REVIEW

Gut and Liver, Vol. 1, No. 2, December 2007, pp. 118-125

Recent Advances of Endoscopy in Inflammatory Bowel Diseases

Jae Hee Cheon and Won Ho Kim

Department of Internal Medicine and Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Korea

Endoscopy plays a key role in the diagnosis and treatment in inflammatory bowel disease (IBD). The most valuable tool for distinguishing different types of IBD is a complete ileocolonoscopy with mucosal biopsy. Endoscopic localization of the disease not only aids in determining prognosis and appropriateness of medical therapies but also aids decision-making in those undergoing surgical therapy. With regard to therapeutic applications, obstructive symptoms caused by benign fibrotic strictures can be treated adequately by endoscopic balloon dilation. Epidemiological studies have demonstrated an increased risk of colorectal cancer in patients with both ulcerative colitis and colonic Crohn's disease (CD). Colonoscopy is currently considered to be the gold standard for cancer surveillance. Published guidelines recommend that two to four biopsy samples should be obtained every 10 cm in the colorectum, necessitating 20-50 samplings per examination. This may result in standard colonoscopy – which is also very time-consuming and laborious – missing significant numbers of small lesions. Various novel techniques have been applied to reduce the required number of biopsy samples and the duration of examinations, including chromoendoscopy with or without magnification, fluorescence endoscopy, narrow-band imaging, optical coherence tomography, and confocal laser endomicroscopy. Until recently the only way to evaluate the small-bowel mucosa in a patient with CD was by barium small-bowel radiographs and intubation of the distal terminal ileum. Both wireless-capsule endoscopy (WCE) and double-balloon enteroscopy (DBE) allow light to be used in the inspection of the small bowel and may replace radiological methods. WCE is more convenient than DBE for probing small-bowel mucosal changes, but only DBE allows a biopsy sample to be obtained from the deep small bowel, and these two examinations can be considered complementary. The wider application of new techniques in the near future might increase the role played by endoscopy in the management of IBD. **(Gut and Liver 2007;1:118-125)**

Key Words: Endoscopy; Inflammatory bowel disease; Ulcerative colitis; Crohn's disease

INTRODUCTION

Endoscopy plays a key role in the diagnosis and treatment in inflammatory bowel disease (IBD). Clear-cut indications for endoscopy in IBD are recognized as follows: a correct diagnosis, assessment of the disease activity and extension, therapeutic implications, and surveillance of dysplasia or cancer in patients with long-standing chronic colonic IBD.[1] Conventional colonoscopy with ileoscopy has been regarded as the only endoscopic method and the gold standard for IBD evaluation yet. However, the recently developed or developing new technologies can further improve colonoscopic diagnosis and treatment. Moreover, new endosopic diagnostic tools such as wireless capsule endoscoy (WCE) or double balloon enteroscopy (DBE) have been evolved to evaluate the entire small bowel.[2] This review will deal with the recent development in endoscopic techniques and tools and their updated roles as well as conventional endoscopy in IBD.

CONVENTIONAL COLONOSCOPY WITH ILEOSCOPY

1. Diagnosis

At initial presentation, it is important to make a correct diagnosis because treatment strategies differ for two different IBDs, i.e., Crohn's disease (CD) and ulcerative col-

Correspondence to: Won Ho Kim
Department of Internal Medicine, Yonsei University College of Medicine, 134, Sinchon-dong, Seodaemun-gu, Seoul 120-752, Korea
Tel: +82-2-2228-1950, Fax: +82-2-393-6884, E-mail: kimwonho@yuhs.ac
Received on December 6, 2007. Accepted on December 13, 2007.

itis (UC). The single most valuable tool for distinguishing the different forms of IBD is a complete ileocolonoscopy. In addition to direct inspection of mucosal patterns, mucosal biopsy is a critical component of endoscopic examination for patients with suspected IBD. Ileocolonoscopy was found to be accurate in 80-90% in differentiating UC from CD in a prospective study.[3]

