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Prospective Study

PillCamColon2 after incomplete colonoscopy - A prospective multicenter study

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Abstract

AIM

To evaluate the ability of PillCamColon2 to visualize colonic segments missed by incomplete optical colonoscopy (OC) and to assess the diagnostic yield.

METHODS

This prospective multicentre study included 81 patients from nine centres who underwent second-generation colon capsule endoscopy (CCE) following incomplete OC performed by an experienced gastroenterologist (> 1000 colonoscopies). Patients with stenosis were excluded. According to patient preferences, CCE was performed the following day (protocol A) after staying on clear liquids and 0.75 L Moviprep in the morning or within 30 d after new split-dose Moviprep (protocol B). Boosts consisted of 0.75 L and 0.25 L Moviprep, and phospho-soda was given as a rescue if the capsule was not excreted after seven hours.

RESULTS

Seventy-four patients were analysed (51% of them in group A; 49% in group B). Bowel cleansing was adequate in 67% of cases, and CCE could visualize colonic segments missed by incomplete colonoscopy in 90% of patients under protocol A and 97% of patients under protocol B ($P = 0.35$, n.s.). Significant polyps including adenocarcinoma were detected in 24% of cases. Detection rates for all polyps and significant polyps per patient were similar in both protocols. Polyps

were found predominantly in the right colon (86%) in segments that were not reached by OC. Extracolonic findings - such as reflux esophagitis, suspected Barrett esophagus, upper GI-bleeding, gastric polyps, gastric erosions and angiectasia - were detected in eight patients. PillCamColon2 capsule was retained in the ileum of one patient (1.4%) without symptoms and removed during an uneventful resection for unknown Crohn's disease that was diagnosed as the cause of anemia, which was the indication for colonoscopy. CCE was well tolerated. One patient suffered from self-limiting vomiting after consuming the phospho-soda.

CONCLUSION

Second-generation CCE using a low-volume preparation is useful after incomplete OC, and it allows for the detection of additional relevant findings, but cleansing efficiency could be improved.

Key words: Colon capsule endoscopy; PillCamColon2; Incomplete colonoscopy; Low volume prep; Moviprep; Phospho-soda; Cleanliness level; Complementation rate; Polyps

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Core tip: Colonoscopy is the gold standard for visualization of the colon, but it may be incomplete, not reaching the cecum. Second-generation colon capsule endoscopy (CCE) with low-volume preparations could complement incomplete colonoscopies in 90% of cases, and it could help to detect additional relevant colonic and extracolonic findings. Protocols with either CCE the day following an incomplete colonoscopy or within 30 d after a new low-volume preparation were both feasible and well tolerated; however, the protocols could be improved with respect to bowel cleanliness and complete colon visualization.

Baltes P, Bota M, Albert J, Philipper M, Hörster HG, Hagenmüller F, Steinbrück I, Jakobs R, Bechtler M, Hartmann D, Neuhaus H, Charton JP, Mayershofer R, Hohn H, Rösch T, Groth S, Nowak T, Wohlmut P, Keuchel M. PillCamColon2 after incomplete colonoscopy - A prospective multicenter study. *World J Gastroenterol* 2018; 24(31): 3556-3566 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v24/i31/3556.htm> DOI: <http://dx.doi.org/10.3748/wjg.v24.i31.3556>

INTRODUCTION

Flexible optical colonoscopy (OC) is the gold standard to detect and treat colorectal diseases and proved to be safe and effective in colorectal cancer screening (CRC)^[1]. However, OC may be incomplete for various reasons, with completion rates between 90% and 98%^[2-5] for screening colonoscopy and 81%-94% in mixed series^[6-9]. Risk factors for incomplete colonoscopy

are female gender, elder patients, previous pelvic or abdominal surgery, diverticulosis, redundant colon, stenosing tumors, poor preparation, inflammatory bowel disease; in contrast sedation, male gender and higher body mass index were reported as protective factors^[4,6,7,10,11]. Of the patients with incomplete OC, 4.3% had advanced neoplasia in the right colon^[5]. A five-year follow-up study showed a higher risk for colorectal cancer in patients with failed colonoscopy^[12], demonstrating the need for additional investigations in these patients. PillCamColon has been cleared by the US Food and Drug Administration (FDA) for detection of colon polyps in patients after an incomplete optical colonoscopy with adequate preparation. Later the indication had been expanded to the detection of colon polyps in patients with evidence of lower gastrointestinal origin and major risks for colonoscopy or moderate sedation.

First-generation PillCamColon1 with a constant rate of two frames per second (fps) had limited sensitivity compared to a colonoscopy^[13-15]. Technical improvements of the second-generation PillCamColon2 that was used in the present study included adaptive frame rates (4 fps and 35 fps) and an increased viewing angle. It also included automatic small bowel detection with consecutive timing of boosters to shorten transit times and to improve cleansing levels^[16], which was shown to have a significantly higher diagnostic yield for polyps^[17]. A decisive factor for CCE accuracy is bowel cleansing; recent data have shown that low-volume Polyethylene glycol (PEG)-based protocols may be feasible instead of high-volume preparations^[18,19].

