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Pillcam Colon 2 in Crohn's Disease: Pan-enteric Tool for a Pan-enteric Disease

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Introduction

Crohn's Disease (CD) is a chronic idiopathic inflammatory bowel disease that may affect any segment of the digestive tract, from mouth to anus. The disease affects the small bowel in approximately 80% of cases, and nearly one half of patients have involvement of both the small bowel and the colon [1]. While ileocolonoscopy remains the mainstay for the diagnosis of CD, the location and extent of the disease in the upper gastrointestinal tract and the small bowel upstream of the terminal ileum should also be assessed, as it may have both prognostic and therapeutic implications [2]. Indeed, although the terminal ileum is the most commonly affected segment, up to half of the patients suffering from ileal CD may have concomitant jejunal lesions which negatively affect the prognosis [3,4] Moreover, in some patients, CD affects only the small bowel proximal to the terminal ileum, which poses a particular diagnostic challenge [1,5]. Gross involvement of the esophagus, stomach, or duodenum is relatively rare and almost always seen in association with disease of the distal small bowel or colon [2].

Capsule Endoscopy in Patients with Crohn's Disease

The evaluation of patients with suspected or known CD is among the clearly established clinical indications for capsule endoscopy [1,6]. Small bowel capsule endoscopy (SBCE) has been shown to have the highest diagnostic yield among all imaging modalities of the small bowel for the detection of CD inflammatory lesions, particularly in the case of superficial lesions and those located in the proximal small bowel [1,7,8]. In patients with suspected CD, it is possible to confidently exclude the diagnosis if no small bowel mucosal changes are identified by the capsule, because it is highly sensitive even for subtle mucosal changes [9,10], thus having a high negative predictive value. SBCE may also be a key diagnostic instrument if it reveals small bowel lesions consistent with CD in adequately selected patients [10-13]. In patients with established CD, capsule endoscopy is useful to evaluate disease extent and activity [3,4], as it may influence therapeutic decisions by detecting previously unknown small bowel lesions [14-16]. SBCE has been used to investigate CD patients with atypical symptoms, unexplained anemia or obscure GI bleeding1, as well as in the post-operative setting [17,18]. Furthermore, it has also been used to assess small bowel mucosal healing after therapy, which is an important endpoint of treatment efficacy, associated with sustained clinical remission and improved outcomes [1,19-21].

PillCam® COLON 2

While ileocolonoscopy is currently the gold standard for endoscopic evaluation of patients with CD, it is restricted to the colon and terminal ileum, and it is an invasive procedure associated with discomfort or pain, often requiring sedation. Moreover, patients with severely active disease undergoing colonoscopy are at increased risk of complications such as perforation [22], and would benefit from a less invasive diagnostic procedure. Recently, a capsule aimed at colonic observation has been developed [23], which has been primarily used for colorectal cancer screening in average risk populations or when colonoscopy is contraindicated or incomplete [24-26]. Although it still requires colon preparation, colon capsule endoscopy does not require insufflation or sedation, and the risks associated with the procedure are minimal [25,27]. Currently on its second-generation, this colon capsule (PillCam® COLON 2, PCC-2) measures 11.6 mm × 31.5 mm and it has one camera at each end, with an angle of view of 172°, allowing for nearly 360° coverage of the colon. PCC-2 captures 4 images per second during the first 3 minutes following activation, and then works at a low rate of 14 images per minute until small bowel images are detected [22]. The capsule then turns into an adaptive frame rate mode, capturing from 4 frames per second when stationary, up to 35 frames per second when in motion [22]. With this technology, the risk of missing lesions while the capsule is moving is reduced, which may be particularly relevant during its rapid passage through the transverse colon, at the same time saving battery energy and optimizing the video length. It is also possible to get the adaptive frame rate mode activated from the beginning of the examination, even before capsule ingestion, in order to improve imaging of the upper GI tract. The data recorder (DR3) assists the medical staff and the patient through the procedure according to a pre-selected preparation protocol, by alerting and displaying on the screen a sequence of instructions, paving the way for PCC-2 to be offered as an out-of-clinic procedure [28]. Figure 1 summarizes the current protocol in our unit. With the DR3 we can use real-time viewing to selectively administer a prokinetic drug to patients with delayed gastric emptying [29]. If the capsule is still remaining in the gastric cavity one hour after ingestion, DR3 will instruct the patient to get a prokinetic such as oral domperidone. DR3 is also able to automatically detect when the capsule starts capturing images of the small bowel, with an estimated sensitivity of 98.3% sensitivity [28], subsequently activating the adaptive frame rate which will capture up to 35 frames per second, and it also alerts the patient to ingest the first booster laxative (sodium phosphate, NaP), which will accelerate small bowel transit time of the capsule and help to maintain the colon cleanliness. DR3 will also notify the patient to have a second booster of NaP, and finally a bisacodyl suppository if the capsule has not been excreted

