

# Severity of Postoperative Recurrence in Crohn's Disease: Correlation Between Endoscopic and Sonographic Findings

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**Background:** Crohn's disease (CD) recurrence is currently assessed by ileocolonoscopy. Small intestine contrast ultrasonography (SICUS) visualizes the small bowel lesions in CD, although its role after curative resection is undefined. We aimed to investigate the accuracy of SICUS in assessing CD recurrence after ileocolonic resection when using ileocolonoscopy as a gold standard. The correlation between the bowel wall thickness (BWT) measured by SICUS and the endoscopic score of recurrence was also assessed.

**Methods:** The analysis included 72 CD patients with ileocolonic resection requiring ileocolonoscopy, undergoing SICUS within 6 months. Recurrence was assessed by ileocolonoscopy using the Rutgeerts' score. SICUS was performed after PEG ingestion and findings compatible with recurrence included: increased BWT (>3 mm), bowel dilation (>25 mm) or stricture (<10 mm).

**Results:** Ileocolonoscopy detected recurrence in 67/72 (93%) patients. SICUS detected findings compatible with recurrence in 62/72 (86%) patients (5 false negative (FN), 4 false positive (FP), 1 true negative (TN), 62 true positive (TP)), showing a 92.5% sensitivity, 20% specificity, and 87.5% accuracy for detecting CD recurrence. The BWT detected by SICUS was correlated with the Rutgeerts' score ( $P = 0.0001$ ;  $r = 0.67$ ). The median BWT, the extent of the ileal lesions, and the prestenotic dilation were higher in patients with an endoscopic degree of recurrence  $\geq 3$  versus  $\leq 2$  ( $P < 0.001$ ) and the lumen diameter was lower in patients with a Rutgeerts' score  $\geq 3$  versus  $\leq 2$  ( $P < 0.0001$ ).

**Conclusions:** Although SICUS and ileocolonoscopy provide different views of the small bowel, SICUS shows a significant correlation with the endoscopic findings. SICUS may represent an

alternative noninvasive technique for assessing CD recurrence after ileocolonic resection.

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**Key Words:** Crohn's disease, postoperative recurrence, ultrasonography, ileocolonoscopy, ileocolonic resection

Surgical resection of the affected bowel is required in almost two-thirds of Crohn's disease (CD) patients.<sup>1</sup> Postoperative recurrence after ileocolonic resection is a feature of CD.<sup>2–6</sup> Follow-up of CD patients after surgery includes the assessment of both clinical and endoscopic recurrence, ileocolonoscopy representing the gold standard for this purpose. As ileocolonoscopy is quite an invasive procedure,<sup>2</sup> alternative noninvasive techniques are needed in order to assess the postoperative recurrence of CD.<sup>7–17</sup>

Transabdominal ultrasonography (TUS) has been proposed for detecting small bowel lesions in patients with suspected or known CD, showing a sensitivity of 67%–84% and 81%–95%, respectively.<sup>18–25</sup> The use of oral contrast significantly increases the sensitivity of ultrasonography for assessing small bowel lesions in CD patients with suspected or known diagnosis (>95%).<sup>24–26</sup> In particular, small intestine contrast ultrasonography (SICUS) performed by an experienced sonographer may visualize not only established CD lesions (i.e., stenosis with possible prestenotic dilation), but also minor changes of the small bowel wall.<sup>26–28</sup> In experienced hands, SICUS has been shown to detect intestinal lesions in patients with suspected small bowel diseases with a high (>95%) sensitivity and specificity, when compared with small bowel follow-through and enema.<sup>26</sup> SICUS has been shown to be more accurate than TUS for assessing small bowel CD lesions, although the experience of the sonographer significantly affects the accuracy of both techniques, particularly of TUS.<sup>26</sup>

The sensitivity of TUS as assessed by the bowel wall thickness (BWT) in identifying the endoscopic CD recurrence after ileocolonic resection has been investigated in 2 studies, showing 82% sensitivity.<sup>29,30</sup> The use of a noninvasive technique, such as ultrasonography, in the follow-up of CD patients after surgery is advisable in order to reduce the radiation exposure and the use of the quite invasive ileocolonoscopy.

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The possible role of SICUS in the assessment of CD recurrence is under investigation as, to our knowledge, only 2 studies evaluated this issue.<sup>31,32</sup> In a prospective longitudinal study, our findings supported the usefulness of SICUS for assessing CD recurrence after ileocolonic resection when using ileocolonoscopy as a gold standard.<sup>31</sup> This finding was confirmed by a different group, reporting that a BWT >4 mm assessed by SICUS is the best cutoff for differentiating the severity of CD recurrence.<sup>32</sup>

Current management of CD patients after curative resection includes a more aggressive medical treatment in patients with early postoperative asymptomatic recurrence, for possible relapse prevention.<sup>33</sup> Therefore, the development of noninvasive and repeatable techniques able to detect CD recurrence in the early postoperative period are needed for proper follow-up and treatment of resected patients.

On the basis of these observations, we aimed to investigate the possible usefulness of SICUS for assessing the postoperative recurrence of CD in patients under regular follow-up after ileocolonic resection. The specific aim was to evaluate the possible correlation between the severity of CD recurrence as assessed by SICUS and by ileocolonoscopy, considered the gold standard.

