

# Bowel Wall Thickness at Abdominal Ultrasound and the One-Year-Risk of Surgery in Patients with Crohn's Disease

Fabiana Castiglione, M.D., Ilario de Sio, M.D., Antonio Cozzolino, M.D., Antonio Rispo, M.D., Francesco Manguso, M.D., Giovanna Del Vecchio Blanco, M.D., Elena Di Girolamo, M.D., Luigi Castellano, M.D., Carolina Ciacci, M.D., and Gabriele Mazzacca, M.D.  
*Divisions of Gastroenterology, University of Naples "Federico II"; and The Second University of Naples, Naples, Italy*

- OBJECTIVES:** Abdominal ultrasound can assess the extent and localization of Crohn's disease, and an increased bowel wall thickness is the most common finding. Our aim was to correlate bowel wall thickness at ultrasound, with the risk of short-term surgical outcome in patients with Crohn's disease.
- MATERIALS AND METHODS:** From 1997 to 2000 we performed ultrasound in 174 consecutive patients with Crohn's disease. Surgical operations were recorded over a 1-yr follow-up. Logistic regression analysis was performed to identify clinical and ultrasound risk factors for surgery.
- RESULTS:** Fifty-two patients underwent surgery within 1 yr. Indication for surgery was strictures in most of the cases. Median bowel wall thickness was higher in patients with surgery (8 mm) than those without surgery (6 mm) ( $p < 0.0001$ ). A receiver operating characteristic (ROC) curve was constructed taking into account bowel wall thickness for selecting patients with a high risk of surgery. The optimized cut-off for equally important sensitivity and specificity was calculated at 7.008 mm. The binary regression analysis showed that CDAI  $> 150$ , absence of previous surgery, stricturing-penetrating pattern, the presence of intestinal complications, and intestinal wall thickness  $> 7$  mm were associated with an increased risk of surgery. Patients with intestinal wall thickness  $> 7$  mm at ultrasound had the highest risk (OR: 19.521, 95% CI: 5.362–71.065).
- CONCLUSIONS:** Data suggest that bowel wall thickness  $> 7$  mm at ultrasound is a risk factor for intestinal resection over a short period of time. Routine use of abdominal ultrasound during evaluation of patients with Crohn's disease may identify a subgroup that is at high risk for surgery.

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## INTRODUCTION

The chronic course of Crohn's disease (CD) is characterized by the occurrence of intestinal complications, namely strictures, fistulae, or abscesses. Bowel strictures of clinically significant importance occur at some time during the natural history of the disease in approximately 50% of affected patients (1). Predominantly due to these complications the majority of patients with CD undergo surgery, often numerous times during their life time.

Standard diagnostic procedures such as ileocolonoscopy or barium studies can reliably visualize bowel obstruction (2), but are of limited usefulness with regard to fistulae and abscesses (3). Furthermore, on clinical grounds, when a stricture is diagnosed at radiology, it is difficult to differentiate symptoms of active inflammation that can be ameliorated by medical therapy, from those of fibrotic obstruction, which

requires surgical treatment. Thus, it is a hard task for the clinician to decide the correct indication and timing for surgery.

Over the past 2 decades, abdominal ultrasound (AUS) had emerged as a useful and simple clinical tool for the diagnosis and evaluation of CD patients (4–6). Abdominal ultrasound can visualize and locate transmural bowel inflammation showing the alteration of the echo-architecture of the bowel wall in CD (7–10). It has been reported that the technique is accurate in diagnosing CD (11), in the differential diagnosis of ulcerative colitis (12), and in the determination of the extent of disease, with the exception of the stomach and of the deep pelvic part of the sigmoid colon (13). Many authors have found that AUS is an accurate method for the detection of intestinal complications in CD and that it compares favorably with enteroclysis in the detection of obstruction, being able to correctly identify 90% of strictures documented by small bowel enema and confirmed at operation (14–17).

Furthermore, AUS has proven effective for the diagnosis of postsurgical recurrence (18, 19).

Contrarily, conflicting results have been published about the correlation of AUS findings and clinical activity or laboratory signs of inflammation (4, 20–22).

