

Role of wireless capsule endoscopy in the follow-up of inflammatory bowel disease

Ioannis V Mitselos, Dimitrios K Christodoulou, Konstantinos H Katsanos, Epameinondas V Tsianos

Ioannis V Mitselos, Dimitrios K Christodoulou, Konstantinos H Katsanos, Epameinondas V Tsianos, Department of Gastroenterology, University Hospital of Ioannina, Faculty of Medicine, School of Health Sciences, University of Ioannina, 45110 Ioannina, Greece

Author contributions: All authors contributed to this manuscript.

Conflict-of-interest: The authors declare that there are no conflicts of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Dimitrios K Christodoulou, MD, PhD, Associate Professor of Gastroenterology, Department of Gastroenterology, University Hospital of Ioannina, Faculty of Medicine, School of Health Sciences, University of Ioannina, PO Box 1186, 45110 Ioannina, Greece. dchristo@uoi.gr
Telephone: +30-26-51099618
Fax: +30-26-51007883

Received: October 27, 2014
Peer-review started: October 28, 2014
First decision: November 27, 2014
Revised: January 15, 2015
Accepted: February 9, 2015
Article in press: February 11, 2015
Published online: June 10, 2015

Abstract

The introduction of wireless capsule endoscopy in 2000 has revolutionized our ability to visualize parts of the small bowel mucosa classically unreachable by the conventional endoscope, and since the recent

introduction of colon capsule endoscopy, a promising alternative method has been available for the evaluation of large bowel mucosa. The advantages of wireless capsule endoscopy include its non-invasive character and its ability to visualize proximal and distal parts of the intestine, while important disadvantages include the procedure's inability of tissue sampling and significant incompleteness rate. Its greatest limitation is the prohibited use in cases of known or suspected stenosis of the intestinal lumen due to high risk of retention. Wireless capsule endoscopy plays an important role in the early recognition of recurrence, on Crohn's disease patients who have undergone ileocolonic resection for the treatment of Crohn's disease complications, and in patients' management and therapeutic strategy planning, before obvious clinical and laboratory relapse. Although capsule endoscopy cannot replace traditional endoscopy, it offers valuable information on the evaluation of intestinal disease and has a significant impact on disease reclassification of patients with a previous diagnosis of ulcerative colitis or inflammatory bowel disease unclassified/indeterminate colitis. Moreover, it may serve as an effective alternative where colonoscopy is contraindicated and in cases with incomplete colonoscopy studies. The use of patency capsule maximizes safety and is advocated in cases of suspected small or large bowel stenosis.

Key words: Small bowel capsule endoscopy; Colon capsule endoscopy; Crohn's disease; Ulcerative colitis; Indeterminate colitis; Postoperative; Ileal pouch-anal anastomosis; Refractory pouchitis

© **The Author(s) 2015.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Wireless capsule endoscopy is a valuable diagnostic tool for the evaluation of lesions located on the small intestine and large bowel mucosa since the recent introduction of colon capsule endoscopy. It plays an important role in the early recognition of recurrence on postsurgical Crohn's disease patients, offers valuable

information on the evaluation of intestinal disease, and aids significantly in patient management, treatment tailoring and disease reclassification in patients with a previous diagnosis of ulcerative or indeterminate colitis. Patency capsule maximizes safety and is advocated in suspected small or large bowel stenosis.

Mitselos IV, Christodoulou DK, Katsanos KH, Tsianos EV. Role of wireless capsule endoscopy in the follow-up of inflammatory bowel disease. *World J Gastrointest Endosc* 2015; 7(6): 643-651 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v7/i6/643.htm> DOI: <http://dx.doi.org/10.4253/wjge.v7.i6.643>

INTRODUCTION

The follow-up of patients with known inflammatory bowel disease consists in close disease monitoring for the maintenance of clinical remission, early detection of biochemical or clinical relapse and early recognition, as well as prevention, of disease and treatment related complications. Since various studies^[1-4] have provided strong evidence that the inflammation of the intestinal mucosa is not firmly associated with patients' symptoms and laboratory markers of inflammation, the treatment goal has evolved to a new concept, the achievement and maintenance of deep remission. Its definition includes the concurrent abatement of symptoms, a score < 150 as measured with Crohn's Disease Activity Index (CDAI), mucosal healing, a term referring to the endoscopic restoration of normal mucosal appearance of a previously inflamed region and the complete absence of ulceration as well as macroscopic and histological signs of inflammation^[5], and diminution of inflammatory markers. In the absence of a consensus on mucosal healing definition in ulcerative colitis patients, this could involve the disease's clinical and endoscopic remission^[6-8]. In Crohn's disease patients, deep remission is associated with a better health-related quality of life and minimization of disease related complications requiring hospitalization or surgery^[6].

Despite its invasive character, colonoscopy is considered the gold standard method for the evaluation of intestinal mucosa lesions as it provides accurate assessment of disease extension and localization, offering the ability of tissue sampling of abnormal mucosal segments. By contrast to colonoscopy, the introduction of wireless capsule endoscopy in 2000^[9], a non-invasive well-tolerated diagnostic method, allowed the visualization of parts of the small intestine beyond the reach of conventional endoscopes and also the large bowel mucosa, since the recent introduction of wireless colon capsule endoscopy. Current research does not support the use of colon capsule endoscopy over colonoscopy for the evaluation of mucosal healing and disease activity^[10] although results of a recent study^[11] demonstrate that colon capsule endoscopy findings can result in changes of the initial diagnosis, in favor of Crohn's disease. The aim of this review is to

evaluate the importance of wireless capsule endoscopy in mucosal healing assessment, treatment management and disease reclassification of inflammatory disease patients, their follow-up in the post-operative period, as well as to highlight its possible future roles.

CAPSULE ENDOSCOPY: BENEFITS, DRAWBACKS, LIMITATIONS AND SAFETY

Capsule endoscopy is a non-invasive, well-tolerated method, allowing direct visualization of the small bowel mucosa and having a significant higher diagnostic yield compared to other diagnostic methods^[12].

Its main disadvantages (Table 1) are the procedure's higher cost compared to other modalities, the inability of tissue sampling, the significant incompleteness rate which in several trials^[13-15] is reported to range from 15% to 30%, the risk of aspiration and the risk of capsule retention, which in Crohn's disease patients is estimated to be 2.6%^[15] and may require surgery for the removal of the retained capsule.

The use of capsule endoscopy is contraindicated in patients with known stricturing or obstructing disease and in selected cases, radiology may still be necessary to exclude the presence of strictures. It is considered to be a safe technique^[16] and the administration of a dissolvable patency capsule to patients with suspected strictures prior to the procedure, provides adequate assessment of the gastrointestinal patency and maximizes safety^[17,18]. In cases of known gastroparesis or in patients unable of swallowing, the videocapsule can be administered endoscopically. The relative contraindication of wireless capsule administration in patients with electromedical devices is in question, as according to recent research^[19] it is considered safe.

