasia in IBD

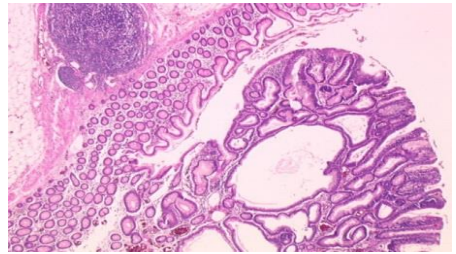
A



B







SCENIC International Consensus Statement on Surveillance and Management of Dysplasia in Inflammatory Bowel Disease

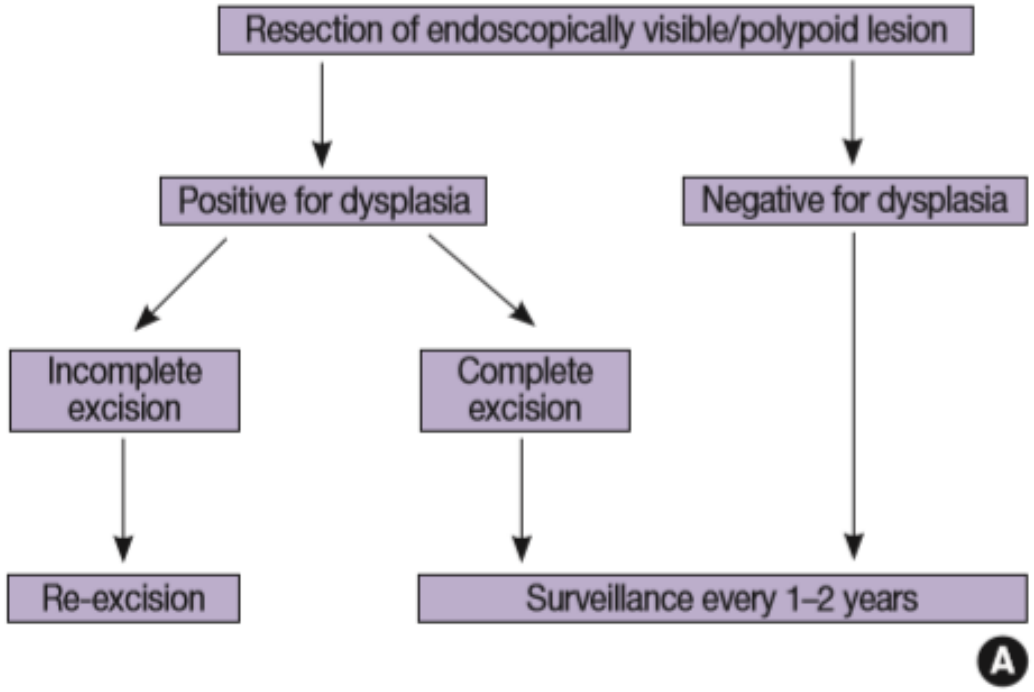
Loren Laine,[1,2] Tonya Kaltenbach,[3] Alan Barkun,[4] Kenneth R. McQuaid,[5] Venkataraman Subramanian,[6] and Roy Soetikno,[3] for the SCENIC Guideline Development Panel

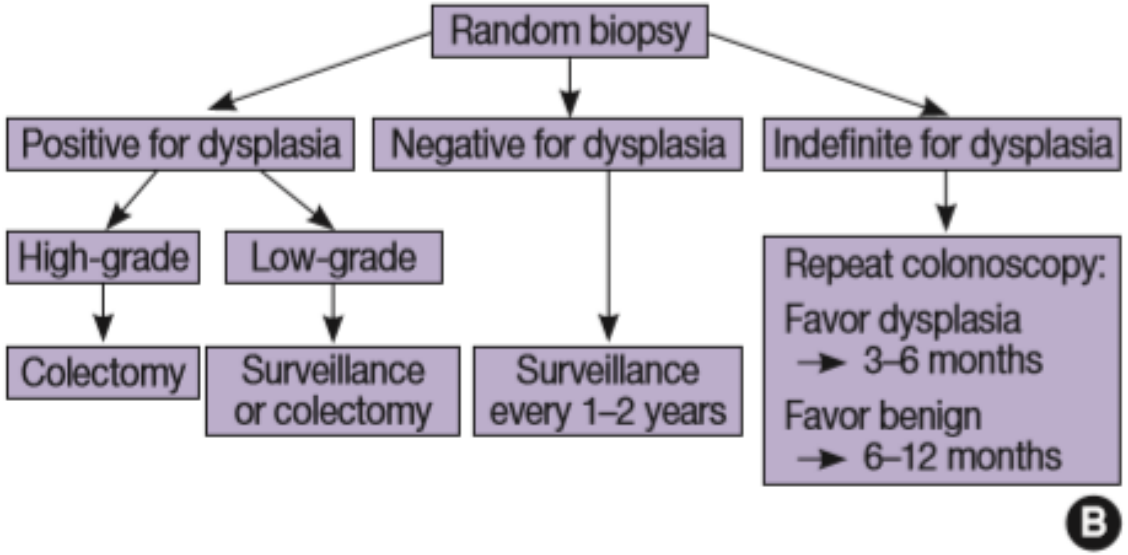
Table 2. The SCENIC consensus statement on morphologic terminology for reporting findings on colonoscopic surveillance of patients with inflammatory bowel disease .

Term	Definition
Visible dysplasia	Dysplasia identified on targeted biopsies from a lesion visualized at colonoscopy
Polypoid	Lesion protruding from the mucosa into the lumen ≥2.5 mm
Pedunculated	Lesion attached to the mucosa by a stalk
Sessile	Lesion not attached to the mucosa by a stalk: entire base is contiguous with the mucosa
Nonpolypoid	Lesion with little (<2.5 mm) or no protrusion above the mucosa
Superficial elevated	Lesion with protrusion but <2.5 mm above the lumen (less than the height of the closed cup of a biopsy forceps)
Flat	Lesion without protrusion above the mucosa
Depressed	Lesion with at least a portion depressed below the level of the mucosa
General descriptors	
Ulcerated	Ulceration (fibrinous-appearing base with depth) within the lesion
Border	
Distinct border	Lesion's border is discrete and can be distinguished from surrounding mucosa
Indistinct border	Lesion's border is not discrete and cannot be distinguished from surrounding mucosa
Invisible dysplasia	Dysplasia identified on random (non-targeted) biopsies of colon mucosa without a visible lesion

Kaltenbach et al, Gastrointestinal Edndoscopy 2017

Algorithms for management of endoscopically visible/polypoid dysplasia versus invisible/flat dysplasia in IBD patients





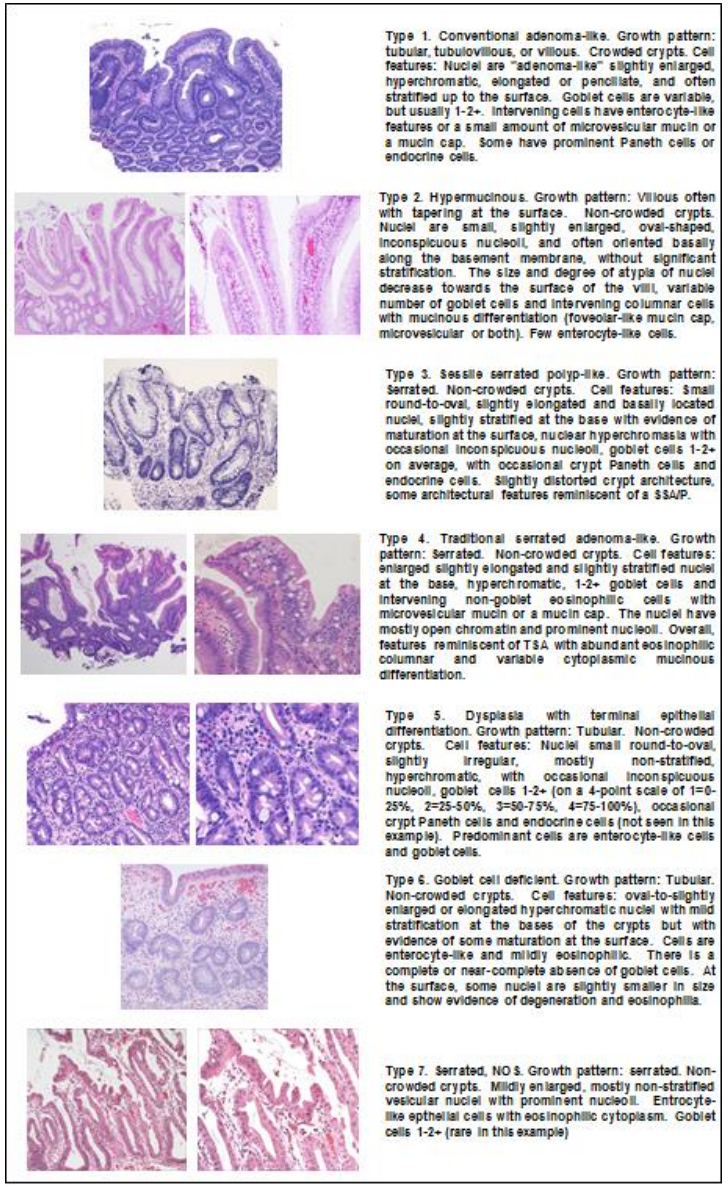
Choi et al., JPTM 2021

Non-conventional dysplastic subtypes in IBD

1. Hypermucinous dysplasia
2. Goblet cell deficient dysplasia
3. Crypt cell dysplasia (or dysplasia with terminal epithelial differentiation)
4. Dysplasia with increased Paneth cell differentiation
5. Sessile serrated lesion-like dysplasia
6. Traditional serrated adenoma-like dysplasia
7. Serrated dysplasia, not other specified

