Anatomic Reasons for Failure to Visualize the Appendix With Graded Compression Sonography: Insights From Contemporaneous CT

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OBJECTIVE. The purpose of this study is to identify the anatomic locations of appendixes on CT when graded compression sonography fails to visualize the appendix.

MATERIALS AND METHODS. The study included 197 patients with suspected appendicitis whose appendixes were not visualized on graded compression sonography performed with typically used transducers of at least 10 MHz, who underwent CT within 48 hours following graded compression sonography, and who had available either pathologic examination following surgery or 6-week follow-up if surgery was not performed. Appendixes were retrospectively localized using four transverse quadrants (including the posteromedial quadrant) centered on the ileocecal valve and projected vertically, the craniocaudal level relative to the iliac crests, and the depth of the appendix as measured from the surface of the skin. Data were assessed using the Fisher exact test, *t* test, multinomial test, binomial distribution, ANOVA, and linear regression.

RESULTS. Appendixes were most frequently located in the posteromedial quadrant (123 of 197 patients [62.4%]; 95% CI, 55.3–69.2%) at a statistically significantly greater frequency than that expected by chance ($p < 0.00001$). Appendixes were located above the iliac crests in 19.8% of patients (39/197; 95% CI, 14.5–26.1%) and at depths exceeding the penetration of typical transducers of at least 10 MHz in 19.3% of patients (38/197; 95% CI, 14.0–25.5%). All appendixes (95% CI, 98.1–100.0%) were located within the range of 6-MHz transducers.

CONCLUSION. Appendixes that are not visualized on graded compression sonography are most frequently located in the posteromedial quadrant and are often located above the iliac crests or at depths too great for visualization with typically used transducers of at least 10 MHz. Accordingly, when the appendix is not visualized on graded compression sonography, targeted scanning of the posteromedial quadrant and the region above the iliac crests, and scanning with 6-MHz transducers, may enable visualization of the appendix and are recommended additions to scanning protocols.

Keywords: appendicitis, diagnostic imaging, ultrasonography

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Compared with CT, graded compression sonography offers several advantages in the evaluation of patients with suspected appendicitis, including the absence of both ionizing radiation and iodine-based contrast media as well as lower cost [1–5]. However, the lower rate of appendiceal visualization on graded compression sonography remains an ongoing challenge [1–10]. Nonvisualization of the appendix on graded compression sonography may be considered an inconclusive finding and, as such, often leads to CT scanning, with its attendant radiation exposure, further delays, and additional costs [2, 5, 6, 11]. Known challenges for graded compression sonography include large body habitus, retrocecal appendixes, and bowel gas [6, 9, 12–14].

Among these challenges, the location of the appendix may be uniquely amenable to innovations in scanning methodology. For example, recent implementation of a three-step sequential positioning algorithm significantly improved appendiceal visualization and decreased the utilization of CT after graded compression sonography [9]. Nonetheless, appendiceal visualization rates of graded compression sonography remain inferior to those of CT, with the former ranging from 2.4% to greater than 70% and the latter ranging up to 100% [2, 8, 14–19]. Accordingly, new methods that improve visualization of the appendix on sonography potentially can increase the utility of graded compression sonography in the evaluation of suspected appendicitis and decrease patients' exposure to CT.

