Invited Review

Endoscopy in Inflammatory Bowel Disease

D. Panagiotakopoulos[1], M. Panos[2]

SUMMARY

Endoscopy is essential in the diagnosis, assessment and management of patients with Inflammatory Bowel Disease (IBD). It is useful in distinguishing between Ulcerative Colitis and Crohn's Disease and to exclude other diagnoses with similar presentation. Accurate diagnosis in patients with IBD has important implications for medical therapy, selection of surgical options and in predicting overall prognosis. New emerging technologies allow detailed assessment of the affected gut and enable targeted tissue sampling. Various endoscopic therapeutic interventions can be applied in the case of some complications that may arise due to IBD. In this article we review the indications for the use of endoscopy in IBD, focusing on its role in diagnosis, assessment of extent and severity, surveillance for dysplasia and cancer, and in addition, we discuss the potential use of emerging endoscopic technologies in the diagnosis and management of IBD patients.

Key words: Endoscopy, Inflammatory Bowel Disease, Diagnosis

INTRODUCTION

Endoscopy not only provides direct visualisation of the affected gut in patients with IBD, but also allows tissue sampling, thus adding essential histological information to the clinical information, radiographic findings and laboratory results. In addition, it enables the endoscopist to determine the extent and severity of the disease, monitor the response to therapy and finally apply therapeutic interventions to deal with complications related to IBD. In the case of conventional endoscopy, white-light permits only the inspection of the surface of the mucosa and the visible network of branching vessels at a relatively low magnification. Newer techniques like chromoendoscopy with magnification endoscopy, optical coherence tomography and endosonography extend the ability of the endoscopist to assemble more detailed information about the mucosal and deeper structures of the bowel wall. As it becomes more widely available this kind of information may prove useful in the surveillance for dysplastic changes and cancer of the bowel mucosa in longstanding IBD. Furthermore the use of wireless capsule endoscopy expands our capacity to visualise areas of the gut which are inaccessible to standard endoscopy.

[1]Department of Gastroenterology, Royal Bournemouth Hospital, Bournemouth, United Kingdom, [2]Department of Gastroenterology, Euroclinic of Athens, Athens, Greece

Author for correspondence:

Dr Dimitris Panagiotakopoulos, Royal Bournemouth Hospital, Castle Lane, Bournemouth, Dorset, BH7 7DW, United Kingdom

Use of Endoscopy in the diagnosis of IBD

There is no single pathognomonic test for the diagnosis of IBD; the diagnosis should be based on a combination of clinical, endoscopic, histological and radiological findings. It is crucial to establish the correct diagnosis at initial presentation, or as early as possible, because the medical and surgical management for Ulcerative Colitis (UC) and Crohn's Disease (CD) differ considerably.

Ulcerative Colitis

The experienced endoscopist can recognise the typical mucosal changes of UC. The early mucosal changes noted are diffuse erythema and vascular congestion, which represent increased blood flow to the affected area. As the disease progresses the mucosal vascular architecture becomes obscured as a result of associated oedema. Individual heaps of oedematous mucosa interspersed with colonic crypts results in a fine granular appearance occasionally described as *'wet sandpaper'*. The mucosa is friable with minimal trauma from the endoscope. As inflammation progresses small ulcers develop and gradually coalesce to form larger ulcers. The ulcers in UC, in contrast with CD, are within a background of diffuse colonic inflammation.[1]

During remission the mucosa may appear normal but in patients who have had recurrent attacks over several years the colon appears featureless with loss of the haustral folds and luminal narrowing and the mucosa becomes atrophic.[2] Additionally, atrophy of the mucosa may leave behind isolated remnants, which can acquire the appearance either of a mucosal bridge or polyp-like projections called *pseudopolyps* or *inflammatory polyps*. Although the latter are almost invariably benign,[3] biopsy or polypectomy may be considered if they have an atypical appearance or cause problems with intussusception or obstruction.[4]

The mucosal changes in UC start from the anorectal junction and affect the colon proximally in a continuous fashion. The endoscopic changes may be confined to the rectum (proctitis), affect the left side of the colon (distal or left-sided colitis) or extend beyond the splenic flexure to affect the transverse colon or the caecum and ascending colon as well (pancolitis). The cut-off from the affected to the normal mucosa is usually abrupt but occasionally it is gradual.[5]

Although conventionally it is accepted that rectal sparing or patchy involvement should raise suspicions of CD, there are circumstances where patchiness can be observed in UC. This may be seen in patients who have received prior local or systemic therapy.[6] Rectal sparing in particular, usually occurs if the patient has applied topical enemas. Bernstein *et al*.[6] studied prospectively 39 cases of treated UC, 17 (44%) of whom had endoscopic evidence of patchiness, including 5 (13%) with rectal sparing. Thirteen (33%) had histological evidence of patchiness, including 6 (15%) with rectal sparing. Both endoscopic and histologic patchiness were seen in 9 patients (23%). The patchy and non-patchy groups did not differ in regard to the use of rectal therapy. They concluded that in patients with treated UC, the finding of rectal sparing or patchiness should not necessarily indicate a change in the diagnosis to CD.

