

# Utility of Capsule Endoscopy in the Diagnosis and Management of Crohn's Disease

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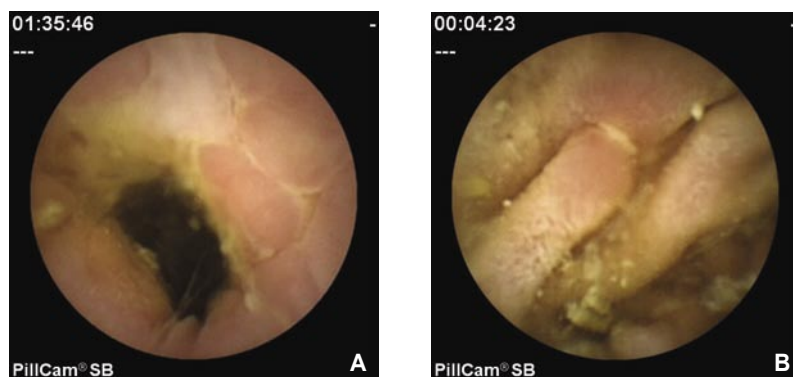
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**Abstract:** Clinicians currently have access to an expanding range of diagnostic modalities for assessment of the small intestine when diagnosing or evaluating the extent of Crohn's disease. Although complete endoscopic examination of the colon with a standard videoendoscope is routine, endoscopic assessment of the entire small intestine by enteroscopy is not feasible as a routine diagnostic test. Capsule endoscopy (CE) has gained increasing acceptance as a highly sensitive small bowel imaging modality, though concerns have been raised regarding the risk of false-positive examinations and complications arising from capsule retention proximal to stenotic lesions. This review will examine current data on the utility of CE in suspected and established Crohn's disease in comparison to other modalities such as push enteroscopy, computed tomography, magnetic resonance enterography, and small bowel follow-through. Current suggested indications for CE in patients with known or suspected Crohn's disease will be evaluated in order to offer a potential framework for the safe and appropriate use of capsule examinations in these patients.

Crohn's disease is a chronic inflammatory bowel disorder that can involve any portion of the gastrointestinal tract, with small bowel mucosal inflammation seen in the majority of cases. The diagnosis is made on the basis of a combination of clinical, biochemical, radiologic, and endoscopic findings, and, when possible, histologic changes that corroborate the diagnosis. In most cases, colonoscopy with intubation and examination of the terminal ileum (ileoscopy) identifies abnormal mucosa accessible to biopsy. However, as a minority of patients have involvement of only the more proximal small intestine, a normal ileocolonoscopy examination does not exclude the diagnosis. In such cases, dedicated imaging of the small bowel is usually required to either confirm or exclude Crohn's disease. Radiologic imaging of the small bowel is usually sufficient. However, in instances where patients have persistent gastrointestinal complaints and suspected Crohn's disease despite normal small bowel imaging and ileocolonoscopy, capsule endoscopy (CE) can be utilized. CE may also play a role in the rare



**Figure 1.** Small bowel mucosal lesions demonstrated by capsule endoscopy. Ulcerated segment of the small intestine with stenosis identified in a young woman with suspected Crohn's disease (A). Focal ulceration in the jejunum seen in a young man with iron-deficiency anemia related to nonsteroidal anti-inflammatory drug use (B).

Capsule images courtesy of Peter Legnani, MD, of the Mount Sinai School of Medicine, New York.

instances where the terminal ileum cannot be intubated at colonoscopy.

In patients with known Crohn's disease, dedicated small bowel imaging is routinely utilized to determine the presence and extent of small bowel involvement. A range of endoscopic and radiologic techniques are available to evaluate the small intestine in these circumstances; CE is merely one of these options, and clinicians must decide whether its reported greater sensitivity for mucosal lesions outweighs its low specificity and inability to assess extraintestinal structures.

There is a range of potential indications for the use of CE in patients with established Crohn's disease. Once a diagnosis of Crohn's disease is confirmed and therapy is initiated, periodic re-assessment may be required to evaluate treatment responses objectively. Additionally, CE has the ability to assess for recurrence of mucosal disease at the anastomosis following surgical resection. Other possible indications for CE include known Crohn's disease with persistent gastrointestinal symptoms or laboratory abnormalities (eg, iron-deficiency anemia, raised inflammatory markers) when radiologic and endoscopic evaluations are unrevealing. CE can potentially be employed in all of the above circumstances, as well as assessment of localized small bowel lesions or investigation of occult or overt gastrointestinal bleeding in patients with Crohn's disease.

