**Name ofournal: World Journal of Gastroenterology**

**ESPS Manuscript NO: 10058**

**Columns: TOPIC HIGHLIGHT**

WJG 20th Anniversary Special Issues (19): Capsule endoscopy

**Capsule endoscopy in pediatrics: A 10-years journey**

Oliva S *et al.* Capsule endoscopy in pediatrics

Salvatore Oliva, Stanley A Cohen, Giovanni Di Nardo, Gianfranco Gualdi, Salvatore Cucchiara, Emanuele Casciani

**Salvatore Oliva, Salvatore Cucchiara, Giovanni Di Nardo,** Department of Pediatrics, Pediatric Gastroenterology Unit, Sapienza University of Rome, 00161 Rome, Italy

**Emanuele Casciani, Gianfranco Gualdi,** Radiology DEA, Sapienza University of Rome, University Hospital Umberto I, 00161 Rome, Italy

**Stanley A Cohen,** Children's Center for Digestive Health Care, Atlanta, GA 30342, United States

**Author contributions:** All authors contributed equally to this paper.

**Correspondence to: Emanuele Casciani, MD,** Radiology DEA, Sapienza University of Rome, University Hospital Umberto I, Viale Regina Elena 324, 00161 Rome, Italy. emanuelecasciani@gmail.com

**Telephone:** +39-64-9979537 **Fax**: +39-64-9979537

**Received:** March 11, 2014 **Revised:** July 8, 2014

**Accepted:** August 13, 2014

**Published online:**

**Abstract**

Video capsule endoscopy (CE) for evaluation the esophagus (ECE), small bowel (SBCE) and the colon (CCE) is particularly useful in pediatrics, because this imaging modality does not require ionizing radiation, deep sedation or general anesthesia. The risk of capsule retention appears to be dependent on indication rather than age and parallels the adult experience by indication, making SBCE a relatively safe procedure with a significant diagnostic yield. The newest indication, assessment of mucosal change, greatly enhances and expands its potential benefit. The diagnostic role of CE extends beyond the SB. The use of ECE also may enhance our knowledge of esophageal disease and assist patient care. Colon CCE is a novel minimally invasive and painless endoscopic technique allowing exploration of the colon without need for sedation, rectal intubation and gas insufflation. The limited data on ECE and CCE in pediatrics does not yet allow the same conclusions regarding efficacy; however, both appear to provide safe methods to assess and monitor mucosal change in their respective areas with little discomfort. Moreover, although experience has been limited, the patency capsule may help lessen the potential of capsule retention; and newly researched protocols for bowel cleaning may further enhance CE's diagnostic yield. However, further research is needed to optimize the use of the various CE procedures in pediatric population~~s~~.

© 2014 Baishideng Publishing Group Inc. All rights reserved.

**Key words:** Capsule endoscopy; Children; Small bowel; Pediatric endoscopy

**Core tip:** Recent investigations using capsule endoscopy as a tool to monitor mucosal change with therapy and to improve bowel cleaning (which potentially will increase the diagnostic yield) and new capsules to evaluate the esophagus and colon present an enhanced value to be gained from capsule endoscopy, 10 years after investigations began in pediatrics.

Oliva S, Cohen SA, Di Nardo G, Gualdi G, Cucchiara S, Casciani E. Capsule endoscopy in pediatrics: A 10-years journey. *World J Gastroenterol* 2014; In press

**INTRODUCTION**

Since 2001, capsule endoscopy (CE) has been used to evaluate small bowel pathology in adults. In patients of 10 to 18 years of age, these evaluations began in January 2004[1]. In 2009, CE was also approved by United States Food and Drug Administration (FDA) for use in children 2 years of age and older[2]. As a result, the use of CE has expanded in the pediatric population over the past decade, largely because of the possibility of avoiding ionizing radiation, deep sedation and general anesthesia. That success has prompted CE evaluations of the esophagus and colon as well while broader indications and applications of CE are being defined in the diagnosis and monitoring of gastrointestinal disease.

**SMALL BOWEL CAPSULE ENDOSCOPY**

Because the small intestine was often considered as the mysterious “black box” of the GI tract, small bowel capsule endoscopy (SBCE) has become particularly valuable for pediatric patients to achieve a definite diagnosis in cases with small bowel pathologies (*i.e.,* Crohn’s disease (CD) or obscure gastrointestinal bleeding) such that the small bowel is no longer the frontier that it had been in the past[3].

***Indications***

The American Society for Gastrointestinal Endoscopy developed indications for SBCE[4]. However, the relative frequency of indications in compiled pediatric reports differs from that in data regarding adults. In adults, 66% of CEs have been for obscure gastrointestinal bleeding (OGIB) including iron deficiency anemia (IDA); 11% for clinical symptoms only (*e.g.,* pain, diarrhea, and weight loss without OGIB); 10% for CD; with the balance (13%) for other indications[5-25]. In pediatric patients, 60% of CE have been for CD, 15% for OGIB, 10% for abdominal pain/diarrhea, and 8% for polyposis[15-16]. More than half of the procedures for IBD indications are related to evaluation of CD and colitis, with 44% due to the suspicion of CD, 16% related to evaluation of known CD, 2% to differentiate indeterminate colitis (IC), and 1% to further evaluate ulcerative colitis (UC). Abdominal pain and diarrhea account for another 10% of the procedures and might be considered as evaluations for the same indications.