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three hours after administering the second NaP booster, in order to accelerate colonic peristalsis and get images from the left colon and rectum before the capsule battery exhaustion. Colon capsule endoscopy appears to be a feasible and very safe procedure, with a very low rate of technical failures (~3%) and a high capsule excretion rate of about 90% [30]. In the setting of colorectal cancer screening, it has demonstrated a high sensitivity for the detection of polyps, with a clinically very meaningful negative predictive value of 97% [26,31,32]. Some recent studies have focused on the potential role of colon capsule endoscopy in patients with ulcerative colitis [33,34] and colonic CD [35], generally showing that it may be useful to monitor inflammation and to screen for colorectal cancer, having a good correlation with standard flexible colonoscopy, although some data showed that the severity and extension of the inflammation could be underestimated by the capsule [36]. Thus, international recommendations currently indicate that there are still insufficient data to support the use of colon capsule endoscopy in the diagnostic work-up or in the surveillance of patients with suspected or known IBD [1,30].

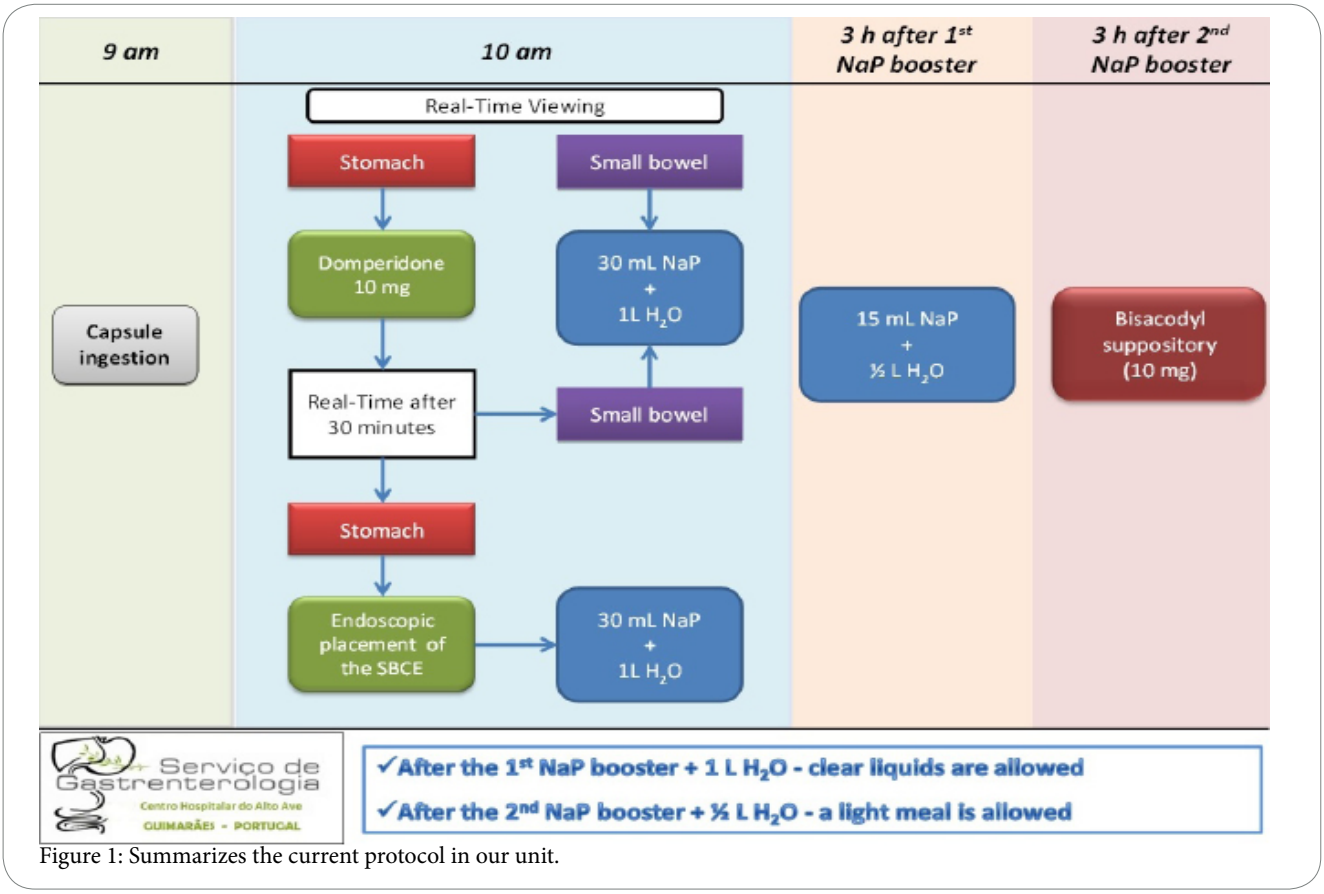

Figure 1: Summarizes the current protocol in our unit.

Pan-endoscopy in Crohn's Disease

The availability of PCC-2 triggered a new concept, based on the possibility to perform a complete examination of the whole GI tract from mouth to anus (pan-endoscopy) with a single non-invasive procedure [37]. Although the exploration of the esophagus and stomach rests sub-optimal with the currently available capsule models, the feasibility of remotely controlled prototypes has been demonstrated, making it expectable to have such limitations overcome in a near future [38-43]. Although there are currently no specific recommendations to routinely perform upper GI endoscopy in adult CD patients, it may contribute to establish the diagnosis, to assess disease extension and severity and to aid in tailoring therapy in selected patients1. PCC-2 is expected to offer at least the same accuracy as SBCE