This review will first evaluate the utility of CE as a front-line diagnostic test in patients with suspected Crohn's disease and then examine its role in patients with established disease. In both contexts, published studies on the performance of CE relative to other small bowel imaging modalities will be reviewed. Current data on the complications of capsule examinations will also be reviewed. Finally, we will attempt to integrate the findings into a framework to guide appropriate use of CE in the diagnosis and ongoing management of Crohn's disease.

### Capsule Endoscopy in the Diagnosis of Crohn's Disease

CE is quite sensitive and has a significant yield of abnormal findings in any symptomatic patient population. One study demonstrated abnormal findings in 95 of 250 patient examinations (38%), with the yield even higher in patients with suspected Crohn's disease.<sup>1</sup> These results were confirmed by another small prospective multicenter study.<sup>2</sup> However, one must keep in mind that many of these abnormal findings are not specific for Crohn's disease. In fact, minor mucosal abnormalities are seen in approximately 14% of asymptomatic individuals (those not taking nonsteroidal anti-inflammatory drugs [NSAIDs])<sup>3</sup> and in up to two thirds of people using NSAIDs regularly.<sup>4</sup>

The value of CE in patients with suspected Crohn's disease is debatable. A number of studies have examined CE findings in patients with suspected small bowel Crohn's disease and found that Crohn's disease was diagnosed in 26–71% of cases with previously negative (ileo)colonoscopy and small bowel follow-through (SBFT).<sup>5–9</sup> This wide variation is due to a number of factors. It is at least partially explained by differences in the criteria used to define suspected small bowel Crohn's disease. Another major issue is the variation in the extent or severity of mucosal changes required for making an endoscopic diagnosis of Crohn's disease (Figure 1). Despite efforts to standardize the reporting of mucosal lesions that were identified on CE,<sup>10,11</sup> interpreting the significance of minor mucosal lesions remains problematic and may lead to overdiagnosis of Crohn's disease. On the other hand, advocates of CE suggest that earlier use of CE in the evaluation of suspected small bowel Crohn's disease is more cost-effective<sup>12</sup> and reduces the total number of diagnostic tests required to arrive at a final diagnosis.

When determining the best method for assessment of the small bowel in patients with suspected Crohn's

disease, clinicians face a choice between the use of CE or an alternative radiologic or endoscopic assessment. Various studies have performed head-to-head comparisons of CE against radiologic techniques for assessing small bowel morphology, in particular comparing their ability to detect small intestinal Crohn's disease. For many years, SBFT was the primary means of radiologic assessment of the small intestine, and it remains a well-established and widely available technique for small bowel evaluation. Although some have reported a reasonable correlation between SBFT and CE for detection of Crohn's disease,<sup>13</sup> others have demonstrated a significant miss rate of small bowel mucosal lesions with SBFT compared to capsule examination.<sup>14-18</sup> Additionally, onset of Crohn's disease symptoms can predate the discovery of abnormal findings on SBFT by several years, suggesting that it may lack sensitivity for detection of early-stage disease.

More recently, radiologic evaluation of the small intestine has been shifting away from contrast-enhanced plain radiography and toward dedicated computed tomography (CT) or magnetic resonance (MR) imaging of the small intestine. Of the two techniques, CT remains more widely available, and direct comparisons of CE with CT in evaluation of the small intestine have been performed. Two studies have evaluated CT enteroclysis in comparison to CE and yielded similar findings.<sup>19,20</sup> The larger of the two studies examined 41 patients with Crohn's disease who were deemed suitable to undergo both examinations. Jejunal or ileal lesions were identified in 25 patients by CE and in 12 individuals by CT, whereas detection of lesions in the terminal ileum/neoterminal ileum was not significantly different.<sup>20</sup> Although the differences were explained by the ability of CE to detect subtle mucosal abnormalities such as aphthous ulcerations, erosions, or villous denudation, the authors reported changes in therapy related to capsule findings in 10 (24%) of the patients studied. Five of these patients had normal imaging, and Crohn's disease was diagnosed based upon CE findings alone. Many clinicians suggest, however, that the higher sensitivity of CE for minor mucosal lesions involves an inevitable trade-off for lower specificity, with a risk of unnecessary treatment for false-positive abnormalities.<sup>21</sup>