## MATERIALS AND METHODS

From May 2004 to April 2008, all patients with ileocolonic resection for CD performed at any time before enrolment, requiring ileocolonoscopy according to clinical criteria, and under regular follow-up in our Gastrointestinal Unit were prospectively enrolled. Clinical activity was assessed at time of endoscopy according to the Crohn's Disease Activity Index (CDAI).<sup>34</sup>

### Study Protocol

Patients underwent both ileocolonoscopy and SICUS within 6 months. In all patients, SICUS and ileocolonoscopy were performed by 2 independent investigators (E.C., L.B.) unaware of previous endoscopic or sonographic findings. At the end of the study the usefulness of SICUS for assessing CD recurrence was analyzed when considering ileocolonoscopy as a gold standard.

For all patients, clinical details (CDAI, hematoclinical assessment, treatment) were available on the basis of records prospectively recorded during the follow-up.

### Ileocolonoscopy

Indication for ileocolonoscopy included conventional clinical criteria for all patients.<sup>33</sup> The degree of recurrence was assessed according to Rutgeerts' score (0–4).<sup>3</sup> Endoscopic findings were documented in all patients by photographic verification. Ileocolonoscopy was performed in 46 (64%) patients in deep sedation (propofol), in 16 (22%) patients with midazolam alone, and in 10 (14%) patients without sedation, according to patients' request.

### SICUS

SICUS was performed as previously described,<sup>26–28</sup> after the ingestion of 375 mL (range 250–500 mL) of oral contrast solution (Promefarm, Milano, Italy) using 3.5- and 5-MHz convex and linear-array transducers (Hitachi, EUB 6500, Japan). Sonographic findings compatible with CD recurrence included an increased BWT (>3 mm) for at least 4 cm at the perianastomotic area, as previously reported.<sup>26</sup> The following additional sonographic findings were considered compatible with CD lesions: 1) small bowel dilation, defined as a lumen diameter >2.5 cm; 2) small bowel stricture, defined as lumen diameter <1 cm, measured at the level of maximally distended loop, independently from the presence of prestenotic dilation; 3) fistulae, defined as hypoechoic tract with or without hyperechoic content; 4) mesenteric adipose tissue alteration and/or masses; and 5) abscesses identified as roundish anechoic lesions, with an irregular wall, often presenting internal echoes and posterior echo enhancement.

### Statistical Analysis

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of SICUS in detecting CD recurrence was calculated using ileocolonoscopy as a gold standard. This analysis was performed by considering both the whole group of 72 patients and, separately, patients subgrouped according to clinical characteristics of the disease, including the time interval from surgery (at different years and separately <3 versus ≥3 years) and the prevalent pattern of the lesions at time of surgery (fibrostricturing versus fistulating). The correlation between the severity of recurrence as assessed by these 2 techniques was investigated by considering the perianastomotic BWT (mm) as assessed by SICUS and the endoscopic degree of recurrence (Rutgeerts' score: 0–4). Differences between patients subgrouped according to clinical, endoscopic, or sonographic parameters were searched using the unpaired Student's *t*-test.

## RESULTS

Clinical characteristics of the study population are reported in Table 1. As indicated, during the study period 72 patients (38 female; median age 44, range 16–73 years, 58 clinically inactive, median disease duration 114 months, range 12–492) with ileocolonic resection for CD had ileocolonoscopy and SICUS performed within 6 months. All 14 patients clinically active at the time of endoscopy underwent SICUS within a median of 1 month (range 1–90 days), and in both clinically active and inactive ( $n = 58$ ) patients the CDAI was comparable at the time of the 2 investigations. Treatment at time of endoscopy and SICUS was similar, including anti-TNF $\alpha$  therapies in 3 patients

**TABLE 1.** Clinical Characteristics of the 72 CD Patients with Previous Ileocolonic Resection

Females	38 (52.7%)
Disease location	
Neoterminal ileum	37 (51%)
Neoterminal ileum and colon	31 (44%)
Colon only	1 (1%)
Jejunum and neoterminal ileum	3 (4%)
Disease behavior	
Fibrostricturing	42 (58%)
Fistulating	30 (42%)
Smoking habits	
Nonsmoker (%)	32 (44.5%)
Smoker (%)	21 (29%)
Exsmoker (%)	19 (26.5%)
Surgical resections	
1	54 (75%)
≥ 2	18 (25%)
Indication for surgery	
Abscesses	14 (19.5%)
Occlusion	52 (72 %)
Fistulae (2 E-E, 1 E-V, 1 E-C)	4 (5.5%)
Suspected appendicitis	2 (3%)
Time from the last resection (months)	18 (3-396)
CDAI (median, range)	85 (0-416)

E-E, entero-enteric; E-V, entero-vesical; E-C, entero-cutaneous.

(2 certolizumab, 1 infliximab; with concomitant azathioprine [AZA], and/or 5-aminosalicylate [5-ASA] in 2), steroids in 17 (prednisone 2, budesonide 15, with concomitant AZA, 1), AZA in 3, 5-ASA only in 47, while 2 patients used no drugs.

