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***Retrospective Study***

**PillCam COLON 2 in Crohn’s disease: A new concept of pan-enteric mucosal healing assessment**

Carvalho PB *et al.* Mucosal healing in CD with PCC2

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**Informed consent:** All patients provided written consent to undergo total colonoscopy, small bowel capsule endoscopy and pan-enteric endoscopy with PCC2.

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**Abstract**

**AIM**: To evaluate mucosal healing in patients with small bowel *plus* colonic Crohn's disease (CD) with a single non-invasive examination, by using PillCam COLON 2 (PCC2).

**METHODS:** Included patients with non-stricturing non-penetrating small bowel *plus* colonic CD in sustained corticosteroid-free remission. Patients had been submitted to ileocolonoscopy (identifying active CD lesions, such as ulcers and erosions) and small bowel capsule endoscopy-assessing the Lewis Score (LS) - at diagnosis.After ≥ 1 year of follow-up, patients underwent entire gastrointestinal tract evaluation with PCC2. Primary endpoint: assessing CD mucosal healing, defined as no active colonic CD lesions and a LS < 135.

**RESULTS:** Twelve patients were included, 7 male; mean age was 32 years, mean follow-up was 38 mo. The majority (83.3%) of patients was medicated with immunosuppressive therapy. Three patients (25%) achieved mucosal healing in both the small bowel and the colon, while in 5 patients (42%) disease activity was limited to either the small bowel or the colon. It was possible to observe the entire gastrointestinal tract in ten of the twelve patients (83%) undergoing PCC2.

**CONCLUSION:** Only three patients in sustained corticosteroid-free clinical remission achieved mucosal healing in both the small bowel and the colon, highlighting the limitations of clinical assessment when stratifying disease activity and need for pan-enteric endoscopy to guide therapeutic adjustment.

**Key words:** Crohn's disease; Mucosal healing; Capsule endoscopy; Small bowel diseases; Inflammatory bowel disease

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**Core tip:** Our study reports for the first time the use of PillCam COLON2 Capsule (PCC2) to evaluate mucosal healing of the entire intestinal tract in small bowel plus colonic Crohn's disease. Only 25% of our patients in corticosteroid-free clinical remission achieved mucosal healing in both the small bowel and the colon, while in 42% there was disease activity limited to either the small bowel or the colon. Endoscopic evaluation of the entire gastrointestinal tract with PCC2 was both feasible and safe. Our results highlight the limitations of clinical assessment when stratifying disease activity and emphasize the need for pan-enteric endoscopy in order to guide therapeutic adjustment.

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**INTRODUCTION**

Crohn's disease (CD) is a chronic inflammatory bowel disease whose prevalence has been rising over the past decades[[1](#_ENREF_1)]. In CD, there is a transmural inflammatory process that may affect the entire gastrointestinal tract, from the mouth to the anus, and in half the patients there is both a small bowel and colonic distribution[[2](#_ENREF_2)]. Although the terminal ileum, easily accessible through ileocolonoscopy, is the most commonly affected small bowel segment in CD (around 80%)[[2](#_ENREF_2)], up to half of the patients suffering from ileal CD have concomitant jejunal mucosal damage[[3](#_ENREF_3)]. Furthermore, one third of patients presents with isolated proximal lesions, associated with an increased risk of relapse and poorer disease outcomes[[3](#_ENREF_3)], but whose observation has been often challenging or incomplete.

Capsule endoscopy first became available in 2001[[4](#_ENREF_4)], revolutionizing the investigation on small bowel diseases. In the most recent European Crohn's and Colitis Organization guidelines[[2](#_ENREF_2)], SBCE established itself as a valid and important diagnostic tool in the diagnosis and evaluation of CD. SBCE was shown to be superior to small bowel follow-through and computed tomography enterography (CT-E) in the small bowel evaluation[[5](#_ENREF_5)]. When compared to magnetic resonance enterography (MRI-E), small studies showed that SBCE had better sensitivity for proximal small bowel mucosal lesions[[6](#_ENREF_6)]. Capsule endoscopy is highly sensitive for superficial mucosal lesions, with a strong negative predictive value[[7](#_ENREF_7),[8](#_ENREF_8)]. In established CD, capsule endoscopy may be used to evaluate disease extent and activity[[3](#_ENREF_3),[9](#_ENREF_9)], often impacting therapeutic decisions[[10](#_ENREF_10)-[12](#_ENREF_12)].