MR enterography has also recently emerged as an alternative to CT, and a number of studies have sought to evaluate the performance of MR imaging of the small intestine in comparison to CE. The largest prospective study of this type evaluated 52 patients, approximately half of whom had known Crohn's disease (and the remainder suspected Crohn's disease). In nearly 30% of cases, CE was not performed due to radiologic evidence of strictures. CE showed slightly greater sensitivity for mucosal lesions, but MR imaging performed better at identifying transmural inflammation, extraluminal abnormalities, inflammatory

collections, and fistulae.<sup>22</sup> Three smaller studies of MR enterography have shown broadly similar findings with CE superior for evaluation of gastrointestinal bleeding (mainly in non-inflammatory bowel disease patients)<sup>23</sup> and superior for detection of mucosal lesions in other small studies specific to patients with Crohn's disease.<sup>24,25</sup>

Attempts have been made to compare CE head-to-head with all of the other commonly used techniques for small bowel evaluation (though MR-based techniques were unfortunately not incorporated). The largest (n=41) of two prospective studies to compare all four of the most widely available small bowel imaging techniques (CE vs CT enterography, SBFT, and ileocolonoscopy) excluded patients taking NSAIDs, a common reason for false-positive findings.<sup>26</sup> In spite of this, the specificity of CE (53%) remained significantly lower than that of other modalities, whereas the sensitivity of CE (83%) was not significantly better than CT enterography. One limitation was that 17% of subjects had asymptomatic partial small bowel obstruction on initial radiology and did not undergo capsule examination. Despite this, 1 of the 28 patients who did undergo CE developed transient capsule-associated small bowel obstruction. A second smaller study of 20 patients showed similar trends.<sup>27</sup> CE appeared to have higher sensitivity when compared with SBFT, but the study failed to detect significant differences. One patient required surgery for capsule retention (in a stricture not identified on SBFT).

In addition to the various radiologic techniques for small bowel imaging, a range of other endoscopic methods can be employed to visualize the small intestinal mucosa. Relative to these other endoscopic techniques for evaluating the small intestine, CE has the advantage of being less invasive. However, it does not allow biopsy or endoscopic therapy for identified lesions. A retrospective review comparing CE to push enteroscopy looked at 155 cases (in approximately half of which both CE and push enteroscopy were used, and the other half push enteroscopy alone) for a range of indications, including assessment for Crohn's disease.<sup>28</sup> No significant difference was observed in the diagnostic yield overall with the addition of CE. However, other studies have suggested that CE has a significantly greater sensitivity than push enteroscopy for small bowel lesions in patients with known or suspected Crohn's disease.<sup>29</sup> CE can play a useful role in determining whether invasive enteroscopy is indicated (to obtain biopsies or facilitate therapy such as argon plasma coagulation) and in determining the optimum (initial) route for the more invasive examination.<sup>30</sup>

Double-balloon enteroscopy is a novel, but relatively invasive, endoscopic technique that may allow for direct visualization of most, or all, of the small intestinal mucosa. A meta-analysis comparing double-balloon enteroscopy

with CE suggested that the diagnostic yield of both techniques for small bowel disease was broadly comparable.<sup>31</sup> Double-balloon enteroscopy can not only facilitate biopsy to characterize identified mucosal lesions but potentially can also provide therapy such as stricture dilatation.<sup>32</sup>