Even within the pediatric population, these clinical indications are age-stratified (Table 1). In a review of 83 procedures in children aged 1.5–7.9 years (when CD is less prevalent), the most common indication for CE was OGIB, accounting for 30 (36%) procedures, with positive yields in 16 (53%)[21]. Suspicion of CD accounted for 20 (24%) procedures, with positive findings in 11 (55%). Abdominal pain accounted for another 12 procedures (14%), and CD was the indication in 3 patients. CD was found in 14 (31%) of the patients where a positive diagnosis was made. Investigation of malabsorption and protein loss required 12 and 9 procedures (14% and 11%), respectively, with positive findings in 6 each. In contrast, OGIB in older children (age 10–18 years) accounted for only 13%–24% of all indications[5,9,11,17,19,23].

Additionally, SBCE is being used to identify eosinophilic enteropathy (with areas of erythematous, denuded mucosa)[9]. an ulcerative inflammatory enteropathy in cystic fibrosis[26] graft versus host disease[8]. monitoring medical therapy in CD[5-27]. and to evaluate the graft's integrity after small bowel transplantion[7,8].

***Preparation***

The inability to establish the exact location of the capsule in the small intestine, and the inability to flushing or suction fluids make adequate bowel cleaning of particular importance for SBCE. Debris, biliary secretion, bubbles and blood, especially in the distal small bowel, and failure of the capsule to reach the cecum have the potential to limit the diagnostic yield[28].

Since cleaning the small intestine prior to examination may improve the diagnostic yield, CE-preparation regimens-mainly using the same products adopted for colonoscopy preparation-have been proposed[29]. But the optimal preparation regimen is yet to be established[30]. A clear liquid diet the evening before CE and an overnight fast appears to be associated with poor visibility of the terminal ileum in the majority of patients[30]. Since simethicone seems to improve mucosal visualization and tolerability by reducing air bubbles, flammable gas (namely, hydrogen) and abdominal discomfort[31], a combination of simethicone and polyethylene glycol (PEG) has frequently been promulgated as an effective means to increase the visibility of the small intestine (SB)[4,33-35].

The only pediatric study to date prospectively evaluated 198 patients with five different preparation regimens[35]. The mucosal visibility of the SB was assessed at five equal time points. After preparation with PEG and simethicone, discomfort was lessened and mucosal visualization improved significantly in the distal ileum, which is the portion most often affected by debris. However, the overall diagnostic yield was not affected except in the last section of SB.

The least amount of PEG solution tested, 1.75 g/25 mL per kg (up to 1 Lt) of PEG solution (70 g /1000 mL) the night before the procedure plus 20 mL (376 mg) oral simethicone 30 min before capsule ingestion appears to be the preparation of choice for SBCE in children. No significant differences were found regarding gastric and small-intestinal transit times or in the proportion of patients in whom the cecum was not visualized. However, intestinal transit is much faster in children than adults and therefore bowel preparation might not impact intestinal transit time in the pediatric age group compared to adults.

***Patient Outcomes***

A meta-analysis[5] and additional reports from the pediatric literature,6,7 comprised 995 patients who underwent 1013 CE procedures with positive findings in 511 (61.4%; 95%CI: = 52.7%–69.7%). Studies were complete (*i.e., t*he capsule reached or passed the ileocecal valve by the end of the recording period) in 846 procedures. (86.0%; 95%CI: 81.6%–89.9%)[5-7]. In the studies for which ingestion was reported, a total 824 (88.4%) children swallowed the capsule uneventfully (95%CI: 86.4%–90.3%)[15]. The youngest child to swallow the capsule was 4 years old[23]. Only 1 patient in the reports could not swallow the capsule and refused endoscopic placement, although the inability to swallow the capsule or the fear of gagging and choking doing so are not infrequent occurrences in clinical practice[11].

A new diagnosis was established in 162 patients (66.0%; 95%CI: 45.4%–83.9%) including patients where the capsule did not enter the colon[12,17,18,23]. A change in therapy followed for 115 of the patients (71.3%; 95%CI: 45.2%–91.5%) where those parameters were quantified.

CD was the most prevalent diagnostic outcome of SBCE studies performed in the pediatric population, based on the criteria of at least 3 mucosal ulcers as previously reported by Fireman and colleagues[36] and Mow and colleagues[37]. In one study, SBCE examination reclassified 4 of 5 patients with UC and 1 of 2 patients with IC (total 5 of 7, or 71%) to CD due to newly recognized SB mucosal lesions[12].In various studies, a change in medical therapy resulted for 75%–92% of patients with known CD[12,13,17].

