Pathologic Continuum of Acute Appendicitis

Sonographic Findings and Clinical Management Implications

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Abstract: Appendicitis is one of the most common causes of the acute abdomen often requiring emergent surgery. Delayed diagnosis leads to the progression of uncomplicated appendicitis to complicated (gangrenous, perforated) appendicitis, often changing clinical management. Computed tomography and ultrasound are imaging modalities of choice to preoperatively diagnose appendicitis. Recent concerns of radiation exposure and cost have renewed interest in using ultrasound as an initial, diagnostic study. A sonographic pictorial and histopathologic review of the continuum of appendicitis is presented. A comprehensive sonographic examination of the appendix should investigate the size (maximal diameter), the echogenic submucosal layer integrity, the mural color Doppler signature, the presence of a fecalith, and the periappendiceal changes. Features of an uncomplicated appendicitis include size greater than 6 to 7 mm, hyperemia on color Doppler, mural thickening, and an intact echogenic submucosal layer. Gangrenous appendicitis is characterized by loss of the echogenic submucosal layer with absent color Doppler flow. Loculated pericecal fluid, prominent pericecal fat, and circumferential loss of the submucosal layer are suggestive of perforation. Sonographic staging can triage management of appendicitis by directing urgent laparoscopic appendectomy for uncomplicated appendicitis, open appendectomy for complicated appendicitis, and conservative management (antibiotics with percutaneous drainage) for perforated appendicitis with abscess formation.

Key Words: appendicitis, sonography, abscess, phlegmon, complicated appendicitis, uncomplicated appendicitis

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CLINICAL OVERVIEW

Appendicitis is one of the most common causes of the acute abdomen in the Western world and is one of the most frequent indications for abdominal surgery.[1] It occurs in 7% to 12% of the general population, and although it may occur at any age, it is most common in the 10- to 19-year-old age group (233/100,000 population annually).[1] Each year, 280,000 appendectomies are performed in the United States to avoid the potential complications of perforated appendicitis.[1] Perforation rates are correlated with delayed diagnosis and age. Young children and the elderly have the highest rates of perforation (40%–57% and 55%–70%, respectively).[2] Of note is the fact that, in the past 2 decades, the negative appendectomy rate has been relatively constant with slight decline after 2000, but the rates for perforated appendicitis seem to be increasing.[2] The clinical diagnosis may be difficult to make without a classic presentation of periumbilical pain migrating to the right lower quadrant or in particular patient populations such as women of child bearing age whose gynecologic pathologies may present similarly. Owing to its increased morbidity, there is an ongoing need for early and accurate diagnosis of appendicitis before the onset of perforation.

Depending on the pathologic stage of appendicitis, there are a variety of surgical and nonsurgical treatment options including laparoscopic or open appendectomy, primary antibiotic therapy, or percutaneous drainage of periappendiceal abscesses.[3–8] Appropriate patient management is based on distinguishing complicated (gangrenous or perforated appendicitis) from uncomplicated appendicitis. In addition, in patients with perforated appendicitis, it is important to differentiate liquefied abscesses from indurated soft tissue masses (phlegmonous inflammation).

For more than 20 years, computed tomography (CT) and sonography have been the primary imaging methods used in the diagnosis of appendicitis.[9] Despite its slightly higher sensitivity and specificity, there are increasing concerns about the radiation burden and cost of CT; thus, there is renewed interest in the role of sonography.[10] In this article, we review the sonographic findings along the pathologic continuum of acute appendicitis emphasizing important luminal, mural, and periappendiceal features that are helpful in differentiating complicated from uncomplicated appendicitis.

THE APPENDIX

The cecum and appendix develop from the midgut, which rotates and descends to its final position in the right iliac fossa. The mean length of the adult appendix measures approximately 9 cm and typically arises from the posteromedial border of the cecum approximately 1.7 to 2.5 cm below the terminal ileum.[11] The appendix can be found in almost any position relative to the cecum, and Wakeley[12] described 5 locations in a review of 10,000 anatomic cases: retrocecal (65.3%), descending/pelvic (directed downward on the psoas) (31%), subcecal in the iliac fossa (2.3%), preileal (1.0%), and postileal 0.4%.

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PATHOPHYSIOLOGY AND PATHOLOGIC STAGES OF ACUTE APPENDICITIS

The most commonly accepted pathogenesis of appendicitis is the obstruction of the appendiceal lumen by a fecalith, lymphoid hyperplasia, foreign bodies, parasites, or primary or metastatic tumors.[9] There may be a higher perforation risk with the detection of an appendicolith as suggested by a study where 49% of perforated cases had an appendicolith compared with 27% in nonperforated cases with $P = 0.049$.[13] However, other studies cite that an appendicolith is neither highly sensitive (50%) nor specific (70%) for the detection of perforation and does not represent a statistically significant association.[14,15]

The early stage of appendicitis develops when obstruction leads to fluid accumulation, elevation of intraluminal pressure, and luminal distention. On gross pathology, uncomplicated appendicitis is characterized by a dull appearance of the normally glistening serosal surface and dilation of the serosal vessels, causing an injected appearance.[16]

