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Critical review

Usefulness of capsule endoscopy in digestive tract tumours

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Abstract

Introduction

This review presents a critical evaluation and a practical approach of capsule endoscopy utility in the diagnosis of digestive tract malignancy, which is based on our long-time experience combined with numerous studies regarding capsule endoscopy.

Discussion

Our observations support the restrictive utility of oesophageal capsule endoscopy. Colon capsule endoscopy cannot be regarded as a proper investigation method for colorectal cancer diagnosis or screening. On the other hand, capsule endoscopy is useful in colorectal polyp screening, and small bowel malignancies are rarely diagnosed. It can be used to identify the tumour when there is a high clinical suspicion and when the usual imagistic methods fail to identify the proliferate area. Surveillance of small bowel Crohn's disease or coeliac disorder by capsule endoscopy may identify neoplasia that might complicate these two disorders: adenocarcinoma or lymphoma. Small bowel tumours can be the source of obscure gastrointestinal bleeding, and capsule endoscopy is the most accurate method for diagnosis of tumours in such cases. The diagnostic yield of capsule endoscopy for small bowel tumours can be optimised by using colon capsule with a modified protocol in order to examine the small bowel completely.

Conclusion

Gastrointestinal tumours can be diagnosed using capsule endoscopy. The utility of oesophageal device for Barrett's oesophagus is limited, as the biopsies are required.

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Introduction

The invention of capsule endoscopy (CE) in 2001 represented a major progress in the direction of exploration of the small bowel mucosa and generated tremendous hope, challenging the development of non-invasive endoscopy for a high-accuracy examination of the entire digestive tract. Technical improvements in small bowel CE, followed by the development of colon and oesophageal devices represented progress and promise for gastroenterology[1–5]. The experience acquired in the last 10 years was followed by numerous studies regarding the diagnostic yield of oesophageal, small bowel and colon capsule in various disorders[6–9]. In this article, we also summarise our personal experience with CE performances in order to evaluate the initial promises. In daily practice, it is important to know the performances of every device (oesophageal, small bowel, colon CE, etc.), the right indications and the accuracy of examination in the diagnosis of digestive tract neoplasia in order to know which device is the best for a specific indication. Our experience is based on the PillCam CE, the software being provided by Given; there are no reported major differences between the available CE systems[7–11].

Discussion

The authors have referenced some of their own studies in this review. These referenced studies have been conducted in accordance with the Declaration of Helsinki (1964) and the protocols of these studies have been approved by the relevant ethics committees related to the institution in which they were performed. All human subjects, in these referenced studies, gave informed consent to participate in these studies.

Oesophageal capsule endoscopy

In 2004, oesophageal CE (ESO CE) was developed and technically improved in 2007. The examination time is 20 minutes, during which the device acquires images from both the ends at a combined rate of 14 images per second (7 images from each side of the capsule). With this instrument, the real-time observation is possible, and this requires patient to be in a specific position. Main indications of ESO CE are oesophageal varices and Barrett's oesophagus screening[5,12,13].

The accuracy of ESO CE for Barrett's oesophagus is very high; the sensitivity is 92% and the specificity is 95%, which strongly recommend the utility of this device for screening and follow-up of this pathology. The main purpose of screening is adenocarcinoma prevention, and there are serious counterarguments against this procedure. Barrett's oesophagus is a very rare condition, hence screening is cannot be cost-efficient. In Western Europe, the prevalence of Barrett's oesophagus is below 2%[14]. In endoscopy units, the frequency of Barrett's oesophagus diagnosis is 4%, which is elevated (9%) for men older than 50 years[15]. Oesophageal cancer is rare and 40% of cases develop without Barrett's esophagus[16]. Even if the screening programme includes only men older than 50 years, with a history of

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reflux symptoms, the utility of ESO CE is not justified. The studies on the high diagnostic accuracy of ESO CE for Barrett's oesophagus[5,6,17] appreciate only macroscopic lesions; even the correct diagnosis is based on microscopic confirmation of intestinal metaplasia on salmon-coloured mucosa (with or without goblet cells), most importantly is the presence of low or high dysplasia on microscopic examination. The entire strategy of follow-up, treatment and post-therapeutic monitoring is based on biopsies and histological examination. Even if the ESO CE magnifies the images 8×, which allows a better detection of small mucosal lesions (ulcers or elevations) than standard endoscopy, the impossibility of biopsy limits the utility of this device. For Barrett's oesophagus with high-degree dysplasia, the follow-up must be performed with high magnification endoscopy techniques (high-definition, NBI, chromoendoscopy or other vital stain methods) for adequate biopsy level[17–19].

