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Is there a role for colon capsule endoscopy beyond colorectal cancer screening? A literature review

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Abstract

Colon capsule endoscopy is recommended in Europe alternatively to colonoscopy for colorectal cancer screening in average risk individuals. The procedure has also been proposed to complete colon examination in cases of incomplete colonoscopy or when colonoscopy is contraindicated or refused by the patient. As tissue samples cannot be obtained with the current capsule device, colon capsule endoscopy has no place in diagnosing ulcerative colitis or in dysplasia surveillance. Nevertheless, data are accumulating regarding its feasibility to examine ulcerative colitis disease extent and to monitor disease activity and mucosal healing, even though reported results on the capsule's performance in this field vary greatly. In this review we present the currently available evidence for the use of colon capsule endoscopy to complement colonoscopy failure to reach the cecum and its use to evaluate ulcerative colitis disease activity and extent. Moreover, we provide an outlook on issues requiring further investigation before the capsule becomes a mainstream alternative to colonoscopy in such cases.

Key words: Colon; Capsule endoscopy; Incomplete colonoscopy; Ulcerative colitis; Gastrointestinal endoscopy

Core tip: Colon capsule endoscopy has a potential to become an endoscopic modality to investigate the colon after incomplete colonoscopy and to estimate ulcerative colitis extent and activity. While for the former indication strong evidence has been accumulating, for the latter the evidence is still limited.

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INTRODUCTION

Video capsule endoscopy (VCE) using an orally ingested recording device was originally introduced by Given Imaging Ltd (Yoqneam, Israel) in 2000 as an endoscopic modality to examine the mucosa of the small bowel[1], an area of limited access to conventional endoscopy. Since then, four more companies manufacture capsule endoscopes and small bowel capsule endoscopy has gained significant diagnostic value as a tool for indications such as obscure gastrointestinal bleeding, mapping and treatment response evaluation in Crohn's disease, celiac disease diagnosis and diagnosis of small bowel tumors and polyposis syndromes[2-4]. Moreover, the emergence of

capsule endoscopes to investigate colonic and esophageal mucosal lesions (PillCam™ Colon and PillCam™ ESO, Given Imaging Ltd, Yoqneam, Israel) has augmented our endoscopy armamentarium[5,6].

Our aim is to review the latest evidence regarding: (1) the performance of colon capsule endoscopy (CCE) as a complementation procedure to incomplete colonoscopy; and (2) the feasibility of CCE to accurately estimate ulcerative colitis disease activity and extend.

Technical aspects of the colon capsule

The first generation of PillCam™ Colon (CCE1) was introduced in 2006; it consisted of a small bio-friendly coated capsule with a diameter of 11 mm and length of 31 mm, with two cameras, one at each side. It was able to obtain four images-frames-per second (fps), covering an area of 156° and spent approximately 90 min in sleeping mode soon after its ingestion in order to save on recording time for colonic video capture[7].

Recently, the second generation of PillCam™ Colon (CCE2) was introduced in the market featuring enhanced technical properties, such as wider coverage angle (almost 360°), adaptive frame capture rate of 4 to 35 fps depending on its location and movement speed and capability of recording images for approximately 10 h. Its new sophisticated recording device can accurately locate the capsule in the small intestine in real time and it can generate visual and audio signals according to the capsule's location, guiding the patient to drink the purgative boosts[7]. This makes an examination of the colon at home feasible for the first time[8].

Based on experience from our center and others, video interpretation time varies according to the level of training and familiarity of the endoscopist with the procedure, ranging from 20 min for experts to 1 h - or even more- for less experienced physicians.

Bowel preparation and precautions

The current European Society of Gastrointestinal Endoscopy (ESGE) recommendation[7] for colon capsule endoscopy preparation is for using four liters polyethylene glycol solution administered split-dose (two liters the day before the examination and 2 liters before capsule ingestion) combined with oral use of prokinetics, low-volume sodium phosphate (NaP) boosters and bisacodyl suppositories to assist capsule propulsion and excretion. Caution should be exercised when NaP is administered to elderly, patients with dehydration or renal disease as well as those receiving angiotensin-converting enzyme inhibitors. Moreover, there are patients difficulties to adhere to this preparation protocol and its overall efficacy for adequate bowel cleansing and capsule propulsion is questionable[7] leaving room for active investigation for more efficacious regiments, even using lower volumes[7]. The possibility of retention of the colon capsule in the small bowel or colon is very low, but its occurrence should prompt endoscopic or surgical intervention[7], possibly leading to discovery of bowel stenoses or other significant findings predisposing to the device's inability to advance through the intestinal lumen.