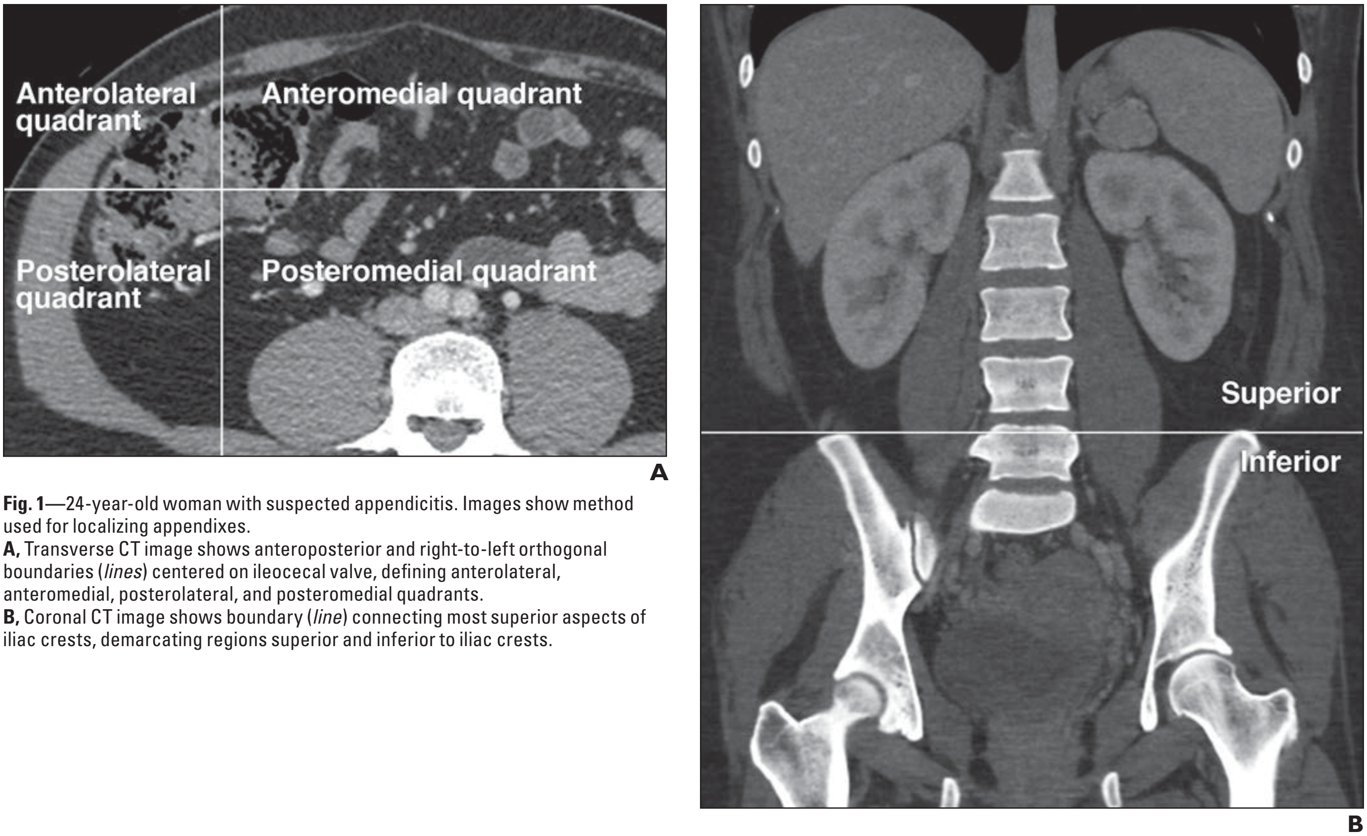


Fig. 1—24-year-old woman with suspected appendicitis. Images show method used for localizing appendixes.
A, Transverse CT image shows anteroposterior and right-to-left orthogonal boundaries (*lines*) centered on ileocecal valve, defining anterolateral, anteromedial, posterolateral, and posteromedial quadrants.
B, Coronal CT image shows boundary (*line*) connecting most superior aspects of iliac crests, demarcating regions superior and inferior to iliac crests.

For many years, graded compression sonography has been the first-line imaging modality of choice at our institution for evaluating patients with suspected appendicitis. Sonography is the modality preferred by the American College of Radiology for pediatric patients [20] and has been proposed for adults in view of concerns about radiation exposure associated with CT [1, 8, 11, 21–25]. On the basis of our earlier experience, we elected to investigate potential anatomic reasons for nonvisualization of the appendix and determine whether nonvisualized appendixes are located in the deep posterior pelvis beyond the cecum or within the abdomen superior to the iliac crests (regions not specifically emphasized in our laboratory or in much of the literature [7, 11, 26–31], although they were identified in a previous study [32]), or are located at depths beyond the range of the transducers of at least 10 MHz that are typically used in our laboratory. We sought to evaluate these possibilities by evaluating patients who underwent CT soon after appendiceal graded compression sonography failed to visualize the appendix.

Materials and Methods

This study was HIPAA compliant. The requirement to obtain informed consent was waived by the institutional review board at Stanford University School of Medicine, in view of the retrospective nature of the investigation.

Patient Selection

An institutional database was searched to identify patients who had undergone graded compression sonography and CT for suspected appendicitis between mid-October 2012 and mid-March 2015. Inclusion criteria were as follows: the initial imaging examination performed was appendiceal graded compression sonography, the appendix was not visualized on graded compression sonography, CT was performed within 48 hours of graded compression sonography and revealed the appendix, and reference standards were available, including pathologic evaluation of resected specimens for patients treated with appendectomy and 6-week follow-up for patients who did not undergo surgery. A total of 197 patients met these criteria.

Scanning Technique

All imaging studies were performed by licensed CT technologists and one of six licensed sonographers with at least 5 years of clinical experience in graded compression sonography. These technologists and sonographers were supervised by attending radiologists, fellows, and residents in our body imaging and pediatric imaging sections. Additional scanning was performed by radiologists, as needed, for clarification of findings, as is typical in our practice. The appendix was identified as a blind-ending tubular structure associated with the cecal tip [2, 7, 14, 29, 31]. Final imaging reports were generated by attending radiologists with 5 years to more than 25 years of experience.

Graded Compression Sonography

Graded compression sonography was performed using Logiq 9 ultrasound equipment (GE Healthcare). A three-step sequential positioning algorithm was used [9]. In this algorithm, when the appendix was not visualized on initial traditional scanning performed with the patient in the supine position, the patient was placed in a 45° left posterior oblique position and was scanned through the right flank to examine the retrocecal region. When the appendix still was not visualized, the patient was returned to the supine position to undergo a second-look evaluation. We typically use linear array transducers of at least 10 MHz for appendiceal studies performed in our laboratory. By agreement with our emergency medicine and surgery departments, patients with a body mass index (weight in kilograms divided by the square of height in meters) of 30 or more, or with peritoneal signs, were evaluated with CT rather than sonography.

CT

Abdominopelvic CT was performed with collimation of 0.625–1.25 mm using 16- or 64- MDCT scanners (LightSpeed VCT, GE Healthcare) without oral or rectal contrast medium. Adults received 150 mL of iohexol contrast medium (Omnipaque 350, GE Healthcare) injected at a rate of 3 mL/s. Pediatric patients received 2 mL of contrast medium per kilogram of body weight, which was injected at a rate of 2 mL/s. Portal venous phase images of the abdomen and pelvis were reconstructed at a slice thickness of 1.25–5 mm with sagittal and coronal reformations obtained at a slice thickness of 2 mm.

Review of CT Examinations

Each CT examination was retrospectively evaluated by two independent reviewers, with discrepancies thereafter resolved by consensus. The position of the appendix was defined by the location of the appendiceal tip because the blind-ended tip provides a recognizable and essential landmark for identifying the appendix [2, 7, 14, 29, 31] and is a unique point in space that is identifiable on both sonography and CT. Each tip was localized in the transverse plane to one of four quadrants demarcated by straight lines centered on the ileocecal valve, extending anteroposteriorly and from right to left and projected vertically, including the anterolateral quadrant, anteromedial quadrant, posterolateral quadrant, and posteromedial quadrant (Figs. 1 and 2). Localization also was performed craniocaudally, with the appendiceal tip identified as being located either superior or inferior to a line connecting the most superior aspects of the iliac crests that divide the pelvis from the abdomen [32, 33] (Fig. 1). Appendiceal tips lying on boundary lines were localized using the immediately adjacent portion of the appendix. Finally, appendiceal depth was defined on axial images, with the use of the shortest distance from the tip to the skin surface without intervening osseous structures, reflecting the closest-approach application of a sonographic transducer.