Excellent diagnostic agreement for each dysplasia category (by expert GI pathologist)

Highest diagnostic agreement for types 1, 2 and 3



Type 1. Conventional adenoma-like. Growth pattern: tubular, tubulovillous, or villous. Crowded crypts. Cell features: Nuclei are "adenoma-like" slightly enlarged, hyperchromatic, elongated or pencillate, and often stratified up to the surface. Goblet cells are variable, but usually 1-2+. Intervening cells have enterocyte-like features or a small amount of microvesicular mucin or a mucin cap. Some have prominent Paneth cells or endocrine cells.

Type 2. Hypermucinous. Growth pattern: Villous often with tapering at the surface. Non-crowded crypts. Nuclei are small, slightly enlarged, oval-shaped, inconspicuous nucleoli, and often oriented basally along the basement membrane, without significant stratification. The size and degree of atypia of nuclei decrease towards the surface of the villi, variable number of goblet cells and intervening columnar cells with mucinous differentiation (foveolar-like mucin cap, microvesicular or both). Few enterocyte-like cells.

Type 3. Sessile serrated polyp-like. Growth pattern: Serrated. Non-crowded crypts. Cell features: Small round-to-oval, slightly elongated and basally located nuclei, slightly stratified at the base with evidence of maturation at the surface, nuclear hyperchromasia with occasional inconspicuous nucleoli, goblet cells 1-2+ on average, with occasional crypt Paneth cells and endocrine cells. Slightly distorted crypt architecture, some architectural features reminiscent of a SSA/P.

Type 4. Traditional serrated adenoma-like. Growth pattern: Serrated. Non-crowded crypts. Cell features: enlarged slightly elongated and slightly stratified nuclei at the base, hyperchromatic, 1-2+ goblet cells and intervening non-goblet eosinophilic cells with microvesicular mucin or a mucin cap. The nuclei have mostly open chromatin and prominent nucleoli. Overall, features reminiscent of TSA with abundant eosinophilic columnar and variable cytoplasmic mucinous differentiation.

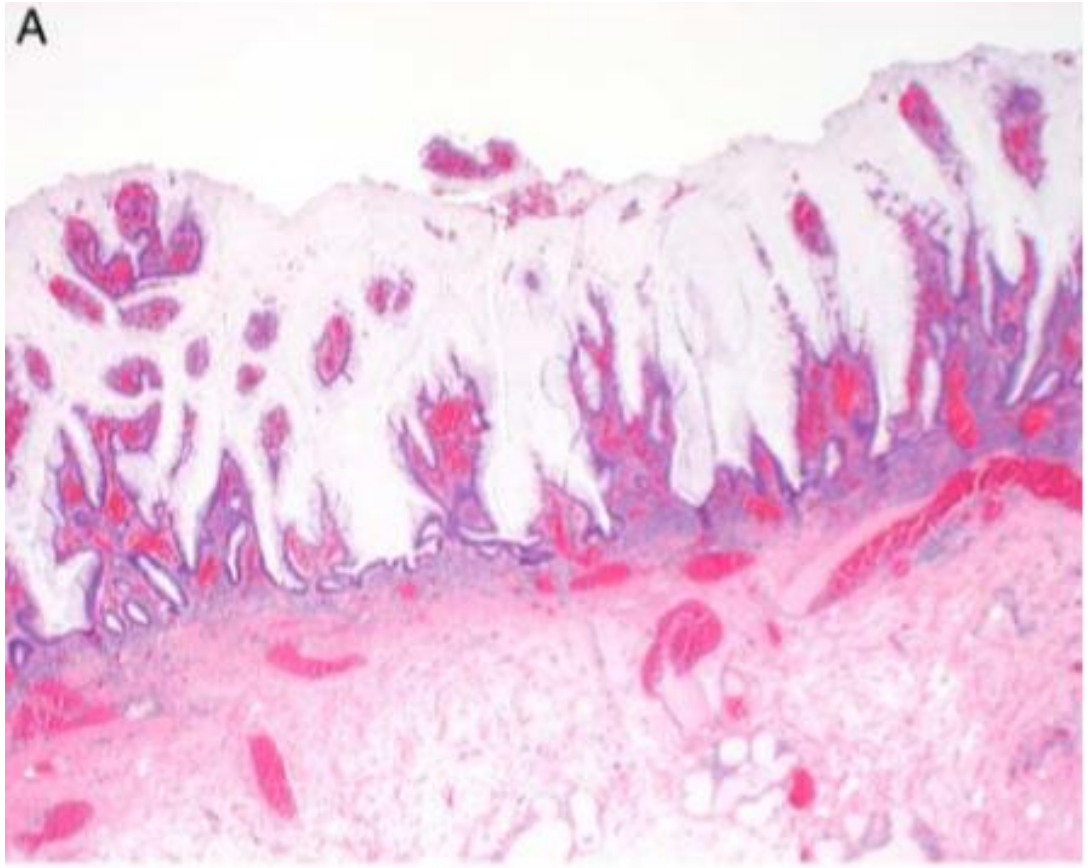
Type 5. Dysplasia with terminal epithelial differentiation. Growth pattern: Tubular. Non-crowded crypts. Cell features: Nuclei small round-to-oval, slightly irregular, mostly non-stratified, hyperchromatic, with occasional inconspicuous nucleoli, goblet cells 1-2+ (on a 4-point scale of 1=0-25%, 2=25-50%, 3=50-75%, 4=75-100%), occasional crypt Paneth cells and endocrine cells (not seen in this example). Predominant cells are enterocyte-like cells and goblet cells.

Type 6. Goblet cell deficient. Growth pattern: Tubular. Non-crowded crypts. Cell features: oval-to-slightly enlarged or elongated hyperchromatic nuclei with mild stratification at the bases of the crypts but with evidence of some maturation at the surface. Cells are enterocyte-like and mildly eosinophilic. There is a complete or near-complete absence of goblet cells. At the surface, some nuclei are slightly smaller in size and show evidence of degeneration and eosinophilia.

Type 7. Serrated, NOS. Growth pattern: serrated. Non-crowded crypts. Mildly enlarged, mostly non-stratified vesicular nuclei with prominent nucleoli. Entrocyte-like epthelial cells with eosinophilic cytoplasm. Goblet cells 1-2+ (rare in this example)

With the courtesy of Noam Harpaz

Hypermucinous dysplasia



Choi et al., Adv Anat Pathol 2021

Rare (2%); likely underdiagnosed
Long history of IBD (mean duration: 21 to 23 y) and often concurrent history of PSC (up to 29%)
UC>>CD

Large polypoid lesion (mean size: 2.1 to 2.5 cm) in the left colon (57% to 64%); flat/invisible dysplasia (42%)

May be the only dysplastic subtype identified (up to 57%

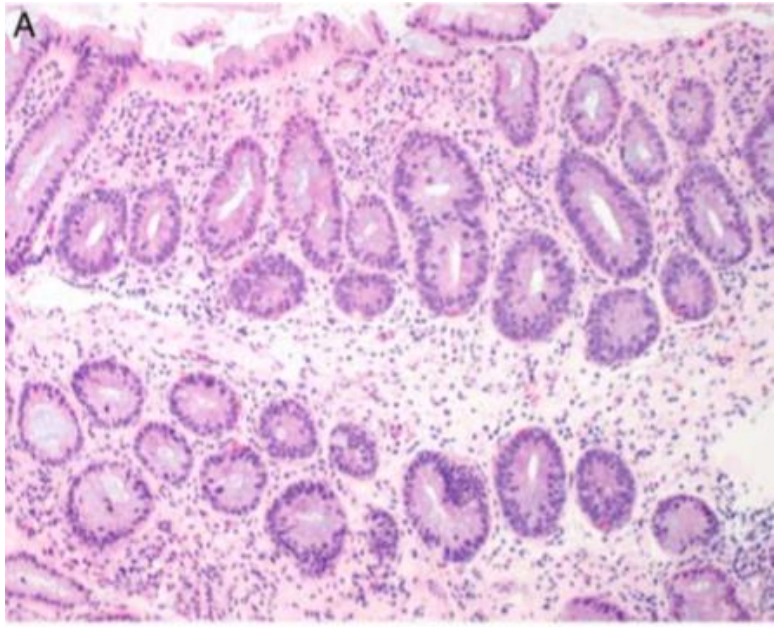
Tubulo-villous architecture++ (76%)