Another interesting feature where patchy distribution may be confusing, is the peri-appendiceal inflammation or *caecal patch* that is seen occasionally in cases of left-sided UC.[5] The incidence of peri-appendiceal inflammation varies and ranges from 15 to 75% of patients with UC.[5,7] Matsumoto *et al*.[8] studied the clinical significance of the presence of a caecal patch in UC and noted that the endoscopic remission rate at twelve months was higher in patients with peri-appendiceal inflammation as compared to those without (84% vs. 40%, $p < 0.05$).

In patients with pancolitis there is usually an abrupt change of the colon mucosa to normal at the ileocaecal valve. Although there is no small bowel involvement in UC, the terminal ileum can be inflamed, a condition known as *backwash ileitis*. In a retrospective study from Germany backwash ileitis was shown to have a strong association with colorectal cancer (CRC) in UC.[9] The reason for this association is not clear. Backwash ileitis is also commonly associated with Primary Sclerosing Cholangiitis (PSC) in patients with UC.[10]

Crohn's Disease

CD can affect any part of the alimentary tract including the perianal area. Defining the distribution of the disease is important in planning medical or surgical treatment. A complete ileo-colonoscopy with mapping biopsies of the affected areas is important to confirm the diagnosis and its extent. Visualization and biopsy of the terminal ileum can be accomplished as a routine by an experienced endoscopist in nearly all patients (80 to 97 percent).[11,12] In a study of 110 patients with suspected CD the positive predictive value of ileoscopy was 96 percent; there was only one false positive result on colonoscopy (due to *Yersinia enterocolitica* infection).[13]

The lesions encountered endoscopically are aphthous ulcers, skip lesions, cobblestoning, longitudinal ulcers and on occasions fistular and sinus tract orifices. The most common endoscopic findings consist of superficial (93%) and deep erosions (74%).[14] Aphthous ulcers are small, discreet and are surrounded by an erythematous halo. In CD as the disease becomes chronic, aphthae may coalesce into larger ulcers with a linear or *serpiginous* appearance. The cobblestone appearance represents a network of ulcers surrounding relatively normal mucosa and prominent submucosal oedema. Large ulcers, sinus tracts, fistulae and strictures, are late findings in CD.

The distribution of the disease in CD tends to be patchy and segmental. In a series of 1084 patients entered into the National Cooperative Crohn's Disease Study, involvement of both colon and terminal ileum was present in 55% of patients. The disease was confined to the terminal ileum, other areas of the small intestine, or colon-only in 14%, 3%, and 15% of patients, respectively.[15] The discontinuous segmental nature of the disease is an important clue to the diagnosis and has a high positive predictive value (98 per cent).[16]

Taking mucosal biopsies at the time of colonoscopy does not add any significant risk to the procedure and should always be performed. Biopsies should be obtained at several levels, even if the mucosa looks normal, as up to 40% of specimens obtained from normal appearing

tissue in patients with suspected IBD show inflammation on histological evaluation. The biopsies should be labelled according to segments, since a patchy pattern of inflammation can be helpful in differentiating CD from UC.[17] Obtaining specimens from micro-ulcers (less than 5mm in size) have the highest diagnostic yield, followed by the edge of larger ulcers.[18]

Upper gastrointestinal endoscopy is indicated in patients with suspected or known CD who complain of upper gastrointestinal symptoms. The use of upper gastrointestinal endoscopy can be useful in cases of indeterminate colitis, where the diagnosis of CD or UC is not clear, since evidence of inflammation in the upper gut makes the diagnosis of CD more likely.

