

Review

Innovative Techniques for the Endoscopic Diagnosis in Inflammatory Bowel Diseases

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REZUMAT

Metode inovatoare de diagnostic endoscopic în bolile inflamatorii intestinale

Diagnosticul de boală inflamatorie intestinală este fundamentat pe asocierea unor criterii endoscopice, radiologice și anatomopatologice. Endoscopia are un rol central în diagnosticul și management-ul pacienților cu boli inflamatorii intestinale, datorită abilității de vizualizare în mod direct a mucoasei și posibilității de a preleva biopsii pentru confirmarea histologică a diagnosticului. Leziunile cu localizare esofagiană, gastrică sau duodenală sunt accesibile diagnosticului prin endoscopie digestivă superioară, iar cele colonice celui prin endoscopie digestivă inferioară; mai greu de evaluat endoscopic este intestinul subțire, leziunile cu această localizare fiind evaluate de obicei inițial prin videocapsulă și mai recent direct prin enteroscopie, care este o metodă endoscopică mai puțin accesibilă, laborioasă și care necesită sedarea pacientului și un endoscopist cu experiență. Actual, primele tipuri de enteroscopie: push-enteroscopia și enteroscopia intraoperatorie, au fost înlocuite de tehnici endoscopice inovatoare: enteroscopia cu balon și enteroscopia spirală, mai puțin invazive și mai eficiente în vizualizarea completă a întregului intestin subțire. Odată cu evoluția tehnologică, examinarea cu videocapsulă și enteroscopia vor deveni disponibile pe scară largă, fiind întocmite deja ghiduri de utilizare a acestora în diagnosticul leziunilor digestive atât în Europa cât și în SUA.

Cuvinte cheie: boli inflamatorii intestinale, diagnostic, videocapsula endoscopică, enteroscopie cu balon, enteroscopie spirală

ABSTRACT

Inflammatory bowel diseases are diagnosed based on a combination of endoscopic, radiological and pathological criteria. Endoscopy plays a central role in the diagnosis and management of patients with inflammatory bowel disease, because of its ability to directly view the lining mucosa and due to the possibility of taking biopsies for the histological confirmation of the diagnosis. Lesions localized in the esophagus, stomach or duodenum are accessible for diagnostic upper gastrointestinal endoscopy, and the colonic lesions can be diagnosed by lower gastrointestinal endoscopy; more difficult to assess endoscopically is the small

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bowel, lesions in this location being usually evaluated initially by videocapsule endoscopy, and recently directly through enteroscopy, which is still a less accessible endoscopic method, being also laborious and requiring patient sedation and an experienced endoscopist. In present, the first types of enteroscopy: push-enteroscopy and intraoperative enteroscopy, were replaced by innovative endoscopic procedures: balloon-enteroscopy and spiral enteroscopy, which are less invasive and more efficient in complete visualization of the entire small bowel. With the evolution of technology, videocapsule examination and enteroscopy will become widely available, guidelines for their use in the diagnosis of gastrointestinal lesions being already prepared both in Europe and in the USA.

Key words: inflammatory bowel diseases, diagnosis, videocapsule endoscopy, balloon-enteroscopy, spiral enteroscopy

Inflammatory bowel diseases, Crohn's disease (CD) and ulcerative colitis (UC), are chronic conditions in which idiopathic inflammation of the gastrointestinal tract wall is the characteristic feature.

The etiology of these disorders is not fully elucidated, proposed causes including environmental, immunological and genetic factors. A consensus hypothesis is that in genetically susceptible individuals, both exogenous factors (eg. Intestinal flora) and factors related to the host (barrier function of epithelial cells, innate and acquired immune response function) produce a chronic immune dysfunction in the intestinal mucosa which is further modified by the action of environmental factors (eg. smoking).

In the absence of a specific etiological agent, these diseases are diagnosed based on clinical, endoscopic and pathological criteria.

