World Journal of Gastrointestinal Endoscopy

Online Submissions: http://www.wjgnet.com/1948-5190office
wjge@wjgnet.com
doi:10.4253/wjge.v3.i2.23

World J Gastrointest Endosc 2011 February 16; 3(2): 23-29
ISSN 1948-5190 (online)

EDITORIAL

Small bowel video capsule endoscopy in Crohn's disease: What have we learned in the last ten years?

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Received: October 19, 2010 Revised: January 25, 2011
Accepted: February 1, 2010
Published online: February 16, 2011

Abstract

Since its introduction in 2001, capsule endoscopy (CE) has become the most important advance in the study of small bowel disease, including Crohn's disease (CD). This technique has been demonstrated to be superior to all other current forms of radiological investigation in detecting mucosal abnormalities of small bowel non-stricturing CD. CE has proven to be extremely useful in diagnosing CD in patients with inconclusive findings from ileocolonoscopy and x-ray-based studies. Almost half of all patients with CD involving the ileum also present lesions in proximal intestinal segments, with the small bowel being exclusively involved in up to 30% of all CD cases. Despite the widespread use of CE, several questions concerning the utility of this technique remain unanswered. The lack of commonly agreed diagnostic criteria for defining CD lesions with the aid of CE may have had an influence on the variation in diagnostic results for CE reported in the literature. The utility of CE in monitoring CD and in guiding therapy has also been proposed. Furthermore, CE could be a useful second-line technique for patients with an established diagnosis of CD and unexplained symptoms. Finally, as no threshold for CD diagnosis has been agreed upon, a severity scale of mucosal disease activity has not been universally followed. None of the available activity indexes based on CE findings has been independently validated. This article discusses several cutting-edge aspects of the usefulness of CE in CD 10 years after its introduction as a sensible method to study the small intestine.

Key words: Capsule endoscopy; Crohn's disease; Inflammatory bowel disease

Peer reviewers: Robert J Richards, MD, Gastroenterology/Hepatology, Stony Brook University HSC, Stony Brook, NY 11793, United States; Reena Sidhu, MRCP, MD, Department of Gastroenterology, Royal Hallamshire Hospital, 15 Barncliffe Road, Fulwood, Sheffield S10 4DF, United Kingdom

Lucendo AJ, Guagnozzi D. Small bowel video capsule endoscopy in Crohn's disease: What have we learned in the last ten years? *World J Gastrointest Endosc* 2011; 3(2): 23-29 Available from: URL: http://www.wjgnet.com/1948-5190/full/v3/i2/23.htm DOI: http://dx.doi.org/10.4253/wjge.v3.i2.23

INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disorder with complex phenotypes regarding age of onset, location, and disease behavior. The diagnosis of CD is based on clinical history and a physical exploration with compatible data, suspicious x-ray images, and the presence of endoscopic lesions with a compatible histology[1]. This combination of diagnostic methods is necessary because there is no single gold standard diagnostic test for CD and, therefore, no isolated finding is sufficient to diagnose this disease accurately.

The most frequent location of CD is in the terminal ileum and the colon. As such, an effective diagnosis can be made with the aid of ileocolonoscopy and biopsies in most cases. However, in one third of all CD patients the

disease is confined to the small bowel[2,3]. For many of these individuals, diagnosis and follow-up management with traditional endoscopic and radiological procedures is of limited value. In fact, the small bowel is the most difficult area to access for diagnostic purposes via endoscopy or x-rays. Capsule endoscopy (CE), a recently introduced diagnostic procedure, thus represents an extremely important technical advance in the identification of mucosal lesions in the small bowel. Initially recommended for the investigation of obscure gastrointestinal bleeding after inconclusive upper endoscopy and colonoscopy results[4],the extensive availability of CE has allowed diagnosticians to extend its use to other small bowel pathologies, including CD, malabsorption syndromes[5], some cases of abdominal pain with unclear origin[6,7], small bowel transplantation, and graft-versus-host disease[8,9].

