Video capsule endoscopy in children with Crohn's disease – review article and single center experience

Video kapsulna endoskopija pri otrocih s Crohnovo boleznijo – pregledni članek in naše izkušnje

Tina Kamhi Trop, Rok Orel

Clinical Department of Gastroenterology, Hepatology and Nutrition, University Children's Hospital Ljubljana, Slovenia

Korespondenca/ Correspondence:
Tina Kamhi Trop, MD, Teaching assistant of pediatrics, Clinical Department of Gastroenterology, Hepatology and Nutrition, University Children's Hospital Bohoričeva 20, SI–1525 Ljubljana, Slovenia
Email: tina.kamhi@kclj.si

Ključne besede:
kapsulna endoskopija, Crohnova bolezen, otroci

Key words:
capsule endoscopy, Crohn's disease, children

Citirajte kot/Cite as:
Zdrav Vestn 2013; 82 supl 1: I-7–14

Prispelo: 19. apr. 2013,
Sprejeto: 9. avg. 2013

Abstract

Video capsule endoscopy is a simple, safe, non-invasive, reliable procedure for visualization of the small bowel, well accepted and tolerated by patients, which can be safely performed in pediatric population as well as in adults.

In this review we describe the video capsule endoscopy system and its clinical applications for use. We discuss the importance of capsule endoscopy in small bowel visualization patients with Crohn's disease. Contraindications and technical limitations of the procedure are listed. Furthermore, we review the literature for diagnostic effectiveness of the procedure, and compare the capsule endoscopy to other modalities for imaging of the small bowel. We describe possible complication of the procedure, capsule retention, and ways to minimize the risk of its occurrence.

At the end, we report our experience with capsule endoscopy use in pediatric patients with Crohn's disease.

Izvleček

Video kapsulna endoskopija je enostavna, varna in neinvazivna metoda za prikaz tankega črevesa, ki jo bolniki dobro prenašajo in jo varno uporabljajo tako pri pediatrični populaciji kot pri odraslih bolnikih. V tem preglednem članku opišemo sistem video kapsulne endoskopije in njene izvedbe za klinično uporabo. Razpravljamo o pomenu kapsulne endoskopije pri pregledu tankega črevesa bolnikov s Crohnovo boleznijo. Naštejemo kontraindikacije in tehnične omejitve preiskave. Poleg tega navajamo pregled objavljene literature o diagnostični učinkovitosti kapsulne endoskopije in jo primerjamo z drugimi slikovnimi tehnikami, ki so na voljo za preiskavo tankega črevesa. Opišemo možni zaplet preiskave, zastoj kapsule, in opišemo način, kako se tveganju za ta pojav čim bolj izognemo.

Na koncu navajamo svoje izkušnje z uporabo kapsulne endoskopije pri pediatričnih bolnikih s Crohnovo boleznijo.

Introduction

Inflammatory bowel disease (IBD) is a group of inflammatory disorders of the gastrointestinal tract that mostly affect adults, with a peak patient age between 20 and 40 years, but can occur in children as well. Pediatric IBD accounts for up to 25 % of all IBD cases.[1]

IBD includes two major diseases, Crohn's disease (CD) that can affect any part of the gastrointestinal tract, and ulcerative colitis (UC) affecting only the colon. There is a

third entity comprising this group of intestinal disorders, known also as indeterminate colitis (IC), with which we describe the disease that cannot be classified endoscopically or histologically either as Crohn's disease or as ulcerative colitis.

Crohn's disease affects the small bowel in 70 % of patients, with as many as 30 % of Crohn's disease patients having lesions limited to the small bowel only.[2] Typical symptoms of Crohn's disease include abdominal pain, diarrhea, bloody stools, and typically in pediatric IBD patients weight loss or failure to thrive and growth retardation. The disease usually follows a chronically relapsing course, with remissions lasting for up to several months.