Indications

Most of the literature on CCE to date involves colorectal cancer (CRC) screening. The diagnostic value of the capsule in detecting significant colonic lesions (polyps ≥ 6 mm or ≥ 3 polyps regardless of size) has been investigated in prospective trials[9-20] and two meta-analyses[21,22]. By pooling the data, the sensitivity and specificity for detection of significant polyps was 58% and 85%, respectively for CCE1[9-11,13-17]; method's sensitivity and specificity greatly improved with the introduction of CCE2 to 83% and 89%, respectively[18-20]. Although these performance characteristics are derived from mixed (average and high CRC risk) populations, a different performance of the capsule is not expected in the setting of average risk CRC screening population with significant polyps being a surrogate marker of advanced neoplastic potential[7]. Based on the above data, ESGE recommends CCE as an alternative to colonoscopy in average risk individuals (*i.e.*, without alarm symptoms and without family or personal history of colorectal neoplasia)[7]. While data on cost-effectiveness of introducing CCE as a screening tool for CRC are lacking, a presumed increased uptake rate of the test by the general population might provide a reasonable basis for this approach[7].

Further to CRC screening, ESGE identified future potential applications of colon capsule endoscopy, although data were scarce at that time. Areas of potential application of CCE include completion of the diagnostic work-up of patients that have undergone incomplete colonoscopy (IC), colon examination in cases of contradicted or informed refused colonoscopy, as well as, diagnosis and evaluation of patients with ulcerative colitis[7]. We will therefore present the evidence that has been accumulated since 2012 for extending the indications of colon capsule endoscopy.

INCOMPLETE COLONOSCOPY

Conventional colonoscopy is the gold standard for diagnosing colonic disease and screening for colorectal neoplasia[23]. Nevertheless, incompleteness of the procedure is being encountered in 4%-20% of performed colonoscopies, mostly due to anatomical reasons (*e.g.,* acute angulations of the bowel, adhesions due to past surgery, diverticulosis, hernias, obstructive lesions) or patient intolerance[24-26]. Currently following an incomplete colonoscopy, patients are usually referred for CT colonography (CTC), especially when the reason for colonoscopy failure is bowel obstruction. In this setting CTC may reveal synchronous lesions and extra-colonic findings that might alter the clinical course of the patients[27]. However, as reported in a large American asymptomatic patient series CTC may miss lesions ≥ 10 mm in diameter in up to 10% of patients[28]. CTC accuracy for the detection of lesions that do not protrude in the lumen (*e.g.*, flat adeno-

mas) is also low, while operator dependency and exposure to radiation are additional issues.

Other options after incomplete colonoscopy include repetition of the examination by expert endoscopists or under general anesthesia, the use of small caliber or variable stiffness endoscopes, device assisted colonoscopy, cap-assisted or water immersion technique[29-32]. These procedures however are not widely available and may not lead to completion of the examination in 100% of the cases.

CCE, a minimally invasive and painless method that does not require sedation, may prove to be the "next-step" after colonoscopy failure. Technically, complementation of colonoscopy by CCE is considered successful when a landmark already seen in colonoscopy (*e.g.*, biopsy spot, surgical anastomosis, tumor, tattooing) is also detected in the capsule recording. Excretion of the capsule or visualization of the rectum or hemorrhoidal plexus confirms completeness of the CCE procedure.

In 2008 Spada *et al*[33] used for the first time CCE1 after colonoscopy failure to inspect the colon further to the sigmoid due to inflammatory stenosis in the left colon. CCE identified the lesion observed in colonoscopy and additionally revealed polyps proximally to the stenosis. Subsequently, in a retrospective series of 12 patients with incomplete colonoscopy due to anatomical reasons or obstructing colonic lesions[34], CCE1 reached and visualized the colon segment at which colonoscopy stopped in 50% of the patients. Moreover, four patients needed further work-up after the two procedures with obvious questions arising on the cost-effectiveness of the CCE approach. Inadequate bowel preparation was also an issue in this report since it was poor in 36% of patients, making images interpretation difficult. At the same period, a new case of successful CCE colon examination in a patient with incomplete colonoscopy due to multiple intra-abdominal adhesions appeared in the literature[35]. All three reports did not identify any safety concern for the use of CCE in this setting.

Based on the aforementioned reports and on the preliminary data of a Greek prospective study[36], ESGE recommended CCE as a feasible and safe tool for visualization of the colon in patients with incomplete colonoscopy without obstruction[7].