Although it was only approved by the Food and Drug Administration in 2001, CE has already proven to be more accurate in the diagnosis of CD than radiological techniques[10-13]. The use of CE has facilitated the detection of previously unknown proximal small bowel lesions in half of all patients with a previous diagnosis of CD involving the distal ileum[14]. In addition, CE may be useful for correctly classifying patients diagnosed with ulcerative colitis and atypical features or with unclassified inflammatory bowel disease[15,16].

CE poses specific risks in patients with CD, the main complication being the retention of the capsule, defined as the failure to progress along the gastrointestinal tract (i.e. a capsule remains in the bowel for a minimum of 2 wk or even permanently, unless extracted surgically or endoscopically)[17]. Capsule retention occurs in 1% of patients with suspected CD, but retention ratios of between 4% to 6% have been reported in patients with confirmed CD[18]. A detailed clinical history for occlusive symptoms and possibly an Agile patency capsule exam should be carried out in higher risk patients as this has been demonstrated to be as safe and effective method for minimizing the risk of capsule retention[19].

USEFULNESS OF CE IN SUSPECTED CD

Several studies have been published recently on the usefulness of CE in diagnosing suspected CD patients, particularly those in whom there remains a high clinical suspicion of CD despite negative results from ileocolonoscopy and/or radiological examinations[18].

In fact, CE has proven to be superior to all current forms of radiological testing of the small intestine in detecting the mucosal abnormalities of nonstricturing CD[16,20]. It shows an incremental diagnostic yield of 20% to 40% over other diagnostic modalities such as barium studies and CT scanning, and a high negative predictive value in cases of suspected CD[21]. A review published in 2005 estimated a diagnostic yield for CD of over 70% in patients with negative or inconclusive findings from previous ileocolonoscopy and x-ray studies[18].

Nevertheless, the success rate of CE is low when performed in patients with either abdominal pain alone or with abdominal pain and diarrhea. The presence of biochemical markers of inflammation in patients with symptoms suggestive of CD as opposed to the presence of suggestive symptoms alone increases the diagnostic success rate of CE[22]. For this reason, and on the basis of ICCE consensus, patients with these symptoms plus either extraintestinal manifestations, inflammatory markers, or abnormal imaging results from SB series, CT scans, *etc*, should be considered as possible CD sufferers. Indeed, when any one of these criteria is added, the CE diagnostic success rate increases. These results were recently corroborated in a meta-analysis[23] which demonstrated that CE was superior to small bowel radiography, CT scans, and ileocolonoscopy in evaluating patients with suspected CD. There is also increasing evidence of the utility of magnetic resonance (MR) in the assessment of small bowel CD, with positive preliminary results indicating it as a frontline technique for CD diagnosis and follow up[24]. Unfortunately, comparative studies between CE and MR have not been carried out on patients suspected of having CD[23]. Larger prospective studies are thus needed to define the proper place of CE in the diagnostic algorithm for CD.

CE findings specific to CD

One of the main problems which arose after the spread of CE as a diagnostic tool was the lack of commonly accepted terminology to describe endoscopic findings during explorations. This led to the proposal of structured terminologies in order to standardize the description and definition of CE results[25,26].

This is especially important since previous studies which used various diagnostic criteria to define CD lesions in the small bowel produced extremely varied results, probably due in large part to the absence of a unified terminology. CD-associated lesions described using CE results are thus in great need of more precise definitions and of commonly accepted defining criteria as, currently, the definition of CD through CE could, to some extent, be considered arbitrary[27].

Currently, the most widely and commonly used diagnostic criterion for CD is the presence of more than 3 ulcerations in the absence of nonsteroidal anti-inflammatory drugs (NSAIDs), as proposed by Mow *et al*[28] in 2004. In addition, the location and length of the intestinal segments involved and the topographical distribution of lesions along the small intestine should be considered as relevant diagnostic criteria for CD since the number of ulcers tends to increase progressively as CE approaches the distal ileum[29]. Using the presence of 3 or more ulcers to indicate an abnormal CE result, a recent article set out to define the utility of CE in patients with suspected CD after inconclusive CT scans, small bowel follow-through, and endoscopy. The authors observed a sensitivity of 77% and a specificity of 89%, with a positive predictive value of 50% and a negative predictive value of 96%[30].