The diagnosis of Crohn's disease is usually based on a combination of clinical, laboratory, endoscopic, histologic, and radiologic/imaging findings.

Until about a decade ago, the small bowel was very difficult to explore with the available endoscopic and radiological techniques; in routine practice, only the last few centimeters of the ileum are accessible to visualization by ileocolonoscopy, the majority of the small bowel being inaccessible for a classic endoscope. There are different types of enteroscopies available for the exploration of the small bowel, such as push, single and double-balloon, or intraoperative enteroscopies, but those procedures are all invasive, and are poorly tolerated by patients.[3,4] Lately, computed tomography (CT) and magnetic resonance imaging (MRI) enteroscopies have also become available for diagnostics of the small bowel, but their diagnostic yield, compared to that of the VCE, is deemed to be inferior. In addition, radiation exposure with CT examination is a particular concern in pediatric patients. In general, patients find capsule endoscopy more comfortable and convenient than the above mentioned radiological examinations.

Video-capsule endoscopy (CE) can provide a simple, safe, non-invasive, reliable procedure for visualization of the small bowel, which is well accepted and tolerated by patients. It can be safe and effective even in small pediatric patients.[5] This technique evaluates the whole small bowel with high resolution images, avoiding any sedation, surgery or radiation exposure,[6,7] which makes it even more appealing for use in pediatric patients.

It is an endoscopic procedure for direct visualization of the small bowel mucosa, but contrary to the standard endoscopy which uses a flexible endoscopic tube, this procedure uses a small vitamin tablet-sized (measuring 11 mm × 26 mm and weighing 3.7 g) pill containing a camera, a battery with 8-hour life, a light source, and a transmitter. The image filed of the camera is 140 degrees, magnification is × 8 and the depth of view is 1 to 30 mm.[8,9] It takes 2 images per second, thus recording approx. 55,000 images during the 8-hour procedure, and transmits them by means of radio frequency to a sensor array with 8 sensors that are placed on the patient's abdomen, and from here to a data recorder device, which the patient carries with him during the whole procedure. After the examination, the images are transferred to a workstation and an 8-hour video is created with specially designed software. Reading and interpreting of the CE video is a timely job, and requires a skillful eye; it takes on average 40–60 minutes to read these images,[10] usually even more. The capsule is excreted with feces and can be disposed of; it is designed for single-use. The patient is asked to observe the stools, if he does not pass the capsule in approximately 7 days, he should be checked for capsule retention with plain radiograph.[11]

Currently, capsule endoscopy systems are manufactured by four companies.[7] The initial capsule endoscope was approved in Europe by the European Medicines Agency and in the United States by the Food and Drug Administration in 2001.[12] Almost all of the information provided in different studies, as well as in this review, is based on published data collected with Given Imaging PillCams.[7]

Use of video capsule endoscopy in Crohn's disease

Indications for capsule endoscopy include obscure gastrointestinal (GI) bleeding, small-bowel Crohn's disease, suspected tu-

mors of the small intestine and surveillance in patients with polyposis syndromes, and suspected or refractory malabsorption syndromes. In patients with CD, it is useful for establishing diagnosis, assessing disease prognosis, activity and mucosal healing post therapy, and to define the extent and severity of the disease within small bowel.[7,13,14]

Capsule endoscopy seems to be very useful in evaluating already established inflammatory bowel disease. It can result in alteration of the management of patients whose small bowel is examined by VCE,[15] and reclassification of IBD from UC/IC to definitive CD. In a study by Cohen et al., 28 patients underwent capsule endoscopy for the evaluation of IBD and in 71 % had their disease reclassified to CD, based upon newly diagnosed small-bowel mucosal lesions detected by CE, 62 % patients with established CD were found to have more extensive small bowel disease, with newly diagnosed jejunal disease found in 12 of 13 (92 %) patients.[16] Significant modification in the therapeutic management of CD patients as a result of VCE examination of small-bowel mucosa has been described by other authors as well.[17]