Our study aimed to assess the impact of second-generation CCE after incomplete colonoscopies by analyzing the complementation rates and incremental diagnostic yields with two different low-volume cleansing protocols. Patients were offered to either stay on clear liquids with a CCE the next day or to start a new bowel preparation procedure within 30 d.

MATERIALS AND METHODS

Study design and population

This prospective, multicentre study including nine centres (tertiary care hospitals or private endoscopy offices) in Germany. It was approved by the ethics committee of Hamburg Chamber of Physicians (PV3467, 20.05.2010). The www.clinicaltrials.gov identifier is NCT01480635.

All patients included in the study were 18 years or older who had incomplete colonoscopies that were performed by an experienced endoscopist (> 1000 colonoscopies performed). Incomplete OC was defined as a failure to reach the cecum or ileo-cecal anastomosis due to looping, bowel angulation, adhesions, and intolerance of sedation or inflammation. The presumed area of the colon reached by OC was documented, as were reasons for termination, detection of polyps and

tumours, other findings and adverse events. Patients with stenosis, inadequate preparation, or exchange of endoscope were excluded. Other exclusion criteria for CCE have been described previously^[18]. Written informed consent was obtained from all patients.

Study protocol

After an incomplete colonoscopy, patients were rescheduled for the following day (protocol A) or they were given a separate appointment within 30 d (protocol B), according to their preference. CCE was performed with PillCamColon2 (Given Imaging, Yoqneam, Israel) after a low-volume cleansing regimen with PEG and ascorbic acid (Moviprep, Norgine, Marburg/Lahn, Germany). Following capsule ingestion, the boosts consisted of 0.75 L after small bowel detection and 0.25 L Moviprep if the capsule had not been excreted five hours after ingestion. 30 mL sodium picosulfate (NaP; Fleet, Recordati, Ulm, Germany) was used as an additional boost if the capsule was not excreted seven hours after ingestion. In protocol A, patients stayed on clear liquids after the colonoscopy, and they received an additional cleansing of 0.75 L Moviprep the next morning (at the latest, one hour before CCE). In protocol B, patients were allowed to eat after the OC. A new bowel cleansing procedure was performed within 30 d: split-dose 1 L of Moviprep was consumed in the evening and 1 L was consumed in the morning, each followed by 1 L of water. Boosts with Moviprep or NaP were identical in both protocols (Table 1).

CCE studies were read with Rapid7 or Rapid8 software in each centre by an experienced endoscopist with additional experience in capsule endoscopy (> 1000 colonoscopies, > 100 small bowel capsule endoscopies (SBCE) and > 25 CCEs performed). All readers had completed a dedicated two-day CCE evaluation course. Polyp size was estimated with the integrated software tool.

For both examination modalities, cleansing levels were documented, as described previously^[15], using four grades: excellent, good (adequate), fair and poor (inadequate). Each colon segment [that is, cecum, ascending colon (AC), transverse colon (TC), left colon (LC) and rectum, see Figure 1] and overall cleansing status were evaluated.

For CCE, visualization of colonic segments, complementation of previous colonoscopy, completeness of CCE, and adverse events were recorded. Complete CCE was defined as excretion of capsule during recording time or by identification of the haemorrhoidal plexus. Detection of polyps, significant polyps, tumours or other relevant findings were documented for segments reached and not reached by the previous standard colonoscopy. According to previous studies, significant polyps were defined by size (≥ 6 mm) or number (≥ 3)^[19-21]. Other findings were considered important if they explained the indication for the colonoscopy or if they had further diagnostic or therapeutic implications.

Table 1 Study protocols A and B for colon capsule endoscopy after incomplete optical colonoscopy

Time	Procedure	
Evening and morning before colonoscopy	Standard bowel prep for colonoscopy	
After incomplete colonoscopy	Incomplete colonoscopy (OC) Patient's choice of protocol A or B for colon capsule endoscopy (CCE)	
After incomplete colonoscopy	Protocol A (CCE next day)	Protocol B (CCE within 30 d)
2 d before CCE	Patient stays on clear liquids	Patient can eat
Day before CCE	NA	Low residue diet
Evening before CCE		Clear liquids only
Morning of CCE	0.75 L Moviprep + water	1 L Moviprep + 1 L water
	Colon capsule ingestion	
Small bowel detection	0.75 L Moviprep + water (1 st boost)	
5 h after ingestion	0.5 L Moviprep + water (2 nd boost) ¹	
7 h after ingestion	30 mL NaP + water ('Rescue boost') ¹	
	Bisacodyl supp ¹	
11 h after ingestion	Removal of equipment ¹	

¹If capsule is not excreted earlier. OC: Optical colonoscopy.

Follow-up took place via a telephone call one week after the procedure. During the call, adverse events were documented, and capsule excretion was confirmed. Any adverse events were recorded, as well as the time of capsule excretion.

Study endpoints

The primary outcome parameter was complementation rate of CCE in patients with incomplete OC, which was defined by visualization of colonic segments not reached by OC. The secondary outcome parameters were as follows: additional (incremental) diagnostic yield of CCE compared to incomplete OC (all polyps, significant polyps defined by size or number and other significant findings) in segments not reached by OC; CCE findings in the upper gastrointestinal (GI) tract and small bowel; rate of complete CCE, as defined above; cleansing level of the colon (overall and segments) following the low-volume protocol for CCE; visualization of the Z-Line; and adverse events (number, type and severity).