CAPSULE ENDOSCOPY SCORING INDEXES FOR THE ASSESMENT OF MUCOSAL INFLAMMATION

In an effort to maximize objectivity on the interpretation of small bowel capsule endoscopy findings and the need of a common language to report severity of small bowel inflammation, two diagnostic scoring systems have been developed, Lewis score (LS) and Capsule Endoscopy Crohn's Disease activity Index (CECDAI).

Developed by Gralnek *et al*^[20] in 2008, LS^[20], an incorporated feature of Given's Rapid Reader software, offers a quantitative assessment of inflammation severity using the Capsule Endoscopy Structured Terminology^[21] for the description of lesions and a grading system for the assessment of inflammation severity. Capsule transit time is used to divide the small bowel in three tertiles and based on the severity of 3 endoscopic variables - villous edema, ulcers and stenosis - each tertile score is calculated individually. The final score ranges from 8 to 4800 points and is the sum of the tertile with the

Table 1 Advantages and disadvantages of wireless capsule endoscopy

Advantages
Non-invasive well-tolerated method
Allows direct visualization of distal and proximal parts of the small bowel (SBCE) and large bowel mucosa (CCE)
Disadvantages
High cost compared to other modalities
Inability of tissue sampling
Significant incompleteness rate (15%-30%)
Risk of capsule retention (2.6%)
Risk of aspiration

SBCE: Small bowel capsule endoscopy; CCE: Colon capsule endoscopy.

greatest score added to the stenosis score. A score below 135 points represents a normal appearing mucosa or clinically insignificant findings.

CECDAI, a quantitative method developed by Gal *et al*^[22] in 2008, employs the variables of inflammation, extent of disease and the presence of strictures as well as a grading system for the assessment severity. Small bowel is divided in proximal and distal segments after the midpoint determination with the use of small bowel transit time. Segmental scores are gauged separately by multiplying the inflammation score by the extent-of-disease score and adding the stricture score. The sum of segmental scores represents the final CECDAI score. Both scores should be interpreted with regard to the patient's history, as they cannot identify the underlying reason of mucosal inflammation. The use of LS and Capsule Endoscopy Crohn's Disease Activity Index is advocated, as they provide an objective non-invasive method for the evaluation of small bowel inflammation and follow up of Crohn's disease^[22-24] and correlate closely with highly sensitive markers of intestinal inflammation such as fecal calprotectin^[25], a protein released from neutrophils and inflamed mucosa. Fecal calprotectin is not able to determinate the cause of intestinal inflammation, however fecal calprotectin levels are demonstrated to correlate closely with intestinal inflammation^[26-29] and are proved to be a valuable selection tool prior to capsule endoscopy studies as despite the presence of symptoms, patients with fecal calprotectin levels between 50 and 100 µg/g, are shown to have negative for findings studies^[30].

THE ROLE OF WIRELESS CAPSULE ENDOSCOPY IN THE ASSESSMENT OF MUCOSAL HEALING AND TREATMENT TAILORING

Clinical remission is not strongly associated with the diminution of inflammatory markers^[4] although C-reactive protein (CRP) is demonstrated to be a useful marker in the evaluation of moderate to severe Crohn's disease^[31]. Moreover, clinical and laboratory improvement of patients under treatment is

not associated with mucosal healing^[31]. Patients continue to have small bowel aphthous ulcerations in video capsule endoscopy studies (Table 2) one month after clinical remission and it is estimated that approximately 6 mo are necessary for the complete endoscopic restoration of small bowel mucosa^[4,32]. In a multicenter prospective study^[3] including 40 patients with known or suspected non-stricturing, non-penetrating Crohn's disease, only one third of the patients who achieved clinical response improved their endoscopic image in capsule endoscopy studies. A cohort of 43 patients with symptomatic small bowel Crohn's disease, under biologic or immunomodulatory treatment, evaluated mucosal healing and deep remission rate on baseline and after 12 and 52 wk on treatment^[1,33]. Their baseline demographics, quality-of-life questionnaires, Harvey-Bradshaw index, CRP and fecal calprotectin levels were collected and Capsule Endoscopy Crohn's Disease Activity Index was used to assess ileitis severity. Active small bowel Crohn's disease was present in 39 patients (90%) on baseline and 28 patients (65%) had an endoscopic re-assessment during week 52. Despite the clinical and biochemical improvement, no patient achieved complete mucosal healing on week 12^[1]. Twelve patients achieved deep remission on week 52 (42%)^[33]. The correlation between capsule endoscopy findings, clinical symptoms (Crohn's Disease Activity Index and Inflammatory Bowel Disease Questionnaire) and laboratory markers of inflammation (CRP) was evaluated in 19 patients with known, moderately active Crohn's disease under treatment^[2]. All patients had a proven functional patency to minimize the risk of capsule retention, and small bowel capsule endoscopy studies at baseline, after 4, 12 and 24 wk on treatment. Mucosal inflammation was evaluated with the use of LS. At baseline, no correlation was found between clinical symptoms, markers of inflammation and LS, and capsule endoscopy findings were not associated with patients' symptoms on 4 and 12 wk of treatment, leading to the conclusion that capsule endoscopy is a reliable, independent and objective diagnostic modality for the assessment of mucosal healing and response to therapy, and on the prognosis of prolonged clinical disease remission^[32]. In addition, data obtained of two recent retrospective studies^[34,35] indicate that capsule endoscopy findings assist on decision making, treatment changes or initiation of new pharmaceutical agents, in a significant proportion of inflammatory bowel disease patients.

THE ROLE OF WIRELESS CAPSULE ENDOSCOPY IN THE POSTOPERATIVE PERIOD OF INFLAMMATORY BOWEL DISEASE PATIENTS

Recurrence

The introduction of biologic therapy for the treatment of inflammatory bowel disease did not eliminate

Table 2 Key studies describing the role of wireless capsule endoscopy on the assessment of mucosal healing in Crohn's disease patients under treatment

Ref.	Treatment	Indication	Patients (n)	Conclusion
CD Niv <i>et al</i> ^[2]	Yes	SB mucosa evaluation of known CD patients	19	Mucosal findings are independent from clinical and laboratory parameters
CD Hall <i>et al</i> ^[11]	Yes	SB mucosal healing and deep remission rates assessment on 12 wk of treatment of known symptomatic CD patients	43	Symptomatic and biochemical response to treatment is not mirrored by mucosal healing
CD Hall <i>et al</i> ^[33]	Yes	SB mucosal healing and deep remission rates assessment on 52 wk of treatment of known symptomatic CD patients	43	Symptomatic and biochemical response to treatment appears to be mirrored by endoscopic remission in 42% of individuals
CD Efthymiou <i>et al</i> ^[3]	Yes	SB mucosal healing assessment of known symptomatic CD patients	40	Clinical response does not correlate closely with mucosal healing in patients with CD of the small bowel
CD Tsibouris <i>et al</i> ^[32]	Yes	Assessment of detection rate of small bowel ulcerative lesions and completion rate in CD patients in acute phase and remission	102	SB aphthous ulcers are present a month after entering clinical remission