### Ileocolonoscopy

Recurrence was detected by ileocolonoscopy in 67/72 (93%) patients. The degree of recurrence was Grade 4 in 34/67 (51%) patients (associated with stenosis not passed by the endoscope in 22), Grade 3 in 9/67 (13%) patients, Grade 2 in 17/67 (25%) patients, and Grade 1 in 7/67 (11%) patients (Grade 0 in 5 patients). The median degree of endoscopic recurrence in the 67 patients was 3 (range 1–4). Among the 22 patients with endoscopic stenosis, at the time of investigation 6 were clinically active (4 with subobstructive symptoms) and 16 inactive (2 undergoing ileocolonic resection within 3 months for subobstructive symptoms). The endoscopic degree of recurrence was significantly correlated with the CDAI value ( $r = 0.27$ ;  $P = 0.03$ ).

The time from the last resection showed a marked variation between patients (Table 1). A comparable amount

of patients were observed when subgrouped according to previous resection performed in the previous <3 or ≥3 years ( $n = 39$  and  $n = 33$ , respectively). When the frequency of endoscopic recurrence was compared in these 2 subgroups, no significant difference was observed between patients with ileocolonic resection performed <3 versus ≥3 years before ileocolonoscopy (patients with recurrence: 37/39; 94.8% versus 30/33; 90.9%, respectively;  $P = NS$ ).

Additional endoscopic findings were observed in 13 out of 72 (18%) patients, including: information regarding the colorectal anastomosis in the only 2 patients with both ileocolonic and colocolonic anastomoses (showing recurrence in 1), inflammatory micropolyps (<0.5 cm) ( $n = 4$ ), angiodysplasia ( $n = 1$ ), aphthoid or deep ulcers in the colon ( $n = 5$ ), diverticulae in the sigmoid colon ( $n = 1$ ).

### SICUS

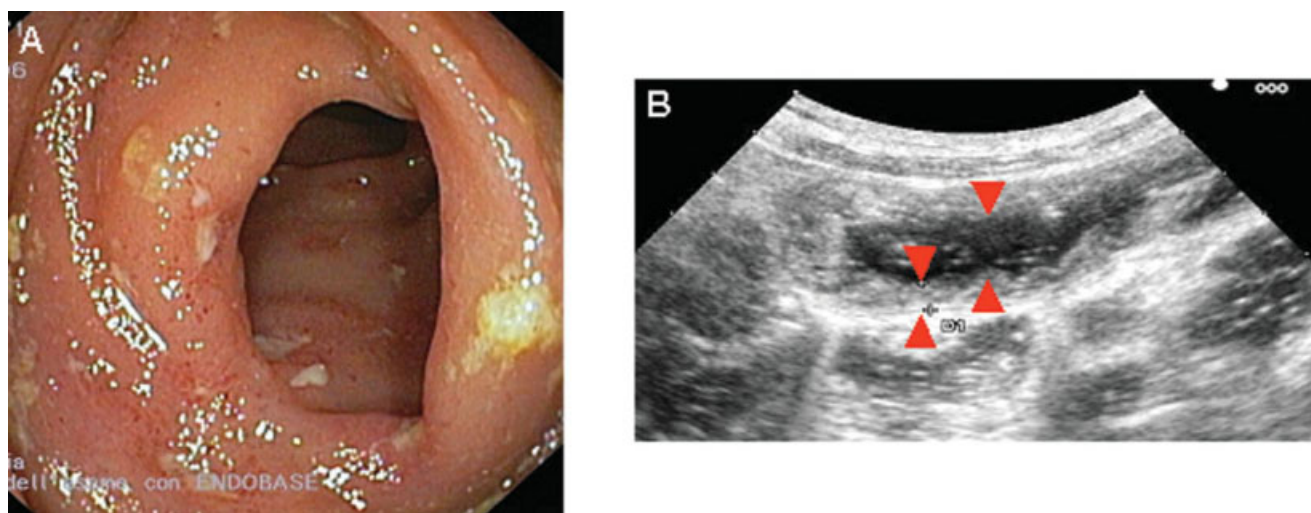
SICUS was well tolerated in all patients and no side effects were observed during or after this procedure. Sonographic findings compatible with recurrence were detected in 62/72 (86%) patients. When considering the whole group of 72 patients, the median BWT was 5 mm (range 3.5–10 mm). SICUS detected strictures in 31/72 (43%) patients, associated with bowel dilation above stricture in 16/31 (51.6%), showing a median lumen of 28 mm (range 25–32). Different from the endoscopic score, no significant correlation was observed between the BWT and CDAI value at time of sonographic assessment ( $r = 0.2$ ;  $P = 0.1$ ). When subgrouping patients according to indication for surgical resection, the BWT did not significantly differ between patients with fistulating ( $n = 32$ ) versus fibrostricturing ( $n = 40$ ) disease (BWT: 5 mm, range 3–9.5 versus 4.5 mm, range 3–10;  $P = NS$ ).

Additional sonographic findings included: enteroenteric fistulae in 3/72 (4%), lymph nodes enlargement in 1/72 (1.4%), mesenteric adipose tissue alteration 5/72 (7%), and jejunal involvement in 6/72 (8%) patients. No abdominal abscesses were detected.

SICUS provided additional findings in the subgroup of 22 patients showing at endoscopy a stenosis not allowing visualization of the ileum. In this subgroup of 22 patients, SICUS allowed the assessment of the neoterminal ileum above the anastomotic stenosis, showing the extent of the ileal lesions (median 13.75 cm, range 5–25), the presence of lumen narrowing at the anastomotic level in all 22 patients (median 4.5 mm, range 2–9), and ileal dilation above anastomotic stenosis in 9 out of 22 patients (41%) (median 20 mm, range 20–35).

