

The role of endoscopy in inflammatory bowel disease

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Abstract. – Endoscopy is an essential tool for diagnosis, management and prognostic evaluation of inflammatory bowel disease. However discomfort, potential risks and costs associated to endoscopic examinations should contribute to the narrowing of indications to those cases in which the result of endoscopy is essential to determine a variation in the management strategy.

Ileocolonoscopy performed by an expert endoscopist allows accurate diagnosis of Crohn's disease or ulcerative colitis in up to almost 90% of cases.

Colonoscopy has a prognostic role during a severe flare of disease (the occurrence of severe endoscopic lesions have a negative prognostic value with significantly higher risk not to respond to medical treatment) both in ulcerative colitis and in Crohn's disease; moreover in Crohn's disease the evaluation of recurrent lesions at anastomosis after curative surgery has a strong prognostic role (endoscopic recurrence closely correlates with clinical/surgical recurrence) and preliminary data suggest that mucosal healing assessed with endoscopy after biologic treatments could be associated with a better prognosis.

Finally colonoscopy is essential for cancer surveillance during the long-term follow-up.

Furthermore there are new endoscopic techniques under evaluation in inflammatory bowel disease, like wireless capsule endoscopy or double balloon enteroscopy for the imaging of small bowel, or endoscopic ultrasound for evaluation of strictures or of perianal disease. Finally some operative techniques like balloon dilation could possibly be employed more frequently in the future in the management of Crohn's disease.

Future perspectives in endoscopy for IBD are chromoendoscopy and newer endoscopic imaging techniques, possibly leading to an "in-vivo histology".

Key Words:

Inflammatory bowel disease, Endoscopy, Diagnosis, Prognosis.

Background

Inflammatory bowel diseases (IBD), Crohn's disease (CD) and ulcerative colitis (UC), are inflammatory processes localised to the gastrointestinal tract. Endoscopy can identify features and elemental lesions, useful in the diagnosis of IBD and to differentiate IBD from enterocolitides with known aetiology.

At present the most important and widespread endoscopic technique for the evaluation of IBD is (ileo-) colonoscopy, while the diagnostic field of upper endoscopy is restricted to paediatric patients and to patients with symptoms suggestive of upper gastrointestinal location of Crohn's disease.

In this paper we will review the role of lower endoscopy in IBD, with regards to:

- Diagnosis
- Prognosis
- Cancer surveillance
- Therapy
- Future perspectives

An added value of endoscopy in the diagnosis of IBD is the possibility to obtain biptic sampling of the mucosa, for histological examination.

Endoscopy for Diagnosis of Inflammatory Bowel Disease

Although IBD diagnosis is not a single examination result, to date the most accurate diagnostic technique for inflammatory bowel disease is ileo-colonoscopy, when performed by expert endoscopists.

Endoscopic lesions in IBD are not absolutely specific, nonetheless the contemporary presence of more than one suggestive

finding, together with clinical history and histopathological data could reliably lead to diagnosis.

First of all an expert endoscopist should differentiate IBD from enterocolitides with known aetiology, namely infectious colitides (psudomembranous colitis, Salmonella, Shigella, other infectious or self limiting colitides), ischaemic, radiation or NSAIDS colitides.

Secondly, when IBD is diagnosed, the endoscopist should differentiate whenever possible Crohn's disease from ulcerative colitis. Endoscopic investigation in patients with chronic colitis is fairly accurate for differential diagnosis between ulcerative colitis and Crohn's disease. A prospective study by Pera and colleagues¹ analysed 606 colonoscopies performed in 357 IBD patients and demonstrated an accurate diagnosis in 89% of cases, while in 7% of cases the diagnosis was indeterminate ("IBD, type uncertain", according to Hogdson definition²) and in 4% of cases there were errors in diagnosis. The wrong diagnoses were more frequent (9%) in the subgroup of patients in which endoscopy was performed during a severe flare of disease. The combination of 11 different endoscopic characteristics, more suggestive of Crohn's disease or of ulcerative colitis, was considered for an endoscopic diagnostic score (CD was more likely if values were greater than 4, while UC was more likely if the resulting score was 4 or less), in Table I we report the endoscopic score.