Suppurative appendicitis (intramural infection without necrosis) results from increasing intraluminal pressure that exceeds capillary perfusion pressure, causing venous outflow obstruction and ultimately arterial compromise. This results in mucosal ischemia that allows bacterial invasion of the appendiceal wall. In some patients with early uncomplicated appendicitis, these inflammatory changes are confined to the tip of the appendix due to a reduced blood supply from the terminal capillary branches of the appendiceal artery.[16] With the onset of mural infection, there is edematous thickening of the appendix wall due to intramural edema and infiltration by inflammatory cells. This mural thickening is often noted in conjunction with dilation of the lumen. On gross pathology, the external appendix appears distended and hyperemic, and there may be early edematous changes within the mesoappendix.[16]

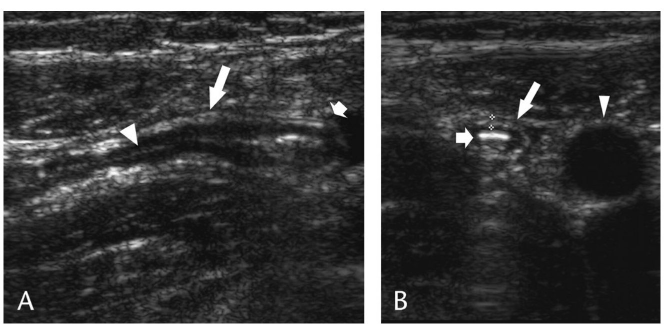

FIGURE 1. A and B, Normal appendix. Panel A is a longitudinal scan of the normal appendix. Note the well-preserved submucosal layer (long arrow), blind-ending tip (short arrow), and acoustic reflection from the collapsed luminal interface (arrowhead). Outer anteroposterior dimensions of appendix were 4.4 mm, well within the reference range of less than 5 mm. Panel B is a transverse scan of the normal appendix in the same patient with graded compression. Note the ovoid shape of the normal appendix (long arrow) with reverberation echoes. Gas (short arrow) is seen within distal tip of appendix lateral to external iliac artery (arrowhead).

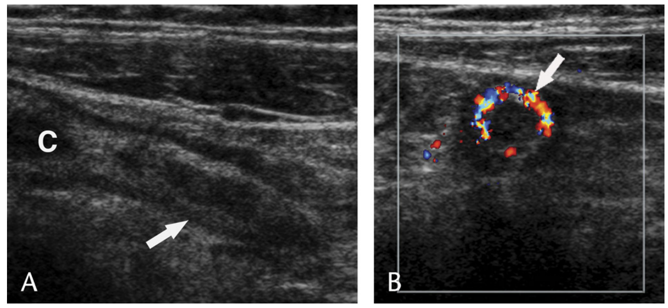

FIGURE 2. A and B, Early uncomplicated acute appendicitis. A, Longitudinal scan of the appendix, demonstrates distended appendix (arrow) originating from the base of the cecal tip (''C''). The echogenic submucosal layer is preserved throughout. B Transverse color Doppler image of the same patient. Note the intramural hyperemia circumferentially seen within the wall of the appendix, indicating early appendicitis (arrow).

Unless diagnosed and surgically treated at an early stage, appendiceal inflammation may ultimately progress to gangrene and perforation. Gangrenous appendicitis results when increasing intramural inflammatory change leads to appendiceal ischemia and transmural necrosis with serosal exudate. This is characterized by a friable serosa surface that may have a purple, green, or black discoloration. As with early intramural inflammation, early gangrenous changes leading to perforation may be confined to the tip and or distal appendix.[16] In many patients with appendiceal perforation, a liquefied abscess forms either in the peritoneal cavity (RLQ or pelvis) or in the retroperitoneum (often the right anterior pararenal space) with retrocecal appendicitis. The size and the degree of "localization" of the abscesses are both highly variable. In other patients with perforated appendicitis, an indurated inflammatory mass (phlegmon) develops involving the surrounding soft tissues involving the mesoappendix, omentum, small bowel, and its adjacent mesentery.[3]

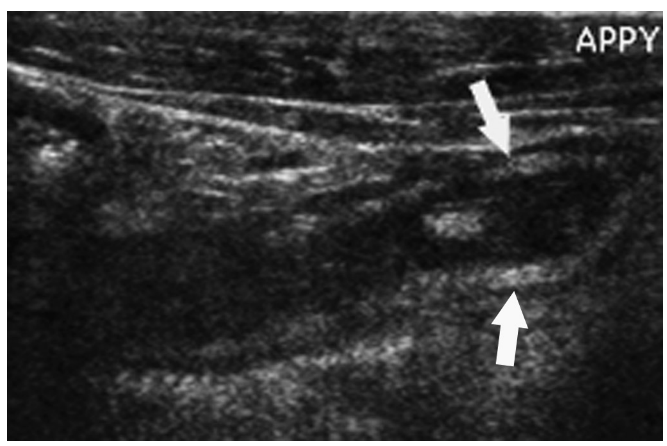

FIGURE 3. Early uncomplicated acute appendicitis. Longitudinal scan demonstrates distended appendix (arrows) with preserved echogenic submucosal layer throughout the entire length of the appendix.