Differentiation between Crohn's Disease and Ulcerative Colitis

Differentiation between CD and UC has important ramifications for medical therapy, surgical planning, cancer surveillance and prognosis. The distribution of the inflammatory changes in the gut on endoscopy is often helpful to distinguish between CD and UC. The distinction between CD and UC can be made endoscopically with 89% accuracy on presentation with a 4% error margin.[16] The accuracy improves to 95% with re-examination and passage of time. The most useful endoscopic features in this prospective series of 357 IBD patients where discontinuous involvement, anal lesions and cobblestoning of mucosa for CD, and erosions or micro-ulcers and granularity for UC.[16]

Isolated right sided UC has been described but care must be taken to rule out other conditions that may affect the colon such as Yersinia, Behçet's disease and ischaemia.[19]

An abrupt change of the colon mucosa to normal at the ileocaecal valve is more consistent with UC. In CD the valve typically is involved, stenosed and rigid commonly with involvement of the terminal ileum. Routine examination of the terminal ileum is useful not only for diagnosis but also to confirm the completeness of the examination.[20]

Patients without specific features of UC and CD on clinical, endoscopic, radiological and histological grounds are said to have indeterminate colitis (IC). As many as 10-15% of patients with IBD are classified as indeterminate.[21] Usually passage of time tends to resolve the issue and around half of the patients with IC will be given the diagnosis of UC or CD, with the majority diagnosed as UC.[22] Immunological markers may help to discriminate between UC and CD in cases of diagnostic uncertainty. The presence of perinuclear anti-neutrophil cytoplasmic antibodies (pANCA) correlate with UC, where anti-*Saccharomyces cerevisiae* antibodies (ASCA) correlate with CD.[23,24] The clarification of the diagnosis in cases of IC has implications for surgical therapy especially if proctocolectomy with an ileoanal pouch is considered. Upper gastrointestinal endoscopy in IC can be useful in the diagnostic workup as the presence of granulomas or other features of IBD makes the diagnosis of CD most likely.[25]

Patients initially diagnosed with either UC or CD may demonstrate with time additional features which may support or be against the initial diagnosis. In a study from Norway from 527 patients initially diagnosed with UC, 88% had their diagnosis confirmed on follow up in 1-2 years. From 228 patients with CD, 91% had their diagnosis confirmed in the same follow-up period. Thirty six patients were diagnosed originally to have IC. On follow-up 33% of them were re-classified as UC and 17% as CD. The re-evaluation was based on clinical review, small bowel radiology if necessary and colonoscopy (77% of patients). The study illustrates the importance of the re-evaluation of the initial diagnosis, as up to 10%, both among patients with UC and CD, were reclassified at follow up.[26]

A further study to support the need of re-evaluation of the diagnosis in IBD showed that in 96 patients with an initial diagnosis of ulcerative proctitis, 14% of them developed features of CD in 29 months of follow-up.[27] It is therefore advisable in patients with proctitis and elevated CRP, ESR, anaemia or hypoalbuminaemia to pursue an ileo-colonoscopy or proceed to radiological assessment of the small bowel as they may have underlying CD.

The most important distinguishing endoscopic criteria are summarised in Table 1.[16, 28, 29]

The use of upper gastrointestinal endoscopy in CD

Most patients with upper gastrointestinal tract involvement from CD are asymptomatic although symptoms like dyspepsia, dysphagia and pyrosis are not uncommon. Although gastrointestinal involvement was considered rare previously,[12,30] new studies indicate a frequency between 2-60%.[31,32] The most common sites of involvement are the antrum and the duodenum, and include findings of erythema, aphthous ulceration, thickened folds, nodules, ulcers, strictures and cobblestoning.[33]

Although granulomas are seen more commonly in biopsies from abnormal areas they can be found even

Table 1. The most important distinguishing endoscopic criteria for IBD

- Aphthous ulcers, typical of CD (occasionally seen in other forms of IBD)
- Cobblestoning, characteristic of CD
- Small ulcers in diffusely inflamed mucosa, typical of UC
- Small to large, irregular ulceration in otherwise normal mucosa, typical of CD
- Granularity and friability (common in UC, less common in CD)
- Focal and asymmetrical distribution, typical in CD
- Continuous disease from the rectum extending proximally, typical of UC
- Distorted vascular pattern, typical of UC
- Granulomas from endoscopic biopsies, characteristic of CD (10-25% of patients)

from biopsies of completely normal mucosa. Routine upper gastrointestinal endoscopy with biopsies may be valuable in defining the diagnosis in cases of IC. Absence of specific upper gastrointestinal symptoms does not preclude the presence of upper gastrointestinal inflammation in CD.[25]

Use of endoscopy in the differential diagnosis of IBD from other disorders

Other diagnoses that are considered commonly in the differential diagnosis of IBD are ischaemic, radiation-induced, microscopic, infective, drug-induced and other colitides.