### Comparison Between Sonographic and Endoscopic Findings

Sonographic findings compatible with recurrence were detected in 62/72 (86%) patients showing endoscopic



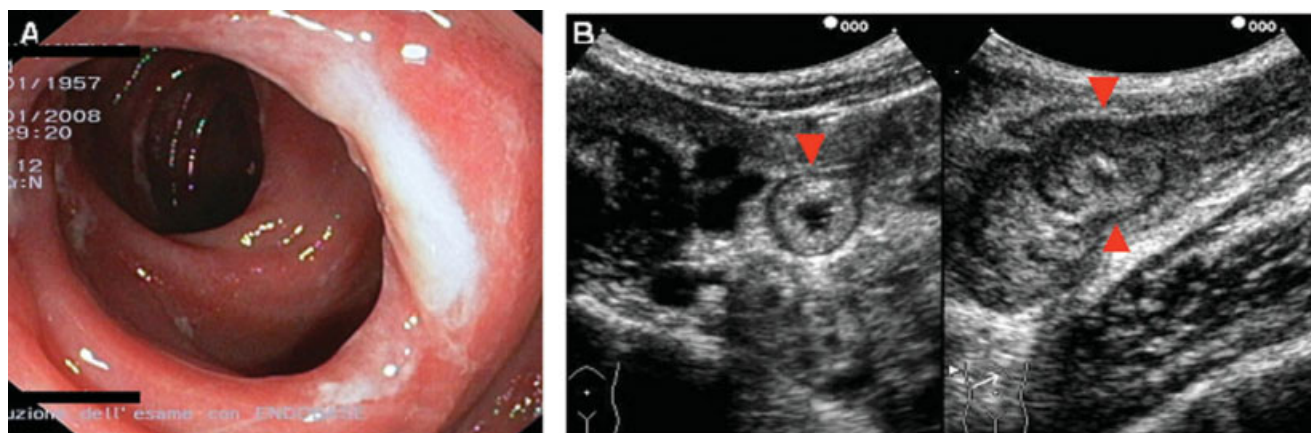
**FIGURE 1.** A,B: Perianastomotic area from a CD patient (P.M.) with ileocolonic anastomosis (side-to-side), as assessed by ileocolonoscopy (A) and SICUS (B) 6 months after surgery. A: ileocolonoscopy showing CD recurrence at the anastomosis and a diffuse aphthous ileitis in neoterminal ileum (Rutgeerts' score: Grade 3). B: Perianastomotic area from the same patient, showing an increased BWT (5 mm; n.v.  $\leq 3$  mm) (arrows), with no stricture or loop dilation above lesions.

recurrence (Figs. 1A,B, 2A,B). When using ileocolonoscopy as a gold standard for assessing CD recurrence, using SICUS there were 4 FP, 62 TP, 1 TN, and 5 FN findings. SICUS therefore showed a 92.5% sensitivity, 20% specificity, 94% PPV, 16.6% NPV, and 87.5% accuracy in detecting CD recurrence. The endoscopic degree of recurrence was  $\leq 2$  in all 5 patients showing FN sonographic findings (Grade 2:  $n = 4$ ; Grade 1:  $n = 1$ ). The BWT was  $\leq 4.5$  mm in all 4 patients showing FP sonographic findings (3.5 mm:  $n = 1$ ; 4 mm:  $n = 2$ ; 4.5 mm:  $n = 1$ ). Figure 3 shows, for each patient, the BWT and the endoscopic degree of recurrence, including FP and FN findings. As

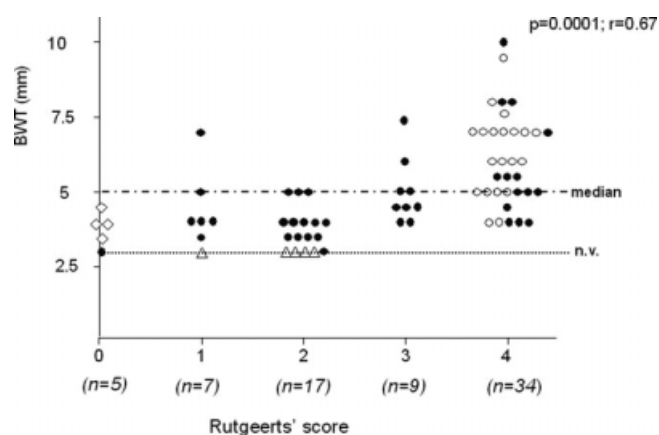
indicated, a significant correlation was observed between the perianastomotic BWT and the Rutgeerts' score ( $P < 0.0001$ ;  $r = 0.67$ ) (Fig. 3).

A significant correlation was also observed between the perianastomotic BWT and the endoscopic degree of recurrence when subgrouping patients according to the time interval from surgery ( $\geq 3$  years:  $P = 0.001$ ,  $r = 0.63$  in 33 patients;  $< 3$  years:  $P = 0.0001$ ,  $r = 0.57$ ;  $n = 39$ ) (Fig. 4A,B).