Statistical analysis

Continuous variables were reported as mean and standard deviation, and categorical variables were reported as percentage. The null hypothesis (H0) for the primary endpoint (complementation of incomplete colonoscopy) was constructed using data from a former study that used PillCamColon1 and that showed a complementation rate of 50%^[22]. Accordingly, H0 was set to $\mu = 0.5$ with an expectation for complementation of OC by PillCamColon2 of 0.67. Using the Fisher exact test with a power of 80% (which is equal to $1-\beta$), 74 patients had to be recruited. Categorical values were compared using a chi-squared test (χ^2), while continuous values with a normal distribution were compared by a Student's *t*-test. *P* values < 0.05 were considered significant. An intention-to-treat (ITT) analysis was performed for complementation rates, cleansing levels, detection of significant polyps and safety. Statistical review was performed by one of the

authors (Peter Wohlmuth).

RESULTS

Demographics

Eighty-one consecutive patients were enrolled from nine participating centres between 2010 and 2013. Seven patients (four in the protocol A group and three in the protocol B group) had to be excluded due to technical failure ($n = 1$), protocol noncompliance as a result of incorrect timing of CCE ($n = 4$), exchange of colonoscope ($n = 1$) or early removal of recorder by the patient ($n = 1$) (Figure 2). In total, data of 74 patients were analysed per protocol. Demographics are shown in Table 2.

Reasons for referral to colonoscopy were CRC screening (22%), anemia (15%), hematochezia (15%), irregular stool (12%), abdominal pain (12%), B symptoms (7%), colitis (5%) and other reasons (12%). Thirty-six patients (48.6%) had prior abdominal surgery, while 14 patients (19%) had more than one surgical intervention. Most common surgeries were appendectomies (23%) and hysterectomies (19%). Only three patients had colonic surgery (4%), one patient had an ileocecal and one patient had a Billroth II anastomosis.

Standard OC

An experienced endoscopist (> 1000 colonoscopies performed) performed OC with a standard colonoscope. The mean duration of the procedure was 45 ± 17 min (range: 15-101 min). Unfavourable anatomy was the reason for termination in 92% of procedures. OC reached the sigmoid colon in 27% of cases, the descending colon (DC) in 4% of cases, the splenic flexure in 12% of cases, the TC in 14% of cases, the hepatic flexure in 35% of cases and the AC in 8% of cases. Adequate cleansing was achieved in 76% of procedures. In 12 of 74 patients (16%), polyps were detected, with a mean size of 6 ± 4.2 mm. Six