CD: Crohn's disease; SB: Small bowel; CRP: C-reactive protein.

the need for surgical intervention^[36-40]. Eventually, 20%-30% of ulcerative colitis patients^[41,42] and up to 75% of Crohn's disease patients^[43], will require surgery for the management of uncontrolled inflammatory bowel disease and disease related complications. A common and undesirable postsurgical outcome is the development of disease recurrence. In Crohn's disease patients, recurrence rate increases with time^[44] and is demonstrated to be higher in smokers^[45], patients with ileocolonic involvement^[46], perforating disease^[47] and 5-ASA-treated patients with end-to-end anastomosis^[44]. The introduction of Rutgeerts endoscopic scoring system^[48] has provided a valuable modality for the quantified assessment of postoperative recurrence of the ileocolonic anastomosis or neoterminal ileum, and a valuable prognostic tool of Crohn's disease recurrence^[48-50], since endoscopic recurrence precedes the development of symptoms^[48] and does not correlate with CDAI^[51]. The follow-up of postoperative patients is directed towards recognition of endoscopic recurrence (Table 3), as severe endoscopic recurrence rate is estimated at 50.2% (95%CI: 28-73; range: 30-79) and early identification and initiation of treatment may prevent clinical recurrence^[52,53].

In a prospective study of 22 Crohn's disease patients, capsule endoscopy was reported to have comparable results with other noninvasive tests on the detection of recurrence^[54]. Moreover, based on the results of a prospective study^[55] including 35 patients who had undergone ileocolonic or partial ileal resection, wireless capsule endoscopy was not shown to be superior to ileocolonoscopy for the detection of recurrence on the neoterminal ileus although it enabled the visualization of lesions beyond colonoscope's reach in two out of three patients and aided significantly in the detection of recurrence in two patients missed by ileocolonoscopy. However, capsule endoscopy was the diagnostic modality preferred by patients in a small prospective study^[56] including 24, symptom-free Crohn's disease patients under no prophylactic

treatment, who had undergone ileocolonic anastomosis. In the same study, the authors concluded that capsule endoscopy was more effective in the detection of a significant number of Crohn's disease recurrence missed by colonoscopy and an effective diagnostic alternative for the visualization of the neoterminal ileum of patients with incomplete colonoscopy studies. Current research supports the use of baseline capsule endoscopy, shortly after the resection, for the detection of true cases of recurrence, as many ulcerations near the anastomotic site are formed due to factors related to surgery, such as disturbed blood flow and sutures^[57], but its preoperative use is reported to be of little value for the prognosis of recurrence^[58]. The use of wireless capsule endoscopy in suspected or known luminal stenosis is contraindicated^[54,57].

Anemia

Based on the results of a small study of 17 ulcerative colitis patients with ileal pouches and persistent iron deficiency anemia^[59], the authors concluded that wireless capsule endoscopy is a well-tolerated procedure to provide additional information on the reason of anemia. Patients with persistent anemia, 12 mo after ileal pouch-anal anastomosis (IPAA) or continent ileostomy, were evaluated with upper gastrointestinal endoscopy, pouch endoscopy and videocapsule endoscopy, and they had laboratory screening to exclude celiac disease. The reason of anemia was identified in 5 patients (29.4%). In one patient, arterio-venous malformations of the small bowel were only recognized by capsule endoscopy.

Pouchitis in patients with IPAA

Surgical removal of the colon and rectum with the creation of an artificial pouch, the IPAA, may be the only treatment option for ulcerative colitis patients with medically uncontrolled disease, who are unwilling to receive immunomodulatory or biologic therapy, or suffering from severe disease complications.

Table 3 Key studies on the role of wireless capsule endoscopy on postoperative Crohn's disease recurrence

Patient group	Ref.	No. of patients	WCE findings/(n)	Ileocolonoscopy findings/(n)
CD	Bourreille <i>et al</i> ^[55]	32	21/(32)	19/(32)
CD	Pons Beltrán <i>et al</i> ^[56]	24	15/(22)	6/(19)
CD	Biancone <i>et al</i> ^[54]	22	16/(17)	21/(22)
CD	Kono <i>et al</i> ^[57]	19	14/(18)	NA

CD: Crohn's disease; WCE: Wireless capsule endoscopy; WCE findings: Number of patients with findings on WCE; WCE (n): Total number of patients who had undergone WCE; Ileocolonoscopy findings: Number of patients with findings on ileocolonoscopy; Ileocolonoscopy (n): Total number of patients who had undergone ileocolonoscopy; NA: Not available.

Pouchitis is the most common complication, with a cumulative probability of nearly 50% ten years after IPAA performed^[60] requiring investigation for the recognition of the underlying cause.

Results based on trials of ulcerative colitis patients with IPAA and symptomatic pouchitis^[35,61,62] (Table 4), support the use of capsule endoscopy for the evaluation of small bowel mucosa on the suspicion of Crohn's disease and on differentiating intermediate colitis.

THE ROLE OF WIRELESS CAPSULE ENDOSCOPY ON DISEASE RECLASSIFICATION

Inflammatory bowel disease patients may undergo multiple imaging studies, endoscopic procedures and biopsies before reaching a definitive Crohn's disease or ulcerative colitis diagnosis, while 10%-15% of patients will remain unclassified^[63]. Capsule endoscopy has become an important tool for the reclassification of disease (Table 5) in patients with an initial diagnosis of ulcerative colitis or inflammatory bowel disease unclassified/indeterminate colitis. The importance of wireless capsule endoscopy in the diagnostic workup of inflammatory bowel disease was demonstrated in a recent study of 23 known ulcerative colitis patients^[64] where small bowel lesions (13 patients, 57%) and erosions (8 patients, 35%) were identified in the majority of them.

Corresponding results from the initial experience with small bowel capsule endoscopy^[65] have demonstrated that the identification of small bowel lesions by wireless capsule in patients with isolated colitis, lead to further investigation with ileocolonoscopy with biopsies, and a change of diagnosis in favor of Crohn's disease. In a retrospective trial^[62] including 120 patients with known ulcerative colitis or indeterminate colitis undergone capsule endoscopy, 19 patients (15.8%) had findings suggestive of small bowel Crohn's disease involvement. Interestingly, patients with the highest proportion of small bowel disease were those with a history of colectomy (7 out of 21 patients, 33%) compared to the patients who did not undergo colectomy (12

Table 4 Key studies on the role of wireless capsule endoscopy on pouchitis patients

Patient group	Ref.	No. of patients	WCE findings/(n)	CD reclassification
UC (IPAA)	Calabrese <i>et al</i> ^[61]	16	15/(15)	None
UC (IPAA)	Mehdizadeh <i>et al</i> ^[62]	21	7/(21)	7
UC (IPAA)	Long <i>et al</i> ^[35]	23	13/(23)	3