Small bowel capsule endoscopy

CE was first intended for small bowel examination. In our opinion, this part of the digestive tract remains the main indication of CE. The disorders that can be diagnosed with CE procedures are obscure gastrointestinal bleeding (overt of occult) and inflammatory bowel disorders. Coeliac disease complications and small bowel tumours are less frequent indications for CE[20]. The utility of CE in small bowel pathology has an important impact on detection of neoplasic lesions.

Tumours

Neoplasia of the small bowel is a rare pathology; only 3–6% of all digestive cancers have this localisation[21]. Small tumours or those that have an extraluminal development (especially stromal tumours) could be missed by CE[21,22]. Multiple tumours such as familial adenomatous polyposis or Peutz-Jeghers syndrome have higher chances to be visualised than a unique tumour[23]. Larger tumours, more than 10–15 mm, are identified by imaging methods such as small bowel follow-through, CT or MRI. Duodenal or periampullary tumours are frequently missed by CE that passes with high speed at this level[24].

In daily practice, a small bowel tumour is identified by CE performed for obscure gastrointestinal bleeding (overt or occult), for refractory coeliac disease or follow-up of patients with familial adenomatous polyposis or Peutz-Jeghers syndrome (Figure 1). Chances of detecting a small bowel tumour were higher in our experience when we used colon CE devices for small bowel investigation after external activation of the optimal frame rate. This is explained by the double image numbers obtained.

Overt obscure gastrointestinal bleeding represents almost 5% of all gastrointestinal bleeding incidences and the majority are caused by a small bowel lesion[25–27], which is the main indication for small bowel CE. The term 'overt obscure gastrointestinal lesion' is used for clinically manifest bleeding (melaena or haematochesia), with negative repeated upper and lower gastrointestinal endoscopies. The colonoscopy usually reveals blood in the proximal colon and terminal ileum. The performances of CE in identifying the bleeding site and the lesion are remarkable, which are superior to other diagnostic procedures and also cost-efficient. It reduces the hospitalisation period, the time until the cause is identified and the transfusion requirements[28–31].

Occult obscure gastrointestinal bleeding is diagnosed in patients with iron-deficiency anaemia with or without positive faecal occult blood

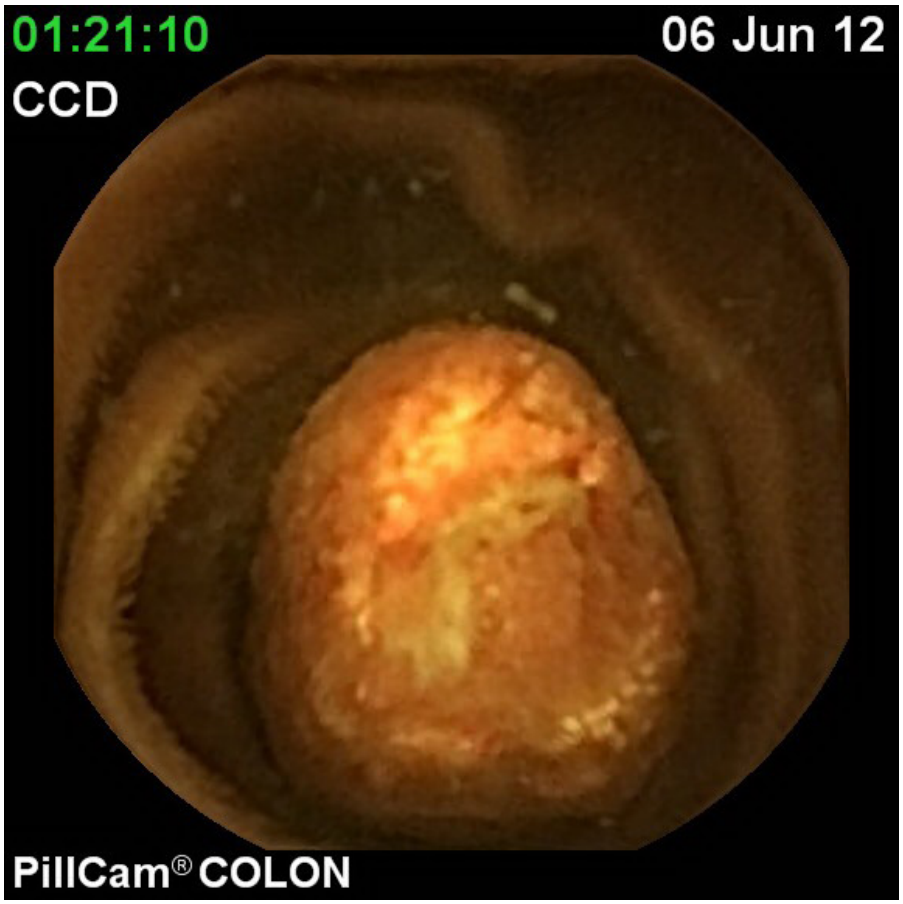

Figure 1: Small bowel polyp in a patient with Peutz-Jeghers syndrome.