Challenging and underestimated diagnostic problems are diagnosis of indeterminate colitis and differentiation of IBD from other intestinal disorders. IBD should be differentiated from other ileocolonic diseases resembling IBD. Unfortunately, despite careful history taking of patients even with various endoscopic and histologic findings, in some cases it might be difficult to distinguish enteric infections from IBD. In a prospective study investigating patients with acute mucoid bloody diarrhea, up to one third were found to have an infectious etiology.[4] Some of infectious diseases such as Salmonella, Shigella or Camphylobacter enterocolitis have endoscopic features similar with UC while other infections such as Yersinia or Cytomegalovirus (CMV) enterocolitis resemble CD. Superimposed infections on IBD by *Clostridium difficille* or CMV, make situations more complicated in some instances. Moreover, in endemic areas of tuberculosis, it is not an easy task to differentiate between CD and intestinal tuberculosis clinically, and somehow, even after histopathological examinations despite the fact that some of endosocpic characteristics of each disease are typical.[5] For example, direction of ulcer is usually longitudinal in CD, whereas transverse in tuberculosis. Sometimes a therapeutic trial with anti-tuberculous medications enables differentiation. A recent systematic analysis revealed that colonoscopic findings were very useful in the differential diagnosis between intestinal tuberculosis and CD.[6] In this study, professor Yang's group suggested a scoring system for differentiation and demonstrated that anorectal lesions, longitudinal as well as aphthous ulcers, and cobblestone appearance were parameters favoring CD, while localized involvement, patulous ileocecal valve, transverse ulcers, and scar or pseudopolyp were parameters favoring intestinal tuberculosis. Moreover, clinical features and histological parameters in colonoscopic mucosal biopsy specimens may be of value in differentiating between the two diseases.[7]

Over the years, use of the term indeterminate or intermediate colitis has broadened to include colonoscopic, radiographic, or histologic appearances that show an overlap of diagnostic criteria for UC and CD. Although ileocolonoscopic and histologic evaluation can differentiate between UC and CD in most cases, approximately 10% of patients have indeterminate colitis.[8] In this context, radiology, serologic testing (ASCA; anti-Saccharaomyces cerevisiae and ANCA; anti-neutrophil cytoplasmic antibody), and upper endoscopy combined with random biopsies for evaluating granuloma are recommended.[9] Although endoscopic ultrasonography had been initially recognized to be effective in differentiating between CD and UC, it is now considered to have a limited function in this setting.[10] Novel diagnostic tools as wells as conventional endoscopy are needed to positively identify this group. The role of WCE in indeterminate colitis will be discussed later.

Because of similar gastrointestinal symptoms and extra-intestinal manifestations, in addition to the presence of intestinal ulcers, differentiation between intestinal Behcet's disease and CD might be difficult in some cases. Typical endoscopic findings in intestinal Behcet's disease which is not a rare disease in Korea include single or a few, large, deep, round or oval ulcers with discrete margin in ileocecal area.[11] We have analyzed endoscopic characteristics of both diseases and found that not only involved segments but also several characteristic of ulcers including number, shape and depth, are also significantly dissimilar between the two diseases. From these findings, we have reported that a simple statistical method called classification and regression tree is useful for differentiation. By sequential application of two variables, i.e., ulcer shape and distribution of lesions, 92% of patients can be accurately diagnosed.[12]

2. Assessment of extent and severity of disease

Localization of disease aids in determining prognosis and appropriateness of medical therapies and helps to stratify risk of colon cancer. Moreover, it can help decision making in those undergoing surgical therapy. An accurate delineation of the affected location may be important for planning surgical interventions. However, the endoscopic appearance often underestimates the extent of disease in UC.[13,14] Thus, it is suggested by some authors that biopsy specimens should be taken from beyond the most proximal extent of endoscopic inflammation to define the proximal extent of disease.[15] With regard to CD, the utility of assessing the extent and severity of endoscopic disease has remained problematic. In the late 1980s, GETAID group developed a quantitative endoscopic index of severity (CDEIS) by dividing the bowel in to 5 segments and generating numeric score based on surface involvement by disease and the presence of deep or superficial ulcerations.[16] However, it was found that the endoscopic severity or extent was not correlated with Crohn's disease activity index (CDAI).[17]

3. Assessment of response to treatments and prediction of relapse

Clinical remission in active UC is associated with endoscopic and histologic remission in about 50-70% of patients. However, repeated endoscopy to assess mucosal healing generally is not recommended because there are few instances in which the endosopic findings would change management. Moreover, UC patients often report symptom flares after colonoscopy.[18] Clinicians should recognize this side-effect of colonoscopy in patients with UC. At present, there are no guidelines on when or how often to repeat the endoscopic evaluation in patients with improved or quiescent UC.[15] However, some of clinical trials require endoscopic assessments of severity in UC and several endoscopic severity criteria such as Baron classification are commonly used.[19]

It is well known that clinical symptoms are not correlated with endoscopic lesions and clinical remission is often discordant with mucosal healing in CD. In a prospective study assessing the value of colonoscopic monitoring in CD patients that achieved clinical remission with prednisolone, only 27% of these patients were in endoscopic remission.[20] Thus, it was suggested that endoscopic monitoring of patients with CD receiving corticosteroids is not beneficial. In contrast, a recent trial evaluating the efficacy of infliximab therapy in CD patients demonstrated that when significant mucosal healing was achieved with infliximab the time to relapse was significantly prolonged.[21] Endosopic appearances in CD might be a better predictor of the future clinical course than CDAI.