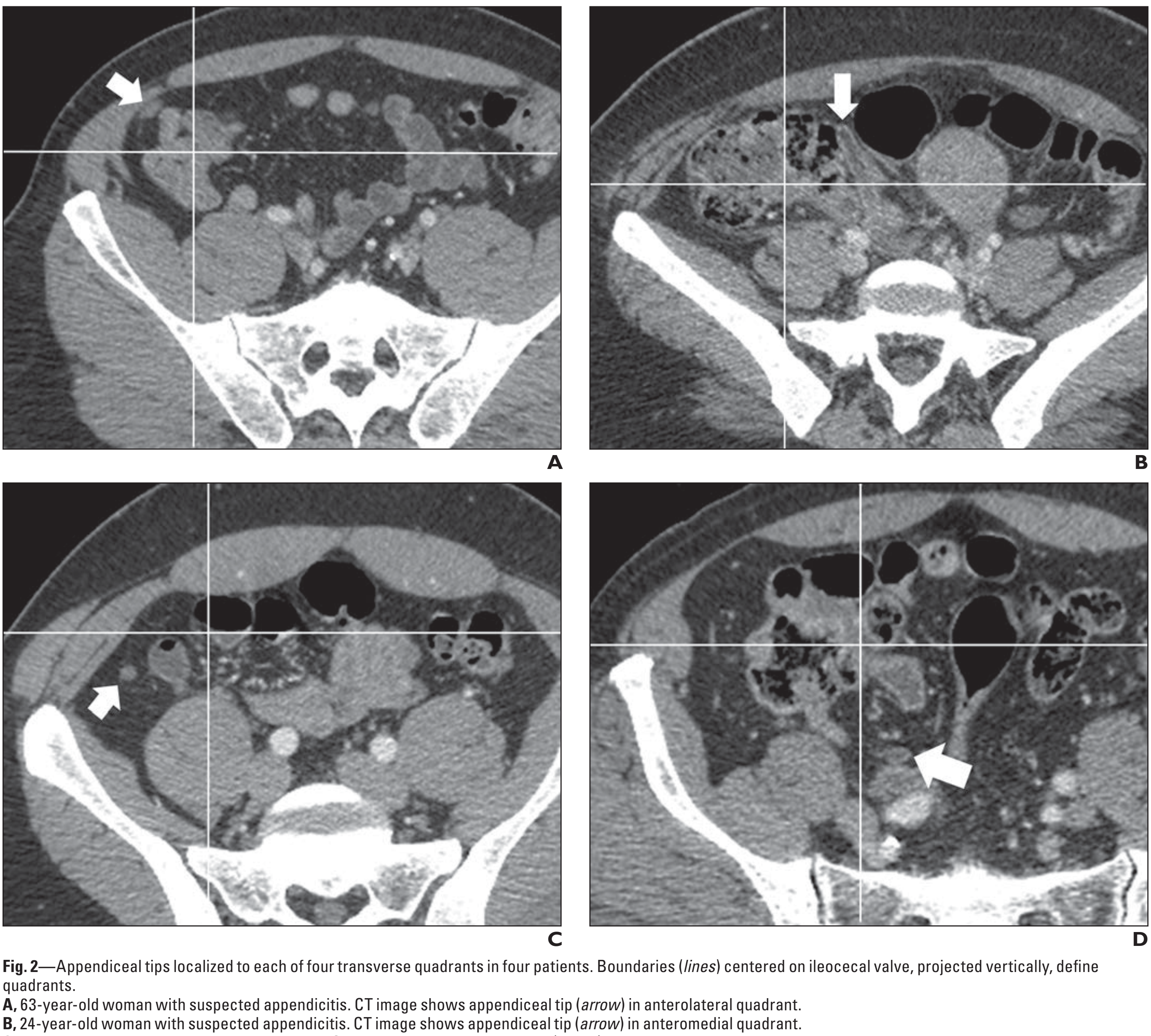


Fig. 2—Appendiceal tips localized to each of four transverse quadrants in four patients. Boundaries (*lines*) centered on ileocecal valve, projected vertically, define quadrants.
A, 63-year-old woman with suspected appendicitis. CT image shows appendiceal tip (*arrow*) in anterolateral quadrant.
B, 24-year-old woman with suspected appendicitis. CT image shows appendiceal tip (*arrow*) in anteromedial quadrant.
C, 37-year-old man with suspected appendicitis. CT image shows appendiceal tip (*arrow*) in posterolateral quadrant.
D, 85-year-old man with suspected appendicitis. CT image shows appendiceal tip (*arrow*) in posteromedial quadrant.

TABLE 1: Sonographically Nonvisualized Appendixes, Stratified by Quadrant Where Appendix Was Located, Patient Group, and Level of Appendix Relative to Iliac Crests