Mucosal healing, defined as the resolution of active inflammatory lesions in the gut[[13](#_ENREF_13)], is now recognized as a major determinant on the outcome of CD[[13](#_ENREF_13)]. Ileocolonoscopy is the gold standard for mucosal healing evaluation, but it is an invasive procedure, associated with discomfort and pain-often requiring sedation and analgesia - and reaching only to the terminal ileum. Procedural risks such as perforation are significantly increased in patients with severe disease[[14](#_ENREF_14)]-such patients would benefit from a less invasive diagnostic procedure. Capsule endoscopy, particularly when coupled with scoring systems such as the Lewis Score (LS)[[2](#_ENREF_2)] or the Capsule Endoscopy Crohn's Disease Activity Index (CECDAI or Niv Score)[[2](#_ENREF_2)], has the potential for assessing and quantifying mucosal healing in the small bowel CD[[2](#_ENREF_2)].

Recently, a capsule aimed at colonic observation has been developed[[15](#_ENREF_15)], PillCam COLON 2© (PCC2, Given Imaging©), which has been primarily used for colorectal cancer screening in average risk populations or when colonoscopy is contraindicated or incomplete[[16](#_ENREF_16)-[18](#_ENREF_18)]. Some recent studies have focused on the potential role of colon capsule endoscopy in patients with ulcerative colitis[[19](#_ENREF_19),[20](#_ENREF_20)] and colonic CD[[21](#_ENREF_21)]. PCC2 allows for the continuous and non-invasive observation of the entire intestinal tract (pan-endoscopy), and new studies are emerging to analyze its effectiveness in such evaluation[[22](#_ENREF_22)]. Although it still requires bowel preparation, colon capsule endoscopy does not require insufflation or sedation; the risks associated with the procedure are minimal, although capsule retention and potential bowel obstruction are more significantly more frequent in patients with established CD[[4](#_ENREF_4),[17](#_ENREF_17)].

We aimed to evaluate mucosal healing in patients with small bowel *plus* colonic Crohn’s disease on corticosteroid-free clinical remission, with at least one year of follow-up after diagnosis, using the PCC2 for pan-endoscopy.

**MATERIALS AND METHODS**

Retrospective single centre study, based on prospectively collected database, including all patients with small bowel *plus* colonic CD at diagnosis, with a non-stricturing, non-penetrating phenotype (Montreal Classification L3, B1[[1](#_ENREF_1)]) in corticosteroid-free remission (defined for an Harvey-Bradshaw Index < 5[[1](#_ENREF_1)]), at least one year of follow-up and age above 18 years. Exclusion criteria comprised pregnancy, known intestinal obstruction or current obstructive symptoms, non-steroidal anti-inflammatory drug use in the 4 wk prior to enrolment as well as previous intestinal surgery Inclusion and exclusion criteria are summarized in table 1. Small bowel radiological imaging was not mandatory prior to inclusion in this study; patients with no clinical features of stricturing or penetrating disease and no stricture at the index ileocolonoscopy were allowed to undergo capsule endoscopy without previous small bowel imaging.

All patients were submitted to both SBCE (PillCam SB2, Given Imaging©) and ileocolonoscopy at diagnosis per department protocol. Small bowel disease activity was assessed using the LS. The LS is calculated through a specific formula using the presence of villous oedema, ulcers and stenosis, and classifies small bowel inflammatory activity in three grades: LS < 135 (no activity), 135 ≤ LS < 790 (mild activity) and LS ≥ 790 (moderate to severe activity); in this study, patients with LS ≥ 135 were included[[23](#_ENREF_23),[24](#_ENREF_24)]. Capsule observation was performed by three physicians with experience in capsule endoscopy, and the images were read at a maximum of 10 frames per second. Colonic lesions for inclusion were the following: ulcers and aphthous ulcerations, while other lesions such as pseudopolyps, granularity without mucosal breaks or nodularity were considered non-active CD. Disease activity, measured with Harvey-Bradshaw Index (HBI), therapy (salicylates, corticosteroids, immunomodulators and anti-TNFα) and disease complications were evaluated during follow-up.