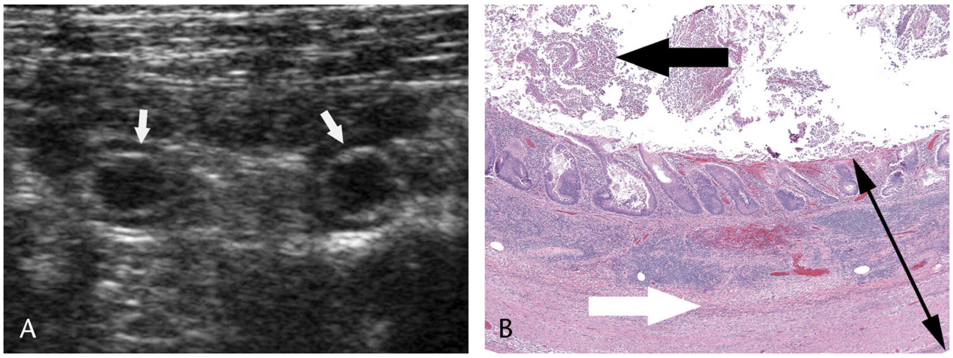

FIGURE 4. A and B, Early uncomplicated appendicitis with primary finding of distension. A, Transverse scan of RLQ demonstrating proximal and distal portions of the appendix cut in cross section (arrows) with luminal distension. There were no other findings to indicate acute appendicitis, and the appendix measured 6.5 mm. B, Photomicrograph demonstrating early, uncomplicated appendicitis with acute, luminal inflammation (black arrow) and mild, acute inflammation of the muscularis propria (white arrow) with diffuse wall thickening (double headed arrow).

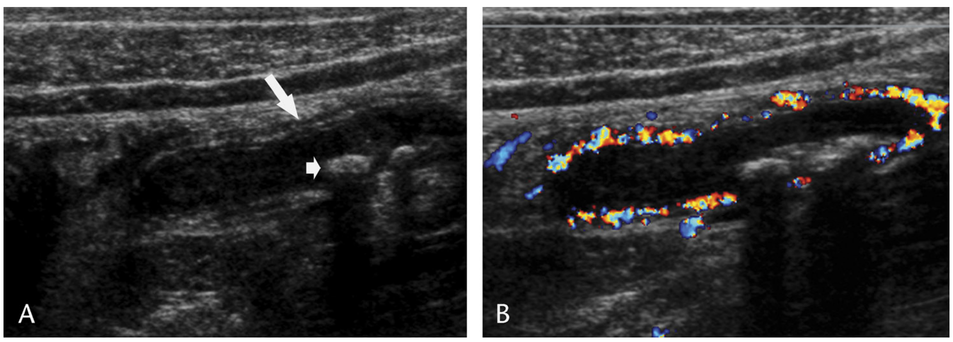

FIGURE 5. A and B, Hyperemia in acute uncomplicated appendicitis. A, Longitudinal scan showing dilated appendix (long arrow) with multiple appendicoliths (short arrow). B, Longitudinal color Doppler scan of the same patient. Note the marked flow within the wall of the appendix, indicating early acute appendicitis.

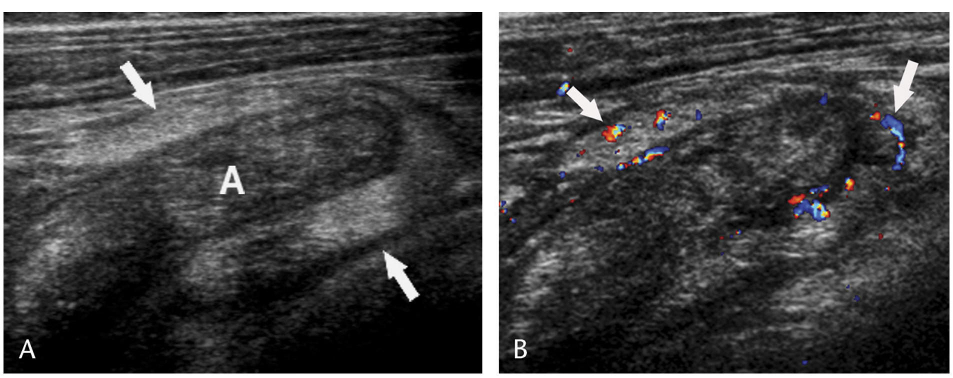

FIGURE 6. A and B, Suppurative appendicitis with transmural inflammation and inflamed periappendiceal fat. A, Longitudinal scan of the appendix demonstrating dilated appendix (''A'') with increased echogenicity within periappendiceal fat (arrow) and poor delineation of echogenic submucosal layer, indicating transmural inflammation. B, Longitudinal color Doppler image of the same patient. Note the slight increased flow within the inflamed periappendiceal fat (arrows).

ULTRASOUND AND CT OF THE APPENDIX

Graded compression sonographic technique allows the displacement of normal gas-filled bowel by slow sustained pressure with the ultrasound (US) transducer, which helps a patient with peritonitis better tolerate the procedure.[9] Scanning begins at the edge of the right hepatic lobe, moving downward into the right iliac fossa to locate the ascending colon. The ileocecal valve can be identified by its fatty component and the appendix should be located nearby. Although typically seen easily on transverse images, the origin of the appendix may be better visualized arising from the cecum on longitudinal images.[17] In cases when the appendix may extend into the pelvis, transvaginal sonography may be a useful adjunct to avoid missing a diagnosis of appendicitis. Criteria for a normal appendix include a compressible, tubular, blind ending structure, with wall thickness of 3 mm or less, absence of peristalsis, and normal hyperechoic periappendiceal fat without inflammatory involvement of the cecum. It rarely exceeds 5 mm in the outer anterior-posterior dimension and often demonstrates an ovoid rather than a rounded shape (Fig. 1).[18] The normal bowel wall layers of the appendix can be distinguished progressing from the lumen to the serosa by alternating echogenicity: hypoechoic mucosa, hyperechoic mucosal interface and submucosa, hypoechoic muscularis propria, and hyperechoic serosa.[17] These criteria are important to avoid false-positive studies where other structures (eg, dilated fallopian tube or dilated ureter) can mimic a dilated appendix.