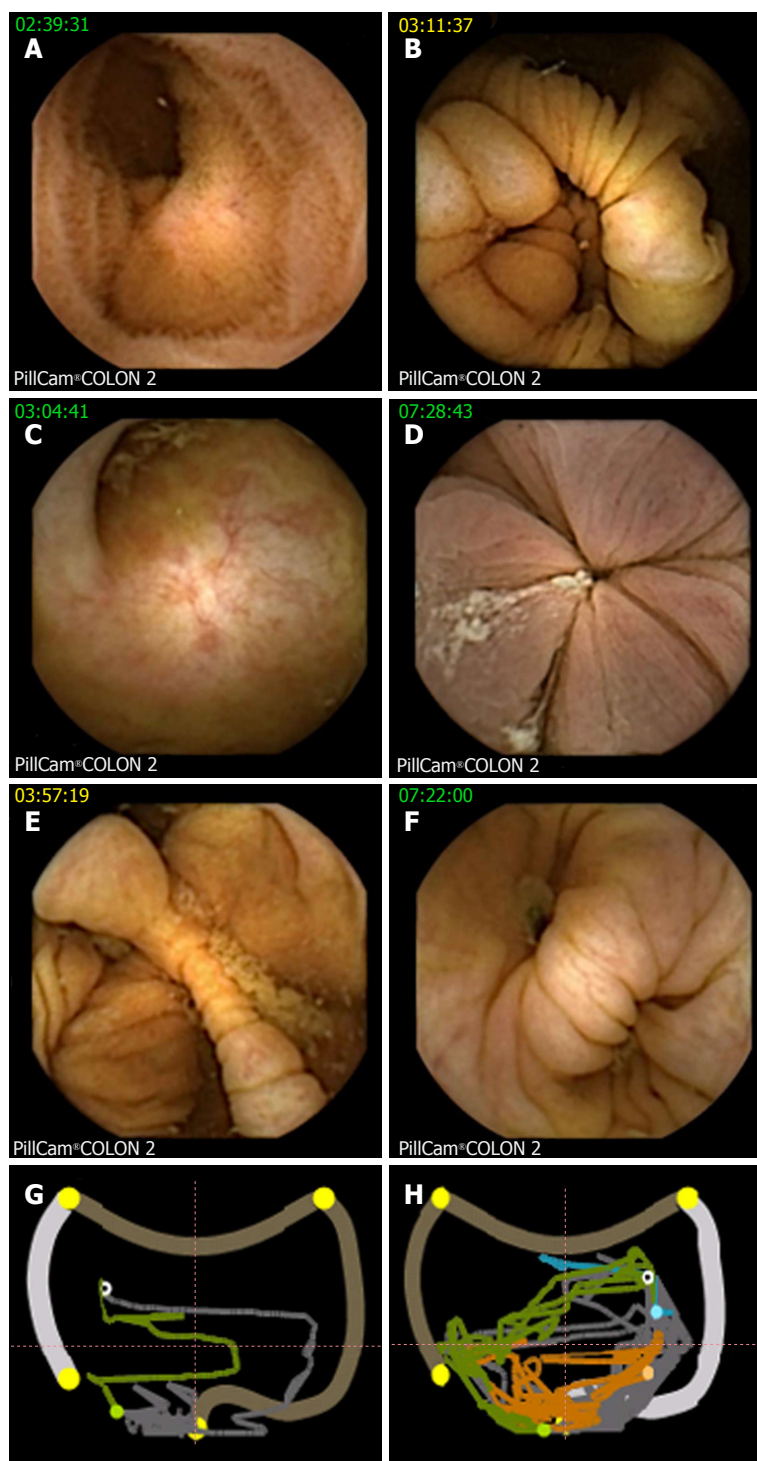


Figure 1 Landmarks at colon capsule endoscopy. A: Terminal ileum; B: IC valve; C: Appendix; D: Hemorrhoidal plexus, hepatic flexure - CCE image (E) with corresponding localization trace (G), white circle showing actual capsule position, green colon already displayed, grey colon yet to be analyzed, orange small bowel, blue stomach, outer pictogram the position to the colonic segment as manually defined by setting the landmarks; F and H: CCE image and localization trace of splenic flexure in another patient. CCE: Colon capsule endoscopy.

patients had more than one polyp (range: 2-5 polyps). Diverticula were found in 35 patients. Other findings were diverticulitis, erosions, angiectasias and erythema.

Colon capsule endoscopy

Primary endpoint: complementation of incomplete colonoscopy: Incomplete colonoscopy could

be complemented by CCE in 69 of 74 patients (93%; see Table 2). Complete CCE was achieved in 48 of 74 patients (65%). In four additional patients, the capsule reached the rectum but did not visualize the haemorrhoidal plexus (5%).

Complementation of OC could be achieved by CCE with protocol A in 89.5% of procedures and with protocol

Table 2 Demographics, reasons for termination of optical colonoscopy, and results of colon capsule endoscopy for protocol A and B *n* (%)

	Protocol A (CCE next day)	Protocol B (CCE within 30 d)	Significance
Demographics			
Patients	38 (51.4)	36 (48.6)	
Female	20/38 (52.6)	24/36 (66.7)	
Age, mean \pm SD	68.0 \pm 12.8 yr	63.9 \pm 13.0 yr	
Body mass index	26.0 \pm 3.9	26.5 \pm 4.9	
Reasons for termination of colonoscopy			
Looping of colon	23/38 (60.5)	23/36 (63.9)	
Angulation of colon	6/38 (15.8)	5/36 (13.9)	
Susp. adhesions	5/38 (13.2)	6/36 (16.7)	
Risk of perforation	2/38 (5.3)	0	$P = 0.710$ (NS); χ^2 test
Sedation problems	2/38 (5.3)	2/36 (5.6)	
Results of CCE			
Complete CCE	24/38 (63.3)	24/36 (66.7)	$P = 0.560$ (NS); χ^2 test
Complementation of colonoscopy	34/38 (89.5)	35/36 (97.2)	$P = 0.350$ (NS); χ^2 test
Adequate cleansing	25/36 (69.4)	23/36 (63.9)	$P = 0.820$ (NS); χ^2 test
Patients with significant colon polyps	10/38 (26.3)	11/36 (30.6)	$P = 0.500$ (NS); χ^2 test
Patients with other colon findings	0	Angiectasia ($n = 3$) Diverticulitis ($n = 1$)	$P = 0.045$; χ^2 test
Patients with small bowel findings	Angiectasia ($n = 1$) Crohn's disease ($n = 1$)	0	$P = 0.174$ (NS); χ^2 test
Patients with upper GI findings	Reflux esophagitis ($n = 1$) Upper GI-bleeding ($n = 1$) Gastric polyps ($n = 1$)	Reflux-esophagitis ($n = 1$) Susp. Barrett esophagus ($n = 1$) Gastric erosions ($n = 1$)	$P = 0.949$ (NS); χ^2 test

CCE: Colon capsule endoscopy.

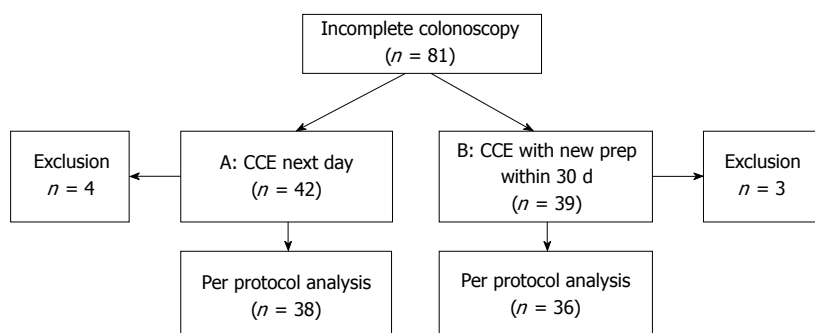


Figure 2 Flow chart protocol A (colon capsule endoscopy the day after colonoscopy) and protocol B (colon capsule endoscopy within 30 d after incomplete colonoscopy).