Probably, the only real contraindication for CE is known or suspected GI obstruction, strictures or fistulas. The procedure may be contraindicated in patients with swallowing difficulties, however, in these patients the capsule can be delivered endoscopically, usually under general anesthesia, thus making the whole procedure invasive.[7,14] Many children under 10 years of age are unable to swallow the large capsule. For these children a special device can be used to place the capsule into the proximal duodenum. Deployment of the capsule during standard upper endoscopy can be facilitated using real-time viewer connected to the capsule data recorder. This has been shown to significantly improve visualization of capsule placement in pediatric population.[18] Use of the real-time viewer during capsule endoscopy procedure can also be practical to detect the position of the capsule after ingestion (usually after one hour), and to verify that the capsule has successfully passed into the duodenum. This is particularly useful in patients with slow passage of bowel contents; patient may be advised to change to lateral side position, to walk around, or a prokinetic drug may be administered at this point.

According to the manufacturer, VCE is contraindicated in patients with cardiac pacemakers and implantable cardioverter defibrillators. Recent studies have demonstrated that CE is increasingly applied in such patients, and seems to be safe; although some interference can occur between CE and ECG-telemetry leading to loss of images or an impaired quality of the CE video.[19,20] However, this may not present a large issue in pediatric population dealing with patients who usually do not have many concomitant diseases.

Technical limitations of the procedure are that CE cannot be used to obtain biopsy specimens or for endoscopic treatment and it cannot be controlled remotely.[12] CE has also some clinical limitations, such as problems in sizing and exact locating small--bowel lesions.[6]

Studies that have evaluated the value of CE in patients with typical symptoms of Crohn's disease showed diagnostic yields as high as 70 %.[21,22] CE has a higher sensitivity for assessing small-bowel mucosal lesions compared to other imaging techniques. The working group on capsule endoscopy in the setting of suspected Crohn's disease agreed that capsule endoscopy is superior to all other methods in identifying subtle mucosal inflammatory changes, ulcers, or erosions in the small bowel.[23] Usefulness of CE in pediatric setting was first evaluated in a study by Sant'Anna et al.; their study compared diagnostic yield of capsule endoscopy with traditional endoscopic and radiologic testing for obscure small-bowel disease in children, and it showed superiority of capsule endoscopy compared to other modalities.[24] Also, a large meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small-bowel Crohn's disease performed by Triester and his co-workers suggests that capsule endoscopy is more diagnostic than small-bowel follow-through (SBFT), CT enterography or classic ileoscopy.[25] An analysis of four prospective comparative

studies, including a total of 115 adult patients, showed a diagnostic yield of 61 % for CE compared to 46 % for ileo-colonoscopy in the detection of small bowel Crohn's disease.[26] CE was also able to identify the extent of disease proximal to the terminal ileum.[27] Another comparison of diagnostic yield of CE to SBFT showed that capsule endoscopy is diagnostic for detecting lesions within the small bowel in 45 % as opposed to SBFT which was diagnostic only in 20 %; furthermore, 65 % of patients with normal SBFT had suspected or diagnostic findings on CE.[28] Other authors reported similar superiority in the performance of VCE compared to other modalities in its ability to detect early small-bowel mucosal changes.[29] The superiority of capsule endoscopy was also shown in comparison with computed tomographic enterography (CTE) in adult patients. The yield for CE was 75 % in comparison with 37 % for CTE. This suggests that mucosal abnormalities possibly representing early Crohn's disease exist below the resolution of CTE.[30-32] A study that compared the diagnostic yield of small-bowel magnetic resonance imaging (MRI) with capsule endoscopy showed 60 % of diagnostic yield for CE and only 40 % for MRI.[33] Literature suggests that other imaging techniques, particularly CT and MRI enterographies, are complementary techniques in the evaluation of the small bowel in IBD. The VCE provides better visualization of smaller mucosal changes not visible on MRI or CT, whereas CT and MRI offer better assessment of the intestinal wall, masses that do not have a mucosal component, and additional information on extraintestinal involvement.[34,35]