Sonography can be very limited in obese patients, and CT is often preferred in this population. Similarly, the normal appendix on CT appears as a tubular, pericecal structure that is collapsed or filled with fluid, contrast, or air, with outer diameter that does not exceed 6 mm, wall thickness less than 3 mm, and homogeneous periappendiceal fat. In appendicitis, CT demonstrates a distended, fluid-filled, blind-ending, tubular structure arising from the cecum with mural thickening and hyperenhancement. Linear fat stranding and local fascial thickening indicate periappendiceal inflammation. An appendicolith is variably present.[9] For perforated appendicitis, there are 5 CT findings that are 100% specific but have low sensitivity: abscess, phlegmon, extraluminal air, extraluminal appendicolith, and focal defect in the appendix wall.[13,19]

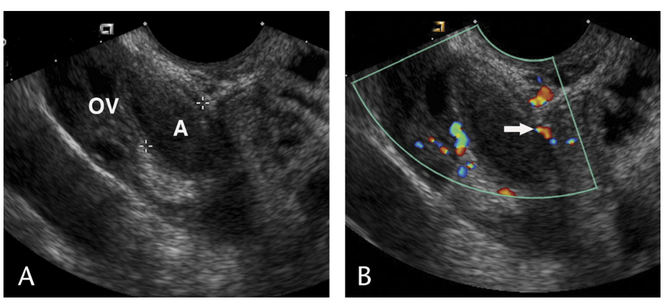

FIGURE 7. A and B, Pelvic appendicitis adjacent to the ovary. A, Coronal endovaginal scan of the right adnexa demonstrating dilated appendix (''A'') immediately adjacent to the right ovary (''OV''). B, Endovaginal coronal color Doppler image. Note the slight hyperemia of the appendix with flow in the appendiceal wall on color Doppler (arrow). At surgery, early acute uncomplicated appendicitis was noted in the pelvic appendix immediately adjacent to the ovary.

FIGURE 8. Gross pathologic specimen of gangrenous appendicitis. Note bluish-black discoloration of the gangrenous appendix (short arrow). In addition, there is marked edema of the mesoappendix with areas of fat necrosis (long arrow).

US CORRELATION WITH PATHOLOGIC STAGE

Uncomplicated Appendicitis

Uncomplicated appendicitis may demonstrate a combination of luminal and mural changes. Using a threshold measurement of 6 mm for the outer dimensions of a noncompressible appendix results in a sensitivity of 100% for appendicitis but a specificity of only 68%.[20] If the size

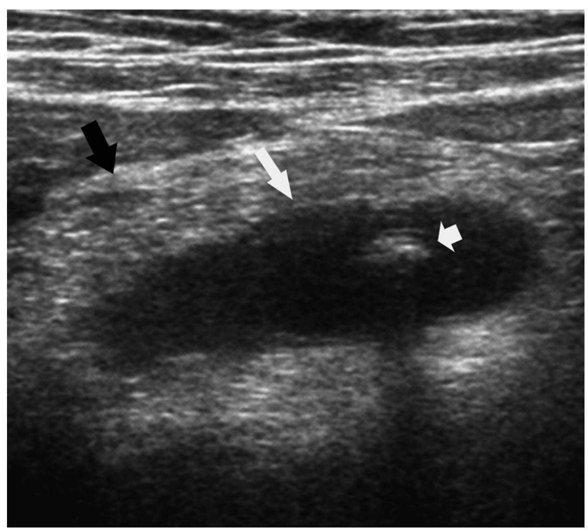

FIGURE 9. Gangrenous appendicitis on longitudinal scan. Note dilated appendix (long arrow) with complete global loss of echogenic submucosal layer and appendicolith (short arrow) within the lumen of the appendix. There is marked increased echogenicity within the surrounding periappendiceal fat (black arrow).

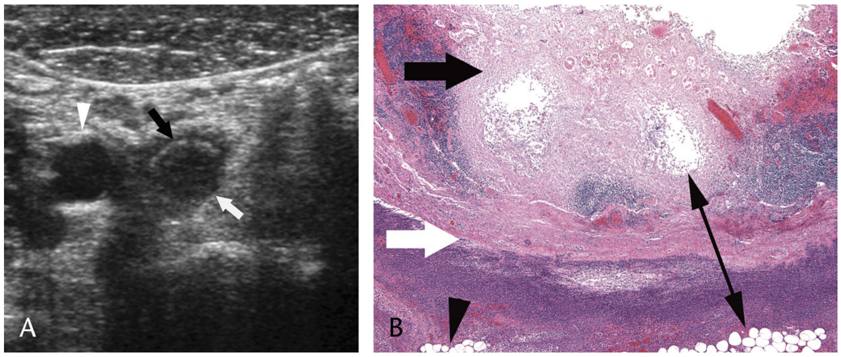

FIGURE 10. A, Transverse scan of gangrenous appendix demonstrating focal loss of echogenic submucosal layer (white arrow) indicating focal gangrenous change within appendix. Note that the anterior aspect of the submucosal layer is intact (black arrow), indicating no circumferential gangrene of appendix. Note that the external iliac artery (arrowhead) is lateral to the appendix. B, Photomicrograph demonstrating gangrenous appendicitis with mucosal necrosis (black arrow), full-thickness suppurative inflammation of the muscularis propria (white arrow), and periappendiceal soft tissues (arrowhead), with diffuse wall thickening (double-headed arrow).