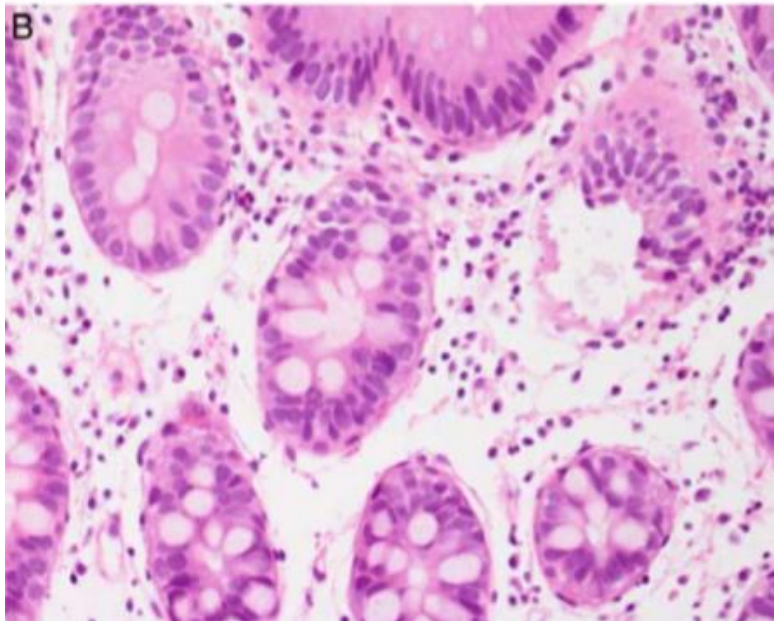
Tall, prominent mucinous cells representing >50% of the lesion; typically mild nuclear atypia, more prominent in the lower portion of crypts

Higher risk for advanced neoplasia compared with conventional dysplasia

Molecular alterations: aneuploidy, *KRAS, TP53*

Crypt cell dysplasia





Rare (4%); underrecognized entity; frequent concurrent history of PSC; UC++

Usually flat, invisible; left colon

Crowded, midly enlarged, round-to-oval or slightly elongated, nonstratified nuclei limited to the crypt base; frequent increased mitoses

No significant active inflammation or ulceration to suggest reactive changes

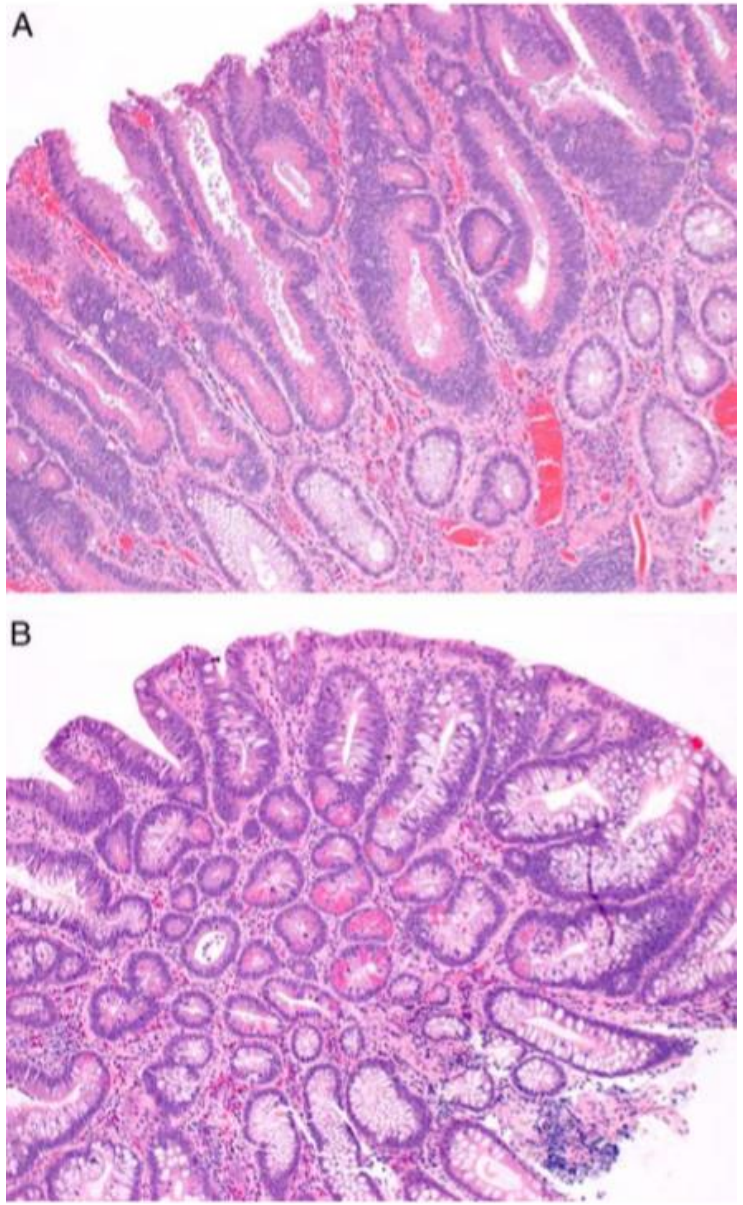
Significant interobserver variability

Aternative term « crypt cell atypia »

Higher risk for advanced neoplasia compared with conventional dysplasia

Molecular alterations: aneuploidy, *TP53, KRAS,*

Dysplasia with increased paneth cell differentiation



Common (13%); UC patients with long history of IBD; very rare concurrent history of PSC (9%)

Usually polypoid/visible

Right colon

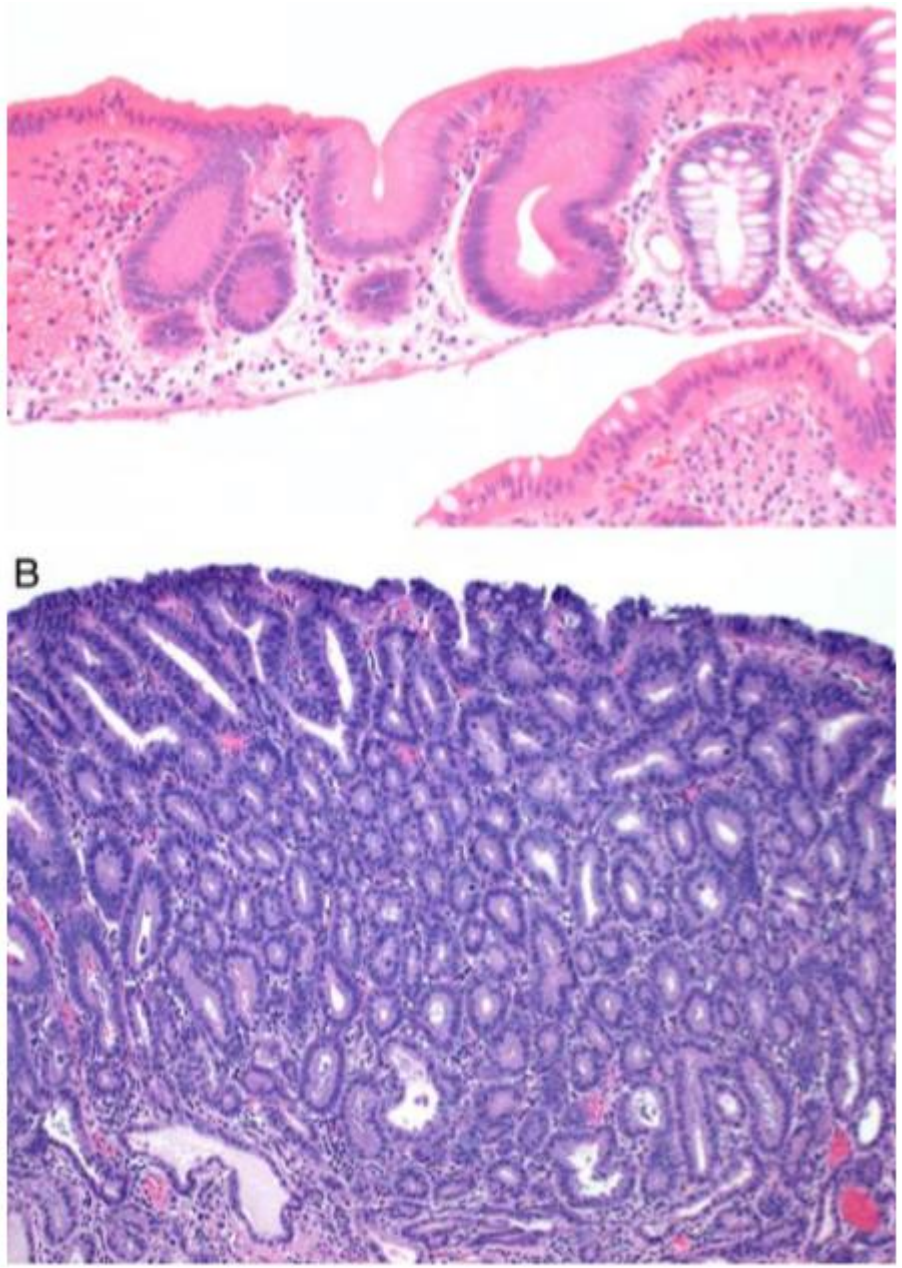
Tubular

Increased Paneth cell differentiation involving at least 2 contiguous dysplastic crypts in 2 different foci