A scoring system has been proposed for assessing the activity of Crohn's disease. The small bowel is divided into tertiles, and three parameters are assessed in each tertile: villous oedema, ulcer and stenosis. A total score < 135 is designated as normal or clinically insignificant mucosal inflammatory change, a score between 135 and 790 is mild, and a score ≥ 790 is moderate to severe.[36] Recently, some studies have suggested that Lewis score may be a valuable diagnostic tool in the setting of suspected Crohn's disease.[37] It has been suggested to have a positive correlation with biomarkers of the disease and that it objectively characterizes small bowel involvement in CD.[38] So far, it has been used mostly for academic purposes; larger clinical trials to evaluate its appropriateness and clinical correlation have to be performed in the future to further validate its use.

Nevertheless, it is important to realize that mucosal breaks seen on CE may be due to conditions other than Crohn's disease, and may be seen in a subgroup of normal individuals as well.[39] Up to 23 % of normal healthy asymptomatic individuals may have variously defined mucosal breaks and other lesions on CE.[39,40]

A normal small-bowel series does not exclude the presence of small-bowel strictures and thus does not protect the patient from having capsule retention.[41] The retention of the device is the main complication of the procedure and is defined when CE remains in the digestive tract for a minimum of 2 weeks. Capsule removal may require medical, endoscopic or surgical intervention. Causes of capsule retention include use of non-steroidal anti-inflammatory drugs, Crohn's disease, small-bowel tumors or larger polyps, anatomic malformations, and surgical anastomotic strictures.[23,41] The risk for VCE retention varies, depending mostly on the clinical indication for CE, and ranges from 0 % in healthy subjects, to 1.5 % in patients with obscure gastrointestinal bleeding, and is estimated as 4 % to 13 % in patients with suspected Crohn's disease.[7,42,43] To determine whether the patient is at risk for retention, a patency capsule system has been developed. It is a simple and convenient accessory that is intended to verify functional patency of the small bowel with known or suspected strictures prior to administration of the capsule for CE. The patency capsule is a self-disintegrating capsule of the same size as the capsule for CE, with lactose filled body and a small radio frequent ID (RFID) tag (12 × 2 mm). It starts disintegrating approximately 30 hours after ingestion, if it is not excreted before that. The capsule remnants can pass through even small orifices.[7] The patency of small bowel is confirmed if the patency capsule is excreted within 30 hours of ingestion or if it is excreted intact at any

time after ingestion. It can be detected using a special handheld patency scanner; the patency capsule is also radiopaque and can be detected on a plain radiograph. It has been shown that the patency capsule can be safely used in pediatric population.[5] In cases when the patency cannot be confirmed with such as patency system, one of the other available imaging modalities is advocated to exclude possible stenoses or strictures of the small bowel, e.g. MRI and CT enterography, or barium follow-through.

Two factors that impair the diagnostic yield of VCE are: firstly, the presence of food residue, air bubbles and intraluminal fluid, and secondly, the failure of capsule to visualize the entire small bowel due to delayed gastric or small bowel transit times.[7] It has been described that the capsule does not reach the caecum in approximately 20 % of patients within the recording time period of 8 hours.[44] There has been a lot of discussion on whether or not the patients have to be prepped before capsule endoscopy. There is still no clear consensus on this issue, as it is unclear what would be the optimal timing for prep procedure. The capsule manufacturer recommends fluid diet from lunch on the day before, and fasting 10 hours prior to the examination. Findings of some studies support this as adequate preparation for CE, and it is generally better tolerated by patients.[45,46] Nandi, on the other hand, has shown that in about 30 % of time this classic small-bowel prepping is inadequate.[47]. Furthermore, studies have shown that prepping the patients for capsule endoscopy with purgatives warrants better visualization of the small bowel and improves the diagnostic yield of the examination, whereas it does not influence passage times and completion rates of the capsule.[7,48,49] Polyethylene glycol has been mostly used for prepping. In addition, it has been demonstrated that the administration of simeticone in order to reduce air bubbles improves visibility of the mucosa of at least the proximal part of the small bowel during VCE recording.[50] Use of prokinetics has been shown to affect transit time in some CE studies. No consistent clinical benefit has been demonstrated, though.[51] Some authors describe that chewing gum might affect the small bowel transit time,[52] whereas others have shown that chewing does not significantly reduce gastric and small-bowel transit times and caecal completion rate.[44]