	Location of Appendix				p[a]	
Patient Group, and Level of Appendix Relative to Iliac Crests	Anterolateral Quadrant	Anteromedial Quadrant	Posterolateral Quadrant	Posteromedial Quadrant	By Multinomial Test[b]	By Fisher Exact Test[c]
All levels						
All patients ($n = 197$)						
No. of patients	13	18	43	123	< 0.0001	
Percentage of patients (95% CI)	6.6 (3.6–11.0)	9.1 (5.5–14.1)	21.8 (16.3–28.3)	62.4 (55.3–69.2) $p < 0.00001$[d]		
Patients with appendicitis ($n = 31$)						
No. of patients	2	3	11	15	0.0015	
Percentage of patients (95% CI)	6.5 (0.8–21.4)	9.7 (2.0–25.8)	35.5 (19.2–54.6)	48.4 (30.2–66.9) $p = 0.0056$[d]		
Patients without appendicitis ($n = 166$)						
No. of patients	11	15	32	108	< 0.0001	0.21
Percentage of patients (95% CI)	6.6 (3.4–11.5)	9.0 (5.1–14.5)	19.3 (13.6–26.1)	65.1 (57.3–72.3) $p < 0.00001$[d]		
Level superior to iliac crests						
All patients ($n = 39$)						
No. of patients	11	10	5	13	0.32	
Percentage of patients (95% CI)	28.2 (15.0–44.9)	25.6 (13.0–42.1)	12.8 (4.3–27.4)	33.3 (19.1–50.2) $p = 0.27$[d]		
Patients with appendicitis ($n = 6$)						
No. of patients	2	2	2	0	0.74	
Percentage of patients (95% CI)	33.3 (4.3–77.7)	33.3 (4.3–77.7)	33.3 (4.3–77.7)	0.0 (0.0–45.9) $p = 0.35$[d]		
Patients without appendicitis ($n = 33$)						
No. of patients	9	8	3	13	0.10	0.11
Percentage of patients (95% CI)	27.3 (13.3–45.5)	24.2 (11.1–42.3)	9.1 (1.9–24.3)	39.4 (22.9–57.9) $p = 0.069$[d]		
Level inferior to iliac crests						
All patients ($n = 158$)						
No. of patients	2	8	38	110	< 0.0001	
Percentage of patients (95% CI)	1.3 (0.2–4.5)	5.1 (2.2–9.7)	24.1 (17.6–31.5)	69.6 (61.8–76.7) $p < 0.0001$[d]		
Patients with appendicitis ($n = 25$)						
No. of patients	0	1	9	15	< 0.0001	
Percentage of patients (95% CI)	0.0 (0.0–13.7)	4.0 (0.1–20.4)	36.0 (18.0–57.5)	60.0 (38.7–78.9) $p = 0.00021$[d]		
Patients without appendicitis ($n = 133$)						
No. of patients	2	7	29	95	< 0.0001	0.48
Percentage of patients (95% CI)	1.5 (0.2–5.3)	5.3 (2.1–10.5)	21.8 (15.1–29.8)	71.4 (63.0–78.9) $p < 0.00001$[d]		

Note—Please note that percentages may not total 100% because of rounding.
[a]All p values other than inequalities are presented to two significant digits after the decimal.
[b]Multinomial test with exhaustive enumeration was used to evaluate overall frequencies of appendixes in four quadrants across each row.
[c]The Fisher exact test is a 2×4 comparison of the distribution of appendixes in four quadrants in patients with appendicitis versus patients without appendicitis.
[d]The null hypothesis is 25.0% distribution in each of the four quadrants.

Relationship Between Depth Measurements on Graded Compression Sonography and CT

Because graded compression sonography is performed under compression and CT is not, the depth measurements of the two modalities were related using linear regression. With a random sample of 40 patients (20 male patients and 20 female patients) chosen from among the 197 patients by use of statistical software (Stata, version 14.1, StataCorp), the distance from the anterior skin surface to a recognizable deep point along the right external iliac artery was measured for each patient in side-by-side evaluations of both modalities performed by one reviewer, with the conformation of the vessel as well as the adjacent boney and muscular features used as landmarks. Regression analysis was used to evaluate relationships of appendiceal depth on graded compression sonography to depth on CT, producing the equation $Y = mX + b$, where Y denotes depth on graded compression sonography, m denotes slope, X denotes depth on CT, and b denotes the y-intercept. Regression analysis was also applied to sex, age, and diagnosis as revealed in the medical record.

Appendiceal Depth on Graded Compression Sonography and Transducer Penetration

Using the relationship that transducer penetration in centimeters equals approximately 60 divided by the frequency in megahertz [34], the regression model was solved for the CT depth measurement corresponding to the lowest-frequency penetration of our typical transducers of at least 10 MHz. Patients whose appendiceal depths exceeded this value were then identified. Similar computations were performed for 6-MHz transducers.

Review of Medical Records

Electronic medical records were reviewed by an individual not otherwise involved in the study who recorded demographic information for each patient. Final pathology reports following surgery for patients who underwent appendectomy, and 6-week postpresentation chart reviews for patients who did not undergo surgery, were used as diagnostic reference standards to establish the presence or absence of appendicitis.

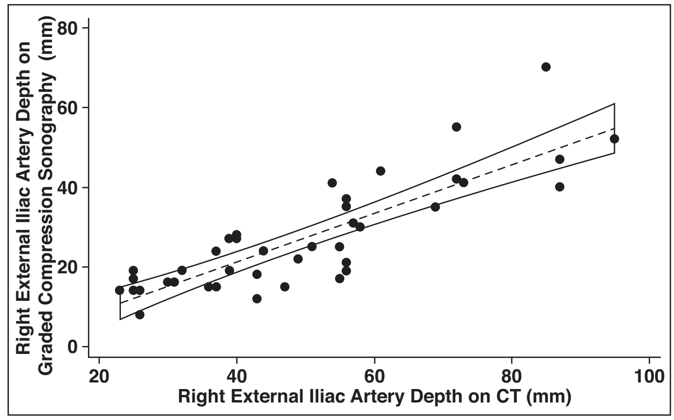


Fig. 3—Scatterplot of depth of recognizable point of right external iliac artery measured with both CT and graded compression sonography, with linear regression relating measurements of two modalities. Circles denote individual patients, dashed line denotes regression line, and area outlined by black line denotes 95% CI.

Statistical Analysis

Statistical analysis was performed using Stata software, utilizing the exact binomial distribution to evaluate 95% CIs of proportions and appendiceal frequencies in individual quadrants, the multinomial exact test with exhaustive enumeration to compare overall four-quadrant distributions within single groups, the 2 × 4 Fisher exact test to compare four-quadrant distributions between groups, one-way ANOVA with the Bonferroni method to adjust for multiple comparisons and a t test to compare depth measurements, and linear regression to relate depth measurements between graded compression sonography and CT. Results with $p < 0.05$, including those indicated by nonoverlapping 95% CIs, were considered significant.

Results

The 197 patients who met the inclusion criteria included 42 male patients (age, 3–65 years; mean, 21.9 years) and 155 female patients (age, 2–74 years; mean, 27.0 years). Of these patients, 13 male patients (31.0%; 95% CI, 17.6–47.1%) and 18 female patients (11.6%; 95% CI, 7.0–77.7%) underwent appendectomy and had appendicitis as defined by the pathologic reference standard. All patients who underwent appendectomy had appendicitis according to this reference standard, and no patients who were managed without surgery presented with appendicitis during follow-up.

