Colon Capsule Endoscopy in incomplete colonoscopy

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"Optical colonoscopy is the standard method for evaluating the colon. However, in routine clinical practice the cecal intubation rate is often suboptimal. CT colonography (CTC) has been recommended as the imaging modality of choice in cases of incomplete colonoscopy. Alternatively, colon capsule endoscopy (CCE) is a new, minimally invasive, painless endoscopic technique that is able to explore the colon without requiring sedation, gas insufflation, and radiation exposure. In several studies, CCE was performed to complement a previous incomplete colonoscopy, being able to visualize the colonic segments not seen by previous incomplete colonoscopy. Recently, a study compared the performance of CCE and CTC. One-hundred consecutive patients with a previous incomplete colonoscopy underwent CCE and CTC followed by colonoscopy in the case of positive findings on either test. CCE and CTC were both able to achieve complete colonic evaluation in 98% of cases. In a per-patient analysis for polyps ≥ 6 mm, CCE detected 24 patients (24.5%) and CTC detected 12 patients (12.2%). Positive predictive values for polyps ≥ 6 mm and ≥ 10 mm were 96% and 85.7%, and 83.3% and 100%, for CCE and CTC, respectively. No missed cancers occurred at clinical follow-up of a mean of 20 months. The overall diagnostic yield of CCE was superior to CTC (mainly because of a higher accuracy for small and/or nonpolypoid lesions). In conclusion, CCE is a highly technically feasible examination for patients with previously incomplete colonoscopy and it should be considered as a first-choice technique in such a setting."

Incomplete colonoscopy: a practical challenge

Optical colonoscopy is the standard method for evaluating the colon [1]. This technique allows evaluation of the entire colon in most patients. Cecal intubation is associated with an increased detection rate of advanced neoplasia, as 33–50% of advanced neoplasias are located in the proximal colon [2]. Despite a recommendation of ≥ 90% and ≥ 95% cecal intubation rates in routine clinical practice and in screening colonoscopies, respectively [3], the actual cecal intubation rate is often suboptimal [4-11]. After an incomplete optical colonoscopy, patients are required to undergo another test in order to exclude clinically relevant lesions and to reduce the risk of proximal cancer, which has been shown to increase twofold when colonoscopy is incomplete [12]. Both endoscopic and radiological options to complete the colon assessment have been available in recent decades. Multiple alternative endoscopic techniques – such as colonoscopy with thinner colonoscopes, gastroscopes, and device-assisted enteroscopes – have been described [13, 14]. However, none of these has been clearly standardized. Alternatively, double-contrast barium enema (DCBE) has traditionally been used to image the colon after failed or incomplete colonoscopy. However, data from the National Polyp Study Work Group already indicated a disappointing 48% sensitivity of DCBE for > 10 mm polyps [15]. CT colonography (CTC) has also been recommended by the American Gastroenterological Association (AGA) as the imaging modality of choice in cases of incomplete colonoscopy [16]. In large, randomized trials in symptomatic patients [17, 18], CTC has been shown to be substantially more effective than DCBE – and equally as effective as colonoscopy – for the detection of large colorectal polyps and already-developed colorectal cancers.

Colon capsule endoscopy: a valid option ?

Colon capsule endoscopy (CCE) (Given Imaging Ltd, Yoqneam, Israel) is a new, minimally invasive, painless endoscopic technique that is able to explore the colon without requiring sedation, gas insufflation, and radiation exposure. Recently, a second-generation CCE has been released that provides a higher frame rate and a larger -angle lens [19,20]. Preliminary data suggest that CCE is a feasible and safe tool for visualization of the colonic mucosa in patients with incomplete

colonoscopy without stenosis, being able to guide further work-up [21-23]. CCE has also recently been approved by the FDA, specifically for a previously incomplete colonoscopy. However, studies comparing CCE with radiological imaging, and in particular with CTC, are lacking. Potential advantages of CCE over CTC are the lack of ionizing radiation, the limited availability of CTC due to saturation of the time-machine with other indications, and the possibility to directly visualize the colorectal mucosa by CCE.
In several studies [21-27], CCE was proven to be able to complement a previous incomplete colonoscopy, being able to visualize the colonic segments not visualized by previous incomplete conventional colonoscopy. Finally, CCE detected additional findings that would have been missed as they were localized in unseen segments(*table 1*).