A recent pilot study evaluating dietary intervention in pediatric CD[27] assessed small bowel mucosal change using CE since 38% of pediatric CD is isolated to the small intestine and 80% of pediatric CD have small bowel involvement[38]. Using the Lewis score, a validated, weighted index of 3 parameters (stenosis, ulceration and villous edema)[39], mucosal improvement was seen at 12 and 52 wk from baseline, providingobjective evidence of mucosal change, which can be used to complement standard clinical IBD research scoring methods that can be affected by the subjective reports from the patients and their families. In pediatric patients investigated for OGIB or IDA by SBCE, 38.4% had confirmed diagnoses[14]. This compares with 59.4% positive results in adults[40]. Forty-six lesions were diagnosed by SBCE[8-11,13,18]: 15 vascular malformations, 7 CD; 14 nonspecific enteropathies; 3 polyps; 2 marked lymphoid hyperplasias; and 1 case each of Meckel’s diverticulum, nonsteroidal anti-inflammatory drug–induced lesions, lymphangiectasia, leukemia-related– and graft-versus-host disease. In patients younger than age 8 years, there were 4 cases of polyps, 2 of angiodysplasias, 2 blue rubber bleb hemangiomas, 2 Meckel’s diverticulae, 1 anastomotic ulcer, and 1 intestinal duplication[23]. In the adult meta-analysis, vascular abnormalities also were the most common cause of OGIB (50%), followed by inflammation and ulcers (27%), and neoplasia (9%)[40]. Evaluation of polyposis syndromes, accounted for 8.0% of the indications in 81 pediatric patients, with positive results in 80.2% of procedures compared to adult diagnostic yield of 55.9% for neoplastic lesions[41].

Although SBCE is rarely performed for evaluation of malabsorption, it is useful since intestinal lymphangiectasia can appear beyond the reach of the endoscope[5]. The infrequency of celiac disease seen in pediatric patients may reflect the infrequency of CE use for evaluation of malabsorption in this population[4] or the decreased time of gluten exposure with potentially patchy or very subtle mucosal changes in childhood at histological levels of Marsh I or II, for which the sensitivity of CE is low[42]. Although lymphonodular hyperplasia and intussusceptions are often seen, they are normally non-pathogenic conditions indigenous to the pediatric population[5].

***Adverse Events***

Capsule retention in the SB occurred in 18 and gastric retention occurred in 4 of 1013 procedures in the meta analysis,producing a pooled retention rate of 2.3% (*n* = 22/1013; 95%CI: 1.5%–3.4%)[5-7,15].Endoscopy was used to remove 5 capsules including 4 from the stomach[9-15] and 1 from an ileal pouch[5]; 13 were retrieved surgically while taking appropriate measures to mitigate the cause of the retention[8,10,13,17]. A retained capsule was successfully evacuated by bowel prep at 22 d post-ingestion[10].

The greatest risk factors for capsule retention include known IBD (5.2% risk), previous small bowel follow-through (SBFT) demonstrating small bowel CD (35.7% risk) and a body mass index below the fifth percentile combined with known IBD (43% risk), although retention has occurred despite the absence of stricture on SBFT[14]. Among 4 patients with CD having capsule passage lasting longer than 5 days (with 3 continuing on to retention), age was significant (18.8 ± 0.9 *vs* 14.6 ± 3.5), but not height or weight, compared to patients who did not have retention.17 Retention rates for indications of OGIB, CD, and neoplastic lesions were 1.2% (95%CI: 0.9%–1.6%), 2.6% (95%CI: 1.6%–3.9%), and 2.1% (95%CI: 0.7%–4.3%), respectively, with a pooled rate of 1.4% (95%CI: 1.2%–1.6%) for those procedures[43]. On a per-procedure basis, this pattern is similar in adults, where retention in OGIB, CD, and polyps occurs at rate of 1.4%, 2.2%, and 1.2%, respectively[40]. Thus, it appearsthat the risk of retention is dependent on the clinical indication, with an higher incidence in patients with suspected chronic small bowel obstruction[43]. Rare cases of perforation, aspiration, or small bowel obstruction have been reported in adults but none have been reported in children. Minor mucosal trauma has occurred in children in which capsules were placed with the Roth net[21]. A specific capsule placement device is now available (AdvanCE, United States Endsocopy, Mentor, OH[44] ).

**Patency capsule:** The majority of capsule retentions have occurred in patients with normal small bowel radiological studies, yet functional patency may be present in patients with radiologically documented strictures. To avoid this concern, an identically sized patency capsule (PC) containing a mixture of barium, lactose and a radiofrequency identity tag was developed. The first version had a single timer plug that degraded at 40 hours. The currently available version has dual timer plugs that gradually implodes if passage does not occur within 30 h.