Similar risk for advanced neoplasia compared with conventional dysplasia

Molecular alterations: aneuploidy

Goblet cell deficient dysplasia



Rare (3%); UC patients with long history of IBD; not uncommon concurrent history of PSC (up to 14%)

Often flat/invisible

Equally common in both right and left colon

Complete or near complete absence of goblet cells; tubular architecture with nuclear anomalies meeting the criteria of LGD (both crypts and surface epithelail cells)

More likely to be associated with conventional dysplasia than hypermucinous and crypt cell dysplasia

Higher risk for advanced neoplasia compared with conventional dysplasia

Molecular alterations: aneuploidy, *PIK3CA, TP53, KRAS*

Serrated lesions in IBD: a challenge

- Two considerations:
  - (i) serrated lesions that occur in the population may also occur in IBD patients.
  - (ii) IBD-associated dysplastic lesions may show serration
- Similar clinical and molecular features of IBD-associated serrated lesions with their sporadic counterpart
- The gross or endoscopic appearance (large irregular ill-defined area vs polyp/lesion), size and histology may be helpful to distinguish sporadic SL from serrated IBD-associated dysplasia

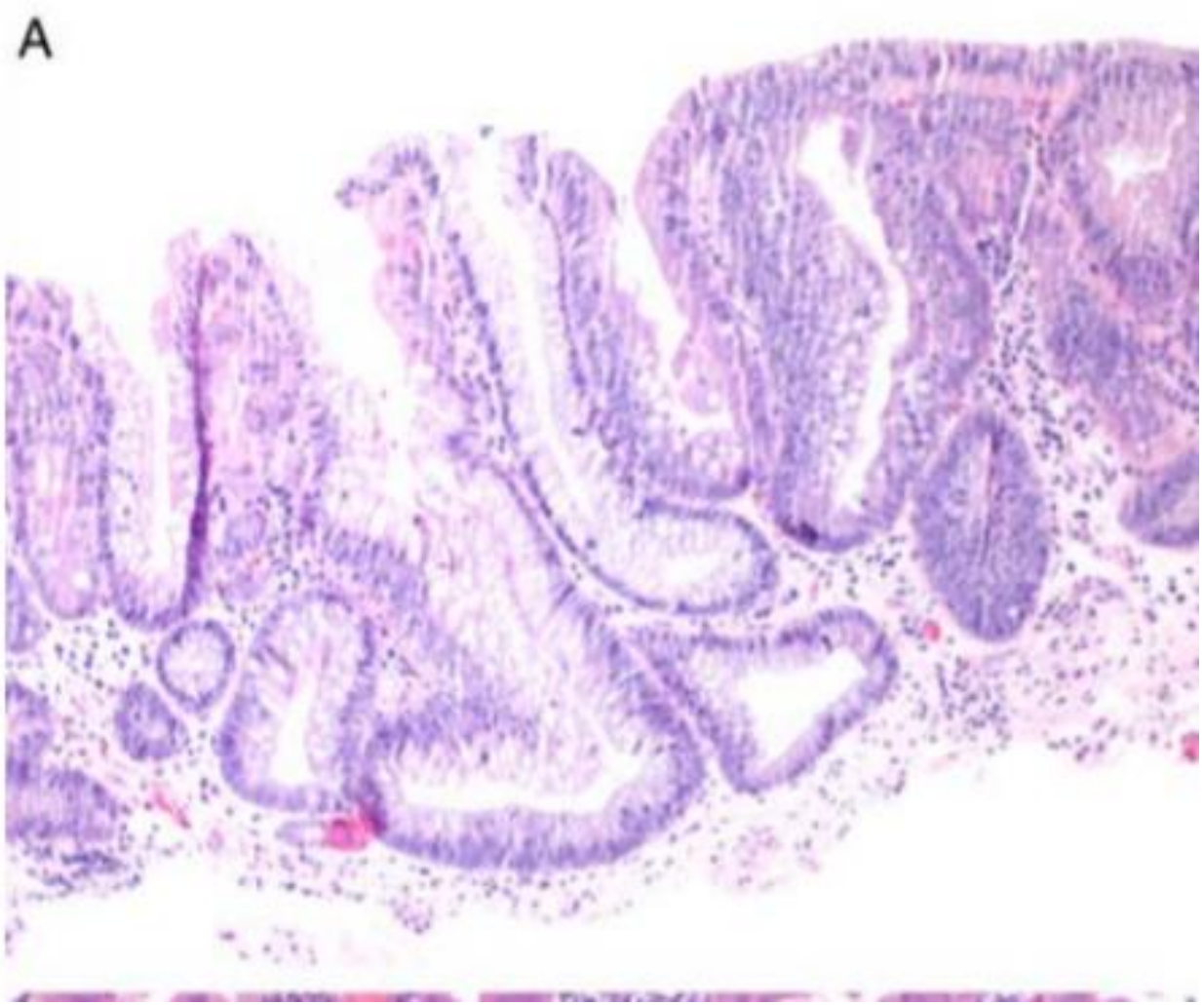
Serrated dysplasia

TABLE 1. Morphologic, Clinicopathologic, and Molecular Features of Nonconventional Dysplastic Subtypes

	Hypermucinous Dysplasia	Crypt Cell Dysplasia	Dysplasia With Increased Paneth Cell Differentiation	Goblet Cell Deficient Dysplasia	Sessile Serrated Lesion-like Dysplasia	Traditional Serrated Adenoma-like Dysplasia	Serrated Dysplasia, Not Otherwise Specified
Characteristic morphologic features	Tall, prominent mucinous cells with typically mild nuclear atypia	Crowded, mildly enlarged, round-to-oval or slightly elongated, nonstratified nuclei limited to the crypt base	Increased Paneth cell differentiation involving at least 2 contiguous dysplastic crypts in 2 different foci	Complete or near-complete absence of goblet cells	Dilatation and/or lateral spread of the crypt base (ie, dilated L-shaped or inverted T-shaped crypts)	Ectopic crypts and intensely eosinophilic cytoplasm	Complex serrated profile without definite features of sessile serrated lesion-like dysplasia or traditional serrated adenoma-like dysplasia
Incidence (% of all dysplastic lesions)	Rare (2%)	Rare (4%)	Common (13%)	Rare (3%)	Rare (1%)	Rare (1%)	Rare (< 1%)
Most common location	Left colon	Left colon	Right colon	Equally common in both right and left colon	Right colon	Left colon	Unknown
Association with PSC	Common	Common	Rare	Not uncommon	Rare	Rare	Unknown
Endoscopic appearance	Often polypoid/visible	Usually flat/invisible	Usually polypoid/visible	Often flat/ invisible	Usually polypoid/ visible	Usually polypoid/ visible	Usually polypoid/visible
Mean size (cm)	2.1-2.5	Not applicable	1.0	1.7-1.9 (when visible)	1.2	1.2	Unknown
Most common histologic architecture	Tubulovillous/villous	Flat	Tubular	Tubular	Tubular	Tubulovillous/ villous	Unknown
Risk for advanced neoplasia compared with conventional dysplasia	Higher	Higher	Similar	Higher	Similar	Similar	Unknown
Molecular alterations	Aneuploidy, *KRAS*, *TP53*	Aneuploidy, *TP53*, *KRAS*	Aneuploidy	Aneuploidy, *PIK3CA*, *TP53*, *KRAS*	*TP53*, *BRAF*	Aneuploidy, *KRAS*, *BRAF*	Unknown

