Small Intestine Contrast Ultrasonography in Pediatric Crohn's Disease

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Objective To evaluate the diagnostic accuracy of small intestine contrast ultrasonography (SICUS) in pediatric Crohn's disease (CD).

Study design A total of 51 consecutive patients (median age 15 years; range 3-20, 31 male patients), 21 with suspected and 30 with proven CD, were studied. All patients underwent standard ultrasonography (ie, transabdominal ultrasonography [TUS]), SICUS, small bowel follow-through, and upper and lower endoscopy. SICUS was performed in patients after they ingested an oral contrast solution. TUS and SICUS were compared with small bowel follow-through and endoscopy via use of the final diagnosis as reference standard.

Results In undiagnosed patients, the sensitivity and specificity of TUS and SICUS in detecting CD small bowel lesions were 75% and 100% and 100% and 100%, respectively. In patients with proven CD, the sensitivity and specificity of TUS and SICUS were 76% and 100% and 96% and 100%, respectively. The agreement (k) with radiology for site of lesions was almost perfect for SICUS (0.93), both for jejunal and ileal lesions, and it was fair (0.40) for jejunal and substantial (0.68) for ileal lesions for TUS. Compared with radiology SICUS correctly assessed the length of lesions, whereas TUS underestimated it (P = .0001).

Conclusions The radiation-free technique SICUS is comparable with radiology and more accurate than TUS in assessing small bowel lesions in pediatric CD, mainly in the detection of proximal small bowel disease. *(J Pediatr 2013;163:778-84)*.

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Crohn's disease (CD) is an inflammatory bowel disease (IBD) that may affect any part of the gastrointestinal (GI) tract. Small bowel involvement, in addition to other sites, is present in as many as two-thirds of pediatric patients, and the disease is confined to small bowel in up to 30% of cases.[1,2] Small bowel disease is of clinical relevance in pediatric CD because of its impact on growth and pubertal development. Moreover, patients with small bowel CD are more likely to develop intestinal strictures and, less commonly, fistulas.[3,4] Therefore, assessment of the small bowel is a cornerstone in the evaluation of children with suspected CD as well as in the follow-up of patients with a proven diagnosis.

Traditionally, small bowel barium contrast studies (ie, small bowel follow-through [SBFT] and small bowel enteroclysis) have been considered the reference standard for detecting small bowel lesions in pediatric patients with CD.[5,6] Because of the unremitting nature of the disease, however, several assessments of the GI tract may be required over a lifetime, and emerging data show a high level of radiation exposure in children with IBD, particularly CD.[7,8] Therefore, during the past few years more and more interest has been focused on the implementation of radiation-free, cross-sectional techniques, such as magnetic resonance (MR)[9-11] and ultrasonography (US),[12-14] for the evaluation of small bowel in pediatric patients with CD.

Transabdominal ultrasonography (TUS) is currently a well-established noninvasive, inexpensive, and easily available tool in the diagnosis of intestinal lesions and related complications of CD either in adults and pediatric patients. However, TUS has inherent limitations because of the virtual gut lumen and the presence of intestinal gas that makes hardly visible the intestinal wall. This is highlighted by the observations that TUS, even when performed in tertiary referral centers, has a variable, and sometimes unsatisfactory, sensitivity (74%-88%) in detecting CD lesions, particularly small bowel lesions outside of the terminal ileum.[15,16] The ingestion of an oral nonabsorbable anechoic contrast solution (macrogol 4000, Giuliani, Milano, Italy)

CD	Crohn's disease
GI	Gastrointestinal
IBD	Inflammatory bowel disease
MR	Magnetic resonance
SBFT	Small bowel follow-through
SICUS	Small intestine contrast ultrasonography
TUS	Transabdominal ultrasonography
US	Ultrasonography

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fulfills the small bowel lumen, thus enabling to dissociate one intestinal loop from another and providing the opportunity to visualize the entire small bowel, from the Treitz angle to the ileocecal valve.[17] In adult patients with suspect or known CD, this technique, known as small intestine contrast ultrasonography (SICUS), has been shown to be comparable with conventional radiology as well as with surgical and pathological findings in detecting the presence, number, site(s), and extension of small bowel lesions.[16,18-21]

This is a prospective study aimed to evaluate, as the primary outcome, the diagnostic accuracy of SICUS to detect the presence, number, site(s), and extension of small bowel lesions in pediatric patients with suspected or known CD. The secondary aim was to compare the accuracy of TUS and SICUS by assessing the level of agreement with the established techniques (ie, SBFT, endoscopy).