Assessment of mucosal healing on follow-up was performed with the PCC2, using our own modified protocol from Herrerias-Gutierrez *et al*[[25](#_ENREF_25),[26](#_ENREF_26)]. Patients were instructed to keep a low-fibre diet and ingest at least 10 glasses of water 2 d before the procedure; on the day before the procedure, a clear liquid diet (water, tea, transparent beverages) was prescribed, as well as 1 L of polyethylene glycol solution *plus* 500 mL of water between 7 and 9 pm; on the day of the procedure, another litre of this solution *plus* 500 mL of water was ingested (between 6:30 and 8:30 am), and fasting was warranted afterwards. At 9 am patients were instructed to ingest the capsule. Prior to the ingestion, real-time viewing (Rapid Access Real Time; Given Imaging©) was initiated and the adaptive frame rate mode was activated to ensure the visualization of the entire

small bowel (Figure 1).

One hour later, using the real-time viewing system, capsule progression to the small-bowel was confirmed - 10 mg of domperidone were administered if the capsule was yet in the stomach. Thirty minutes later, capsule progression was assessed - in case of delayed stomach emptying, endoscopic capsule placement in the small bowel was performed. When the small bowel was reached, a booster of 30 mL of sodium phosphate solution (Fleet Phospho Soda; Casen-Fleet Laboratories©) was administered, followed by the ingestion of 1 L of water; 3 h later a second booster of sodium phosphate (15 mL) was administered (plus 500 mL of water) if the capsule was not excreted by then, and after an additional 3 h, a bisacodyl suppository was given. In the event of an incomplete examination, unless the patient reported capsule excretion, an abdominal X-ray was performed after a period of 15 d or if obstructive symptoms developed.

Capsule observation was performed by a physician with experience in capsule endoscopy, blinded to both the initial endoscopic procedures and current therapy. The images were read at a maximum of 10 frames per second, using both cameras sequentially for colonic evaluation and a single camera for the remainder of the gastrointestinal tract. Small bowel, colon (segmented as follows: cecum, ascending, transverse, descending/sigmoid colon and rectum) and upper gastrointestinal CD lesions were described, and LS was calculated. Gastric transit time (from the first gastric frame to first duodenum frame), small bowel transit time (from the first duodenum frame to first cecum frame) and colonic transit time (from the first cecum frame to last rectal frame) were registered, in minutes. In the case of incomplete examination (capsule not excreted during battery time) a colon transit time was defined from the first cecal frame to the last registered colon frame. Small bowel and colon preparation quality was classified with a grading scale ranging from 1 to 4, where 1 is excellent (no more than small bits of residue), 2 is good (some residue, not enough to interfere with the examination), 3 is fair (enough residue to preclude a completely reliable examination) and 4 is poor (large amount of residue)[[25](#_ENREF_25)].

A blood panel was performed both at diagnosis and on the day of the pan-endoscopy (complete blood count, c-reactive protein, erythrocyte sedimentation rate, ferritin and albumin). Anaemia was defined for Hgb < 12 g/dL in women and < 13 g/dL in men; iron deficiency was defined for ferritin levels < 100 μg/L, leukocytosis was defined for a white blood count > 11.000/μL, elevated CRP was defined for values ≥ 3 mg/L, elevated ESR was defined for values > 20 mm/h and hypoalbuminemia was defined for albumin levels < 3,5 mg/dL, according to our laboratory reference range.

The Ethics Committee of the Centro Hospitalar do Alto Ave, E.P.E approved this study. All patients gave their written informed consent before enrolment. Data was analyzed anonymously to preserve the patient’s confidentiality. Statistical analysis of frequencies was performed using the Statistical Package for Social Sciences (SPSS, v.21.0, IBM©).