Although endoscopy plays an important role in evaluating postoperative recurrence in CD patients who have undergone prior bowel resections, routine postoperative endoscopic surveillance is often not indicated.

4. Therapeutic endoscopy for complications of IBD

Strictures may complicate CD, and to a lesser extent UC. Endoscopy is indicated for assessment and biopsy to exclude possible malignancy, especially in the setting of UC. Obstructive symptoms caused by benign fibrotic strictures can be treated adequately by using balloon dilation.[22,23] Corticosteroid injection into the stricture at the time of balloon dilation may improve outcome.[24] Gastrointestinal bleeding is another common complication of IBD. However, the presence of an endoscopically treatable lesion is uncommon and endoscopy plays more of a diagnostic and less of a therapeutic role in the management of bleeding.

5. Surveillance of dysplasia and colorectal cancer

Epidemiological studies have demonstrated an increased risk of colorectal cancer in patients with UC.[25] Moreover, it has been shown that the risk of cancer in CD involving colon is similar to that of UC. In general, there is an increased risk for colorectal cancer associated with younger age at onset of IBD, longer duration of colitits, and more extensive disease.[26] Currently, colonoscopy is considered to be the gold standard for surveillance of patients with IBD.[27] Indications may differ according to the extent and duration of disease. Because growth pattern of dysplastic lesions in UC is often multifocal and flat, published guidelines recommend that 2-4 biopsies should be taken every 10 cm in the colorectum, rendering 20-50 biopsies per examination.

Rubin et al. retrospectively reviewed database of 1339 surveillance colonoscopies in patients with UC at University of Chicago and found that surprisingly almost 2/3 of neoplastic lesions are visible by white light. Because most of neoplastic lesions in UC were endoscopically visible, they suggested modification of surveillance guideline.[28] Considering many problems, current recommendation is not only far from perfect and may miss significant numbers of small lesions but also very time-consuming and laborious. To overcome those problems, there have been many efforts to reduce biopsies taken and time of examinations through various novel techniques, which will be discussed later. Importantly, cancer surveillance in IBD patients should be optimally conducted in clinical remitted state to minimize the impact of inflammation on the examination.

NEW ENDOSCOPIC TECHNIQUES

1. Chromoendoscopy and magnifying endoscopy

Chromoendoscopy is a technique in which different dyes are topically applied to the gastrointestinal mucosa during endoscopy in order to better characterize and highlight specific changes in the mucosa.[29] Chromoendoscopy may not only increase the detection of mucosal lesions but may also help to predict neoplastic changes during the procedure. Endoscopists have mainly used indigocarmine and methylene blue and sometimes cresol violet for enhancing visualization. Although indigocarmine is often used to screen for sporadic adenoma due to convenience, methylene blue as an absorptive stain offers advantages in patients with UC due to its longer stable staining pattern. Magnifying endoscopy utilizes a movable lens controlled by the endoscopists to vary the degree of magnification, which ranges from $\times 1.5$ to $\times 150$.[30] The

techniques of chromoendoscopy and magnifying endoscopy are often used simultaneously to analyze surface structure. High resolution and magnification endoscopic systems can offer image quality that is significantly better than that of conventional endoscopy and have the ability to discriminate details. The glandular openings of adenomatous tissues can be seen and differentiated from surrounding normal mucosa. In this regard, Kudo et al. developed a classification system that divides colorectal lesions into 5 categories, which permits a prediction of the nature of the detected lesion. Types 1 and 2 are staining patterns that predict non-neoplastic lesions, whereas types 3 to 5 predict neoplastic lesions.[31] Many recent investigations have demonstrated the high efficiency of these techniques in detecting early colorectal neoplasia.[32,33] Moreover, they help to predict neoplastic changes during the endoscopic procedure.

