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Basic Endoscopic Findings — Normal and Pathological Findings

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Abstract

Since its inception, colonoscopy has evolved to become the cornerstone for colorectal imaging. The increasing indications for endoscopic evaluation and potential therapeutic intervention parallels technological advances and the expanding diagnostic and therapeutic capabilities of colonoscopy. The diagnostic and therapeutic yield of colonoscopy is highly user dependent. Thus, it is essential for the clinical endoscopist to perform a thorough endoscopic evaluation and be cognizant of normal and pathologic findings. This review details normal and pathologic endoscopic findings in a variety of disease states that are often encountered by the clinical endoscopist including colon polyps, inflammatory bowel disease, and infectious and non-infectious colitides. In addition, we review the diagnostic and therapeutic role of colonoscopy in the evaluation of an acute lower gastrointestinal bleed.

Keywords: Polyp, pseudopolyp, hyperplastic polyp, adenoma, tubular adenoma, tubulovillous adenoma, sessile adenoma, sessile serrated adenoma, colitis, diverticulosis, hemorrhoids, anal fissure

1. Introduction

The advent of retrograde colonoscopy in June 1969 revolutionized the field of gastroenterology [1]. It has since evolved to become the gold standard for colorectal imaging [2, 3].

As technology continues to advance, so too does the diagnostic utility and therapeutic capabilities of colonoscopy. Thus, it becomes imperative for the clinical endoscopist to perform a thorough colonoscopic evaluation and be cognizant of normal and pathologic findings as indications for colonoscopy expand. Here, we detail normal and pathologic endoscopic findings in a variety of disease states that are often encountered by the clinical endoscopist

including colon polyps, inflammatory bowel disease (IBD), and infectious and non-infectious colitides. In addition, we review the diagnostic and therapeutic role of colonoscopy in the evaluation of an acute lower gastrointestinal bleed.

2. Polyps and potential progression to colorectal cancer

Colorectal cancer is the third most common cancer among men and women, and the third leading cause of cancer-related death in the United States [4]. It is estimated that in 2014, 71,830 men and 65,000 women were diagnosed with colorectal cancer with approximately 50,000 mortalities (26,270 men and 24,040 women) as a result of the disease. Globally, colorectal cancer is the fourth leading cause of cancer-related death accounting for approximately 700,000 deaths in 2012 [5]. The vast majority of colorectal cancers stem from benign polyps arising from the mucosal layer. Winawer et al. were among the first to demonstrate that colorectal adenomas have the potential to progress to colorectal adenocarcinoma, thus stressing the importance of colonoscopic polypectomy in colorectal cancer prevention [6]. Subsequent long term data has validated the importance of colonoscopy and colonoscopic polypectomy in the prevention of colorectal cancer-related deaths [7]. To date, colonoscopy remains the cornerstone in colorectal cancer prevention. Unfortunately, the “miss rate” of colonoscopy for colorectal cancer and adenomas larger than 1 cm has been reported to be as high as 6% [8] and 17% [9, 10], respectively.

Adenomas and hamartomatous polyps, later discussed in depth, are polyps that carry malignant potential. They are indolent in nature, typically growing slowly over the span of a decade or more. There is a direct correlation between the size of the adenoma and its risk of developing future advanced adenomas or carcinoma with studies demonstrating this risk to be as high as 7.7% [11], 15.9% [11], and 19.3% [12], for adenomas <5mm, 5–20mm, and >20mm, respectively.

Chromosomal instability and common point mutations occurring in colorectal cancer-related tumor suppressor genes (e.g., APC, P53) or tumor promoter genes (e.g., K-Ras) architect the progression from benign polyps to colorectal cancer. Figure 1 depicts key point mutations and its impact on morphologic changes of a benign polyp to colorectal cancer. There is, however, considerable genetic and epigenetic heterogeneity resulting in different pathways to tumorigenesis [13]. Luo et al. sought to evaluate the effect of these alterations on the progression to colorectal cancer by conducting genome-wide array-based studies and comprehensive data analysis of aberrantly methylated loci in normal colon tissue (n=41), colon adenomas (n=42), and colorectal cancer (n=64) [14]. They identified three classes of cancers and two classes of adenomas, high-frequency methylation and low-frequency methylation based on their DNA methylation patterns. Mutant K-Ras was found in a subset of high-frequency methylated adenomas. In addition, they found the methylation signatures of high-frequency methylation adenomas to be similar to those of cancer with low or intermediate levels of methylation, and low-frequency methylation adenomas to have methylation signatures similar to that of normal colon tissue. These findings demonstrated genome-wide alterations in DNA methylation to

occur during the early stages of progression of adenomas to colorectal cancer, and the presence of heterogeneity in tumorigenesis, even at the adenoma step of the process.

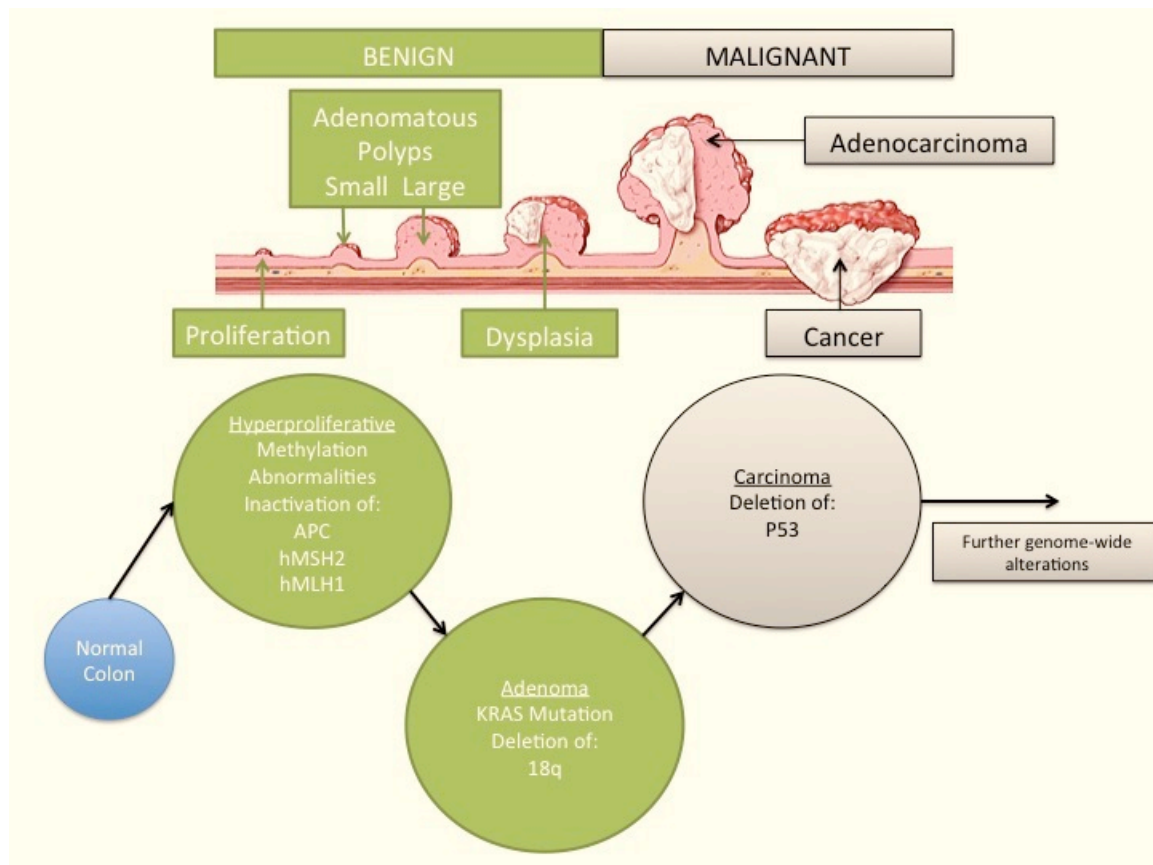


Figure 1. Key point mutations and its impact on morphologic changes of a benign polyp to colorectal cancer.

3. Polyps and pseudopolyps

In 2003, the Paris Endoscopic Classification arose to describe polyp morphology [15], which can potentially guide the endoscopist toward its malignancy potential [16–18]. Figure 2 provides a schematic overview of the Paris Endoscopic Classification and Figure 3 provides an endoscopic view of differing polyp morphology under traditional white-light colonoscopy. A recent study by van Doorn et al. evaluated the interobserver agreement for the Paris Endoscopic Classification among seven expert endoscopists [19]. The seven expert endoscopists assessed 85 endoscopic video clips depicting polyps. Afterwards, they underwent a digital training module and then assessed the same 85 polyps again. A calculated Fleiss kappa of 0.42 and a mean pairwise agreement of 67% suggested moderate interobserver agreement among the seven experts. In addition, the proportion of lesions labeled as “flat” lesions ranged between 13–40% ($p < 0.001$). The interobserver agreement did not change significantly after the digital training module, which led the investigators to conclude there to be only moderate

interobserver agreement among experts for this classification system and that use of this classification system in daily practice is questionable and unsuitable for comparative endoscopist research. Thus, the need for a simplified classification system is necessary to better aid the clinical endoscopist.

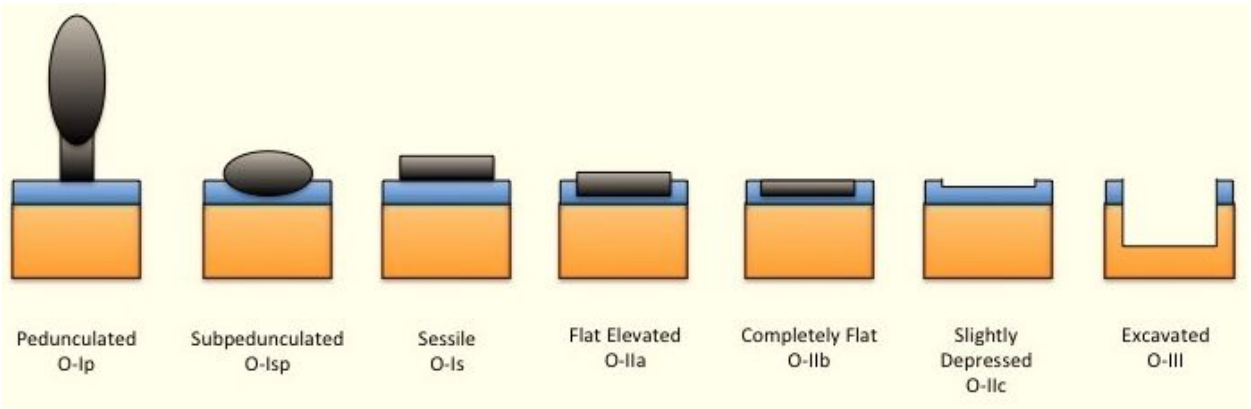


Figure 2. The Paris Classification based on polyp appearance.