**RESULTS**

Twelve patients were included at baseline, and all completed the study protocol. Five patients were female (41.7%); the mean age was 32 years (18-50 years), with a mean follow-up of 40 mo (14-65 mo). Mean HBI at diagnosis was 9.64 (6-17). Two patients reported regular tobacco consumption (10-20 cig/d), three were ex-smokers and seven were non-smokers.

On baseline SBCE, mean LS was 1022 (± 810; 168-2980) and highest in the third tercile (mean 994 ± 838; 112-2980); mild inflammatory activity (135 ≤ LS < 790) was present in five patients and moderated to severe inflammatory activity (LS ≥ 790) was found in the other seven. No small bowel stenoses were observed. On baseline ileocolonoscopy, eight patients (66.7%) presented with a segmental pattern of colonic lesions, the majority in the right colon (*n* = 5); in four patients, there was extensive mucosal damage throughout the entire colon. The laboratorial results at diagnosis and at the time of the PCC2 are summarized in Table 2.

The majority (83.3%) of patients was medicated with immunosuppressive therapy. Two patients were treated with combination immunomodulation therapy (adalimumab plus azathioprine), 8 with azathioprine in monotherapy and 2 with oral mesalazine

Mean gastric transit time was 45 min (± 38 min; 3-90 min); domperidone administration was warranted in 4 patients, and endoscopic placement needed in 3 of them, with no subsequent complications. Mean small bowel transit time was 90 min (± 37 min; 21-162). Mean colon transit time was 321 min (± 308 min; 20-936). Two pan-endoscopy procedures were incomplete (17%), the splenic flexure being reached in both of them. In these patients, the colon transit time was 895 and 936 min (total battery time for the PillCam COLON 2© is 1020 min).

Small bowel cleanliness was excellent in 5 (42%) patients, good in 6 (50%), and fair in 1 (8%), while the colonic preparation was excellent in two patients (17%), good in 6 (50%) patients, fair in 2 (17%) and poor in two (17%) patients.

PCC2 findings in the small bowel were as follows: complete mucosal healing of the small bowel (LS < 135) was achieved in 4 patients (33%), three of them under azathioprine monotherapy, while the other patient was treated with mesalazine; one patient (8%) with previous moderated to severe inflammatory activity treated with anti-TNFα plus azathioprine presented with mild inflammatory activity, and moderated to severe inflammatory activity was found in the remaining patients (*n* = 7, 58%). In four patients (33%), a single stenosis was found on the small bowel, in all on the third tercile, and it was ulcerated in two of them; the stenoses were traversed in all patients, causing no obstructive symptoms.

Mean LS was 1551 (± 1999; 0-5392), and was highest in the third tercile (1126 ± 1213; 0-3040). Colonic lesions were found in half the patients (*n* = 6); two patients presented with ulcers throughout the entire colon, while segmental inflammatory activity was found in the remaining four. Six patients (50%) achieved complete mucosal healing of the colon; in three of them (25%), there was concomitant small bowel mucosal healing. Patients' characteristics, CD therapy and endoscopic findings are summarized in Table 3.

**DISCUSSION**

In our study, investigating patients in corticosteroid-free clinical remission, we found significant inflammatory activity in 9/12 (75%) of the patients, and crucially, in 5 (42%) patients, disease with previous both small bowel and colonic involvement was on follow-up limited to one of those segments, highlighting the limitations of clinical disease assessment when stratifying disease activity and need for therapeutic adjustment.

Moreover, in 3 out of 6 of the patients with normal colonic mucosa, there was involvement of the proximal small bowel, an independent risk factor for disease relapse[[3](#_ENREF_3)]. Conversely, two patients where no significant inflammatory activity was found in the small bowel (LS < 135) were shown to have multiple ulcers in the colonic mucosa. Finally, moderated to severe activity in the small bowel, as well as colon disease, was confirmed in a third of our patients.

Adequate small bowel preparation was achieved in all twelve patients, and in only two patients was the colon preparation poor. These results are comparable to the ones reported in the literature for both the small bowel and the colon[[4](#_ENREF_4)], but warrant a consideration on whether it is possible to further optimize colon preparation.

