Role of bowel ultrasound as a predictor of surgical recurrence of Crohn's disease

This is the author's manuscript

Original Citation:

Availability:
This version is available http://hdl.handle.net/2318/1632791 since 2019-07-30T14:09:20Z

Published version:
DOI:10.3109/00365521.2013.777774

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Role of Bowel Ultrasound as a predictor of surgical recurrence of Crohn's disease.

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Abstract

In Crohn's disease natural history, about 80% of the patients require surgery, which is not curative: unfortunately, the disease recurs in many patients.

Objective: To investigate the role of intestinal ultrasound to predict the risk of post-operative surgical recurrence in Crohn's disease.

Material and methods: 196 patients, with ileal or ileocolonic Crohn's disease, undergoing intestinal resection, were retrospectively enrolled. All patients underwent bowel ultrasonography 6–15 months after resection. Wall thickness at the anastomosis level was measured, and thickening > 3[mm] was evaluated as risk factor of long-term need for reoperation.

Results: Patients who have a bowel wall thickness > 3[mm] have a RR of surgical recurrence = 2.1 (95% CI = 1.12 – 3.74) higher than those with a thickness of ≤ 3[mm]. The absolute incidence of new surgical intervention is 13% in patients with thickness of 3[mm], 28% in patients with thickness > 3[mm], 29.1% with thickness > 4[mm], 34% with thickness > 5[mm], 40% with thickness > 6[mm].

Conclusions: Bowel wall thickness > 3[mm] at ultrasound may be a non-invasive predictor of early surgical recurrence after ileo-colonic resection.

Key words: Bowel ultrasonography; Crohn's disease; Post-surgical recurrence.
1. Introduction

About 80% of the patients with Crohn's disease require surgery [1]. Smoking, prior bowel surgery, penetrating disease behavior, perianal location, extended resection of the small intestine, no prophylactic treatment are predictors of early recurrence after ileo-colonic resection [1].

Endoscopic recurrence predicts clinical recurrence and severe endoscopic recurrence predicts poor prognosis [2]. None invasive examinations include [3]: wireless capsule endoscopy that, after excluding stricture, seems accurate in small series, but no validated score is available; CT enteroclysis, but ionising radiation exposure limits its use; MR that may be as powerful as ileocolonoscopy in diagnosing postoperative recurrence and in predicting the clinical outcome.

Many studies show that bowel ultrasonography is valuable for predicting the risk of surgical intervention in patients never surgically treated [4,5], and for identifying post-surgical recurrence (Fig. 1) [6-10].

Fig. 1.

Only one study considers bowel ultrasound as a predictor of post-surgical recurrence in patients treated with conservative surgery (strictureplasty) [11].

2. Methods
We performed a retrospective study on 196 patients that underwent ileal or ileo-colonic resection with ileo-colonic anastomosis between December 1993 and March 2009 (all diagnosis of Crohn’s disease was confirmed at histologic examination). All patients underwent bowel ultrasound after at least 6 months from surgery.

The study was reviewed and authorized by Local Ethical Committee. Bowel ultrasound was performed in these years with the following ultrasonographic equipments: ESAOTE AU4, ESAOTE Technos, ESAOTE My Lab 70, TOSHIBA Aplio. A first evaluation of the bowel was made with a convex transducer (frequency 3.5[MHz]) and then with a high frequency linear-array transducer (7.5–10[MHz]).

The 4 ultrasonographers who performed the examinations were all radiologists having at least 3 years’ experience in ultrasound scanning of patients with intestinal bowel diseases and working in the same department. Each investigation was performed by one radiologist, C. T., S. A, R. D., D. P., that respectively performed 69, 55, 39 and 33 investigations. During the procedure the involved tract wall was examined in a transverse section, from the central hyperechoic line of the lumen to the outer hyperechoic margin of the wall with a linear-array transducer. Wall thickness of the ileo-colonic anastomosis was calculated as the average of at least 3 measurements; at the end of the US investigation measurements of intestinal wall at the level of ileo-colonic anastomosis were reported on a standardized form.