In IBD settings, these techniques are being under investigations in two main objectives, i.e., early detection and prediction of premalignant lesions and early prediction of disease relapse and inflammation in quiescent or remission status. The first randomized controlled trial to test whether magnifying chromoendoscopy is capable of improving the early detection of intraepithelial neoplasia in patients with UC was published by Kiesslich R et al.[34] In their study, significantly more intraepithelial neoplasias were detected in the chromoendoscopy group than conventional group (32 *vs.* 10). These findings were further supported by Hurlstone DP et al. Early neoplasia in flat mucosal change was observed in 37 lesions, of which 31 were detected using chromoendoscopy.[35] Another trial also suggested that careful mucosal examination aided by pancolonic chromoendoscopy and targeted biopsies of suspicious lesions might be a more effective surveillance methodology than taking multiple non-targeted biopsies.[36] Based on these trials, chromoendoscopy is now incorporated into the US guidelines for surveillance in patients with long-standing UC.[37] Concerning the view of the prediction of histologic changes in UC, through a large prospective study using high-magnification chromoscopic colonoscopy, a good correlation was found between the Saitoh criteria for magnification imaging and Matts' histopathological criteria in patients with UC. Magnifying endoscopy was significantly better at predicting the extent of disease and histopathological grade than conventional endoscopy and the Baron scores of all parameters.[38] Moreover, Nishio et al. investigated the association of pit patterns as assessed by magnifying endoscopy with histological inflammation and mucosal chemokine activity in patients with quiescent UC.[39] In that study, magnifying endoscopic grading was associated the degree of histological inflammation and mucosal interleukin-8 activity.

2. Fluorescence endoscopy

Fluorescence endoscopy after 5-ALA sensitization is a possible method of visualizing dysplastic lesions in the colon that can also be used in patients with UC. By combining fluorescence with red and green reflectance, autofluorescence image (AFI) could be generated. Messmann et al. reported that the sensitivity of fluorescence for dysplastic lesions was high, ranging from 87% to 100% after local sensitization.[40] In contrast, because of low frequency of dysplasia, recent small-sized trial could not confirm the previous data about the efficacy of fluorescence endoscopy on the detection of dysplasia in patients with IBD.[41] However, 2 investigations presented in Digestive Disease Week 2007 reported that AFI showed the similar detection yield of dysplasia with smaller number of biopsies compared with conventional colonoscopy in UC surveillance, suggesting its efficacy.[42,43]

3. Narrow band imaging (NBI)

NBI is an innovative optical technology that can provide clear imaging of the microvascular structure in the mucosal layer. It illuminates the tissue surface through special filters that narrow the red, green, and blue bands with increased intensity of the blue band to enhance the tissue microvascular structure as a result of the differential optical absorption of light by hemoglobin.[44] The resulting images have the similar appearance of chromoendoscopy without dye. It has been reported that NBI and chromoendoscopy showed the same sensitivity and specificity to differentiate neoplastic from nonneoplastic lesions, and both techniques were superior to conventional colonoscopy.[45,46] However, in a recent prospective, randomized crossover study investigating the patients with UC, the sensitivity of the studied first generation NBI system was not superior to conventional colonoscopy in detecting patients with neoplasia.[47] The efficacy of NBI system in this setting should be further validated with newly introduced system.

4. Optical coherence tomography (OCT)

OCT is a new imaging modality, which is similar to B-scan ultrasound apart from its image formation, which relies on differences in optical (infrared light) rather than acoustic backscattering properties of tissue.[48] OCT provides images in real time with a resolution approaching that of conventional histopathology, but without the need for tissue removal. The spatial resolution of OCT is approximately 10 μm. Firstly, Shen et al. investigated the clinical value of optical coherence tomography for differ-

entiating between CD and UC. The disrupted layered structure on OCT, indicating transmural inflammation, had diagnostic sensitivity and specificity levels of 90.0% and 83.3%, respectively.[49] Moreover, in another recent trial, the in vivo OCT correctly detected disease features in endoscopically affected colon segments, but even in apparently normal segments of UC patients.[50] However, the resolution provided by the currently available OCT probes is still unsatisfactory. Improvements in both axial and lateral resolution are needed to further refine the diagnostic possibilities.