Distribution of Appendixes Among Quadrants

As shown in Table 1, the distribution of appendixes among the four quadrants was statistically significantly nonuniform in the entire sample of 197 patients ($p < 0.0001$) as well as in the 31 patients with appendicitis ($p = 0.0015$) and the 166 patients without appendicitis ($p < 0.0001$). A significant majority lay in the posteromedial quadrant among all patients and those without appendicitis (with nonoverlapping 95% CIs between the posteromedial quadrant and each of the other quadrants) and a nonsignificant majority was present in the posteromedial quadrant of patients with appendicitis. In all three patient groups (all patients, patients with appendicitis, and patients without appendicitis), appendixes were significantly more frequently located in the posteromedial quadrant compared with the 25.0% rate expected by chance ($p < 0.00001$, $p = 0.0056$, and $p < 0.00001$, respectively); the null hypothesis was that appendixes are distributed equally among the four quadrants. Overall four-quadrant distributions between patients with and without appendicitis did not differ significantly ($p = 0.21$).

TABLE 2: Appendixes Not Visualized by Sonography, Stratified by Patient Group and Level of Appendix Relative to Iliac Crests

Patient Group	Superior to Iliac Crests	Inferior to Iliac Crests	p^a
All patients ($n = 197$)			
No. of patients	39	158	
Percentage of patients (95% CI)	19.8 (14.5–26.1)	80.2 (73.9–85.5)	
Patients with appendicitis ($n = 31$)			
No. of patients	6	25	
Percentage of patients (95% CI)	19.4 (7.5–37.5)	80.6 (62.5–92.5)	
Patients without appendicitis ($n = 166$)			
No. of patients	33	133	1.00
Percentage of patients (95% CI)	19.9 (14.1–26.8)	80.1 (73.2–85.9)	

[a]By Fisher exact test (a 2 × 2 comparison of the presence or absence of appendicitis with the location of the appendix superior or inferior to the iliac crests). The p value is presented to two significant digits after the decimal.

TABLE 3: Depths of Appendixes Not Visualized by Sonography, Stratified by Patient Group and Quadrant Where Appendix Was Located

Patient Group	Location of Appendix					p[a]
	All Quadrants	Anterolateral Quadrant	Anteromedial Quadrant	Posterolateral Quadrant	Posteromedial Quadrant	
All patients ($n = 197$)						
Range	7–163	27–77	14–123	23–121	7–163	
Mean (95% CI)	78.9 (75.1–82.7)	58 (48.8–67.2)	78.3 (63.7–92.9)	72.8 (65.2–80.4)	83.4 (78.5–88.2)	0.0034
Patients with appendicitis ($n = 31$)						
Range	23–125	63–63	84–96	23–110	42–125	
Mean (95% CI)	75.5 (67.2–83.9)	63.0 (63.0–63.0)	89.3 (74.2–104.5)	75.3 (55.3–95.2)	74.7 (63.4–86.0)	0.65
Patients without appendicitis ($n = 166$)						
Range	7–163	27–77	14–123	42–121	7–163	
Mean (95% CI)	79.5 (75.3–83.8)	57.1 (46.0–68.2)	76.1 (58.5–93.6)	71.9 (63.5–80.3)	84.6 (79.3–89.9)	0.0032
$p = 0.45$[b]					$p = 0.19$[b]	

Note—All depth measurements are expressed in millimeters.
[a]ANOVA with Bonferroni method to adjust for multiple comparisons. The p value is presented to two significant digits after the decimal.
[b]By t test for the comparison of the appendiceal depth in patients with and without appendicitis. The p value is presented to two significant digits after the decimal.

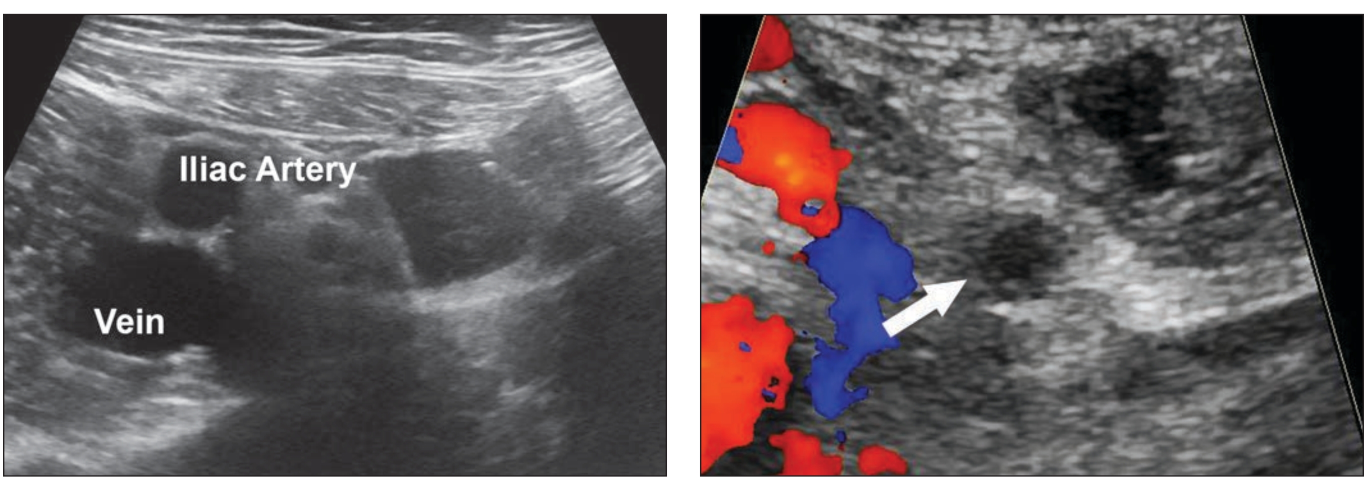
Level of Appendixes Relative to Iliac Crests

As shown in Table 2, a statistically significant majority of appendixes were located inferior to the iliac crests among all patients, patients with appendicitis, and patients without appendicitis, as indicated by the nonoverlapping 95% CIs between appendixes superior and appendixes inferior to the iliac crests for each of these three patient groups. In addition, the presence or absence of appendicitis was not associated with location of the appendix superior or inferior to the iliac crests ($p = 1.00$).