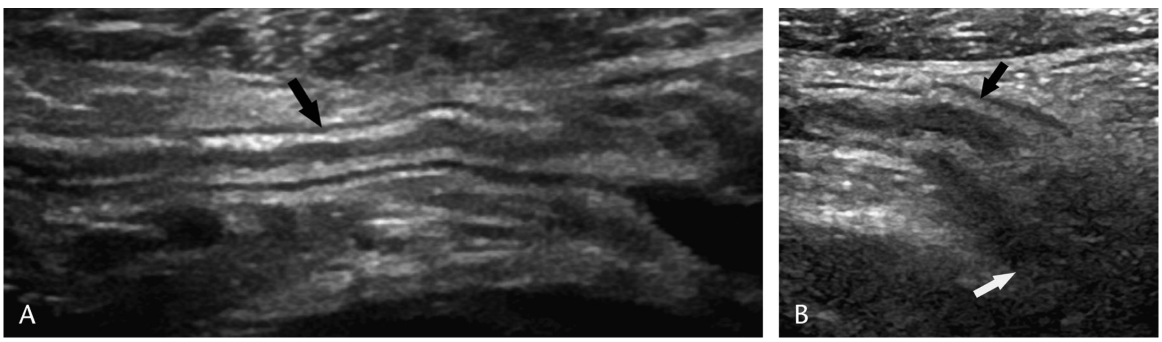

FIGURE 11. A, Sagittal scan of the base of the normal-appearing appendix, with preserved echogenic submucosal layer (black arrow). B, Sagittal scan of the distal appendix of the same patient demonstrating a slight thickening of the echogenic submucosal layer (black arrow) in the midportion of the appendix and complete necrosis with focal loss of the submucosal layer in the distal tip (white arrow). At surgery, the tip of the appendix was necrotic.

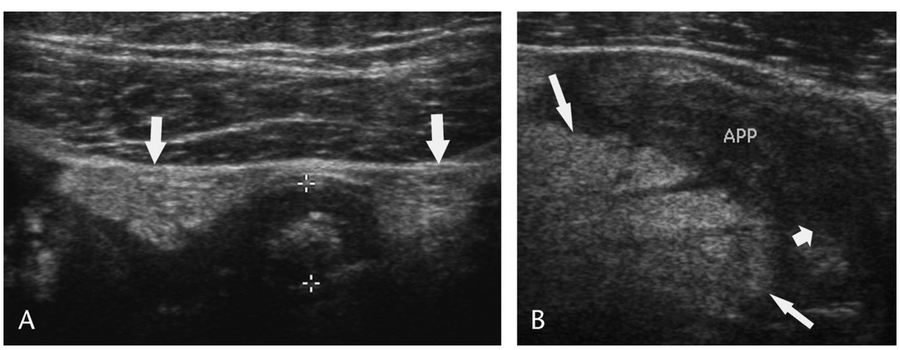

FIGURE 12. A and B, Edematous periappendiceal fat in gangrenous appendicitis on transverse scan. Note gangrenous appendix (calipers) with global loss of echogenic submucosal layer. Note echogenic periappendiceal fat draped over the appendix (white arrows) that mimics appearance of the thyroid gland and the trachea. B, Sagittal scan of the gangrenous appendix of the same patient. Note the prominent echogenic periappendiceal fat (long arrows) and the complete global loss of echogenic submucosal layer in the distal appendix (short arrow). APP indicates appendix.

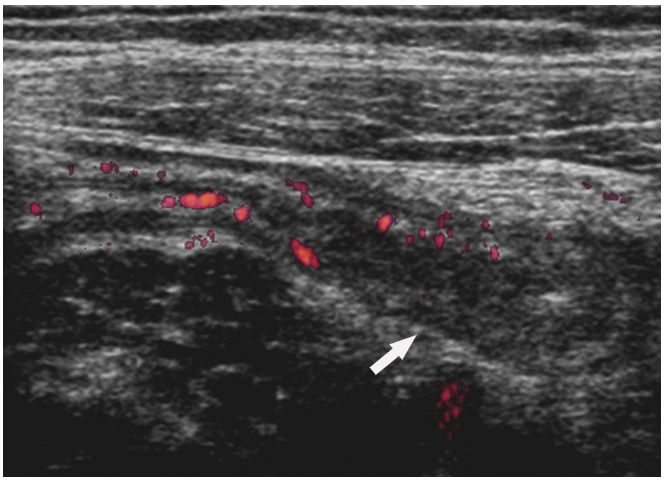

FIGURE 13. Gangrenous tip of the appendix. Note focal loss of echogenic submucosal layer and lack of blood flow within the necrotic distal tip of the appendix (white arrow).

threshold is increased to 7 mm, however, the sensitivity drops to 94%, but the specificity increases to 88%.[20] When the appendix measures between 6 and 7 mm, demonstration of intramural hyperemia on color Doppler may be a valuable aid in establishing the diagnosis in borderline cases because there is usually no visualized flow in the normal appendix (Figs. 2–7).[9]