B in 97.2% of procedures ($P = 0.35$, not significant; Table 2). There were no differences between the rates of complementation using CCE for protocol A or B and the diagnostic yield. In the patients with incomplete visualization of the missing segments ($n = 5$), the capsule was able to display the hepatic flexure in two patients. One patient had a capsule retention in the small bowel because of unknown stenosing Crohn's disease. In one patient, the capsule did not reach the colon during recording time, and in one patient, visualization of the colon was incomplete due to recording gaps. The capsule was excreted within seven hours of ingestion and before the need for an additional NaP booster in 17 of 38 patients (44.7%) following protocol A, and in 12 of 36 patients (33.3%; $P = 0.25$, not significant) in protocol B.

Secondary endpoints: CCE was performed on the

day after colonoscopy in 38 patients (protocol A; 51%) or within 30 d in 36 patients (protocol B; 49%). Overall, cleansing was adequate in 48 of 72 (67%), and cleansing was adequate in the cecum in 58% of cases, in the AC in 65% of cases, in the TC in 77% of cases, in the LC in 70% of cases and in the rectum in 63% of cases (Figure 3); there were no differences between the protocols. Two capsules did not allow for visualization of the colon. Poor cleansing was rare (4 of 72 patients; 5.6%).

CCE detected 76 polyps in 35 of 74 patients (47%; Figure 4). Twenty-one patients (28%) had significant polyps (Table 3), and 14 patients had an insignificant number of polyps. In 9 of 21 patients, polyp size was ≥ 6 mm; in 3 patients, the number of polyps was ≥ 3 ; and in 9 patients, both parameters were positive. A total of 59 polyps (mean size 8 ± 4.5 mm) were detected in the 21

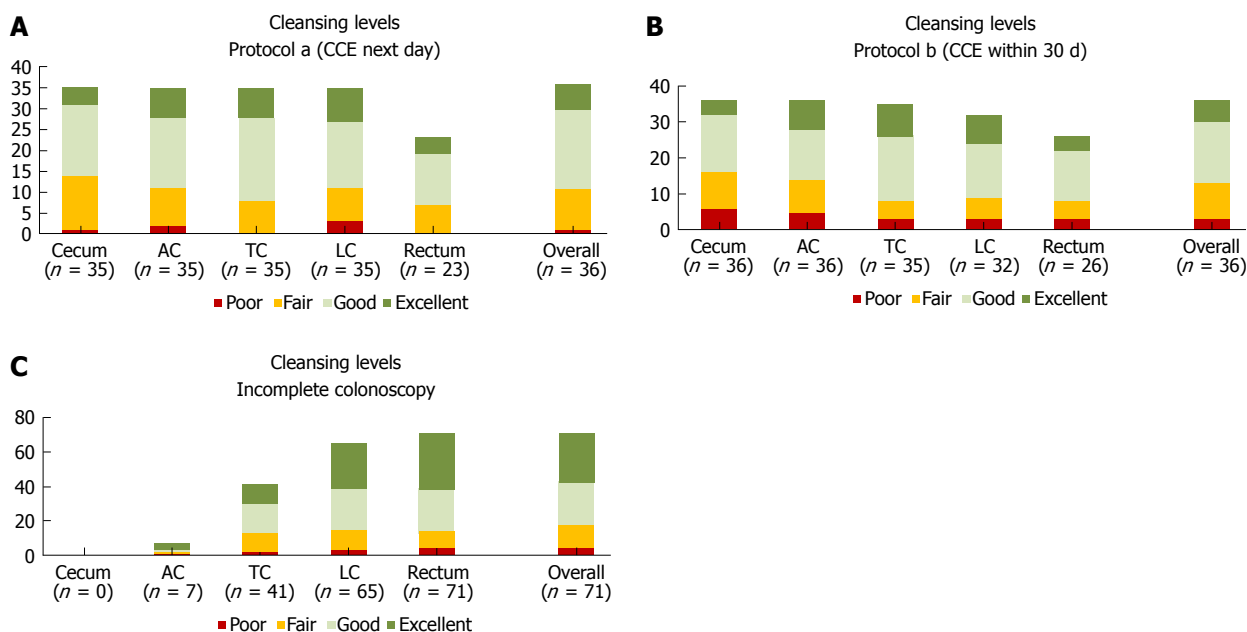


Figure 3 Cleansing levels for the colon segments: cecum, ascending colon, transverse colon, left colon, rectum and overall classification for all segments. Absolute number of patients for each level (poor, fair, good, excellent) are shown A for CCE with protocol a (next day), B for CCE with protocol b (within 30 d), and C for incomplete colonoscopy. AC: Ascending colon; CCE: Colon capsule endoscopy; LC: Left colon; TC: Transverse colon.

patients with significant polyps. Significant polyps were predominantly found in the ascending colon in segments that had not been reached by OC (86%). Incremental diagnostic yield of CCE compared to previous incomplete OC per patient for detecting significant polyps was 24%, and there were no differences between the two protocols. A cecal polyp of 26 mm turned out to be an adenocarcinoma, and hemicolectomy was performed in this patient.