As SICUS allows the detection of small bowel lesions, comparisons between sonographic and endoscopic findings were analyzed separately in patients showing



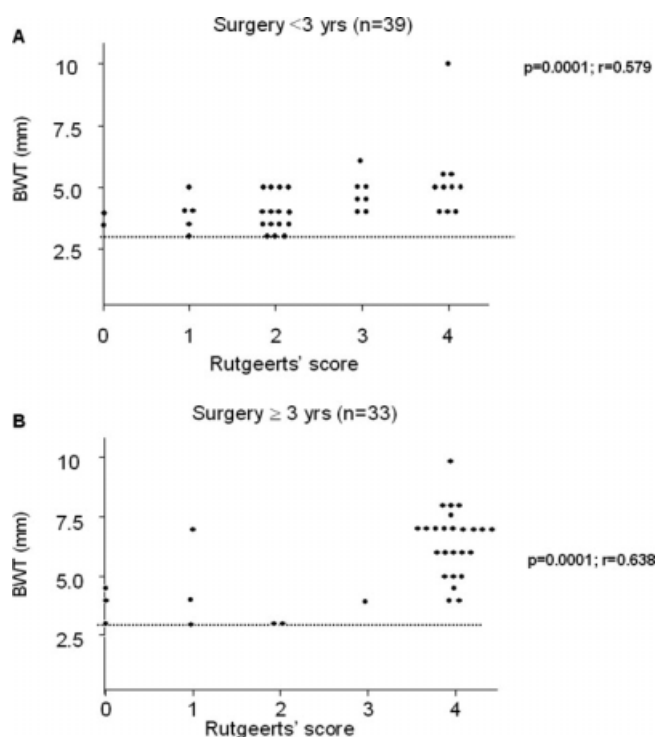
**FIGURE 2.** A,B: Perianastomotic area from a CD patient (D.L.A.) with ileocolonic anastomosis (side-to-side), as assessed by ileocolonoscopy (A) and SICUS (B) 12 months after surgery. A: ileocolonoscopy showing recurrence involving the anastomosis and the neoterminal ileum, with more than 5 aphthae (Rutgeerts' score: Grade 2). B: Perianastomotic area from the same patient showing an increased BWT (6 mm; n.v.  $\leq 3$  mm) (arrows), with no stricture or ileal loop dilation.



**FIGURE 3.** The graph shows, for each of the 72 patients, the correlation between the BWT at the perianastomotic level as assessed by SICUS (mm) and the endoscopic degree of recurrence (Rutgeerts' score) (white squares = FP; white triangles = FN). As shown, a significant correlation was observed ( $r = 0.67$ ;  $P = 0.0001$ ). White circles represent patients with endoscopic score of Grade 4, associated with stenosis. Dotted line indicates the median BWT (n.v. = normal cutoff value of BWT, 3 mm).

established ileal lesions visualized by SICUS (Grade  $\geq 3$ : diffuse aphthous ileitis, larger ulcers, nodules, and/or narrowing) or in patients with recurrence limited to the anastomosis with possible minor ileal lesions (Grade  $\leq 2$ : aphthoid ulcers or lesions confined to the ileocolonic anastomosis).<sup>3</sup> This analysis showed that the median BWT was significantly higher in patients with an endoscopic score of recurrence  $\geq 3$  (5.5 mm, range 4–10;  $n = 43$ ) versus  $\leq 2$  (4 mm, range 3–7;  $n = 29$ ;  $P = 0.0001$ ). In patients with an endoscopic score  $\geq 3$  versus  $\leq 2$ , a significantly higher median BWT, extent of the lesions, and prestenotic dilation were observed (median prestenotic dilation 20 mm, range 20–25 versus 20 mm, range 30–35, respectively;  $P = 0.001$ ) (Table 2). Accordingly, the lumen diameter was significantly lower in patients with a Rutgeerts' score  $\geq 3$  versus  $\leq 2$  (Table 2).

In order to evaluate and compare the clinical outcome in patients grouped according to endoscopic and sonographic findings, among the 58 quiescent CD patients at the time of examination, 11 relapsed within 1 year. When considering the Rutgeerts' score as a predictor, clinical relapse was observed in 1 out of the 25 (4%) patients with a score  $\leq 2$ , and in 10 out of the 33 (30%) patients with a score  $\geq 3$ . However, when considering the sonographic BWT as a predictor, clinical relapse was observed in 5 out of 40 (12.5%) patients with a BWT between 3–5 mm (4 mm in 2; 5 mm in 3 patients), and in 6 out of the 18 (33%) patients with a BWT  $\geq 6$  mm. Additional surgical resection within 1 year was required by only 3 out of the 58 (5%) inactive patients.



**FIGURE 4.** A,B: The graphs show the correlation between the BWT in the perianastomotic area as assessed by SICUS (mm) and the endoscopic degree of recurrence (Rutgeerts' score; Grade 0–4) in patients with ileocolonic resection with a time interval  $< 3$  years ( $n = 39$ ) (A) or  $\geq 3$  years ( $n = 33$ ) (B) from enrolment. As shown, a significant correlation was observed in both subgroups.

