Sonography for Surveillance of Patients With Crohn Disease

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Crohn disease is a chronic inflammatory condition of the bowel characterized by periods of quiescence and inflammatory activity or “disease flares.” Although genetic factors, dysbiosis, and altered immunity are implicated in inflammatory bowel disease, the etiology is unknown. The peak age of onset is early in life, between 15 and 40 years, thus affecting patients during their most productive years with potential for substantial social and personal costs. Crohn disease tends to complicate over time, with the development of fistulas and fibrostenotic lesions. As a result, surgical intervention rates in the prebiologic era were high. However, early and appropriate medical management can alter the course of this disease, with reductions in surgical rates and hospitalization.

Detection of disease activity through objective monitoring is key to changing the long-term outcome and disability. Monitoring clinical symptoms alone is inadequate: the presence or absence of these does not reflect disease activity. Routine endoscopic monitoring is also not feasible because it is an invasive examination with associated risks and the need for preparation. Computed tomography (CT) with dedicated small-bowel imaging or enterography has been the modality of choice to date, but there is mounting evidence questioning its safety and repeatability, given ionizing radiation exposure in these young patients. Magnetic resonance imaging (MRI) is a radiation-free alternative and has also been shown to be effective in detection of inflammatory activity. However, this modality is expensive, and the lack of access precludes routine use.

Transabdominal sonography is a highly effective modality for detecting inflammatory activity in Crohn disease, equal to that of CT or MRI. Sonography is particularly sensitive in detecting ileocecal Crohn disease compared to the reference standard ileocolonoscopy and thus is a useful initial screening tool to aid in diagnosis. Postoperative Crohn disease recurrence is also reliably detected with sonography, a suggested surrogate for endoscopic evaluation. It is an effective modality in the detection of complications such as strictures, fistulas, and abscesses, with surgical pathologic confirmation showing sensitivity as high as 100%. Although there are little existing data on the utility of any transmural modality in routine monitoring of disease activity in asymptomatic patients, there is a move toward more frequent observation, given the disconnect between symptoms and disease. Sonography is a superb modality for monitoring stable patients with a
number of additional advantages: it is inexpensive and widely available, and real-time imaging with potential for 3-dimensional reconstruction can optimally characterize complications such as partial small-bowel obstruction. It is safe and noninvasive with easy repeatability and patient tolerability. Inflammatory activity, reflected by excess blood flow in the bowel wall, is shown on color Doppler imaging and more sensitively with the use of contrast agents, with potential for actual quantification and objective measurement of blood flow and therefore inflammatory activity.15

Although sonography of the bowel is a highly effective modality, there are limitations. First, operator experience and expertise are more important in evaluation of the bowel compared to sonographic evaluation of other abdominal organs. Acquisition of technical expertise and adequate time are essential to survey the entire small and large bowel. The reproducibility of sonographic inflammatory parameters is a commonly suggested limitation of bowel sonography; however, there is strong evidence that inter-rater agreement on key parameters such as bowel wall thickness is high.16

Consistent identification of the anatomic site of inflammation is also identified as a potential limitation. More than 80% of patients with Crohn disease have small-bowel involvement, often the distal terminal ileum. Patients with active Crohn disease generally have a distinctively thickened bowel, which becomes relatively gasless compared to the normal bowel. This condition creates a mass effect. Therefore, as disease worsens, the pathologic characteristics improve the likelihood of detection. Areas that may be more challenging to identify include those deeper within the pelvis (rectum or ileoanal pouch) and proximal small bowel (duodenum). Considerable challenges may also arise with a complex surgical history, and accurate identification of the anatomic location can be limited in this circumstance.

Obesity, particularly body mass indices of 30 or greater, may hamper a sonographic study of any portion of the abdomen. Failure of sonography should not be predicated on body habitus alone, however. A low body mass index with little abdominal wall fat is advantageous for sonography compared to CT and MRI, which are both improved by the presence of intra-abdominal fat.

Complications associated with Crohn disease are well appreciated on sonography, but open fistulas and drainage sites may be problematic in patients with severe fistulizing disease, limiting transducer placement on the skin. In addition, discomfort may further limit examination. Complex fistulizing disease is often readily identified; however, there may be challenges associated with mapping of tracks, given surrounding inflammation and tethering, similar to any other modality. Certainly, partial small-bowel obstructions are shown on real-time sonography, and examination of complex disease is generally well tolerated by patients, given the lack of bowel preparation or need for contrast agents.