Ischaemic colitis is usually segmental and tends to affect the splenic flexure and descending colon area. On the other hand, there are cases of ischaemia affecting other segments of the colon including the caecum[34] or even the rectum, especially in the elderly.[35] Endoscopy can demonstrate the sharp transition between the almost pathognomonic violaceous hue of the ischaemic mucosa and the normal colonic mucosa. Additionally, submucosal nodules, oedema and bluish-black blebs are also diagnostic for ischaemia.[36] The distribution of the endoscopic features in the colon in addition with histological assessment helps clarifying the diagnosis in most cases.

Radiation proctitis can be confused with UC, but a history of prior radiation for prostatic or uterine cancer for example, even if temporally distant, helps the diagnosis. Non-steroidal anti-inflammatory drugs (NSAID), gold, methyldopa and penicillamine can occasionally cause a diffuse mild colitis. NSAID injury to the bowel may mimic IBD by causing discreet ulceration, diffuse changes and strictures.[37,38] Caution should be exercised in the case of patients with salicylate-induced colitis as the administration of 5-ASA drugs can make them worse.[39]

The endoscopic appearances of the mucosa and the histologic changes in infective and inflammatory colitis may be virtually indistinguishable. A third of patients presenting with mucoid bloody diarrhoea and suspected IBD have an infective aetiology.[40] To complicate matters, patients with IBD have the propensity for bacterial superinfection.[41] The most common enteric pathogens implicated are *Campylobacter, Salmonella, Shigella, Amoeba* and *Clostridium difficile*. In the majority of cases the history, presentation, serological tests and stool cultures help in the differentiation between infective colitides and IBD. In culture-negative patients with persistent symptoms endoscopic evaluation either with flexible sigmoidoscopy or full colonoscopy can be helpful.[42]

Endoscopic features favouring infection include yellow, tenacious exudates, luminal mucopus and intensely erythematous mucosa. In a study by Surawicz *et al*.[43] seven criteria were used to discriminate between infection and IBD. The features with a high predictive probability (87%-100%) of diagnosing idiopathic IBD were distorted crypt architecture, increased numbers of both round cells and neutrophils in the lamina propria, a villous surface, epithelioid granulomas, crypt atrophy, basal lymphoid aggregates and basally located isolated giant cells. One or more of these features were present in 79% of all idiopathic IBD cases and were seen in both acute and chronic cases. The authors concluded that the histological diagnosis of acute self-limited colitis is primarily based on the absence of histologic criteria favouring idiopathic IBD.

Tuberculosis of the terminal ileum and caecum can mimic CD. The presence of caseating granulomas or acid fast bacilli on biopsy specimens establishes the diagnosis of tuberculosis.[44] Endoscopic features suggestive of tuberculosis are mucosal nodules predominantly around the ileocaecal valve, pseudopolypoid folds, mucosal protuberance and destruction of the ileocaecal valve. Caseating granulomas may be difficult to identify due to their deep location; thus, their absence does not rule out tuberculosis.[44] Other infections that can cause terminal ileitis and confusion with CD include *Yersinia enterocolitica, Campylobacter, Shigella,* and *Salmonella*.

Pseudomembranous colitis may resemble IBD in some cases. Small areas of pseudomembranes can grossly look like the aphthous ulcers of CD. Usually a recent history of treatment with antibiotics and a positive toxin

assay for *Clostridium difficile* clarifies the diagnosis.

Assessment of extent and severity of IBD

Defining disease extent in IBD is important in choosing the appropriate medical and surgical therapy and in determining the cancer risk. Total colonoscopy with ileal intubation and mapping biopsies is the most important step in defining the disease extent and severity.

Ulcerative Colitis

Although the diagnosis of UC by colonoscopy is quite accurate in the majority of cases, obtaining biopsies at the time of endoscopy enhances the diagnostic yield. In patients with UC biopsies should be taken not only from the obviously affected area of the colon but also from the normal-appearing mucosa. This is useful in defining the true extent of the disease.[45] Pancolitis was diagnosed in twice as many patients examined with endoscopy as compared to double contrast barium enema and in three times as many patients by using histology.[16] Furthermore, in a prospective study by Kiesslich *et al*.,[46] the use of chromoendoscopy improved the accuracy of the diagnosis and the establishment of the extent and severity of the disease in patients with UC when compared with conventional colonoscopy.