Single center experience

At the Clinical Department of Gastroenterology, Hepatology and Nutrition of the University Children's Hospital Ljubljana, Slovenia, capsule endoscopy has been used in pediatric patients since 2006. From October 2006 to April 2013, VCE was performed in 112 pediatric patients (62 ♂, 50 ♀), with mean age 12.9 years (the youngest patient was 2 years of age). The capsule had to be positioned endoscopically under general anesthesia in 11 patients. All patients had upper and lower GI endoscopy before the procedure, and up until mid 2009, most of them also had SB follow-through prior to VCE study to minimize the possibility of capsule retention due to possible stenosis. From June 2009, a patency capsule system became available at our unit and was used to confirm patency of the small bowel, without unnecessarily exposing patients to radiation. Since then, we have used the patency capsule in 47 patients, and small-bowel patency was confirmed in 44. The remaining 3 had subsequently been shown to have a small-bowel stenosis on SBFT (all due to Crohn's disease) and were not appropriate candidates for capsule endoscopy. All patients receive simeticone upon ingestion of the capsule, and lately we prep all our patients using polyethylene glycol prior to the procedure. We have noticed greatly improved visualization since the patients are better prepped; also the completion rate has improved. VCE was performed in 57 patients with established CD (50.9 %), 16 patients with previously diagnosed IC (14.3 %), and 14 patients with suspected IBD (12.5 %). Other indications for capsule endoscopy were: unexplained bleeding (12 patients), ulcerative colitis with severe clinical course (4 patients), Peutz-Jeghers syndrome (4 patients), other polyposis syndromes, unexplained entheropathy and hereditary intestinal lymphangiectasia – 1 patient each). In 63 patients VCE confirmed

SB mucosal lesions; total diagnostic yield was 56 %. In 15 patients the VCE findings resulted in reclassification of the disease; 7 patients initially diagnosed as IC were reclassified to CD, and 4 patients had their diagnosis of IC reclassified to UC upon negative result of the VCE. In 3 patients suspected of having IBD, the disease was confirmed as CD based on the new SB mucosal changes seen on VCE. The procedure was generally well tolerated in most of our patients.[53-55] Complications occurred in 3 patients: one retention due to stricturing Crohn's disease that was misdiagnosed as non-stricturing upon prior small-bowel follow-through (the patient remained asymptomatic for 5 months of retention which resolved spontaneously upon disease remission), and two failures to position the capsule endoscopically (the patients were too small). No other adverse effects, such as abdominal pain or discomfort were reported. The costs for pediatric capsule endoscopy in Slovenia are paid by the national health insurance company.

Conclusions

Video capsule endoscopy is a reliable, non-invasive method for endoscopic visualization of the small-bowel mucosa in pediatric patients with inflammatory bowel disease, particularly with Crohn's disease. It is mostly used to evaluate the extent of disease within the small bowel; it may also help in reclassification of IBD from indeterminate colitis to either Crohn's disease or ulcerative colitis. In addition, previously diagnosed patients with CD may be found to have a more significant burden of SB disease. It is performed safely and has good diagnostic yield, comparable to that in adult VCE series and studies using different diagnostic modalities, as reported in the literature. It is the only imaging method that can provide direct visualization of the entire small-bowel mucosa that is friendly to the patient, noninvasive and effective.