On grayscale imaging, the normal wall of the appendix is less than 3 mm. Mural thickening is an important sonographic finding in appendicitis.[9] Specifically, thickening of the echogenic submucosal layer is a sign of submucosal edema. Because appendicitis may be confined to the tip of the appendix, it is important to identify the "blind end" of the appendix in order not to miss early luminal or mural changes. Preservation of a normal submucosal echogenic layer, especially in the distal and tip of the appendix, is an important observation indicating uncomplicated appendicitis due to lack of mural necrosis or gangrenous change.[21–23]

The progressive enlargement of the intact submucosal layer signals suppurative appendicitis, with further transmural inflammation causing appendiceal wall thickening, then thinning from destruction of the mucosa, enlargement of the muscular layer, and an increase in distal appendiceal diameter due to intraluminal accumulation of pus. Periappendiceal fat changes are seen as well as false membranes from serosal infection. Color Doppler shows severe hyperemia.[24]

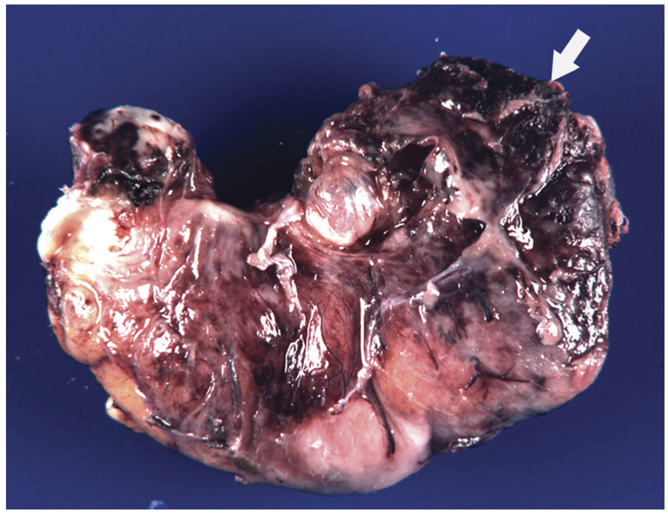

FIGURE 15. Gross pathology specimen of perforated appendicitis. Note black discoloration at the necrotic tip of the appendix that was perforated at gross pathology and surgery.

Complicated Appendicitis (Gangrenous or Perforated Appendicitis)

Increasing intramural inflammation of the appendix ultimately results in ischemia and appendiceal gangrene (Fig. 8). In patients with a strong clinical suspicion of perforated appendicitis due to high fever and leukocytosis, contrast CT is often the imaging modality of choice because of the difficulty in performing graded compression sonography in patients with perforation and peritonitis. However, when technically satisfactory, sonography may demonstrate characteristic findings. Either focal or global loss of the echogenic submucosal layer is a key sonographic observation indicating gangrenous appendicitis (Figs. 9–12).[25] Unlike the hyperemic

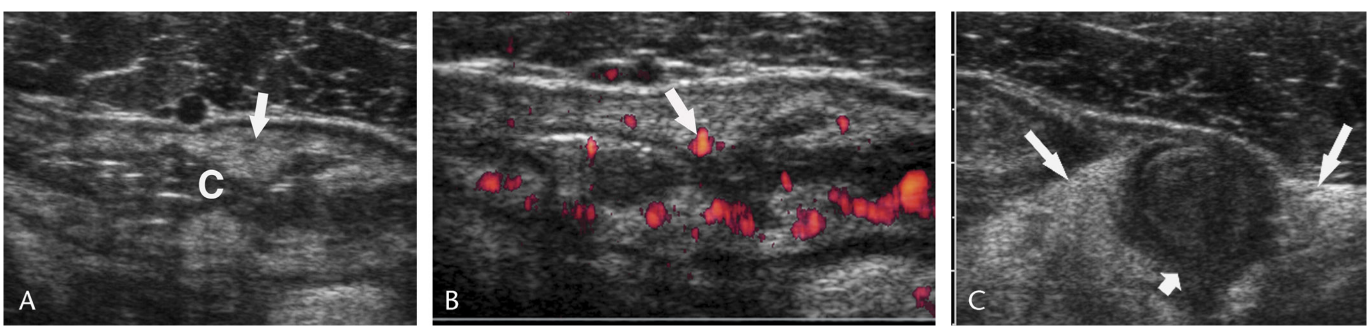

FIGURE 14. A–C, Transverse scan of cecum ("C") in a patient with gangrenous appendix demonstrating marked thickening of the submucosal layer (arrow) that is strikingly echogenic, indicating submucosal edema within the cecum. In B, in the same patient, note marked hyperemia within the cecum (arrow) on a transverse power Doppler image. In C, a transverse image of the appendix of the same patient, note the echogenic periappendiceal fat (long arrows) and loss of echogenic submucosal layer from the dilated appendix with gangrenous change (short arrow).