Voderholzer *et al*[31] suggested that finding more than 10 aphthae in a CE examination was also strongly

suggestive of CD. The presence of several small alterations such as villous edema, villous denudation (loss of villi), erosions, erythema, vasculitis, cobblestone appearance, nodular lymphoid hyperplasia, and lymphangiectasia have been considered to be early manifestations of CD in some series[12,20,22,32,33], but not in others[34-36]. The finding of previously undetected stenosis has also been considered an important diagnostic criterion by some authors[36-38].

The various CE-based criteria outlined above are not considered to be of equal value in diagnosing CD. Thus, while ulcers and multiple aphthae may directly lead to a CD diagnosis in a suitable clinical context, an isolated simple mucosal edema or mucosal erythema is probably insufficient to establish a clear diagnosis. Different observers report that the discovery of mucosal breaks such as ulcers and aphthae (which can be described as 'major findings'), as well as of circumferentially ulcerate stenosis, have a high diagnostic correlation[37,39] while the presence of more subtle lesions ('minor findings') is less well correlated with a diagnosis of CD[39]. Nevertheless, observing only 'minor findings' in patients clinically and/or analytically suspected of having CD should not definitively exclude a diagnosis of CD, since such patients can show clinical improvement when treated for CD[20]. This further obliges medical professionals to develop standardized, prospectively validated diagnostic criteria and to perform more follow-up studies.

CD-like findings on CE

It is important to note that the accuracy of CE in diagnosing CD is limited by the lack of specificity of mucosal findings. In fact, up to 14% of healthy subjects have mucosal breaks and erosions in the small bowel[40], which only serves to bolster the idea that CE mucosal findings alone are insufficient to confirm a diagnosis of CD.

It is also worth noting that not all mucosal breaks found in the small intestine are due to CD. Several lesions properly described as CD are actually non-specific and can be found in a large proportion of patients treated with NSAIDs[41,42] as well as in patients with other types of small bowel disorders. For this reason, recent intake of NSAIDs should be excluded in all patients undergoing CE, and, if possible, such therapy should be interrupted several weeks before the CE exploration to ensure accuracy. Such measures would help improve the predictive values of the technique.

CE AS A CD MONITORING TECHNIQUE

CE has also been proposed as a method for determining the extent and severity of lesions, postoperative recurrence, and mucosal healing under therapies in patients with an established CD diagnosis. Because CE is also more sensitive than x-ray-based techniques in monitoring CD, some authors have proposed that CE be used to assess the activity or recurrence of the disease, thereby limiting a patient's exposure to unnecessary radiation[16]. However, the exact role of CE for this indication has yet to be established[27]. In fact, some of the available data are contradictory and in clinical practice, indications for CE are limited to patients with a proven diagnosis of CD.

CE and mucosal healing

The major goals for medical therapies to combat CD should include modifying the clinical course, halting the progression of the disease, and avoiding the need for surgery, hospitalization, and the use of corticosteroids. In this context, early healing of the intestinal mucosa has recently been proposed as the primary objective of medical therapies[43]. In fact, early healing has been demonstrated to be a strong predictor for improved long term outcome in CD, with fewer complications and surgical interventions[44]. CE may have a potential role in assessing mucosal healing after drug therapy[27], but it is still unclear whether the presence of endoscopic lesions in the small bowel mucosa identified with the aid of CE in CD patients is directly related to the activity of the disease itself. It remains to be seen whether CE findings can lead to a change in the therapeutic management of CD patients[45] similar to that of ileocolonoscopy during CD flare-ups. Part of the problem is that the clinical response does not always correlate with mucosal healing in patients with small bowel CD[46].

A study published by Mehdizadeh *et al*[29] in 2010, retrospectively analyzed 147 CE procedures performed on 134 patients who had previously been diagnosed with CD and who exhibited symptoms suggestive of active disease. CE identified lesions indicative of activity in about half the symptomatic patients, with the number of lesions progressively increasing as the CE approached the distal ileum. This study concluded that a clear correlation between symptoms and endoscopic lesions cannot be established in CD patients since symptoms suggesting activity may occur in the absence of small bowel lesions.