As shown in Table 1, the distribution of appendixes below the iliac crests among the four quadrants was statistically significantly nonuniform for all three patient groups ($p < 0.0001$, for each). For each patient group, most appendixes found below the iliac crests were located within the posteromedial quadrant, at a frequency that significantly exceeded the 25.0% frequency expected by chance (for all patients, $p < 0.00001$; for patients with appendicitis, $p = 0.00021$; and for patients without appendicitis, $p < 0.00001$). Above the iliac crests, however, relatively few appendixes were present and none of the three patient groups exhibited significant four-quadrant nonuniformity, a majority in the posteromedial quadrant, or posteromedial quadrant frequency that exceeded the 25.0% rate expected by chance. Overall four-quadrant distributions between patients with appendicitis and patients without appendicitis did not differ significantly whether the appendix was found above ($p = 0.11$) or below ($p = 0.48$) the iliac crests.

Depth of Appendixes on CT

Appendiceal depth on CT ranged from 7 to 163 mm (mean, 78.9 mm) among the 197 patients, and it did not differ significantly between patients with appendicitis and patients without appendicitis ($p = 0.45$) (Table 3).



A B

Fig. 4—38-year-old woman with appendicitis who was not included in sample of 197 patients. Sonographic images show value of sonography performed with 6-MHz transducer after nonvisualization of appendix on sonography performed with 10-MHz transducer.
A, Initial gray-scale sonographic image obtained at 10 MHz shows no appendix within posteromedial quadrant.
B, Color Doppler image obtained at 6 MHz after image shown in **A** shows appendix (*arrow*) and vessels in posteromedial quadrant.

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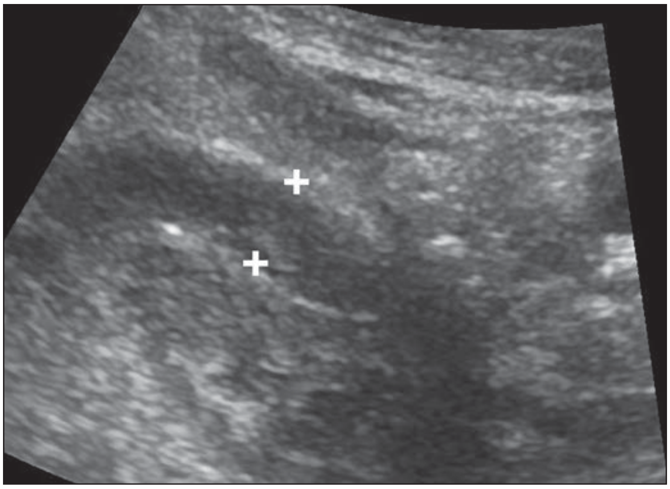


C

Fig. 4 (continued)—38-year-old woman with appendicitis who was not included in sample of 197 patients. Sonographic images show value of sonography performed with 6-MHz transducer after nonvisualization of appendix on sonography performed with 10-MHz transducer.
C, Gray-scale ultrasound image obtained at 6 MHz permits measurement of enlarged 9-mm appendix (between *calipers*) in posteromedial quadrant.

As evaluated with ANOVA (Table 3), all patients and patients without appendicitis had significant nonuniformity in mean appendiceal depth among the four quadrants (p = 0.0034 and p = 0.0032, respectively); these findings reflected significant pairwise differences between the posteromedial quadrant and the anterolateral quadrant (and only between the posteromedial quadrant and anterolateral quadrant) for these two patient groups (p = 0.0070 and p = 0.0090, respectively). Patients with appendicitis exhibited neither significant nonuniformity among the four quadrants by ANOVA (p = 0.65) (Table 3) nor significant pairwise differences among the four quadrants (p = 1.00, for each pairwise combination). Appendiceal depth in the posteromedial quadrant did not differ significantly between patients with appendicitis and patients without appendicitis (p = 0.19) (Table 3).

Relationship Between Depth Measurements on Graded Compression Sonography and CT

In linear regression analysis of the subset of 40 randomly selected patients, depth measurements on CT correlated significantly with depth measurements on graded compression sonography in both univariate ($p < 0.001$) and multivariate analysis ($p < 0.001$). Sex, age, and diagnosis did not correlate significantly with depth on graded compression sonography in univariate analysis or multivariate analysis (for sex, p = 0.29 and p = 0.46, respectively; for age, p = 0.30 and p = 0.44, respectively; and for diagnosis, p = 0.63 and p = 0.58, respectively), and were excluded from further calculations. Linear regression of depth on graded compression sonography as a function of depth on CT yielded a slope of 0.61 (95% CI, 0.48–0.73), a y-intercept of –3.03 mm, $p < 0.001$, and R^2 = 0.71 (Fig. 3).

Appendiceal Depth on Graded Compression Sonography Versus Transducer Penetration

Using the relationship between transducer penetration and frequency reported by Szabo and Lewin [34], transducers of at least 10 MHz, such as those typically used in our laboratory, would penetrate to a maximum depth of 60 mm. Substituting this value into the linear regression model yielded an equivalent CT depth of 103 mm.