Thereafter, three European prospective studies using the first generation CCE after incomplete or contraindicated colonoscopy have been published so far. In a large prospective trial from France, 107 patients in whom colonoscopy was either incomplete or contraindicated for reasons precluding anesthesia administration underwent colon examination with CCE1, either one day after colonoscopy or within 14 d later. A significant diagnosis was made in 31% of the asymptomatic and in 35% of the symptomatic patients respectively, including polyps, colon cancer, angiodysplasias, diverticulitis, ischemia or inflammatory bowel disease. No CCE related adverse event was reported, and patients were followed for 1 year in order to confirm validity of CCE results. Importantly, the low-volume preparation administered during the study yielded adequate bowel preparation in 76% of cases[37]. The main limitation of this study is that the results are not reported for the colonoscopy failure cases (n = 77) separately, making comparisons to the following studies impossible. However, it is until now the largest study that examined the value of CCE in the setting of colonoscopy contraindication[37]. Another similar study using CCE2 reported almost identical results, although adequate bowel preparation rate was low[38]. The final results of an ongoing large French multicenter prospective study of CCE in cases of contradicted or informed refused colonoscopy are still awaited.

A recent Spanish study prospectively employed CCE1 in 34 patients with non-occlusive incomplete colonoscopy reporting overall colonoscopy complementation in 85.3% and study completion in 77% of the cases, respectively. In 60% of the patients the procedure was conclusive, while inconclusive CCE was mainly attributed to inadequate bowel cleansing (12/14 cases). During the 1-year follow-up of patients with normal CCE, none received additional intervention. A full colonoscopy preparation regimen with polyethylene glycol in combination with prokinetics, purgative boosters and a laxative suppository used in this study yield relatively low overall bowel preparation adequacy (64.7%) and mild adverse events (nausea, pain, vomiting) attributed to the regimen[39].

Finally, in a prospective trial from Greece, CCE1 was performed in 75 patients, either immediately after colonoscopy failure (one third of them) or within the next 21 d. Capsule endoscopy successfully complemented colonoscopy in 91% of cases. Significant findings in areas unreached by colonoscopy where observed in 44% of the patients. Overall, further work-up was requested for 23 patients; 15 of them ultimately underwent a third examination and 9 undertook a therapeutic intervention. The major issue detected in this study was inadequate colon preparation (in approximately 40% of the cases) that was responsible for the majority of incomplete CCE cases[40]. The major strength of the study is that it showed for the first time that CCE can be performed effectively and safely immediately after incomplete colonoscopy, thus minimizing the burden for the patients. Other strengths include the assessment of patients' acceptance rate for CCE - 82% of the patients would undergo the procedure again if needed - and the 2-year follow-up period during which no significant missed lesion was diagnosed, overcoming, at least partially, the lack of a reference study to CCE examination[40].

All three[37,39,40] fully published studies have several methodological limitations. Mixed[37] or relatively selected[39,40] study population, use of first generation capsule endoscopes[37,39,40] and use of preparation regimens that are currently not recommended[37,39,40] might prevent the generalizability of the results. Moreover, uncertainty regarding the documentation of the successful CCE colonoscopy complementation[39,40], small and unjustified sample size[39], absence of blinded central CCE reading[40]

Table 1 Performance of colon capsule endoscopy after incomplete colonoscopy

	n	PillCam Colon™ capsule generation	Same day CCE	Colon preparation regiment	Preparation adequacy	Completion of CCE	Complementation of IC	Additional Findings	Study design details
Spada *et al*[33], 2008	1	First	0	4 L of PEG + NaP boosters	Fair	100%	100%	100%	Case report
Triantafyllou *et al*[34], 2009	12	First	0	4 L of PEG + NaP boosters	58%	8%	50%	30%	Retrospective Case series
Fernández-Urién *et al*[35], 2011	1	First	0	NR	NR	100%	100%	None	Case report
Pioche *et al*[37], 2012	107	First	0	1 or 2 L of PEG (MoviPrep®) + NaP boosters	76%	83.20%	NR	33.6%	Prospective cohort study; results are not reported separately for the incomplete colonoscopy cases (n = 77)
Alarcón-Fernández *et al*[39], 2013	34	First	0	3 L of PEG + NaP boosters	64.70%	77%	85.30%	23.5%	Prospective cohort study
Triantafyllou *et al*[40], 2014	75	First	33%	1 L of PEG + NaP boosters or 4 L of PEG[1]	60%	76%	91%	44%	Prospective cohort study
Baltes *et al*[41], 2013	45	Second	0	PEG (MoviPrep®) + PEG/NaP boosters	70%	80%	87%	18%	Prospective cohort study (preliminary data)
Spada *et al*[42], 2013	50	Second	0	4 L of PEG	83%	NR	98%	14%	Prospective cohort study (preliminary data); compares CCE-CTC
Nogales *et al*[43], 2013	96	Second	NR	NR	NR	72%	93%	58%	Prospective cohort study
Negreanu *et al*[44], 2014	3	Second	0	4 L of PEG + PEG boosters	NR	NR	100%	100%	Case series