### Capsule Endoscopy As a Guide to Crohn's Disease Management

In addition to a potential role in the initial diagnosis and staging of Crohn's disease, CE has also been employed in a range of circumstances as part of the ongoing management and assessment of patients with established Crohn's disease. A recent meta-analysis examining the yield of CE compared to other diagnostic modalities in Crohn's disease demonstrated a greater diagnostic yield for CE compared to barium radiography, ileocolonoscopy, CT enterography/enteroclysis, and MR enterography. It is important to note that the incremental yield observed for CE was not in the initial diagnosis (where differences were not significant), but rather in patients with established nonstricturing Crohn's disease being evaluated for small bowel involvement.<sup>33</sup> On the basis of such findings, some have advocated that CE is better utilized as a tool for monitoring disease extent and activity than as a primary diagnostic modality. Additionally, there is concern regarding cumulative radiation exposure from repeated diagnostic imaging in patients with Crohn's disease.<sup>34</sup> CE has the advantage of no radiation exposure. However, whether monitoring patients with established Crohn's disease with CE alters long-term management remains unclear. There are certain circumstances in which CE may have an added benefit in patients with inflammatory bowel disease, and these are worthy of review.

One instance where CE may prove useful is in those patients with indeterminate colitis or inflammatory bowel disease—unclassified. In the 10–15% of newly diagnosed inflammatory bowel disease cases that cannot easily be classified as either Crohn's disease or ulcerative colitis, CE, with its greater sensitivity for small bowel mucosal lesions, appears to allow a more definitive diagnosis. Studies have suggested that patients with recently diagnosed inflammatory bowel disease—unclassified have a sufficient number of small bowel lesions in 15–20% of cases, allowing them to be reclassified as Crohn's disease.<sup>35,36</sup>

CE also has been examined as a minimally invasive method for assessment of postoperative recurrence of Crohn's disease, either as an alternative to colonoscopy or when the anastomosis is not readily accessible to endoscopic examination. The yield of CE for identification of lesions proximal to the anastomosis is greater, with lesions detected above the endoscopically accessible segment in a significant proportion of patients.<sup>37,38</sup> However, at least

one prospective study has suggested that CE has a lower sensitivity for detection of postoperative recurrence in the neoterminal ileum after ileocelectomy.<sup>38</sup> Another small prospective study demonstrated equivalency of both CE and small intestine contrast ultrasonography with ileocolonoscopy.<sup>39</sup> Patient acceptability, assessed in one study, was reported to be superior for CE compared to ileocolonoscopy.<sup>37</sup>

In addition to laboratory indices and radiologic examinations, CE can be used to provide an objective assessment of disease activity in patients with known small bowel Crohn's disease. This can be clinically useful in assessing treatment responses (ie, endoscopic healing), though persistent aphthous ulceration does not predict clinical response to treatment.<sup>40</sup> Another potential role of CE is the evaluation of symptoms that persist despite apparently adequate therapy or a lack of objective evidence of active disease on radiology or ileocolonoscopy. CE may be able to demonstrate significant ulceration that has been missed on other modalities.<sup>17,20,22</sup> A specific capsule-related Crohn's Disease Activity Index has been developed and validated, and it can be employed precisely to track objective responses.<sup>41</sup> The utility of such indices outside of clinical trials is somewhat unclear, but, nonetheless, CE does appear to have a role in evaluating select patients with comorbid irritable bowel syndrome and Crohn's disease to help identify the origin of symptoms,<sup>42</sup> particularly in those who fail to respond to standard anti-inflammatory therapies. Distinguishing between active Crohn's disease and irritable bowel syndrome or other causes of gastrointestinal symptoms can be challenging, but it is clearly vital in determining the proper course of therapy.

CE has also been established as a useful adjunct in evaluating recurrent iron-deficiency anemia and obscure gastrointestinal bleeding (OGIB), though few studies have specifically examined this in patients with inflammatory bowel disease. However, a recent meta-analysis showed that, for the most part, patients with Crohn's disease undergoing evaluation for OGIB had the highest diagnostic yield with CE (over other methods such as push enteroscopy, small bowel barium radiography, and CT enterography).<sup>43</sup>

### Complications of Capsule Endoscopy

CE is minimally invasive, and there does appear to be a role for it in both the initial diagnosis and ongoing assessment of Crohn's disease patients; however, CE is not an entirely benign procedure, and complications can occur. Although transient abdominal discomfort and other minor abdominal symptoms are frequently reported in clinical trials, persistent capsule retention is the major complication arising from videocapsule

examination. Reports have estimated the incidence of retention to be approximately 2% of all examinations, predominantly due to capsule retention proximal to benign or malignant strictures.<sup>44</sup> More recent large case series estimated the risk of capsule retention to be between 1.4% and 2.5%.<sup>45,46</sup> Given the tendency for stricturing to arise from chronic small intestinal inflammation, patients with Crohn's disease are at particular risk of capsule retention. One series reported retention in 13% of examinations in patients with known Crohn's disease, most of whom were not known to have strictures in advance of the procedure.<sup>47</sup> Normal radiologic imaging of the small bowel does not guarantee the absence of a stricture. Despite normal imaging, patients with Crohn's disease remain at risk for capsule retention.<sup>26,27</sup>

