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Colon capsule endoscopy

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ABSTRACT

PillCam colon capsule endoscopy (CCE) (Covidien, USA, formerly Given Imaging, Yoqneam, Israel) is a noninvasive technique that enables endoscopic evaluation of the colon without sedation, ionizing radiation, or air insufflation. Recently, a new generation of colon capsule was included in the portfolio of capsule endoscopy. The new generation of CCE was demonstrated to be accurate to detect colonic lesions, such as polyps and tumors. To date, CCE is not an alternative to screening colonoscopy. It is a complementary test for average-risk patients unwilling to undergo optical colonoscopy, in case of incomplete colonoscopy, or in case of patients unable to safely undergo optical colonoscopy. In the United States, it is approved by the Food and Drug Administration only for incomplete colonoscopy owing to technical reasons. CCE has been also cleared by Japan's Pharmaceuticals & Medical Devices Agency (PMDA) for diagnosis of colonic disease when colonoscopy is required but difficult to conduct, including patients unwilling or unable to undergo colonoscopy. Other potential applications of CCE, such as in colorectal cancer screening or diagnostic surveillance of inflammatory bowel disease (IBD), remain to be clarified.

1. Introduction

PillCam colon capsule endoscopy (CCE) (Covidien, USA, formerly Given Imaging, Yoqneam, Israel) is a noninvasive technique that enables endoscopic evaluation of the colon without sedation, ionizing radiation, or air insufflation. CCE was initially released in 2006 [1,2]. Recently, a new generation of colon capsule was included in the portfolio of capsule endoscopy. The technology has been implemented, and a second generation of CCE is now available. The second generation of CCE (PillCam Colon 2, Covidien) (CCE-2) was proven to be an accurate tool to detect colonic neoplastic lesions when used in average risk individuals [3,4]. To date, the evidence supports the use of CCE-2 in case of optical colonoscopy failure, in patients unwilling to undergo optical colonoscopy, and when standard optical colonoscopy is contraindicated. In the United States, it is approved by the Food and Drug Administration only for incomplete colonoscopy owing to technical reasons. Similarly, in Japan, CCE was cleared by Japan's Pharmaceuticals & Medical Devices Agency (PMDA) for diagnosis of colonic disease when colonoscopy is required but difficult to conduct, including patients unwilling or unable to undergo colonoscopy. Other potential applications, such as colorectal cancer screening or diagnostic surveillance of inflammatory bowel disease (IBD), need to be clarified [5].

2. Colon capsule endoscopy system

The CCE system is composed of 3 main subsystems: an ingestible capsule endoscope (second-generation colon capsule), a data recorder, and a RAPID workstation. The second-generation CCE (PCC-2) is 11.6 mm × 31.5 mm in size [3,4]. The capsule has a battery lasting approximately 10 hours and has 2 cameras, one at each end, with an angle of view of 172° for each camera, allowing a near-full visual coverage of the colon lumen. To enhance colon mucosal visualization and to save battery energy and video reading time, the capsule is equipped with an adaptive frame rate (AFR), which alternates from 35 images per second while in motion to 4 images per second when the capsule is stationary. At the moment of capsule ingestion, the capsule works using this AFR, allowing proper visualization of the esophagus also; then it slows down to 14 images per minute. When small bowel images are detected, the system switches on the capsule into the AFR mode. This advanced system [3,4,6] for the control of capsule image rate is the result of a bidirectional communication between the capsule and the data recorder, which constantly analyzes and recognizes the transmitted images and adapts in a split second the frame rate. The data recorder also alerts the patient by means of visual and audio signals. The data recorder buzzes, vibrates, and shows instructions on its liquid crystal display to instruct the patient during the day of the procedure (ie, to ingest the colon cleansing booster after the capsule

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has left the stomach and entered the small bowel). On completion of the examination, data from the data recorder are downloaded to the workstation that includes dedicated software (Rapid Software) for video processing and viewing.

3. Bowel preparation

During the colon capsule procedure, it is not possible to clean the colon. Therefore, colonic preparation is crucial, as even small amounts of debris could interfere with colon capsule capability to identify colonic polyps and ultimately with the outcome of the procedure. Colonic preparation should achieve 3 goals: (1) to provide an adequate cleansing level, (2) to distend the colonic wall filling the lumen of clean liquids, and (3) to promote capsule propulsion and excretion. A protocol of preparation combining high volumes of PEG (4 L) and boosts with sodium phosphate (75 ml) was adopted and has been demonstrated to allow a complete colon examination in most cases [3,4,7]. Subsequent studies proposed modifications in the timing and doses of these components. In particular, because of the known concerns related to the administration of sodium phosphate, other boosters have been investigated. Unfortunately, these studies resulted in unsatisfactory outcomes in terms of significant reduction of capsule excretion and completion rates [7,8]. For these reasons, to date, most of the evidence support a regimen of preparation that includes a split regimen of PEG (2 L + 2 L) to improve the cleansing level and sodium phosphate boosters to achieve a reasonable capsule excretion rate (ie, complete colonoscopy). As a booster, a low dose of sodium phosphate (45-55 mL) was shown to achieve an adequate capsule excretion rate with the significant advantage of decreasing the risk of sodium phosphate toxicity (acute nephropathy, electrolyte imbalance, and kidney failure) [5] (Table 1).