There is an inter-observer variability in the description of mucosal changes in UC. Various endoscopic scores have been devised to describe the changes in UC (Table 2). An alternative and more reliable overall scoring system of severity can be based on a simple three-grade scale, i.e. normal pattern, moderate activity, severe activity.[47]

In severe UC the decision for surgical intervention is largely dependent on clinical criteria as set in the seminal paper of Edward and Truelove.[48] Surgery may be life saving in the deteriorating patient with UC. Triage may be more precisely defined by performing colonoscopy in patients on whom surgery is being contemplated. Careful colonoscopy with gentle insufflation can be performed safely in patients with acute severe colitis. No procedure associated increase in morbidity or mortality was observed.[49] Ulcer depth in severe UC is correlated with the need for surgery.[50] Carbonnel *et al.*[51] defined two groups of patients with acute colitis. In 85 patients with acute colitis, 46 patients had extensive deep ulcers at endoscopy. Forty-three had colectomy as a failure to respond to steroids (38 patients) or because of toxic megacolon (5 patients). In 42 out of the 43 patients there were deep ulcers extending to, or beyond the circular muscle layer on histology. The second group of 39 had moderate changes on endoscopy and 30 of these responded to medical therapies alone. Nine required surgery. Six of them had a colonoscopy prior to surgery. Severe colitis was seen in all 6 and deep ulceration reaching the circular muscle layer was found on subsequent pathological examination of the resected specimen.

Table 2. Endoscopic Grading of Ulcerative Colitis

Grade 0
Pale colonic mucosa with well-demarcated vessels.
Fine submucosal nodularity with nodules identifiable beneath the normal-coloured mucosa (in healed or resolving colitis).
Tertiary arborisation (neovascularisation of the terminal arterioles)
Grade I
Oedematous, erythematous, smooth and glistening mucosa with masking of the normal vascular pattern
Grade II
Oedematous, erythematous mucosa with a fine granular surface.
Sporadic areas of spontaneous mucosal haemorrhage (petechiae).
Friability to gently endoscopic pressure.
Grade III
Oedematous, erythematous, granular and friable mucosa with spontaneous haemorrhage and mucopus in the lumen.
Occasional mucosal ulceration.

(Adapted from Baron JH, Connell AM, Lennard-Jones JE: Variation between observers in describing mucosal appearances in proctocolitis. Br Med J 1964;1:89.)

In another retrospective study by Alemayehu *et al*.[49] twenty out of 34 patients with severe colitis did not have severe lesions on endoscopy despite resistance to 10 days of intravenous therapy. Medical therapy was continued and at 5 years 12 out of 17 patients had avoided colectomy and remained well. On the basis of the above evidence, it is recommended that patients with severe UC who do not seem to respond initially to medical therapy, colonoscopic assessment can help with decision making in terms of carrying on with medical means or proceeding to surgery.

Clinical remission may not be accompanied by complete endoscopic or histological remission.[52] The endoscopic response is seen in up to 75% of the patients but tends to lag behind the clinical response to therapy.

Crohn's Disease

The endoscopic evaluation of the extent and severity of CD has been problematic. Some of the reasons for this are the lack of a reliable endoscopic score, the inter-

observer variability in describing mucosal lesions, the transmural nature of the disease and the inability to visualise all the involved areas of the gut. The extent of CD in the intestine can be reliably assessed if the results from the endoscopic assessment are combined with radiological studies.

Push enteroscopy with a flexible 200cm enteroscope or the 160cm paediatric colonoscope can be used to examine the small bowel beyond the reach of the conventional gastroscope. This usually requires an overtube to reduce looping in the stomach. The overtube adds discomfort and an increased risk to the procedure and usually permits examination up to the mid-jejunum. Recently the double-balloon enteroscope appears to offer inspection of the small bowel in its entirety.[53] In addition biopsies can be obtained and therapeutic interventions applied, but its role in IBD remains to be assessed.

Lately, wireless capsule endoscopy (WCE) has been introduced in the evaluation of patients with CD of the small bowel. First results demonstrate WCE to have a high diagnostic yield in patients with suspected CD and to be superior to endoscopy, barium follow-through and CT enteroclysis.[54-56] WCE is contraindicated in patients with intestinal strictures as entrapment of the capsule in one of them may necessitate a laparotomy. For that reason most centres perform small bowel imaging prior to the use of WCE. Another method that is becoming popular in centres using WCE is the use of the so called "patency" capsule (Given Imaging Ltd - Yoqneam, Israel). This self-dissolving capsule that is the same size as the video capsule is taken by the patient initially and painless egestion of an intact patency capsule indicates safety of WCE. Recently, a useful study from Berlin[57] showed that patients without obstructive symptoms do not require either small-bowel radiography or a patency capsule study prior to WCE.

The clinical severity of CD is not dependent on the nature, extent or severity of the endoscopic lesions.[14] In a study by Mary and Modigliani in the GETAID group[58] using a quantitative endoscopic index of CD severity (CDEIS), there was no correlation between clinical activity and endoscopically demonstrated disease. In addition, it was shown that resistance to steroids cannot be predicted from the endoscopic findings.