An increased bowel wall thickness (BWT) at ultrasound is the most common finding in patients with CD (8, 12, 20, 23). Bowel wall thickness depends on the transmural extension of inflammation and its consequent fibrosis and may represent the physiopathological mechanism that determines, in most cases, the need of a surgical intervention. Some researchers have suggested that in patients with BWT >8 mm and quiescent disease, there is a high prevalence of strictures and a frequent need for surgical resection (4, 19).

The aim of this study was to evaluate whether BWT, as assessed by AUS, might be considered a valuable parameter in predicting surgical outcome during a short-term period (1-yr) in patients with CD.

## PATIENTS AND METHODS

During the period under survey (1997–2000) we performed AUS in 174 consecutive patients with CD who had attended the Inflammatory Bowel Disease Clinic in our department (100 male, 74 female, median age (interquartile range (IQR)) 34.5 (19.25) yr). Three further cases observed within this period that had an immediate indication for surgery due to the presence of abdominal complications were not considered for the analysis.

Table 1 summarizes the main clinical features of the 174 evaluable patients.

After AUS patients underwent bimonthly clinical controls with a monitoring of serological parameters. Assessment of disease activity was performed at the time of AUS by the Crohn's disease activity index (CDAI) (24).

AUS was performed in the morning after an overnight fast by an Aloka SSD-1700 with a convex probe 3.5–6 MHz. No special preparation was prescribed. Abdominal ultrasound was performed by one of two investigators who alternatively did all examinations. Interobserver and intraobserver agreement evaluation was not planned. At the moment of AUS the investigator was not privy to the results of the biochemistry

and morphological investigations performed during the same period. The physicians were aware of any surgical resection previously performed.

In every patient the entire abdomen was systematically scanned starting from the right iliac fossa.

The BWT was measured both in longitudinal and transverse sections and was considered normal up to 3 mm (25). In accordance with Maconi *et al.* (14), stenosis was considered present at AUS examination when there was the coexistence of thickened (more than 4 mm) and stiff intestinal wall, narrowed intestinal lumen along with distended fluid, or echogenic content-filled loops just above the thickened intestinal tract. Enterocutaneous or enteroenteric fistulas were considered present when detection of hypoechoic duct-like structures with fluid or air content was seen between skin and intestinal loops or between one loop and another loop, respectively. The presence of abscesses was considered according to the current literature (15).

To appraise the discrimination ability of the intestinal wall thickness (mm) at ultrasonography in prediction of surgery, a receiver operating characteristic (ROC) curve was constructed and the area under the curve was calculated. The optimal cut-off point was identified for sensitivity and specificity; both of equal importance. Binary logistic regression was used to evaluate the relationship between surgery as the dependent and independent variables. For the selection of independent variables to be included in the multivariate model, we chose those with  $p < 0.2$  at the univariate analysis. In fact, it is sustained that variables may contribute to a multiple regression model in an unforeseen way because of the complex interrelationships among variables.

## Statistical Analysis

Data were previously examined by a normality test. Because of the non-Gaussian distribution of continuous variables, data are presented as median and IQR and compared to nonparametric means with the Mann-Whitney U test. For categorical variables the Pearson  $\chi^2$ -test was performed unless the Fisher's exact test was required for frequency tables when more than 20% of the expected values were less than 5. Binary logistic regression was used to examine the relationship between surgery as the dependent variable and possible predictors as the independent variables. The model was performed by using the stepwise backward method (Wald). The coefficients obtained from the logistic regression analysis were also expressed in terms of odds of event occurrence. A  $p$ -value of 0.05 or less was considered significant. The SPSS software package for Windows (release 11.0.1—Nov 15, 2001; SPSS, Inc., Chicago, IL) was used for statistical analysis. The ROC curve was obtained with StatsDirect statistical software (ver. 2.2.9).

## RESULTS

Three patients were excluded because at the time of AUS they had a clear indication for immediate surgery. All the

**Table 1.** Clinical Features of the 174 CD Patients Evaluated by AUS

Sex (M/F)	100/74
Age (IQR) yr*	34.5 (19.25)
Previous surgical resection	42
Length of CD (IQR) months*	33 (76)
CD intestinal localization	
Colonic	21
Ileo-colonic	56
Small bowel	97
CDAI <150/> 150	86/88

Data are expressed as numbers except where indicated.

\*Median (interquartile range).