Both a retrospective[5] and a prospective study[45] have been performed in pediatric IBD using the first iteration of the PC prior to SBCE. Of the 19 who were evaluable in the retrospective analysis, patency was established and subsequent CE was performed successfully in all but 1 patient who had a retained capsule from CE the following week. The prospective trial of 18 patients (age 10-16 years) who ingested the PC, 15 of whom excreted an intact PC (mean 34.5 h) without any PC or CE retentions or adverse events[45]. CD was eventually diagnosed in all patients having PC transit of more than 40 h and in 9 of 12 who passed the patency capsule in 40 h or less. There were no capsule retentions or adverse events. Thus, the PC can serve as a useful guide and may lessen the likelihood of CE retention, particularly in known CD where the risk of retention is greatest**.**

**Esophageal and colon capsules:** Esophageal capsule endoscopy (ECE) was approved by the US FDA and introduced for clinical use in 2004 with a second iteration (ESO 2; Given Imaging) released in 2007. However, clinical trials and apparent pediatric use (or at least, the reporting of that use) have been limited. Only 2 small pediatric trials of the first ECE capsule have appeared. Both focused on portal hypertension, finding that variously sized varices and other esophageal and duodenal findings could be seen despite a rapid transit time in pediatric patients[46-48].

Similarly, colon capsule endoscopy (CCE; Given Imaging Ltd, Yoqneam, Israel)[49-54] has been aided by a recently released, second-generation CCE device (CCE-2)[51,52],Consensus guidelines of ESGE on CCE have proposed that CCE-2 may be useful to monitor inflammation in UC, which may help guide therapy[53]. To date, there have been few studies conducted in adults, with only one using the second generation of CCE[54-57]. There is only one pilot study using CCE-2 in 29 pediatric patients with ulcerative colitis[58]. Sensitivity of CCE-2 in detecting disease activity was 96% (95%CI: 79-99) and specificity was 100% (95%CI: 61-100), corresponding to an overall accuracy of 97% (95%CI: 90-100). The positive and negative predictive values were 100% (95%CI: 85-100) and 85% (95%CI: 49-97), respectively. Optimal preparation is yet to be adequately studied or established.

**CONCLUSION**

SBCE is a useful diagnostic tool that has particular benefit in pediatrics because it does not usually require ionizing radiation, deep sedation or general anesthesia. The risk of retention appears to be dependent on indication rather than age and parallels the adult experience by indication, making SBCE a relatively safe procedure with a significant diagnostic yield. Recent investigations to improve bowel cleaning and establish CE as a useful tool to monitor mucosal change may further expand its utility.

The limited data on ECE and CCE in pediatrics do not warrant the same conclusions as yet; however, both appear to provide safe methods to assess and monitor mucosal change in their respective anatomic areas with little discomfort. However, further investigations are needed to maximize the impact of this burgeoning area of mucosal assessment and to determine whether CE can pre-empt traditional studies in order to lessen cost and improve tolerability of needed procedures.

**REFERENCES**

1 **United States Food and Drug Administration.** Center for Devices and Radiological Health. PC Patency System and Pillcam Platform with Pillcam SB Capsules. Available from: URL: http: //www.accessdata.fda.gov/cdrh\_docs/pdf9/K090557.pdf. Accessed February 10, 2010.

2 **Swaminath A**, Legnani P, Kornbluth A. Video capsule endoscopy in inflammatory bowel disease: past, present, and future redux. *Inflamm Bowel Dis* 2010; **16**: 1254-1262 [PMID: 20155845 DOI: 10.1002/ibd.21220]

3 **Eisen GM**. Small-bowel endoscopy. *Gastrointest Endosc* 2012; **76**: 521-524 [PMID: 22898411 DOI: 10.1016/j.gie.2012.07.002]

4 **Mishkin DS**, Chuttani R, Croffie J, Disario J, Liu J, Shah R, Somogyi L, Tierney W, Song LM, Petersen BT. ASGE Technology Status Evaluation Report: wireless capsule endoscopy. *Gastrointest Endosc* 2006; **63**: 539-545 [PMID: 16564850]

5 **Cohen SA**, Klevens AI. Use of capsule endoscopy in diagnosis and management of pediatric patients, based on meta-analysis. *Clin Gastroenterol Hepatol* 2011; **9**: 490-496 [PMID: 21440674 DOI: 10.1016/j.cgh.2011.03.025]

6 **Cohen SA**, Ephrath H, Lewis JD, Klevens A, Bergwerk A, Liu S, Patel D, Reed-Knight B, Stallworth A, Wakhisi T, Gold BD. Pediatric capsule endoscopy: review of the small bowel and patency capsules. *J Pediatr Gastroenterol Nutr* 2012; **54**: 409-413 [PMID: 21760541 DOI: 10.1097/MPG.0b013e31822c81fd]