Although this was a single centre retrospective study with a small number of patients, it was based on prospectively collected data, with strict inclusion criteria, and it focuses on a very relevant hot topic in CD that has not previously been investigated - the simultaneous evaluation of post-treatment mucosal healing in both the small bowel and colon with a single non-invasive endoscopic examination.

In CD, symptom remission has not been shown to alter the natural course of the disease[[13](#_ENREF_13)], particularly regarding complication and surgical rates[[27](#_ENREF_27)], arguably because the correlation between clinical and inflammatory activities is poor[[28](#_ENREF_28)]. In the era of biologic therapy, a new concept, mucosal healing, has arisen. In contrast to clinical symptoms, mucosal healing has been associated with significantly reduced rates of surgery[[29](#_ENREF_29)] and hospitalization[[30](#_ENREF_30)] as well as with the achievement of long term steroid-free remission[[31](#_ENREF_31)].

Optimal assessment of mucosal healing is still debated. Ileocolonoscopy is so far the gold standard for evaluating mucosal healing, but it is an invasive procedure and restricted to the colon and distal ileum[[32](#_ENREF_32)]. Several surrogate markers for mucosal healing exist, but none without limitations. Fecal markers, such as calprotectin, have shown promising discriminating power to predict disease relapse[[33](#_ENREF_33)], but the results regarding ileal disease are unremarkable[[34](#_ENREF_34)]. Cross-sectional imaging, particularly CT-E and MR-E, allows for the evaluation of the small bowel and colonic mucosa, as well as deep-tissue assessment, and has shown good correlation with both clinical and endoscopic activity[[13](#_ENREF_13)]. However, CT poses a cumulative radiation risk, and MR-E is expensive and not widely available in clinical practice. SBCE has shown superior diagnostic accuracy to cross-sectional imaging in small bowel CD[[6](#_ENREF_6),[35](#_ENREF_35),[36](#_ENREF_36)], particularly in detecting proximal and superficial lesions[[5](#_ENREF_5),[6](#_ENREF_6)], and was recently reported to be safe in established small bowel CD, even in patients with previously known stenotic lesions[[32](#_ENREF_32)], but does not allow for colon observation.

The colon capsule was recently developed for colon observation, particularly in patients who refuse colonoscopy or in whom such procedure is not possible[[17](#_ENREF_17)]. Although it still requires colon preparation, there is no need for insufflation or sedation, and the risks associated with the procedure are minimal[[4](#_ENREF_4),[17](#_ENREF_17)].

Colon capsule endoscopy implementation to detect mucosal inflammation in the colon was previously described in ulcerative colitis patients[[19](#_ENREF_19),[20](#_ENREF_20)], and was recently shown to have a good correlation with colonoscopy when evaluating colon mucosal damage in patients with colonic CD[[21](#_ENREF_21)].

The use of colon capsule endoscopy for the whole intestinal tract observation was previously reported by Remes-Troche *et al*[[22](#_ENREF_22)] and by Negreanu *et al*[[37](#_ENREF_37)]. In both studies, PCC2 allowed for a thorough examination of both the small bowel and the colon, with very good tolerability and no complications

No stenosis was encountered during SBCE at diagnosis, but single small bowel stenoses were found in 4 patients on PCC2. These patients reported no obstructive symptoms either previous or during the procedure, and such results are consistent with the ones reported by Niv *et al*[[32](#_ENREF_32)], where 6 patients with ulcerated small bowel stenoses underwent repeated SBCE with no incidence of retention or complications.

The cecum was reached in all patients, allowing for the crucially important observation of the terminal ileum, ileocecal valve and the cecum. Despite optimized protocol and prolonged battery life (maximum 17 h), the procedure was incomplete in 2 patients.

Gastric transit time was per protocol always under 90 min. In contrast to other colon capsule preparation regimens[[22](#_ENREF_22),[25](#_ENREF_25)], we used real-time viewing to adjust drug administration, allowing for criterious use of prokinetic drugs only in patients with delayed gastric emptying, as well as for determining the ideal timing for phosphate soda booster delivery.