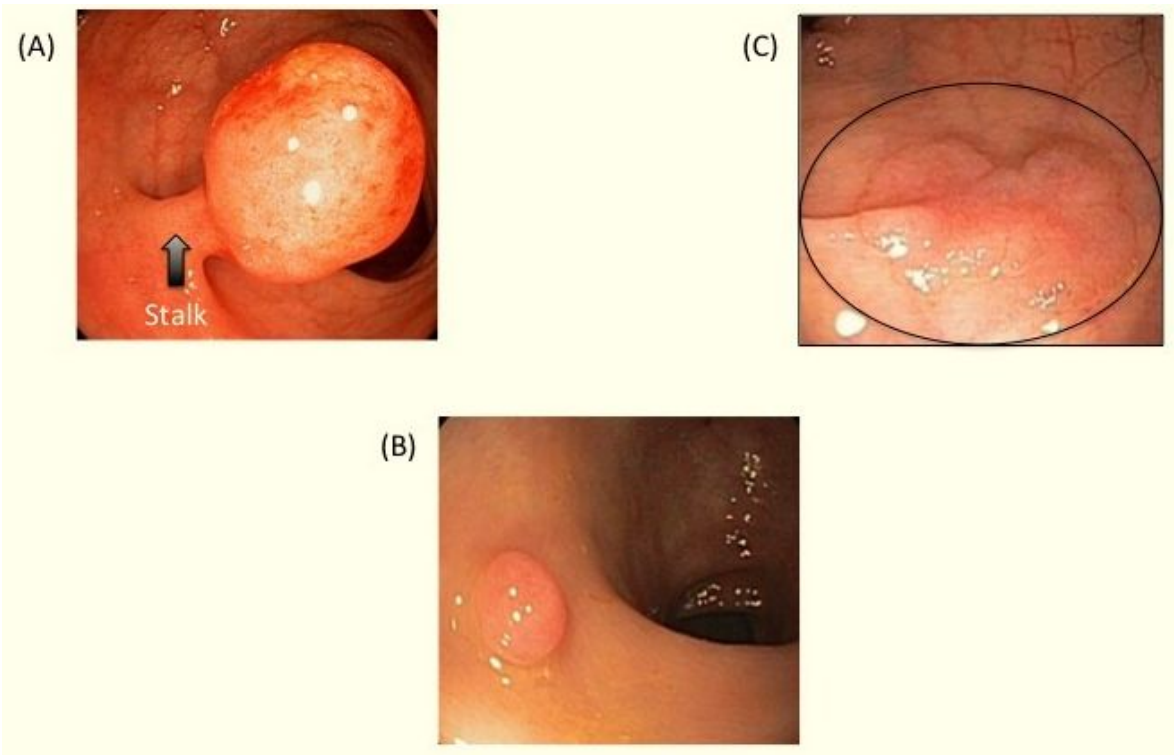


Figure 3. Endoscopic views of differing polyp morphology under traditional white-light colonoscopy: (A) Pedunculated polyp, (B) Sessile polyp, (C) Flat polyp.

In addition to traditional white-light colonoscopy, several studies have demonstrated the utility of narrow-band-imaging (NBI) to be useful in adenoma detection [20–23]. Under NBI,

adenomas appear to have thicker and higher volumes of microvasculature compared to normal mucosa and hyperplastic polyps, resulting in distinct pit patterns that may increase diagnostic yield [23]. This section will review the morphology and histology, malignant potential, and provide endoscopic and pathologic depictions of different polyp subtypes.

3.1. Adenomas

Adenomatous polyps by definition are dysplastic and thus carry malignant potential. They can further be characterized as being an advanced adenoma, synchronous adenoma, or metachronous adenoma. An advanced adenoma is defined as an adenoma with high-grade dysplasia, an adenoma with a size >10 mm, an adenoma with significant villous components (>25%), or an adenoma with evidence of invasive carcinoma [24]. Synchronous adenomas are polyps that are diagnosed at the same time as an index colorectal cancer and metachronous adenomas are ones diagnosed at least six months before or after the diagnosis of an index colorectal cancer [25]. The diagnosis of synchronous and metachronous adenomas are of utmost importance as it can potentially identify individuals at risk for hereditary conditions, thus impacting therapeutic intervention and screening intervals for relatives [26].

3.1.1. Tubular, villous, and tubulovillous adenomas

Adenomas are characterized as tubular, villous, or tubulovillous (a mixture of the two) based on their glandular architecture. Tubular adenomas, which account for the vast majority of colon adenomas, are characterized by a network of branching adenomatous epithelium and a tubular component of >75% [16]. Figure 4 depicts a histologic representation of a tubular adenoma in the background of normal colon tissue. Villous adenomas, which account for up to 15% of adenomas, are characterized by long glands that extend straight down to the center of the polyp from its surface with a villous component of >75% [16]. Figure 5 depicts a histologic representation of a villous adenoma in the background of normal colon tissue. Lastly, tubulovillous adenomas, which account for up to 15% of adenomas, are a mixture of the two previous adenomas with a villous component of anywhere from 26–75%. Figure 6 depicts a histologic representation of a tubulovillous adenoma in the background of normal colon tissue.

The CpG island methylator phenotype (CIMP) pathway is composed of methylated promoter regions of multiple putative tumor suppressor genes occurring in colorectal cancer and also in adenomatous polyps [27]. Kakar et al. examined villous/tubulovillous adenomas (n=32) and tubular adenomas (n=30) for *BRAF*/K-Ras mutations and CIMP-status (characterized by methylation of three or more loci at hMLH1, p16, HIC1, RASSF2, MGMT, MINT1, and MINT31) [28]. They found 44% of villous/tubulovillous to be CIMP-positive compared with 27% of tubular adenomas (p=0.08). In addition, villous/tubulovillous adenomas demonstrated significantly higher methylation rates at MGMT (87% vs. 37%; p<0.01) and RASSF2 (94% vs. 70%; p=0.02) when compared to tubular adenomas. Lastly, CIMP-positive adenomas correlated with increased size, right-sided location, and increased villous component in villous/tubulovillous adenomas. This led the authors to conclude that CIMP status is indicative of size, location, and malignant potential, and that methylation of MGMT and RASSF2 increases as adenomas progress from tubular adenomas to villous/tubulovillous adenomas.

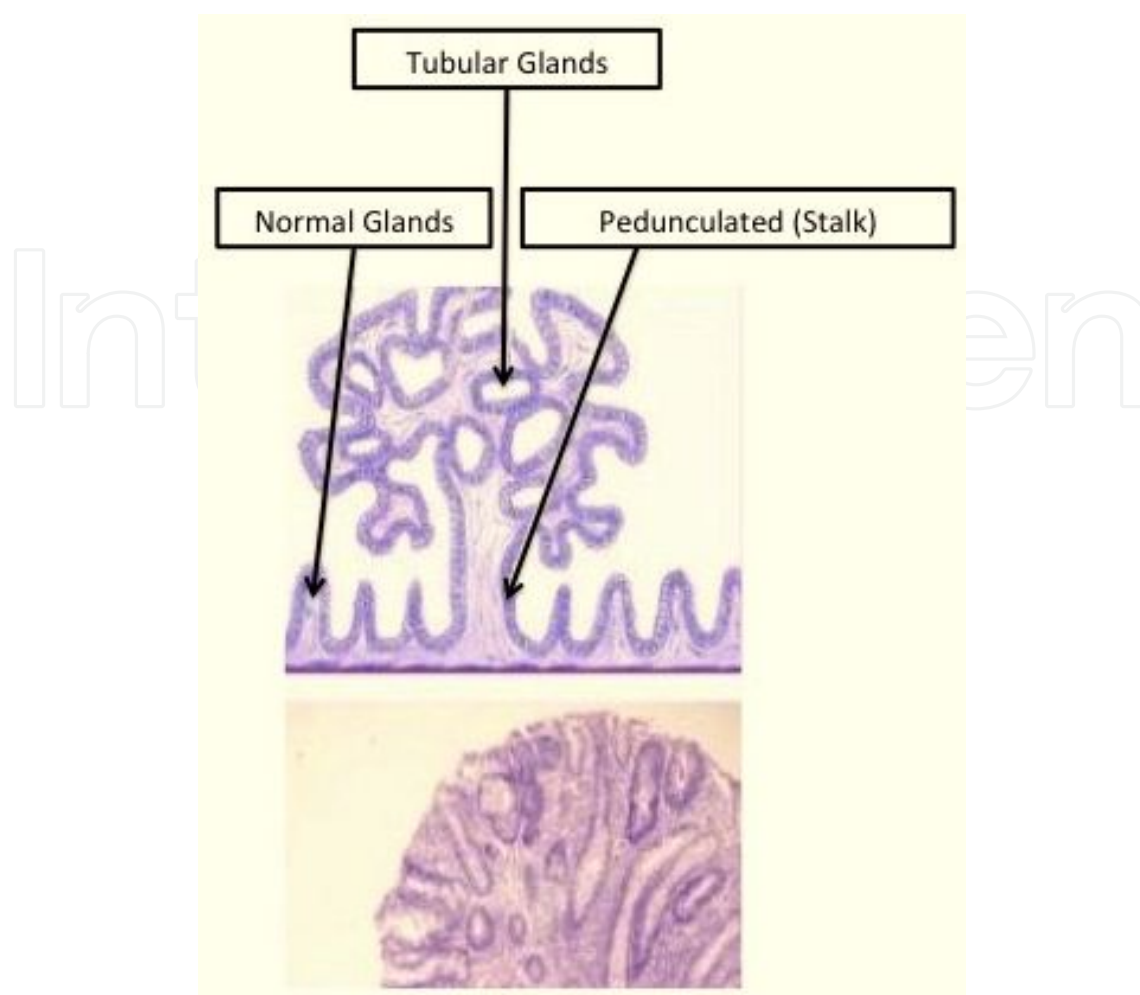


Figure 4. Histologic representation of tubular adenoma in the background of normal colon tissue.

3.1.2. Sessile serrated adenomas, traditional serrated adenomas, and hyperplastic polyps

Serrated lesions account for approximately 30% of colorectal cancers, arising via the serrated neoplasia pathway characterized by widespread DNA methylation and *BRAF* mutations [29]. They are classified histologically as sessile serrated adenomas/polyps (SSA/Ps), traditional serrated adenomas (TSAs), or hyperplastic polyps, with only SSA/Ps and TSAs carrying malignant potential [30]. SSA/Ps typically lack classic dysplasia, however, those that demonstrate foci of classic histologic dysplasia and molecular profiles exhibiting methylation of DNA repair genes (e.g., *MLH-1*) are thought to be precursor lesions to sporadic unstable microsatellite (MSI-H) cancers. SSA/Ps also exhibit activation of the *BRAF* oncogene, a feature seen in many sporadic MSI-H cancers [31]. Figure 7 depicts two potential molecular pathways of serrated neoplasia.

SSA/Ps tend to be more prominent in the proximal colon [32] as compared with TSAs [33] and hyperplastic polyps [34], which tend to be more prominent in the rectosigmoid. Thus, expert recommendations are to completely remove all serrated lesions proximal to the sigmoid colon and all serrated lesions in the rectosigmoid >5mm [30]. They may be more difficult to detect

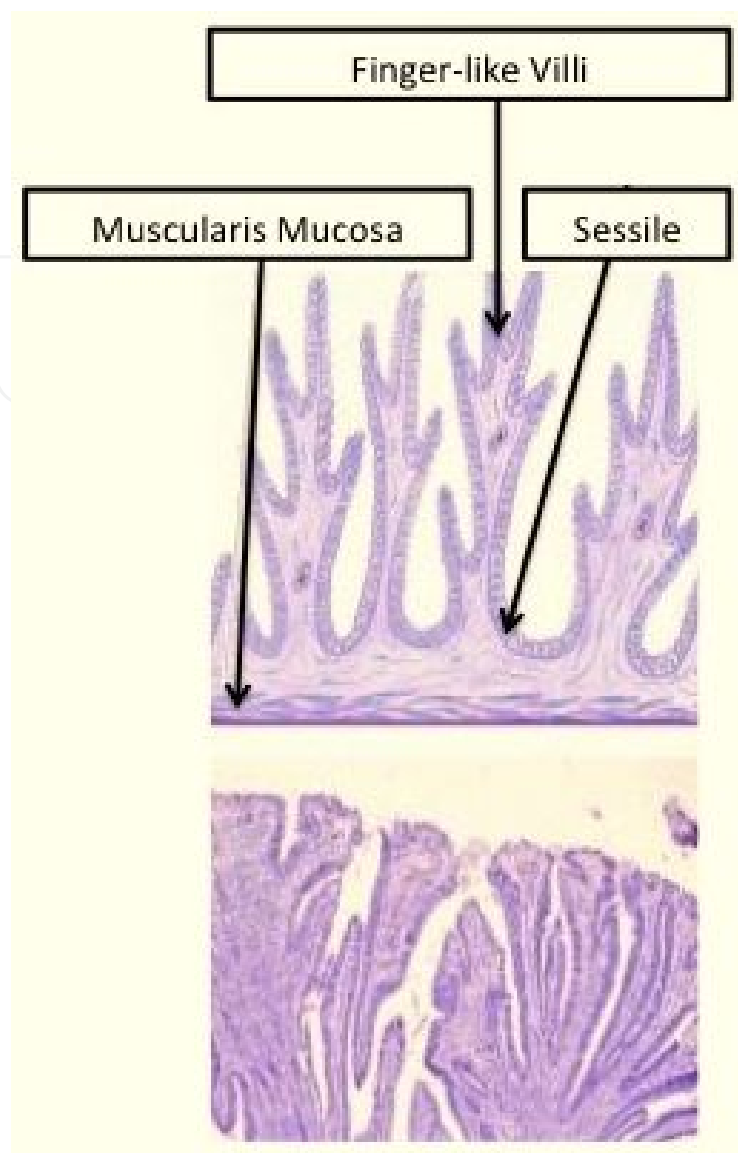


Figure 5. Histologic representation of villous adenoma in the background of normal colon tissue.

than conventional adenomatous polyps, in particular SSA/Ps, since they are more likely to be flat lesions, and so recent studies have advocated for a longer withdrawal time to increase serrated lesion detection rates [35, 36].