Z-line was visualized in 45 of 74 patients (60.8%). CCE findings in the upper GI tract were reflux esophagitis ($n = 2$), suspected Barrett’s esophagus ($n = 1$), hemorrhagic gastropathy ($n = 1$), gastric polyps ($n = 1$; consecutive gastroscopy revealed foveolar hyperplasia in previously undiagnosed atrophic gastritis with vitamin B12 deficiency) and upper GI bleeding ($n = 1$).

In the small bowel, angiectasia and previously unknown Crohn’s disease was detected in one patient each. In colon segments missed by incomplete colonoscopy, angiectasias were detected in three patients and diverticulitis was detected in one patient (all patients were part of protocol B).

ITT analysis of all 81 patients found a complementation rate of 89%, adequate cleansing in 65%, significant polyps in 26% of patients, and no additional adverse events. The low complementation rate that was observed in this cohort is consistent with the exclusion criteria [technical problems, $n = 1$, and noncompliance of study protocol, $n = 6$ (for example, early removal of recorder and incorrect CCE timing)].

In one patient (protocol A), the capsule was retained in the small bowel without symptoms. Surgery was indicated following a new diagnosis of stenosing and fistulating Crohn’s disease with iron deficiency anemia (indication for

colonoscopy). During an uneventful surgery, the capsule was retrieved. Another patient (protocol B) complained of self-limiting nausea and vomiting after the NaP boost.

DISCUSSION

In this prospective, multicentre study, second-generation CCE allowed for the visualization of colon segments that were not reached by a previously incomplete colonoscopy in 93% of 74 patients. Fifty-one percent of patients opted for protocol A, and 49% for protocol B. The complementation rate following incomplete OC was higher in group B (97%) compared with group A (89%), but the results did not reach statistical significance. There were no differences between the rate of complete CCE, the cleansing level, the diagnostic yield or the number of adverse events.

The complementation rate identified in the present study corresponded well with results from recent trials using a first-generation colon capsule. A Spanish study found a complementation rate of incomplete colonoscopies of 85.3% and a diagnostic yield of 45%^[23]. A French trial including patients as well with contraindicated as incomplete OC, complete CCE was achieved in 83% of patients. An Italian trial reported a complete PillcamColon2 CCE after incomplete OC in 98% of patients using a separate preparation with Senna tablets, 4 L of PEG and two boosters with NaP and gastrografin^[24]. This rate was higher than in our low-volume protocol, but it was accompanied more often by preparation-related complaints (28.0% vs 1.4%). Nevertheless, our primary aim to complement colon visualization was achieved in 93% of patients, which was similar to a Greek study that achieved results