7 **Gralnek IM**, Cohen SA, Ephrath H, Napier A, Gobin T, Sherrod O, Lewis J. Small bowel capsule endoscopy impacts diagnosis and management of pediatric inflammatory bowel disease: a prospective study. *Dig Dis Sci* 2012; **57**: 465-471 [PMID: 21901253]

8 **Tokuhara D**, Watanabe K, Okano Y, Tada A, Yamato K, Mochizuki T, Takaya J, Yamano T, Arakawa T. Wireless capsule endoscopy in pediatric patients: the first series from Japan. *J Gastroenterol* 2010; **45**: 683-691 [PMID: 20143103 DOI: 10.1007/s00535-010-0209-5]

9 **Guilhon de Araujo Sant'Anna AM**, Dubois J, Miron MC, Seidman EG. Wireless capsule endoscopy for obscure small-bowel disorders: final results of the first pediatric controlled trial. *Clin Gastroenterol Hepatol* 2005; **3**: 264-270 [PMID: 15765446]

10 **Jensen MK**, Tipnis NA, Bajorunaite R, Sheth MK, Sato TT, Noel RJ. Capsule endoscopy performed across the pediatric age range: indications, incomplete studies, and utility in management of inflammatory bowel disease. *Gastrointest Endosc* 2010; **72**: 95-102 [PMID: 20472231 DOI: 10.1016/j.gie.2010.01.016]

11 **Antao B**, Bishop J, Shawis R, Thomson M. Clinical application and diagnostic yield of wireless capsule endoscopy in children. *J Laparoendosc Adv Surg Tech A* 2007; **17**: 364-370 [PMID: 17570790]

12 **Cohen SA**, Gralnek IM, Ephrath H, Saripkin L, Meyers W, Sherrod O, Napier A, Gobin T. Capsule endoscopy may reclassify pediatric inflammatory bowel disease: a historical analysis. *J Pediatr Gastroenterol Nutr* 2008; **47**: 31-36 [PMID: 18607266 DOI: 10.1097/MPG.0b013e318160df85]

13 **de' Angelis GL**, Fornaroli F, de' Angelis N, Magiteri B, Bizzarri B. Wireless capsule endoscopy for pediatric small-bowel diseases. *Am J Gastroenterol* 2007; **102**: 1749-157; quiz 1748, 1758 [PMID: 17686071]

14 **Atay O**, Mahajan L, Kay M, Mohr F, Kaplan B, Wyllie R. Risk of capsule endoscope retention in pediatric patients: a large single-center experience and review of the literature. *J Pediatr Gastroenterol Nutr* 2009; **49**: 196-201 [PMID: 19561547 DOI: 10.1097/MPG.0b013e3181926b01]

15 **Cohen S.** Pediatric capsule endoscopy. *Tech Gastrointestinal Endosc* 2013; **15**: 32-35

16 **Casciani E**, Masselli G, Di Nardo G, Polettini E, Bertini L, Oliva S, Floriani I, Cucchiara S, Gualdi G. MR enterography versus capsule endoscopy in paediatric patients with suspected Crohn's disease. *Eur Radiol* 2011; **21**: 823-831 [PMID: 20922391 DOI: 10.1007/s00330-010-1976-3]

17 **Moy L**, Levine J. Wireless capsule endoscopy in the pediatric age group: experience and complications. *J Pediatr Gastroenterol Nutr* 2007; **44**: 516-520 [PMID: 17414156]

18 **Ge ZZ**, Chen HY, Gao YJ, Gu JL, Hu YB, Xiao SD. Clinical application of wireless capsule endoscopy in pediatric patients for suspected small bowel diseases. *Eur J Pediatr* 2007; **166**: 825-829 [PMID: 17103187]

19 **Argüelles-Arias F**, Caunedo A, Romero J, Sánchez A, Rodríguez-Téllez M, Pellicer FJ, Argüelles-Martín F, Herrerías JM. The value of capsule endoscopy in pediatric patients with a suspicion of Crohn's disease. *Endoscopy* 2004; **36**: 869-873 [PMID: 15452782]

20 **Urbain D**, Tresinie M, De Looz D, Demedts I, Hauser B, Mana F, Macken E, Hoffmann I, Scaillon M, Van Callie-Bertrand M, Van Gossum A, Louis E, Vandenplas Y. Capsule endoscopy in paediatrics: multicentric Belgian study. *Acta Gastroenterol Belg* 2007; **70**: 11-14 [PMID: 17619532]

21 **Barth BA**, Donovan K, Fox VL. Endoscopic placement of the capsule endoscope in children. *Gastrointest Endosc* 2004; **60**: 818-821 [PMID: 15557968]

22 **Shamir R**, Hino B, Hartman C, Berkowitz D, Eshach-Adiv O, Eliakim R. Wireless video capsule in pediatric patients with functional abdominal pain. *J Pediatr Gastroenterol Nutr* 2007; **44**: 45-50 [PMID: 17204952]