Serrated lesions have a distinct endoscopic appearance albeit often very subtle. A retrospective analysis of high-resolution endoscopic video clips by Tadepalli et al. analyzed the gross morphologic characteristics of 158 SSPs [37]. They found the most prevalent visual descriptors to be the presence of a mucous cap (which may be yellow or green in white light and red under NBI) (63.9%), rim of debris or bubbles (51.9%), alteration of the contour of a fold (37.3%), and interruption of underlying vascular pattern (32%). Figure 8 depicts an SSP under traditional white-light colonoscopy with a superficial mucous cap, its appearance under NBI, and a histologic representation.

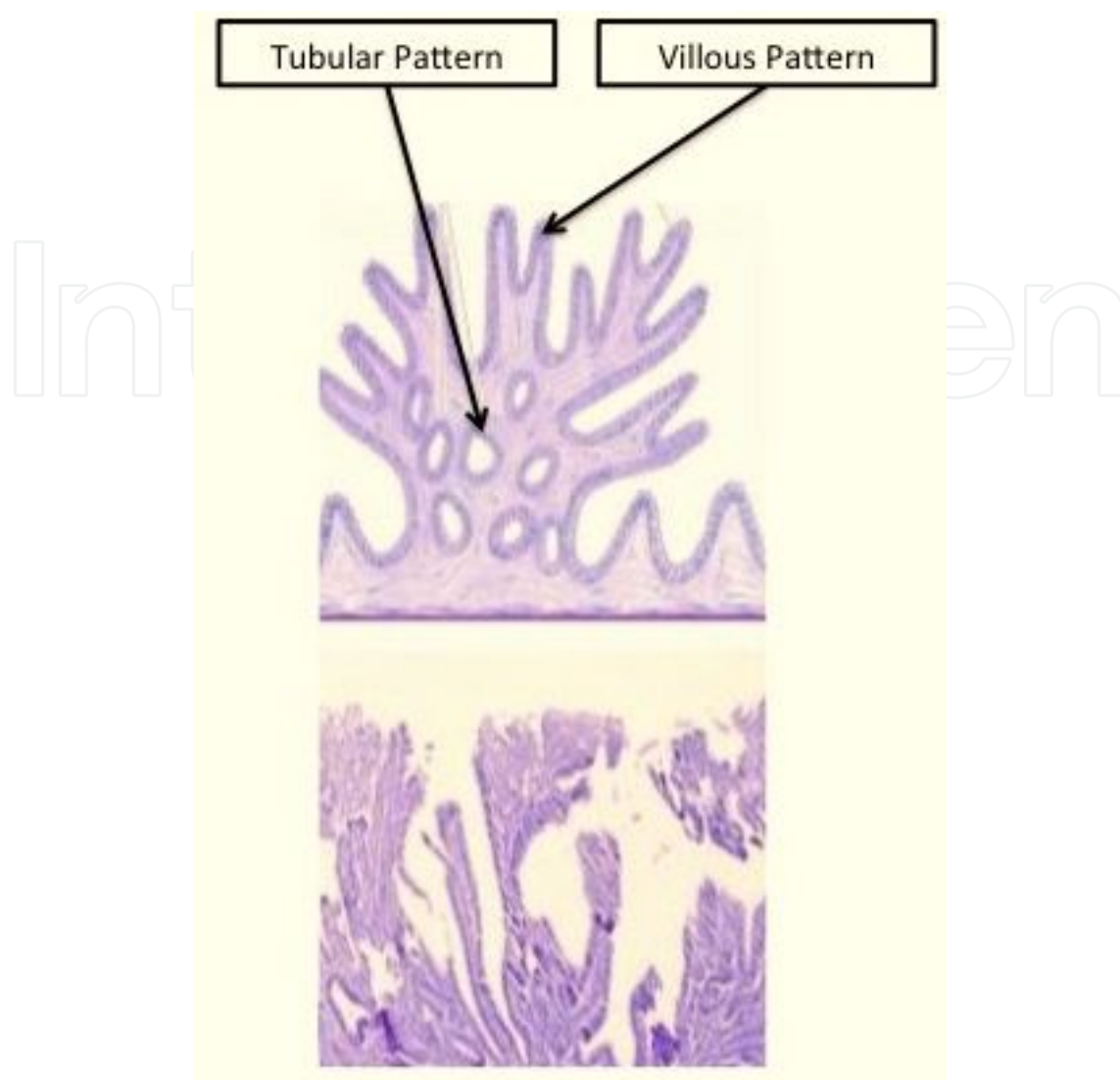


Figure 6. Histologic representation of a tubulovillous adenoma in the background of normal colon tissue.

Hyperplastic polyps are the most common non-neoplastic polyps in the colon; however, they are oftentimes grossly indistinguishable from adenomatous polyps. Histologically, hyperplastic polyps resemble normal colonic tissue with the exception of proliferation in the basal portion of the crypt and a characteristic “saw tooth” pattern along the crypt axis [38]. The relationship between diminutive hyperplastic polyps in the left colon and proximal neoplasia has long been a topic of debate with studies producing mixed results [39–42]. Hyperplastic polyps found proximal to the left colon, however, have consistently been shown to carry malignant potential and should be resected [39, 43].

3.2. Hamartomatous polyps

Hamartomatous polyps are polyps that may grossly resemble normal colonic tissue but are histologically a mixture of tissues growing in disarray. Histologically, they contain mucous-filled glands, retention cysts, abundant connective tissue, and/or chronic eosinophilic infiltra-

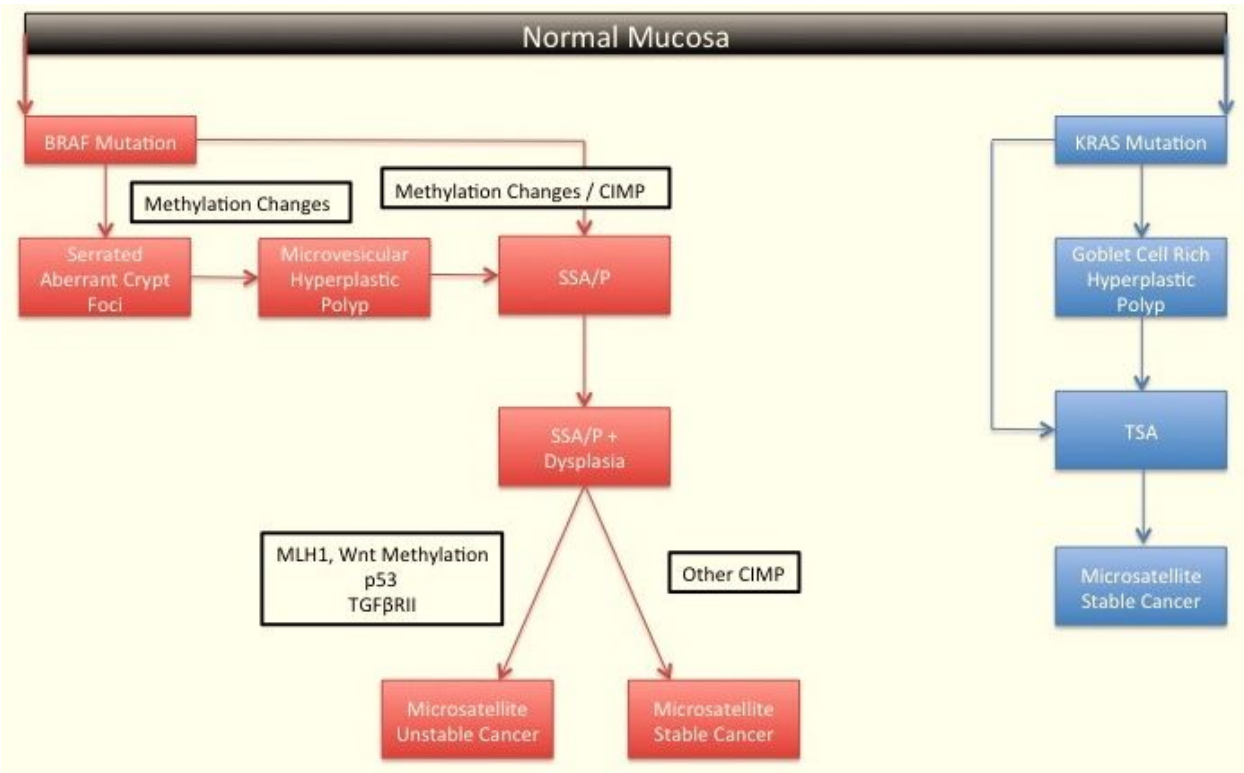


Figure 7. Potential molecular pathways of serrated neoplasia.