CD or UC diagnosis is based on a combination of endoscopic, radiological and pathological criteria documenting granulomatous, segmental and asymmetrical transmural intestinal inflammation in CD or continuous inflammation of the colonic mucosa in UC. (1)

Formulating a proper diagnosis of CD or UC must include the extension, clinical-evolutive pattern, severity of inflammatory flare, intestinal and extraintestinal complications.

Endoscopy plays a central role in the diagnosis and management of patients with inflammatory bowel disease, because of its ability to directly view the lining mucosa and due to the possibility of taking biopsies for the histological confirmation of the diagnosis.

Endoscopy is frequently used in the investigation of patients with various gastrointestinal symptoms,

and plays an important role in the early paraclinical evaluation if the patient presents with digestive hemorrhage, occlusive syndrome / subocclusion or significant abdominal pain, which are relatively frequently described symptoms in people with inflammatory bowel disease.

Lesions localized in the esophagus, stomach or duodenum are accessible for diagnostic upper gastrointestinal endoscopy, and the colonic lesions can be diagnosed by lower gastrointestinal endoscopy; more difficult to assess endoscopically is the small bowel, lesions in this location being usually evaluated initially by videocapsule endoscopy (2-7) and less directly through enteroscopy, which is a less accessible endoscopic method, being also laborious and requiring patient sedation and an experienced endoscopist.

Lower endoscopy (colonoscopy) is the most commonly used endoscopic investigation in the assessment of inflammatory bowel disease, due to the colonic location of UC and the frequent ileo-colonic localisation of Crohn's disease, and serves to: (1) diagnosis of inflammatory bowel disease localised in the large bowel or terminal ileum, (2) differentiation between CD and UC, (3) determination of extension and severity of the disease, (4) evaluation of treatment response, (5) screening for dysplasia (by sampling biopsies or brushing cytology), (6) therapy (eg.: pneumatic dilatation of benign strictures).

Severe colitis, with the presence of deep ulcers or stretched mucosal denudation, is a relative contraindication and complications like perforation or toxic megacolon are absolute contraindications for performing colonoscopy.

The early lesions detected in CD is the aphthoid ulceration, a superficial yellowish-white loss of

substance, of small dimension, well shaped and surrounded by hyperemic halo (**Fig. 1**). Aphthoid ulcers are usually numerous and the lining mucosa interposed between them is apparently normal. As the disease progresses, ulcers increase in size and are stretching both in surface and in depth, giving rise to large and deep ulcers. Ulcers present in advanced stages of the disease often have serpiginous character, each intersecting another and delineating areas of unaffected mucosa ("skip areas"). All these give rise to the appearance of "paving stone" (cobblestone) (**Fig. 2**), highly characteristic endoscopic lesion in CD. Segmental distribution with discontinuous and asymmetric lesions is another characteristic endoscopic feature for CD.

Similar changes may be present in the esophagus, stomach and duodenum at the evaluation by upper gastrointestinal endoscopy. They usually accompany small or large bowel lesions, rarely being described strictly upper gastrointestinal damage in Crohn's disease. In addition, the detection of granulomas or active gastritis in the absence of *Helicobacter pylori* infection in gastric biopsies may help establish the diagnosis of CD. (8)

In UC, lower endoscopy (colonoscopy) performed for diagnostic purpose can be resumed at sigmoidoscopy with biopsy sampling, given the constant involvement of the rectum. Toxic megacolon is an absolute contraindication for performing colonoscopy. The distribution of endoscopic lesions is characteristic in UC: lesions are continuous, with strictly colonic involvement, beginning from the rectum which is always affected and extending proximally till a variable distance. Normally it doesn't outreach the ileocecal valve and in almost all cases there is a strict line of demarcation between the ulcerated and the normal mucosa (1) However it can extend diffusely to the terminal ileum determining the so-called backwash ileitis.(2) An other characteristic feature is the limitation of the damage to the mucosa, the submucosa and the muscular layer being involved only in fulminant forms.