### DISCUSSION

The growing use of radiologic techniques in CD management, together with the younger age at diagnosis of CD during the last years,<sup>35</sup> is raising concern about the radiation exposure, indicating the need of radiation-sparing techniques in these patients. We therefore investigated the role of sonography using oral contrast for evaluating the postoperative recurrence of CD in patients with ileocolonic resection when using ileocolonoscopy as a gold standard. Although sonography is promoted in continental Europe,<sup>36</sup>

**TABLE 2.** SICUS Findings in Patients with an Endoscopic Degree of Recurrence  $\leq 2$  vs.  $\geq 3$  (Rutgeerts' Score)

SICUS Parameters	Rutgeerts' Score $\leq 2$ ( $n = 29$ )	Rutgeerts' Score $\geq 3$ ( $n = 43$ )	P-value
BWT (mm)	4 (3-7)	5.5 (4-10)	$P = 0.0001$
Lumen diameter (mm)	10 (5-15)	6.5 (2-15)	$P = 0.0001$
Lesion extent (cm)	5 (0-15)	10 (4-30)	$P = 0.0001$

Results are expressed as median and range.

very few studies investigated the possible role of this technique for assessing the postoperative recurrence of CD, reporting a high sensitivity (81%–82%), and specificity (86%–100%).<sup>29,30</sup> The use of oral contrast, together with operator experience, significantly increases the accuracy of sonographic assessment of ileal lesions in CD,<sup>26–28</sup> although only 2 studies investigated the usefulness of this technique in assessing CD recurrence.<sup>31,32</sup> As recent evidence supports the need of a more aggressive treatment in patients with early endoscopic recurrence, even if asymptomatic,<sup>33,37</sup> a noninvasive technique in the early postoperative period may identify patients at risk of a more aggressive course after surgery. These observations prompted us to investigate the possible usefulness of SICUS for assessing the postoperative recurrence of CD. In our series, SICUS showed a high sensitivity (92.5%), PPV (94%), and accuracy (87.5%) for detecting lesions compatible with CD recurrence as assessed by ileocolonoscopy. These results were observed by 2 independent investigators unaware of previous endoscopic or sonographic findings, but not blind in terms of both a previous diagnosis of CD and of an ileocolonic anastomosis for the disease. However, in our CD population SICUS showed a low specificity (20%) and NPV (16.6%), most likely in relation to the low number of TN findings ( $n = 5$ ). When compared with previous findings, a lower sensitivity (82%) and a comparable PPV (93%) was observed, although associated with a higher specificity (94%) and NPV (84%).<sup>32</sup> Discrepancies between the 2 studies are most likely related to the different number of tested patients (72 versus 40), particularly regarding the subgroup with no recurrence (5 versus 18) and to the different time intervals from surgery.<sup>32</sup>

In our CD population, 5 FN findings were detected by SICUS when using 3 mm as a normal cutoff value.<sup>26,38</sup> However, all these 5 FN findings were detected in patients showing an endoscopic degree of recurrence  $\leq 2$ , and therefore included patients with no established ileal lesions detectable by SICUS (i.e.,  $< 5$  aphthoid ulcers and/or anastomosis). We also detected 4 FP findings, in 4 patients with a BWT ranging from 3.5–4.5 mm, including values below the observed median BWT in our study population (5 mm). Discrepant findings arising from sonographic and endoscopic assessment of CD recurrence may also be related to the different view of the lesions provided by these 2 techniques. While sonography allows the visualization of the bowel wall, ileocolonoscopy shows the inner mucosal surface. Nevertheless, when pooling sonographic and endoscopic findings from the whole group of 72 CD patients with ileocolonic resection, we unexpectedly found a significant correlation between the BWT detected by SICUS and the Rutgeerts' score of recurrence ( $r = 0.67$ ;  $P = 0.0001$ ). This finding appeared not related to the time interval from surgery, as a significant correlation was also observed

when subgrouping patients resected  $< 3$  versus  $\geq 3$  years before enrolment. Although this cutoff value was quite arbitrary, it was chosen in relation to a comparable amount of patients included in each subgroup. Different from the present findings, in our previous study<sup>31</sup> correlation between severity of recurrence as assessed by endoscopy and SICUS at 1 year was at the limit of statistical significance ( $P = 0.05$ ;  $r = 0.42$ ). The observed discrepancy may be related to the different number of tested patients (72 versus 22) and/or to the different time interval between surgery and recurrence assessment.<sup>31</sup> The time interval between the 2 techniques (within 6 months) may limit the relevance of this study. However, in all 72 patients both clinical activity (CDAI) and treatment strategies (steroids or biologics) were comparable at the time of SICUS and ileocolonoscopy. These observations suggest that the time interval between the 2 procedures may not significantly influence our findings.

In the present study the time interval from surgery included a wide range (3–396 months). The protocol was indeed designed as a cross-sectional study in order to assess the role of SICUS in evaluating CD recurrence in any patient with a previous ileocolonic resection performed at any time before assessment. This issue may assume relevance in clinical assessment of resected CD patients referred for the first time to an IBD service including an available expert sonographer.

Although the retrospective analysis and the small number of patients relapsing within 1 year limit the search for a role of endoscopy versus SICUS as predictors of clinical relapse, our findings further support that a higher Rutgeerts' score is associated with early relapse and also suggest that a higher BWT is observed in almost one-third of patients undergoing relapse.

The finding of a significant correlation between the CDAI and the endoscopic score of recurrence, but not between the CDAI and the BWT, may well be explained by the different view of the lesions provided by these 2 techniques. Different from our study, a significant correlation between the CDAI and BWT has been reported by Maconi et al,<sup>41</sup> although this finding was observed in a study population including a higher number of CD patients not selected on the basis of a previous ileocolonic resection.<sup>39</sup> The clinical relevance of the observed statistically significant difference between patients with an endoscopic score  $< 2$  versus  $> 3$  in terms of prestenotic dilation needs further investigation.