**Table 2.** Indication for Surgery in the 52 Patients Operated on During a One-Year Follow-Up after AUS

Chronic bowel obstruction*	29
Abscesses	16
Fistulae	3
Refractory disease**	2
Perforation	1
Occlusion	1

Data are expressed as numbers of patients.

\* Symptomatic chronic bowel obstruction with fixed stricture and proximal dilatation.

\*\* Chronic active disease not responsive to steroids and azathioprine.

other patients were considered for the study and analyzed. Fifty-two (32 male, 20 female; 25 ileum, 24 ileo-colonic, 3 colonic) out of 174 patients underwent surgery within 1 yr after AUS. Table 2 shows the indication for surgery in the 52 patients operated during a 1-yr follow-up after AUS. Chronic bowel obstruction (no. 29), abscesses (no. 16), and fistulae (no. 3) were the most frequent indications. Strictures, fistulae, and abscesses were evident at AUS in most cases. In four patients fistulae were not observed by AUS and were found at surgery. In four patients, in whom AUS showed a single stricture, a picture of multiple strictures was found at laparotomy.

### Univariate Analysis

Patients' characteristics were analyzed using univariate analysis. The main data on CD patients divided into those with surgery and without surgery in the year after AUS are given in Table 3. The distribution of age, sex, smoking habit, duration

of the disease, and previous surgery did not vary between the two groups.

At AUS, the median BWT was higher in patients with surgery (8 mm) than in those without surgery (6 mm) ( $p < 0.0001$ ). Patients with complications at AUS were 36.5% within the surgery group and 4.9% in those without surgery with a significant difference of the proportion ( $p < 0.0001$ ). No difference was found for bowel loops distension at AUS.

Out of 132 patients 44 (33%) without previous surgery and 8 out of 42 patients (19%) with previous surgery were surgically treated during the study period ( $p = \text{NS}$ ). The ileo-colonic involvement was more frequently observed in operated patients (46.2%), while patients who did not undergo surgery during the study had more frequently small bowel (59%) or colonic (14.7%) involvement ( $p = 0.02$ ). The presence of a stricturing or penetrating pattern was more frequently observed in patients with surgery (88.5%) than in those without surgery (31.3%) ( $p < 0.0001$ ). Patients with CDAI  $> 150$  at time of AUS were more frequent in the surgery group (88.5 vs 34.4%;  $p < 0.0001$ ). CRP was increased in 78.8% of patients with surgery and in 62.3% of those without surgery ( $p = 0.03$ ), while no difference was found for ESR. Azathioprine consumption was not different between the two groups, while steroid treatment was more frequently observed in the surgery group (78.8 vs 62.3%;  $p = 0.03$ ).

### ROC Curve

A ROC curve was constructed taking into account the bowel thickness at AUS. Patients were divided into a "condition" present group defined as those who submitted to abdominal

**Table 3.** Characteristics of 174 Patients with Crohn's Disease Classified for Having Received Surgery During their 1-Yr Follow-Up after AUS

	Surgery		<i>p</i>
	No (122 pts)	Yes (52 pts)	
Age (yr)*	35 (18)	31.5 (19.75)	0.12**
Sex (M/F)	56/44	61/39	0.48†
Smokers	52	56	0.62†
Duration of the disease (months)*	36 (78)	27.5 (53.50)	0.45**
Previous surgery	28	15	0.08†
Localization of disease			
Colonic	15	6	0.02†
Ileo-colonic	26	46	
Small bowel	59	48	
Pattern (non stricturing–nonpenetrating/stricturing–penetrating)	69/31	11/89	$<0.0001^\dagger$
CDAI $> 150$	34	89	$<0.0001^\dagger$
ESR*	24 (28)	29 (35.25)	0.25**
CRP (increased)	62	79	0.03†
Steroid treatment	19	35	0.03†
Azathioprine	9	6	0.56†
Bowel wall thickness (mm)*	6 (2)	8 (2)	$<0.0001^{**}$
Complications at AUS	4.9	36.5	$<0.0001^\dagger$
Bowel loop distension	20	33	0.09†