Appendiceal depths on CT exceeded 103 mm in 38 of the 197 patients (19.3%; 95% CI, 14.0–25.5%). As shown in Table 4, the distribution of appendixes with a depth exceeding 103 mm was statistically significantly nonuniform among the four quadrants for all patients and for patients without appendicitis ($p < 0.0001$ for both patient groups), with the posteromedial quadrant accounting for a statistically significant majority of appendixes in both patient groups (with nonoverlapping 95% CIs between the posteromedi-

TABLE 4: Appendixes Not Visualized by Sonography and Located at Depths Exceeding the Penetration of Transducers of at Least 10 MHz, Stratified by Patient Group and Quadrant Where Appendix Was Located

Patient Group	Location of Appendix				p^a	
	Anterolateral Quadrant	Anteromedial Quadrant	Posterolateral Quadrant	Posteromedial Quadrant	By Multinomial Test[b]	By Fisher Exact Test[c]
All patients (n = 38)						
No. of patients	0	4	7	27	< 0.0001	
Percentage of patients (95% CI)	0 (0.0–9.3)	10.5 (2.9–24.8)	18.4 (7.7–34.3)	71.1 (54.1–84.6) $p < 0.00001^d$		
Patients with appendicitis (n = 5)						
No. of patients	0	0	3	2	0.18	
Percentage of patients (95% CI)	0.0 (0.0–52.2)	0.0 (0.0–52.2)	60.0 (14.7–94.7)	40.0 (5.3–85.3) $p = 0.60^d$		
Patients with appendicitis (n = 33)						
No. of patients	0	4	4	25	< 0.0001	0.046
Percentage of patients (95% CI)	0.0 (0.0–10.6)	12.1 (3.4–28.2)	12.1 (3.4–28.2)	75.8 (57.7–88.9) $p < 0.00001^d$		

[a]All p values other than inequalities are presented to two significant digits after the decimal.
[b]Multinomial test with exhaustive enumeration was used to evaluate overall frequencies of appendixes in four quadrants across each row.
[c]The Fisher exact test is a 2 × 4 comparison of the distribution of appendixes in four quadrants in patients with appendicitis versus patients without appendicitis.
[d]The null hypothesis is 25.0% distribution in each of the four quadrants.

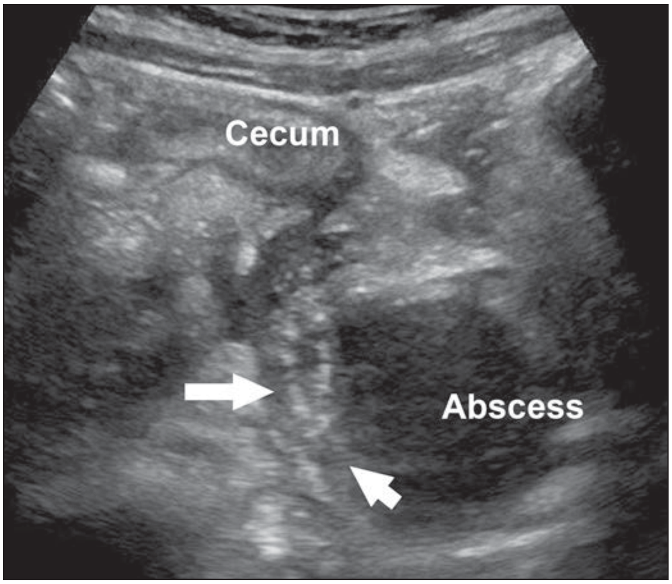


Fig. 5—26-year-old woman with appendicitis and periappendiceal abscess who was not included in sample of 197 patients. Sonographic image obtained at 6 MHz shows appendix (*long arrow*) in posteromedial quadrant, cecum, abscess, and focal loss of submucosal layer at appendiceal tip (*short arrow*) immediately after nonvisualization of appendix on initial sonography performed at 10 MHz.

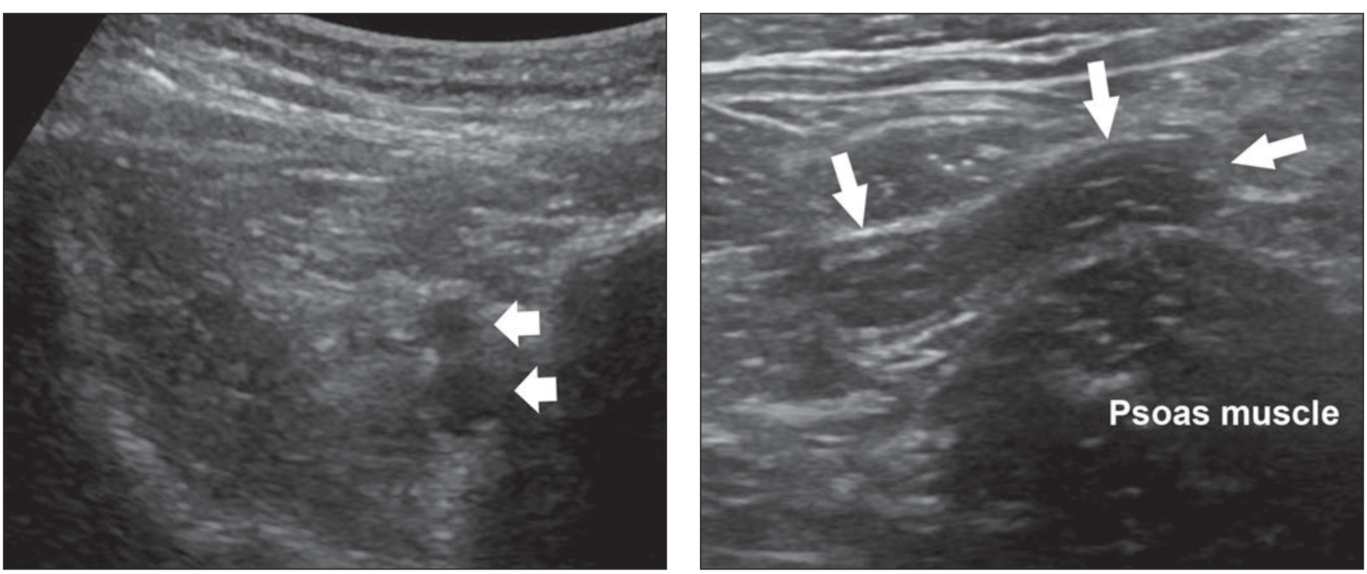
al quadrant and each of the other quadrants) at frequencies significantly greater than the 25.0% expected by chance for both patient groups ($p < 0.0001$, for both groups). Although comparison of the overall four-quadrant distributions between patients with and without appendicitis was of borderline statistical significance ($p = 0.046$), caution is in order because very few patients with appendicitis had appendixes deeper than 103 mm.