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test, with negative repeated upper and lower endoscopies. The diagnostic yield of CE is lower than that in overt gastrointestinal bleeding. A unique lesion such as small tumour might not be identified[32,33]. In a recent systematic review, the percentage of incidence of neoplasia in patients investigated with CE for obscure gastrointestinal bleeding was 8.8%[34].

The initial management of obscure gastrointestinal bleeding (overt or occult) involves repeating the upper and lower endoscopies if previous were negative[26,35]. The same decision might be required with CE, even if the cost is high. For an initial proper examination of small bowel without increasing the costs, we used the colon CE device after external activation of optimal frame rate. The first device for colon CE was swallowed after 1 hour and 48 minutes after external activation. As our interest was in the small bowel examination, the battery capacity allowed us an entire and optimal examination of small bowel. With the second generation of colon CE we preferred also the external activation of optimal frame rate. As we have two registrations, the chances of identifying the source of bleeding are higher as we double the number of images obtained. It is like a second small bowel CE examination. Using this protocol, in some cases we identified the bleeding lesions only in one registration from the two colour video cameras. We preferred to make the examination of the small bowel with the colon capsule, as fast as possible, without preparation, even in haemodynamically unstable patients. The chance of identifying the source of bleeding is higher when the time from the start of the bleeding until the examination, is shorter.

Coeliac disease

Capsule endoscopy is used in coeliac disease because of its high accuracy for specific duodenal atrophic lesions and its excellent correlation with standard endoscopy[36]. There are some studies that have demonstrated a good correlation between macroscopic images obtained by CE and histological aspects[37].

The main indication of CE in coeliac disease is the persistence of symptoms despite a gluten free diet[38–41]. The CE examination might reveal the persistence of atrophic mucosa (not restrictive diet or refractory coeliac disease) or the development of complications: ulcerative jejunoileitis or T cell lymphoma (Figure 2). The malignancy develops in 10%–15% of coeliac disease patients[42,43], the most frequent being T cell lymphoma[44]. The adenocarcinoma is also found in coeliac patients older than 50 years. The surveillance of coeliac disease, especially those with refractory mucosal lesions to gluten free diet or those with specific symptoms such as abdominal pain, weight loss or intestinal bleeding by CE permits a correct and early diagnosis than other imagistic techniques such as entero CT or small bowel follow-through. After a correct identification of the lesions and the approximate localisation, enteroscopy might be necessary for biopsies.

In the largest series of complicated coeliac patients investigated with CE published by Culliford and coworkers in 2005 the percentage of malignancy reported was 2.1%[45].

Crohn's disease

In Crohn's disease, the small bowel is frequently involved as the only localisation or in association with colon lesions[46]. Long-term Crohn's disease