23 **Fritscher-Ravens A**, Scherbakov P, Bufler P, Torroni F, Ruuska T, Nuutinen H, Thomson M, Tabbers M, Milla P. The feasibility of wireless capsule endoscopy in detecting small intestinal pathology in children under the age of 8 years: a multicentre European study. *Gut* 2009; **58**: 1467-1472 [PMID: 19625281 DOI: 10.1136/gut.2009]

24 **Postgate A**, Hyer W, Phillips R, Gupta A, Burling D, Bartram C, Marshall M, Taylor S, Brown G, Schofield G, Bassett P, Spray C, Fitzpatrick A, Latchford A, Fraser C. Feasibility of video capsule endoscopy in the management of children with Peutz-Jeghers syndrome: a blinded comparison with barium enterography for the detection of small bowel polyps. *J Pediatr Gastroenterol Nutr* 2009; **49**: 417-423 [PMID: 19543117 DOI: 10.1097/MPG.0b013e31818f0a1f]

25 **Thomson M**, Fritscher-Ravens A, Mylonaki M, Swain P, Eltumi M, Heuschkel R, Murch S, McAlindon M, Furman M. Wireless capsule endoscopy in children: a study to assess diagnostic yield in small bowel disease in paediatric patients. *J Pediatr Gastroenterol Nutr* 2007; **44**: 192-197 [PMID: 17255830]

26 **Werlin SL**, Benuri-Silbiger I, Kerem E, Adler SN, Goldin E, Zimmerman J, Malka N, Cohen L, Armoni S, Yatzkan-Israelit Y, Bergwerk A, Aviram M, Bentur L, Mussaffi H, Bjarnasson I, Wilschanski M. Evidence of intestinal inflammation in patients with cystic fibrosis. *J Pediatr Gastroenterol Nutr* 2010; **51**: 304-308 [PMID: 20512061 DOI: 10.1097/MPG.0b013e3181d1b013]

27 **Cohen SA,** Gold BD, Oliva S, Lewis J, Stallworth A, Koch B, Eshee L, Mason D.Clinical and Mucosal Improvement with the Specific Carbohydrate Diet in Pediatric Crohn's Disease: A Prospective Pilot Study. *J Pediatr Gastroenterol Nutr* 2014; [PMID: 24897165]

28 **Niv Y**. Efficiency of bowel preparation for capsule endoscopy examination: a meta-analysis. *World J Gastroenterol* 2008; **14**: 1313-1317 [PMID: 18322940 DOI: 10.3748/wjg.14.1313]

29 **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; **104**: 219-227 [PMID: 19098872 DOI: 10.1038/ajg.2008.63]

30 **Ladas SD**, Triantafyllou K, Spada C, Riccioni ME, Rey JF, Niv Y, Delvaux M, de Franchis R, Costamagna G. European Society of Gastrointestinal Endoscopy (ESGE): recommendations (2009) on clinical use of video capsule endoscopy to investigate small-bowel, esophageal and colonic diseases. *Endoscopy* 2010; **42**: 220-227 [PMID: 20195992 DOI: 10.1055/s-0029-1243968]

31 **Chen HB**, Huang Y, Chen SY, Song HW, Li XL, Dai DL, Xie JT, He S, Zhao YY, Huang C, Zhang SJ, Yang LN. Small bowel preparations for capsule endoscopy with mannitol and simethicone: a prospective, randomized, clinical trial. *J Clin Gastroenterol* 2011; **45**: 337-341 [PMID: 20871410 DOI: 10.1097/MCG.0b013e3181f0f3a3]

32 **Faigel DO**, Baron TH, Adler DG, Davila RE, Egan J, Hirota WK, Jacobson BC, Leighton JA, Qureshi W, Rajan E, Zuckerman MJ, Fanelli R, Wheeler-Harbaugh J. ASGE guideline: guidelines for credentialing and granting privileges for capsule endoscopy. *Gastrointest Endosc* 2005; **61**: 503-505 [PMID: 15812400]

33 **Villa F**, Signorelli C, Rondonotti E, de Franchis R. Preparations and prokinetics. *Gastrointest Endosc Clin N Am* 2006; **16**: 211-220 [PMID: 16644451]

34 **Spada C**, Riccioni ME, Familiari P, Spera G, Pirozzi GA, Marchese M, Bizzotto A, Ingrosso M, Costamagna G. Polyethylene glycol plus simethicone in small-bowel preparation for capsule endoscopy. *Dig Liver Dis* 2010; **42**: 365-370 [PMID: 19736051 DOI: 10.1016/j.dld.2009.07.017]

35 **Oliva S**, Cucchiara S, Spada C, Hassan C, Ferrari F, Civitelli F, Pagliaro G, Di Nardo G. Small bowel cleansing for capsule endoscopy in paediatric patients: a prospective randomized single-blind study. *Dig Liver Dis* 2014; **46**: 51-55 [PMID: 24041737 DOI: 10.1016/j.dld.2013.08.130]