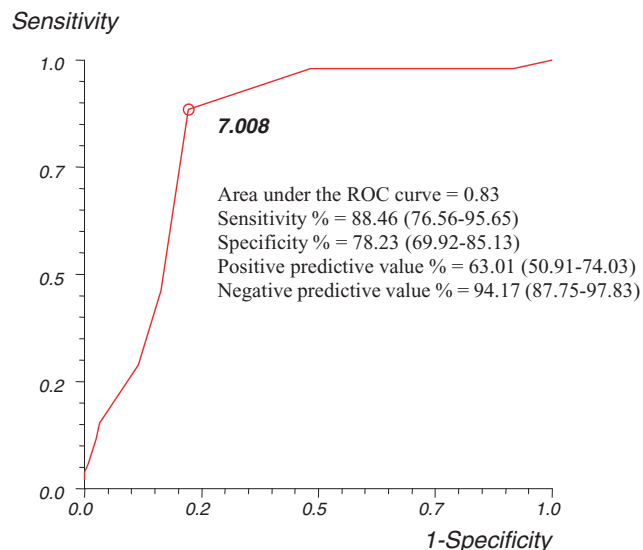
Data are expressed as percentage except where indicated.

\*Median (IQR); IQR = interquartile range.

\*\*By Mann-Whitney U test.

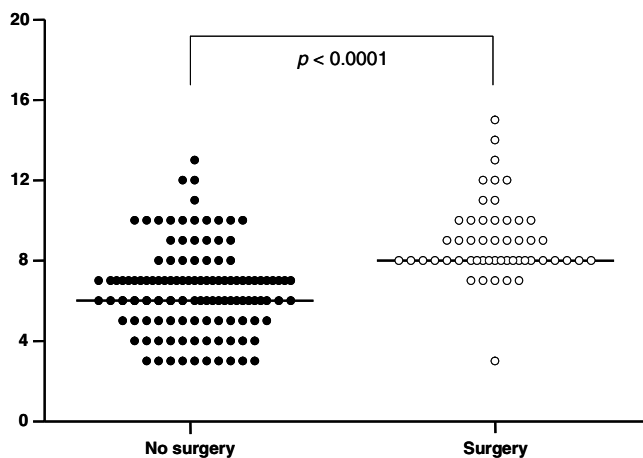
†By Pearson  $\chi^2$ -test.

‡By Fisher's exact test.



**Figure 1.** Plot of a receiver operating characteristic (ROC) curve to define cut-off point to appraise the discrimination ability of the intestinal wall thickness (mm) at ultrasonography in order to predict surgery. The area under the curve, sensitivity, specificity, and positive and negative predictive values are also shown.

surgery and a “condition” absent group where there was no abdominal surgery. The optimized cut-off for equally important sensitivity and specificity was calculated at 7.008 mm (Fig. 1). After this analysis a BWT of  $>7$  mm at AUS was subsequently chosen as value for selecting CD patients with a high risk of undergoing intestinal surgery. Bowel wall thickness for all patients is reported in Figure 2. Six percent of patients with BWT  $<7$  mm underwent surgery, while 37% of patients with BWT  $>7$  mm were not operated in the period under survey. Figure 3 shows the ultrasound image of a CD patient with a BWT  $>7$  mm of an affected ileal segment.



**Figure 2.** Scatter plot showing bowel wall thickness (mm) measured with abdominal ultrasound in patients with Crohn's disease stratified in those with and without surgery during 1-yr follow-up. The line represents the median.  $p$  by the Mann-Whitney  $U$  test.

### Multivariate Analysis

At the univariate analysis the following variables had  $p < 0.2$ : CRP, CDAI, nonstricturing–nonpenetrating/stricturing–penetrating pattern, localization of disease, steroid treatment, bowel loop distension, age at ultrasonography, wall thickness, previous surgery, and intestinal complications at AUS (Table 3). The predictive value of surgery by binary logistic regression analysis is shown in Table 4. CDAI  $> 150$ , the absence of previous intestinal surgery, a stricturing–penetrating pattern, the presence of intestinal complications at AUS, and intestinal wall thickness  $>7$  mm are associated with a significantly increased risk of intestinal surgery. In particular, patients with intestinal wall thickness  $>7$  mm at abdominal ultrasound had the highest risk (OR: 19.521; 95% CI: 5.362–71.065) of intestinal surgery, while previous intestinal surgery was protective (OR: 0.117; 95% CI: 0.026–0.523).