Ileocolonoscopy was performed in a little percentage of patients and in different time respect to bowel ultrasound because of the invasiveness of a
colonoscopy in patients that underwent resection for Crohn disease of the ileum, so is impossible to prove any correlation.

The CDAI was calculated in the follow up visits. Bowel wall thickness (whose normal value is \( \leq 3\text{[mm]} \) \[12\]) was evaluated as a predictor of surgical recurrence: we assumed a wall thickness at the anastomosis level > 3[mm] as a predictive value for the risk of surgical recurrence.

*Statistical analysis*

Predictive value were calculated for bowel wall thickness thresholds more or less than 3[mm]. Confidence interval (CI) was set at 95%, being statistical significance set at p value less than 0.05.

All statistical analyses were performed using MedCalc software (MedCalc Software, version 9.2.1.0).

**3. Results**

Clinical characteristics of the study population are reported in Table I.

Other data: 176 patients were clinically inactive (CDAI < 150 at the time of the bowel ultrasound); bowel ultrasound was performed after a mean time of 12 months (range 6–15 months) after the resection.

*Table I*
The average follow-up was 114 months (range: 25–205 months) after surgery.

Major surgical complications occurred in 12 out of 196 patients (6%). Obviously, our final analysis refers to the reoperation for the disease recurrence and not to the reoperation for these immediate complications (Table II).

Table II

The rate of surgical recurrence for the whole population was 20.4% (40 of 196 patients), at a mean distance of 78 months from previous surgery (range: 20 months - 175 months).

4. Discussion

This is the largest retrospective study with the longest follow-up period in our knowledge.

We think that knowing how many patients, 1 year after surgery, had a physiological bowel thickness (3[mm]) (50.5%) and how many had a pathological bowel thickness (> 3[mm]) (49.5%) is interesting in order to assess the entity of changes in the management of the subpopulation at greater risk of surgical recurrence (i.e. how many patients might be affected by a change of therapy to better their disease natural history) (Fig. 2).
Patients with bowel wall thickness at the anastomosis > 3[mm] run a double relative risk (statistically significant) of undergoing surgery compared to patients with a thickness of 3[mm] (Table III).

**Table III**

The absolute incidence of new surgical intervention is 13% in patients with thickness of 3[mm], 28% in patients with thickness > 3[mm], 29.1% with thickness > 4[mm], 34% with thickness > 5[mm], 40% with thickness > 6[mm]. (Fig 3).

Although the population with a wall thickness > 3[mm] had taken steroids or immunosuppressants or biologics in a greater percentage (45% vs. 36%), it revealed a higher percentage of surgical recurrence (28% vs. 13%). The data suggest that these patients would have had an even more aggressive natural history of the disease if they had followed the same therapy as the population with a thickness ≤ 3[mm] (Fig. 4).
Some critical issues should be considered. The retrospective design of the study represents a limitation and this is the reason because some patients were examined by ultrasound precociously and other late, but the same reasons are also the strength of the study: the “real world” setting of the data, the long follow-up period and the fact that all patients were treated in these years by the same doctor (A. M.).

In conclusion, bowel wall thickness at the anastomosis > 3[mm] at bowel ultrasound performed 1 year after surgery could be added to the non-invasive predictors of early recurrence after ileo-colonic resection besides those implying a double risk of recurrence, such as smoking [13], previous bowel surgery, penetrating behavior of the disease, perianal location, extensive small bowel resection, absence of prophylactic treatment. A prospective study would be useful, in which the population with bowel wall thickness > 3[mm] 1 year after surgery would be treated with more aggressive drugs (topical or systemic steroids, immunosuppressants, biological agents), to investigate the possibility of bettering their disease natural history and extending their surgical recurrence-free interval. Ileocolonoscopy remains the gold standard in predicting recurrence. MR represent alternative tool for this indication; wireless capsule endoscopy appear promising, but it will require further investigation [3].
5. References