Recently, in a large multicenter trial, sodium phosphate was replaced by Suprep (sodium sulfate, potassium sulfate, and magnesium sulfate) (Braintree Lab Inc, United States), maintaining the split dose of PEG [9]. Results of this trial were comparable to those of other previous trials (where sodium phosphate was adopted): capsule excretion within 10 hours occurred in 91% of patients, and the cleansing level was adequate in 80% of cases. If further trials confirm these results, Suprep, where available, might represent a viable alternative to sodium phosphate.

4. Accuracy

4.1. Neoplastic lesions

CCE was demonstrated to be a feasible and reliable tool to detect colonic lesions, such as polyps and tumors (Figure) [3,4,9-11].

Table 1
Regimen of preparation according to the ESGE Guidelines [5].

Schedule		Intake
Day 2	Bedtime	Senna, 4 tablets (48 mg)
Day 1	All day	Clear liquid diet
	Evening (7-9 pm)	2-L PEG
Exam day	7-9 am	2-L PEG
	10 am (~1 h after last intake of PEG)	Capsule ingestion*
	After small bowel detection	1st Boost 30-mL NaP + 1-L water
	3 h after first boost	2nd Boost †15-ml NaP + 0.5-L water
	2 h after second boost	Suppository †10-mg Bisacodyl

* 10 mg Metoclopramide tablet if capsule delayed in stomach > 1 h.
† Only if capsule not excreted yet.

To date, more than 1100 patients were involved in comparative trials that used standard optical colonoscopy as the gold standard (Table 2). Although studies were heterogeneous in terms of regimen of preparation and procedure, CCE sensitivity is between 72% and 95% for patients with polyps ≥ 6 mm and between 75% and 92% for patients with polyps ≥ 10 mm [3,4,9-11]. Specificity ranges between 64% and 91% for patients with polyps ≥ 6 mm and between 89% and 100% for patients with polyps ≥ 10 mm [3,4,9-11]. The low specificity observed in trials was mainly related to a consistent number of false-positive cases generated by size mismatching between standard optical colonoscopy and CCE. Only a minority of false positives was related to findings visualized by CCE but not confirmed by optical colonoscopy, being not possible to exclude the risk of missed polyps by colonoscopy (ie, false negative at optical colonoscopy).

Specific trials that evaluate the accuracy of CCE in detecting colorectal cancers are missing. Nevertheless, gathering such information from comparative trials, to date, 10 cancers have been detected by conventional colonoscopy in comparative trials: CCE identified cancers in all these cases, suggesting a potential 100% sensitivity for CCE [3,4,6,9-11].

4.2. Inflammatory bowel disease

The diagnosis of ulcerative colitis (UC) requires biopsy and histologic confirmation; therefore, CCE cannot be recommended for initial diagnosis [5]. However, it is potentially a useful tool to guide therapy, especially for checking mucosal healing when considering discontinuation of medication. A few studies have evaluated the role of CCE in patients with UC and reported discordant results [12]. These studies may not be comparable as they differ in terms of adopted technology (first- or second-generation of CCE), methodology, and measured outcomes. Some studies showed good correlation between CCE and optical colonoscopy. The first and largest study was a multicenter study carried out by Sung et al [13] involving 100 suspected or known patients with UC. The sensitivity of CCE to detect active colonic inflammation was 89% and the specificity was 75%, with positive and negative predictive values of 93% and 65%, respectively. Hosoe et al [14] and Kobayashi et al [15] reported a strong correlation between CCE and optical colonoscopy in all colonic segments (mean $r = 0.797$). Ye et al [26] found significant correlation ($p < 0.001$) in terms of severity and extent of UC between CCE and optical colonoscopy. Similarly, San Juan-Acosta et al [16] reported a good agreement (73%) in determining severity and extent of UC between CCE and colonoscopy. Conversely, other studies showed lower agreement between CCE and colonoscopy findings. Manes et al [17] reported a 56% and 61% agreement between CCE and colonoscopy in assessing mucosal activity and disease extent, respectively. Such low performance of CCE in evaluating patients with UC was also described by Singeap et al [18], who reported only a 60% agreement between CCE and colonoscopy. Meister et al [19] recommended the preferential use of optical colonoscopy in the assessment of inflammation in patients with UC, as they reported that the severity and extent of disease were both underestimated by CCE compared with conventional colonoscopy. These studies have all been conducted in adults. Recently, the potential role of CCE (ie, second-generation CCE) in IBD was evaluated in 30 consecutive pediatric patients with UC [20]. The sensitivity of CCE for disease activity was 96% and specificity was 100%. The positive and negative predictive values of CCE-2 were 100% and 85%, respectively. In the same trial, rather than colonoscopy, CCE had a higher overall tolerability, and interobserver agreement was excellent in all cases (≥ 0.86) [20].