Use of endoscopy in surveillance for neoplasia in IBD

Although colorectal cancer (CRC) complicating UC and CD, only accounts for 1-2% of all cases of CRC in the general population,[59] it is a serious complication and accounts for approximately 15% of all deaths in IBD patients.[60-62] There is a considerable variation in CRC incidence as reported through population-based studies. The magnitude of the risk of colon cancer for patients with IBD increases by 0.5-1.0% yearly, 8-10 years after diagnosis. When considering duration of the disease, it is important to remember that colitis may be present long before the day it was confirmed, and that 10% of the patients at the time of the index colonoscopy for surveillance may have dysplasia or cancer.[63,64] The CRC risk increases with early age of IBD diagnosis, longer duration of symptoms and extent of the disease.[61,65-67] The risk of CRC in patients with Crohn's colitis parallels that of UC if matched for duration and extent of disease.[68]

Although the majority of carcinomas in the general population develop through the adenoma-carcinoma sequence[69] in UC the carcinomas tend to develop without the transition through a mass lesion. The tumours instead tend to develop through a dysplasia-carcinoma sequence.[1]

Dysplasia is recognised as a group of histologic abnormalities that are neoplastic and include oedematous and villous alterations in the mucosa and cellular modifications including pleomorphism and stratification of hyperchromatic nuclei that have lost their normal polarity.[1] To simplify the diagnosis of dysplasia a scheme of dysplasia diagnoses that include negative, low-grade (LGD), high-grade (HGD) and indeterminate was devised.[70]

Endoscopically dysplastic foci present as flat lesions which may present as discoloured areas, velvety villous lesions or fine nodular thickening.[70] The dysplasia can also be associated with a visible polypoid-like mass. This kind of dysplasia is called Dysplasia Associated Lesion or Mass (DALM) and carries a sufficiently high risk for CRC, thereby constituting a strong indication for colectomy.[71] In the report by Blackstone *et al*.,[71] 12 out of 112 patients with long standing colitis were found to have a DALM. In 7 of these 12 cases carcinoma was subsequently found. In 5 of the 7 cases the DALM's where single and polypoid and all 5 contained carcinoma in situ. In only 2 of the 7 patients the dysplasia in the biopsies was graded as severe, in the other 5 only mild or moderate.

There has been no uniform approach to dysplasia surveillance in terms of number of biopsies or number of sites in published studies[63] and this has led to a lack of uniform approach in clinical practice.[72,73] Most surveillance programs start at 8-10 years from diagnosis.[74,75] One should pursue a full dysplasia-surveillance endoscopy be-

fore 8 years from diagnosis if there are additional risk factors like PSC or a first degree relative with CRC. Having a first-degree relative with CRC but unaffected by IBD increases the risk of cancer in the UC patient.[76] It is important therefore to enquire about a family history of CRC and to look for clues for PSC in all patients with IBD. A proposed approach for endoscopic surveillance in UC is illustrated in Table 3.

If the index surveillance colonoscopy is negative for dysplasia the incidence of developing dysplasia is estimated at around 3%.[63,72] Therefore after two consecutive negative dysplasia-surveillance colonoscopies one should extend the surveillance interval to every 3 years. At 20 years of disease the risk rises at a sharper rate and it is prudent to conduct surveillance endoscopies annually.[77]

It is recommended to biopsy the colon at 10cm intervals with 4 quadratic biopsies in each site. Biopsies should be labelled separately. It has been estimated that 33 biopsies are required to give 90% confidence in the detection of dysplasia if it is indeed present.[78] By increasing the number of biopsies to 63 the sensitivity increases to 95%.[79] More biopsies should be taken from the rectosigmoid colon since inflammation is more pronounced in this area and it tends to be the most common site of cancer presentation.

Table 3. Proposed Approach for Endoscopic Surveillance in UC

1. Begin surveillance at 8 years of disease onset
2. Take 4 biopsies from at least 9 sites throughout the colon, ensuring at least 4 sites from the rectum and sigmoid
3. If there is no endoscopic inflammation from mid or right colon, 2 biopsies may be sufficient in loci from these sites, unless it is known there is microscopic evidence of disease
4. If the biopsies are negative for dysplasia at the first surveillance, then repeat the endoscopic surveillance at 1 year, and then if negative, pursue repeat endoscopies every 3 years until 20 years of disease
5. At 20 years pursue dysplasia surveillance annually
6. If biopsies are indeterminate for dysplasia then maximise anti-inflammatory therapy and repeat the endoscopic surveillance in 3-6 months
7. Special circumstances: If patients have PSC or first-degree relative with sporadic colon cancer, consider endoscopic surveillance prior to 8 years of disease duration and consider a reduced interval between 9 and 20 years of disease progression