The blood flow in the anastomosis was not measured in our CD population, also in relation to previous studies showing that surgical resection may affect superior mesenteric artery blood flow.<sup>40,41</sup>

When comparing sonography versus endoscopy in terms of additional findings, ileocolonoscopy was obviously

more appropriate in the only 2 patients with not only ileocolonic, but also colocolonic anastomosis. No significant additional lesions were detected by endoscopy. Different from ileocolonoscopy, SICUS also detected extraluminal lesions, including enteroenteric fistulae (4%), lymph nodes enlargement (1.4%), mesenteric adipose tissue alterations (7%), and proximal small bowel involvement (8%). This relatively low frequency of additional findings may be related to the quite short time interval from surgery in most of the patients. In our study, the role of SICUS appeared more relevant in visualizing the neoterminal ileum in patients showing an anastomotic stenosis not passed by the endoscope. In all 22 patients showing a stenosis of the ileocolonic anastomosis, SICUS indeed provided additional information regarding the neoterminal ileum, including the presence and extent of lesions compatible with recurrence and possible dilation above stenosis. These findings suggest that in CD patients with suspected anastomotic stenosis, SICUS is more appropriate than colonoscopy, as the visualization of the neoterminal ileum provided by sonography may avoid the need of small bowel radiology after colonoscopy. In our study, a comparable amount of time was required to perform SICUS (median 40 minutes, range 35–90) and colonoscopy.

Taken together, results from the present study suggest that sonography using oral contrast is a noninvasive technique useful for assessing CD recurrence after ileocolonic resection, providing findings comparable to colonoscopy. Different from colonoscopy, SICUS also allows the visualization of the neoterminal ileum in patients with a stenosis of the anastomosis not allowing passage of the endoscope. However, FN findings may be observed by using SICUS in patients with minor lesions related to CD recurrence. Results from our cross-sectional study, however, suggest that SICUS performed by an experienced sonographer is a noninvasive technique useful for assessing CD recurrence in patients with ileocolonic resection, particularly in those patients at high risk for complications related to colonoscopy (i.e., older age or comorbidities), as also in young patients with a history of high radiation exposure.

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#### REFERENCES

- Sales DJ, Kirsner JB. Prognosis of inflammatory bowel disease. *Arch Intern Med*. 1983;143:294–299.
- Rutgeerts P, Geboes K, Vantrappen G, et al. Natural history of recurrent Crohn's disease at the ileocolonic anastomosis after curative surgery. *Gut*. 1984;25:665–672.
- Rutgeerts P, Geboes K, Vantrappen G, et al. Predictability of the postoperative course of Crohn's disease. *Gastroenterology*. 1990;99:956–963.
- Sachar DB. The problem of postoperative recurrence of Crohn's disease. *Med Clin North Am*. 1990;74:183–188.
- Olaisson G, Smedh K, Sjudahl R. Natural course of Crohn's disease after ileocolonic resection: endoscopically visualised ileal ulcers preceding symptoms. *Gut*. 1992;33:331–335.
- Pallone F, Boirivant M, Stazi MA, et al. Analysis of clinical course of postoperative recurrence in Crohn's disease. *Dig Dis Sci*. 1992;37:215–219.
- Olaisson G, Smedh K, Sjudahl R. Natural course of Crohn's disease after ileocolonic resection: endoscopically visualised ileal ulcers preceding symptoms. *Gut*. 1992;33:331–335.
- Rutgeerts P. Strategies in the prevention of postoperative recurrence in Crohn's disease. *Best Pract Res Clin Gastroenterol*. 2003;17:63–73.
- Farmer RG, Whelan G, Fazio VW. Long-term follow up of patients with Crohn's disease. Relationship between the clinical pattern and prognosis. *Gastroenterology*. 1985;88:1818–1825.
- Tibble JA, Sightorsson G, Bridger S, et al. Surrogate markers of intestinal inflammation are predictive of relapse in patients with inflammatory bowel disease. *Gastroenterology*. 2000;111:15–22.
- Tibble J, Teahon K, Thjodleifsson B, et al. A simple method for assessing intestinal inflammation in Crohn's disease. *Gut*. 2000;47:506–513.
- Orlando A, Modesto I, Castiglione F, et al. The role of calprotectin in predicting endoscopic postsurgical recurrence in asymptomatic Crohn's disease: a comparison with ultrasound. *Eur Rev Med Pharmacol Sci*. 2006;10:17–22.
- Boirivant M, Pallone F, Leoni M, et al. Usefulness of fecal alpha-1-antitrypsin clearance as an early indicator of asymptomatic postoperative recurrence in Crohn's disease. *Dig Dis Sci*. 1991;36:347–352.
- Biancone L, Scopinaro F, Ierardi M, et al. 99m-Tc-HMPAO granulocyte scintigraphy in the early detection of postoperative asymptomatic recurrence in Crohn's disease. *Dig Dis Sci*. 1997;42:1549–1556.
- Biancone L, Fiori R, Tosti C, et al. Virtual colonoscopy compared with conventional colonoscopy for stricturing postoperative recurrence in Crohn's disease. *Inflamm Bowel Dis*. 2003;9:343–350.
- Rispo A, Imbriaco M, Celentano L, et al. Noninvasive diagnosis of small bowel Crohn's disease: combined use of bowel sonography and Tc-99m-HMPAO leukocyte scintigraphy. *Inflamm Bowel Dis*. 2005;11:376–382.
- Bourreille A, Jarry M, D'Halluin PN, et al. Wireless capsule endoscopy versus ileocolonoscopy for the diagnosis of postoperative recurrence of Crohn's disease: a prospective study. *Gut*. 2006;55:978–982.
- Horsthuis K, Bipat S, Bennis R, et al. Inflammatory bowel disease diagnosed with US, MR, scintigraphy, and CT: meta-analysis of prospective studies. *Radiology*. 2008;247:64–79.
- Sonnenberg A, Erckenbrecht J, Peter P, et al. Detection of Crohn's disease by ultrasound. *Gastroenterology*. 1982;83:430–434.
- Pedersen BH, Gronvall S, Dorff S, et al. The value of dynamic ultrasound scanning in Crohn's disease. *Scand J Gastroenterol*. 1986;21:969–972.
- Pera A, Cammarota T, Comino E, et al. Ultrasonography in the detection of Crohn's and in the differential diagnosis of inflammatory bowel disease. *Digestion*. 1988;41:180–184.
- Lindberg B. Diagnosis of acute ulcerative colitis and colonic Crohn's disease by colonic sonography. *J Clin Ultrasound*. 1989;17:25–31.
- Linberg B, Osswald B. Diagnosis and differential diagnosis of ulcerative colitis and Crohn's disease by hydrocolonic sonography. *Am J Gastroenterol*. 1994;89:1051–1057.
- Schwerk WB, Beckh K, Raith M. A prospective evaluation of high resolution sonography in the diagnosis of inflammatory bowel disease. *Eur J Gastroenterol Hepatol*. 1992;4:173–182.
- Hata J, Haruma K, Suenaga K, et al. Ultrasonographic assessment of inflammatory bowel disease. *Am J Gastroenterol*. 1992;87:443–447.
- Calabrese E, La Seta F, Buccellato A, et al. Crohn's disease: a comparative prospective study of transabdominal ultrasonography, small intestine contrast ultrasonography, and small bowel enema. *Inflamm Bowel Dis*. 2005;11:139–145.
- Parente F, Greco S, Molteni M, et al. Oral contrast enhanced bowel ultrasonography in the assessment of small intestine Crohn's disease. A prospective comparison with conventional ultrasound, x-ray studies, and ileocolonoscopy. *Gut*. 2004;53:1652–1657.