Small bowel transit time was under 3 h in all patients. Despite some evidence that the small bowel transit time correlates with diagnostic yield in SBCE[[38](#_ENREF_38)], the possibility that the shortening of small bowel transit time might reduce the diagnostic yield with PCC2 would probably not be an issue as its dynamic frame rate allows for the capture of up to 35 frames per second in accelerated movement.

Colon transit times averaged 320 min, and we encountered two incomplete studies, whose colon transit times were 895 and 936 min - a completion rate of 83.3%. No colon lesions were found in these patients despite the splenic flexure being reached in both of them. Both patients reported the excretion of the capsule on the following day with no complications. The completion rate for colon capsule endoscopy is reported to range between 76- 100%[[18](#_ENREF_18),[19](#_ENREF_19),[22](#_ENREF_22),[39](#_ENREF_39)], comparable to our own (83%). Finally, we report no technical failures.

Our study has some limitations: it was an exploratory single centre study, which included a limited number of patients due to strict inclusion criteria, particularly the requirement of both ileocolonoscopy and SBCE at diagnosis, minimum follow-up of one year after the initiation of CD therapy, and corticosteroid-free clinical remission, prior to mucosal healing assessment with PCC2. Secondly, as the objective of the study was to demonstrate the feasibility of PCC2 for the evaluation of small bowel and colonic mucosal healing, no control group or gold standard was employed. Prospective multicenter studies would enable the inclusion of a significantly larger number of patients, in order to validate our preliminary results, with the primary outcome of assessing complete mucosal healing in both small bowel and colonic mucosa; ideally, new studies should use new or adapted scoring systems that could measure inflammatory activity both in the small bowel and the colon, as this novel concept becomes widespread in the investigation of this pan-enteric disease, based on a compromise of high diagnostic accuracy, less invasiveness and convenience for patients. Further investigations should be able to evaluate whether complete (absence of endoscopically visible lesions) *versus* partial (improvement with lower inflammatory activity scores) mucosal healing in each and/or both “segments” (small bowel and/or colon) have a significant prognostic value, by following patients to assess for endpoints such as the rate of clinical relapses, hospitalizations or surgeries. Although the possibility of fully assessing mucosal healing during the course of CD by means of a single non-invasive procedure seems a very attractive concept, there is currently not enough evidence that such strategy could positively impact disease outcomes; moreover, key practical drawbacks such as the high cost of each examination, the time required to read the videos, and the relatively scarce availability of adequately trained medical staff to read PCC2 videos, are some of the issues that currently limit its widespread generalization for use in clinical practice, beyond patients unwilling or unable to undergo conventional ileocolonoscopy.

In conclusion, the PillCam COLON 2© allows for a new concept of non-invasive, safe and well tolerated examination of the entire gastrointestinal tract. Additionally, in a population currently in corticosteroid-free clinical remission, we found significant inflammatory activity in all but three patients (25%); of relevance, 5 patients (42%) with previous activity in both the small-bowel and colon presented with disease limited to one of them, reinforcing the importance of the entire gut visualization before any management decisions regarding CD patients. In the future, this procedure may be used to evaluate mucosal healing in small bowel, particularly with proximal distribution, and colonic Crohn's Disease.

**COMMENTS**

***Background***

Crohn's disease (CD) is a chronic inflammatory bowel disease characterized by periods of remission and periods of relapse. Both the small bowel and colonic mucosa are affected in half the CD patients, and mucosal healing has been recently shown to associate with improved clinical outcomes. Capsule endoscopy has been developed for the study of the small bowel and colon, and with the new Pillcam Colon Capsule 2 (PCC2), it is now possible to observe the entire intestinal tract (pan-endoscopy).

***Research frontiers***

In our study, we aimed to evaluate the presence of mucosal healing in patients with small bowel plus colonic CD in clinical remission, with at least one year of follow-up after diagnosis, using the PCC2 for pan-endoscopy.

***Innovations and breakthroughs***

We've reported for the first time the use of capsule endoscopy to assess mucosal healing of the entire intestinal tract in patients with CD. Mucosal healing for both the small bowel and the colon was achieved in 25% of the patients, and in 42%, there was disease activity limited to either the small bowel or the colon. Pan-endoscopy with PCC2 was safe and feasible in our study.