Persistent capsule retention usually requires attempts at endoscopic retrieval<sup>48,49</sup> or surgical intervention.<sup>50,51</sup> Although stricture resection may be of broader therapeutic value, increasing efforts have focused on identifying strictures likely to cause capsule retention prior to performance of diagnostic examinations. Recently, the use of dissolvable patency capsules to help identify previously unrecognized strictures in Crohn's disease patients has been explored. A number of small studies have suggested that the passage of a patency capsule within 72 hours (without abdominal pain) predicts minimal risk of retention of a capsule endoscope that is administered subsequently.<sup>52,53</sup> However, the original patency capsules were slow to dissolve and caused abdominal pain or small bowel obstruction not infrequently when they became impacted in a stricture. Although this was usually a transient phenomenon, there were cases that necessitated surgery when the obstruction failed to resolve with conservative measures.<sup>54,55</sup> A new patency capsule has been devised to avoid these complications and appears safe for use in patients with strictures.<sup>56</sup>

Unlike patients with known Crohn's disease, patients with suspected Crohn's disease do not appear to be at a greatly increased risk for capsule retention. In one study that compared capsule retention in patients with known and suspected Crohn's disease, the risk of capsule retention in patients with suspected Crohn's disease was 1.6%, similar to that of the general patient population (vs 13% in patients with known Crohn's disease).<sup>47</sup>

## Conclusion

CE is a sensitive, noninvasive, and relatively safe technique for assessment of the small intestinal mucosa. Its role as a primary diagnostic tool for Crohn's disease is disputed. Despite its enhanced sensitivity for the detection of small mucosal erosions and aphthae,<sup>20</sup> the significance

of such findings is unclear. Its specificity appears lower than that of other small bowel imaging techniques.<sup>26</sup> It remains our view, therefore, that a diagnosis of Crohn's disease should rarely, if ever, be made on the basis of capsule findings alone and that CE should be used very selectively in the initial evaluation of suspected small bowel Crohn's disease.

Data suggest that CE may play a more useful role in monitoring Crohn's disease activity and extent. Despite its greater ability for detection of mucosal lesions, however, it is probably best suited as an adjunctive tool to other imaging techniques. CT and MR enterography generally perform well and also provide clinically useful information on extraluminal abnormalities such as fluid collections and fistulae, which CE cannot identify.<sup>22</sup> It is recommended that small bowel imaging be performed prior to CE to evaluate for stricturing and identify patients at risk of capsule retention.<sup>57</sup> However, a normal small bowel radiologic examination does not obviate the risk of capsule retention.

CE is a suitable means for evaluation of postoperative recurrence of Crohn's disease in individuals reluctant to undergo ileocolonoscopy or in whom the anastomosis is not readily accessible to standard endoscopy. Due to higher specificity, colonoscopy remains the examination of choice for assessment of recurrence after ileocelectomy.<sup>38</sup>

CE also constitutes a useful test to evaluate persistent iron deficiency or OGIB in patients with Crohn's disease<sup>43</sup> and to assess persistent symptoms despite apparently adequate therapy and normal small bowel imaging.<sup>42</sup> CE findings should nonetheless be interpreted with caution (Figure 1). Even in patients with known Crohn's disease, the significance of minor mucosal abnormalities remains a topic of dispute. Use of NSAIDs should always be ruled out in these instances, and it should be remembered that minor mucosal changes can be seen in as many as 13.8% of asymptomatic healthy individuals undergoing CE.<sup>3</sup> The development of scoring systems to quantify the extent and severity of small bowel mucosal inflammatory changes with the aim of defining a threshold for clinically significant changes is welcomed,<sup>58</sup> as it is crucial that overtreatment of Crohn's disease patients with potent immunomodulation on the basis of minor mucosal abnormalities should be avoided. In addition, capsule retention remains an important consideration, and informed consent for capsule examinations in patients with established Crohn's disease must emphasize the increased risk of capsule retention in undiagnosed strictures and clearly state the risk of surgery in the event of persistent capsule retention. It should be understood that capsule retention may lead to surgery in patients who might otherwise be managed medically.<sup>59</sup>