5. Confocal laser endomicroscopy

Recently, a miniatured confocal microscope integrated into the distal tip of a conventional endoscope was developed. This new confocal laser endomicroscopy allows subsurface analysis of the intestinal mucosa and in vivo histologic examination during ongoing endoscopy.[51] It has been shown that surface and subsurface analysis at cellular and subcellular resolutions can be used to predict mucosal neoplasias with high accuracy. However, this technique is not suitable for screening of the entire colonic surface in UC to predict neoplasias in flat mucosa because of the time required for examination of large surface areas. To overcome this problem, there has been a trial using chromoendoscopy-guided endomicroscopy to identify potential neoplastic lesions and to diagnose colitis-associated mucosal neoplasias in UC.[52] It was found that 4.75-fold more neoplasias could be detected ($p=.005$) than with conventional colonoscopy, although 50% fewer biopsy specimens ($p=.008$) were required by using chromoscopy with endomicroscopy. In addition, endomicroscopic analysis was highly sensitive and specific. Thus, endomicroscopy based on in vivo histology might determine whether UC lesions identified by chromoscopy should undergo biopsy examination, thereby increasing the diagnostic yield and reducing the need for biopsy examinations.

In the near future, these new techniques could be used as a multi-modality approach in time and labor effective surveillance. For example, fluorescence imaging could be used firstly for rapid detection of suspected lesion, followed by confocal endomicroscopy for detailed evaluation.

NEW ENDOSCOPIC TOOLS FOR SMALL BOWEL EVALUATION

1. Capsule endoscopy

Until recently the only way to evaluate the small bowel mucosa in a patient with CD was by barium small bowel radiographs and intubation of the distal terminal ileum. WCE is a sensitive way to evaluate the mucosa of the small intestine. Many prospective trials, including a multicenter study conducted by Korean capsule endoscopy study group, have shown the superiority of WCE over small bowel radiography for the evaluation of small bowel lesions.[53,54] Moreover, a recent meta-analysis of the yield of WCE compared to other diagnostic modalities in patients with non-stricturing small bowel CD.[55] WCE was superior to all other modalities for diagnosing non-stricturing small bowel CD, with a number needed to test (NNT) of 3 to yield one additional diagnosis of CD over small bowel barium radiography and NNT of 7 over colonoscopy with ileal intubation. Although there remains significant uncertainty regarding the role of capsule endoscopy in the setting of IBD, WCE is likely to be the most objective tool to evaluate the entire small bowel in patients who have CD. It is now under investigations to evaluate the efficacy of WCE in examining the extent of disease, unexplained symptoms, isolated colits, postoperative recurrence, and mucosal healing.[56] For the diagnosis of small bowel CD, standardized scoring index is necessary and a recently developed scoring index that utilizes parameters consisting of villous edema, ulceration, and stenosis is promising.[57] Although negative WCE does not exclude further diagnosis of CD, WCE might be a potentially clinically useful technique for categorizing a subgroup of patients with indeterminate colitis. Maunoury et al. reported that WCE could display endoscopic features suggestive for CD in 5 of 30 patients with indeterminate colitis.[58]

There is a controversy concerning the sensitivity of WCE in detecting recurrence in the neoterminal ileum.[59,60] Therefore, at present, it seems that WCE cannot replace ileocolonoscopy in the regular management of patients after surgery.

However, WCE should be used with caution in the setting of suspected or known CD because of the potential for capsule retention. In a retrospective study by Cheifetz et al., capsule retention occurred in 13% of patients with known CD.[61] Capsule retention could cause small bowel obstruction and/or lead to a need for surgery to remove the capsule in a patient who otherwise might have been treated medically. Small bowel radiology can not predict capsule retention, while patency capsule made with starch may reduce this serious side-effect.

2. Double balloon endoscopy

It is difficult to evaluate mucosal changes in the deep small bowel by radiographic examination. Both WCE and DBE allow light to be used in the inspection of entire small bowel and may replace previous radiological me-

thods. WCE is more convenient than DBE for probing small bowel mucosal changes, but only DBE allows a biopsy to be obtained, and these two examinations can be considered complementary. As expected, Oshtani et al. demonstrated superiority of DBE on radiological study in detecting minor lesions, such as aphthae, erosions, and small ulcers in the ileum.[62] DBE also enabled some therapeutic implications such as removal of the retended capsule in the stenosing segment of small bowel. However, DBE is a considerably invasive technique that could potentially induce serious complications such as perforation or hemorrhage in the setting of small bowel CD. It should be further validated for the appropriate selection of patients to avoid unnecessary DBE examinations.

CONCLUSION

The major indications for endoscopy in IBD are to establish the diagnosis, to differentiate between UC and CD, to define the extent and severity of disease activity, as well as to diagnose and manage complications. In this regard, conventional endoscopy is still essential, but recently developed or developing technologies may provide more rapid, more convenient, and more accurate diagnosis that leads to proper management.