In contrast, another study by Lorenzo-Zúñiga *et al*[47] showed that therapy was changed in 64% of patients previously diagnosed with CD after a CE exam was performed due to anemia, abdominal pain, or because the location of the disease needed to be reevaluated. These results indicate that CE findings can bring about a change in therapeutic approach in a large number of CD patients. However, further research must be done on the usefulness of CD in monitoring mucosal healing during the natural course of small bowel CD[45].

CE in assessing postoperative recurrence of CD

Diagnosis of post-operative recurrence may be based on clinical symptoms and/or endoscopic findings. To date, ileocolonoscopy is viewed as the gold standard for defining the presence and severity of morphologic recurrence and predicting the clinical course of the disease. Recent studies have shown that performing a CE exam 6 to 12 mo after surgery seems to have comparable sensitivity, specificity, and positive/negative predictive values to ileocolonoscopy in diagnosing post-operative recurrence of CD[48,49]. The advantage of CE is that it has higher tolerability and a better probability of reaching the neoileum, which is not always accessible *via* colonoscopy.

Table 1 Lewis capsule endoscopy scoring table[38]

	Regions[1]				
	Duodenum	Jejunum	Proximal ileum	Distal ileum	
	Lesions				
	Number	Distribution pattern	Longitudinal extent	Shape	Size (by circumference)
Erythema		Localized = 1 Patchy = 2 Diffuse = 3	Short segment = 1 Long segment = 2 Whole region = 3		
Edema		Localized = 1 Patchy = 2 Diffuse = 3	Short segment = 1 Long segment = 2 Whole region = 3		
Nodularity	Single = 1 Few = 2 Multiple = 3	Localized = 1 Patchy = 2 Diffuse = 3	Short segment = 1 Long segment = 2 Whole region = 3		
Ulcer	Single = 3 Few = 5 Multiple = 7	Localized = 3 Patchy = 5 Diffuse = 7	Short segment = 1 Long segment = 2 Whole region = 3	Circular = 3 Linear = 5 Irregular = 7	< ¼ = 3 ¼ - ½ = 5 > ½ = 7
Stenosis	None = 0 Single = 10 Multiple = 20	Traversed = 10 Not traversed = 20	Nonulcerated = 5 Ulcerated = 10		

[1]Score by region by adding points listed.

However, the value of CE in diagnosing post-operative recurrence in the ileum and particularly in the jejunum has not yet been systematically studied. Further studies are thus needed before a definitive conclusion can be reached.

Indexes for evaluating the severity of CD

Once CE had been widely accepted as a good diagnostic tool, several activity indexes were developed to assess the severity and extension of small bowel CD. The various CE proposed indexes primarily assess 4 parameters to define CD severity: (1) the presence of mucosal lesions that are felt to explain the patient's reasons for referral (including disturbances in villous appearance and presence of ulcers); (2) the size of ulcers; (3) the location and extension of ulcers; and (4) the presence of stenosis with or without mucosal lesions. Apart from these parameters, each index has its own particularities.

The first index created to evaluate CD severity was proposed in 2004 by Kornbluth *et al*[38]. It makes use of five parameters previously defined in structured terminology developed specifically for CE: erythema, edema, nodularity, ulcers, and stenosis. This Lewis Capsule Endoscopy Score[38] exhaustively analyses each parameter over four small bowel segments (duodenum, jejunum, proximal ileum, and distal ileum) (Table 1), adding up the individual points to obtain the final score by region. The complete score highlights the distribution and longitudinal extent of lesions found through CE.

In 2005, Gralnek *et al*[39] carried out a study in order to develop and test a simple, user-friendly CE scoring index for CD activity based on the previously proposed endoscopic findings associated with the disease. These were individually scored as three equal parts (or tertiles) into which the small bowel transit time was divided (Table 2). The final scoring index included three endoscopic variables among which the authors found excellent inter-observer agreement: villous edema, ulcers, and stenosis. Index parameters are measured by number, longitudinal extent, and additional descriptors. Using these parameters, the authors established a score ranging from 8 to 4800 points: a score < 135 was designated as normal or clinically insignificant mucosal inflammatory change while a score between 135 and 790 was considered to indicate mild CD and a score ≥ 790 indicated moderate to severe CD.