UC: Ulcerative colitis; IPAA: Ileal pouch-anal anastomosis; WCE findings: Number of patients with findings on WCE; WCE (n): Total number of patients who had undergone WCE; CD: Crohn's disease; WCE: Wireless capsule endoscopy.

out of 99 patients/12%), indicating the importance of capsule endoscopy studies prior to colectomy in ulcerative colitis patients. Similarly, data obtained from a study of 30 inflammatory bowel disease unclassified patients with negative serology^[66] showed that wireless capsule endoscopy findings resulted in disease reclassification in favor of Crohn's disease in five of them. Another significant conclusion of this study was that negative for findings capsule endoscopy studies, do not exclude small bowel Crohn's disease, as further investigation with ileocolonoscopy and biopsies in six patients led to a diagnosis of Crohn's disease in five patients and ulcerative colitis in one patient. In two studies that enrolled pediatric patients^[67,68] capsule endoscopy resulted in reclassification of more than half of the ulcerative colitis, inflammatory bowel disease unclassified/indeterminate colitis patients to Crohn's disease.

POSSIBLE FUTURE INDICATIONS OF WIRELESS CAPSULE ENDOSCOPY IN THE FOLLOW UP OF INFLAMMATORY BOWEL DISEASE PATIENTS

Research on the prognostic value of mucosal healing on treatment response^[69-72], has shown that assessment of mucosal healing on certain time points can predict the likelihood of prolonged deep remission. The data of 127 patients^[73] who had participated in the SONIC trial, were used to estimate the prognostic value of ileocolonoscopy findings on treatment response. Patients Simple Endoscopic Score for Crohn's Disease and the Crohn's Disease Endoscopic Index of Severity were calculated on baseline, after week 26 and week 50. Namely, the endoscopic response and mucosal healing in week 26 identified the patients who would be on corticosteroid-free clinical remission on week 50. The study's results provided confirmatory evidence that assessment of mucosal healing in certain time points during therapy has a significant prognostic value on the response of treatment.

Growing evidence^[74-76] in the corresponding literature, indicate the strong association between disease location and disease complications. Patients with ileal

Table 5 Key studies evaluating the role of wireless capsule endoscopy on disease reclassification

Patient group	Ref.	No. of patients	SB findings of inflammation	Reclassified to CD
UC/IC	Gralnek <i>et al</i> ^[68]	4	2	2
UC	Higurashi <i>et al</i> ^[64]	23	13	None
UC/IC	Cohen <i>et al</i> ^[67]	7	5	5
UC/IBDU	Mehdizadeh <i>et al</i> ^[62]	120	19	NA
IBDU	Maunoury <i>et al</i> ^[66]	30	5	5
UC/IC	Mow <i>et al</i> ^[65]	21	12	5

UC: Ulcerative colitis; IC: Indeterminate colitis; IBDU: Inflammatory bowel disease unclassified; SB: Small bowel; CD: Crohn's disease; NA: Not available.

Crohn's disease were shown to have a greater risk of stricturing and penetrating disease development as well as disease progression compared to those with colonic involvement.

There is no supporting evidence for the use of wireless capsule endoscopy on treatment response, on risk stratification and as a prognostic tool for prolonged remission, but given videocapsule endoscopy's non invasive nature and the advantage of detailed imaging of the entire small intestine, it could be a promising tool towards this direction.

Wireless capsule endoscopy could play an important role in the early detection of ulcerative colitis related panenteritis^[77], a new and rare entity related to colectomy which typically occurs after colectomy, and its histological picture is not compatible with Crohn's disease. In a small case series of 6 patients^[78], the use of ileocolonoscopy identified ulcerative colitis related panenteritis findings in 5 patients, resulting in treatment step-up and clinical improvement. One patient had to be evaluated with capsule endoscopy to confirm small bowel mucosa inflammation leading to the conclusion that video capsule endoscopy could offer an alternative method for the early detection of this rare complication.

CONCLUSION

Wireless capsule endoscopy is a valuable, non-invasive tool for the follow-up of inflammatory bowel disease, offering direct and detailed visualization of the entire intestine. Even though it cannot replace the role of traditional endoscopy, its use is advocated when there is high suspicion of small bowel disease involvement and as an alternative method in incomplete colonoscopy studies or when colonoscopy is contraindicated. Wireless capsule endoscopy's important disadvantages comprise the inability of tissue sampling and the limited, or in selected cases, prohibited application on patients with known stenosis or obstruction of the intestinal lumen, due to the high risk of capsule retention. Unnecessary capsule endoscopy studies can be avoided with the use of fecal calprotectin levels to identify patients who will probably not benefit from the procedure, and the use of patency capsule to identify patients that are

likely to experience capsule retention. Lewis Score and Capsule Endoscopy Crohn's Disease Activity Index are validated, objective and reliable scoring systems developed to minimize interobserver agreement and provide a standardized reporting system of small-bowel inflammation. Assessment of mucosal inflammation has a positive impact on treatment tailoring and is proven to be a reliable prognostic tool for disease remission. Videocapsule endoscopy studies in the postoperative period of ulcerative colitis and inflammatory bowel disease unclassified/indeterminate colitis patients provide valuable information on the differential diagnosis of Crohn's disease as well as postoperative complications, and can aid significantly in the early recognition of recurrence for the timely initiation of immunomodulatory or biologic treatment, before obvious clinical and laboratory relapse. Wireless Capsule endoscopy may have potentially significant roles in the prognosis of treatment response as well as the occurrence of potential complications and the early diagnosis of ulcerative colitis related panenteritis, a recently described rare entity, affecting patients with ulcerative colitis after colectomy.