Choi et al., Adv Anat Pathol 2021

Sessile serrated lesion-like dysplasia



Sessile Serrated Lesion-like Dysplasia	Traditional Serrated Adenoma-like Dysplasia	Serrated Dysplasia, Not Otherwise Specified
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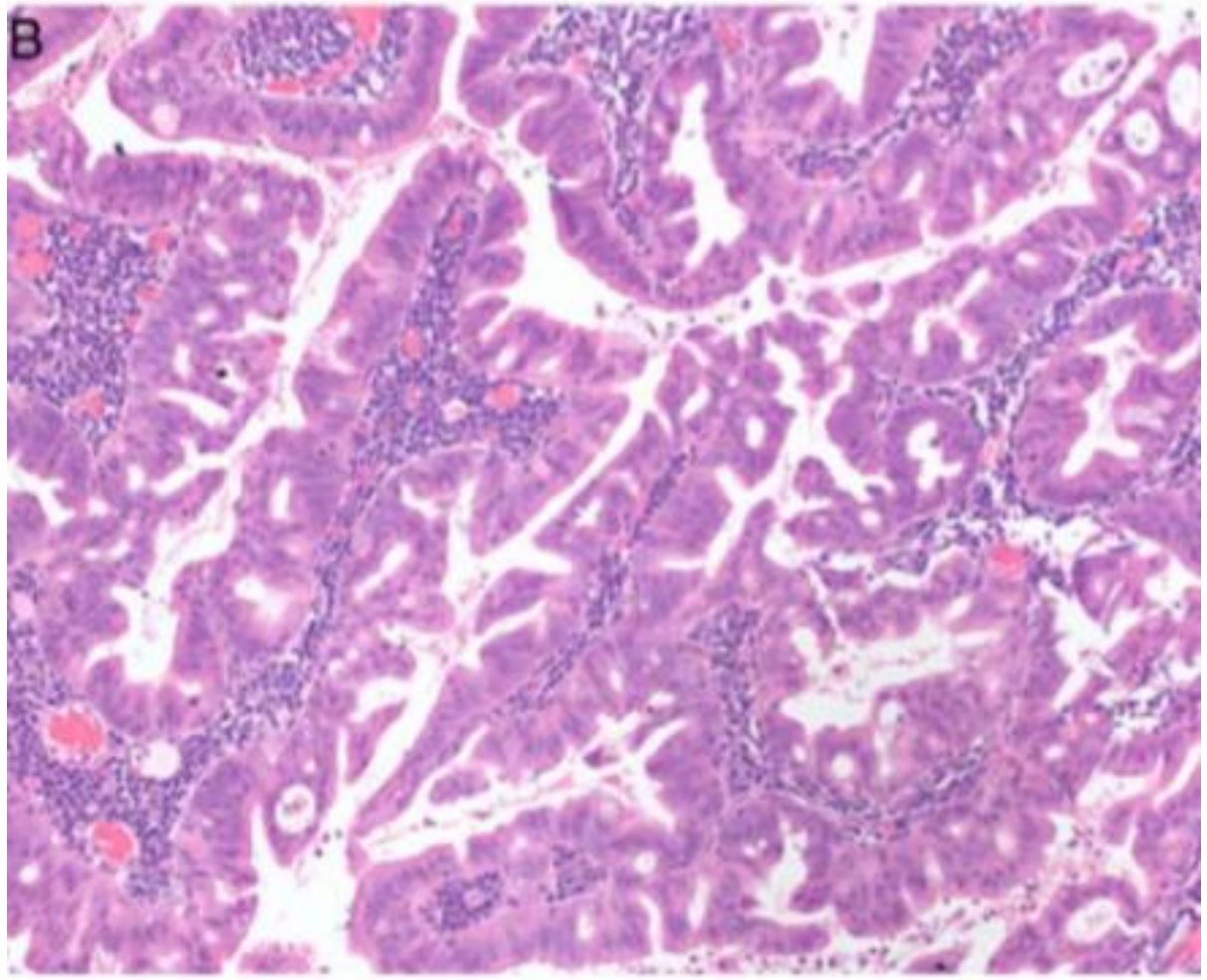
Rare (1%)	Rare (1%)	Rare (< 1%)
Right colon	Left colon	Unknown
Rare Usually polypoid/ visible 1.2	Rare Usually polypoid/ visible 1.2	Unknown Usually polypoid/visible Unknown
Tubular	Tubulovillous/ villous	Unknown
Similar	Similar	Unknown
TP53, *BRAF*	Aneuploidy, *KRAS*, *BRAF*	Unknown

Choi et al., Adv Anat Pathol 2021

Traditional serrated adenoma-like dysplasia



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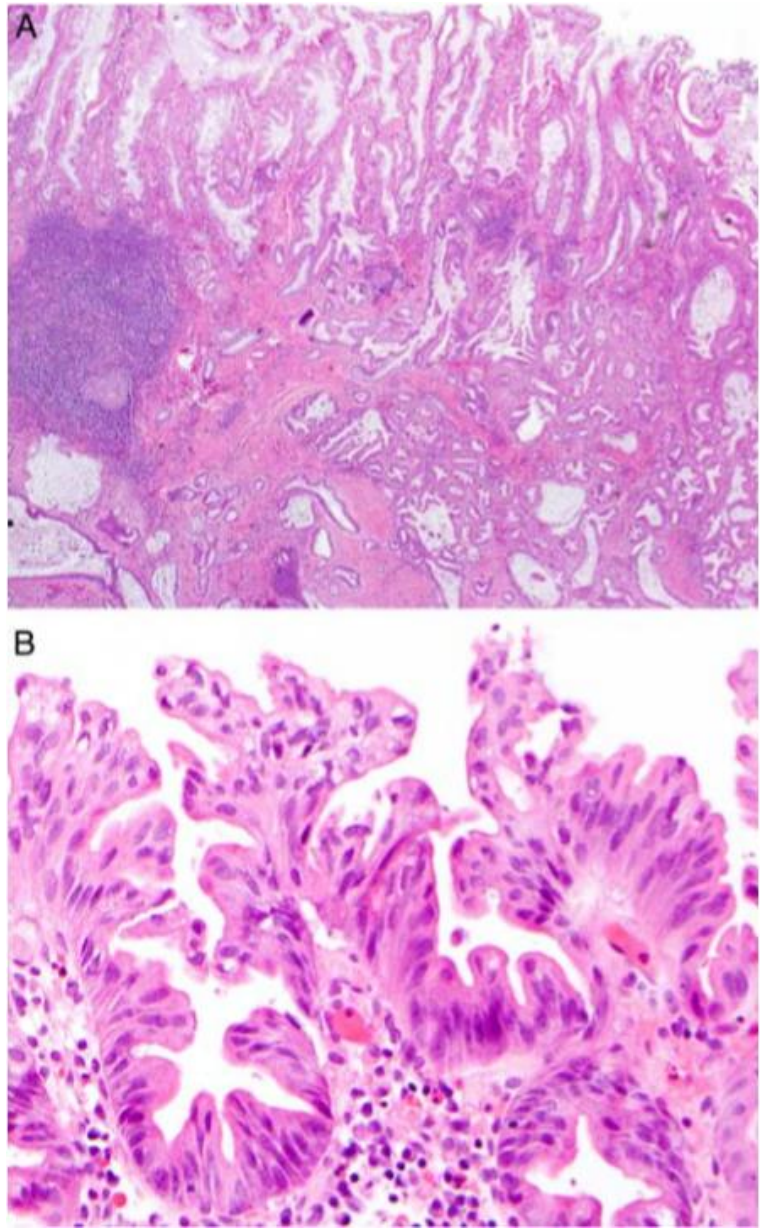
Right colon	Left colon	Unknown
Rare Usually polypoid/ visible	Rare Usually polypoid/ visible	Unknown Usually polypoid/visible
1.2	1.2	Unknown
Tubular	Tubulovillous/ villous	Unknown
Similar	Similar	Unknown
TP53, *BRAF*	Aneuploidy, *KRAS*, *BRAF*	Unknown

Choi et al., Adv Anat Pathol 2021

Serrated dysplasia, not otherwise specified



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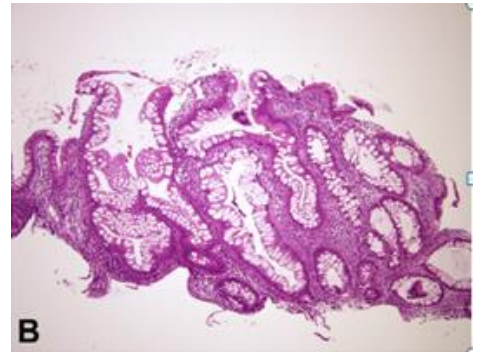
Right colon	Left colon	Unknown
Rare Usually polypoid/ visible	Rare Usually polypoid/ visible	Unknown Usually polypoid/visible
1.2	1.2	Unknown
Tubular	Tubulovillous/ villous	Unknown
Similar	Similar	Unknown
TP53, *BRAF*	Aneuploidy, *KRAS*, *BRAF*	Unknown