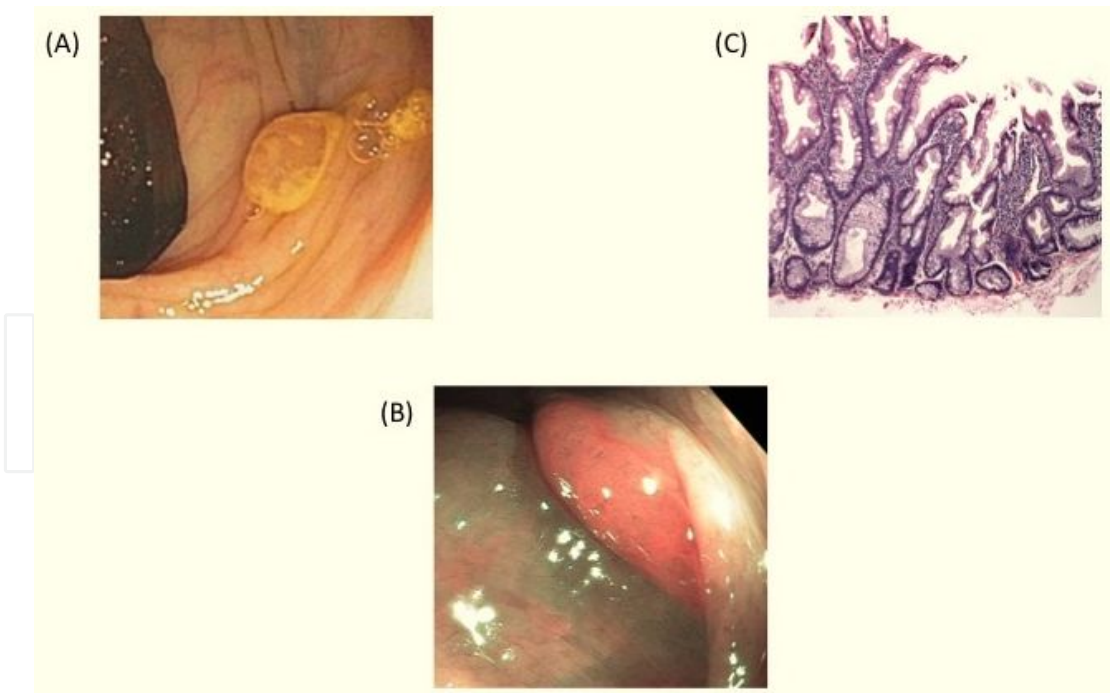


Figure 8. A) Sessile serrated polyp with mucosal cap under white-light colonoscopy. (B) Sessile serrated polyp under NBI. (C) Histology of sessile serrated polyp demonstrating expanded crypt proliferative zone, exaggerated architecture in crypt region with basilar crypt dilation, inverted crypts, and a predominance of crypts with minimal cell maturation.

tion [44]. Traditionally, they have been classified as non-neoplastic but several associated polyposis syndromes (e.g., Juvenile Polyposis Coli, Peutz-Jegher Syndrome, Cronkhite Canada Syndrome, and Cowden Syndrome) do carry a predilection towards colorectal cancer and other gastrointestinal malignancies.

Juvenile polyps are a type of hamartomatous polyp characterized by dilated cystic glands rather than an increased number of epithelial cells [44]. They can be found at any age, but as the name implies, are more commonly diagnosed during childhood. They are typically removed due to their propensity to bleed. Peutz-Jegher polyps are a type of hamartomatous polyp characterized by glandular epithelium supported by smooth muscle cells contiguous with the muscularis mucosa. Figure 9 depicts an endoscopic view of a hamartomatous polyp and histologic view of a Peutz-Jegher polyp.

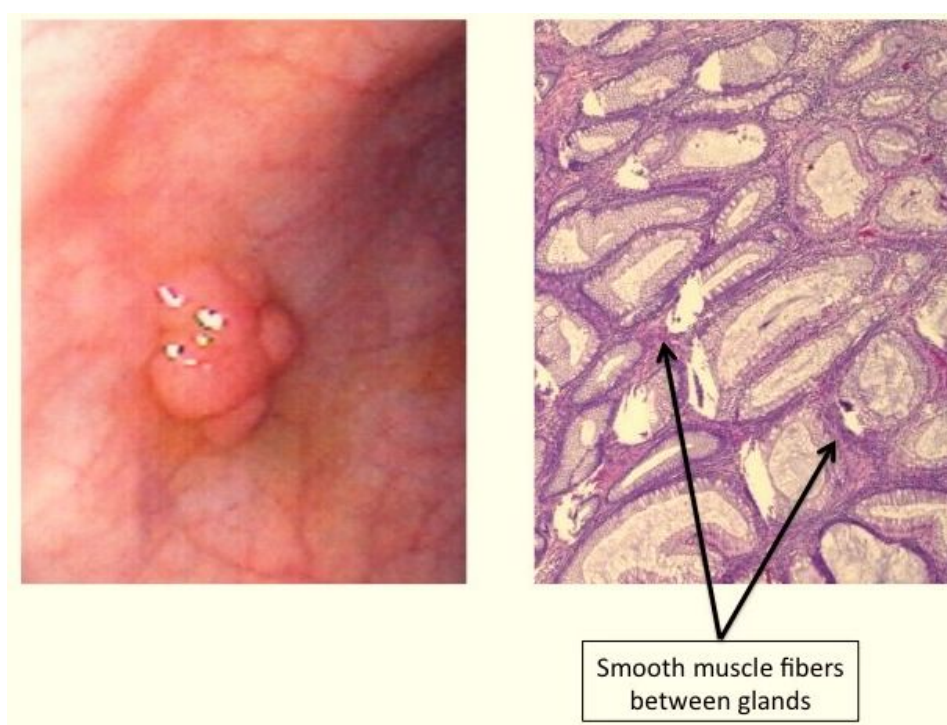


Figure 9. Endoscopic view of a hamartomatous polyp and histologic view of a Peutz-Jegher polyp.

3.3. Inflammatory pseudopolyps

Inflammatory polyps, typically seen in IBD, are indicative of regenerative and/or healing phases of mucosal ulceration and possess no malignant potential. They are formed from discrete islands of residual intact colonic mucosa that result from the ulceration and tissue reparation that is inherent to the disease course [45]. Scattered throughout the colitic region of the colon, they are often numerous, filiform, and can be large enough to encompass the lumen resulting in intussusception or luminal obstruction [45, 46]. The clinical endoscopist ought to be cognizant of clusters of localized giant pseudopolypoidosis as they may be associated with occult dysplasia [47]. Histologically, inflammatory pseudopolyps are characterized by

inflamed lamina propria and distorted colonic epithelium [48]. Surface erosions, congestion, hemorrhage and/or crypt abscesses may also be present [48]. Figure 10 depicts an endoscopic and histologic view of an inflammatory pseudopolyp.

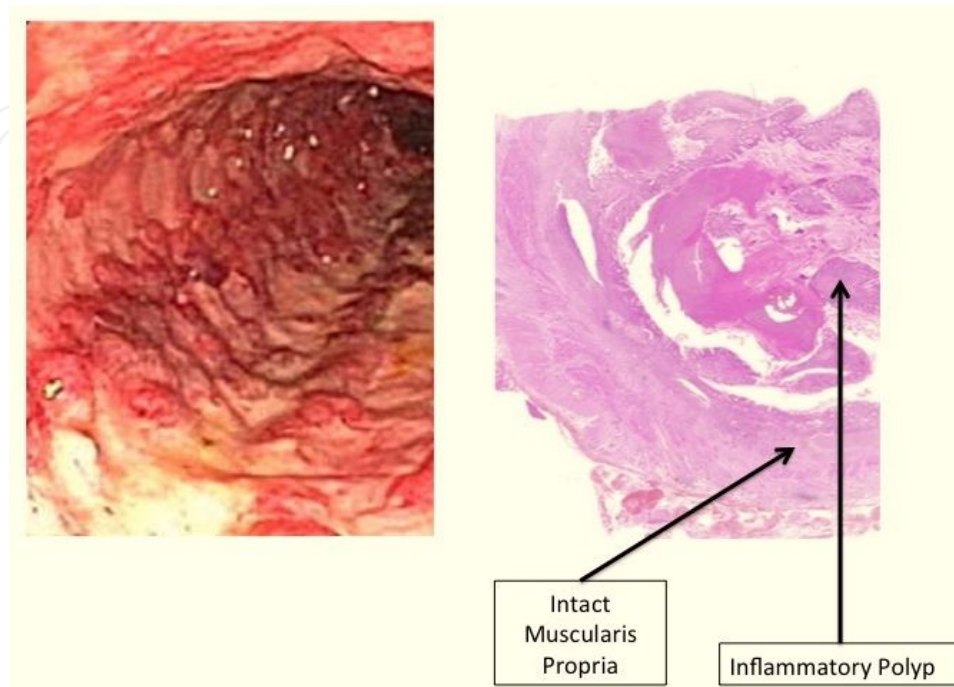


Figure 10. Endoscopic and histologic view of an inflammatory pseudopolyp.

4. Colitis

4.1. Inflammatory bowel disease

In patients with a clinical presentation suggestive of IBD, colonoscopy with ileoscopy can be used to make the initial diagnosis as it allows for direct visualization and biopsy of rectal, colonic, and terminal ileum mucosa [49]. In addition, it can assess disease activity and monitor therapeutic response, provide surveillance of dysplasia or neoplasia, and lastly provide therapeutic intervention such as stricture dilation [49] or closure of fistulae and anastomotic leakages [50].

The use of endoscopic appearance in distinguishing IBD from other non-IBD colitides is limited [51] as there are a number of 'IBD mimickers' including but not limited to colonic tuberculosis [52], Behçet's disease [53], and segmental colitis associated with diverticular disease [54]. In addition to tuberculosis, there are hosts of other infectious colitides that can also endoscopically mimic IBD [51, 55]. Table 1 provides an endoscopic description of various infectious colitides. Once these other etiologies have been excluded, colonoscopy can often shed light in distinguishing Crohn's disease (CD) from ulcerative colitis (UC), which is important for

disease management. The data gathered from an index colonoscopy is of utmost importance owing to the fact that once therapy is initiated for IBD, discriminating features of CD from UC may be obscured [56, 57].

Infectious Etiology	Endoscopic Appearance
<i>Apergillus</i>	Hemorrhagic ulcerations
<i>Campylobacter</i>	Colonic erythema and ulceration
<i>Chlamydia</i>	Perianal abscesses, ulcerations, and fistulae
<i>C. difficile</i>	Pseudomembranes and moderately severe colitis, predominantly left sided
<i>Cytomegalovirus</i>	Colitis with ulceration (typically punched out and shallow)
<i>Entamoeba</i>	Acute colitis with ulceration
<i>E. coli</i> 0157:H7	Moderately severe colitis
<i>Herpes</i>	Proctitis with ulceration, there may be perianal involvement as well.
<i>Histoplasma</i>	Moderately severely colitis, predominantly right sided
<i>Klebsiella</i>	Hemorrhagic colitis
<i>Mycobacterium</i>	Ileal ulceration, may be transverse or circumferential
<i>Nessieria</i>	Proctitis with ulceration, there may be perianal involvement as well
<i>Salmonella</i>	Friable mucosa, ileal and colonic hemorrhages often present
<i>Schistosoma</i>	Extensive colitis may be segmental, polyps often times present
<i>Shigella</i>	Intense patchy colonic erythema that can also include the ileum
<i>Treponema</i>	Proctitis with ulceration, there may be perianal involvement as well
<i>Yersinia</i>	Patchy colitis with ileal ulceration (aphthoid)

Table 1. Endoscopic description of various infectious colitides [54].

4.1.1. Endoscopic features of UC and Mayo Scoring System

Endoscopically, classic UC starts in the rectum and progresses proximally, sometimes as far as the ileo-cecal valve, in a circumferential and contiguous fashion with diffused and continuous inflammation [58]. Endoscopic features suggestive of UC include erythema, edema resulting in a loss of the usual vascular patter, granular appearing mucosa, increased friability, and small superficial erosions and ulcers surrounded by diffuse inflammation [59]. These classic visual features are used to endoscopically score the extent of the disease. The Mayo

Scoring System was derived in order provide an objective measure describing the endoscopic extent of the disease. Lemmens et al. sought to evaluate the correlation between endoscopy and histology with use of the Mayo Scoring System [60]. This retrospective study included 236 biopsy sets from 131 patients with known UC. Endoscopy was performed by IBD specialists and graded using the Mayo Scoring System. Biopsy specimens were analyzed by expert gastrointestinal pathologists using the Geboes and Riley histologic scoring systems. They found that at both extremes, inactive and severely active disease, there was a very high concordance rate. For mild disease, however, there were important differences, as histologic examination seemed to have detected more severe disease than endoscopically suspected, thus stressing the need for a combined histologic and endoscopic scoring system when assessing disease activity. Figure 11 depicts the classic endoscopic appearance of UC in relation to the Mayo Scoring System.