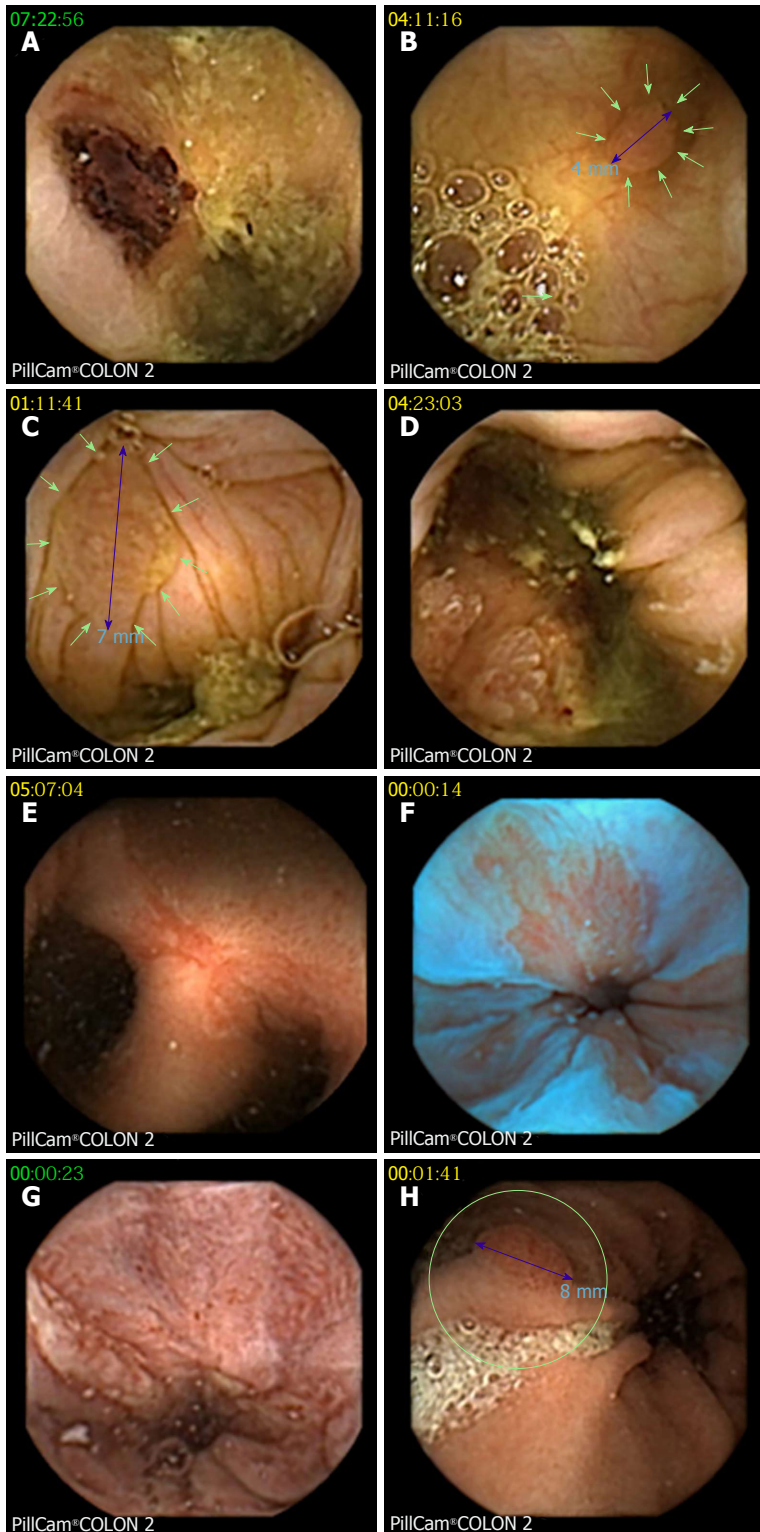


Figure 4 Examples of findings at colon capsule endoscopy. A: Biopsy tattoo after optical colonoscopy; B: One of three 4 mm polyps in the ascending colon, confirmed at consecutive balloon enteroscopy as tubular adenoma; C: Significant (7 mm) polyp; D: Cecal adenocarcinoma (confirmed by surgery); E: Fistulating and stenosing Crohn's disease of the ileum (confirmed by enteroclysis, CT scan, and surgery); F: Irregular Z-line suggestive of Barrett's esophagus (blue mode image); G: Reflux esophagitis; H: Gastric polyp (consecutive gastroscopy found foveolar hyperplasia and autoimmune gastritis with vitamin B12 deficiency).

using PillCamColon1 in 91% of patients^[14]. In the present study, unfavourable anatomy was the reason for terminating the colonoscopy, which was usually performed under propofol sedation, in 92% of patients. In contrast, pain was reported by 45% of patients as

the reason for incomplete colonoscopy in the Italian trial. This selection bias toward unfavourable anatomy might have also influenced the rate of complete consecutive CCEs (65%) in the present study. It may also be relevant when comparing our results to series

Table 3 Details of the 21/74 patients in whom significant polyps/tumors were detected during colon capsule endoscopy

No.	Significance based on	Size of largest polyp (mm)	Number of polyps	Localization of polyps	Farest point reached in OC	All segments with polyps in CCE reached by colonoscopy
1	Size/number	6	5	Rectum	HF	Yes
2	Size	8	2	Sigma	SF	Yes
3	Size/number	8	3	Sigma	AC	Yes
4	Size/number	8	3	2 × Cecum, 1 × AC	TC	No
5	Size	14	1	AC	HF	No
6	Size	26	1	AC	SF	No
7	Size	6	2	AC	Sigma	No
8	Size/number	10	3	2 × AC, 1 × TC	SF	No
9	Size/number	10	3	2 × LC, 1 × AC	Sigma	No
10	Size	10	1	AC	SF	No
11	Size/number	9	3	2 × AC, 1 × LC	HF	No
12	Size	6	1	AC	Sigma	No
13	Size	8	2	1 × AC/1 × LC	HF	No
14	Size	7	1	HF	Sigma	No
15	Number	5	4	AC, TC, 2 × sigma	Sigma	No
16	Size/number	12	4	1 × Cecum, 1 × AC, 1 × LC, 1 × rectum	Sigma	No
17	Number	4	3	1 × Cecum, 2 × rectum	TC	No
18	Number	5	5	2 × AC, 1 × TC, 2 × LC	HF	No
20	Size/number	10	7	4 × AC, 3 × LC	TC	No
20	Size	9	2	2 × Cecum	LC	No
21	Size/number	12	3	AC	LC	No

AC: Ascending colon; HF: Hepatic flexure; TC: Transverse colon; SF: Splenic flexure; LC: Left colon; OC: Optical colonoscopy.

with unselected patients without previously incomplete colonoscopies. In these trials, complete CCE was achieved in 76% of patients using a similar low-volume preparation^[18], in 88% of patients using PEG^[25], in 76% of patients using NaP^[14] and in 98% of patients using a PEG-, NaP- or gastrografin-based regimen^[24].

In the present study, colon cleansing using a low-volume preparation was adequate in 67% of patients, and the results were similar in both protocols. These results are comparable to other studies that used PillCamColon1 for incomplete colonoscopies with PEG preparation and NaP boosts (65%)^[23], and 60% vs 63% in the right and left colon, respectively^[14]. Adequate cleansing following use of the PillcamColon1 was observed in 76% of patients following consumption of 1-2 L Moviprep and two NaP boosts in a mixed cohort, including 28% of patients with contraindicated colonoscopy without anatomical problems^[19]. A recent Spanish multicentre trial found adequate cleansing levels in 75% of patients using a standard 4 L PEG preparation with a NaP booster for PillCamColon2 after an incomplete colonoscopy^[26]. Even in a large trial in a screening population without negative selection towards unfavorable anatomy, CCE was technically insufficient in 9% of patients due to inadequate cleansing or rapid transit of the capsule^[27].