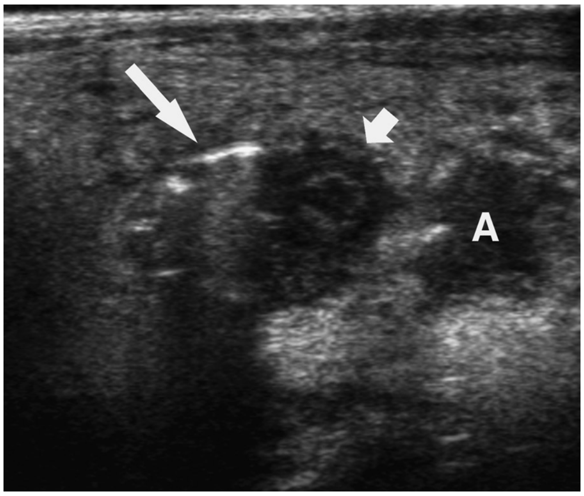

FIGURE 16. Transverse scan of perforated appendicitis demonstrating marked circumferential wall thickening of the appendix (short arrow) with adjacent gas collection (long arrow) indicating gas-forming periappendiceal abscess. Note second adjacent abscess (''A'') medial to the appendix.

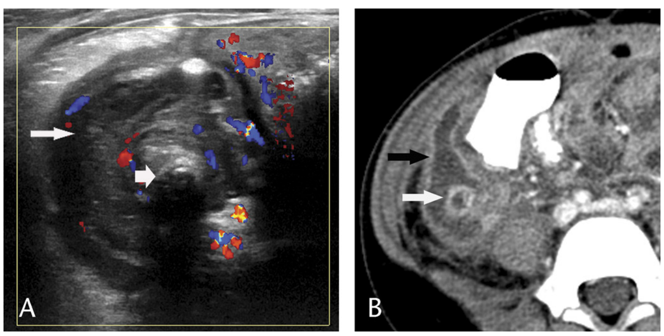

FIGURE 17. A and B, Perforated appendix with periappendiceal abscess on CT and US. In A, transverse color Doppler scan demonstrates abscess cavity (long arrow) surrounding appendicolith (short arrow). Note hyperemia surrounding the abscess on color Doppler flow. In B, contrast-enhanced CT demonstrates abscess (black arrow) surrounding the appendix (white arrow).

portions of the appendiceal wall that are merely inflamed but not necrotic, areas of gangrenous necrosis are typically avascular on color Doppler because the blood supply to these portions of the appendiceal wall is absent (Fig. 13).[21] Transmural inflammatory exudate results in edema, first within the fat of the mesoappendix, then into the cecum and pericecal fat, and finally to the mesenteric or omental fat. The inflamed fat appears echogenic on grayscale imaging and hyperemic on color Doppler (Fig. 14).[25,26] As previously emphasized, it is of critical importance to adequately visualize the tip of the appendix where gangrenous changes and perforation preferentially occur.

In perforating appendicitis, the necrotic appendix may no longer be visible sonographically or only a small residual portion of the appendix may be identified (Fig. 15).[25] Periappendiceal abscesses are often apparent sonographically as hypoechoic fluid collections or masses. In some cases, an extruded appendicolith is evident within the abscess cavity and casts an acoustic shadow (Fig. 16). This finding helps confirm that the abscess is due to perforated appendicitis and not some other gastrointestinal source. Because of the proteinaceous content of the pus, periappendiceal abscesses often exhibit relatively little enhanced through sound transmission unlike other simple fluid collections.[21] When "walled off" by surrounding inflamed omental and mesenteric fat, the fat is often strikingly echogenic on grayscale imaging and hyperemic on color Doppler (Figs. 17–19).[25,26]

In some patients with perforating appendicitis, there is relatively little liquefied pus and only intense inflammation of the surrounding tissues. Often this results in a "mass-like" phlegmonous infiltration due to an indurated soft tissue mass (Fig. 20).[3,25] As with other forms of inflamed fat, this phlegmonous inflammation often appears as an echogenic mass that is hyperemic on color Doppler imaging.

In differentiating between perforated and nonperforated appendicitis, the sonographic criteria specific for perforation include loculated pericecal fluid, prominent pericecal fat, and circumferential loss of submucosal layer. Although none of these individual findings had a specificity greater than 59%, combining one or more of these findings improved the overall sensitivity and specificity for the diagnosis of perforation to

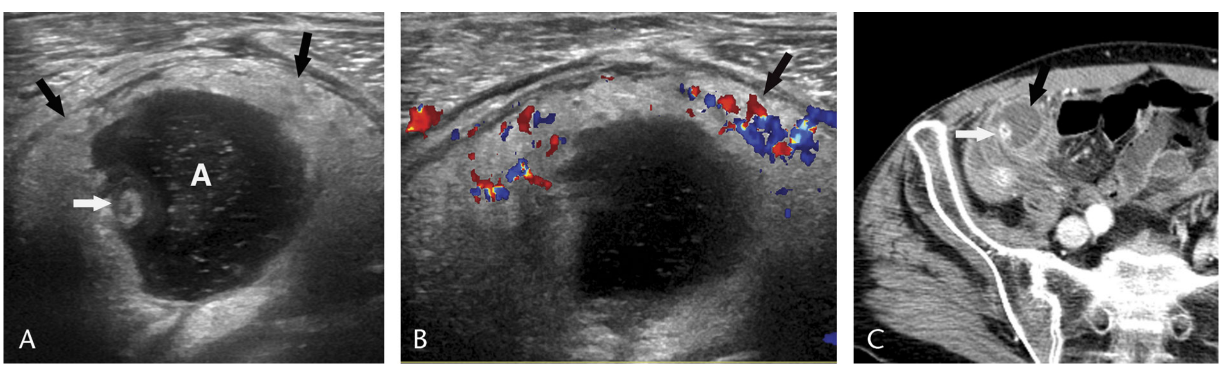

FIGURE 18. A–C, Perforated appendix with periappendiceal abscess. A, The transverse sonogram demonstrating large abscess (''A'') surrounding the appendix (white arrow). Note the echogenic fat (black arrows) walling off the abscess. B, Color Doppler sonogram of the same patient, demonstrates marked hyperemia (black arrow) within the inflamed fat walling off the abscess. C, Contrast-enhanced CT in same patient demonstrates abscess (black arrow) surrounding calcified appendicolith (white arrow).