In 2008, a new activity index was developed by Gal *et al*[37]. The CECDAI (Capsule Endoscopy Crohn's Disease Activity Index) (Table 3) uses a methodology similar to that of the previously described index, but with two important differences. First, small bowel transit time is divided into proximal and distal parts. In both the proximal and distal bowel, three parameters are calculated separately by multiplying the inflammation score (A) by the extent-of-disease score (B) and adding the stricture score (C). The second particularity of this index is that villous appearance and ulcers are considered to be opposite extremes of a wide range of inflammation rather than as independent variables, as was the case in the Gralnek index. Furthermore, and in contrast to both of the aforementioned indexes, the number of lesions is not considered in calculating the score. In the case of identifying different inflammatory lesions in the same bowel segment (i.e. moderate edema and a large ulcer in the distal section), the more serious lesion is used for calculating the index. The same occurs with regard to the stricture index.

An important limitation in the use of CE severity indexes is that none of them has been independently validated and no studies comparing the different indexes have been conducted to date. Another important disadvantage of the use of indexes in CD is that clinical indexes do not

Table 2 Parameters and weightings for the capsule endoscopy scoring index[39]

	Parameters	Number	Longitudinal extent	Descriptors
First tertile	Villous appearance	Normal = 0 Edematous = 1	Short segment = 8 Long segment = 12 Whole segment = 20	Single = 1 Patchy = 14 Diffuse = 17
	Ulcer	None = 0 Single = 3 Few = 5 Multiple = 10	Short segment = 8 Long segment = 12 Whole segment = 20	< ¼ = 9 ¼ to ½ =12 > ½ = 18
Second tertile	Villous appearance	Normal = 0 Edematous = 1	Short segment = 8 Long segment = 12 Whole segment = 20	Single = 1 Patchy = 14 Diffuse = 17
	Ulcer	None = 0 Single = 3 Few = 5 Multiple = 10	Short segment = 8 Long segment = 12 Whole segment = 20	< ¼ = 9 ¼ to ½ = 12 > ½ = 18
	Villous appearance	Normal = 0 Edematous = 1	Short segment = 8 Long segment = 12 Whole segment = 20	Single = 1 Patchy = 14 Diffuse = 17
	Ulcer	None = 0 Single = 3 Few = 5 Multiple = 10	Short segment = 8 Long segment = 12 Whole segment = 20	< ¼ = 9 ¼ to ½ =12 > ½ = 18
Third tertile	Villous appearance	Normal = 0 Edematous = 1	Short segment = 8 Long segment = 12 Whole segment = 20	Single = 1 Patchy = 14 Diffuse = 17
	Ulcer	None = 0 Single = 3 Few = 5 Multiple = 10	Short segment = 8 Long segment = 12 Whole segment = 20	< ¼ = 9 ¼ to ½ =12 > ½ = 18
Stenosis-rated for whole study	Stenosis	None = 0 Single = 14 Multiple = 20	Ulcerated = 24 Non-ulcerated = 2	Traversed = 7 Not traversed = 10

Table 3 Capsule endoscopy Crohn's disease activity index scoring system[37]

	Proximal	Distal
A. Inflammation score	0 = None 1 = Mild to moderate edema/hyperemia/denudation 2 = Severe edema/hyperemia/denudation 3 = Bleeding, exudates, aphthae, erosion small ulcer (< 0.5 cm) 4 = Moderate ulcer (0.5 cm - 2 cm), pseudopolyp 5 = Large ulcer (> 2 cm)	
B. Extent of disease score	0 = None 1 = Focal disease (single segment) 2 = Patchy disease (multiple segments) 3 = Diffuse disease	
C. Narrowing (stricture)	0 = None 1 = Single-passed 2 = Multiple-passed 3 = Obstruction	
Segmental score = A × B + C Total score = (A1 × B1 + C1) + (A2 × B2 + C2)		

estimate the severity of mucosal lesions while endoscopic indexes only assess small bowel mucosal changes, not necessarily their effect on the disease. Indeed, the main advantage of having different types of indexes available is their prognostic value, as they allow medical professionals to observe the changes caused by the disease over time.