### DISCUSSION

Our data suggest that abdominal ultrasound can identify a group of patients with CD characterized by a bowel wall thickening  $>7$  mm that carries a significant risk for intestinal resection over a short period of time.

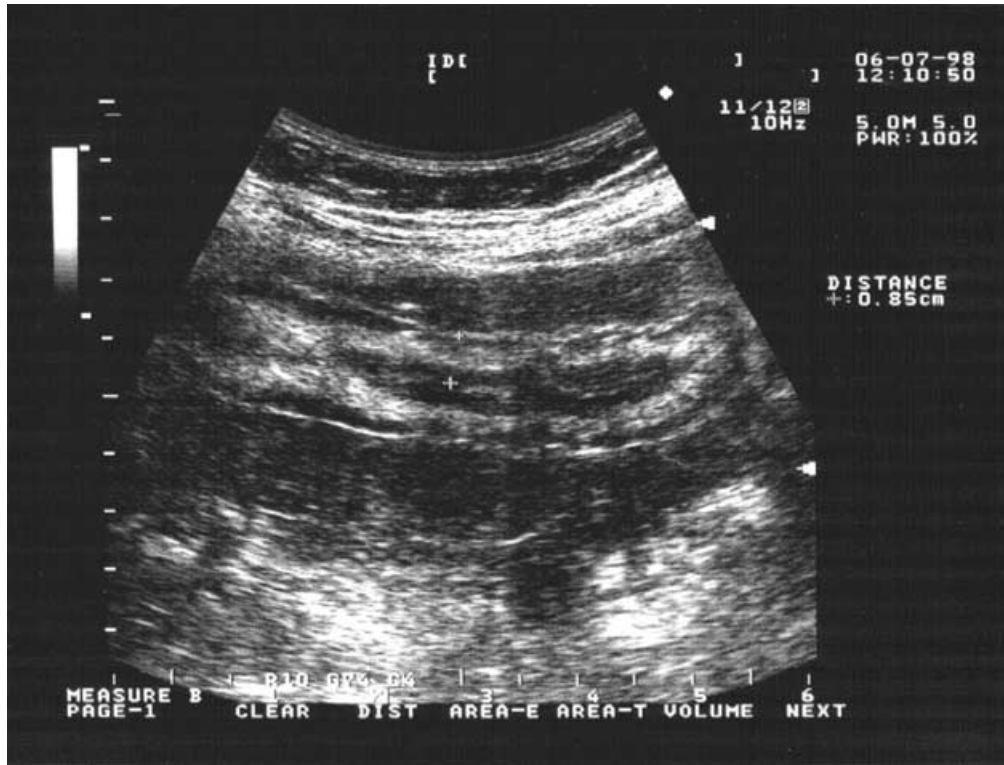
A number of studies have shown in recent years that AUS enables us to obtain information about the transmural intestinal changes in inflammatory bowel disease (7–10). The technique compares favorably with endoscopy and X-ray double-contrast studies in defining the location of the intestinal segments involved, being less sensitive in the study of the bowel mucosa (25, 26). On the contrary, AUS has the significant advantage of being a simple and noninvasive diagnostic method that is able to accurately diagnose peri-intestinal complications such as fistulae and abscesses (14, 15).

Many authors have investigated the relationship between AUS findings and clinical activity, although conflicting data have been reported (4, 20, 21, 22). In a recent report in 32 pediatric patients with CD, a significant correlation between BWT and CDAI was described (20). On the contrary, Futagami *et al.* (21) showed in 55 adult patients only a tenuous association between an ultrasonographic activity index (based on BWT and wall stratification) and CDAI.

An increased BWT is one of the more frequent findings at AUS in CD patients. The normal value of BWT is normally considered at 3-mm (23, 25).

Maconi *et al.* (4) have investigated the association between BWT, CDAI, and biological indices of inflammation. In their study they found only a tenuous association and were able to identify a subgroup of patients with a CDAI  $< 150$  and a BWT  $> 8$  mm who were characterized by a higher prevalence of strictures and more frequent need of surgical resections. The cut-off of 8 mm was chosen being the mean value found in 110 patients with CD (4). More recently these authors have suggested that AUS may contribute toward distinguishing the inflammatory and/or fibrotic nature of CD strictures, helping to identify patients at high risk for surgery (4, 19).