36 **Fireman Z**, Mahajna E, Broide E, Shapiro M, Fich L, Sternberg A, Kopelman Y, Scapa E. Diagnosing small bowel Crohn's disease with wireless capsule endoscopy. *Gut* 2003; **52**: 390-392 [PMID: 12584221]

37 **Mow WS**, Lo SK, Targan SR, Dubinsky MC, Treyzon L, Abreu-Martin MT, Papadakis KA, Vasiliauskas EA. Initial experience with wireless capsule enteroscopy in the diagnosis and management of inflammatory bowel disease. *Clin Gastroenterol Hepatol* 2004; **2**: 31-40 [PMID: 15017630]

38 **Griffiths AM**. Specificities of inflammatory bowel disease in childhood. *Best Pract Res Clin Gastroenterol* 2004; **18**: 509-523 [PMID: 15157824]

39 **Lewis BS**, Eisen GM, Friedman S. A pooled analysis to evaluate results of capsule endoscopy trials. *Endoscopy* 2005; **37**: 960-965 [PMID: 16189768]

40 **Liao Z**, Gao R, Xu C, Li ZS. Indications and detection, completion, and retention rates of small-bowel capsule endoscopy: a systematic review. *Gastrointest Endosc* 2010; **71**: 280-286 [PMID: 20152309 DOI: 10.1016/j.gie.2009.09.031]

41 **Cohen SA**. The potential applications of capsule endoscopy in pediatric patients compared with adult patients. *Gastroenterol Hepatol (N Y)* 2013; **9**: 92-97 [PMID: 23983653]

42 **Gay G,** Fassler I, Florent C, Delvaux M. Malabsorption in Halpern M, Jacob H. Atlas of Capsule Endoscopy. Norcross, GA. Given Imaging 2002; 84-90

43 **Singeap AM,** Trifan A, Cojocariu C, Sfarti C, Stanciu C. Outcomes after symptomatic capsule retention in suspected small bowel obstruction. *Eur J Gastroenterol Hepatol* 2011; **23**: 886-890 [PMID: 21811157 DOI: 10.1097/MEG.0b013e328349efa4]

44 **Uko V**, Atay O, Mahajan L, Kay M, Hupertz V, Wyllie R. Endoscopic deployment of the wireless capsule using a capsule delivery device in pediatric patients: a case series. *Endoscopy* 2009; **41**: 380-382 [PMID: 19340746 DOI: 10.1055/s-0029-1214491]

45 **Cohen SA**, Gralnek IM, Ephrath H, Stallworth A, Wakhisi T. The use of a patency capsule in pediatric Crohn's disease: a prospective evaluation. *Dig Dis Sci* 2011; **56**: 860-865 [PMID: 20652742 DOI: 10.1007/s10620-010-1330-2]

46 **Fox V.** Esophageal capsule endoscopy in children and young adults with portal hypertension. 6th International Conference on Capsule Endoscopy (ICCE) 2006; Madrid: AB887874.

47 **Schaible TD,** Olive AP, Wilson DS, Fishman DS. Use of esophageal capsule endoscopy in pediatric patients with portal hypertension. *Gastrointest Endosc* 2010; **71**: M1562 [DOI: 10.1016/j.gie.2010.03.563]

48 **de Franchis R**, Eisen GM, Laine L, Fernandez-Urien I, Herrerias JM, Brown RD, Fisher L, Vargas HE, Vargo J, Thompson J, Eliakim R. Esophageal capsule endoscopy for screening and surveillance of esophageal varices in patients with portal hypertension. *Hepatology* 2008; **47**: 1595-1603 [PMID: 18435461 DOI: 10.1002/hep.22227]

49 **Schoofs N**, Devière J, Van Gossum A. PillCam colon capsule endoscopy compared with colonoscopy for colorectal tumor diagnosis: a prospective pilot study. *Endoscopy* 2006; **38**: 971-977 [PMID: 17058159]

50 **Van Gossum A**, Munoz-Navas M, Fernandez-Urien I, Carretero C, Gay G, Delvaux M, Lapalus MG, Ponchon T, Neuhaus H, Philipper M, Costamagna G, Riccioni ME, Spada C, Petruzziello L, Fraser C, Postgate A, Fitzpatrick A, Hagenmuller F, Keuchel M, Schoofs N, Devière J. Capsule endoscopy versus colonoscopy for the detection of polyps and cancer. *N Engl J Med* 2009; **361**: 264-270 [PMID: 19605831 DOI: 10.1056/NEJMoa0806347]

51 **Eliakim R**, Yassin K, Niv Y, Metzger Y, Lachter J, Gal E, Sapoznikov B, Konikoff F, Leichtmann G, Fireman Z, Kopelman Y, Adler SN. Prospective multicenter performance evaluation of the second-generation colon capsule compared with colonoscopy. *Endoscopy* 2009; **41**: 1026-1031 [PMID: 19967618 DOI: 10.1055/s-0029-1215360]