[1]Depending on the timing of the procedure. IC: Incomplete colonoscopy; NR: Not reported; PEG: Polyethylene glycol solution; MoviPrep®: Trade mark of a lower-dose polyethylene glycol based solution; NaP: Sodium phosphate; CCE: Colon capsule endoscopy; CTC: Computed tomography colonography.

and most of all, the lack of a reference procedure that could serve as a gold standard[37,39,40] are issues that are expected to be adequately addressed by the ongoing studies.

During the 2013 United European Gastroenterology Week held in Berlin, Germany, the results of 3 more studies on the use of CCE after incomplete colonoscopy were presented. Firstly, preliminary data from a German prospective trial involving 45 patients who undertook second generation CCE showed that the capsule complemented incomplete colonoscopy in 87% of patients and detected polyps in segments unreached by colonoscopy in 18% of them. A low volume regimen of polyethylene glycol was administered in this study, leading to adequate colon cleanness in 70% of cases[41]. Secondly, data from a recently completed prospective Italian trial comparing second generation CCE with CTC after incomplete colonoscopy in 100 patients showed that CCE displayed superior diagnostic yield than CTC in finding polyps ⩾ 6 mm; CCE's complementation rate was almost 100%[42]. Thirdly, results from a prospective trial from Spain enrolling 96 patients after colonoscopy failure showed that CCE2 complemented colonoscopy in 93% of cases, despite the relatively low procedure completion rate (72%); findings leading to medical or surgical intervention were detected in 43 patients[43].

To complete the literature puzzle, a recent case series showed that the use of CCE2 in 3 patients with incomplete colonoscopies undergoing Crohn's disease work-up revealed erosions in the stomach, small bowel and colon, leading to correct evaluation of the disease extend and effective treatment decisions[44].

Table 1 provides a summary of existing data regarding the performance of CCE in the setting of incomplete colonoscopy. The final results of the German and Spanish studies[41,43] are expected to clarify the performance of the second generation colon capsule endoscope in incomplete colonoscopy cases and probably elucidate the efficacy and safety of new, lower dose colon preparation regiments. Moreover, the full publication of the Italian study[42] results is expected to strengthen the role of CCE in colon evaluation with equal performance characteristics to CT colonography that is currently recommended as the first alternative examination after incomplete colonoscopy. Furthermore, in the era of fiscal austerity[45] the use of an expensive modality like CCE might not be justified in certain countries with limited resources and cost-utility studies might be requested in certain settings.

ULCERATIVE COLITIS

Recent data highlight the importance of mucosal healing (*i.e.*, absence of friability, erosions or ulcerations at endoscopy) for treatment decisions and prognosis of ulcerative colitis (UC). Achieving this endoscopic goal leads to lower rates of hospitalization, surgery and dysplasia development in UC patients, with high impact on their quality of life[46-49].

The performance of CCE for the diagnosis of UC was firstly published in 2012[50]. One hundred patients with possible or known ulcerative colitis were studied; conventional colonoscopy bowel preparation regimen assisted by NaP boosters, prokinetics and a laxative was used and CCE was performed prior to colonoscopy using the first generation capsule endoscope. The procedure was completed in 96 patients and bowel preparation was adequate in 64% of the cases. With colonoscopy serving as the gold-standard, CCE displayed a sensitivity and specificity of 89% and 75%, respectively for the diagnosis of active ulcerative colitis. The authors concluded that the procedure is safe, but its low specificity, mainly attributed to poor preparation and rapid colon transit, precluded its use for the grading of disease activity. The absence of disease extent documentation and the interpretation of CCE images by a single physician were the main limitations of the study. Manes *et al*[51] commented on this study, highlighting the issue of poor bowel preparation attributed, according to the authors, to the unpredictable efficacy of laxatives in the inflamed bowel mucosa. Presenting their experience in 18 patients, they showed that bowel preparation was adequate in only 44% of them and CCE1 agreed with colonoscopy findings in 55% and 61% of cases regarding activity and extent of disease, respectively.