References

1. Cosnes J, Gower-Rousseau C, Seksik P, Cortot A. Epidemiology and natural history of inflammatory bowel diseases. Gastroenterology 2011; 140: 1785–1794. Jevon GP, Madhur R. Endoscopic and histologic findings in pediatric inflammatory bowel disease. Gastroenterol Hepatol 2010; 6(3): 174–180.
2. Lashner B. Clinical features, laboratory findings, and course of Crohn's disease, 5th ed. Philadelphia, PA: Saunders, 2000.
3. Galmiche JP, Coron E, Sacher-Huvelin S. Recent developments in capsule endoscopy. Gut.2008; 57: 695–703.
4. Teshima CW, Kuipers EJ, Veldhuyzen SZ, Mensink PB. Double balloon enteroscopy and capsule endoscopy for obscure gastrointestinal bleeding. J Gastroenterol Hepatol. 2011; 26(5): 796–801.
5. Cohen SA, Ephrath H, Lewis JD, et al. Pediatric capsule endoscopy: review of the small bowel and patency capsules. JPGN 2012; 54: 409–413.
6. Rondonotti E, Villa F, Mulder CJ, Jacobs MA, de Franchis R. Small bowel capsule endoscopy in 2007: indications, risks and limitations. World J Gastroenterol. 2007; 13: 6140–6149.
7. Ladas et al. ESGE Recommendations on VCE in investigation of small-bowel, esophageal, and colonic diseases. Endoscopy 2010; 42: 220–227.
8. Davis BR, Harris H, Vitale GC. The evolution of endoscopy: wireless capsule cameras for the diagnosis of occult gastrointestinal bleeding and inflammatory bowel disease. Surg Innov. 2005; 12: 129–133.
9. Iddan G, Meron G, Glukhovsky A, Swain P. Wireless capsule endoscopy. Nature. 2000; 405: 417.
10. Pennazio M. Capsule endoscopy: where are we after 6 years of clinical use? Dig Liver Dis.2006; 38: 867–878.
11. Swain P. Wireless capsule endoscopy and Crohn's disease. Gut 2005; 54: 323–6.
12. Nakamura T, Terano A. Capsule endoscopy: past, present, and future. J Gastroenterol. 2008; 43: 93–99.
13. *Rey* J-F *et al*. ESGE Guideline for Video Capsule *Endoscopy*. *Endoscopy 2004*; 36: 656–658.
14. *Mishkin* DS, Chuttani R, Croffie J, *et al*: ASGE Technology Status Evaluation Report: Wireless capsule endoscopy. *Gastrointest Endosc 2006*; *63*: *539–545*.
15. Thomson M, Fritscher-Ravens A, Mylonaki M, et al. Wireless capsule endoscopy in children: a study to assess diagnostic yield in small bowel disease in pediatric patients. JPGN 2007; 44: 192–197.
16. Cohen SA, Gralnek IM, Ephrath H, Saripkin L, Meyers W, et al. Capsule endoscopy may reclassify pediatric inflammatory bowel disease: a historical analysis. J Pediatr Gastroenterol Nutr. 2008; 47: 31–36.
17. Castro FD, Rosa B, Moreira MJ, Cotter J. Impact of capsule endoscopy on management of Crohn's disease: a single center experience. Gastrointest Endosc 2012; 75(4):Supp AB 1719.
18. Bass LM, Misiewicz. Use of real-time viewer for endoscopic deployment of capsule endoscope in pediatric population. JPGN 2012; 55: 552–555.