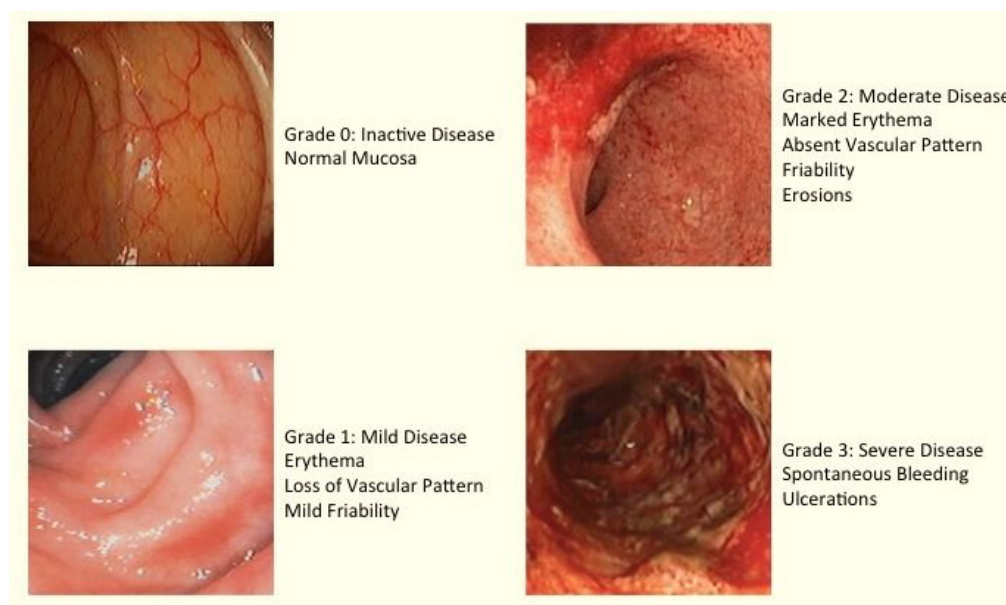


Figure 11. Classic endoscopic appearance of UC in relation to the Mayo Scoring System.

4.1.2. Endoscopic features of CD and the Simple Endoscopic Score for CD (SES-CD)

Inflammation in CD can span the entire gastrointestinal tract with nearly 55% of cases involving the terminal ileum and colon, 40% involving exclusively the ileum, and 25% involving the colon alone [61]. Rectal involvement occurs in up to 50% of patients with CD [62]. It should be noted that while terminal ileal involvement is strongly suggestive of CD, it might also occur in patients with UC, particularly pan-colitic UC, by way of “backwash” of cecal contents or “backwash ileitis” [63, 64]. The exact pathogenesis of “backwash ileitis” remains poorly understood, however it is believed that in patients with pan-colitic UC, the terminal ileum becomes inflamed stemming from chronic exposure to cecal contents.

Endoscopically, classic CD appears as “skip lesions” or areas of inflammation interposed between islands of normal mucosa, “cobblestone” appearance of the mucosal surface due to

submucosal inflammation and edema, and deep, longitudinal, polycyclic ulcers [55]. In 2004, the SES-CD was derived in order to provide an objective measure describing the endoscopic extent of the disease [65]. To date, prospective data evaluating the utility of SES-CD in predicting corticosteroid-free clinical remission and long-term disease progression is lacking [66, 67]. Figure 12 depicts the classic endoscopic appearance of CD as well as the SES-CD. Table 2 illustrates the key endoscopic differences between UC and CD.

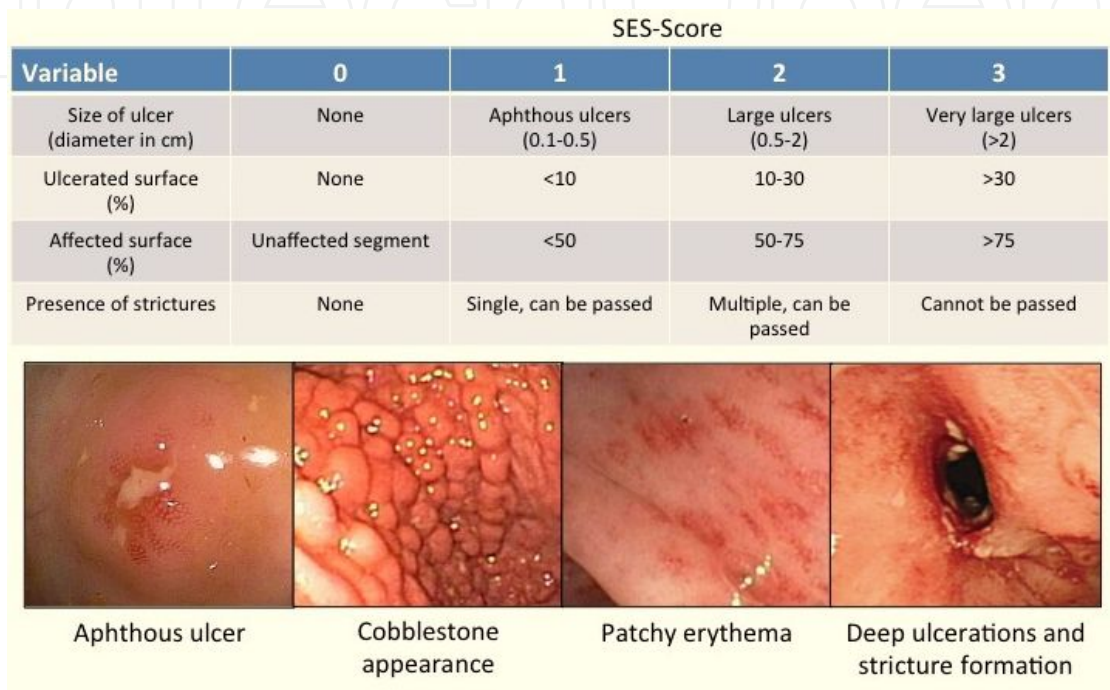


Figure 12. Classic endoscopic appearance of CD as well as the SES-CD.

Endoscopic Features	Ulcerative Colitis	Crohn’s Disease
Aphthous Ulcers	√	√√√
Cobblestone Appearance	x	√√
Deep Ulcers	x	√√√
Erythema	√√√	√√
Granular Mucosa	√√√	√
Ileal Ulcers	x	√√√
Loss of Vascular Pattern	√√√	√
Pseudopolyp	√√√	√√√
Patchy Inflammation	x	√√√
Rectal Involvement	√√√√	√√

Table 2. Key endoscopic differences between UC and CD [54].

4.2. Microscopic (Lymphocytic and collagenous) and eosinophilic colitis

While microscopic colitis by definition is a histologic diagnosis, emerging data suggests that it may not always present with normal endoscopic findings [68–72]. Microscopic colitis is further subdivided into lymphocytic colitis and collagenous colitis depending on the presence of lymphocytic predominant infiltration or collagen deposition, respectively [73]. There have been several macroscopic lesions associated with collagenous colitis including longitudinal ulcers [69,70], hypervascularity [71], loss of normal vascularity [72], and exudative bleeding [73]. A retrospective study by Park et al. sought to investigate macroscopic lesions seen on the endoscopy in 14 patients with diagnosed lymphocytic colitis [68]. Patients with more severe diarrhea demonstrated macroscopic lesions on colonoscopy that included hypervascularity and exudative bleeding, which led to the conclusion that lymphocytic colitis may not always present with a normal endoscopically appearing mucosa. Figure 13 depicts lymphocytic colitis associated with hypervascular mucosa and exudative bleeding.

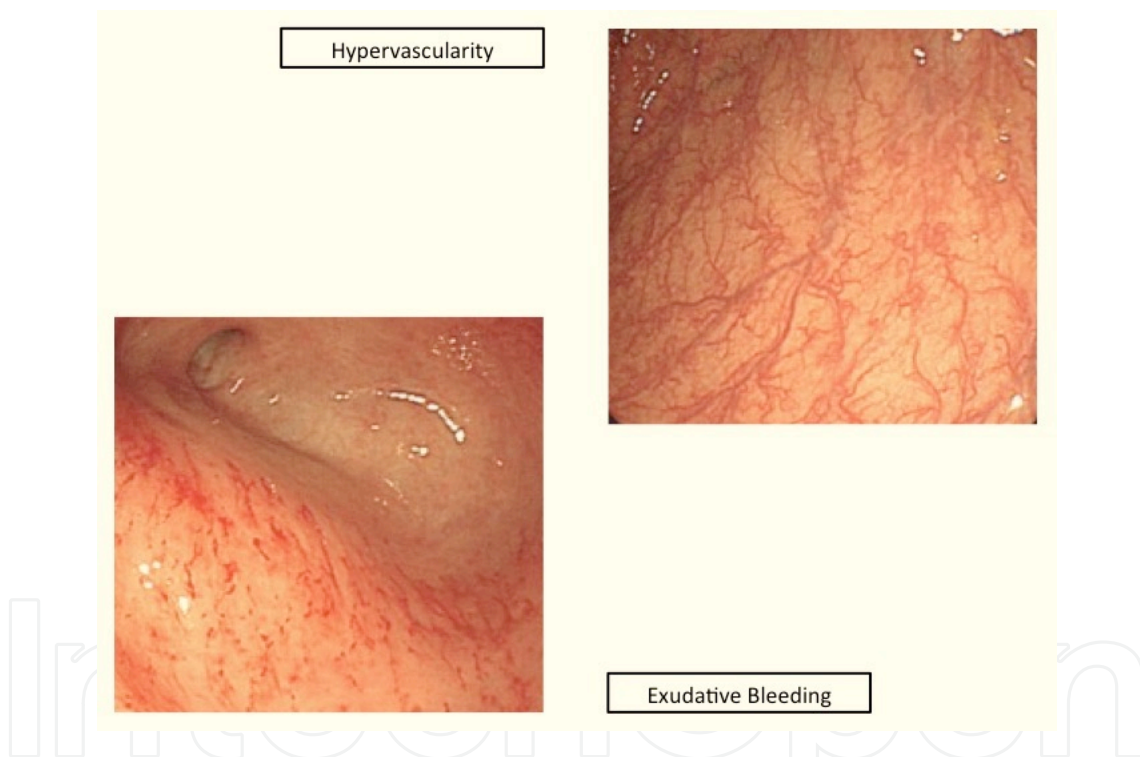


Figure 13. Hypervascular mucosa and exudative bleeding associated with lymphocytic colitis.

Eosinophilic disorders can span the entirety of the gastrointestinal tract, including the esophagus (eosinophilic esophagitis), stomach and small intestine (eosinophilic gastroenteritis), and the colon (eosinophilic colitis). Eosinophilic colitis is the least frequent manifestation of primary eosinophilic gastrointestinal disorders with only a few reports reported over the last four decades [74]. Secondary eosinophilic colitis can stem from several conditions including parasitic infections (e.g., *Strongyloides stercoralis* [75], *Enterobius vermicularis* [76], and *Trichuris trichiura* [77]), drug-induced (e.g., clozapine [78], carbamazepine [79], rifampicin [80], non-steroidal anti-inflammatory drugs [81, 82], tacrolimus [83], and gold [84]), auto-immune

disorders (e.g., scleroderma [85], dermatomyositis and polymyositis [86, 87], and vasculitides (e.g., Churg-Strauss syndrome [88]). Endoscopic features suggestive of eosinophilic colitis include an edematous mucosa with loss of normal vascular pattern, patchy erythema, and superficial ulcerations [74].