for the evaluation of the small bowel, while enabling the additional atractive feature of also exploring the colon within the same non-invasive examination. Having this concept in mind, our centre is currently using PCC-2 to evaluate post-therapy mucosal healing in patients with small bowel plus colonic CD on corticosteroid-free clinical remission, which had been submitted to both ileocolonoscopy and SBCE at diagnosis and with at least one year of follow-up. Interim analysis after inclusion of 12 patients, mostly (~80%) treated with azathioprine and/or biological therapy, revealed that only 3 patients (25%) achieved mucosal healing in both the small bowel and the colon, despite being in corticosteroid-free clinical remission (unpublished data). This highlights the limitations of clinical disease assessment when stratifying disease activity and when identifying patients in need for therapeutic adjustment. Moreover, 5 patients (42%) had mucosal healing in only one segment (small bowel or colon), which emphasizes the importance of full endoscopic evaluation of both the small bowel and colon to assess mucosal healing in CD. PCC-2 allowed for a non-invasive, safe and well tolerated examination of the entire gastrointestinal tract, achieving nearly 85% complete examinations, with good or excellent bowel preparation in approximately two thirds of patients.

In order to increase objectivity and inter observer agreement in the evaluation of small bowel inflammatory activity, the use of standardized endoscopic scoring systems such as the Lewis Score (LS)44 and the Capsule Endoscopy Crohn's Disease Activity Index (CECDAI or Niv Score)45 has been recommended1. In a near future, the development of a new score that will apply to PCC-2 pan-endoscopy in CD, integrating both small bowel and colonic pathology,

may be expected as this is steadily emerging as a new exciting concept for the investigation of this pan-enteric disease, based on a compromise of high diagnostic accuracy with less invasiveness and convenience for patients.

Competing Interests

The authors have no competing interests with the work presented in this manuscript.

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