(Adapted from Berstein CN. Ulcerative Colitis With Low-Grade Dysplasia. Gastroenterology 2004;127:950-959)

Neoplasia in UC is significantly correlated with both histologic and endoscopic inflammation.[80] Macroscopically normal areas should be biopsied as well, possibly by taking two rather than four biopsies as this would determine the presence of microscopic involvement of the colon, which in turn would warrant increased sampling the next time surveillance is pursued. In a study by Mathy *et al*.,[81] it is emphasised that areas of non-inflamed mucosa in UC should be biopsied, as UC-related neoplasia can occur in areas of the colon not grossly involved with colitis.

The risk of CRC in patients with left-sided colitis is lower compared to patients with pancolitis.[82] The British Society of Gastroenterology recommends that the onset of surveillance starts at 15 years of disease in left-sided UC.[74] This would be valid if there was a way to evaluate the possibility of disease progression from the left side to beyond the splenic flexure. It is safer therefore to pursue a similar strategy regardless of the disease extent.[77] Patients with proctitis have not been shown to be at increased risk for CRC as compared to the general population.[83]

Some clinicians support enhanced surveillance for LGD until either HGD or a more advanced lesion is found. The discovery of LGD may create a false sense of security. There is a perceived sense that an evolution from LGD to HGD is a continuum. But when LGD is present, nearly 1 in 5 patients may have cancer.[63] Furthermore, it is well recognised that LGD is the only dysplasia found near frank colon cancer in UC in 50% of the cases.[84] Additionally, LGD has been shown to advance to HGD in 35-50% of patients by 5 years.[64, 85] For this reason, waiting on LGD makes little sense for the patient's best interest unless the patient is a poor surgical candidate. The key issue is to gain agreement that dysplasia is truly present by seeking a second opinion from a histopathologist with special interest in gastrointestinal pathology. The surgical options should then be discussed with the patient. Thirty to 50% of colectomy specimens from patients with UC and HGD harbour concomitant carcinoma hence the general agreement that this finding is an indication for colectomy.[63,64]

Although dysplasia in the rectum is associated with occurrence of neoplasia more proximally,[86] the practice of looking for dysplasia in the rectum as a reflection of dysplasia elsewhere in the colon has not been validated, since a significant number of patients with dysplasia proximally (up to 90%) may not have concomitant dysplasia in the rectum.[87]

As random colonic biopsies represent just a minute fraction of the entire mucosal surface, a considerable sampling error accompanies surveillance colonoscopy. The diagnostic yield for dysplasia increases by targeting mucosal irregularities.[88] Chromoendoscopy has been shown to detect more dysplastic lesions as compared to routine surveillance.[46,89] In addition, chromoendoscopy with indigo carmine, with or without high resolution endoscopy, may be useful in detecting small flat neoplasia.[89,90]

Use of endoscopy in the management of complications in IBD

Strictures

Benign strictures often complicate the course of IBD, mainly in patients with CD. The strictures are usually a result of circumferential fibrosis which is commonly associated with an inflammatory component. Strictures can be single or multiple and can be involving the small or large bowel or both. In UC they are most commonly seen in long-standing disease but they are also occasionally seen at an early stage.[3,91,92] Small bowel strictures in CD have a very low malignant potential in marked contrast with colonic strictures in both CD and UC.

Cancer in CD is often manifested as a stricture. In a cohort of 980 patients with colonic CD, 132 (13.5%) patients had one or more strictures. There was a tenfold increase in prevalence of malignancy in patients with strictures compared to those without (6.9% vs. 0.7%) so presence of a stricture in CD should raise the suspicion of cancer. With increasing duration of disease the percentage of strictures harbouring malignancy increased significantly from 3% in patients with disease duration of less than 20 years to 11% in patients with 20 or more years of disease. Compared to benign strictures, malignant strictures did not differ in presenting symptoms, duration of disease or mean age of onset of CD.[93]

In a series of 1156 patients with UC,[92] seventy strictures were found in 59 patients giving an incidence of 5%. The rate of malignancy in UC stricture group was 29%. The characteristic features of malignant strictures included long-standing disease, proximal location and obstructive symptoms. Mean duration of UC in benign strictures was 14.5 years compared to 25 years in the malignant group. Although left-sided strictures were more common (63 distal to splenic, 3 in transverse and 4 right-sided) the probability of malignancy was higher in proximal lesions. Obstructive symptoms were 100% predictive. The prevalence of malignant strictures varies in other studies. In the series of Hunt[94] only 12.5% of strictures were malignant whereas Grandquist[95] found no cancer in 14 patients with colonic strictures.