## References

1. Van Tuyl SA, Van Noorden JT, Kuipers EJ, Stolk MF. Results of videocapsule endoscopy in 250 patients with suspected small bowel pathology. *Dig Dis Sci*. 2006;51:900-905.
2. May A, Manner H, Schneider M, Ipsen A, Ell C. Prospective multicenter trial of capsule endoscopy in patients with chronic abdominal pain, diarrhea and other signs and symptoms (CEDAP-Plus Study). *Endoscopy*. 2007;39:606-612.
3. 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.
4. Maiden L, Thjodleifsson B, Theodors A, Gonzalez J, Bjarnason I. A quantitative analysis of NSAID-induced small bowel pathology by capsule endoscopy. *Gastroenterology*. 2005;128:1172-1178.
5. Valle J, Alcantara M, Perez-Gruoso MJ, Navajas J, Munoz-Rosas C, et al. Clinical features of patients with negative results from traditional diagnostic work-up and Crohn's disease findings from capsule endoscopy. *J Clin Gastroenterol*. 2006;40:692-696.
6. Herrerias JM, Caunedo A, Rodriguez-Tellez M, Pellicer F, Herrerias JM Jr. Capsule endoscopy in patients with suspected Crohn's disease and negative endoscopy. *Endoscopy*. 2003;35:564-568.
7. Girelli CM, Porta P, Malacrida V, Barzaghi F, Rocca F. Clinical outcome of patients examined by capsule endoscopy for suspected small bowel Crohn's disease. *Dig Liver Dis*. 2007;39:148-154.
8. Fireman Z, Mahajna E, Broide E, Shapiro M, Fich L, et al. Diagnosing small bowel Crohn's disease with wireless capsule endoscopy. *Gut*. 2003;52:390-392.
9. Fireman Z, Eliakim R, Adler S, Scapa E. Capsule endoscopy in real life: a four-centre experience of 160 consecutive patients in Israel. *Eur J Gastroenterol Hepatol*. 2004;16:927-931.
10. Korman LY, Delvaux M, Gay G, Hagenmuller F, Keuchel M, et al. Capsule endoscopy structured terminology (CEST): proposal of a standardized and structured terminology for reporting capsule endoscopy procedures. *Endoscopy*. 2005;37:951-959.
11. Delvaux M, Friedman S, Keuchel M, Hagenmuller F, Weinstein M, et al. Structured terminology for capsule endoscopy: results of retrospective testing and validation in 766 small bowel investigations. *Endoscopy*. 2005;37:945-950.
12. Goldfarb NI, Pizzi LT, Fuhr JP Jr, Salvador C, Sikirica V, et al. Diagnosing Crohn's disease: an economic analysis comparing wireless capsule endoscopy with traditional diagnostic procedures. *Dis Manag*. 2004;7:292-304.
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. Park CH, Kim JO, Choi MG, Kim KJ, Kim YH, 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.
15. Eliakim R, Suissa A, Yassin K, Katz D, Fischer D. Wireless capsule video endoscopy compared to barium follow-through and computerized tomography in patients with suspected Crohn's disease-final report. *Dig Liver Dis*. 2004;36:519-522.
16. Eliakim R, Fischer D, Suissa A, Yassin K, Katz D, 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.
17. Costamagna G, Shah SK, Riccioni ME, Foschia F, Mutignani M, et al. A prospective trial comparing small bowel radiographs and video capsule endoscopy for suspected small bowel disease. *Gastroenterology*. 2002;123:999-1005.
18. Dubcenco E, Jeejeebhoy KN, Petroni R, Tang SJ, Zalev AH, et al. 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.
19. Voderholzer WA, Ortner M, Rogalla P, Beinholz J, Lochs H. Diagnostic yield of wireless capsule endoscopy in comparison with computed tomography enteroclysis. *Endoscopy*. 2003;35:1009-1014.
20. Voderholzer WA, Beinholz J, Rogalla P, Murrer S, Schachschal G, et al. Small bowel involvement in Crohn's disease: a prospective comparison of wireless capsule endoscopy and computed tomography enteroclysis. *Gut*. 2005;54:369-373.
21. Lashner BA. Sensitivity-specificity trade-off for capsule endoscopy in IBD: is it worth it? *Am J Gastroenterol*. 2006;101:965-966.
22. Albert JG, Martiny F, Krummnerl A, Stock K, Lesske J, et al. Diagnosis of small bowel Crohn's disease: a prospective comparison of capsule endoscopy with magnetic resonance imaging and fluoroscopic enteroclysis. *Gut*. 2005;54:1721-1727.