Until today, the Hong Kong study[50] is the largest published on this field. For the purpose of the review, we will briefly summarize the rest of the existing evidence regarding the use of CCE to evaluate ulcerative colitis disease activity and extend. The reader should have in mind that this evidence has accumulated through case reports or small patients' cohorts providing very weak evidence to support this CCE indication.

There are 3 more published small studies that included 67 patients overall, reporting controversial results on the performance of CCE in UC patients. Meister *et al*[52] compared CCE1 to colonoscopy for the evaluation of disease activity and extent in 13 patients with known UC. Bowel preparation using PEG was deemed adequate in 90% of the patients and CCE was complete in 10 of them. Investigators reported that CCE underestimated disease activity and did not reliably characterize disease extent. The main strength of the study was the evaluation of results by six blinded physicians, while the small size of the cohort was its main limitation. Almost at the same period, a Japanese feasibility study presented data from 29 patients with known UC who underwent CCE2 with same day colonoscopy, after bowel preparation with low-volume polyethylene glycol solution and prokinetics. Results showed a strong correlation of CCE with colonoscopy findings regarding disease activity, especially in areas proximal to the left colon, although the modified preparation regimen led to adequate cleansing in less than half of the cases[53]. Finally, significant agreement between the two procedures for the assessment of severity ($\kappa = 0.751$, $P < 0.001$) and disease extent ($\kappa = 0.522$, $P < 0.001$) was demonstrated in a study that included 25 UC patients. Despite the use of lower volume preparation colon cleansing adequacy was 80% and all procedures were completed[54].

During the 2013 European Crohn's and Colitis Organization annual meeting, preliminary data of 4 more studies were presented. A Spanish study that included 19 UC patients reported that colonoscopy and CCE findings correlated regarding disease activity and extent ($\kappa = 0.184$ and ($\kappa = 0.709$), respectively[55]. Similarly, Singeap *et al*[56] investigated the correlation of CCE2 with colonoscopy findings in 15 UC, Crohn's disease and unclassified colitis patients. In 6 patients CCE displayed findings consistent to those of colonoscopy regarding severity and extent of disease, while in two more the capsule guided the differential diagnosis between Crohn's disease and UC diagnosis. The level of agreement between the two modalities was related to the quality of bowel preparation. Exploring the uncertainty about the type of bowel preparation regiment for UC patients undergoing CCE, Kobayashi *et al*[57] evaluated the efficacy of a low-volume preparation regimen consisting of two liters of polyethylene glycol or polyethylene glycol plus isotonic magnesium citrate solution, with the later leading to higher CCE completion rate (85% *vs* 69%) and higher adequacy of colon preparation. CCE findings were comparable to colonoscopy findings in both groups. Finally, Oliva *et al*[58] investigated the performance of CCE2 in 29 pediatric UC patients. The sensitivity specificity, positive predictive value and negative predictive value of CCE for inflammation detection were 95%, 100%, 100% and 85%, respectively. There was no significant difference between CCE and colonoscopy in assessing disease activity and no serious adverse events occurred. The main strength of the study was the independent review of CCE and colonoscopy images by blinded to the procedures physicians. These very promising results highlight for the first time the usefulness of a non-invasive and painless procedure like CCE in the sensitive pediatric population.

Details of the aforementioned studies on the performance of CCE in UC patients are summarized in Table 2. Unfortunately, the quality (small, unjustified sample sizes and inadequate methodology) of the available, the different preparations schemes administered in the studies and the inconsistent results do not firmly support the use of CCE for evaluating the activity and the extent of the disease. Large, controlled trials employing more effective preparation regimens and assuring evaluation of CCE and colonoscopy images by blinded investigators are needed before CCE becomes a mainstream alternative to