52 **Spada C**, Hassan C, Munoz-Navas M, Neuhaus H, Deviere J, Fockens P, Coron E, Gay G, Toth E, Riccioni ME, Carretero C, Charton JP, Van Gossum A, Wientjes CA, Sacher-Huvelin S, Delvaux M, Nemeth A, Petruzziello L, de Frias CP, Mayershofer R, Amininejad L, Dekker E, Galmiche JP, Frederic M, Johansson GW, Cesaro P, Costamagna G. Second-generation colon capsule endoscopy compared with colonoscopy. *Gastrointest Endosc* 2011; **74**: 581-589.e1 [PMID: 21601200 DOI: 10.1016/j.gie.2011.03.1125]

53 **Spada C**, Hassan C, Galmiche JP, Neuhaus H, Dumonceau JM, Adler S, Epstein O, Gay G, Pennazio M, Rex DK, Benamouzig R, de Franchis R, Delvaux M, Devière J, Eliakim R, Fraser C, Hagenmuller F, Herrerias JM, Keuchel M, Macrae F, Munoz-Navas M, Ponchon T, Quintero E, Riccioni ME, Rondonotti E, Marmo R, Sung JJ, Tajiri H, Toth E, Triantafyllou K, Van Gossum A, Costamagna G. Colon capsule endoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline.*Endoscopy* 2012; **44**: 527-536 [PMID: 22389230 DOI: 10.1055/s-0031-1291717]

54 **Sung J**, Ho KY, Chiu HM, Ching J, Travis S, Peled R. The use of Pillcam Colon in assessing mucosal inflammation in ulcerative colitis: a multicenter study. *Endoscopy* 2012; **44**: 754-758 [PMID: 22696193 DOI: 10.1055/s-0032-1309819]

55 **Ye CA**, Gao YJ, Ge ZZ, Dai J, Li XB, Xue HB, Ran ZH, Zhao YJ. PillCam colon capsule endoscopy versus conventional colonoscopy for the detection of severity and extent of ulcerative colitis. *J Dig Dis* 2013; **14**: 117-124 [PMID: 23134295 DOI: 10.1111/1751-2980.12005]

56 **Meister T**, Heinzow HS, Domagk D, Dortgolz A, Lenze F, Ross M, Domschke W, Lügering A. Colon capsule endoscopy versus standard colonoscopy in assessing disease activity of ulcerative colitis: a prospective trial. *Tech Coloproctol* 2013; **17**: 641-646 [PMID: 23307507 DOI: 10.1007/s10151-012-0965-8]

57 **Hosoe N**, Matsuoka K, Naganuma M, Ida Y, Ishibashi Y, Kimura K, Yoneno K, Usui S, Kashiwagi K, Hisamatsu T, Inoue N, Kanai T, Imaeda H, Ogata H, Hibi T. Applicability of second-generation colon capsule endoscope to ulcerative colitis: a clinical feasibility study. *J Gastroenterol Hepatol* 2013; **28**: 1174-1179 [PMID: 23517279 DOI: 10.1111/jgh.12203

58 **Oliva S**, Di Nardo G, Hassan C, Spada C, Aloi M, Ferrari F, Redler A, Costamagna G, Cucchiara S. Second-generation colon capsule endoscopy vs. colonoscopy in pediatric ulcerative colitis: a pilot study. *Endoscopy* 2014; **46**: 485-492 [PMID: 24777427 DOI: 10.1055/s-0034-1365413]

**P-Reviewer:** Ahboucha S, **Andus T,** Stanciu C, Triantafyllou K **S-Editor:** Qi Y

**L-Editor: E-Editor:**

**Table 1 Clinical indications, outcomes and adverse events by different age groups**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | | **Adult** | **Pediatric** | **< 8 yr** |
| **Indications** (%) | | |  |  |  |
| OGIB + IDA | | | 66 | 15 | 36 |
| CD /UC /IC | | | 10 | 63 | 24 |
| Abdominal pain | | | 11 | 10 | 14 |
| Polyps/Neoplasms | | | 3 | 8 | - |
| Other | | | 10 | 4 | 25 |
| **Outcomes (% positive findings for different indications)** | | | | |  |
| OGIB + IDA | 61 | 42 | | | **-** |
| CD /UC /IC | 55 | 65 | | | - |
| Abdominal pain | 23 | 43 | | | - |
| Polyps/Neoplasms | 56 | 75 | | | - |
| Overall | 59 | 61 | | | 67 |
| **Adverse events** **(%)** |  |  | | |  |
| Capsule retention | 1.4 | 2.6 | | | 0.5 |
| Incomplete examinations | 16 | 13 | | | 7 |
| Other | 1.1 | 0.9 | | | - |

CD: Crohn’s disease; IDA: Iron deficiency anemia; OGIB: Obscure gastrointestinal bleeding; IC: Indeterminant colitis; UC: Ulcerative colitis.