Table 1. Summary of studies that used Colon capsule endoscopy (CCE) in case of incomplete colonoscopy.

	Number of patients	Completeness (%)	CCE Complementary Findings (%)
Pioche *et al.* [25]	107	83	34
Alarcon-Fernandez *et al.* [22]	34	85	23.5
Triantafyllou *et al.* [23]	75	90.7	44
Spada *et al.* [26]	100	98	24⋆
Nogales *et al.* (UEGW, 2013)	96	93	45⋆ °°
Baltes *et al.* [27]	74	95	49/28⋆ °°

⋆ significant polyps; °° cancers.
Nogales O, *et al.* Utility of colon capsule endoscopy after an incomplete colonoscopy. Multicentric spanish study. UEGW 2013 P 793
UEGW: United European Gastroenterology Week.

In detail, regarding full papers, few studies, all performed using the first generation of colon capsule, have evaluated the role of CCE in

patients with an incomplete colonoscopy [22, 23, 25]. Pioche *et al.* [25] reported for the first time, in a prospective multicenter series of 107 patients (*i.e.* 77 with a colonoscopy failure and 30 with a contraindication), a 93% capsule completion rate and a 33.6% CCE diagnostic yield. Alarcon-Fernandez *et al.* [22] evaluated the effects of CCE on medical decision-making in patients with incomplete colonoscopy in 34 patients. These authors reported that CCE was able to exceed the most proximal point reached by conventional colonoscopy in 85% of patients and to allow formulation of a specific medical plan in 59% of patients. Triantafyllou *et al.* [23] studied 75 patients who underwent CCE either immediately after incomplete colonoscopy, or rescheduled to a different day. CCE reached or went beyond the colonic segment where colonoscopy stopped in 91% of patients and detected additional findings in 44% of patients . Data available in the literature, thus, homogenously suggest that CCE can be considered as a complementary procedure in cases of incomplete colonoscopy and can yield significant findings

Head-to-head comparison of CCE and CTC

Despite previously published trials on either of the two techniques, the comparison between CCE (using the second generation of colon capsule) and CTC in this group of patients was never evaluated. Recently, a study [26] was published with the aim to compare the performances of CCE and CTC in a prospective cohort of patients with a previously incomplete colonoscopy. Consecutive patients with a previous incomplete colonoscopy underwent CCE and CTC followed by colonoscopy in the case of positive findings on either test (polyps/mass lesions ≥ 6 mm). CTC was performed either after colon capsule excretion or 10–12 hours post ingestion. Since the gold standard colonoscopy was performed only in positive cases, both diagnostic yield and positive predictive values of CCE and CTC were used as study endpoints. As patients underwent CCE and CTC on the same day, the regimen of preparation that is usually recommended was slightly modified [21] (Table 2). Briefly, this consisted of the standard regimen of preparation for CCE as previously described, with the inclusion of sodium-amidotrizoate and meglumine-amidotrizoate (75 mL) (Gastrografin, Bayer, Italy), which was added to the sodium-phosphate booster for fecal tagging.

Table 2. Regimen of preparation for Colon capsule endoscopy (CCE) used in the comparison of CCE and CT colonography (CTC) [26].