19. Bandorski D, Jakobs R, Brück M, Hoeltgen R, Wieczorek M, Keuchel M. Capsule Endoscopy in Patients with Cardiac Pacemakers and Implantable Cardioverter Defibrillators: (Re)evaluation of the Current State in Germany, Austria, and Switzerland 2010. Gastroenterol Res Pract. 2012; 2012: 717408.
20. Bandorski D, Lotterer E, Hartmann D, et al. Capsule endoscopy in patients with cardiac pacemakers and implantable cardioverter-defibrillators–a retrospective multicenter investigation. J Gastrointestin Liver Dis. 2011 Mar; 20(1): 33–7.
21. Fireman Z, Mahajna E, Broide E, *et al.* Diagnosing small bowel Crohn's disease with wireless capsule endoscopy. Gut 2003; 52: 390–2.
22. Herrerias JM, Caunedo A, Rodriguez-Tellez M, *et al.* Capsule endoscopy in patients with suspected Crohn's disease and negative endoscopy. Endoscopy 2003; 35: 564–8.
23. Lewis BS, Rey JF, Sediman EG. Capsule endoscopy 2005: results of the 2005 International Consensus Conference – introduction. Endoscopy 2005; 37(10): 1038–1039.
24. Sant'Anna AM, Dubois J, Miron MC, et al. Wireless capsule endoscopy for obscure small-bowel disorders: final results of the first pediatric controlled trial. Clin Gastroenterol Hepatol 2005; 3: 264–270.
25. *Triester SL*, Leighton JA, Leontiadis GI et al. A *meta-analysis* of the *yield* of *capsule endoscopy compared* to *other diagnostic modalities* in *patients* with *non-stricturing small bowel Crohn's disease*. Am J Gastroenterol 2006; 101(5): 954–64.
26. Kornbluth A, Colombel JF, Leighton JA, et al. ICCE Consensus for Inflammatory bowel disease. Endoscopy 2005; 37: 1051–4.
27. Sidhu R, Sanders DS, Morris AJ, McAlindon ME. Guidelines on small bowel enteroscopy and capsule endoscopy in adults. Gut 2008; 57: 125–136.
28. Costamagna G, Shah SK, Riccioni ME, *et al.* A prospective trial comparing small bowel radiographs and video capsule endoscopy for suspected small bowel disease. Gastroenterology 2002; 123: 999–1005.
29. Dionisio PM, Gurudu SR, Leighton JA, et al. 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.
30. Voderholzer WA, Ortner M, Rogalla P, *et al.* Diagnostic yield of wireless capsule enteroscopy in comparison with computed tomographic enteroclysis. Endoscopy 2003; 35: 1009–14.
31. Eliakim R, Suissa A, Yassin K et al. Wireless capsule video endoscopy compared to barium follow--through and computerized tomography in patients with suspected Crohn's disease: fina report. Dig Liv Dis 2004; 36: 519–522.
32. Hara AK, Leighton JA, Sharma VK et al. Imaging of small bowel disease: comparison of capsule endoscopy, standard endoscopy, barium examination, and CT. RadioGraphics 2005; 25: 697–711.
33. Goelder SK, Schreyer AG. Comparison of capsule endoscopy and magnetic resonance (MR) enterocylsis in suspected small bowel disease. Int J Colorectal Dis 2006; 21(2): 97–104.
34. Akin E, Demirezer Bolat A, Buyukasik S, Algin O, Selvi E, Ersoy O. Comparison between Capsule Endoscopy and Magnetic Resonance Enterography for the Detection of Polyps of the Small Intestine in Patients with Familial Adenomatous Polyposis.Gastroenterol Res Pract. 2012; 2012: 215028.
35. 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 Mar; 54(3): 369–73.)
36. Gralnek IM, Defranchis R, Seidman E, et al. Development of a capsule endoscopy scoring index for small bowel mucosal inflammatory change. Aliment Pharmacol Ther 2008; 27(2): 146–54.
37. 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(6): 692–7.
38. Rodrigues S, Magro F, Cardoso H, et al. Role of capsule endoscopy in the evaluation of different segments of the small bowel in Crohn's disease: correlation of clinical parameters, biomarkers, endoscopy and Lewis score. Gastroenterol 2012; 142(5):Supp AB Tu1258.
39. Goldstein JL, Eisen G, Lewis BS et al. Video capsule endoscopy to prospectively assess small bowel injury with celecoxib, naproxen plus omeprazole, and placebo. Clin Gastroenterol Hepatol 2005; 3: 133–141.
40. Lewis JR, Pashinsky Y, Tinsley A, Lewis BS. Capsule endoscopy in healthy individuals. Gastroenterol 2012; 142(5):Supp AB 215.
41. Cave D, Legnani P, de Franchis R, Lewis BS. ICCE consensus for capsule retention. Endoscopy.2005; 37: 1065–1067.
42. Mow WS, Lo SK, Targan SR, *et al.* Initial experience with wireless capsule enteroscopy in the diagnosis and management of inflammatory bowel disease. Clin Gastroenterol Hepatol 2004; 2: 31–40.
43. Mata A, Llach J, Bordas JM. Wireless capsule endoscopy. World J Gastroenterol. 2008; 14: 1969–1971.
44. Svarta S, Ou G, Enns RA. The effect of chewing gum on small bowel transit time: a prospective randomized trial. Gastrointest Endosc 2012; 75(4):Supp AB 149.
45. Maqboul N, Murugananthan AU, Hong TP, et al. Prep, no prep or more prep? a prospective randomised study comparing two bowel preparation regimes with no preparation on quality of capsule endoscopy. Gastrointest Endosc 2012; 75(4):SuppAB Sa1759.
46. Beltran VP et al. Evaluation of different bowel preparations for small bowel capsule endoscopy: a prospective, randomised, cotrolled study. Dig Dis Sci 2011; 56: 2900–2905.
47. Nandi N, Brotz C, Schroeder T, Conn M, Daskalakis C, DiMarino M, Infantolino A, Katz L, Kastenberg D. The standard preparation for wireless capsule endoscopy is substandard. Gastrointest Endosc; 2007. (Presented at DDW, 2007, and ICCE, Madrid, Spain, 2007).
48. Rokkas T, Papaxoinis K, Triantafyllou K, Pistiolas D, Ladas SD. Does purgative preparation influence