28. Pallotta N, Tomei E, Viscido A, et al. Small intestine contrast ultrasonography: an alternative to radiology in the assessment of small bowel disease. *Inflamm Bowel Dis*. 2005;11:146–153.
29. Di Candio G, Mosca F, Campatelli A, et al. Sonographic detection of postsurgical recurrence of Crohn's disease. *Am J Roentgenol*. 1986;146:523–526.
30. Andreoli A, Cerro P, Falasco G, et al. Role of ultrasonography in the diagnosis of postsurgical recurrence of Crohn's disease. *Am J Gastroenterol*. 1998;93:1117–1121.
31. Biancone L, Calabrese E, Petruzzello C, et al. Wireless capsule endoscopy and small intestine contrast ultrasonography in recurrence of Crohn's disease. *Inflamm Bowel Dis*. 2007;13:1256–1265.
32. Castiglione F, Bucci L, Pesce G, et al. Oral contrast-enhanced sonography for the diagnosis and grading of postsurgical recurrence of Crohn's disease. *Inflamm Bowel Dis*. 2008;14:1240–1245.
33. Travis SP, Stange EF, Lemann M, et al. European evidence based consensus on the diagnosis and management of Crohn's disease: current management. *Gut*. 2006;55:i16–35.
34. Best WR, Becktel JM, Singleton JW, et al. Development of a Crohn's disease activity index. National Cooperative Crohn's Disease Study. *Gastroenterology*. 1976;70:439–444.
35. Jess T, Riis L, Vind I, et al. Changes in clinical characteristics, course, and prognosis of inflammatory bowel disease during the last 5 decades: a population-based study from Copenhagen, Denmark. *Inflamm Bowel Dis*. 2007;13:481–489.
36. Nikolaus S, Schreiber S. Diagnostics of inflammatory bowel disease. *Gastroenterology*. 2007;133:1670–1689.
37. Hanauer SB, Korelitz BI, Rutgeerts P, et al. Postoperative maintenance of Crohn's disease remission with 6-mercaptopurine, mesalamine, or placebo: a 2-year trial. *Gastroenterology*. 2004;127:723–729.
38. Fraquelli M, Colli A, Casazza G, et al. Role of US detection of Crohn's disease: meta-analysis. *Radiology*. 2005;236:95–101.
39. Maconi G, Parente F, Bollati S, et al. Abdominal ultrasound in the assessment of extent and activity of Crohn's disease: clinical significance and implication of bowel wall thickening. *Am J Gastroenterol*. 1996;9:1604–1609.
40. Maconi G, Parente F, Bollani S, et al. Factors affecting splanchnic haemodynamics in Crohn's disease: a prospective controlled study using Doppler ultrasound. *Gut*. 1998;43:645–650.
41. van Oostayen JA, Wasser MN, Griffioen G, et al. Diagnosis of Crohn's ileitis and monitoring of disease activity: value of Doppler ultrasound of superior mesenteric artery flow. *Am J Gastroenterol*. 1998;93:88–91.