REFERENCES

- Hall BJ, Holleran GE, Smith SM, Mahmud N, McNamara DA. A prospective 12-week mucosal healing assessment of small bowel Crohn's disease as detected by capsule endoscopy. *Eur J Gastroenterol Hepatol* 2014; **26**: 1253-1259 [PMID: 25264865 DOI: 10.1097/MEG.000000000000194]
- Niv E, Fishman S, Kachman H, Arnon R, Dotan I. Sequential capsule endoscopy of the small bowel for follow-up of patients with known Crohn's disease. *J Crohns Colitis* 2014; **8**: 1616-1623 [PMID: 24666976 DOI: 10.1016/j.crohns.2014.03.003]
- Efthymiou A, Viazis N, Mantzaris G, Papadimitriou N, Tzourmakliotis D, Raptis S, Karamanolis DG. Does clinical response correlate with mucosal healing in patients with Crohn's disease of the small bowel? A prospective, case-series study using wireless capsule endoscopy. *Inflamm Bowel Dis* 2008; **14**: 1542-1547 [PMID: 18521929 DOI: 10.1002/ibd.20509]
- Peyrin-Biroulet L, Reinisch W, Colombel JF, Mantzaris GJ, Kornbluth A, Diamond R, Rutgeerts P, Tang LK, Cornillie FJ, Sandborn WJ. Clinical disease activity, C-reactive protein normalisation and mucosal healing in Crohn's disease in the SONIC trial. *Gut* 2014; **63**: 88-95 [PMID: 23974954 DOI: 10.1136/gutjnl-2013-304984]
- Feagan BG, Lemann M, Befrits R, Connell W, D'Haens G, Ghosh S, Michetti P, Ochsenkühn T, Panaccione R, Schreiber S, Silverberg M, Sorrentino D, van der Woude CJ, Vermeire S, Rutgeerts P. Recommendations for the treatment of Crohn's disease with tumor necrosis factor antagonists: an expert consensus report. *Inflamm Bowel Dis* 2012; **18**: 152-160 [PMID: 22038857 DOI: 10.1002/ibd.21870]
- Orlando A, Guglielmi FW, Cottone M, Orlando E, Romano C, Sinagra E. Clinical implications of mucosal healing in the management of patients with inflammatory bowel disease. *Dig Liver Dis* 2013; **45**: 986-991 [PMID: 23993738 DOI: 10.1016/j.dld.2013.07.005]
- D'Haens G, Sandborn WJ, Feagan BG, Geboes K, Hanauer SB, Irvine EJ, Lemann M, Marteau P, Rutgeerts P, Schölmerich J, Sutherland LR. A review of activity indices and efficacy end points for clinical trials of medical therapy in adults with ulcerative colitis. *Gastroenterology* 2007; **132**: 763-786 [PMID: 17258735 DOI: 10.1053/j.gastro.2006.12.038]

- 8 **Travis SP**, Higgins PD, Orchard T, Van Der Woude CJ, Panaccione R, Bitton A, O'Morain C, Panés J, Sturm A, Reinisch W, Kamm MA, D'Haens G. Review article: defining remission in ulcerative colitis. *Aliment Pharmacol Ther* 2011; **34**: 113-124 [PMID: 21615435 DOI: 10.1111/j.1365-2036.2011.04701.x]
- 9 **Iddan G**, Meron G, Glukhovskiy A, Swain P. Wireless capsule endoscopy. *Nature* 2000; **405**: 417 [PMID: 10839527 DOI: 10.1038/35013140]
- 10 **Meister T**, Heinzow HS, Domagk D, Dortgolz A, Lenze F, Ross M, Domschke W, Lügering A. Colon capsule endoscopy versus standard colonoscopy in assessing disease activity of ulcerative colitis: a prospective trial. *Tech Coloproctol* 2013; **17**: 641-646 [PMID: 23307507 DOI: 10.1007/s10151-012-0965-8]
- 11 **San Juan-Acosta M**, Caunedo-Álvarez A, Argüelles-Arias F, Castro-Laria L, Gómez-Rodríguez B, Romero-Vázquez J, Belda-Cuesta A, Pellicer-Bautista F, Herrerías-Gutiérrez JM. Colon capsule endoscopy is a safe and useful tool to assess disease parameters in patients with ulcerative colitis. *Eur J Gastroenterol Hepatol* 2014; **26**: 894-901 [PMID: 24987825 DOI: 10.1097/MEG.000000000000125]
- 12 **Dionisio PM**, Gurudu SR, Leighton JA, Leontiadis GI, Fleischer DE, Hara AK, Heigh RI, Shiff AD, Sharma VK. Capsule endoscopy has a significantly higher diagnostic yield in patients with suspected and established small-bowel Crohn's disease: a meta-analysis. *Am J Gastroenterol* 2010; **105**: 1240-1248; quiz 1249 [PMID: 20029412 DOI: 10.1038/ajg.2009.713]
- 13 **Koulaouzidis A**, Giannakou A, Yung DE, Dabos KJ, Plevris JN. Do prokinetics influence the completion rate in small-bowel capsule endoscopy? A systematic review and meta-analysis. *Curr Med Res Opin* 2013; **29**: 1171-1185 [PMID: 23790243 DOI: 10.1185/03007995.2013.818532]
- 14 **Westerhof J**, Weersma RK, Koornstra JJ. Risk factors for incomplete small-bowel capsule endoscopy. *Gastrointest Endosc* 2009; **69**: 74-80 [PMID: 18691709 DOI: 10.1016/j.gie.2008.04.034]
- 15 **Liao Z**, Gao R, Xu C, Li ZS. Indications and detection, completion, and retention rates of small-bowel capsule endoscopy: a systematic review. *Gastrointest Endosc* 2010; **71**: 280-286 [PMID: 20152309 DOI: 10.1016/j.gie.2009.09.031]
- 16 **Marmo R**, Rotondano G, Piscopo R, Bianco MA, Cipolletta L. Meta-analysis: capsule enteroscopy vs. conventional modalities in diagnosis of small bowel diseases. *Aliment Pharmacol Ther* 2005; **22**: 595-604 [PMID: 16181299 DOI: 10.1111/j.1365-2036.2005.02625.x]
- 17 **Spada C**, Spera G, Riccioni M, Biancone L, Petruzzello L, Tringali A, Familiari P, Marchese M, Onder G, Mutignani M, Perri V, Petruzzello C, Pallone F, Costamagna G. A novel diagnostic tool for detecting functional patency of the small bowel: the Given patency capsule. *Endoscopy* 2005; **37**: 793-800 [PMID: 16116528 DOI: 10.1055/s-2005-870246]