CONCLUSION

CE represents the most important technical advance in the diagnosis of small bowel diseases and constitutes an irreplaceable method for studying CD. However, difficulties in clearly establishing commonly accepted diagnostic criteria and the possibility of finding typical lesions of CD without histological confirmation in subjects not suffering from the disease have limited the diagnostic success of this method. Diagnostic yield of CE in CD increases when finding are interpreted within a suitable clinical and analytical context. Some studies suggest that CE may be a useful technique for monitoring CD as well as an interesting tool in guiding treatment. Proposed activity indexes could be useful for predicting the prognosis of CD by assessing mucosal changes caused by the disease or the therapy, although further research should be carried out to confirm this potential.

REFERENCES

1 **Lennard-Jones JE**. Classification of inflammatory bowel

disease. *Scand J Gastroenterol Suppl* 1989; **170**: 2-6; discussion 16-19
2 **Petruzziello C**, Onali S, Calabrese E, Zorzi F, Ascolani M, Condino G, Lolli E, Naccarato P, Pallone F, Biancone L. Wireless capsule endoscopy and proximal small bowel lesions in Crohn's disease. *World J Gastroenterol* 2010; **16**: 3299-3304
3 **Lashner B**. Clinical features, laboratory findings, and course of Crohn's disease. In: Kirsner JV, editor. Inflammatory bowel disease. 5th edn. Philadelphia: Saunders, 2000: 305-314
4 **Molinié F**, Gower-Rousseau C, Yzet T, Merle V, Grandbastien B, Marti R, Lerebours E, Dupas JL, Colombel JF, Salomez JL, Cortot A. Opposite evolution in incidence of Crohn's disease and ulcerative colitis in Northern France (1988-1999). *Gut* 2004; **53**: 843-848
5 **Raju GS**, Gerson L, Das A, Lewis B. American Gastroenterological Association (AGA) Institute technical review on obscure gastrointestinal bleeding. *Gastroenterology* 2007; **133**: 1697-1717
6 **Cellier C**, Green PH, Collin P, Murray J. ICCE consensus for celiac disease. *Endoscopy* 2005; **37**: 1055-1059
7 **Bardan E**, Nadler M, Chowers Y, Fidder H, Bar-Meir S. Capsule endoscopy for the evaluation of patients with chronic abdominal pain. *Endoscopy* 2003; **35**: 688-689
8 **Spada C**, Pirozzi GA, Riccioni ME, Iacopini F, Marchese M, Costamagna G. Capsule endoscopy in patients with chronic abdominal pain. *Dig Liver Dis* 2006; **38**: 696-698
9 **de Franchis R**, Rondonotti E, Abbiati C, Beccari G, Merighi A, Pinna A, Villa E. Capsule enteroscopy in small bowel transplantation. *Dig Liver Dis* 2003; **35**: 728-731
10 **Beckurts KT**, Stippel D, Schleimer K, Schäfer H, Benz C, Dienes HP, Hölscher AH. First case of isolated small bowel transplantation at the university of cologne: rejection-free course under quadruple immunosuppression and endoluminal monitoring with video-capsule. *Transplant Proc* 2004; **36**: 340-342
11 **Voderholzer WA**, Ortner M, Rogalla P, Beinhölzl J, Lochs H. Diagnostic yield of wireless capsule enteroscopy in comparison with computed tomography enteroclysis. *Endoscopy* 2003; **35**: 1009-1014
12 **Eliakim R**, Suissa A, Yassin K, Katz D, Fischer D. Wireless capsule video endoscopy compared to barium follow-through and computerised tomography in patients with suspected Crohn's disease--final report. *Dig Liver Dis* 2004; **36**: 519-522
13 **Buchman AL**, Miller FH, Wallin A, Chowdhry AA, Ahn C. 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
14 **Marmo R**, Rotondano G, Piscopo R, Bianco MA, Siani A, Catalano O, Cipolletta L. Capsule endoscopy versus enteroclysis in the detection of small-bowel involvement in Crohn' s disease: a prospective trial. *Clin Gastroenterol Hepatol* 2005; **3**: 772-776