Table I. Endoscopic diagnostic score for differentiation between Crohn's disease (> 4) and ulcerative colitis (≤ 4), adapted from 1

Endoscopic characteristic	Score
<i>Crohn's disease more likely</i>	
Segmental mucosal involvement	+55
Cobblestoning	+8
Aphthoid/serpiginous/linear ulcers	+4
Large/deep ulcers	+4
Spare rectum	+5
Anal lesions	+15
<i>Ulcerative colitis more likely</i>	
Continuous mucosal involvement	-2
Granularity	-3
Loss of vascular pattern	-2
Erosions	-7
Rectal involvement	-2

Prognostic Role of Endoscopy

Endoscopy is indicated in ulcerative colitis during severe flares of disease, for its prognostic value. Although it looks to be overall safe³, it is advisable to perform examination without bowel cleansing, with minimal or no insufflation, and to stop the examination when severe lesions are detected, as further examination has no additional prognostic values, and is potentially more at risk for perforation.

Carbonnel et al.⁴ demonstrated that total colonoscopy is feasible in 86% of cases in severe UC (73/85), and when severe endoscopic lesions (Table II) are present, colectomy is much more likely: only 3/46 patients with severe endoscopic lesions (7%) compared with 29/39 patients without such lesions (74%) retained their colon after medical treatment (OR 41).

Data on the prognostic role of severe endoscopic lesions are confirmed by Travis and colleagues⁶ and in a large retrospective series of 149 episodes of severe ulcerative colitis⁷. In the group of severe UC studied at our Institution⁷, 91% of non-responders to medical treatment compared with 34% of responders had severe endoscopic lesions at colonoscopy (OR > 20).

The presence of the same severe endoscopic lesions in patients with Crohn's colitis is equally a negative prognostic marker for the risk of colectomy for refractoriness to medical treatments. Patients with active Crohn's disease and severe endoscopic lesions had a relative risk of 6.7 compared to patients without severe lesions⁵. This findings support the role of endoscopic examination also in Crohn's disease acute colitis.

Ileo-colonoscopy is indicated in Crohn's disease for its prognostic role after surgical resection. An examination performed 3, 6 or 12 months after surgery allows to detect early recurrence of the disease, and the type and severity of the lesions visible at the anastomosis correlate with the likelihood of clinical recurrence or of need for further surgical operations. Clinical recurrence occurs in about 50% of cases at 3 years, while endoscopic recurrence is much more frequent (up to 60-70% at 6-12 months). However patients with less severe endoscopic lesions according to Rutgeerts' score⁸ (less than 5 aphthoid ulcers at anastomosis site), have a lower risk of clin-

Table II. Definition of severe lesions according to Carbonnell et al⁴.

Severe endoscopic lesions	Moderate endoscopic lesions
Large deep ulcers Loss of mucosal layer (with or without mucosal isles) 'Well-like' ulcers Large mucosal abrasions	Erythematous mucosa Superficial ulcers Deep ulcers involving less than 10% of the surface

ical recurrence, with cumulative 7 years recurrence risk of 9% compared with 100% risk at 4 years for patients with more severe endoscopic recurrence (Rutgeerts' score i_2 or greater, Table III).

Some studies have shown that endoscopic healing cannot be achieved with steroids⁹⁻¹¹, while thiopurine drugs treatment results in a slow but significant mucosal healing^{12,13}. Recently it was demonstrated that infliximab treatment induces a rapid and significant mucosal healing¹⁴, and it was shown that mucosal healing with infliximab is associated to significantly less health care consumption^{15,16}.

This interest focused on assessment of endoscopic healing and therefore on endoscopic activity measurement lead to re-evaluation of possible activity scores. To date the most widespread endoscopic activity score for CD is the CDEIS¹⁷, however although the CDEIS is reproducible^{9-11,17,18}, the scoring system is time consuming, complicated and not very user-friendly, so that it is practically unfit for daily practice outside clinical trials.

Recently a European multicenter prospective study was carried out in order to develop and validate a new and simpler score of endoscopic activity for Crohn's disease, the Simple Endoscopic Score for Crohn's Disease, or "SES-CD"¹⁹.

This study showed that the variables considered are highly reproducible, with excellent interobserver agreement for their scor-

ing, and that clinical-endoscopical correlation is significant, although not different for the SES-CD or the CDEIS. In Table IV there are the definitions of SES-CD variables; SES-CD results from the sum of all the scores given for all the endoscopic variables in the explored ileocolonic segments (Table V shows the scoring form for SES-CD)¹⁹. At present the use of endoscopic activity scores, however, has no role outside clinical trials and should not be considered in routine clinical examinations.

Although it is a common practice in some referral centers, there is less agreement for the indication to colonoscopy in patients affected by UC, in order to monitor mucosal healing after medical treatment of a flare of disease. Limited data in favour of this strategy are published to date, and they would suggest that in patients with complete healing, remission would last longer²⁰. At present this is not a strict indication to endoscopy for UC patients.