Although the above factors are considerations in the choice of sonography for the study of the bowel, as avid ultrasound enthusiasts, we support the use and choice of sonography as a first-line modality for evaluation of all patients with Crohn disease, both for routine surveillance and for evaluation at the time of acute exacerbation.

Case Description

A 38-year-old man with long-standing ileocolonic Crohn disease diagnosed at 21 years of age underwent emergent ileocolonic resection at presentation for suspected acute appendicitis. He was well for a decade, but after symptoms of intermittent severe abdominal pain developed, he was referred to gastroenterology. Ileocolonoscopy revealed an ulcerated and stenosed ileocolic anastomosis with a completely normal colon. He also had a cutaneous perianal opening with active drainage on perianal examination, consistent with a perianal fistula. He was given combination therapy of infliximab and methotrexate and was in clinical remission for 2 years with normal blood test results and a lack of perianal symptoms. A sonographic examination performed 1 year after initiation of medical therapy showed no abnormalities with no evidence of inflammatory activity, including the perianum.

One year later, the patient continued to be in clinical remission, with no symptoms of Crohn disease, other than intermittent scant drainage from his known perianal cutaneous opening. Subsequent surveillance sonographic examinations, however, revealed dramatic interval deterioration with extensive small-bowel thickening (Figure 1, A and B), hyperemia of the bowel on color Doppler imaging (Figure 1, C and D), abundant mesenteric inflammatory fat, and proximal disease in a skip lesion distribution. There were also multiple sites of narrowing with incomplete mechanical bowel obstruction (Figure 1, E–G), evidenced by fluid-filled dilated segments of the small bowel with to-and-fro peristalsis before segments with constant luminal apposition and wall thickening. The total length of the abnormal bowel was estimated to be 40 cm. Maximal wall thickness was measured at 8 mm. In addition, a clear intersphincteric rectocutaneous fistulous tract was identified on transperineal sonography (Figure 1H) without associated complications, specifically no ischiorectal fossa abscess.
Figure 1. Images from a 38-year-old man with Crohn disease for 17 years who previously underwent ileocolic resection. He was feeling well after 2 years of taking infliximab and methotrexate for recurrent disease in the neoterminal ileum. A previous sonographic examination 1 year earlier yielded normal findings, showing a marked initial positive response to therapy. The following images are from a surveillance scan. A and B. Long-axis and axial images of the neoterminal ileum show marked wall thickening with some loss of wall layering. The bowel measures 9 mm in thickness (threshold is 3 mm). C and D. Corresponding color Doppler images. The profuse easily shown blood flow is a reflection of active inflammation. (continued)
Commentary

The lack of clinical symptoms despite active disease, confirmed on endoscopy, is well documented. Furthermore, postoperative recurrence of Crohn disease is almost inevitable over time, and the need for a second operation in the absence of medical therapy is high. Many of these patients remain asymptomatic despite disease recurrence. Alternatively, the number of patients with Crohn disease who have typical symptoms such as diarrhea and abdominal pain in the context of quiescent disease is high, approaching 60%. Therefore, differentiating active from inactive disease clinically is challenging. Serologic measures of inflammation such as C-reactive protein are also unreliable in consistently detecting disease. Therefore, other noninvasive means of routinely evaluating the inflammatory activity in patients with Crohn disease is imperative to detect disease and prevent complications even when patients feel well. Sonography is an ideal modality for this purpose. It is key in the routine management of inflammatory bowel disease in a number of countries in Europe and in our department.

Figure 1. (continued) E, Fixed angulation of a very thick and black neoterminal ileum, well proximal to the anastomosis. On the left, the lumen shows fixed apposition, and on the right, there is fluid distention suggesting an element of stricture. There is abundant echogenic inflammatory fat. F, At a point more proximal in the neoterminal ileum, there is dilated bowel on the left with an abrupt transition to thick bowel with luminal apposition on the right, suggestive of another stricture with incomplete mechanical bowel obstruction. G, At yet another point more proximal, there is a fixed, very acute angulation of a thickened segment. Dilated fluid-filled bowel is shown both proximally and distally. H, Axial transperineal view of the anal canal. There is a hypoechoic inflammatory mass (arrows) posterolateral to the left side of the anal canal. The internal opening, in the 6-o’clock position directly posterior, is slightly more caudal and not shown here. Impression: active recurrent disease of the neoterminal ileum. There is a multifocal stricture, fixed acute angulation, incomplete mechanical bowel obstruction, and a perianal inflammatory mass.
The interval or frequency for transmural monitoring of Crohn disease is uncertain. In the case described here, the surveillance interval was likely too long: despite highly effective medical therapy and the absence of clinical symptoms, the patient had severe active persistent disease detectable 1 year after an examination yielded normal findings. This situation is not uncommon: a substantial number of patients who respond initially to biologic therapy lose the response over time. The reference standard target for assessing the response to medical therapy is endoscopic, to establish mucosal healing, but frequent routine endoscopic evaluation is not acceptable to most patients. There are no clearly established surrogates for mucosal healing in widespread use, but sonographic assessment is certainly a candidate. There is a need for a validated scoring system reflecting sonographic inflammatory activity to be included with other measures of disease activity.