REFERENCES

1. Leighton JA, Shen B, Baron TH, et al. ASGE guideline: endoscopy in the diagnosis and treatment of inflammatory bowel disease. Gastrointest Endosc 2006;63:558-565.
2. Mackalski BA, Bernstein CN. New diagnostic imaging tools for inflammatory bowel disease. Gut 2006;55:733-741.
3. Pera A, Bellando P, Caldera D, et al. Colonoscopy in inflammatory bowel disease. Diagnostic accuracy and proposal of an endoscopic score. Gastroenterology 1987;92: 181-185.
4. Tedesco FJ, Hardin RD, Harper RN, Edwards BH. Infectious colitis endoscopically simulating inflammatory bowel disease: a prospective evaluation. Gastrointest Endosc 1983;29:195-197.
5. Tandon HD, Prakash A. Pathology of intestinal tuberculosis and its distinction from Crohn's disease. Gut 1972;13:260-269.
6. Lee YJ, Yang SK, Byeon JS, et al. Analysis of colonoscopic findings in the differential diagnosis between intestinal tuberculosis and Crohn's disease. Endoscopy 2006;38:592-597.
7. Kirsch R, Pentecost M, Hall Pde M, Epstein DP, Watermeyer G, Friederich PW. Role of colonoscopic biopsy in distinguishing between Crohn's disease and intestinal tuberculosis. Clin Pathol 2006;59:840-844.
8. Tremaine WJ. Indeterminate colitis-definition, diagnosis and management. Aliment Pharmacol Ther 2007;25:13-17.
9. Alcantara M, Rodriguez R, Potenciano JL, Carrobles JL, Munoz C, Gomez R. Endoscopic and bioptic findings in the upper gastrointestinal tract in patients with Crohn's disease. Endoscopy 1993;25:282-286.
10. Lew RJ, Ginsberg GG. The role of endoscopic ultrasound in inflammatory bowel disease. Gastrointest Endosc Clin N Am 2002;12:561-571.
11. Lee CR, Kim WH, Cho YS, et al. Colonoscopic findings in intestinal Behcet's disease. Inflamm Bowel Dis 2001;7: 243-249.
12. Kim TI, Kim WH, Lee JH, et al. Diffrential diagnosis of intestinal Behcet's disease and Crohn's disease by colonoscopic findings. J Gastroenterol Hepatol 2001;16:30AB.
13. Floren CH, Benoni C, Willen R. Histologic and colonoscopic assessment of disease extension in ulcerative colitis. Scand J Gastroenterol 1987;22:459-462.
14. Yantiss RK. Odze RD. Pitfalls in the interpretation of nonneoplastic mucosal biopsies in inflammatory bowel disease. Am J Gastroenterol 2007;102:890-904.
15. Fefferman DS, Farrell RJ. Endoscopy in inflammatory bowel disease: indications, surveillance, and use in clinical practice. Clin Gastroenterol Hepatol 2005;3:11-24.
16. Modigliani R, Mary JY, Simon JF, et al. Clinical, biological, and endoscopic picture of attacks of Crohn's disease. Evolution on prednisolone. Groupe d'Etude Therapeutique des Affections Inflammatoires Digestives. Gastroenterology 1990;98:811-818.
17. Olaison G, Sjodahl R, Tagesson C. Glucocorticoid treatment in ileal Crohn's disease: relief of symptoms but not of endoscopically viewed inflammation. Gut 1990;31:325-328.
18. Menees S, Higgins P, Korsnes S, Elta G. Does colonoscopy cause increased ulcerative colitis symptoms? Inflamm Bowel Dis 2007;13:12-18.
19. Baron JH, Connell AM, Lennard-Jones JE. Variation between observers in describing mucosal appearances in proctocolitis. Br Med J 1964;5375:89-92.
20. Landi B, Anh TN, Cortot A, et al. Endoscopic monitoring of Crohn's disease treatment: a prospective, randomized clinical trial. The Groupe d'Etudes Therapeutiques des Affections Inflammatoires Digestives. Gastroenterology 1992; 102:1647-1653.
21. D'haens G, Van Deventer S, Van Hogezand R, et al. Endoscopic and histological healing with infliximab anti-tumor necrosis factor antibodies in Crohn's disease: A European multicenter trial. Gastroenterology 1999;116: 1029-1034.
22. Ajlouni Y, Iser JH, Gibson PR. Endoscopic balloon dilatation of intestinal strictures in Crohn's disease: safe alternative to surgery. J Gastroenterol Hepatol 2007;22:486-490.
23. Nomura E, Takagi S, Kikuchi T, et al. Efficacy and safety of endoscopic balloon dilation for Crohn's strictures. Dis Colon Rectum 2006;49(Suppl 10):S59-67.
24. Brooker JC, Beckett CG, Saunders BP, Benson MJ. Long-acting steroid injection after endoscopic dilation of anastomotic Crohn's strictures may improve the outcome: a retrospective case series. Endoscopy 2003;35:333-337.
25. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 2001;48: 526-535.
26. Gillen CD, Walmsley RS, Prior P, Andrews HA, Allan RN. Ulcerative colitis and Crohn's disease: a comparison of the