The Role of Endoscopy in Cancer Surveillance

Another accepted indication for endoscopy in ulcerative colitis (but also in long standing Crohn's colitis) is its use in the cancer surveillance of long-standing disease. At present guidelines²¹ prescribe one colonoscopy every 3 years during the second decade of disease, every 2 years during the third decade, and

Table III. Rutgeerts' score for endoscopic recurrence of Crohn's disease⁸.

Degree	Endoscopic findings
i_0	No lesion in the neoterminal ileum
i_1	≤ 5 aphtoid lesions
i_2	> 5 aphtoid lesions, with normal mucosa between, or skip areas or larger lesions limited to anastomosis
i_3	Diffuse aphtoid ileitis, with mucosa extensively inflamed
i_4	Diffuse inflammation, large ulcers, nodules and/or stenoses

Table IV. Definitions of SES-CD variables¹⁹.

Variable	SES-CD values			
	0	1	2	3
Size of ulcers	None	Aphthous ulcers (Ø 0.1 to 0.5 cm)	Large ulcers (Ø 0.5 to 2 cm)	Very large ulcers (Ø > 2 cm)
Ulcerated surface	None	< 10%	10-30%	> 30%
Affected surface	Unaffected segment	< 50%	50-75%	> 75%
Presence of narrowings	None	Single, can be passed	Multiple, can be passed	Cannot be passed

yearly afterwards in case of pancolitis. After 8-10 years of disease it is advisable to perform a total colonoscopy in every patient, in order to verify the real extent of disease involvement²¹. Although no prospective study was published on the item, it is common feeling that such an intensive surveillance program, together with adequate bioptic sampling and dedicate histopathologic examination could lead to early detection of precancerous lesions and to minimize the risk of diagnosing colon cancer in a more advanced stage.

In this field it is possible that newer molecular biology techniques could allow a better selection of patients at higher risk (to submit to more aggressive surveillance programs) or to detect more reliably early changes in the cellular cycle, before cancer develops (stool tests, molecular tests on tissue samples, ...).

Therapeutic Role of Endoscopy

During the past years some techniques used in routine operative endoscopy were adopted also for the treatment of complication of IBD. Endoscopic pneumatic balloon dilation of Crohn's strictures (both post-surgical and in non-operated patients) was proposed instead of mini-invasive surgical procedures^{22,23}, and it was also proposed to add to this standard strategy the infiltration of long-lasting steroids, with the goal to reduce the risk of recurrence²⁴. Although long lasting results were reported with this technique²⁵, the exact role of balloon dilation in the management of colonic and anastomotic strictures is not clearly stated.

Future Perspectives of Endoscopy in IBD

Although colonoscopy is essential for IBD management, the great majority of the small

Table V. SES-CD scoring form¹⁹.

	Ileum	Right colon	Transverse colon	Left colon	Rectum	Total	
Presence and size of ulcers (0-3)							+
Extent of ulcerated surface (0-3)							+
Extent of affected surfac (0-3)							+
Presence and type of narrowings (0-3)							+
SES-CD =							

bowel is not accessible to classic endoscopy; other endoscopic techniques are under investigation or in use for evaluation of small bowel lesions: push enteroscopy, wireless video-capsule enteroscopy²⁶, double balloon enteroscopy²⁷. The diagnostic yields and the prognostic value of elemental lesions observed with these techniques are still a matter of investigation, but their field of application is growing constantly.

One of the problems with normal endoscopy is the detection of dysplasia during surveillance colonoscopy. To overcome this issue several strategies were proposed, like chromoendoscopy²⁸, magnification endoscopy, narrow band imaging²⁹, fluorescence imaging, elastic scattering spectroscopy or optical coherence tomography, but none of these techniques became a standard in routine endoscopy nor in IBD patients endoscopy. If newer molecular techniques could allow a selection of patients at higher risk, these newer ancillary endoscopic techniques could be employed allowing a more targeted bioptic sampling or leading to a real “*in vivo histology*”.

Finally some techniques, like endoscopic ultrasound (EUS), are advocated for evaluation of strictures or of perianal/penetrating disease; at present the role of EUS in the diagnostic evaluation of IBD patients have still to be assessed outside the field of perianal disease. Endoscopic operative techniques (like balloon dilation of stenoses) commonly used in routine endoscopy were used also in IBD, although a careful selection of cases is needed. Other more “futuristic” operative endoscopic approaches could be studied in IBD, for example endoscopic anastomoses could be studied in selected cases with indication to conservative surgery, in order to minimize invasiveness of surgical procedures.

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