- 18 **Spada C**, Shah SK, Riccioni ME, Spera G, Marchese M, Iacopini F, Familiari P, Costamagna G. Video capsule endoscopy in patients with known or suspected small bowel stricture previously tested with the dissolving patency capsule. *J Clin Gastroenterol* 2007; **41**: 576-582 [PMID: 17577114 DOI: 10.1097/01.mcg.0000225633.14663.64]
- 19 **Harris LA**, Hansel SL, Rajan E, Srivathsan K, Rea R, Crowell MD, Fleischer DE, Pasha SF, Gurudu SR, Heigh RI, Shiff AD, Post JK, Leighton JA. Capsule Endoscopy in Patients with Implantable Electromedical Devices is Safe. *Gastroenterol Res Pract* 2013; **2013**: 959234 [PMID: 23710168 DOI: 10.1155/2013/959234]
- 20 **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* 2008; **27**: 146-154 [PMID: 17956598 DOI: 10.1111/j.1365-2036.2007.03556.x]
- 21 **Korman LY**, Delvaux M, Gay G, Hagenmuller F, Keuchel M, Friedman S, Weinstein M, Shetzline M, Cave D, de Franchis R. Capsule endoscopy structured terminology (CEST): proposal of a standardized and structured terminology for reporting capsule endoscopy procedures. *Endoscopy* 2005; **37**: 951-959 [PMID: 16189767 DOI: 10.1055/s-2005-870329]
- 22 **Gal E**, Geller A, Fraser G, Levi Z, Niv Y. Assessment and validation of the new capsule endoscopy Crohn's disease activity index (CECDAI). *Dig Dis Sci* 2008; **53**: 1933-1937 [PMID: 18034304 DOI: 10.1007/s10620-007-0084-y]
- 23 **Niv Y**, Ilani S, Levi Z, Hershkowitz M, Niv E, Fireman Z, O'Donnell S, O'Morain C, Eliakim R, Scapa E, Kalantzis N, Kalantzis C, Apostolopoulos P, Gal E. Validation of the Capsule Endoscopy Crohn's Disease Activity Index (CECDAI or Niv score): a multicenter prospective study. *Endoscopy* 2012; **44**: 21-26 [PMID: 22125196 DOI: 10.1055/s-0031-1291385]
- 24 **Rosa B**, Moreira MJ, Rebelo A, Cotter J. Lewis Score: a useful clinical tool for patients with suspected Crohn's Disease submitted to capsule endoscopy. *J Crohns Colitis* 2012; **6**: 692-697 [PMID: 22398099 DOI: 10.1016/j.crohns.2011.12.002]
- 25 **Koulaouzidis A**, Douglas S, Plevris JN. Lewis score correlates more closely with fecal calprotectin than Capsule Endoscopy Crohn's Disease Activity Index. *Dig Dis Sci* 2012; **57**: 987-993 [PMID: 22057284 DOI: 10.1007/s10620-011-1956-8]
- 26 **Langhorst J**, Elsenbruch S, Koelzer J, Rueffer A, Michalsen A, Dobos GJ. Noninvasive markers in the assessment of intestinal inflammation in inflammatory bowel diseases: performance of fecal lactoferrin, calprotectin, and PMN-elasticase, CRP, and clinical indices. *Am J Gastroenterol* 2008; **103**: 162-169 [PMID: 17916108 DOI: 10.1111/j.1572-0241.2007.01556.x]
- 27 **Sipponen T**, Björkstén CG, Färkkilä M, Nuutinen H, Savilahti E, Kolho KL. Faecal calprotectin and lactoferrin are reliable surrogate markers of endoscopic response during Crohn's disease treatment. *Scand J Gastroenterol* 2010; **45**: 325-331 [PMID: 20034360 DOI: 10.3109/00365520903483650]
- 28 **van Rheenen PF**, Van de Vijver E, Fidler V. Faecal calprotectin for screening of patients with suspected inflammatory bowel disease: diagnostic meta-analysis. *BMJ* 2010; **341**: c3369 [PMID: 20634346 DOI: 10.1136/bmj.c3369]
- 29 **Summerton CB**, Longlands MG, Wiener K, Shreeve DR. Faecal calprotectin: a marker of inflammation throughout the intestinal tract. *Eur J Gastroenterol Hepatol* 2002; **14**: 841-845 [PMID: 12172403]
- 30 **Koulaouzidis A**, Douglas S, Rogers MA, Arnott ID, Plevris JN. Fecal calprotectin: a selection tool for small bowel capsule endoscopy in suspected IBD with prior negative bi-directional endoscopy. *Scand J Gastroenterol* 2011; **46**: 561-566 [PMID: 21269246 DOI: 10.3109/00365521.2011.551835]
- 31 **Yang L**, Ge ZZ, Gao YJ, Li XB, Dai J, Zhang Y, Xue HB, Zhao YJ. Assessment of capsule endoscopy scoring index, clinical disease activity, and C-reactive protein in small bowel Crohn's disease. *J Gastroenterol Hepatol* 2013; **28**: 829-833 [PMID: 23425203 DOI: 10.1111/jgh.12146]
- 32 **Tsibouris P**, Periklis A, Chrissostomos K, Antonios Z, Panagiota M, Erasmia V, Georgios A. When Crohn's disease is in remission, more patients complete capsule endoscopy study but less lesions are identified. *Saudi J Gastroenterol* 2013; **19**: 63-68 [PMID: 23481131 DOI: 10.4103/1319-3767.108468]
- 33 **Hall B**, Holleran G, Chin JL, Smith S, Ryan B, Mahmud N, McNamara D. A prospective 52 week mucosal healing assessment of small bowel Crohn's disease as detected by capsule endoscopy. *J Crohns Colitis* 2014; **8**: 1601-1609 [PMID: 25257546 DOI: 10.1016/j.crohns.2014.09.005]
- 34 **Dussault C**, Gower-Rousseau C, Salleron J, Vernier-Massouille G, Branche J, Colombel JF, Maunoury V. Small bowel capsule endoscopy for management of Crohn's disease: a retrospective tertiary care centre experience. *Dig Liver Dis* 2013; **45**: 558-561 [PMID: 23238033 DOI: 10.1016/j.dld.2012.11.004]
- 35 **Long MD**, Barnes E, Isaacs K, Morgan D, Herfarth HH. Impact of capsule endoscopy on management of inflammatory bowel disease: a single tertiary care center experience. *Inflamm Bowel Dis* 2011; **17**: 1855-1862 [PMID: 21830264 DOI: 10.1002/ibd.21571]
- 36 **Burke JP**, Velupillai Y, O'Connell PR, Coffey JC. National trends in intestinal resection for Crohn's disease in the post-biologic era. *Int J Colorectal Dis* 2013; **28**: 1401-1406 [PMID: 23604410 DOI: 10.1007/s00384-013-1698-5]

