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

Teresa Cammarota <sup>a</sup>, Davide Giuseppe Ribaldone <sup>b</sup>, Andrea Resegotti <sup>c</sup>,  
Alessandro Repici <sup>d</sup>, Silvio Danese <sup>e</sup>, Gionata Fiorino <sup>e</sup>, Antonino Sarno <sup>a</sup>,  
Daniela Robotti <sup>a</sup>, Paola Debani <sup>a</sup>, Giovanni Bonenti <sup>a</sup>, Rinaldo Pellicano <sup>b</sup>,  
Nicoletta Sapone <sup>b</sup>, Daniele Simondi <sup>b</sup>, Francesca Bresso <sup>f</sup>, Marco Astegiano <sup>b</sup>

<sup>a</sup> Radiologia 5, Department of Radiology, AOU S. Giovanni Battista, Turin, Italy

<sup>b</sup> Department of Gastro-Hepatology, S. Giovanni Battista (Molinette) Hospital, Turin, Italy

<sup>c</sup> 7th Department of Surgery, S. Giovanni Battista (Molinette) Hospital, Turin, Italy

<sup>d</sup> Digestive Endoscopy Unit, IRRCS Istituto Clinico Humanitas, Milano, Italy

<sup>e</sup> Humanitas Clinical and Research Center, Via Manzoni 56, 20089 Rozzano, Milan, Italy

<sup>f</sup> Gastrocentrum medicin, Karolinska university hospital, Stockholm, Sweden

Teresa Cammarota: Radiologia 5, Department of Radiology, AOU S.

Giovanni Battista, Via Cherasco 23, 10126 Turin, Italy; tel

(0039)3336035799, fax (0039)0116335853,

tcammarota@molinette.piemonte.it

Davide Giuseppe Ribaldone: Department of Gastro-Hepatology, S.

Giovanni Battista (Molinette) Hospital - SGAS, Via Cavour, n° 31, 10123

Turin, Italy; tel (0039)3476861126, fax (0039)0116333623,

davrib\_1998@yahoo.com

Andrea Resegotti: 7th Department of Surgery, S. Giovanni Battista

(Molinette) Hospital, Corso Bramante, n° 88, 10126 Turin, Italy; tel

(0039)3358227678, fax (0039)0116335938,

aresegotti@molinette.piemonte.it

Alessandro Repici: Digestive Endoscopy Unit, IRRCSS Istituto Clinico

Humanitas, Milano, Italy; alessandro.repici@humanitas.it

Silvio Danese: Humanitas Clinical and Research Center, Via Manzoni 56,

20089 Rozzano, Milan, Italy; tel (0039)0282244771, fax

(0039)0282245101, sdanese@hotmail.com

Gionata Fiorino: IBD Center, IRCCS Humanitas Via Manzoni 56, 20089

Rozzano, Milan, Italy; gionata.fiorino@humanitas.it

Antonino Sarno: Radiologia 5, Department of Radiology, AOU S.

Giovanni Battista, Via Cherasco 23, 10126 Turin, Italy; tel

(0039)0116335832, fax (0039)0116335853, antonino.sarno@gmail.com

Daniela Robotti: Radiologia 5, Department of Radiology, AOU S.

Giovanni Battista, Via Cherasco 23, 10126 Turin, Italy; tel

(0039)0116335832, fax (0039)0116335853,

drobotti@molinette.piemonte.it

Paola Debani: Radiologia 5, Department of Radiology, AOU S. Giovanni

Battista, Via Cherasco 23, 10126 Turin, Italy; tel (0039)0116335832, fax

(0039)0116335853, pdebani@molinette.piemonte.it

Giovanni Bonenti: Radiologia 5, Department of Radiology, AOU S.

Giovanni Battista, Via Cherasco 23, 10126 Turin, Italy; tel

(0039)0116335832, fax (0039)0116335853,

gbonenti@molinette.piemonte.it

Rinaldo Pellicano: Department of Gastro-Hepatology, S. Giovanni Battista

(Molinette) Hospital - SGAS, Via Cavour, n° 31, 10123 Turin, Italy; tel

(0039)0116333565, fax (0039)0116333623,

rinaldo\_pellican@hotmail.com

Nicoletta Sapone: Department of Gastro-Hepatology, S. Giovanni Battista

(Molinette) Hospital - SGAS, Via Cavour, n° 31, 10123 Turin, Italy; tel

(0039)0116333565, fax (0039)0116333623, nicoletta.sapone@alice.it

Daniele Simondi: Department of Gastro-Hepatology, S. Giovanni Battista

(Molinette) Hospital - SGAS, Via Cavour, n° 31, 10123 Turin, Italy; tel

(0039)3333917118, fax (0039)0116333623, danisimondi@hotmail.com

Francesca Bresso: Gastrocentrum medicin, Karolinska university hospital,

Hälsovag 7-9, 14183 Stockholm, Sweden; tel +46 8 6089143, fax: +46 8

7745538, Francesca.Bresso@ki.se

Marco Astegiano: Department of Gastro-Hepatology, S. Giovanni Battista

(Molinette) Hospital - SGAS, Via Cavour, n° 31, 10123 Turin, Italy; tel

(0039)3356348383, fax (0039)0116333623,

mastegiano@molinette.piemonte.it

**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  $\leq$  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  $\leq 3$ [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).

**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  $\leq 3$ [mm] (Table III).

**Table III**

The absolute incidence of new surgical intervention is 13% in patients with thickness of  $\leq 3$ [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).

**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  $\leq 3$ [mm] (Fig. 4).

**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].

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**Table I.** Characteristics of the study population

[n = 196 Crohn's disease patients]

Males/Females	115/81
Median age, years (range)	42 (16 – 82)
Duration of Crohn's disease, years (range)	8 (0 – 54)
Smoking habit at surgery, n (%)	
Ever smoker	86 (43.9)
Never smoker	110 (56.1)
Previous surgery, n (%)	
Never	139 (70.9)
1	41 (20.9)
2	14 (7.1)
>2	2 (1.0)
Total length of bowel resection (cm)	
< 50	140 (71.4%)
>= 50	56 (28.6%)
Indications for surgery, n (%)	
Strictures	103 (52.6)
Fistula	54 (27.6)
Refractoriness to medical therapy	34 (17.3)
Perforation	5 (2.6)

**Table II.** Major surgical complications

Patients with major surgical complications	12 (6%)
Complications:	
• anastomotic dehiscence	10
• entero-cutaneous fistula	1
• hemorrhage	1
• occlusion	1
Reoperation	12
# of patients with anastomosis wall thickness > 3[mm] 1 year after operation	6 (50%)
# of patients with surgical recurrence	5 (41.7%)

**Table III.** RR of surgical recurrence

Wall thickness	RR
> 3[mm]	2.1 (95% CI = 1.12 ÷ 3.74)
> 4[mm]	2.0 (95% CI = 1.14 ÷ 3.49)
> 5[mm]	2.2 (95% CI = 1.25 ÷ 3.70)
> 6[mm]	2.5 (95% CI = 1.44 ÷ 4.24)



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.