**Figure 3.** Ultrasound image of a CD patient with a BWT  $> 7$  mm of an affected ileal loop. A thickened intestinal wall (8.5 mm) with narrowed lumen is evident.

In the present study we investigated whether an increased BWT assessed by AUS was associated with a more frequent surgical outcome in a 1-yr period after the examination. The study was performed prospectively in 174 consecutive patients attending our clinic during their follow-up, independently of their previous clinical history and their present disease activity.

In order to appraise the discrimination ability of the intestinal wall thickness at AUS so as to predict surgery, we constructed a ROC curve and calculated that the optimized cut-off for equally important sensitivity and specificity was at a BWT of 7.008 mm. Therefore, a bowel thickness  $> 7$  mm at AUS was chosen as value for selecting CD patients with a high risk of intestinal surgery. With this cut-off only 6% of patients with BWT  $< 7$  mm underwent surgery within 1 yr,

while 37% of the cases with BWT  $> 7$  mm was not operated during the following year.

Binary logistic regression was used to evaluate the relationship between surgery as the dependent variable and independent variables. The absence of previous intestinal surgery, a CDAI  $> 150$ , a stricturing–penetrating pattern, the presence of abscesses or fistula, and intestinal wall thickness  $> 7$  mm were associated with a significantly increased risk of intestinal surgery at binary logistic regression analysis. We found that patients with intestinal wall thickness  $> 7$  mm at abdominal ultrasound had the highest risk (OR 19.521) of being operated on in the following year compared to the other risk factors. In particular, BWT was the best predictor of surgery compared to a CDAI  $> 150$  or in presence of intestinal complications not requiring an immediate surgical intervention.

**Table 4.** Binary Logistic Regression Analysis Examining the Relationship between Surgery at One Year as a Dependent Variable (no/yes = 0/1) and Clinical and Instrumental Parameters as Independent Variables in Patients with Crohn's Disease. The coefficients obtained from the logistic regression analysis were also expressed in term of the odds of occurrence of an event.

Variable	Regression Coefficient	SE	<i>p</i>	OR	CI
CDAI ( $\leq 150$ / $> 150$ = 0/1)	2.146	0.676	0.001	8.553	2.275–32.154
Previous surgery (no/yes = 0/1)	−2.144	0.763	0.005	0.117	0.026–0.523
Pattern (nonstricturing–nonpenetrating/stricturing or penetrating = 0/1)	2.886	0.669	$< 0.0001$	17.915	4.824–66.539
Complications at AUS (no/yes = 0/1)	1.856	0.785	0.02	6.396	1.373–29.789
Thickness ( $\leq 7$ / $> 7$ mm = 0/1)	2.972	0.659	$< 0.0001$	19.521	5.362–71.065
Intercept	−5.740	0.999			

SE = standard error of estimated coefficient, CI = confidence interval, OR = odds ratio.

The higher risk for surgery in patients with a BWT > 7 mm compared to inflammation parameters (CRP values) or CDAI suggests that a BWT > 7 mm is strongly related to fibrosis other than submucosal edema and cellular inflammation.

As expected, multivariate analysis showed that the penetrating/stricturing pattern of disease was strongly related to the risk of surgery, while a history of previous surgical intestinal resection was protective (27). The latter result is in accordance with the data of the literature showing that the rate of surgery is significantly lower in patients with previous resections compared to patients not operated upon (28, 29).

These data indicate that AUS may be a reliable tool in predicting the risk of surgery and that it may be useful in the selection of patients that can undergo elective surgery. This is a very important goal for the clinicians involved with the care of patients with CD since it is well known that the morbidity and mortality rate of surgery in inflammatory bowel disease is significantly higher in patients who undergo surgery in emergency or in the presence of intestinal complications. The identification of patients with a high risk for surgery may help to select subgroups that could benefit from an intensive follow-up.

In conclusion, our data suggest that a BWT > 7 mm at ultrasound examination in CD patients is predictive of need for intestinal resection over the next year. Routine use of AUS may help in identifying the subgroup of CD patients who will require resection for optimal clinical outcome.

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**Reprint requests and correspondence:** Fabiana Castiglione, M.D., Cattedra di Gastroenterologia, Facoltà di Medicina e Chirurgia, Università "Federico II", Via S. Pansini 5, 80131 Naples, Italy.

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