4.3. Ischemic colitis

Ischemic colitis occurs as a result of inadequate blood supply to the large colon, typically affecting the critically ill and elderly population [89]. A recent retrospective study by Church et al. examined the role of urgent bedside colonoscopy in critically ill patients [90]. This study included 41 patients totaling 49 bedside colonoscopies with the most common indication being to exclude ischemic colitis (n=25). Of those 25, the diagnosis was confirmed in 19 with 14 patients subsequently undergoing surgical intervention, which led the authors to conclude that bedside colonoscopy is helpful in the diagnosis of acute lower gastrointestinal disease and can potentially guide therapeutic management in critically ill patients. There are several endoscopic findings that may assist in the diagnosis of ischemic colitis, one of which is the colon single-stripe sign. Zuckerman retrospectively studied 26 patients with endoscopic evidence of the colon single-stripe sign and compared it with 58 consecutive patients without a stripe [91]. All patients in the colon single-stripe cohort had a stripe that was >5cm in length predominantly in the left colon (89%). Patients with the colon single-stripe sign were significantly more likely to have evidence of a preceding ischemic event (62%) compared to the colitis comparison group (7%). Histologically, patients with the colon single-stripe sign had microscopic evidence of ischemic injury compared to the colitis cohort (75% vs. 13%, respectively; $p < 0.0001$). Next, the clinical course and outcome of the 26 patients with the colon single-stripe sign was compared with 22 patients with circumferentially involved ischemic colitis. None of the patients with the colon single-stripe sign required surgical intervention compared with 27% of patients with circumferential ischemic colitis. In addition, mortality rates were higher in the circumferential ischemic colitis group compared with patients with the colon single-stripe sign (41% vs. 4%, respectively; $p < 0.05$). This led the authors to conclude that the colon-single stripe sign can manifest endoscopically, typically in a milder disease in the clinical spectrum of ischemic colitis [91]. Other endoscopic manifestations of ischemic colitis include petechial hemorrhages, edematous and fragile mucosa, segmental erythema, scattered erosions, and longitudinal ulcerations [92]. The 'watershed areas' (e.g., splenic flexure and transverse colon) are areas most vulnerable to ischemia due to the fact that they have the fewest collateral circulation. Figure 14 depicts various endoscopic manifestations of ischemic colitis.

4.4. Graft-Versus-Host Disease (GVHD)

Acute GVHD is associated with significant morbidity and mortality in the first 100 days following allogeneic hematopoietic progenitor stem cell transplant [93]. Acute GVHD can have GI manifestations (abdominal pain, nausea/vomiting, and diarrhea), obstructive jaundice, or skin rash. Gastroenterologists are often times consulted for endoscopic evaluation to rule out GVHD, when post-transplant patients present with GI manifestations in the absence of liver

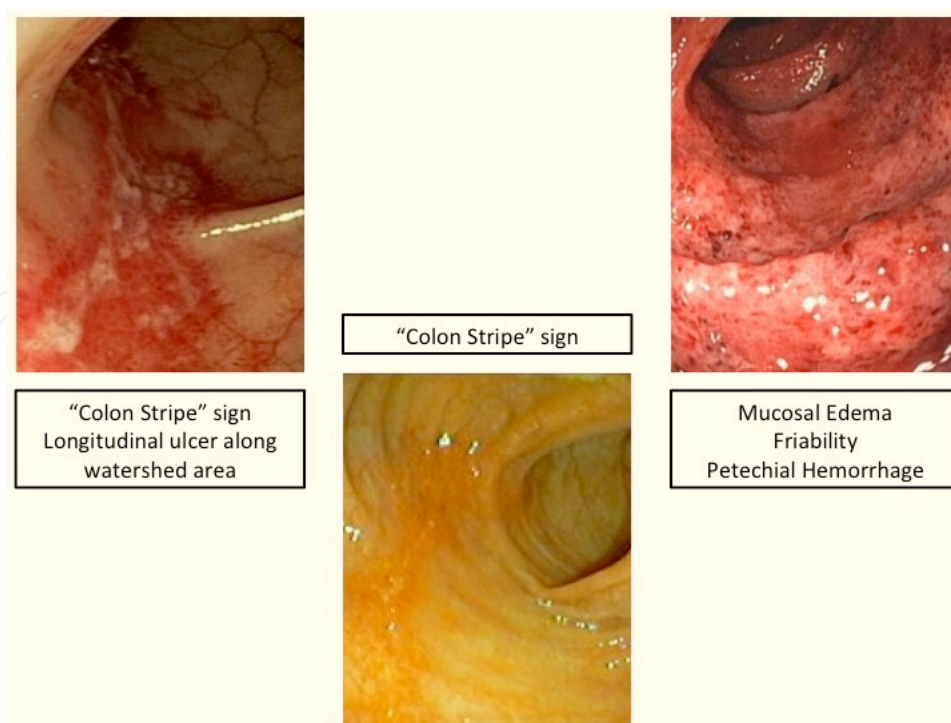


Figure 14. Various endoscopic manifestations of ischemic colitis.

or dermatologic involvement. In a majority of patients, flexible sigmoidoscopy with rectal biopsies allow for histologic diagnosis of GVHD and thus colonoscopy is not necessary [94, 95]. Endoscopic features of GVHD include diffuse edema, hyperemia, patchy erosions, scattered ulcers, sloughing, and active bleeding [96].

5. Evaluation of Lower Gastrointestinal Bleeding (LGIB)

The incidence of LGIB is approximately 20 per 100,000, with an associated all cause mortality of 3.9% [97]. The three most common causes of LGIB include angioectasias, diverticular bleeding, and hemorrhoidal bleeding [98]. Colonic ulcerations secondary to underlying IBD or chronic NSAID use, stercoral ulcer, Dieulafoy's lesion, or colorectal varices are less common etiologies of LGIB. In addition, an upper gastrointestinal source should also be included in the differential being that upwards of 15% of patients with severe hematochezia are found to have an upper gastrointestinal source [99]. In a hemodynamically stable patient, colonoscopy remains the cornerstone in the diagnosis of an LGIB. Figure 15 is a suggested algorithm by Parekh et al. for the role of colonoscopy in the evaluation of a hemodynamically stable LGIB [100].

Diverticulosis of the colon is an out-pouching of colonic mucosa through weakened layers of muscle in the colon wall. The incidence of diverticular increases after the age of 40 [101]. While in itself benign, complications of diverticular disease include diverticulitis, which is the inflammation or infection of diverticula, and painless bleeding, which may be life threatening.

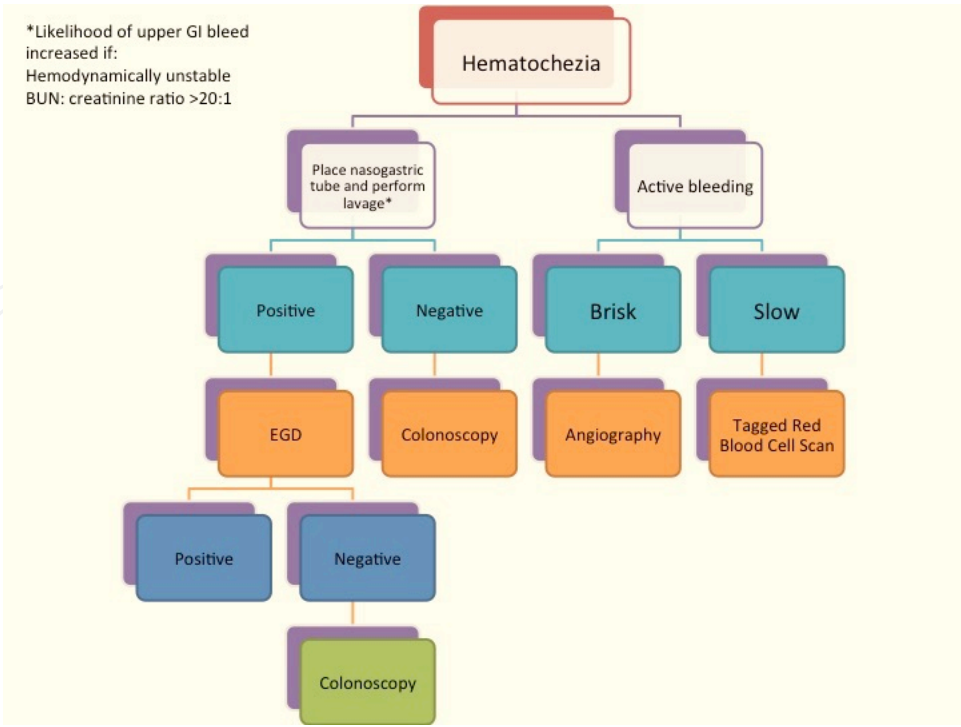


Figure 15. Suggested algorithm by Parekh et al. for the role of colonoscopy in the evaluation of a hemodynamically stable LGIB [100].

Therefore, it is important for the endoscopist to inform the patient of symptoms of potential complications of diverticular disease.

Colonic angioectasias, previously referred to as arteriovenous malformations or angiodysplasias, are a common source of lower gastrointestinal bleeding [102]. They can often times be difficult to identify if not actively bleeding. Figure 16 is an example of colonic diverticula and an angioectasia seen endoscopically.

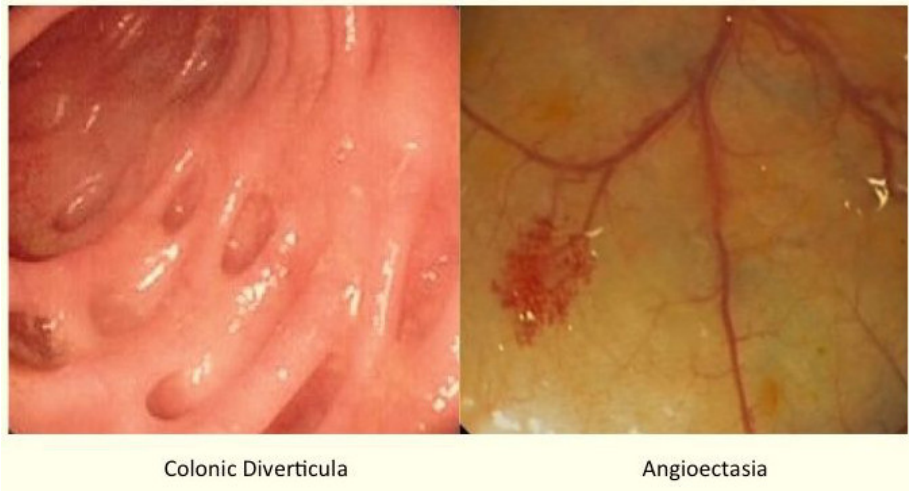


Figure 16. Colonic diverticula and an angioectasia seen endoscopically.

6. Hemorrhoids and anal fissures

Hemorrhoids are vascular structures in the anal canal that act as cushions to help with stool control [103]. When they become swollen or inflamed, internal hemorrhoids (above the dentate line) can present as painless rectal bleeding. External hemorrhoids can result in pain when thrombosed, or painful bleeding if ulceration occurs from pressure necrosis [103]. Skin tags may be evidence of prior thrombosed external hemorrhoids.

An anal fissure is a linear tear or crack in the distal anal canal. It often presents as painful defecation. Initially it usually involves only the epithelium and progresses to include the full thickness of the anal mucosa. Figure 17 is an example of an internal hemorrhoid, external hemorrhoid, skin tag, and an anal fissure.