[13] Bernstein C, Rawsthorne P, Cheang M, Blanchard JF. A population-based case control study of
potential risk factors for IBD. Am J Gastroenterol 2006;101:993-1002.
**Table I.** Characteristics of the study population

[n = 196 Crohn’s disease patients]

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males/Females</td>
<td>115/81</td>
</tr>
<tr>
<td>Median age, years (range)</td>
<td>42 (16 – 82)</td>
</tr>
<tr>
<td>Duration of Crohn’s disease, years (range)</td>
<td>8 (0 – 54)</td>
</tr>
<tr>
<td>Smoking habit at surgery, n (%)</td>
<td></td>
</tr>
<tr>
<td>Ever smoker</td>
<td>86 (43.9)</td>
</tr>
<tr>
<td>Never smoker</td>
<td>110 (56.1)</td>
</tr>
<tr>
<td>Previous surgery, n (%)</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>139 (70.9)</td>
</tr>
<tr>
<td>1</td>
<td>41 (20.9)</td>
</tr>
<tr>
<td>2</td>
<td>14 (7.1)</td>
</tr>
<tr>
<td>&gt;2</td>
<td>2 (1.0)</td>
</tr>
<tr>
<td>Total length of bowel resection (cm)</td>
<td></td>
</tr>
<tr>
<td>&lt; 50</td>
<td>140 (71.4%)</td>
</tr>
<tr>
<td>&gt;= 50</td>
<td>56 (28.6%)</td>
</tr>
<tr>
<td>Indications for surgery, n (%)</td>
<td></td>
</tr>
<tr>
<td>Strictures</td>
<td>103 (52.6)</td>
</tr>
<tr>
<td>Fistula</td>
<td>54 (27.6)</td>
</tr>
<tr>
<td>Refractoriness to medical therapy</td>
<td>34 (17.3)</td>
</tr>
<tr>
<td>Perforation</td>
<td>5 (2.6)</td>
</tr>
</tbody>
</table>
### Table II. Major surgical complications

<table>
<thead>
<tr>
<th>Patients with major surgical complications</th>
<th>12 (6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications:</td>
<td></td>
</tr>
<tr>
<td>• anastomotic dehiscence</td>
<td>10</td>
</tr>
<tr>
<td>• entero-cutaneous fistula</td>
<td>1</td>
</tr>
<tr>
<td>• hemorrhage</td>
<td>1</td>
</tr>
<tr>
<td>• occlusion</td>
<td>1</td>
</tr>
<tr>
<td>Reoperation</td>
<td>12</td>
</tr>
<tr>
<td># of patients with anastomosis wall thickness &gt; 3 [mm] 1 year after operation</td>
<td>6 (50%)</td>
</tr>
<tr>
<td># of patients with surgical recurrence</td>
<td>5 (41.7%)</td>
</tr>
</tbody>
</table>
**Table III.** RR of surgical recurrence

<table>
<thead>
<tr>
<th>Wall thickness</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 3[mm]</td>
<td>2.1 (95% CI = 1.12 ÷ 3.74)</td>
</tr>
<tr>
<td>&gt; 4[mm]</td>
<td>2.0 (95% CI = 1.14 ÷ 3.49)</td>
</tr>
<tr>
<td>&gt; 5[mm]</td>
<td>2.2 (95% CI = 1.25 ÷ 3.70)</td>
</tr>
<tr>
<td>&gt; 6[mm]</td>
<td>2.5 (95% CI = 1.44 ÷ 4.24)</td>
</tr>
</tbody>
</table>
Fig. 1. Ileo-colonic anastomosis with wall thickening in both the ileal (↘) and colonic (←) side.

Fig. 2. Thickness of the bowel wall at ultrasound performed 1 year after surgery.

Fig. 3. Surgical recurrence rate.

Fig. 4. Medications at the time of the bowel ultrasound.