



Endoscopic vs ultrasonographic findings related to Crohn's Disease recurrence: A prospective longitudinal study at 3 years

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(SICUS)

Abstract

Background and aims: Ileocolonoscopy (IC) is the gold standard for assessing Crohn's Disease (CD) recurrence after ileo-colonic resection. In a prospective longitudinal study we compared findings related to CD recurrence when using techniques visualizing either the luminal or the extraluminal surface (IC and small bowel follow through, SBFT vs Small Intestine Contrast Ultrasonography, SICUS).

Methods: From 2003 to 2008, 25 CD patients undergoing ileo-colonic resection were enrolled. Clinical assessment (CDAI) was performed at 1, 2 and 3 years. IC was performed at 1 ($n=25$) and 3 years ($n=15$), SBFT at 2 years ($n=21$) and SICUS at 1 ($n=25$), 2 ($n=21$) and 3 years ($n=15$). Recurrence was assessed by SBFT and SICUS (bowel wall thickness, BWT) when using IC as gold standard.

Results: At 1 year, all patients were inactive and recurrence was detected by IC in 24/25 (96%) and by SICUS in 25/25 patients. At 2 years, 6/21 patients (29%) were active and recurrence was detected by SBFT in 12/21 (57%) and by SICUS in 21/21 patients. At 3 years, 5/15 patients (33%) were active, IC showed recurrence in 14/15 (93%), and SICUS in 15/15 patients. The endoscopic score at 1 year was higher in patients developing relapse at 2 years ($n=5$) than in patients maintaining remission ($n=10$) (median: 4, range 3–4 vs 2, range 0–3; $p=0.003$). The same finding was not observed by using SICUS (median BWT at 1 year: 5, range 4–7 vs 3.7, range 3.5–6; $p=0.19$).

Conclusions: Although IC and SICUS provide a different view of the bowel wall, in experienced hands SICUS provides findings compatible with endoscopic recurrence after ileo-colonic resection for CD. Discrepant findings may be observed in a low proportion of patients with minor lesions related to CD recurrence.

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1. Introduction

Postoperative recurrence after ileo-colonic resection is a feature of Crohn's Disease (CD). Ileocolonoscopy currently represents the gold standard for assessing CD recurrence, graded according to the Rutgeerts' score.^{1,2} Endoscopic recurrence after curative ileo-colonic resection is observed in almost 73% of patients at 1 year and in almost 90% of patients at 3 years, even in the absence of other symptoms.^{1–3} Severe endoscopic recurrence² is observed in about one-third of patients at 3 months and in almost two-thirds of patients at 6 months after surgery.^{1–4} The severity of the lesions as assessed by endoscopy has been shown to predict clinical relapse, and the frequency of symptomatic recurrence parallels the follow up length.^{5–7} Surgical reintervention is indeed required in about 15–40% of CD patients at 10 years and in about 50–70% of patients at 20 years after initial resection.^{5,6} Beside the severity of endoscopic lesions after resection, risk factors for a more aggressive course after surgery include active smoking, especially in women, disease extent and a fistulizing pattern.^{5–9}

Identification of the subgroup of patients undergoing early symptomatic CD recurrence may be useful for a timely treatment and possible relapse prevention. Due to these observations, non-invasive procedures alternative to ileocolonoscopy may well be of use for assessing CD recurrence. Small bowel follow through (SBFT) and enteroclysis have been proposed,^{10,11} although providing a high radiation exposure to the patient. These 2 techniques also show a low sensitivity in terms of visualization of minor lesions related to CD recurrence, even in experienced hands.^{10,11}

More recently, Small Intestine Contrast Ultrasonography (SICUS) has been proposed for detecting small bowel lesions in patients with suspected or known CD (>95%).^{12–14} SICUS findings compatible with CD recurrence include an increased bowel wall thickness (BWT), thus providing the view of the extraluminal small bowel lesions. In a prospective longitudinal study we recently reported that SICUS may represent an alternative non-invasive technique useful for assessing CD recurrence after ileo-colonic resection.^{15,16} However, by our knowledge, no studies compared findings compatible with CD recurrence as assessed by techniques visualizing either the inner or the extraluminal small bowel surface. The possible clinical usefulness of procedures providing different views of the peri-anastomotic area after ileo-colonic resection, as also the natural history of the extraluminal lesions (*i.e.* BWT) associated with CD recurrence is undefined.