The characteristic macroscopic lesions in UC depend on the severity and duration of the illness. Early lesions are the granular appearance of the mucosa with absence of shine, friability and superficial mucosal ulcerations (not exceeding muscularis mucosae). Initially they are small in size, but are increasing along with disease progression and by confluence may denude large areas of mucosa (**Fig. 3**). Muco-purulent exudate is associated with

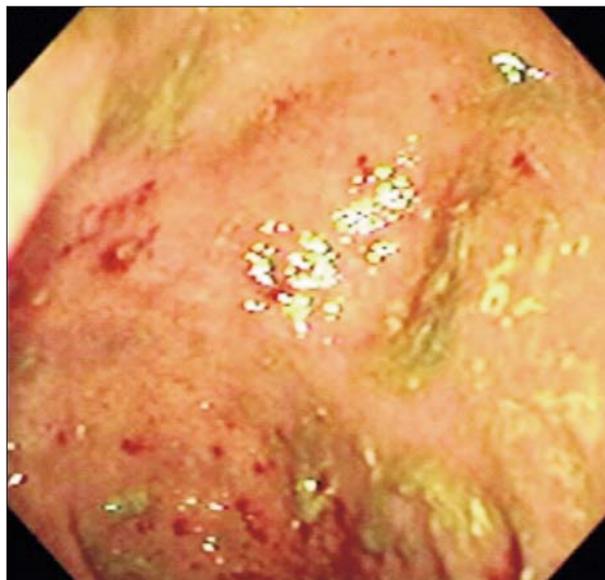


Figure 1. Inflammation in the terminal ileum. Note the areas of inflammation and ulcers in the terminal ileum

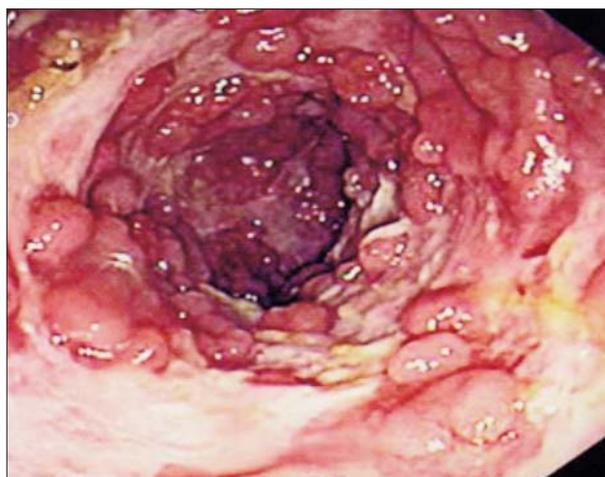


Figure 2. Appearance of "paving stone" highly characteristic of Crohn's disease

the ulcers in active stages of the disease. As colitis is healing, mucosal changes become more restricted (8). The colonic mucosa regenerates by replacing ulcers with granulation tissue and eventually with restitution of mucosal vascular pattern with irregular vascular branches that appear "cut". In areas that were severely inflamed, granulation tissue can protrude in the lumen and by re-epithelization may create the pseudopolyp appearance. These pseudopolyps have no malignant potential, but sometimes it can be difficult to distinguish them macroscopically from adenomatous polyps.

Until recently ulcerative colitis was considered a disease strictly localized in the colon, and for this

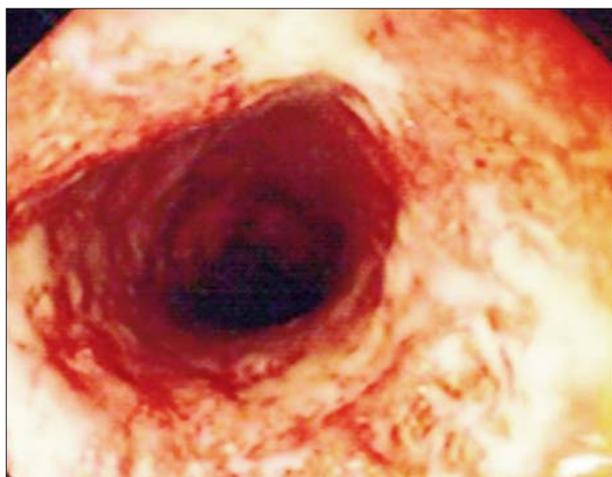


Figure 3. Colonoscopic appearance in UC

reason upper digestive endoscopy was not a part in the investigation plan for its evaluation. However, in the recent years more and more studies reveal the presence of gastric inflammation associated with UC, most often a diffuse *Helicobacter Pylori* negative gastritis, sometimes only identified at the histopathological examination (normal macroscopic appearance at upper digestive endoscopy).