- 37 **Jones DW**, Finlayson SR. Trends in surgery for Crohn's disease in the era of infliximab. *Ann Surg* 2010; **252**: 307-312 [PMID: 20585239 DOI: 10.1097/SLA.0b013e3181e61df5]
- 38 **Poritz LS**, Rowe WA, Koltun WA. Remicade does not abolish the need for surgery in fistulizing Crohn's disease. *Dis Colon Rectum* 2002; **45**: 771-775 [PMID: 12072629]
- 39 **Bewtra M**, Su C, Lewis JD. Trends in hospitalization rates for inflammatory bowel disease in the United States. *Clin Gastroenterol Hepatol* 2007; **5**: 597-601 [PMID: 17382602 DOI: 10.1016/j.cgh.2007.01.015]
- 40 **Windsor A**, Michetti P, Bemelman W, Ghosh S. The positioning of colectomy in the treatment of ulcerative colitis in the era of biologic therapy. *Inflamm Bowel Dis* 2013; **19**: 2695-2703 [PMID: 23846487 DOI: 10.1097/MIB.0b013e318292fae6]
- 41 **Langholz E**, Munkholm P, Davidsen M, Binder V. Colorectal cancer risk and mortality in patients with ulcerative colitis. *Gastroenterology* 1992; **103**: 1444-1451 [PMID: 1358741]
- 42 **Leijonmarck CE**, Persson PG, Hellers G. Factors affecting colectomy rate in ulcerative colitis: an epidemiologic study. *Gut* 1990; **31**: 329-333 [PMID: 2323599]
- 43 **Mekhjian HS**, Switz DM, Watts HD, Deren JJ, Katon RM, Beman FM. National Cooperative Crohn's Disease Study: factors determining recurrence of Crohn's disease after surgery. *Gastroenterology* 1979; **77**: 907-913 [PMID: 467942]
- 44 **Caprilli R**, Corrao G, Taddei G, Tonelli F, Torchio P, Viscido A. Prognostic factors for postoperative recurrence of Crohn's disease. Gruppo Italiano per lo Studio del Colon e del Retto (GISC) *Dis Colon Rectum* 1996; **39**: 335-341 [PMID: 8603558]
- 45 **Reese GE**, Nanidis T, Borysiewicz C, Yamamoto T, Orchard T, Tekkis PP. The effect of smoking after surgery for Crohn's disease: a meta-analysis of observational studies. *Int J Colorectal Dis* 2008; **23**: 1213-1221 [PMID: 18762954 DOI: 10.1007/s00384-008-0542-9]
- 46 **Whelan G**, Farmer RG, Fazio VW, Goormastic M. Recurrence after surgery in Crohn's disease. Relationship to location of disease (clinical pattern) and surgical indication. *Gastroenterology* 1985; **88**: 1826-1833 [PMID: 3996839]
- 47 **Simillis C**, Yamamoto T, Reese GE, Umegae S, Matsumoto K, Darzi AW, Tekkis PP. A meta-analysis comparing incidence of recurrence and indication for reoperation after surgery for perforating versus nonperforating Crohn's disease. *Am J Gastroenterol* 2008; **103**: 196-205 [PMID: 17900320 DOI: 10.1111/j.1572-0241.2007.01548.x]
- 48 **Rutgeerts P**, Geboes K, Vantrappen G, Beyls J, Kerremans R, Hiele M. Predictability of the postoperative course of Crohn's disease. *Gastroenterology* 1990; **99**: 956-963 [PMID: 2394349]
- 49 **Katz JA**. Postoperative endoscopic surveillance in Crohn's disease: bottom up or top down? *Gastrointest Endosc* 2007; **66**: 541-543 [PMID: 17725943 DOI: 10.1016/j.gie.2007.02.060]
- 50 **Blum E**, Katz JA. Postoperative therapy for Crohn's disease. *Inflamm Bowel Dis* 2009; **15**: 463-472 [PMID: 18942739 DOI: 10.1002/ibd.20741]
- 51 **Regueiro M**, Kip KE, Schraut W, Baidoo L, Sepulveda AR, Pesci M, El-Hachem S, Harrison J, Binion D. Crohn's disease activity index does not correlate with endoscopic recurrence one year after ileocolonic resection. *Inflamm Bowel Dis* 2011; **17**: 118-126 [PMID: 20848538 DOI: 10.1002/ibd.21355]
- 52 **Regueiro M**, Schraut W, Baidoo L, Kip KE, Sepulveda AR, Pesci M, Harrison J, Plevy SE. Infliximab prevents Crohn's disease recurrence after ileal resection. *Gastroenterology* 2009; **136**: 441-450.e1; quiz 716 [PMID: 19109962 DOI: 10.1053/j.gastro.2008.10.051]
- 53 **Nguyen DL**, Solaimani P, Nguyen ET, Jamal MM, Bechtold ML. Antitumor necrosis factor α is more effective than conventional medical therapy for the prevention of postoperative recurrence of Crohn's disease: a meta-analysis. *Eur J Gastroenterol Hepatol* 2014; **26**: 1152-1159 [PMID: 25089549 DOI: 10.1097/MEG.0000000000000178]
- 54 **Biancone L**, Calabrese E, Petruzzello C, Onali S, Caruso A, Palmieri G, Sica GS, Pallone F. Wireless capsule endoscopy and small intestine contrast ultrasonography in recurrence of Crohn's disease. *Inflamm Bowel Dis* 2007; **13**: 1256-1265 [PMID: 17577246 DOI: 10.1002/ibd.20199]
- 55 **Bourreille A**, Jarry M, D'Halluin PN, Ben-Soussan E, Maunoury V, Bulois P, Sacher-Huvelin S, Vahedy K, Lerebours E, Heresbach D, Bretagne JF, Colombel JF, Galmiche JP. Wireless capsule endoscopy versus ileocolonoscopy for the diagnosis of postoperative recurrence of Crohn's disease: a prospective study. *Gut* 2006; **55**: 978-983 [PMID: 16401689 DOI: 10.1136/gut.2005.081851]
- 56 **Pons Beltrán V**, Nos P, Bastida G, Beltrán B, Argüello L, Aguas M, Rubín A, Pertejo V, Sala T. Evaluation of postsurgical recurrence in Crohn's disease: a new indication for capsule endoscopy? *Gastrointest Endosc* 2007; **66**: 533-540 [PMID: 17725942 DOI: 10.1016/j.gie.2006.12.059]
- 57 **Kono T**, Hida N, Nogami K, Iimuro M, Ohda Y, Yokoyama Y, Kamikozuru K, Tozawa K, Kawai M, Ogawa T, Hori K, Ikeuchi H, Miwa H, Nakamura S, Matsumoto T. Prospective postsurgical capsule endoscopy in patients with Crohn's disease. *World J Gastrointest Endosc* 2014; **6**: 88-98 [PMID: 24634713 DOI: 10.4253/wjge.v6.i3.88]
- 58 **Murrell Z**, Vasiliauskas E, Melmed G, Lo S, Targan S, Fleshner P. Preoperative wireless capsule endoscopy does not predict outcome after ileal pouch-anal anastomosis. *Dis Colon Rectum* 2010; **53**: 293-300 [PMID: 20173476 DOI: 10.1007/DCR.0b013e3181b71a2c]
- 59 **Shen B**, Remzi FH, Santisi J, Lashner BA, Brzezinski A, Fazio VW. Application of wireless capsule endoscopy for the evaluation of iron deficiency anemia in patients with ileal pouches. *J Clin Gastroenterol* 2008; **42**: 897-902 [PMID: 18360292 DOI: 10.1097/MCG.0b013e318074dd73]
- 60 **Meagher AP**, Farouk R, Dozois RR, Kelly KA, Pemberton JH. Ileal pouch-anal anastomosis for chronic ulcerative colitis: complications and long-term outcome in 1310 patients. *Br J Surg* 1998; **85**: 800-803 [PMID: 9667712 DOI: 10.1046/j.1365-2168.1998.00689.x]
- 61 **Calabrese C**, Fabbri A, Gionchetti P, Rizzello F, Morselli C, Liguori G, Poggioli G, Campieri M, Di Febo G. Controlled study using wireless capsule endoscopy for the evaluation of the small intestine in chronic refractory pouchitis. *Aliment Pharmacol Ther* 2007; **25**: 1311-1316 [PMID: 17509099 DOI: 10.1111/j.1365-2036.2007.03323.x]
- 62 **Mehdizadeh S**, Chen G, Enayati PJ, Cheng DW, Han NJ, Shaye OA, Ippoliti A, Vasiliauskas EA, Lo SK, Papadakis KA. Diagnostic yield of capsule endoscopy in ulcerative colitis and inflammatory bowel disease of unclassified type (IBDU). *Endoscopy* 2008; **40**: 30-35 [PMID: 18058654 DOI: 10.1055/s-2007-995359]
- 63 **Price AB**. Overlap in the spectrum of non-specific inflammatory bowel disease--'colitis indeterminate'. *J Clin Pathol* 1978; **31**: 567-577 [PMID: 670413]
- 64 **Higurashi T**, Endo H, Yoneda M, Hosono K, Sakai E, Takahashi H, Inamori M, Uchiyama S, Kojima T, Kawana K, Natsumeda Y, Nagase H, Nakajima A. Capsule-endoscopic findings of ulcerative colitis patients. *Digestion* 2011; **84**: 306-314 [PMID: 22041924 DOI: 10.1159/000333086]
- 65 **Mow WS**, Lo SK, Targan SR, Dubinsky MC, Treyzon L, Abreu-Martin MT, Papadakis KA, Vasiliauskas EA. Initial experience with wireless capsule enteroscopy in the diagnosis and management of inflammatory bowel disease. *Clin Gastroenterol Hepatol* 2004; **2**: 31-40 [PMID: 15017630]
- 66 **Maunoury V**, Savoye G, Bourreille A, Bouhnik Y, Jarry M, Sacher-Huvelin S, Ben Soussan E, Lerebours E, Galmiche JP, Colombel JF. Value of wireless capsule endoscopy in patients with indeterminate colitis (inflammatory bowel disease type unclassified). *Inflamm Bowel Dis* 2007; **13**: 152-155 [PMID: 17206697 DOI: 10.1002/ibd.20060]
- 67 **Cohen SA**, Gralnek IM, Ephrath H, Saripkin L, Meyers W, Sherrod O, Napier A, Gobin T. Capsule endoscopy may reclassify pediatric inflammatory bowel disease: a historical analysis. *J Pediatr Gastroenterol Nutr* 2008; **47**: 31-36 [PMID: 18607266 DOI: 10.1097/MPG.0b013e318160df85]
- 68 **Gralnek IM**, Cohen SA, Ephrath H, Napier A, Gobin T, Sherrod O, Lewis J. Small bowel capsule endoscopy impacts diagnosis and

