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Capsule endoscopy in pediatrics: A growing experience

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ABSTRACT

Capsule endoscopy (CE) usage and research in pediatrics is in its infancy but is growing. The possibility of avoiding ionizing radiation, deep sedation, and general anesthesia makes CE an appealing tool for diagnosis and disease state monitoring in luminal pediatric gastrointestinal disorders. As such, clinical use is expanding, but research has lagged behind, focusing on inflammatory bowel diseases (IBD) and polyposis syndromes. Food and Drug Administration approval in 2009 for children 2 years of age and older has resulted from the broader application of CE. In turn, this acceptability has fostered use in infants as young as 8 months (and 7.9 kg in weight). With these age differences (within the pediatric population and in comparison with adults), the indications have changed, with continued emphasis on not only patients with IBD but also in younger children who have a lower incidence of IBD, with more concern regarding occult bleeding and additional small bowel disorders, including graft-vs-host disease, Henoch-Schönlein purpura, cystic fibrosis, and lymphangiectasia. The ability to swallow or place the capsule remains a concern, but retention parallels adult indications rather than age. To date, esophageal capsules have been used primarily for the evaluation of varices, although the colon capsule has been used to further understand IBD in both the small bowel and the large bowel. With this varied and expanded use has come comparisons with other diagnostic modalities, attempts to integrate CE with these modalities into effective and cost-effective clinically assessed algorithms, and a plea for further research and the funding to make that possible.

1. Introduction

Small bowel (SB) capsule endoscopy (CE) has become an important part of the diagnostic armamentarium for pediatric gastroenterologists since the United States Food and Drug Administration (FDA) approved its use in evaluating SB pathology in patients older than 10 years [1]. Its use has gradually expanded, largely because of the possibility of avoiding ionizing radiation, deep sedation, and general anesthesia, and has led to FDA approval in 2009 for children 2 years of age and older (although these younger patients often require deep sedation [2] or anesthesia [3] for capsule placement). Additionally, the release of esophageal and colon capsules has allowed for investigations of those areas in the pediatric population while further research has also pursued broader indications and applications of SBCE in otherwise difficult assessments of gastrointestinal disease states in children as well as adults [4].

2. Small bowel capsule endoscopy

2.1. Indications

Organizations such as the American Society for Gastrointestinal Endoscopy have promulgated indications for SBCE [5]. However, systematic analyses demonstrate that, in pediatrics, the relative frequency of indications differs from that in data regarding adults [6]. In pediatric patients, 60% of CEs have been for Crohn's disease (CD), 15% for obscure gastrointestinal bleeding (OGIB), 10% for abdominal pain or diarrhea, and 8% for polyposis [6-25]. In adults, 66% of CEs have been for OGIB including iron-deficiency anemia, 11% for clinical symptoms only (eg, pain, diarrhea, and weight loss without OGIB), 10% for CD, and the remaining (13%) for other indications [26].

The most common indications for SBCE in pediatric patients are the suspicion of CD and evaluation of existing inflammatory bowel disease (IBD), accounting for 63% of the total indications [6]. More

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Table
Clinical indications by age (reproduced from Cohen S. Tech Gastrointest Endosc 2013;15:32-35).

	Adult*	Pediatric†	Age < 8 y‡
Procedures (*n*)	22,840	1013	83
OGIB + IDA	66	15	36
CD, UC, or IC (%)	10	63	24
Abdominal pain (%)	11	10	14
Polyps or neoplasms (%)	3	8	–
Other (%)	10	4	25

Abbreviation: IDA, iron-deficiency anemia.

* Cohen [6].
† Liao [26].
‡ Fritcher-Ravens [23].

than half of the procedures for IBD indications are related to the evaluation of CD and colitis, with 44% owing to the suspicion of CD, 16% related to evaluation of known CD, 2% to indeterminate colitis (IC), and 1% ulcerative colitis (UC). Abdominal pain and diarrhea account for another 10%. Similar indications were noted in a single-center study where the mean age was younger than 10 years (119 months, range: 8-188 months) [27].

Even within the pediatric population, these clinical indications are age stratified (Table). In a review of 83 procedures in European children aged 1.5-7.9 years (for whom CD is less prevalent), the most common indication for CE was OGIB, accounting for 30 (36%) procedures, with positive yields in 16 (53%) [23]. In contrast, OGIB in older children (age 10-18 years) accounted for only 13%-24% of all indications [6,10,12,17,19,22].

In the younger children, 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%) patients in whom 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 a study of Japanese infants and children [2], CE was also performed to evaluate recurrent vomiting and SB lesions associated with intractable Henoch-Schönlein purpura.