***Applications***

Our study highlights the limitations of clinical assessment when stratifying disease activity. Morever, in patients with previous small bowel and colonic CD, we found mucosal healing to be limited to one segment in almost half the patients, emphasizing the need for pan-enteric endoscopy to guide therapeutic adjustment in patients with established CD.

***Terminology***

Pan-endoscopy refers to the endoscopic assessment of both small bowel and colon observation. Mucosal healing corresponds to the resolution of active inflammatory lesions in the gut (erosions, ulcers, friability, haemorrhage). Capsule endoscopy is a recent endoscopic technique where a small device with a camera is swallowed by the patient in order to visualize the mucosa of the gastrointestinal tract.

***Peer-review***

This is an interesting study performed by Carvalho *et al* reporting on a new technique - the use of colon capsule in the assessment of mucosal healing in CD patients. The manuscript is well written, and carefully designed. The procedures are described in great details in the material and methods section.

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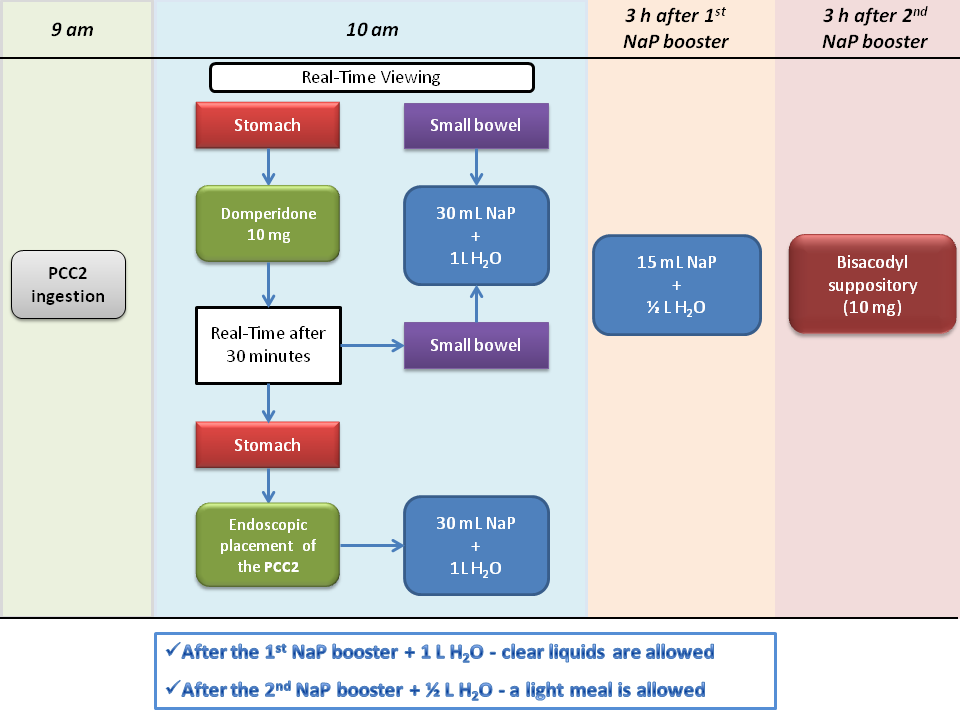
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**P-Reviewer:** Formica V, Ma L, Rolle U **S-Editor:** Qi Y **L-Editor: E-Editor:**

**Figure 1 Department protocol for pan-enteric evaluation with PCC2®.** PCC2: Pillcam colon capsule 2; NaP: Sodium phosphate.