Choi et al., Adv Anat Pathol 2021

Serrated epithelial changes (SEC)



- SEC (serrated epithelial changes) is a histologic finding in longstanding colitis.
- SEC: synonymous with hyperplastic-like mucosal change and flat serrated change
- Histologically: glands with distorted architecture and by crypts which are no longer perpendicular to the muscularis mucosae and which do not necessarily reach the muscularis mucosae. Serration of the epithelium and enlarged goblet cells both extend to the base of the crypts.
- SEC is not a widely recognized histopathologic finding and does not have WHO criteria
- Unclear clinical significance in the development of dysplasia in IBD patients

Non-conventional mucosal lesions (serrated epithelial change, villous hypermucinous change) are frequent in patients with inflammatory bowel disease—results of molecular and immunohistochemical single institutional study

Surgical specimens and/or endoscopical biopsy samples of IBD patients during a 10-year period

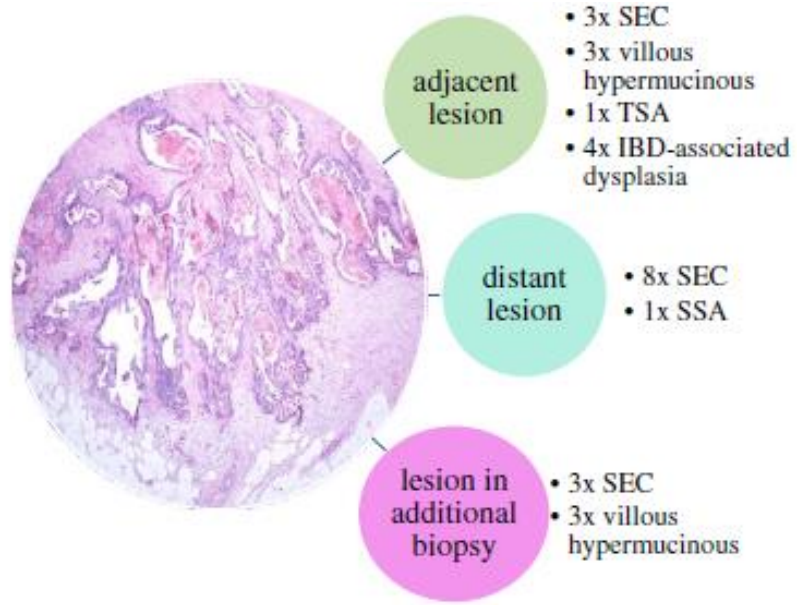
Table 3 Immunohistochemical and molecular characteristics of lesions from all groups (groups 1–3)

	Serrated epithelial change *N* = 41 (100%, $)	Villous hypermucinous change *N* = 6 (100%, $)	Combined serrated and villous lesions *N* = 5 (100%, $)	HP-like lesions *N* = 4 (100%, $)	All PPLs *N* = 56 ($ 100%)	Hyperplastic poly N = 6 (100%)	Sessile serrated adenoma N = 7 (100%)	Traditional serrated adenoma *N* = 2 (100%)	IBD-associated dysplasia N = 6 (100%)	IBD-associated CRC *N* = 11 (100%)
IHC results										
MGMT loss	17 (41%, $ 30%)	4 (67%, $ 7.1%)	2 (40%, $ 3.6%)	2 (50%, $ 3.5%)	25 ($ 44.6%)	2 (33.3%)	7 (100%)	2 (100%)	2 (33.3%)	6 (54.5%)
p53 aberrant expression (complex and basal)	14 (26.9%, $ 19.7%)	2 (33.3%, $ 3.6%)	1 (20%, $ 1.8%)	1 (25%, $ 1.8%)	18 ($ 32.1%)	1 (16.6%)	1 (14.2%)	2 (100%)	3 (50%)	6 (54.5%)
MLH1 loss	0	1 (16.6%, $ 1.8%)	0	0	1	0	0	0	0	0
Molecular results										
KRAS/NRAS mutated	17 (41.5%, $ 30.6%)	2 (33.3%, $ 3.6%)	4 (80%, $ 7.1%)	1 (25%, $ 1.8%)	24 ($ 42.9%)	3 (50%)	4 (57.1%)	2 (100%)	4 (66.6%)	8 (72.7%)
BRAF mutated*	6 (15%, $ 10.7%)	2 (33.3%, $ 3.6%)	0	1 (25%, $ 1.8%)	9 (16.4%, $16.1-%) *	4 (66.6%)	4 (57.1%)	0	0	1 (9.1%)
Concurrent *KRAS(NRAS)* and *BRAF* mutation	3 (7.3%, $ 5.3%)	0	0	0	3 ($ 5.3%)	2 (33.3%)	2 (28.6%)	0	0	0

CRC, colorectal carcinoma; *IBD*, inflammatory bowel disease; *HP*, hyperplastic polyp; *IHC*, immunohistochemistry; *PPLs*, putative precursor lesions

$Percentage of cases counted from all PPLs

*$p = 0.017$ comparing difference between KRAS and BRAF mutations in PPLs



SEC: 46.6% of cases (most common non-conventional mucosal lesion)
SEC: loss of MGMT expression (41%), aberrant P53 expression and KRAS mutation (41.5%)
Association with invasive carcinoma (with same KRAS or BRAF mutation)

Possible neoplastic potential?

The emerging role of histologic disease activity assessment in UC

The emerging role of histologic disease activity assessment in UC

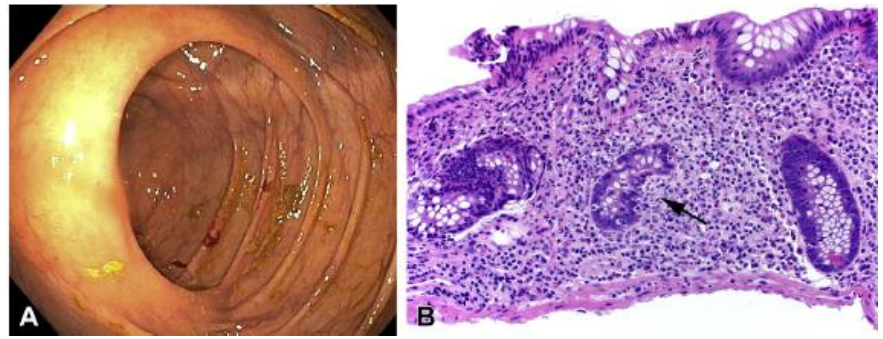
« Mucosal healing » (absence or near absence of macroscopic lesions in the GI mucosa) : treatment target associated with improved long-term outcomes

However, the presence of an apparently healthy mucosa at colonoscopy does not exclude the presence of longstanding microscopic inflammation.

histological remission, an important therapeutic endpoint for UC.

Geboes Score (GS), Robarts Histopathology Index (RHI) and Nancy Index (NH)

Development of numerous scoring systems, not all formally validated



Pai et al., Gastrointestinal Endoscopy 2018

Main histological scoring systems used in UC

Key features
Separately evaluates multiple aspects of mucosal injury
Subscore 0: Architectural changes
0.0: No abnormality
0.1: Mild abnormality
0.2: Mild or moderate diffuse or multifocal abnormalities
0.3: Severe diffuse or multifocal abnormalities
Subscore 1: Chronic inflammatory infiltrate (1.1-1.3)
1.0: No increase
1.1: Mild but unequivocal increase
1.2: Moderate increase
1.3: Marked increase
Subscore 2A: Eosinophils in lamina propria (2A.1-2A.3)
2A.0: No increase
2A.1: Mild but unequivocal increase
2A.2: Moderate increase
2A.3: Marked increase
Subscore 2B: Neutrophils in lamina propria (2B.1-2B.3)
2B.0: No increase
2B.1: Mild but unequivocal increase
2B.2: Moderate increase
2B.3: Marked increase
Subscore 3: Neutrophils in epithelium (3.0-3.3)
3.0: None
3.1: <5% crypts involved
3.2: 5%-50% crypts involved
3.3: >50% crypts involved
Subscore 4: Crypt destruction (4.0-4.3)
4.0: None
4.1: Probable—local excess of neutrophils in part of crypt
4.2: Probable—marked attenuation
4.3: Unequivocal crypt destruction
Subscore 5: Surface epithelial injury (5.0-5.4)
5.0: No erosion, ulceration, or granulation tissue
5.1: Recovering epithelium plus adjacent inflammation
5.2: Probable erosion—focally stripped
5.3: Unequivocal erosion
5.4: Ulcer or granulation tissue

Geboes score (2001):