the diagnostic yield of small bowel video capsule endoscopy?: A meta-analysis. Am J Gastroenterol 2009 Jan; 104(1): 219–27.
49. DeFranchis R et al. Bowel preparation and prokinetics. Endoscopy 2005; 37: 1040–1045.
50. Ge ZZ, Chen HY, Gao YJ, et al. The role of simeticone in small bowel preparation for capsule endoscopy. Endoscopy 2006; 38: 836–840.
51. Mergener K, Ponchon T, Gralnek I, et al. Literature review and recommendations for clinical application of small-bowel capsule endoscopy, based on a panel discussion by international experts. Consensus statements for small-bowel capsule endoscopy, 2006/2007. Endoscopy. 2007; 39(10): 895–909.
52. Apostolopoulos P, Kalantzis C, Gralnek IM, Liatsos C, Tsironis C, Kalantzis N. Clinical trial: effectiveness of chewing-gum in accelerating capsule endoscopy transit time—a prospective randomized, controlled pilot study. Aliment Pharmacol Ther2008; 28: 405–411.
53. Kamhi T, Orel R. Capsule endoscopy in pediatric patients, our experience from the University Children's Hospital Ljubljana, Slovenia (poster). The 41st annual meeting of ESPHGAN, Iguassu Falls, Brazil, 2008.
54. Kamhi Trop T, Orel R. Wireless capsule endoscopy as part of routine work-up of pediatric patients with inflammatory bowel disease (poster). The 44th annual meeting of ESPHGAN, Sorrento, Italy, 2011.
55. Kamhi Trop T, Orel R. Use of Agile patency capsule – our experience (poster). SEEPEG, Bled, Slovenia, 2011.