Twenty-four percent of our patients (ITT 22%) had additional relevant finding following the CCE, which led to a recommendation for further diagnostics or treatment. Similarly, PillCamColon1 was useful in guiding management after failed OC in a Spanish trial^[23].

Most of the significant polyps (86%), including a carcinoma, were found in the AC. Our data confirmed

previous observations^[5] that CCE can identify relevant lesions in segments not reached by incomplete OC (Table 3).

Device-assisted colonoscopy with either spiral endoscopy and double or single balloons have identical rates, similar to CCE, of complementing incomplete OC of about 90%^[28-31]. These flexible endoscopic techniques additionally provide the possibility to directly treat detected lesions, but they require equipment and expertise, and they are restricted to specialized centres. A cap-assisted colonoscopy was also successful in 93% of patients, and one perforation occurred with this technique after failed OC^[32].

Computed tomographic colonography (CTC) after incomplete OC has a good diagnostic yield and may be advantageous if extra-colonic findings are considered^[33], for example, in the case of tumour. However, CTC detected fewer small polyps than CCE^[24]. Furthermore, radiation-free CCE could additionally be used to visualize the Z-line in 60.8% of patients, as previously reported for PillCamColon1 (60%)^[34]. In the present trial, eight patients had relevant extra-colonic findings, seven of which were presumably not detectable with CTC.

Capsule retention occurred in one patient, corresponding to a retention rate of 1.4%, which was similar to the rate reported for SBCE^[35]. This capsule retention resulted in a new diagnosis of Crohn's disease and was considered to be diagnostic rather than a complication. However, possible retention must also be considered when applying CCE to complement incomplete OC and should be included as part of the informed consent discussion. Although adhesions were supposed to be the cause of incomplete OC in some patients, no related clinical problems or capsule retention following CCE

were observed.

In conclusion, second-generation CCE using low-volume bowel preparations is useful, well tolerated and is able to detect additional relevant lesions. Risk of retention is as low as in SBCE, but must be considered. Similar results were found in the present study between the two protocols for the complementation rate and presence of significant polyps.

Limitations

Patients could choose between preparation protocols for CCE without randomization. The area reached by the colonoscopy was described, but tattooing was only optional. Long-term follow-up was not part of the present study.

ARTICLE HIGHLIGHTS

Research background

Optical colonoscopy (OC) is the gold standard for visualization of the colon. However, it may be incomplete e.g. due to unfavorable anatomy. Colon capsule endoscopy (CCE) is cleared by the US Food and Drug Administration for patients with previously incomplete OC. Second generation CCE has been shown to have a higher sensitivity for detection of colon polyps than first generation. Low volume bowel prep with Moviprep has been shown to be feasible for CCE.

Research motivation

Bowel preparation for CCE is more extensive than for OC. Thus, we aimed to evaluate, if second generation CCE is feasible using either repeated low volume bowel prep or staying on clear liquids following an incomplete OC.

Research objectives

Main research objective was the ability of CCE to visualize those colon segments not reached by incomplete OC. Secondary objectives were additional diagnostic yield of CCE, rate of complete colon visualization by CCE, cleansing levels, and safety.

Research methods

In this prospective multicenter study 81 patients underwent second generation colon capsule endoscopy with PillCamColon2 after incomplete OC. CCE was performed either the following day (protocol A) after staying on clear liquids and 0.75 L Moviprep in the morning or within 30 d after new split-dose Moviprep (protocol B). Boosts consisted of 0.75 L and 0.25 L Moviprep, and phospho-soda as rescue if the capsule was not excreted after 7 hours.

Research results

Seventy-four patients were finally analyzed per protocol. Of those, cleansing was adequate in 67% of cases and CCE could visualize the colonic segments missed by incomplete colonoscopy in 90% (protocol A) and 97% (protocol B, $P = 0.35$, n.s.) of the patients. Detection rates were similar with both protocols: Significant polyps and one adenocarcinoma were detected in 24% of cases. Polyps were found predominantly in the right colon (86%) in segments not reached by OC. Extra-colonic findings as reflux esophagitis, suspected Barrett esophagus, upper GI-bleeding, gastric polyps, gastric erosions, and angiectasias were detected in 8 patients. One capsule (1.4%) was retained in the ileum without symptoms and removed during uneventful resection for unknown Crohn's disease diagnosed as cause of unclear anemia. CCE was well tolerated. One patient suffered from self-limiting vomiting after phospho-soda.

Research conclusions

Second generation CCE using low volume prep is useful to complement incomplete OC, detects additional relevant findings including extra-colonic

lesions, and is well tolerated. CCE is feasible the following day after staying on clear liquids or after new prep within 30 d. Potential risk of capsule retention must be considered.

Research perspectives

Future studies should address improvement of colon cleansing levels and completeness of CCE after incomplete OC. Cost-effectiveness of CCE after incomplete OC should be addressed by future research in comparison with other methods as CT colonoscopy, MR colonoscopy, and device assisted colonoscopy.

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