The endoscopic approach to a stricture should include the assessment of its appearance, its length and most importantly the acquisition of multiple targeted biopsies for histological assessment. Endoscopic features suggesting malignancy include rigidity of the edge, an eccentric lumen, an abrupt shelf-like margin and inability to intubate.[96] If the stricture is very tight and can not be negotiated with the smallest available calibre colonoscope after adequate insufflation and gentle pressure, the procedure should be abandoned and surgery advised. Forceful intubation may lead to perforation as the colonic wall is often thin and does not withstand longitudinal pressure force. [1]

Benign strictures can be dilated with 'through-the-scope' (TTS) balloons. The overall symptomatic success is around 60%.[97,98] Balloon dilatations of strictures can be accompanied by steroid injection to prevent or slow down recurrence.[99] In a recent series of 17 patients with CD, 29 stricture dilations were performed on 20 primary and anastomotic strictures with the TTS balloon with or without intralesional steroid injection. Long-term success was achieved in 76.5% patients with a complication rate of 10%. The conclusion from the study was that this mode of therapy appeared safe and effective and could be considered as an alternative to surgery in selected patients with medically refractory CD-associated strictures. Success rates were better in patients who received four quadrant steroid injections. No difference was seen in stricture recurrence rate or complications based on diameter of TTS balloon used.[100]

Bleeding

Although rectal bleeding is a common presenting feature in UC, acute major gastrointestinal bleeding is uncommon in IBD. Most cases of major gastrointestinal haemorrhage are due to CD, without a predilection for site of involvement. The presence of an endoscopically treatable lesion is uncommon. The role of endoscopy in this setting is more diagnostic especially if the diagnosis is not yet known at the time of presentation. In addition, identifying the segment of bowel that could account for the haemorrhage by using endoscopy, can be useful in planning surgical resection.[101]

New technologies

New emerging technologies such as chromoendoscopy with or without magnification endoscopy, immunoscopy and optical coherence tomography that are based on the interaction between the light and the mu-

cosal tissues give us information at a microscopic, cellular and biochemical level. Some of the new technologies may, in the future allow clinical decisions in real time and histologic interpretation without removing tissue.

For example, immunoscopy combines endoscopy and immunofluorescence and has shown some promising results in the detection of CRC in resection specimens.[102] Chromoendoscopy uses various stains to enhance mucosal detail and improve the diagnostic yield of video endoscopy. The main use of chromoendoscopy in IBD is in screening for dysplastic and neoplastic changes in long-standing IBD and to facilitate direct targeted biopsy acquisition. Methylene blue is useful in the detection of flat adenomas and carcinomas and in distinguishing hyperplastic from adenomatous polyps.[103] Indigo carmine dye highlights irregularities in the mucosal architecture as a result of pooling in mucosal crevices and depressed areas. The role of indigo carmine chromoendoscopy includes screening for neoplasia during surveillance colonoscopy, helping in differentiation between benign and malignant lesions and also in pit-pattern analysis using magnifying endoscopes.[104]

Endoscopic ultrasound of the rectum may aid the differential diagnosis between CD, UC and other conditions as mucosal or transmucosal inflammation can be identified.[105,106] There is also a role for it in the evaluation of perirectal and perianal complications of CD. In one study, EUS has been demonstrated to be superior to fistulography, CT and equal to or superior to MRI.[107]

Optical coherence tomography uses backscattered light to offer cross-section imaging in a high resolution (10-25 times higher than is obtained from high-frequency endoscopic ultrasound, computerised tomography and magnetic resonance imaging).[108] In an in vivo colonoscopic optical coherence tomography study of 40 patients with CD and 30 with UC, the disrupted layered structure of the bowel wall as seen with this modality, (indicative of transmural inflammation), had a diagnostic sensitivity of 90.0% (95% CI: 78.0%, 96.5%) for UC and specificity of 83.3% (95% CI: 67.3%, 93.3%) for CD.[109] Some of these technologies are at their infancy and further evaluation is necessary before their widespread use in clinical practice.

Conclusion

Endoscopy plays a crucial role in the initial diagnosis and subsequent management of patients with IBD by allowing detailed assessment of the extent, severity and complications of the condition and may be useful in the management of complications. A detailed endoscopic evaluation of the colon during surveillance in patients with long-standing IBD may potentially reduce the mortality from malignant complications. New endoscopic technologies represent a promising research field but require further evaluation and validation in clinical practice.

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