15 **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
16 **Redondo-Cerezo E**. Role of wireless capsule endoscopy in inflammatory bowel disease. *World J Gastrointest Endosc* 2010; **2**: 179-185
17 **Cave D**, Legnani P, de Franchis R, Lewis BS. ICCE consensus for capsule retention. *Endoscopy* 2005; **37**: 1065-1067
18 **Legnani P**, Kornbluth A. Video capsule endoscopy in inflammatory bowel disease 2005. *Curr Opin Gastroenterol* 2005; **21**: 438-442
19 **Herrerias JM**, Leighton JA, Costamagna G, Infantolino A, Eliakim R, Fischer D, Rubin DT, Manten HD, Scapa E, Morgan DR, Bergwerk AJ, Koslowsky B, Adler SN. Agile patency system eliminates risk of capsule retention in patients with known intestinal strictures who undergo capsule endoscopy. *Gastrointest Endosc* 2008; **67**: 902-909
20 **Swain P**. Wireless capsule endoscopy and Crohn's disease. *Gut* 2005; **54**: 323-326
21 **Triester SL**, Leighton JA, Leontiadis GI, Gurudu SR, Fleischer DE, Hara AK, Heigh RI, Shiff AD, Sharma VK. 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
22 **De Bona M**, Bellumat A, Cian E, Valiante F, Moschini A, De Boni M. Capsule endoscopy findings in patients with suspected Crohn's disease and biochemical markers of inflammation. *Dig Liver Dis* 2006; **38**: 331-335
23 **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
24 **Van Assche G**, Dignass A, Panes J, Beaugerie L, Karagiannis J, Allez M. The second European evidence-based consensus on the diagnosis and management of Crohn's disease: Definitions and diagnosis. *J Crohns Colitis* 2010; **4**: 7-27
25 **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
26 **Delvaux M**, Friedman S, Keuchel M, Hagenmüller F, Weinstein M, Cave D, de Franchis R, Gay G, Korman LY. Structured terminology for capsule endoscopy: results of retrospective testing and validation in 766 small-bowel investigations. *Endoscopy* 2005; **37**: 945-950
27 **Bourreille A**, Ignjatovic A, Aabakken L, Loftus EV Jr, Eliakim R, Pennazio M, Bouhnik Y, Seidman E, Keuchel M, Albert JG, Ardizzone S, Bar-Meir S, Bisschops R, Despott EJ, Fortun PF, Heuschkel R, Kammermeier J, Leighton JA, Mantzaris GJ, Moussata D, Lo S, Paulsen V, Panés J, Radford-Smith G, Reinisch W, Rondonotti E, Sanders DS, Swoger JM, Yamamoto H, Travis S, Colombel JF, Van Gossum A. Role of small-bowel endoscopy in the management of patients with inflammatory bowel disease: an international OMED-ECCO consensus. *Endoscopy* 2009; **41**: 618-637
28 **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
29 **Mehdizadeh S**, Chen GC, Barkodar L, Enayati PJ, Pirouz S, Yadegari M, Ippoliti A, Vasiliauskas EA, Lo SK, Papadakis KA. Capsule endoscopy in patients with Crohn's disease: diagnostic yield and safety. *Gastrointest Endosc* 2010; **71**: 121-127
30 **Tukey M**, Pleskow D, Legnani P, Cheifetz AS, Moss AC. The utility of capsule endoscopy in patients with suspected Crohn's disease. *Am J Gastroenterol* 2009; **104**: 2734-2739
31 **Voderholzer WA**, Beinhoelzl J, Rogalla P, Murrer S, Schachschal G, Lochs H, Ortner MA. Small bowel involvement in Crohn's disease: a prospective comparison of wireless capsule endoscopy and computed tomography enteroclysis. *Gut* 2005; **54**: 369-373
32 **Dubcenco E**, Jeejeebhoy KN, Petroniene R, Tang SJ, Zalev AH, Gardiner GW, Baker JP. Capsule endoscopy findings in patients with established and suspected small-bowel Crohn's disease: correlation with radiologic, endoscopic, and histologic findings. *Gastrointest Endosc* 2005; **62**: 538-544
33 **Figueiredo P**, Almeida N, Lopes S, Duque G, Freire P, Lérias C, Gouveia H, Sofia C. Small-bowel capsule endoscopy in patients with suspected Crohn's disease-diagnostic value and complications. *Diagn Ther Endosc* 2010; **2010**: Epub 2010 Aug 5