**Table 1 Patients' inclusion and exclusion criteria**

|  |
| --- |
| **Patients’ inclusion and exclusion criteria** |
| Inclusion criteria (all of the following) |
| Small bowel plus colonic Crohn's disease |
| Non-stricturing, non-penetrating phenotype |
| Corticosteroid-free remission (Harvey-Bradshaw Index < 5) |
| Follow-up ≥ 1 yr |
| Age ≥ 18 yr |
| Exclusion criteria (any of the following) |
| Pregnancy |
| Intestinal obstruction / obstructive symptoms |
| Intestinal surgery |
| Non-steroidal anti-inflammatory drug use within 4 wk of enrolment |

**Table 2 Patients' hematological results at diagnosis and follow-up**

|  |  |  |  |
| --- | --- | --- | --- |
| **Result (mean ± SD)** | **Diagnosis** | **Follow-up** | **Ref.** |
| Hemoglobin (g/dL) | 13.2 ± 2.8 | 14.2 ± 1.4 | 12.0-18.0 |
| Leucocytes (103 /uL) | 10.100 ± 3.200 | 7.800 ± 2.800 | 4.8-10.8 |
| Platelets (103 /uL) | 363 ± 194 | 265 ± 124 | 150 -350 |
| Erythrocyte sedimentation rate (mm/h) | 28.6 ± 23.8 | 12.3 ± 8.3 | 0-14 |
| C-reactive protein (mg/L) | 42.6 ± 36.4 | 17.2 ± 17.0 | < 2.9 |
| Ferritin (ng/mL) | 120 ± 112 | 74 ± 49 | 26-388 |
| Albumin (ng/mL) | 4.1 ± 0.6 | 3.9 ± 0.3 | 3.1-17.5 |

**Table 3 Patients' characteristics, Crohn's disease therapy and endoscopic findings**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient** | **Age** | **Gender** | **Follow-up**  **(mo)** | **Therapy** | **SBCE LS** | **Index colonoscopy colon findings** | **PCC2 LS** | **PCC2**  **colon findings** |
| 1 | 21 | Male | 48 | Azathioprine 2.5 mg/kg per day | 2980 | Extensive ulcers and erythema in entire colon | 1068 | Extensive ulcers in entire colon |
| 2 | 21 | Female | 63 | Azathioprine 2.5 mg/kg per day  Adalimumab 40 mg eow | 1440 | Extensive ulcers and erythema in entire colon | 2336 | No lesions |
| 3 | 26 | Male | 57 | Azathioprine 2.5 mg/kg per day  Adalimumab 40 mg eow | 1350 | Aphtoid ulcers and erythema in the sigmoid | 562 | No lesions |
| 4 | 48 | Male | 33 | Azathioprine 2.5 mg/kg per day | 1240 | Aphtoid ulcers and erythema in the cecum | 5392 | Extensive ulcers in the ascending and transverse colon |
| 5 | 24 | Male | 39 | Mesalazine 3 g/d | 1104 | Aphtoid ulcers in the cecum | 1518 | Aphtoid ulcers in the cecum |
| 6 | 27 | Female | 14 | Azathioprine 2.5 mg/kg per day | 900 | Extensive ulcers and erythema proximal to the splenic flexure | 0 | Ulcers in the transverse colon |
| 7 | 18 | Male | 14 | Azathioprine 2.5 mg/kg per day | 1690 | Extensive ulcers and erythema in entire colon | 2336 | Ulcers in the cecum, ascending, transverse and descending colon |
| 8 | 35 | Female | 22 | Azathioprine 2.5 mg/kg per day | 314 | Aphtoid ulcers and erythema in the cecum | 5392 | No lesions |
| 9 | 32 | Male | 22 | Mesalazine 3 g/d | 458 | Extensive ulcers and erythema in entire colon | 0 | No lesions |
| 10 | 46 | Female | 49 | Azathioprine 2.5 mg/kg per day | 393 | Extensive ulcers and erythema proximal to the splenic flexure | 0 | No lesions |
| 11 | 50 | Female | 65 | Azathioprine 2.5 mg/kg per day | 225 | Ulcers in the sigmoid | 8 | Ulcerative lesions in the splenic flexure; |
| 12 | 39 | Male | 62 | Mesalazine 3 g/d | 168 | Aphtoid ulcers in the cecum and ascending colon | 0 | No lesions |

SBCE: Small bowel capsule endoscopy; PCC2: PillCam Colon Capsule 2; LS: Lewis Score; eow: Every other week.