

## Atypical indications for small bowel capsule endoscopy

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### Abstract

Obscure bleeding remains the most important indication for small bowel capsule endoscopy, but some other small bowel diseases have also been studied. The aim of this paper is to provide an overview of the recent literature concerning atypical or rare indications for the small bowel capsule endoscopy. (*Acta gastroenterol. belg.*, 2010, 73, 479-483).

**Key words:** "Capsule endoscopy", small bowel, indications, Crohn, pediatrics, OGIB (Obscure GastroIntestinal Bleeding).

### Introduction

Endoscopic examination of the small bowel has known major progress these last years (1). Capsule endoscopy induced a real revolution in this setting since the first official publication announcing its invention (2) followed by the two first publications on clinical applications (3,4). Numerous articles were produced in the literature and the best indication for the Small Bowel Capsule Endoscopy (SBCE) remains the Obscure GastroIntestinal Bleeding (OGIB). However, other indications were explored and published. The aim of this paper is to provide an overview of these "atypical" indications. In Belgium, the SBCE is currently exclusively reimbursed in OGIB and Iron Deficiency Anemia (IDA), after non contributive endoscopic work-up (fibroduodenoscopy and colonoscopy).

OGIB is defined as a digestive tract bleeding after negative upper and lower endoscopic evaluation and occurs in 5% of all patients with gastrointestinal hemorrhage (5). OGIB can be overt (blood loss is visible) or obscure, inducing in this last case unexplained IDA. The most frequent lesions responsible for small bowel hemorrhage are arteriovenous malformations, significant ulceration/inflammation, and polyps/masses (6,7). Multiple prospective studies have shown that the added diagnostic yield of SBCE ranges between 50 and more than 70% in patients with OGIB (8,9). The real added diagnostic yield should be around 50% (10). As a comparison, the added diagnostic yield for push enteroscopy is around 25-30% (11,12). A meta-analysis confirmed a superiority of SBCE in OGIB over push enteroscopy, small bowel radiography, CT enteroclysis, mesenteric angiography and small bowel MRI (13). As for classical push enteroscopy, up to 20% of the lesions encountered during SBCE examination are within the field of classical upper- and lower endoscopy.

The diagnostic yield of the capsule is much higher in overt bleeding, mostly if the examination takes place within two weeks of the acute episode and especially within the first 48 h (14,15). The timing of SBCE in overt OGIB is thus crucial to obtain a maximal diagnostic yield.

In the very recent recommendations published by the European Society of Gastrointestinal Endoscopy (ESGE) (16), SBCE in OGIB (as first-line examination after upper and lower gastrointestinal endoscopy) and unexplained IDA had both a grade B of recommendation, category of evidence 2B (evidence based on non controlled cohort studies).

### Portal hypertension

Vascular abnormalities are frequently found by SBCE in portal hypertension (50% of cases) (17). These abnormalities include angiodysplastic lesions, varices, erythematous spots and the presence of fresh blood. In most patients, vascular abnormalities are multiple. The varices found are theoretically accessible with conventional endoscopy (proximal jejunum and terminal ileum), confirming the fact that varices out of reach of the classical endoscopy are probably infrequent.

SBCE is useful for detecting vascular lesions in portal hypertension, but these findings probably have limited clinical relevance. SBCE in portal hypertension has to be restricted to selected patients.

### Crohn's disease

SBCE is currently not reimbursed for this indication in Belgium. Very recently, the role of the SBCE in the management of patients with inflammatory bowel disease was critically evaluated by an expert panel (18). Most evidence supported assessments (level 2a, 2b) of importance for the clinician were :

- Ileocolonoscopy must be performed prior to SBCE for the diagnosis of Crohn's disease and SBCE should

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generally be preceded by small-bowel cross-sectional imaging.

- SBCE is able to identify lesions compatible with Crohn's in some patients in whom conventional imaging failed to establish a diagnosis.
- Diagnosis of Crohn's disease should not be based on the appearances at SBCE alone
- A normal SBCE examination has a high negative predictive value for active small-bowel Crohn's disease.

As additional comments, we could say that there are indeed no validated endoscopic criteria for diagnosing Crohn's disease by means of SBCE, as NSAID's induced lesions, lymphoid hyperplasia, lymphoma, radiation enteritis, vasculitis or infectious disease can induce similar lesions. Practically, NSAID's should be stopped before SBCE procedure takes place (19). Furthermore, the use of SBCE must be avoided in suspicion of stricturing Crohn's disease. The risk of retention in Crohn's disease has been estimated to be 5%-13% (20). This justifies to perform small-bowel cross-sectional imaging before SBCE should be planned.