23. Golder SK, Schreyer AG, Endlicher E, Feuerbach S, Scholmerich J, et al. Comparison of capsule endoscopy and magnetic resonance (MR) enteroclysis in suspected small bowel disease. *Int J Colorectal Dis*. 2006;21:97-104.
24. Tillack C, Seiderer J, Brand S, Goke B, Reiser MF, et al. Correlation of magnetic resonance enteroclysis (MRE) and wireless capsule endoscopy (CE) in the diagnosis of small bowel lesions in Crohn's disease. *Inflamm Bowel Dis*. 2008;14:1219-1228.
25. Crook DW, Knuesel PR, Froehlich JM, Eigenmann F, Unterweger M, et al. Comparison of magnetic resonance enterography and video capsule endoscopy in evaluating small bowel disease. *Eur J Gastroenterol Hepatol*. 2009;21:54-65.
26. Solem CA, Loftus EV Jr, Fletcher JG, Baron TH, Gostout CJ, et al. Small bowel imaging in Crohn's disease: a prospective, blinded, 4-way comparison trial. *Gastrointest Endosc*. 2008;68:255-266.
27. Hara AK, Leighton JA, Heigh RI, Sharma VK, Silva AC, et al. Crohn disease of the small bowel: preliminary comparison among CT enterography, capsule endoscopy, small bowel follow-through, and ileoscopy. *Radiology*. 2006;238:128-134.
28. Sidhu R, McAlindon ME, Kapur K, Hurlstone DP, Wheeldon MC, Sanders DS. Push enteroscopy in the era of capsule endoscopy. *J Clin Gastroenterol*. 2008;42:54-58.
29. 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.
30. Gay G, Delvaux M, Fassler I. Outcome of capsule endoscopy in determining indication and route for push-and-pull enteroscopy. *Endoscopy*. 2006;38:49-58.
31. Pasha SF, Leighton JA, Das A, Harrison ME, Decker GA, et al. Double-balloon enteroscopy and capsule endoscopy have comparable diagnostic yield in small bowel disease: a meta-analysis. *Clin Gastroenterol Hepatol*. 2008;6:671-676.
32. Sunada K, Yamamoto H, Kita H, Yano T, Sato H, et al. Clinical outcomes of enteroscopy using the double-balloon method for strictures of the small intestine. *World J Gastroenterol*. 2005;11:1087-1089.
33. Triester SL, Leighton JA, Leontiadis GI, Gurudu SR, Fleischer DE, 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.
34. Desmond AN, O'Regan K, Curran C, McWilliams S, Fitzgerald T, et al. Crohn's disease: factors associated with exposure to high levels of diagnostic radiation. *Gut*. 2008;57:1524-1529.
35. Maunoury V, Savoye G, Bourrille A, Bouhnik Y, Jarry M, et al. Value of wireless capsule endoscopy in patients with indeterminate colitis (inflammatory bowel disease type unclassified). *Inflamm Bowel Dis*. 2007;13:152-155.
36. Mehdizadeh S, Chen G, Enayati PJ, Cheng DW, Han NJ, et al. Diagnostic yield of capsule endoscopy in ulcerative colitis and inflammatory bowel disease of unclassified type (IBDU). *Endoscopy*. 2008;40:30-35.
37. Pons Beltran V, Nos P, Bastida G, Beltran B, Arguello L, et al. Evaluation of postsurgical recurrence in Crohn's disease: a new indication for capsule endoscopy? *Gastrointest Endosc*. 2007;66:533-540.
38. Bourrille A, Jarry M, D'Halluin PN, Ben-Soussan E, Maunoury V, 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.
39. Biancone L, Calabrese E, Petruzzello C, Onali S, Caruso A, et al. Wireless capsule endoscopy and small intestine contrast ultrasonography in recurrence of Crohn's disease. *Inflamm Bowel Dis*. 2007;13:1256-1265.
40. Efthymiou A, Viazis N, Mantzaris G, Papadimitriou N, Tzourmakliotis D, et al. 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.
41. 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.
42. Niv Y. Diagnostic value of capsule endoscopy during relapse in co-morbid irritable bowel syndrome and Crohn's disease. *Eur J Gastroenterol Hepatol*. 2004;16:1073-1074.
43. Leighton JA, Triester SL, Sharma VK. Capsule endoscopy: a meta-analysis for use with obscure gastrointestinal bleeding and Crohn's disease. *Gastrointest Endosc Clin N Am*. 2006;16:229-250.