The first studies were performed in the pediatric population with UC and the latest recommendations of international pediatric societies include upper digestive endoscopy in the investigations set for the initial evaluation of inflammatory bowel disease in children.

Articles about gastroduodenal lesions in inflammatory bowel diseases in adults are predominantly isolated case presentations, but there are few studies attesting the presence of diffuse gastritis in UC, unlike in CD in which focal gastritis prevails. In the patients with UC who had undergone proctocolectomy, the presence of diffuse gastritis or duodenitis was proved to be an important predictor of the installation of pouchitis.

It was also found that there is a reduced incidence of gastritis due to *Helicobacter pylori* infection in patients with inflammatory bowel diseases.

The role of upper digestive endoscopy in assessing UC remains a topic of debate for adult patients until a wider experience regarding the upper digestive tract damage in this disease is achieved, but another argument in favor of its use is the need to exclude concomitant gastroduodenal lesions which may be aggravated by the treatments applied for inflammatory bowel disease (such as

ulcers which can be complicated by the corticosteroids or 5-ASA derivatives).

Location of lesions in the small intestine put the biggest problems of diagnosis in Crohn's disease. Capsule endoscopy is used when the disease affects parts of the small intestine that can not be examined by conventional upper or lower gastrointestinal endoscopy. This investigation appears to be more sensitive in detecting early lesions than enterocT or barium enema. (9)

But the existence of a significant risk of capsule retention in patients with asymptomatic strictures, cases in which the surgical removal of the capsule is necessary, is the reason for not using this method widely. (10)

Also, if for the lesions accessible by upper gastrointestinal endoscopy or colonoscopy, biopsy sampling is usually possible since the first assessment, when a pathological change in the small intestine is detected by endoscopic capsule, in order to obtain a definite diagnosis, enteroscopy with intestinal biopsy is required. That is why new enteroscopy techniques were developed, among the first ones used being the push-enteroscopy, which unfortunately can not provide a complete and accurate view of the entire small intestine. (11-13)

Consequently, at the end of the last century intraoperative enteroscopy was developed, the first optic fiber endoscope being used intraoperatively in 1976, (14) and this technique had relatively quickly become the gold standard for investigating small bowel lesions. (15) It allows examination of the entire bowel by introducing an enteroscope through a small enterotomy that the surgeon performs by laparotomy.