	Schedule	Intake
Day -2	Bedtime	Senna, 4 tb (48 mg)
Day -1	All Day	Clear Liquid Diet
Exam-day	Evening	2 L PEG
	7-9 am	2 L PEG
	10 am (~ 1h after last intake of PEG)	Capsule Ingestion*
	After small bowel detection	1st Boost 40 mL NaP + 1 L water with Gastrografin*** (50 mL)
	3 hours after 1st Boost	2nd Boost **20 mL NaP + 0.5 L water with Gastrografin*** (25 mL)
	2 hours after 2nd Boost	Suppository **10 mg Bisacodyl

* 10 mg metoclopramide tablet if capsule delayed in stomach > 1 hour; ** Only if capsule not excreted yet; *** Sodium-amidotrizoate and meglumine-amidotrizoate.

One hundred patients were enrolled. CCE and CTC were both able to achieve complete colonic evaluation in 98% of cases. In a per-patient analysis for polyps ≥ 6 mm, CCE detected 24 patients (24.5%) and CTC detected 12 patients (12.2%). The relative sensitivity of CCE compared with CTC was 2.0 (95% CI, 1.34–2.98), indicating a significant increase in sensitivity for lesions ≥ 6 mm. Regarding diagnostic yield for large polyps (≥ 10 mm), these values were 5.1% for CCE and 3.1% for CTC, respectively (relative sensitivity: 1.67 [95% CI, 0.69–4.00]). Positive predictive values for polyps ≥ 6 mm and ≥ 10 mm were 96% and 85.7%, and 83.3% and 100%, for CCE and CTC,

respectively. No missed cancer occurred at clinical follow-up of a mean of 20 months. The Authors concluded that both CCE and CTC were of comparable efficacy in completing colon evaluation after incomplete colonoscopy. However, the overall diagnostic yield of colon capsule endoscopy was superior to CTC. Interestingly, the superiority of CCE appears mainly to be related to a higher accuracy for small and/or nonpolypoid lesions. This is in line with the suboptimal sensitivity of CTC for such lesions already shown in previous head-to-head CTC-colonoscopy series [28-39]. Such superiority of CCE over CTC challenges the clinical recommendation of CTC for patients with a previously incomplete colonoscopy, with the exception of those with a colonic stricture. In settings where CCE is already available, CCE should always be considered in the case of incomplete colonoscopy and the choice between CCE and CTC will depend on local expertise, patient acceptance, and economic resources.

To note, CCE completion and excretion rates observed in this trial were higher than those observed in previous trials [19; 20]. The volume effect caused by Gastrografin that was included in the regimen of preparation in this trial [26] might have had a role in enhancing the propulsion of the capsule through the colon, and might also have had an effect on the quality of colonic preparation. In this trial, a high rate of good quality examinations was observed with both CCE and CTC. Hence, the overall quality rate was judged adequate in 83% (95% CI 74%-90%) and 90% (95% CI 82%-95%) of cases, respectively [26].

Directions for future research

The role of CCE in cases of a previously incomplete colonoscopy has been widely explored in recent years. To date, there is good evidence that CCE is a highly technically feasible examination for patients with previously incomplete colonoscopy, being able to complete the vast majority of previously incomplete colonoscopies and to detect significant findings not visualized by incomplete colonoscopy. Nevertheless, there are some issues that still need to be clarified. These mainly relate to the timing of capsule endoscopy after incomplete colonoscopy and to how to proceed with the preparation if CCE is performed immediately after colonoscopy. It would be important to know if CCE is feasible and can be performed immediately after an incomplete colonoscopy. This would be crucial since patients would not be asked to

perform an additional preparation and it would allow Endoscopists to complete colonoscopy the same day without referring the patient to other physicians and/or sessions. It is basically unknown how to proceed with the preparation if CCE is feasible immediately after incomplete colonoscopy. In particular, it is not known if in such cases the regimen of preparation for CCE may be limited to the administration of boosters or if additional doses of lavage solutions are required.

Conclusion

Data available in the literature suggest that CCE is a highly technically feasible examination for patients with previously incomplete colonoscopy and that it should be considered as a first-choice technique in such setting.

Conflicts of interest

Cesare Hassan is a consultant for Given imaging Covidien GI Solutions.

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