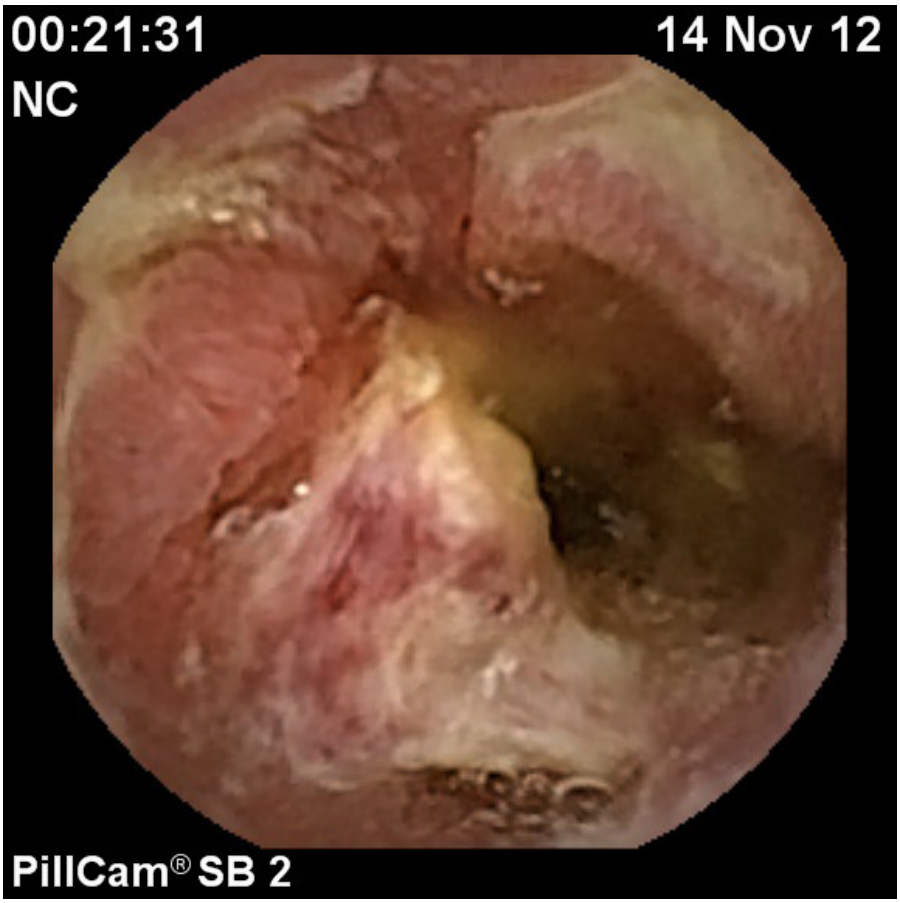

Figure 2: Severe circumferential small bowel mucosal lesions: oedema, erythaema and ulcers suggestive for lymphoma.

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has a high risk for neoplasia, monitoring being required. A recent meta-analysis in patients with Crohn's disease demonstrated a relative risk for small bowel cancer of 28.4 and a relative risk for lymphoma of 1.42[47]. Capsule endoscopy represent a non-invasive procedure in monitoring these patients regarding the assessment of their disease activity and extent, assessment of postsurgical small bowel recurrence and evaluation of mucosal healing[48]. Capsule endoscopy results in management changes in the majority of cases of symptomatic inflammatory bowel disorders[49], meaning the many patients actually do not reach mucosal healing, being at risk for adenocarcinoma development. In these patients repeated examinations are needed, CE being the less aggressive.

Colon CE

There are two generations of colon CE devices. The battery of first device provides 10 hours of image registration, but with an inactive period of one hour and 45 minutes, after the first three active minutes. The second device has a variable frame rate of images acquisition, being able to register till 35 images per second if the speed of capsule is high, which allows a better examination of colonic mucosa[3,4].

The main indications of colon CE are: colorectal cancer screening, colonic polyp detection and inflammatory bowel disorders.

Literature data are confusing regarding the screening of colorectal cancer, as both the diagnosis of colorectal cancer and the polyp detection are considered. Actually, the screening definition is 'a system of checking (a person or a group) for the presence or absence of *a disease'*[50]. We consider that colorectal cancer and colonic polyps must be considered separately[51].

Regarding the colorectal cancer screening, in asymptomatic patients, with medium risk of colorectal cancer, the detection rate was very low: 39%[52,53]. In more selected series the reported detection rate was more elevated: 60%–75% for colorectal cancer and 73% for adenoma. For real life screening in asymptomatic patients, this procedure that misses 2 of 3 cancers could not be a real option, even might increase the adherence to screening programme[54]. Standard colonoscopy has very good results in screening programmes, examination time is very low compared with CE, has the possibility for cleaning improvement also for biopsy and polyp removal and localises more accurate the lesions. Colon CE could be done in symptomatic patients, highly suspected of colonic neoplasia, who refuse or have serious concerns about standard colonoscopy. Only patient preferences, the lack of sedation or analgesia or complication rates are in favour of colon CE.

Regarding colonic polyps, the role of screening is to prevent colorectal cancer through polypectomy. European guidelines recommend for standard colonoscopy a caecum intubation rate of 97% and an adenoma detection rate of 25% for men and 15% for women. These standards are very high, for patients' security and the cost efficiency of screening procedure. For prevention purposes, biopsy and polypectomy are both required[53].