86% and 60%, respectively.[25] A meta-analysis in a pediatric population demonstrated that the relative risk of a false-negative US finding in perforating appendicitis compared with nonperforating appendicitis is 0.34; thus, the sensitivity is increased with perforating appendicitis. Data were insufficient for the adult studies.[27]

Implications for Surgical or Nonoperative Management

In patients with uncomplicated appendicitis, urgent surgical intervention has always been the standard of care to avoid the morbidity and finite mortality associated with appendiceal perforation.[9] For the past decade, there has been an increasing trend toward performing the appendectomy in uncomplicated appendicitis via a laparoscopic approach.[5,27–29] The advantages of laparoscopic appendectomy include smaller incisions that allow for better cosmetic result, fewer wound infections, faster recovery with shorter hospital stay, earlier return to work, and decreased pain.[5,28–31]

The use of laparoscopic appendectomy for gangrenous or perforated appendicitis, however, remains controversial. Some surgical authorities argue for open appendectomy for patients suspected of having complicated appendicitis because there is an increased incidence of postoperative abdominal abscess with the laparoscopic approach in these patients.[30,31]

The identification of a well-defined periappendiceal abscess greater than 3 cm is an indication for treatment with imaging-guided percutaneous drainage and antibiotic therapy.[32] Conversely, perforated appendicitis with a large periappendiceal phlegmon and no drainable pus may be successfully managed by primary antibiotic therapy alone in many patients.[3,32,33]

CONCLUSIONS

Recent concerns for increasing the use of CT include cost, and radiation exposure has renewed interest in sonography for the diagnosis of acute appendicitis. Accurate sonographic evaluation of the appendix requires an understanding of the pathologic and sonographic continuum of uncomplicated and complicated appendicitis that we have presented. The hallmarks of uncomplicated appendicitis include inflammatory changes in the appendiceal wall without necrosis indicated by an enlarged appendiceal diameter (>6–7 mm), hyperemia on color Doppler, mural thickening, and an intact echogenic submucosal layer. Complicated appendicitis is characterized by necrosis and perforation; suspicious sonographic signs are of loculated pericecal fluid, prominent pericecal fat, and circumferential loss of the submucosal layer. Correct identification of the pathologic stage of appendicitis may be of considerable clinical value in guiding appropriate therapy. In particular, the differentiation of complicated versus uncomplicated appendicitis may influence the decision to perform open or laparoscopic appendectomy. Alternatively, larger well-defined periappendiceal abscesses may be treated by percutaneous drainage, whereas periappendiceal phlegmons may be successfully managed with antibiotic therapy alone.

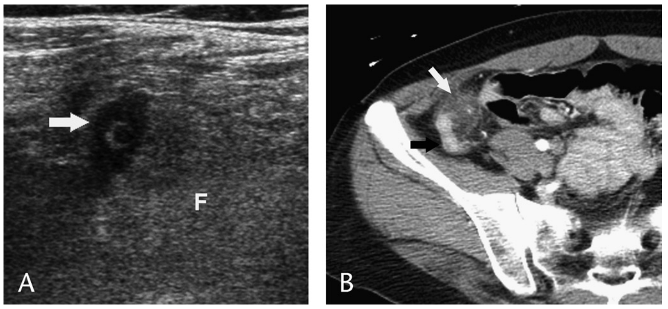

FIGURE 20. A and B, Perforated appendix with periappendiceal phlegmon. A is a transverse sonogram demonstrating an inflamed appendix (arrow) with a marked increased echogenicity within the inflamed periappendiceal fat (''F''). B is a contrast-enhanced CT scan of the same patient demonstrating an abnormal enhancement of the appendix (black arrow) and periappendiceal inflammatory soft tissue infiltration consistent with phlegmon (white arrow).

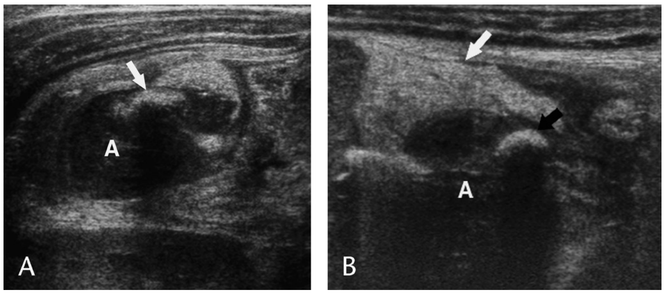

FIGURE 19. A and B, Periappendiceal abscess. In A, transverse sonogram demonstrates hypoechoic periappendiceal abscess (''A'') surrounding extruded appendicolith (arrow). In B, note the marked inflamed fat (white arrow) walling off the abscess (''A'') in same patient. An appendicolith (black arrow) is identified within abscess cavity.

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