- management of pediatric inflammatory bowel disease: a prospective study. *Dig Dis Sci* 2012; **57**: 465-471 [PMID: 21901253 DOI: 10.1007/s10620-011-1894-5]
- 69 **Geboes K**, Rutgeerts P, Opendakker G, Olson A, Patel K, Wagner CL, Marano CW. Endoscopic and histologic evidence of persistent mucosal healing and correlation with clinical improvement following sustained infliximab treatment for Crohn's disease. *Curr Med Res Opin* 2005; **21**: 1741-1754 [PMID: 16307694 DOI: 10.1185/030079905X65457]
- 70 **Baert F**, Moortgat L, Van Assche G, Caenepeel P, Vergauwe P, De Vos M, Stokkers P, Hommes D, Rutgeerts P, Vermeire S, D'Haens G. Mucosal healing predicts sustained clinical remission in patients with early-stage Crohn's disease. *Gastroenterology* 2010; **138**: 463-468; quiz e10-e11 [PMID: 19818785 DOI: 10.1053/j.gastro.2009.09.056]
- 71 **Hébuterne X**, Lémann M, Bouhnik Y, Dewit O, Dupas JL, Mross M, D'Haens G, Mitchev K, Ernault É, Vermeire S, Brixi-Benmansour H, Moreels TG, Mary JY, Marteau P, Colombel JF. Endoscopic improvement of mucosal lesions in patients with moderate to severe ileocolonic Crohn's disease following treatment with certolizumab pegol. *Gut* 2013; **62**: 201-208 [PMID: 22525883 DOI: 10.1136/gutjnl-2012-302262]
- 72 **af Björkesten CG**, Nieminen U, Sipponen T, Turunen U, Arkkila P, Färkkilä M. Mucosal healing at 3 months predicts long-term endoscopic remission in anti-TNF-treated luminal Crohn's disease. *Scand J Gastroenterol* 2013; **48**: 543-551 [PMID: 23477356 DOI: 10.3109/00365521.2013.772230]
- 73 **Ferrante M**, Colombel JF, Sandborn WJ, Reinisch W, Mantzaris GJ, Kornbluth A, Rachmilewitz D, Lichtiger S, D'Haens GR, van der Woude CJ, Danese S, Diamond RH, Oortwijn AF, Tang KL, Miller M, Cornillie F, Rutgeerts PJ. Validation of endoscopic activity scores in patients with Crohn's disease based on a post hoc analysis of data from SONIC. *Gastroenterology* 2013; **145**: 978-986.e5 [PMID: 23954314 DOI: 10.1053/j.gastro.2013.08.010]
- 74 **Thia KT**, Sandborn WJ, Harmsen WS, Zinsmeister AR, Loftus EV. Risk factors associated with progression to intestinal complications of Crohn's disease in a population-based cohort. *Gastroenterology* 2010; **139**: 1147-1155 [PMID: 20637205 DOI: 10.1053/j.gastro.2010.06.070]
- 75 **Smith BR**, Arnott ID, Drummond HE, Nimmo ER, Satsangi J. Disease location, anti-Saccharomyces cerevisiae antibody, and NOD2/CARD15 genotype influence the progression of disease behavior in Crohn's disease. *Inflamm Bowel Dis* 2004; **10**: 521-528 [PMID: 15472511]
- 76 **Aldhous MC**, Drummond HE, Anderson N, Smith LA, Arnott ID, Satsangi J. Does cigarette smoking influence the phenotype of Crohn's disease? Analysis using the Montreal classification. *Am J Gastroenterol* 2007; **102**: 577-588 [PMID: 17338736 DOI: 10.1111/j.1572-0241.2007.01064.x]
- 77 **Corporaal S**, Karrenbeld A, van der Linde K, Voskuil JH, Kleibeuker JH, Dijkstra G. Diffuse enteritis after colectomy for ulcerative colitis: two case reports and review of the literature. *Eur J Gastroenterol Hepatol* 2009; **21**: 710-715 [PMID: 19282770 DOI: 10.1097/MEG.0b013e32831bc400]
- 78 **Hoentjen F**, Hanauer SB, Hart J, Rubin DT. Long-term treatment of patients with a history of ulcerative colitis who develop gastritis and pan-enteritis after colectomy. *J Clin Gastroenterol* 2013; **47**: 52-57 [PMID: 22858512 DOI: 10.1097/MCG.0b013e3182582c1d]

P- Reviewer: Cuadrado-Garcia A, Kopylov U, Maric I, Mais V, Nakajima N, Vynios D **S- Editor:** Ji FF **L- Editor:** A **E- Editor:** Wu HL





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