The detection rate of polyps with colon CE has been reported between 64% and 88%[4,53]. This means that 12%–36% of polyps are missed and the potential risks of cancer remain. These data are explained by an inappropriate colon cleaning in almost 50% of patients, the impossibility to improve cleaning during procedure

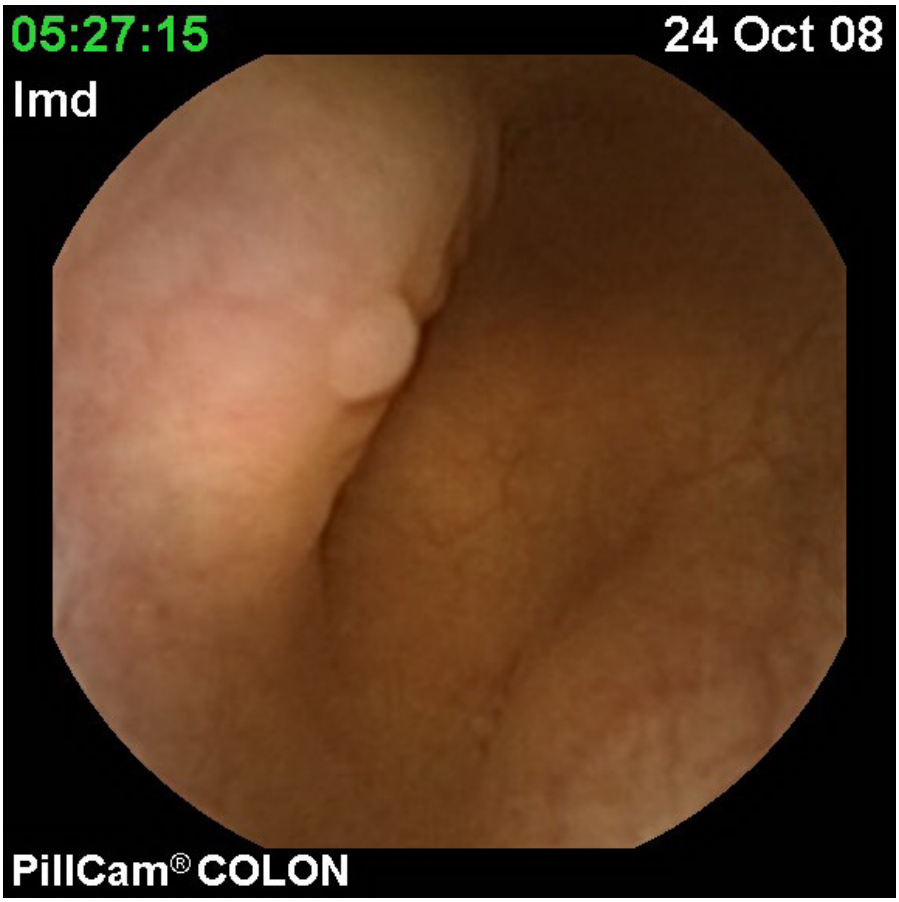

Figure 3: Colonic small polyp.

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and the rapid colon transit in some cases. In case of polyps' identification (Figure 3), standard colonoscopy is mandatory for polypectomy and frequently requires a new preparation, as standard colonoscopy on the same day is not feasible in most endoscopy units and preparation is no longer good at more than ten hours after finishing the CE procedure.

Actually, it is not very important to detect all polyps with colon CE. Detection of one or few polyps is followed by colonoscopy in order to remove all polyps. It is the same situation with sigmoidoscopy-based approach for screening: if an advanced distal polyp is identified during sigmoidoscopy, patients should have a colonoscopy as the risk of proximal advanced polyp is similar or slightly higher in patients with a distal adenoma than in patients with a negative sigmoidoscopy[55]. Using the same strategy with colon CE, the follow-up colonoscopy performed under the most rigorous conditions will overtake the deficiencies of colon CE for polyp detection.

If colon CE is not useful for colorectal cancer screening, it may be useful for colorectal polyp screening. As colon CE is able to magnify eight fold the image it might be helpful for small polyps, flat and serrated adenomas.

Conclusion

Gastrointestinal tumours diagnosis might benefit from capsule endoscopy. The utility of oesophageal device for Barrett oesophagus is limited as the biopsies are required. For small bowel tumours the VCE represent an important diagnostic tool. Small bowel tumours developed spontaneously or as complications of coeliac or Crohn's diseases, being the main reasons to perform capsule endoscopy. Using colon capsule for small bowel improves the tumour detection rate.

For colon cancer diagnosis, colon capsule has low utility. Colorectal cancer screening has no real indications and performances in order to recommend this procedure for practical use. For colorectal polyps screening might represent a real approach, being followed by standard colonoscopy and polypectomy that reduced morbidity from colorectal cancer.

Abbreviations list

CE, capsule endoscopy; ESO CE, oesophageal CE.

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