The most commonly used histological index in UC

Not formally validated

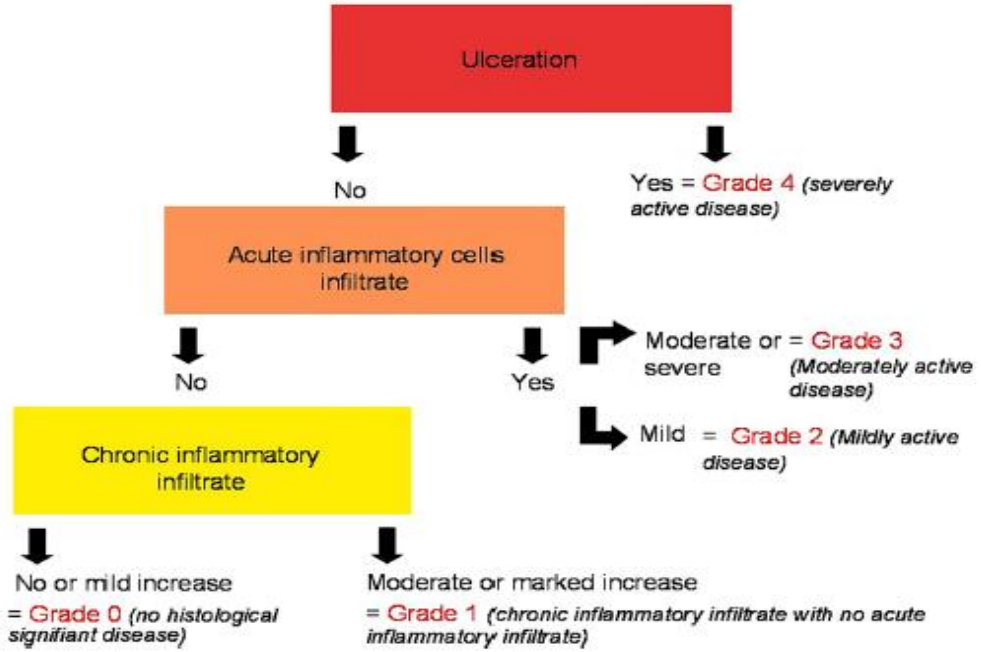
But good reproducibility after interobserver agreement analyses

Progressive classification system based on the existence of six major grades, and subdivision of each grade into four categories

Recent development of a simplified version of this score (Jauregui-Amezaga et al., JCC 2017)

Main histological scoring systems used in UC

The Nancy Index (NI)



Bressenot et al., Gut 2015

The main advantages: its practicality, high intraobserver and interobserver reliability and responsiveness to change

The Robarts Histopathologic Index (RHI)

Based on the Geboes Score; measures items that correlate with histologic severity, are reproducible, and respond to therapy; calculated score that ranges from 0 to 33
RHI = 1 × chronic inflammatory cell infiltrate (0-3) + 2 × lamina propria neutrophils (0-3) + 3 × neutrophils in epithelium (0-3) + 5 × erosions

The main advantages: This histological index has been reported to be reproducible, responsive and valid.

ECCO Position Paper: Harmonisation of the approach to Ulcerative Colitis Histopathology

Fernando Magro,[a,b,c] Glen Doherty[d], Laurent Peyrin-Biroulet[e,f], Magali Svrcek[g], Paula Borralho[h], Alissa Walsh[i], Fatima Carneiro[j,k], Francesca Rosini[l], Gert de Hertogh[m], Luc Biedermann[n], Lieven Pouillon[o], Michael Scharl[n], Monika Tripathi[p], Silvio Danese[q,r], Vincenzo Villanacci[s], Roger Feakins[t]

Magro et al., JCC 2020

- **Specific objectives :**

(i) to standardise the approach to the assessment of histological activity in UC

(ii) to specify which inflammatory cells require assessment

(iii) to define which structural changes (epithelium and/or lamina propria) are important

(iv) to define minimum requirements for histological response, remission and improvement

(v) to recommend the best histological scoring systems

Histological procedures (1) : the pathology report should include all the acute and chronic features of UC

ECCO Histology Position 2.7

The pathology report should mention several histological features that may assist with the assessment of overall severity: [i] neutrophils in the lamina propria, in the surface epithelium, in the crypt epithelium [cryptitis] and within the lumen of crypts [crypt abscesses]; [ii] basal plasmacytosis; [iii] lamina propria chronic inflammatory cell density; [iv] eosinophils in the lamina propria; [v] erosions; [vi] ulcers; [vii] crypt architectural distortion; [viii] crypt atrophy; and [ix] mucin depletion. [Evidence Level 2]—**Agreement 100%**

Histological procedures (2) : eliminating mucosal neutrophils and ulceration/erosion should be the minimum requirement for histological remission

ECCO Histology Position 2.8

Neutrophils are not normally present within the lamina propria or epithelium. [Evidence Level 3]—**Agreement 94%**

ECCO Histology Position 2.9

Histological activity is defined by neutrophil infiltration of epithelium and/or lamina propria. [Evidence Level 3]—**Agreement 100%**

Histological scores (1)

Section 3—Histological Scores

ECCO Histology Position 3.1

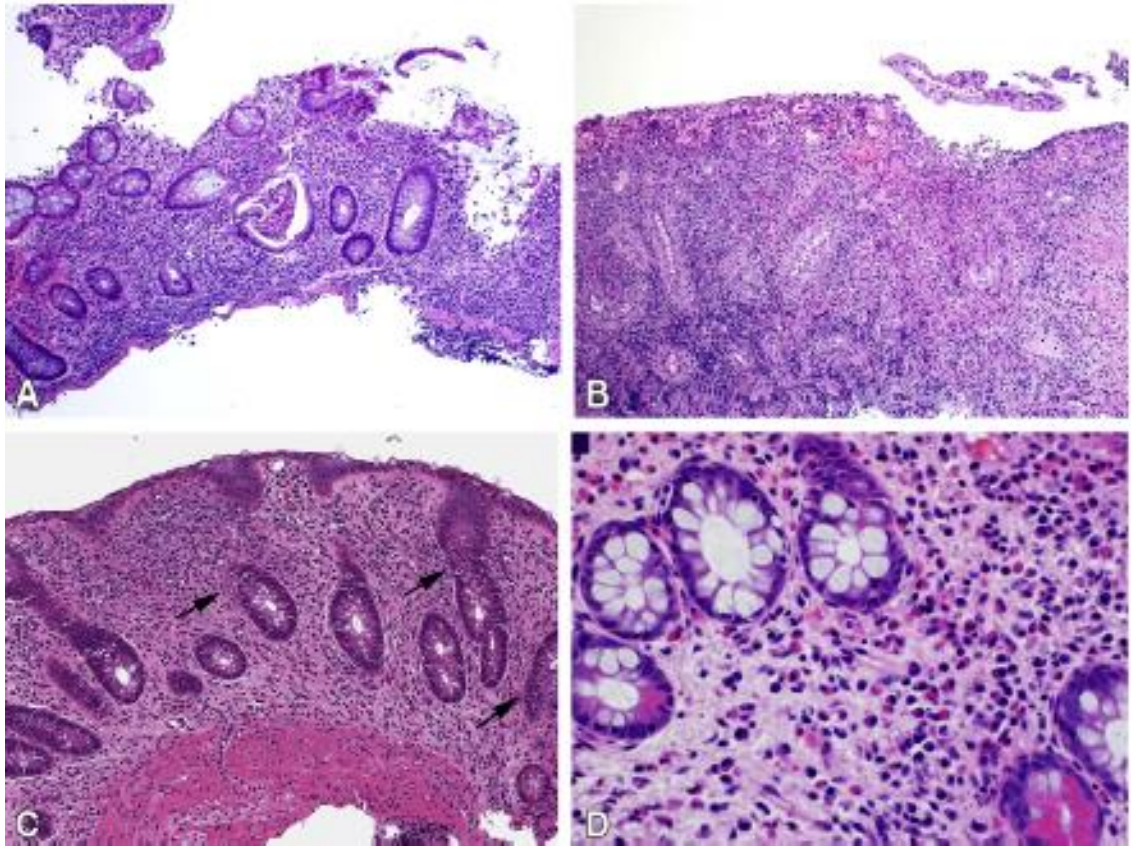
Several scoring systems are available for the assessment of histological inflammation/activity in ulcerative colitis. Direct comparisons are often not possible because criteria for inflammation and activity are inconsistent and study designs are different. [Evidence Level 3]—**Agreement 86%**

ECCO Histology Position 3.2

Only two scores for histological inflammation in ulcerative colitis are fully validated [Robarts histopathology index and Nancy index] and have been cross-validated against one another and against the Geboes score and faecal calprotectin. Geboes score is only partially [not formally] validated but widely used. [Evidence Level 2]—**Agreement 100%**

ECCO Histology Position 3.3

Most scoring systems for ulcerative colitis histology include mucosal architecture, mononuclear cell infiltrate [this is sometimes defined as including eosinophils] and neutrophils [in the lamina propria, in the epithelium, with epithelial damage: cryptitis—crypt abscesses—erosions—ulceration]. [Evidence Level 2]—**Agreement 86%**



Pai et al., Gastrointestinal Endoscopy 2018

Histological scores (2) : histological remission

ECCO Histology Position 3.4

The strictest definition of histological remission is return to normal. [Evidence Level 3]—**Agreement 83%**

ECCO Histology Position 3.5

Definitions of histological remission of the mucosa in ulcerative colitis following treatment include: histological normalization; absence of inflammation; absence of neutrophils/erosion/ulceration; absence of intra-epithelial neutrophils/erosion/ulceration; Robarts histopathology index ≤ 3; Nancy index = 0; Geboes ≤ 2.0. [Evidence Level 3]—**Agreement 85%**

Several definitions of histological remission or histological mucosal healing

In clinical pratice, histopathologists should provide a description of activity and/or use a recognised scoring system, instead of using the word « healing » or « remission »

Histological scores (3) : which score should be used?