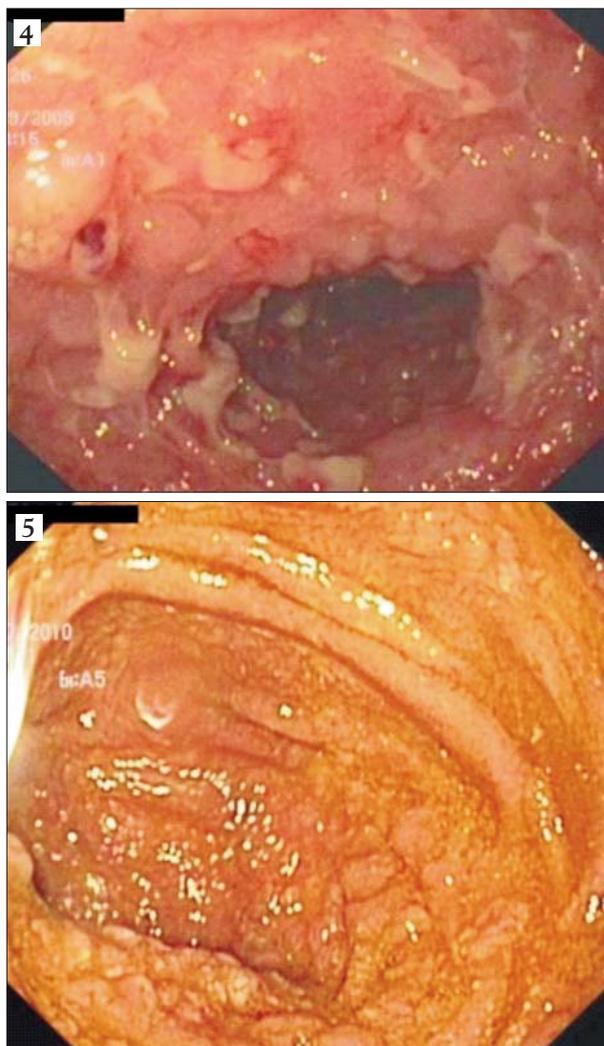
Depending on the situation (location of the lesion established by preoperative imaging methods or intraoperatively by palpation) and on the endoscopy laboratory equipment, small diameter colonoscopes (such as for example the pediatric ones) or even gastroscopes can be used. This invasive approach requires complete equipment of an operating room and anesthesia and aseptic measures similar to those of a conventional abdominal surgery and a good collaboration between the gastroenterologist and the surgeon, knowing that there are only a few surgeons specialized in digestive endoscopy, and even fewer experienced in interventional endoscopy. The risks of this type of intraoperative endoscopy are also not negligible, the most important of them being: the formation of postoperative adhesions, perforation,

intra-abdominal infection risk (abscess or even peritonitis) and wound infection risk, sometimes resulting afterwards in postoperative eventration, plus the anaesthetical risks and other complications such as prolonged postoperative ileus and cardiovascular events during postoperative convalescence. Currently this method is reserved for situations in which an immediate therapeutic intervention is required in continuation of the diagnostic procedure (eg in case of intestinal obstruction or important gastrointestinal bleeding) or when the other less invasive diagnostic methods can not establish the correct diagnosis. (16)

To compensate for the disadvantages of the intra-operative enteroscopy, new endoscopic devices were developed in the early 21st century, which allow the assessment of the small bowel without laparotomy, through natural orifices. In 2001 the Japanese (Yamamoto et al) published the first article about double-balloon enteroscopy (17-18), to whom were added later experiences of other medical centers that have demonstrated the superiority of this technique in the diagnosis of small bowel lesions compared to push-endoscopy (19).

Recently, other enteroscopy techniques have been developed, such as single-balloon enteroscopy, whose diagnostic performances were found to be comparable to those of the double-balloon enteroscopy, and also spiral enteroscopy which allows the small bowel examination in a shorter time (20-24).

Still there are no comparative studies on the effectiveness of these diagnostic methods in the evaluation of patients with small bowel injuries, most of the published research assessing their use in cases of occult gastrointestinal bleeding. Most of the studies published till now still rank videocapsule endoscopy first in the evaluation of small bowel lesions, placing the balloon-enteroscopy second in the line, to be used in case of a positive diagnosis with videocapsule examination - in order to obtain the certain diagnosis by biopsy, or for therapeutic reasons (15,25). However, in the recent years, balloon-enteroscopy techniques tend to become the standard endoscopic visualization method of the small intestine, but is not yet widely available, being reserved for specialized tertiary centers. (Fig. 4, 5) Full intubation of the small intestine has been reported with very different rates in different studies (from 0 to 86%) depending on the presence of factors such as: previous abdominal surgery resulted in postoperative adhesions or obesity, but also



Figures 4-5. Enteroscopy - small bowel involvement in Crohn's disease

according to the endoscopist experience and learning curves (17,18,21,23,26-28).

Some studies are attesting the impossibility of reaching the terminal ileum in a considerable number of cases because of the limited length of the endoscopes (29-31).

However, when balloon- enteroscopy is guided by the results of the previous videocapsule examination, the lesion is found in about 90% of cases (32)

With the evolution of technology, videocapsule examination and enteroscopy will become widely available, guidelines for their use in the diagnosis of gastrointestinal lesions being already prepared both in Europe and in the USA (33,34).

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