colorectal cancer risk in extensive colitis. Gut 1994;35: 1590-1592.
27. Collins PD, Mpofu C, Watson AJ, Rhodes JM. Strategies for detecting colon cancer and/or dysplasia in patients with inflammatory bowel disease. Cochrane Database Syst Rev 2006;2:CD000279.
28. Rubin DT, Rothe JA, Hetzel JT, Cohen RD, Hanauer SB. Are dysplasia and colorectal cancer endoscopically visible in patients with ulcerative colitis? Gastrointest Endosc 2007;65:998-1004.
29. Kiesslich R, Neurath MF. Chromoendoscopy and other novel imaging techniques. Gastroenterol Clin North Am 2006;35:605-619.
30. Nelson DB, Block KP, Bosco JJ, et al. High resolution and high-magnification endoscopy. Guidelines: Technology Status Evaluation Report. Gastrointest Endosc 2000;52: 864-866.
31. Kudo S, Tamura S, Nakajima T, Yamano H, Kusaka H, Watanabe H. Diagnosis of colorectal tumorous lesions by magnifying endoscopy. Gastrointest Endosc 1996;44:8-14.
32. Brooker JC, Saunders BP, Shah SG, et al. Total colonic dye-spray increases the detection of diminutive adenomas during routine colonoscopy: a randomized controlled trial. Gastrointest Endosc 2002;56:333-338.
33. Konishi K, Kaneko K, Kurahashi T, et al. A comparison of magnifying and nonmagnifying colonoscopy for diagnosis of colorectal polyps: a prospective study. Gastrointest Endosc 2003;57:48-53.
34. Kiesslich R, Fritsch J, Holtmann M, et al. Methylene blue-aided chromoendoscopy for the detection of intraepithelial neoplasia and colon cancer in ulcerative colitis. Gastroenterology 2003;124:880-888.
35. Hurlstone DP, McAlindon ME, Sanders DS, Koegh R, Lobo AJ, Cross SS. Further validation of high-magnification chromoscopic-colonoscopy for the detection of intraepithelial neoplasia and colon cancer in ulcerative colitis. Gastroenterology 2004;126:376-378.
36. Rutter MD, Saunders BP, Schofield G, Forbes A, Price AB, Talbot IC. Pancolonic indigo carmine dye spraying for the detection of dysplasia in ulcerative colitis. Gut 2004;53: 256-260.
37. Itzkowitz SH, Present DH; Crohn's and Colitis Foundation of America Colon Cancer in IBD Study Group. Consensus conference: Colorectal cancer screening and surveillance in inflammatory bowel disease. Inflamm Bowel Dis 2005;11: 314-321.
38. Hurlstone DP, Sanders DS, McAlindon ME, Thomson M, Cross SS. High-magnification chromoscopic colonoscopy in ulcerative colitis: a valid tool for in vivo optical biopsy and assessment of disease extent. Endoscopy 2006;38:1213-1217.
39. Nishio Y, Ando T, Maeda O, et al. Pit patterns in rectal mucosa assessed by magnifying colonoscope are predictive of relapse in patients with quiescent ulcerative colitis. Gut 2006;55:1768-1773.
40. Messmann H, Endlicher E, Freunek G, Rummele P, Scholmerich J, Knuchel R. Fluorescence endoscopy for the detection of low and high grade dysplasia in ulcerative colitis using systemic or local 5-aminolaevulinic acid sensitisation. Gut 2003;52:1003-1007.
41. Ochsenkuhn T, Tillack C, Stepp H, et al. Low frequency of colorectal dysplasia in patients with long-standing inflammatory bowel disease colitis: detection by fluorescence endoscopy. Endoscopy 2006;38:477-482.
42. Seaman DL, Gostout CJ, Smyrk TC, et al. Blinded comparison of white light surveillance colonoscopy to endoscopic autofluorescence and narrow band imaging for detection of dysplasia in patients with chronic ulcerative colitis. Gastrointest Endosc 2007;65:AB349.
43. van den Broek FJ, Hardwick JC, Reitsma JB, Stokkers PC, Fockens P, Dekker E. Endoscopic trimodality imaging for detection and classification of neoplsia in patients with longstanding ulcerative colitis. Gastrointest Endosc 2007; 65:AB256.
44. Kuznetsov K, Lambert R, Rey JF. Narrow-band imaging: potential and limitations. Endoscopy 2006;38:76-81.
45. Machida H, Sano Y, Hamamoto Y, et al. Narrow-band imaging in the diagnosis of colorectal mucosal lesions: a pilot study. Endoscopy 2004;36:1094-1098.
46. Watanabe K, Machida H, Kamata N, et al. The efficacy of surveillance colonoscopy for patients with ulcerative colitis associated cancer or dysplasia by using NBI as handy optical pancolonic chromoendoscopy. Gastrointest Endosc 2007; 65:AB333.
47. Dekker E, van den Broek FJ, Reitsma JB, et al. Narrow-band imaging compared with conventional colonoscopy for the detection of dysplasia in patients with longstanding ulcerative colitis. Endoscopy 2007;39:216-221.
48. Brand S, Poneros JM, Bouma BE, Tearney GJ, Compton CC, Nishioka NS. Optical coherence tomography in the gastrointestinal tract. Endoscopy 2000;32:796-803.
49. Shen B, Zuccaro G Jr, Gramlich TL, et al. In vivo colonoscopic optical coherence tomography for transmural inflammation in inflammatory bowel disease. Clin Gastroenterol Hepatol 2004;2:1080-1087.
50. Familiari L, Strangio G, Consolo P, et al. Optical coherence tomography evaluation of ulcerative colitis: the patterns and the comparison with histology. Am J Gastroenterol 2006;101:2833-2840.
51. Kiesslich R, Burg J, Vieth M, et al. Confocal laser endoscopy for diagnosing intraepithelial neoplasias and colorectal cancer in vivo. Gastroenterology 2004;127:706-713.
52. Kiesslich R, Goetz M, Lammersdorf K, et al. Chromoscopy-guided endomicroscopy increases the diagnostic yield of intraepithelial neoplasia in ulcerative colitis. Gastroenterology 2007;132:874-882.
53. Park CH, Kim JO, Choi MG, et al. Utility of capsule endoscopy for the classification of Crohn's disease: a multicenter study in Korea. Dig Dis Sci 2007;52:1405-1409.
54. Eliakim R, Fischer D, Suissa A, et al. Wireless capsule video endoscopy is a superior diagnostic tool in comparison to barium follow-through and computerized tomography in patients with suspected Crohn's disease. Eur J Gastroenterol Hepatol 2003;15:363-367.
55. Triester SL, Leighton JA, Leontiadis GI, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease. Am J Gastroenterol 2006;101:954-964.
56. Buchman AL, Miller FH, Wallin A, et al. Videocapsule endoscopy versus barium contrast studies for the diagnosis of Crohn's disease recurrence involving the small intestine.