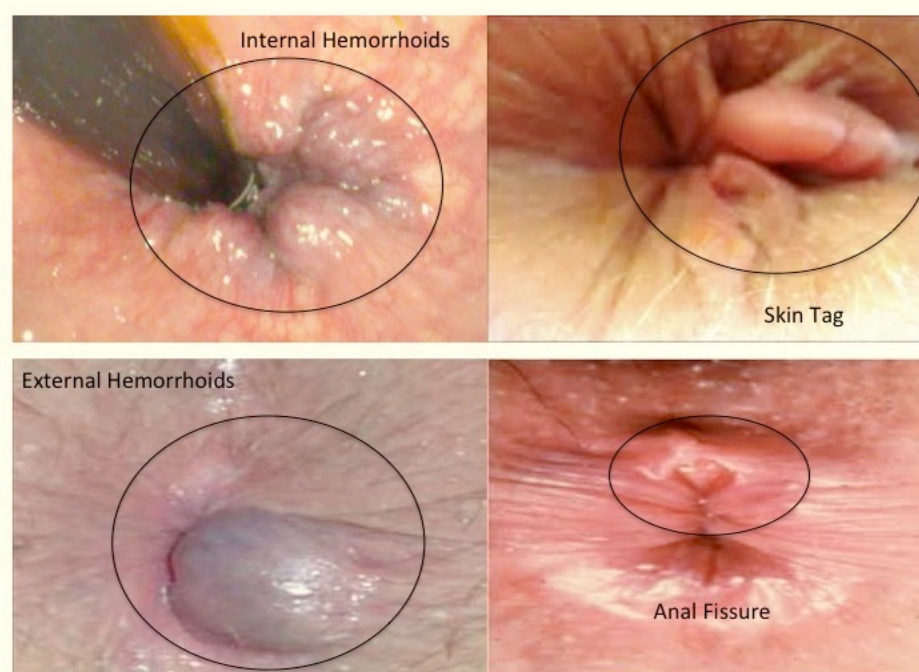


Figure 17. Internal hemorrhoid, external hemorrhoid, skin tag, and an anal fissure.

7. Conclusion

Colonoscopy is important in the diagnosis and therapeutic management of several disease states. To date, colonoscopy remains the gold standard in colorectal cancer prevention. It is the cornerstone in the diagnosis and therapeutic management of IBD, particularly with the recent paradigm shift in the therapeutic management of IBD stressing the importance of endoscopic remission in addition to symptomatic remission. In addition, a thorough colonoscopic exam can aid in the diagnosis of other non-IBD colitides. In the acute setting, findings

during colonoscopy are not only crucial in diagnosing the underlying etiology but also driving therapeutic management. As technology evolves and indications for colonoscopy expand, it becomes increasingly more crucial for the clinical endoscopist to be knowledgeable of normal and pathologic findings during colonoscopy.

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References

- [1] Wolff WI. Colonoscopy: History and development. *Am J Gastroenterol.* 1989;84(9):1017-25.
- [2] Rex DK, Rahmani EY, Haseman JH, Lemmel GT, Kaster S, Buckley JS. Relative sensitivity of colonoscopy and barium enema for detection of colorectal cancer in clinical practice. *Gastroenterology.* 1997;112(1):17-23.
- [3] Winawer SJ, Zauber AG, Fletcher RH, et al. Guidelines for colonoscopy surveillance after polypectomy: A consensus update by the US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society. *CA Cancer J Clin.* 2006;56(3):143-59.
- [4] Siegel R, Desantis C, Jemal A. Colorectal cancer statistics, 2014. *CA Cancer J Clin.* 2014;64(2):104-17.
- [5] Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin.* 2015;65(2):87-108.
- [6] Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. *N Engl J Med.* 1993;329(27):1977-81.
- [7] Zauber AG, Winawer SJ, O'Brien MJ, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. *N Engl J Med.* 2012;366(8):687-96.
- [8] Bressler B, Paszat LF, Chen Z, Rothwell DM, Vinden C, Rabeneck L. Rates of new or missed colorectal cancers after colonoscopy and their risk factors: a population-based analysis. *Gastroenterology.* 2007;132(1):96-102.

- [9] Pickhardt PJ, Nugent PA, Mysliwiec PA, Choi JR, Schindler WR. Location of adenomas missed by optical colonoscopy. *Ann Intern Med.* 2004;141(5):352-9.
- [10] Van gelder RE, Nio CY, Florie J, et al. Computed tomographic colonography compared with colonoscopy in patients at increased risk for colorectal cancer. *Gastroenterology.* 2004;127(1):41-8.
- [11] Lieberman DA, Weiss DG, Harford WV, et al. Five-year colon surveillance after screening colonoscopy. *Gastroenterology.* 2007;133(4):1077-85.
- [12] Martínez ME, Baron JA, Lieberman DA, et al. A pooled analysis of advanced colorectal neoplasia diagnoses after colonoscopic polypectomy. *Gastroenterology.* 2009;136(3):832-41.
- [13] Pancione M, Remo A, Colantuoni V. Genetic and epigenetic events generate multiple pathways in colorectal cancer progression. *Patholog Res Int.* 2012;2012:509348.
- [14] Luo Y, Wong CJ, Kaz AM, et al. Differences in DNA methylation signatures reveal multiple pathways of progression from adenoma to colorectal cancer. *Gastroenterology.* 2014;147(2):418-29.e8.
- [15] The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. *Gastrointest Endosc.* 2003;58(6 Suppl):S3-43.
- [16] O'Brien MJ, Winawer SJ, Zauber AG, et al. The National Polyp Study. Patient and polyp characteristics associated with high-grade dysplasia in colorectal adenomas. *Gastroenterology.* 1990;98(2):371-9.
- [17] Binmoeller KF, Bohnacker S, Seifert H, Thonke F, Valdeyar H, Soehendra N. Endoscopic snare excision of "giant" colorectal polyps. *Gastrointest Endosc.* 1996;43(3):183-8.
- [18] Lieberman D, Moravec M, Holub J, Michaels L, Eisen G. Polyp size and advanced histology in patients undergoing colonoscopy screening: Implications for CT colonography. *Gastroenterology.* 2008;135(4):1100-5.
- [19] Van doorn SC, Hazewinkel Y, East JE, et al. Polyp morphology: An interobserver evaluation for the Paris classification among international experts. *Am J Gastroenterol.* 2015;110(1):180-7.
- [20] Leung WK, Lo OS, Liu KS, et al. Detection of colorectal adenoma by narrow band imaging (HQ190) vs. high-definition white light colonoscopy: A randomized controlled trial. *Am J Gastroenterol.* 2014;109(6):855-63.
- [21] Jin XF, Chai TH, Shi JW, Yang XC, Sun QY. Meta-analysis for evaluating the accuracy of endoscopy with narrow band imaging in detecting colorectal adenomas. *J Gastroenterol Hepatol.* 2012;27(5):882-7.

- [22] East JE, Ignjatovic A, Suzuki N, et al. A randomized, controlled trial of narrow-band imaging vs. high-definition white light for adenoma detection in patients at high risk of adenomas. *Colorectal Dis.* 2012;14(11):e771-8.
- [23] Mizuno K, Kudo SE, Ohtsuka K, et al. Narrow-banding images and structures of microvessels of colonic lesions. *Dig Dis Sci.* 2011;56(6):1811-7.
- [24] Winawer SJ, Zauber AG. The advanced adenoma as the primary target of screening. *Gastrointest Endosc Clin N Am.* 2002;12(1):1-9, v.
- [25] Mattar M, Frankel P, David D, et al. Clinicopathologic significance of synchronous and metachronous adenomas in colorectal cancer. *Clin Colorectal Cancer.* 2005;5(4):274-8.
- [26] Karlitz JJ, Hsieh MC, Liu Y, et al. Population-based lynch syndrome screening by microsatellite instability in patients ≤ 50 : Prevalence, testing determinants, and result availability prior to colon surgery. *Am J Gastroenterol.* 2015.
- [27] Worthley DL, Leggett BA. Colorectal cancer: Molecular features and clinical opportunities. *Clin Biochem Rev.* 2010;31(2):31-8.
- [28] Kakar S, Deng G, Cun L, Sahai V, Kim YS. CpG island methylation is frequently present in tubulovillous and villous adenomas and correlates with size, site, and villous component. *Hum Pathol.* 2008;39(1):30-6.
- [29] Rosty C, Hewett DG, Brown IS, Leggett BA, Whitehall VL. Serrated polyps of the large intestine: current understanding of diagnosis, pathogenesis, and clinical management. *J Gastroenterol.* 2013;48(3):287-302.
- [30] Rex DK, Ahnen DJ, Baron JA, et al. Serrated lesions of the colorectum: Review and recommendations from an expert panel. *Am J Gastroenterol.* 2012;107(9):1315-29.
- [31] Spring KJ, Zhao ZZ, Karamatic R, et al. High prevalence of sessile serrated adenomas with BRAF mutations: A prospective study of patients undergoing colonoscopy. *Gastroenterology.* 2006;131(5):1400-7.
- [32] Sweetser S, Smyrk TC, Sinicrope FA. Serrated colon polyps as precursors to colorectal cancer. *Clin Gastroenterol Hepatol.* 2013;11(7):760-7.
- [33] Anderson JC. Pathogenesis and management of serrated polyps: Current status and future directions. *Gut Liver.* 2014;8(6):582-9.
- [34] Weston AP, Campbell DR. Diminutive colonic polyps: Histopathology, spatial distribution, concomitant significant lesions, and treatment complications. *Am J Gastroenterol.* 1995;90(1):24-8.
- [35] Butterly L, Robinson CM, Anderson JC, et al. Serrated and adenomatous polyp detection increases with longer withdrawal time: Results from the New Hampshire Colonoscopy Registry. *Am J Gastroenterol.* 2014;109(3):417-26.

- [36] Anderson JC, Butterly LF, Goodrich M, Robinson CM, Weiss JE. Differences in detection rates of adenomas and serrated polyps in screening versus surveillance colonoscopies, based on the new hampshire colonoscopy registry. *Clin Gastroenterol Hepatol*. 2013;11(10):1308-12.
- [37] Tadepalli US, Feihel D, Miller KM, et al. A morphologic analysis of sessile serrated polyps observed during routine colonoscopy (with video). *Gastrointest Endosc*. 2011;74(6):1360-8.
- [38] Higuchi T, Sugihara K, Jass JR. Demographic and pathological characteristics of serrated polyps of colorectum. *Histopathology*. 2005;47(1):32-40.
- [39] Provenzale D, Garrett JW, Condon SE, Sandler RS. Risk for colon adenomas in patients with rectosigmoid hyperplastic polyps. *Ann Intern Med*. 1990;113(10):760-3.
- [40] Dave S, Hui S, Kroenke K, Imperiale TF. Is the distal hyperplastic polyp a marker for proximal neoplasia? *J Gen Intern Med*. 2003;18(2):128-37.
- [41] Rex DK, Smith JJ, Ulbright TM, Lehman GA. Distal colonic hyperplastic polyps do not predict proximal adenomas in asymptomatic average-risk subjects. *Gastroenterology*. 1992;102(1):317-9.
- [42] Lin OS, Schembre DB, McCormick SE, et al. Risk of proximal colorectal neoplasia among asymptomatic patients with distal hyperplastic polyps. *Am J Med*. 2005;118(10):1113-9.
- [43] Weston AP, Campbell DR. Diminutive colonic polyps: Histopathology, spatial distribution, concomitant significant lesions, and treatment complications. *Am J Gastroenterol*. 1995;90(1):24-8.
- [44] Calva D, Howe JR. Hamartomatous polyposis syndromes. *Surg Clin North Am*. 2008;88(4):779-817, vii.
- [45] Choi YS, Suh JP, Lee IT, et al. Regression of giant pseudopolyps in inflammatory bowel disease. *J Crohns Colitis*. 2012;6(2):240-3.
- [46] Maldonado TS, Firoozi B, Stone D, Hiotis K. Colocolonic intussusception of a giant pseudopolyp in a patient with ulcerative colitis: a case report and review of the literature. *Inflamm Bowel Dis*. 2004;10(1):41-4.
- [47] Wyse J, Lamoureux E, Gordon PH, Bitton A. Occult dysplasia in a localized giant pseudopolyp in Crohn's colitis: A case report. *Can J Gastroenterol*. 2009;23(7):477-8.
- [48] Popiolek DA, Kahn E, Procaccino JA, Markowitz J. Nodular neuronal hyperplasia: A distinct morphologic type of pseudopolyp in inflammatory bowel disease. *Arch Pathol Lab Med*. 1998;122(2):194-6.
- [49] Leighton JA, Shen B, Baron TH, et al. ASGE guideline: Endoscopy in the diagnosis and treatment of inflammatory bowel disease. *Gastrointest Endosc*. 2006;63(4):558-65.