### Celiac disease

Villous atrophy can reliably be identified by capsule inclusively in parts of the duodenum not accessible for routine endoscopy. The transit of SBCE through the second part of duodenum is however very fast making difficult an adequate visualization of this region by the device. Moreover, the diagnosis of celiac disease can be established by cheaper diagnostic tests. SBCE has been used in some studies in refractory forms of celiac disease and especially for the detection of potentially associated Enteropathy Associated T-cel Lymphoma (EATL) (21, 22) (Fig. 1a and 1b).

### SBCE in Paediatrics

The criteria of reimbursement of SBCE in Belgium are also valuable for pediatric patients. The use of SBCE in children was approved in 2004 by the FDA, but exclusively in children older than 10 years. However, the device has been used in children as young as 1.5 years (23). The youngest child we investigated up to now was 5 years old (24). The limiting step in pediatric patients is the ability of the child to swallow the capsule scope but different devices exist to bypass this limitation (25). In their recent multicentric study, Fritscher-Ravens *et al.* focused on children under the age of 8 years (23). This study found the Advance introducer (US Endoscopy, Mentor Ohio, USA) superior to other techniques for endoscopic placement of the capsule in the stomach or the duodenum. As in adults, suspicion of gastrointestinal bleeding is the most important indication. Findings are however more specific for pediatric diseases: ulcerative jejunitis, polyposis, angiodysplasia, Blue rubber bleb. Suspected Crohn's disease is also an

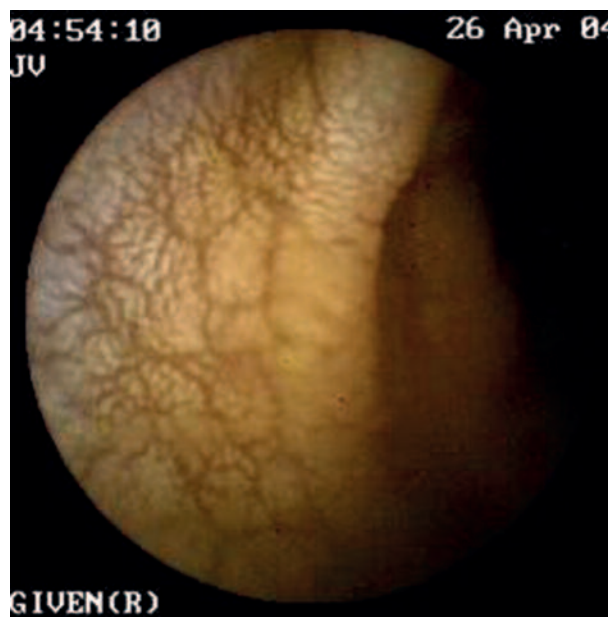


Fig. 1a. — Cracked aspect of small bowel mucosa in a case of refractory celiac disease.

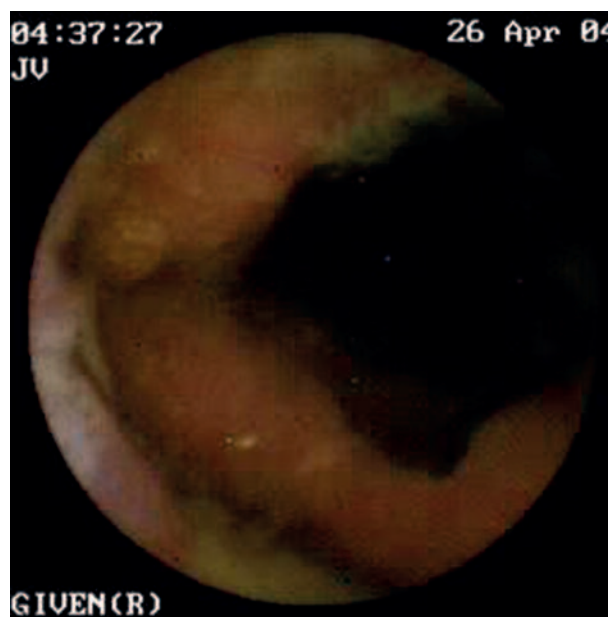


Fig. 1b. — Same patient: Enteropathy Associated T-cel Lymphoma.

important indication, confirming the interest of the pediatricians for Crohn's disease in children (23,26-30). More specifically, the Familial Adenomatous Polyposis (FAP) has been recently reviewed by Pennazio *et al.* (31). In this indication, SBCE should be used at initial diagnosis and thereafter every 2-3 years from the age of 10, and as part of the investigation of patients with symptoms. SBCE was found to be unable to evaluate size or location of polyps and CT and/or MR were found

to be better than capsule for planning subsequent therapy by push enteroscopy or device assisted enteroscopy (32).