Am J Gastroenterol 2004;99:2171-2177.
57. Gralnek IM, Defranchis R, Seidman E, Leighton JA, Legnani P, Lewis BS. Development of a capsule endoscopy scoring index for small bowel mucosal inflammatory change. Aliment Pharmacol Ther; Epub ahead of print.
58. Maunoury V, Savoye G, Bourreille A, et al. Value of wireless capsule endoscopy in patients with indeterminate colitis (inflammatory bowel disease type unclassified). Inflamm Bowel Dis 2007;13:152-155.
59. Bourreille A, Jarry M, D'Halluin PN, et al. Wireless capsule endoscopy versus ileocolonoscopy for the diagnosis of postoperative recurrence of Crohn's disease: a prospective study. Gut 2006;55:978-983.
60. Pons Beltran V, Nos P, Bastida G, et al. Evaluation of postsurgical recurrence in Crohn's disease: a new indication for capsule endoscopy? Gastrointest Endosc 2007; 66:533-540.
61. Cheifetz AS, Kornbluth AA, Legnani P, et al. The risk of retention of the capsule endoscope in patients with known or suspected Crohn's disease. Am J Gastroenterol 2006; 101:2218-2222.
62. Oshitani N, Yukawa T, Yamagami H, et al. Evaluation of deep small bowel involvement by double-balloon enteroscopy in Crohn's disease. Am J Gastroenterol 2006;101: 1484-1489.