34 **Costamagna G**, Shah SK, Riccioni ME, Foschia F, Mutignani M, Perri V, Vecchioli A, Brizi MG, Picciocchi A, Marano P. A prospective trial comparing small bowel radiographs and video capsule endoscopy for suspected small bowel disease. *Gastroenterology* 2002; **123**: 999-1005

35 **Chong AK**, Taylor A, Miller A, Hennessy O, Connell W, Desmond P. Capsule endoscopy vs. push enteroscopy and enteroclysis in suspected small-bowel Crohn's disease. *Gastrointest Endosc* 2005; **61**: 255-261

36 **Hara AK**, Leighton JA, Heigh RI, Sharma VK, Silva AC, De Petris G, Hentz JG, Fleischer DE. Crohn disease of the small bowel: preliminary comparison among CT enterography, capsule endoscopy, small-bowel follow-through, and ileoscopy. *Radiology* 2006; **238**: 128-134

37 **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

38 **Kornbluth A**, Legnani P, Lewis BS. Video capsule endoscopy in inflammatory bowel disease: past, present, and future. *Inflamm Bowel Dis* 2004; **10**: 278-285

39 **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

40 **Goldstein JL**, Eisen GM, Lewis B, Gralnek IM, Zlotnick S, Fort JG. Video capsule endoscopy to prospectively assess small bowel injury with celecoxib, naproxen plus omeprazole, and placebo. *Clin Gastroenterol Hepatol* 2005; **3**: 133-141

41 **Graham DY**, Opekun AR, Willingham FF, Qureshi WA. Visible small-intestinal mucosal injury in chronic NSAID users. *Clin Gastroenterol Hepatol* 2005; **3**: 55-59

42 **Maiden L**, Thjodleifsson B, Seigal A, Bjarnason II, Scott D, Birgisson S, Bjarnason I. Long-term effects of nonsteroidal anti-inflammatory drugs and cyclooxygenase-2 selective agents on the small bowel: a cross-sectional capsule enteroscopy study. *Clin Gastroenterol Hepatol* 2007; **5**: 1040-1045

43 **Pineton de Chambrun G**, Peyrin-Biroulet L, Lémann M, Colombel JF. Clinical implications of mucosal healing for the management of IBD. *Nat Rev Gastroenterol Hepatol* 2010; **7**: 15-29

44 **Schnitzler F**, Fidder H, Ferrante M, Noman M, Arijs I, Van Assche G, Hoffman I, Van Steen K, Vermeire S, Rutgeerts P. Mucosal healing predicts long-term outcome of maintenance therapy with infliximab in Crohn's disease. *Inflamm Bowel Dis* 2009; **15**: 1295-301

45 **Kornbluth A**, Colombel JF, Leighton JA, Loftus E. ICCE consensus for inflammatory bowel disease. *Endoscopy* 2005; **37**: 1051-1054

46 **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

47 **Lorenzo-Zúñiga V**, de Vega VM, Domènech E, Cabré E, Mañosa M, Boix J. Impact of capsule endoscopy findings in the management of Crohn's Disease. *Dig Dis Sci* 2010; **55**: 411-414

48 **Biancone L**, Calabrese E, Petruzziello 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

49 **Pons Beltrán V**, Nos P, Bastida G, Beltrán B, Argüello L, Aguas M, Rubín A, Pertejo V, Sala T. Evaluation of post-surgical recurrence in Crohn's disease: a new indication for capsule endoscopy? *Gastrointest Endosc* 2007; **66**: 533-540

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