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44. Baichi MM, Arifuddin RM, Mantry PS. What we have learned from 5 cases of permanent capsule retention. *Gastrointest Endosc.* 2006;64:283-287.
45. Li F, Gurudu SR, De Petris G, Sharma VK, Shiff AD, et al. Retention of the capsule endoscope: a single-center experience of 1000 capsule endoscopy procedures. *Gastrointest Endosc.* 2008;68:174-180.
46. Cheon JH, Kim YS, Lee IS, Chang DK, Ryu JK, et al. Can we predict spontaneous capsule passage after retention? A nationwide study to evaluate the incidence and clinical outcomes of capsule retention. *Endoscopy.* 2007;39:1046-1052.
47. Cheifetz AS, Kornbluth AA, Legnani P, Schmelkin I, Brown A, 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.
48. Irkorucu O, Tascilar O, Emre AU, Cakmak GK, Karakaya K, et al. Small bowel obstruction secondary to wireless capsule enteroscopy: extraction of the capsule without enterotomy. *Endoscopy.* 2007;39(suppl 1):E286-287.
49. Tanaka S, Mitsui K, Shirakawa K, Tatsuguchi A, Nakamura T, et al. Successful retrieval of video capsule endoscopy retained at ileal stenosis of Crohn's disease using double-balloon endoscopy. *J Gastroenterol Hepatol.* 2006;21:922-923.
50. Bai Y, Gao J, Song B, Zhou YQ, Zou DW, Li ZS. Surgical intervention for capsule endoscope retained at ileal stricture. *Endoscopy.* 2007;39(suppl 1):E268-269.
51. Magdeburg R, Riestert T, Hummel F, Lohr M, Post S, Sturm J. Ileus secondary to wireless capsule enteroscopy. *Int J Colorectal Dis.* 2006;21:610-613.
52. Signorelli C, Rondonotti E, Villa F, Abbiati C, Beccari G, et al. Use of the Given Patency System for the screening of patients at high risk for capsule retention. *Dig Liver Dis.* 2006;38:326-330.
53. Spada C, Shah SK, Riccioni ME, Spera G, Marchese M, et al. 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.
54. Delvaux M, Ben Soussan E, Laurent V, Lerebours E, Gay G. Clinical evaluation of the use of the M2A patency capsule system before a capsule endoscopy procedure, in patients with known or suspected intestinal stenosis. *Endoscopy.* 2005;37:801-807.
55. Gay G, Delvaux M, Laurent V, Reibel N, Regent D, et al. Temporary intestinal occlusion induced by a "patency capsule" in a patient with Crohn's disease. *Endoscopy.* 2005;37:174-177.
56. Herrerias JM, Leighton JA, Costamagna G, Infantolino A, Eliakim R, et al. Agile patency system eliminates risk of capsule retention in patients with known intestinal strictures who undergo capsule endoscopy. *Gastrointest Endosc.* 2008;67:902-909.
57. Sidhu R, Sanders DS, Morris AJ, McAlindon ME. Guidelines on small bowel enteroscopy and capsule endoscopy in adults. *Gut.* 2008;57:125-136.
58. 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.
59. Cheifetz AS, Lewis BS. Capsule endoscopy retention: is it a complication? *J Clin Gastroenterol.* 2006;40:688-691.