ECCO Histology Position 3.6

For randomized control trials in ulcerative colitis, use of the Robarts histopathology index or Nancy index is recommended, as these systems are validated. [Evidence Level 2]—**Agreement 80%**

ECCO Histology Position 3.7

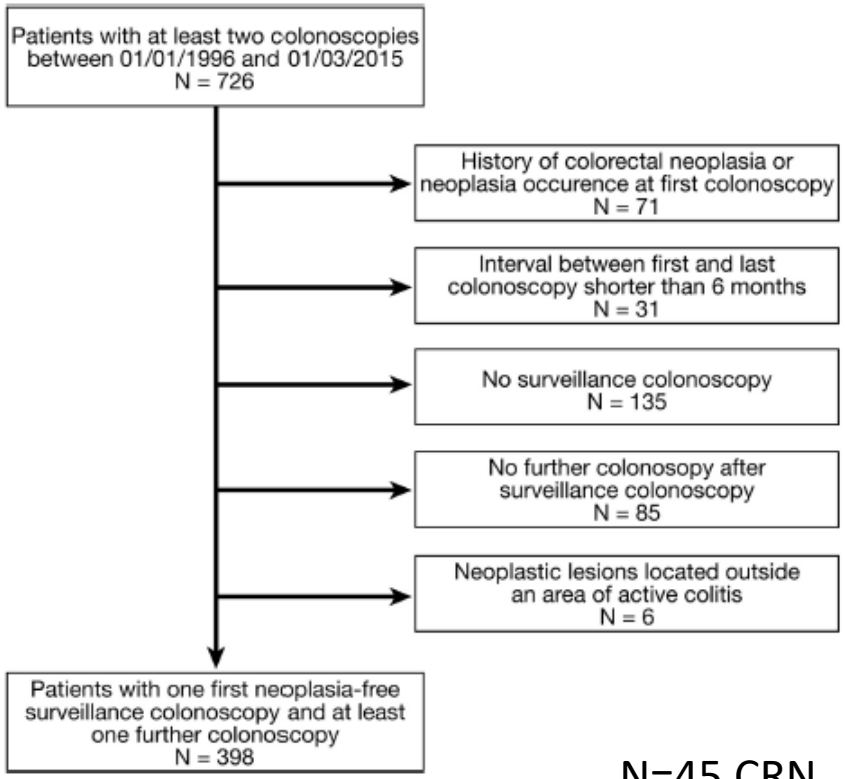
For observational studies or in clinical practice, use of an easy to apply and validated score for ulcerative colitis histology, such as the Nancy index, is recommended. [Evidence Level 5]—**Agreement 100%**

Nancy Index Scores of Chronic Inflammatory Bowel Disease Activity Associate With Development of Colorectal Neoplasia

Julien Kirchgesner,[*,‡] Magali Svrcek,[§] Guillaume Le Gall,[*] Cécilia Landman,[*] Xavier Dray,[*] Anne Bourrier,[*] Isabelle Nion-Larmurier,[*] Nadia Hoyeau,[§] Harry Sokol,[*,‖] Philippe Seksik,[*,‖] Jacques Cosnes,[*] Jean-François Fléjou,[§] and Laurent Beaugerie,[*,‡] for the Saint-Antoine Inflammatory Bowel Disease Network

Clinical Gastroenterology and Hepatology 2020;18:150–157

Aim: To assess the impact of histologic and endoscopic disease activity on the risk for a first CRN in IBD patients after a surveillance colonoscopy negative for dysplasia (assessment of the proper interval between surveillance colonoscopies, stratification of the risk)



y popula-

N=45 CRN

Table 3. Risk Factors of Colorectal Neoplasia: Multivariate Analysis

	Odds ratio (95% CI)	P
Histologic variables		
Mean Nancy histologic index[a]	1.69 (1.29–2.21)	<.001
Age[b,c]	1.04 (1.01–1.07)	.003
Male sex	1.27 (0.64–2.52)	.49
IBD phenotype, UC	1.73 (0.86–3.51)	.13
Primary sclerosing cholangitis	2.65 (1.06–6.61)	.04
Current treatment during >6 mo before neoplasia or end of follow-up period		
Thiopurines	0.55 (0.25–1.21)	.14
Endoscopic variables		
Colonic strictures	2.37 (0.84–6.75)	.11

OR per 1 unit increase

Endoscopic and histologic predictors

	Inflammatory bowel disease	
	Odds ratio (95% CI)	P
Histologic variables		
Mean Nancy histologic index[a]	1.69 (1.29–2.21)	<.001
Maximum Nancy histologic index[a]	1.30 (1.03–1.64)	.03
Endoscopic variables		
Endoscopic ulcerations		
On >50% of colonoscopies	1.24 (0.53–2.91)	.62
On at least 1 colonoscopy	1.75 (0.89–3.44)	.11

The cumulative assessment of histologic disease based on the Nancy histologic index should be included in the risk-stratification strategy for CRN screening in IBD.

Manuscript Doi: 10.1093/ecco-jcc/jjac006

ECCO Position on harmonization of Crohn's disease mucosal histopathology

Statement 10. Neutrophils are not normally present within the lamina propria or epithelium of the intestinal mucosa [EL-3].

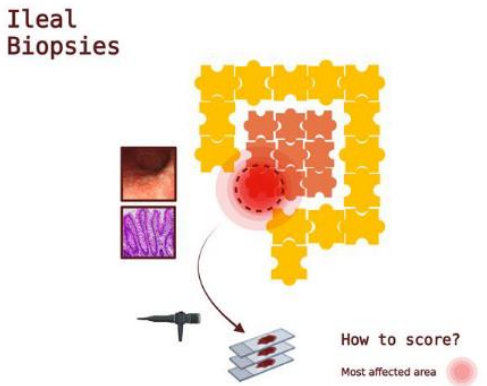
Statement 11. Histological activity in Crohn's disease [CD] is defined by neutrophilic inflammation of the epithelium, lamina propria, or both. The absence of neutrophilic inflammation is an appropriate histological target [EL-3].

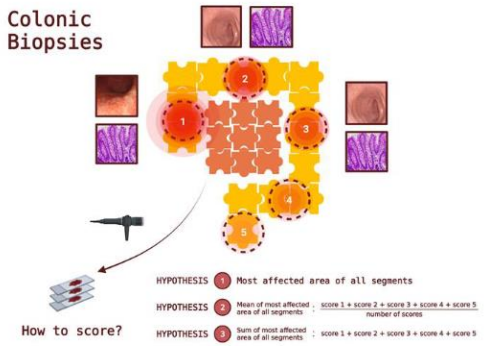
Statement 12. Basal plasmacytosis, mucosal eosinophils, and granulomas are not recommended as markers of histological activity or histological remission in Crohn's disease [CD] [EL-4].

Statement 13. Eosinophils should not be used as a marker of histological activity for Crohn's disease [CD] due to the lack of reproducibility between pathologists and lack of supportive data [EL-4].

Statement 16. Histological healing in the intestine varies with the distribution of disease activity in Crohn's disease [CD] [EL-3].

Statement 17. In Crohn's disease [CD], it is appropriate to score the ileum and colon separately given that patients may present with differential involvement [EL-2].





Statement 21. Histological scoring systems for ulcerative colitis [UC], including the Geboes Score, Robarts Histopathology Index [RHI], and Nancy Histological Index, can be used for scoring intestinal biopsies from Crohn's disease [CD] patients [EL-4].

Statement 22. The Nancy Histological Index can be used for Crohn's disease [CD] biopsies in clinical practice [EL-5].