*Abdominal pain* is an indication frequently encountered in the pediatric literature. In the recent European multicentric study, up to 50% of these children investigated by SBCE had significant lesions (23). The majority of the children with abdominal pain had small intestinal Crohn's disease or typical pediatric findings like lymphonodular hyperplasia. In adults, the diagnostic yield for this indication is very low. Protein losing enteropathy and malabsorption are other relevant indications in children, allowing to diagnoses such as undetected lymphangiectasia (23,33).

### Transit time

Due to the passive transport of the capsule, there are large variations in transit time and caecal completion rate of the capsule. Incomplete examination of the small bowel occurs in approximately 20% due to the limited battery life, which hampers the visualization of the distal small bowel (34,35). There are currently capsule devices with longer battery life. In a recent study, Nakamura *M et al* found that the capsule transit time was useful for the route selection (oral versus anal) for double-balloon endoscopy in OGIB (36). These authors found an accuracy of route selection of 94% (for a cut off value of 50% of the time duodenal bulb to cecum for the position of the lesion).

### SBCE in neoplastic disease

Primary small bowel tumors are rare and mostly consist of adenocarcinomas (30-50%), carcinoids (25-30%) and lymphomas (15-20%). Ileum and duodenum are the most frequent localizations (37). Data concerning the detection of small bowel tumors by capsule endoscopy are more and more available, with an additional diagnostic yield varying between 3.6 and 9% as compared with other techniques (38-40). In a former multicentric study, we also found that the clinical impact on the work-up of patients was as high as 55% (38). More than 90% of the indications in case of diagnosing tumors by SBCE are OGIB.

Small intestinal tumors can also be the result of secondary involvement (more frequently than as primary site of tumors) by a neoplastic disease arising from other organs. Secondary invasion can be by direct invasion or peritoneal spread (colon, stomach, ovary, uterus) or by hematogenous route (lung, breast, melanoma) (41). Metastases from melanoma have been described in 1.5%-4.4% of patients having previously removed skin melanoma and in 58% of postmortem specimens (42). Finding small bowel metastases of melanoma can be important as mentioned in a recent publication, because surgical removal of unique small bowel metastasis of melanoma could improve survival of patients (43). In the indication of detecting small bowel metastases from

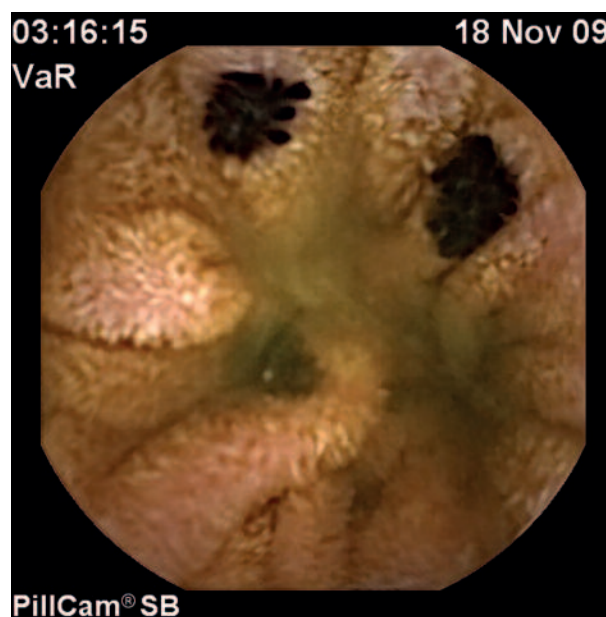


Fig. 2. — Small bowel metastases of melanoma

melanoma, SBCE could be superior to other techniques inclusive the Pet-scan (44,45) (Fig. 2). Limitations of SBCE in neoplastic disease are risk of retention, poor precision in the localization of lesions through the small bowel, absence of specific aspect of the lesions and no possibility to take tissue samples.

In their analyze of a large data base, Lewis *et al.* (46) found that the miss rate of SBCE in neoplastic diseases could be around 18%. This is much lower than that of other diagnostic techniques (63% in the same study) but clearly underlines the limits of the technique. One important limiting feature is probably the fact that discriminating masses from bulges still remains a weak point of SBCE.

### Conclusion

OGIB remains from far the best indication for SBCE, and especially overt OGIB shortly after the bleeding episode. SBCE can help in selected cases of Crohn's disease by identifying lesions compatible with this disease, after imaging failed to establish a diagnosis. While specific findings cannot be expected, it is important to note that a normal SBCE examination is a strong argument against a small bowel localization of the disease. In pediatrics, the experience of SBCE is growing, and additional publications of large series of patients can be expected. SBCE in tumoral diseases is a topic in expansion, especially in situations where secondary involvement of the small bowel has a therapeutic impact, like in melanoma. Most important weak points of the SBCE in

tumors remain the risk of retention and the low capacity discrimination between masses and bulges.

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