Methods

Consecutive patients referred to our tertiary-care pediatric gastroenterology center between January 2008 and June 2011 for symptoms or signs suggestive of small bowel CD or for recurrence of previously diagnosed CD were prospectively enrolled. We specifically inquired about the patients' medical history, abdominal and extra-abdominal complaints, and bowel habits. In children with known CD age at diagnosis, site and behavior of disease according to Paris classification, past surgery, and current and previous medical treatment were also reported. Written informed consent from parents and assent from children were obtained, and the study protocol was approved by the local ethics committee.

All patients underwent a diagnostic work up starting with a standardized clinical interview and a physical examination performed by certified and experienced pediatric gastroenterologists. Patients were consecutively submitted in the same day to TUS and SICUS by an expert intestine-dedicated ultrasonographist (N.P.), who has performed more than 9000 SICUS examinations. All patients underwent upper and lower GI endoscopy under conscious sedation or general anesthesia in accordance with a protocol previously reported,[22] and SBFT was performed on a different day. When necessary, additional investigations, including MR, wireless capsule endoscopy, and single-balloon enteroscopy, were performed. The ultrasonographist was unaware of the clinical suspect as well as of radiologic and endoscopic data in undiagnosed patients; in known patients with CD, she was aware of the diagnosis, history of surgery, and current symptoms but was blinded to the results of the other investigations.

At the end of the diagnostic examination the ultrasonographist and the radiologist reported on a standardized form small bowel abnormalities with particular reference to presence, number, site, and extension in centimeters of intestinal wall and lumen abnormalities; US extraluminal alterations, namely node enlargement, mesenteric involvement, fistulas, and abscesses, also were looked for and reported. We compared TUS and SICUS with radiology and endoscopy and used the final diagnosis as reference standard.

US

Real-time US was performed with Tosbee (Toshiba, Tokyo, Japan) equipment with a 3.5-MHz convex and a 5-MHz linear array transducers. The apparatus can detect a bowel wall thickness variation of 0.1 mm. TUS and SICUS were performed after the patient fasted overnight. SICUS was performed according to a previously published method.[17,18] To summarize, after the patient ingested 125-250 mL of macrogol oral contrast solution (Giuliani, Milano, Italy), and once the contrast was seen flowing through the terminal/neoterminal ileum into the colon, a retrograde follow-through assessment of the entire small bowel was performed to visualize, in a caudocranial sequence, the contrast-filled ileal and jejunal loops. Wall thickness and lumen diameter of maximally distended, and not contracting, intestinal loops, were measured at the level of jejunum, proximal, and distal ileum and terminal ileum at the level.

Contrast Solution. The contrast solution was freshly prepared by dissolving in 250 mL of water a granular powder containing macrogol 4000 (Giuliani), a nondigestible, nonabsorbable, and nonfermentable macromolecule that links water and, once ingested, progresses through the GI tract until rectal evacuation. The iso-osmolar PEG solution, once in the small bowel, remains unchanged, filling the lumen and distending the intestinal loops.

Definitions of CD Lesions and Complications at US

US criteria for presence of small bowel CD lesions were increased wall thickness (≥3 mm),[16-18] reported as the average of at least 3 measurements; loss of stratification of the bowel wall; "stiffness," identified as intestinal loop with increased wall thickness; or distended loop, which remains unchanged during transabdominal compression.[16] The extension of small bowel lesions was reported as the average of at least 3 measurements. Bowel stenosis was defined as lumen diameter <1 cm with or without prestenotic dilatation (**Figure 1**, A-C). Bowel dilation was defined as lumen diameter >2.5 cm.[16,21] Hypoechoic peri-intestinal lesions were defined as fistulas when they were duct-like shaped with a cross-sectional lumen diameter <2.0 cm and as abscesses when they appeared as a round-like mass with a cross-sectional diameter >2 cm.[21] Mesenteric fat hypertrophy was defined as homogeneous hyperechoic tissue surrounding thickened bowel with loss of the normal double-shaped stratification of hypoechoic and hyperechoic layers (**Figure 1**, D).[21]

Radiology

SBFT was performed according to the standard protocol in our unit. According to age, fasting patients drink 250-450 mL of a barium sulfate suspension (Bario HD; Bracco, Milan, Italy) under the intermittent fluoroscopic guidance of a radiologist. Spot filming of the esophagus, stomach, and duodenum was obtained with the patient in an upright and recumbent position. Radiographs were then obtained in the prone position at 15- to 20-minute intervals for the first hour and then every half hour until the terminal ileum and right colon were well visualized. Criteria for presence of small