Table 2 Performance of colon capsule endoscopy for the assessment of inflammation severity and disease extent in ulcerative colitis patients, as compared to colonoscopy

	n	PillCam Colon™ capsule generation	Study main end-point(s)	Preparation regimen	Adequacy of bowel preparation	Completion of CCE	CCE performance compared to colonoscopy	Limitations
Sung *et al*[50], 2012	100	First	Assessment of inflammation	4 L of PEG + NaP boosters	64%	96%	High PPV, low NPV in activity evaluation	Lack of documentation of disease extent, histological proof of activity not reported
Manes *et al*[51], 2013	20	First	Assessment of inflammation and disease extent	3 L of PEG + NaP boosters	44%	90%	Moderate correlation in activity and extent evaluation	Small sample size, histology not reported
Meister *et al*[52], 2013	13	First	Assessment of inflammation and disease extent	2.5 L of PEG (MoviPrep®) prior CCE ingestion and as boosters	90%	77%	CCE underestimates disease activity, poor extent estimation	Small sample size, lack of histological verification of activity, histological proof of disease activity was not obtained
Hosoe *et al*[53], 2013	29	Second	Assessment of inflammation	2 L of PEG	< 50%	69%	Strong correlation for activity evaluation	Small cohort, most patients had mild disease, histological proof of disease activity was not obtained
Ye *et al*[54], 2013	25	First	Assessment of inflammation and disease extent	3 L of PEG + NaP boosters	80%	100%	Strong correlation regarding disease activity/extent	Small sample size
San Juan Acosta *et al*[55], 2013	19	Second	Assessment of inflammation and disease extent	4 L of PEG	NR	84%	Strong correlation in activity/extent evaluation	Small sample size, histology not reported
Singeap *et al*[56], 2013	15	Second Second	Assessment of inflammation and disease extent	NR	NR	93%	Correlates with colonoscopy findings (activity/extent), assists in the accurate diagnosis of undetermined colitis	Small sample size, histology not reported
Kobayashi *et al*[57], 2013	49		Assessment of inflammation	2 L PEG or 700 mL PEG + 900-1500 mL Magnesium Citrate as booster	NR	69%-85%	Comparable evaluation of disease severity	Small sample size, histology not reported
Oliva *et al*[58], 2013	29	Second	Assessment of inflammation and disease extent	PEG + NaP boosters (volumes are not reported)	62%	100%	High PPV (100%) and NPV (85%) regarding disease activity evaluation, high agreement in disease extent	Small sample size, histology not reported

CCE: Colon capsule endoscopy; PEG: Polyethylenoglycol; MoviPrep®: Trade mark of a lower-dose polyethylene glycol based solution; NaP: Sodium phosphate; PPV: Positive predictive value; NPV: Negative predictive value; UC: Ulcerative colitis; NR: Not reported.

colonoscopy for monitoring mucosa inflammation in patients with UC.

CONCLUSION

Colon capsule endoscopy is a relatively novel procedure mainly indicated for colorectal neoplasia screening in average-risk individuals with no alarm symptoms. The procedure may also be offered as an alternative to high-risk patients when colonoscopy is either non acceptable or contraindicated.

Based on the reviewed data and in accordance with the 2012 ESGE recommendations, CCE may also represent a safe and feasible test in patients with non-obstructing incomplete colonoscopy. The non-invasive nature of CCE might encourage patients to complete their work-up after an often displeasing incomplete colonoscopy experience[59]. The results of large scale randomized controlled trials comparing this approach with alternatives such as CT colonography are expected to support this recommendation and define which patients may benefit more from the procedure. Given the fact that the diagnostic yield of CCE is proportional to the adequacy of the bowel preparation, efforts

should be directed to its standardization.

The cost of each of the common colon cancer screening modalities is another issue for consideration. The average cost of a colon capsule endoscopy procedure in the US lies approximately at $950, which is more or less the same as that of a diagnostic colonoscopy[60], even though recent reports from the United States that the cost of the latter may reach significantly higher proportions when costs such as that of anesthesia are included[61]. On the other hand, the charge for a CT-colonography is approximately $500 but the need for more frequent (every 5 years) repetition for screening purposes make it a more costly approach than colonoscopy[62]. In Europe the cost of the capsule is approximately €700, much higher than that of a conventional colonoscopy. Further cost-analysis studies are required to determine the role of CCE in colorectal cancer screening. The reading time of the captured video footage should also be taken under consideration when considering implementation of the capsule as a screening modality.

Since capsule endoscopy cannot perform tissue sampling for histology yet, it cannot replace standard colonoscopy for the diagnosis of UC and for surveillance for inflammation related neoplasia. However, CCE might have a significant role for the endoscopic monitoring of patients treatment; mucosal healing having been established as a main prognostic factor in IBD. This painless, non-invasive tool might also monitor inflammation in UC patients who cannot tolerate colonoscopy. To date, data on this field are scarce and of low quality. Available studies are limited by small population sizes, inappropriate methodology, large variability regarding bowel preparation schemes and inconsistent results regarding evaluation of both disease activity and extent.

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