2.2. Patient outcomes

A systematic meta-analysis [6] along with additional reports from pediatric literature [7,8] includes 995 patients who underwent 1013 CE procedures, with positive findings in 511 (61.4%; 95% CI: 52.7%-69.7%). Studies were complete (ie, the 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%; $P = 0.0003$) [4–6]. In many other studies, diagnostic findings were achieved even though the capsule did not enter the colon [11,15,16,21]. A new diagnosis was established in 162 patients (66.0%; 95% CI: 45.4%-83.9%), with a change in therapy for 101 of the patients (71.3%; 95% CI: 45.2%-91.5%) in whom those parameters were quantified.

A total 824 (88.4%) children in the studies for which ingestion was reported swallowed the capsule uneventfully (95% CI: 86.4%-90.3%; $P < 0.0001$) [14]. The youngest was 4 years of age [7]. Only 1 patient in the reports could not swallow the capsule and refused endoscopic placement, although this can occur in up to 51% of the young population, with endoscopic placement then being used [27]. Subsequent reports indicate successful CE usage in patients until 8 months of age (9-kg body weight) [28].

2.3. Inflammatory bowel disease

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 [29] and Mow and colleagues [30]. In various studies, a change in medical therapy resulted for 75%-92% of patients with known CD [13,14,17]. In 1 study, SBCE examination reclassified 4 of 5 patients with UC and 1 of 2 patients with IC (5/7 or 71%) to CD owing to newly diagnosed SB mucosal lesions [13]. CE success in disease reclassification and improvement in therapeutic decision making have been confirmed in 2 further studies [31,32].

As a result, CE is now an indicated option under the Porto criteria to evaluate the small intestine in suspected IBD cases, with SB imaging considered essential in pediatric patients with CD, IBD-undetermined, or atypical UC. Caution is noted, however, when CE is the only SB imaging technique because of the high number of false-positive results, particularly with nonsteroidal anti-inflammatory drugs use, the risk of retention, and the current lack of validated diagnostic criteria or scoring system in pediatrics [33].

In the past 2 decades, advances in magnetic resonance enterography (MRE) and small intestine contrast ultrasonography have led to widespread use of these noninvasive, radiation-free, and well-tolerated approaches to imaging children with IBD. Computerized tomography has lost favor because of the cumulative radiation dose from often repeated studies and its lower diagnostic yield, in favor of MRE, which too lacks a validated scoring system but can detect extraluminal events and fibrotic vs inflammatory stenosis. Deep or balloon enteroscopy is also felt to be indicated when the other modalities do not allow a definite diagnosis of SB CD [33,34].

Nevertheless, there remains considerable uncertainty regarding their timely application in diagnostic algorithms for suspected CD, as well as in disease activity assessments among those with known CD. A recent pediatric study has compared CE, MRE, and small intestine contrast ultrasonography, showing that an integrated use of these different tools should be suggested to achieve a complete assessment of SB in children with suspected or confirmed CD [35].

Moreover, CE is useful in monitoring mucosal healing in SB CD. A recent pediatric pilot study employed CE to evaluate disease activity before and after dietary intervention [36].

2.4. Gastrointestinal bleeding or undefined anemia

In pediatric patients investigated for OGIB or iron-deficiency anemia by SBCE, 38.4% had confirmed diagnoses [6]. This compares with 59.4% positive results seen in adults [26]. In total, 46 lesions were diagnosed by SBCE [9-12,14,18], including 15 vascular malformations, 7 CD, 14 nonspecific enteropathies, 3 polyps, 2 marked lymphoid hyperplasias, and 1 case each of Meckel diverticulum, nonsteroidal anti-inflammatory drug–induced lesions, lymphangiectasia, leukemia-related disease, and graft-vs-host disease. In patients younger than age 8 years, there were 4 cases of polyps, 2 of angiodysplasias, 2 of blue rubber bleb hemangiomas, 2 of Meckel diverticuli, 1 of anastomotic ulcer, and 1 of 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%) [26].

A recent pediatric study evaluated the role of CE and colon capsule endoscopy (CCE), in a diagnostic algorithm followed by deep enteroscopy, in 22 patients. First-look CE provided positive findings in 64% of cases, whereas adding a second look by CCE brought the diagnostic yield to 73%. Enteroscopy was subsequently able to reach the positive and suspicious findings in all but 2, with intraoperative enteroscopy needed. This combined approach showed positive findings in 21 of 22 cases with a diagnostic yield of 95% and OGIB resolution in 82%, suggesting CE has a decisive role in evaluating OGIB and guiding therapeutic management [37].