- [50] Sulz MC, Bertolini R, Frei R, Semadeni GM, Borovicka J, Meyenberger C. Multipurpose use of the over-the-scope-clip system ("Bear claw") in the gastrointestinal tract: Swiss experience in a tertiary center. *World J Gastroenterol*. 2014;20(43):16287-92.
- [51] Fefferman DS, Farrell RJ. Endoscopy in inflammatory bowel disease: Indications, surveillance, and use in clinical practice. *Clin Gastroenterol Hepatol*. 2005;3(1):11-24.
- [52] Chatzicostas C, Koutroubakis IE, Tzardi M, Roussomoustakaki M, Prassopoulos P, Kouroumalis EA. Colonic tuberculosis mimicking Crohn's disease: Case report. *BMC Gastroenterol*. 2002;2(1):10.
- [53] Lee SK, Kim BK, Kim TI, Kim WH. Differential diagnosis of intestinal Behçet's disease and Crohn's disease by colonoscopic findings. *Endoscopy*. 2009;41(1):9-16.
- [54] Del val JH. Old-age inflammatory bowel disease onset: A different problem? *World J Gastroenterol*. 2011;17(22):2734-9.
- [55] Rameshshanker R, Arebi N. Endoscopy in inflammatory bowel disease when and why. *World J Gastrointest Endosc*. 2012;4(6):201-11.
- [56] Kim B, Barnett JL, Kleer CG, Appelman HD. Endoscopic and histological patchiness in treated ulcerative colitis. *Am J Gastroenterol*. 1999;94(11):3258-62.
- [57] Bernstein CN, Shanahan F, Anton PA, Weinstein WM. Patchiness of mucosal inflammation in treated ulcerative colitis: A prospective study. *Gastrointest Endosc*. 1995;42(3):232-7.
- [58] Jevon GP, Madhur R. Endoscopic and histologic findings in pediatric inflammatory bowel disease. *Gastroenterol Hepatol (N Y)*. 2010;6(3):174-80.
- [59] Tontini GE, Vecchi M, Pastorelli L, Neurath MF, Neumann H. Differential diagnosis in inflammatory bowel disease colitis: State of the art and future perspectives. *World J Gastroenterol*. 2015;21(1):21-46.
- [60] Lemmens B, Arijis I, Van assche G, et al. Correlation between the endoscopic and histologic score in assessing the activity of ulcerative colitis. *Inflamm Bowel Dis*. 2013;19(6):1194-201.
- [61] Freeman HJ. Natural history and clinical behavior of Crohn's disease extending beyond two decades. *J Clin Gastroenterol*. 2003;37(3):216-9.
- [62] Nikolaus S, Schreiber S. Diagnostics of inflammatory bowel disease. *Gastroenterology*. 2007;133(5):1670-89.
- [63] Kaiser AM. Discussion of "Backwash ileitis is strongly associated with colorectal carcinoma in ulcerative colitis". *Gastroenterology*. 2002;122(1):245-6.
- [64] Haskell H, Andrews CW, Reddy SI, et al. Pathologic features and clinical significance of "backwash" ileitis in ulcerative colitis. *Am J Surg Pathol*. 2005;29(11):1472-81.

- [65] Daperno M, D'haens G, Van assche G, et al. Development and validation of a new, simplified endoscopic activity score for Crohn's disease: The SES-CD. *Gastrointest Endosc.* 2004;60(4):505-12.
- [66] Ferrante M, Colombel JF, Sandborn WJ, et al. Validation of endoscopic activity scores in patients with Crohn's disease based on a post hoc analysis of data from SONIC. *Gastroenterology.* 2013;145(5):978-986.e5.
- [67] Khanna R, Bouguen G, Feagan BG, et al. A systematic review of measurement of endoscopic disease activity and mucosal healing in Crohn's disease: Recommendations for clinical trial design. *Inflamm Bowel Dis.* 2014;20(10):1850-61.
- [68] Park HS, Han DS, Ro YO, Eun CS, Yoo KS. Does lymphocytic colitis always present with normal endoscopic findings? *Gut Liver.* 2015;9(2):197-201.
- [69] Nomura E, Kagaya H, Uchimi K, et al. Linear mucosal defects: a characteristic endoscopic finding of lansoprazole-associated collagenous colitis. *Endoscopy.* 2010;42 Suppl 2:E9-10.
- [70] Couto G, Bispo M, Barreiro P, Monteiro L, Matos L. Unique endoscopy findings in collagenous colitis. *Gastrointest Endosc.* 2009;69(6):1186-8.
- [71] Sato S, Matsui T, Tsuda S, et al. Endoscopic abnormalities in a Japanese patient with collagenous colitis. *J Gastroenterol.* 2003;38(8):812-3.
- [72] Giardiello FM, Bayless TM, Yardley JH. Collagenous colitis. *Compr Ther.* 1989;15(2):49-54.
- [73] Pardi DS, Smyrk TC, Tremaine WJ, Sandborn WJ. Microscopic colitis: A review. *Am J Gastroenterol.* 2002;97(4):794-802.
- [74] Alfadda AA, Storr MA, Shaffer EA. Eosinophilic colitis: Epidemiology, clinical features, and current management. *Therap Adv Gastroenterol.* 2011;4(5):301-9.
- [75] Al samman M, Haque S, Long JD. Strongyloidiasis colitis: A case report and review of the literature. *J Clin Gastroenterol.* 1999;28(1):77-80.
- [76] Liu LX, Chi J, Upton MP, Ash LR. Eosinophilic colitis associated with larvae of the pinworm *Enterobius vermicularis*. *Lancet.* 1995;346(8972):410-2.
- [77] Chandrasekhara V, Arslanlar S, Sreenarasimhaiah J. Whipworm infection resulting in eosinophilic colitis with occult intestinal bleeding. *Gastrointest Endosc.* 2007;65(4):709-10.
- [78] Friedberg JW, Frankenburg FR, Burk J, Johnson W. Clozapine-caused eosinophilic colitis. *Ann Clin Psychiatry.* 1995;7(2):97-8.
- [79] Anttila VJ, Valtonen M. Carbamazepine-induced eosinophilic colitis. *Epilepsia.* 1992;33(1):119-21.

- [80] Lange P, Oun H, Fuller S, Turney JH. Eosinophilic colitis due to rifampicin. *Lancet*. 1994;344(8932):1296-7.
- [81] Bridges AJ, Marshall JB, Diaz-arias AA. Acute eosinophilic colitis and hypersensitivity reaction associated with naproxen therapy. *Am J Med*. 1990;89(4):526-7.
- [82] Jiménez-sáenz M, González-cámpora R, Linares-santiago E, Herrerías-gutiérrez JM. Bleeding colonic ulcer and eosinophilic colitis: a rare complication of nonsteroidal anti-inflammatory drugs. *J Clin Gastroenterol*. 2006;40(1):84-5.
- [83] Saeed SA, Integlia MJ, Pleskow RG, et al. Tacrolimus-associated eosinophilic gastroenterocolitis in pediatric liver transplant recipients: role of potential food allergies in pathogenesis. *Pediatr Transplant*. 2006;10(6):730-5.
- [84] Martin DM, Goldman JA, Gilliam J, Nasrallah SM. Gold-induced eosinophilic enterocolitis: Response to oral cromolyn sodium. *Gastroenterology*. 1981;80(6):1567-70.
- [85] Clouse RE, Alpers DH, Hockenbery DM, Deschryver-kecskemeti K. Pericrypt eosinophilic enterocolitis and chronic diarrhea. *Gastroenterology*. 1992;103(1):168-76.
- [86] Barbie DA, Mangi AA, Lauwers GY. Eosinophilic gastroenteritis associated with systemic lupus erythematosus. *J Clin Gastroenterol*. 2004;38(10):883-6.
- [87] Ahmad M, Soetikno RM, Ahmed A. The differential diagnosis of eosinophilic esophagitis. *J Clin Gastroenterol*. 2000;30(3):242-4.
- [88] Avgerinos A, Bourikas L, Tzardi M, Koutroubakis IE. Eosinophilic gastroenteritis associated with Churg-Strauss syndrome. *Ann Gastroenterol*. 2012;25(2):164.
- [89] Huguier M, Barrier A, Boelle PY, Houry S, Lacaine F. Ischemic colitis. *Am J Surg*. 2006;192(5):679-84.
- [90] Church J, Kao J. Bedside colonoscopy in intensive care units: indications, techniques, and outcomes. *Surg Endosc*. 2014;28(9):2679-82.
- [91] Zuckerman GR, Prakash C, Merriman RB, Sawhney MS, Deschryver-kecskemeti K, Clouse RE. The colon single-stripe sign and its relationship to ischemic colitis. *Am J Gastroenterol*. 2003;98(9):2018-22.
- [92] Zou X, Cao J, Yao Y, Liu W, Chen L. Endoscopic findings and clinicopathologic characteristics of ischemic colitis: A report of 85 cases. *Dig Dis Sci*. 2009;54(9):2009-15.
- [93] Sultan M, Ramprasad J, Jensen MK, Margolis D, Werlin S. Endoscopic diagnosis of pediatric acute gastrointestinal graft-versus-host disease. *J Pediatr Gastroenterol Nutr*. 2012;55(4):417-20.
- [94] Aslanian H, Chander B, Robert M, et al. Prospective evaluation of acute graft-versus-host disease. *Dig Dis Sci*. 2012;57(3):720-5.
- [95] Crowell KR, Patel RA, Fluchel M, Lowichik A, Bryson S, Pohl JF. Endoscopy in the diagnosis of intestinal graft-versus-host disease: Is lower endoscopy with biopsy as

effective in diagnosis as upper endoscopy combined with lower endoscopy? *Pediatr Blood Cancer*. 2013;60(11):1798-800.

- [96] Xu CF, Zhu LX, Xu XM, Chen WC, Wu DP. Endoscopic diagnosis of gastrointestinal graft-versus-host disease. *World J Gastroenterol*. 2008;14(14):2262-7.
- [97] Strate LL, Ayanian JZ, Kotler G, Syngal S. Risk factors for mortality in lower intestinal bleeding. *Clin Gastroenterol Hepatol*. 2008;6(9):1004-10.
- [98] Chait MM. Lower gastrointestinal bleeding in the elderly. *World J Gastrointest Endosc*. 2010;2(5):147-54.
- [99] Farrell JJ, Friedman LS. Review article: The management of lower gastrointestinal bleeding. *Aliment Pharmacol Ther*. 2005;21(11):1281-98.
- [100] Parekh PJ, Buerlein RC, Shams R, Vingan H, Johnson DA. Evaluation of gastrointestinal bleeding: Update of current radiologic strategies. *World J Gastrointest Pharmacol Ther*. 2014;5(4):200-8.
- [101] Comparato G, Pilotto A, Franzè A, Franceschi M, Di mario F. Diverticular disease in the elderly. *Dig Dis*. 2007;25(2):151-9.
- [102] Management of gastrointestinal angiodysplastic lesions (GIADs): A systematic review and meta-analysis. *The American Journal of Gastroenterology*. 2014;109(4):474.
- [103] Sanchez C, Chinn BT. Hemorrhoids. *Clin Colon Rectal Surg*. 2011;24(1):5-13.

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