We therefore aimed to compare, in a prospective longitudinal study, findings related to CD recurrence as assessed by procedures visualizing either the luminal surface (*i.e.* ileocolonoscopy or SBFT) or the extraluminal surface (SICUS) in a cohort of CD patients prospectively followed up at 1, 2 and 3 years after ileo-colonic resection. The possible relation between techniques providing different views of the peri-anastomotic area and the clinical outcome at 3 years was also investigated.

2. Materials and methods

2.1. Patients

In a prospective longitudinal study, 25 patients undergoing elective ileo-colonic resection for CD (12 M, median age 35

range 16–69 years) were consecutively enrolled from July 2003 to July 2005, and followed up for 3 years. All patients were under regular follow up at the GI Unit of the Università "Tor Vergata" of Rome, Italy, and resected by the same surgical Unit. The diagnosis of CD was made according to conventional criteria.²

Before surgery, disease assessment was performed within 6 months by using ileocolonoscopy in all 25 patients and also by SBFT in 16 out of the 25 patients.

Clinical characteristics of each patient are summarized in Table 1. Risk factors for recurrence and other characteristics were recorded, including smoking habits (yes: $n=10$; no: $n=12$; ex: $n=3$), familial history of IBD (yes: $n=5$; no: $n=20$), disease site (ileum alone: $n=17$; ileum-colon: $n=8$), age at diagnosis of CD (median 28; range 15–49), disease duration (median 6 years; range 0.5–29), presence of typical CD granuloma at histological examination of the surgical specimen (yes: $n=1$; no: $n=24$). Inclusion criteria included: CD patients under regular follow up undergoing elective ileo-colonic resection, age ranging from 15 to 70 years, surgical resection including all the involved tissue, written informed consent. *Exclusion criteria:* Patients with relevant comorbidities (renal, cardiovascular diseases), body mass index (BMI) >30 (not allowing a proper ultrasonographic assessment), or with low adherence to follow the study protocol, including repeated clinical assessments and procedures for 3 years.

2.1.1. Study protocol

From July 2003 to July 2005, all eligible CD patients with no complications after ileo-colonic resection, fulfilling the above reported inclusion criteria were prospectively enrolled. Reasons for drop out were reported. After surgery, all patients were treated with mesalamine (2.4 gr/day) within 14 days from resection. Treatment changes during the follow up were made according to current clinical criteria.²

Clinical activity was assessed according to the Crohn's Disease Activity Index (CDAI)¹⁷ every 6 months for 3 years after surgery.

At 12 months, all patients underwent clinical assessment (CDAI) and recurrence was assessed by using ileocolonoscopy as a gold standard,² followed by SICUS. The two procedures were performed by 2 independent gastroenterologists, unaware of previous findings. At 24 months, patients in follow up underwent clinical assessment (CDAI), and lesions compatible with CD recurrence were evaluated by using SICUS and SBFT. At 36 months, patients underwent clinical assessment (CDAI) and lesions compatible with CD recurrence were assessed by using ileocolonoscopy and SICUS.

2.1.2. Clinical assessment

Clinical assessment (CDAI) was performed every 6 months for 3 years, together with routine blood tests.

2.1.3. Ileocolonoscopy

Endoscopical assessment of recurrence was made at 1 and 3 years, and the severity of recurrence assessed according to the Rutgeerts' score (0–4)^{1,3} (Fig. 1, panel a). Endoscopic findings were documented in all patients by photographic verification. Ileocolonoscopy was performed with or without sedation (ipnovel *i.v.*), according to patients' request. During

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