Wall thickness measurement is central to sonographic determination of disease activity. However, the addition of color Doppler evaluation of the bowel in this case further illustrates the severity of the disease. This combined demonstration of severe disease strongly substantiates the presence of inflammation; therefore, contrast-enhanced sonography if performed is less additive in this case. Although contrast enhancement is a powerful tool for showing inflammation, this case is an excellent example of demonstrated severe active disease without the requirement for either intravenous access or contrast agent injection.

Given the predilection of Crohn disease for the terminal ileum and right colon, a sonographic examination starts with axial orientation of the right flank from the hepatic edge to the right iliac fossa looking for the wall and gas shadow suggestive of the ascending colon. Once localized, the terminal ileum is identified at the ileocecal valve. The remainder of the colon can generally be continuously followed from the ascending colon to the rectum. Furthermore, because of their fixed mesenteric locations, the segments of the colon can all be identified on the basis of their known locations and positions within the abdomen.

The entire small bowel is systematically evaluated by performing a series of axial scans from the right flank to the left flank with overlap of the scanning planes. The small bowel is not as easy to strictly identify, however, both the location and appearance are helpful. The jejunum is localized in the left upper quadrant with a characteristic feathery appearance of the valvulae conniventes. The small bowel in the 3 remaining quadrants is more likely to be ileum, with a more variable appearance.

Selection of the correct ultrasound probe is critical for successful sonographic evaluation of the bowel. The initial survey may be performed with a 4- to 6-MHz probe for systematic identification of thickened segments of bowel and evidence of complications. These low-frequency evaluations are necessary to avoid overlooking deeply positioned fluid collections. Localized regions of interest should then undergo detailed evaluation with higher-frequency probes (7–9 MHz), either linear or curved, for superior bowel wall resolution. In women, endovaginal probes are ideal to study both the rectosigmoid colon and portions of the terminal ileum located deep in the true pelvis. Finally, the ultrasound machine should be optimized for high contrast and low flow on color Doppler imaging.

For many years, we have performed transperineal sonographic evaluation of the anal canal and perianal soft tissues in patients with Crohn disease who have known fistulas or perianal pain. The technique is established as an accurate modality in both men and women, with potential for the addition of transvaginal scanning to increase accuracy in women. The identification of internal and external openings, inflammatory tracts, and any associated abscess is noninvasive, accurate, and easily repeated, facilitating close monitoring. Thus, monitoring responses to both surgical and medical therapy of perianal disease is readily accessible. Transrectal sonography can facilitate characterization of disease in patients with more proximal disease or supralevator extension of inflammatory changes. This examination can be painful for patients, however, and is infrequently performed for this indication in our center.

Fibrostenotic complications or strictures are areas of fixed luminal apposition with dilated proximal bowel, often accompanied by excess and dysfunctional to-and-fro peristalsis. Accurate assessment of the degree to which the stricture is inflammatory versus fibrotic in nature continues to be a challenge regardless of the transmural imaging modality. The inflammatory activity of a stricture is similar to non-narrowed thickened bowel with an increased blood supply, shown on Doppler imaging, which may be further characterized with microbubble contrast agents. Contrast further increases the sensitivity for detecting inflammation. Elastography used to evaluate bowel wall stiffness is a promising technology that may prove helpful in discerning the predominant etiology of the stricture. It is currently being investigated in our center.
Summary

Crohn disease is a complex chronic systemic inflammatory disease that frequently has complications and requires close monitoring to prevent disability. Current medical therapies have demonstrated success in the alteration of the natural history; however, a substantial number of patients do not respond to medical therapy or lose the response over time, as shown here. There is a shift in the management of Crohn disease to move beyond symptoms in identifying disease activity early and to treat to target, with mucosal healing as the goal, and not just for improvement of symptoms. Sonographic measurements of wall thickness and blood flow to the bowel wall are accurate measures of disease activity. Sonography is an excellent surrogate for mucosal healing, with easy repeatability so that frequent assessments can be made to facilitate early intervention.

References