If 6-MHz transducers been used instead of transducers of at least 10 MHz, penetration on graded compression sonography would have increased to 100 mm [34], and the equivalent depth on CT would have increased to 169 mm in the regression model. This increased penetration would have been sufficient to reach the appendixes of all 197 patients in the sample (100.0%; 95% CI, 98.1–100.0%), which ranged in depth from 7 to 163 mm on CT.

Discussion

On CT performed shortly after graded compression sonography, a statistically significant majority (62.4%) of sonographically nonvisualized appendixes were found in the posteromedial quadrant within the deep posterior pelvis, at frequencies statistically significantly greater than that expected by chance, whether appendicitis was present or not. Additionally, sonographically nonvisualized appendixes were found above the iliac crests in 19.8% of patients and were present at depths beyond the range of our typical transducers of at least 10 MHz in 19.3% of patients. No significant differences were evident between normal appendixes and those with appendicitis with respect to quadrant location, craniocaudal level relative to the iliac crests, or depth from the skin.

Our findings were obtained from evaluations of living patients who were undergoing noninvasive imaging, and thus they may reflect in vivo relationships in ways that previous surgical or postmortem studies have not [35, 36]. To our knowledge, this is the first study to utilize contemporaneous CT to evaluate potential anatomic reasons for nonvisualization of the appendix on graded compression sonography. We employed orthogonal transverse and craniocaudal planes to accomplish localization, using four quadrants centered on the ileocecal valve in the transverse plane as well as the level of the iliac crests in the coronal plane, with the appendiceal tip serving as the unique point for appendiceal localization. In doing this, we sought to produce straightforward, rigorous orthogonal data that could be correlated between CT and graded compression sonography; the region of the ileocecal valve is generally vis-



A B

Fig. 6—27-year-old woman with appendicitis who was not included in sample of 197 patients. Sonographic images show value of scanning above iliac crests after nonvisualization of appendix below iliac crests.
A, Initial transverse gray-scale sonographic image shows iliac artery and vein (*arrows*) but no appendix in region below iliac crests.
B, Transverse gray-scale sonogram obtained after image in **A** shows appendix (*arrows*) adjacent to psoas muscle in region above iliac crests.

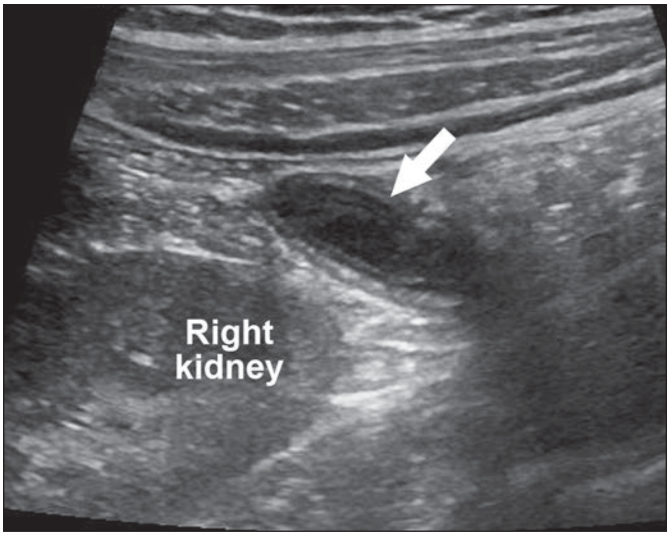


Fig. 7—10-year-old boy with appendicitis who was not included in sample of 197 patients. Sonographic image shows enlarged appendix (*arrow*) above iliac crests immediately after nonvisualization of appendix on initial sonographic image of region below iliac crests.

ible on both modalities, and the iliac crests are visible on CT and are palpable during graded compression sonography.

This design represents a departure from earlier reports that addressed surgical, postmortem, and sonographic subjects, utilized more qualitative categories such as "splenic or post-ileal," "pelvic," and "midpelvic," and variably intermixed transverse and craniocaudal components of location [32, 33, 35, 36]. Moreover, our subjects all had suspected appendicitis with sonographically nonvisualized appendixes and underwent contemporaneous CT, characteristics that may differentiate them from subjects in earlier reports yet currently characterize these individuals as a clinically important and diagnostically challenging group of patients.

The preponderance of appendixes in the posteromedial quadrant evident in our results may reflect several factors. First, anteriorly located appendixes (those located in the anterolateral or anteromedial quadrant) are closer to the skin than are posteriorly located appendixes (those located in the posterolateral or anteromedial quadrant), as evidenced by their significantly lesser mean depth. Additionally, as opposed to the posterolateral quadrant, the posteromedial quadrant likely affords a tapering acoustic window during the left posterior oblique step of the three-step sequential positioning algorithm that we use [9]; the acoustic beam likely narrows as it passes behind the cecum before reaching the posteromedial quadrant. Also, we found that a statistically significant majority of appendixes in the posteromedial quadrant were located beyond the range of the transducers of at least 10 MHz that we routinely use. In addition, the deep posterior pelvis beyond the cecum is an area not previously emphasized during evaluations in our laboratory or in much of the previous literature [7, 11, 26–31]. In our sample, some of the appendixes in the posteromedial quadrant and posterolateral quadrant could be considered retrocecal in location; however, definitions of retrocecal location are not uniform in the literature, and the reported frequencies of retrocecal appendixes vary widely (e.g., from 26.5–28.6% in studies using graded compression sonography to 65.28% in large autopsy studies and 20.2–74% in postmortem and surgical studies [32, 33, 35, 36]. Although the preponderance of appendixes found in the posteromedial quadrant in our study could reflect the anatomy of the population in general, this is uncertain given the substantial variability that exists in the literature regarding appendiceal positions.

Our results revealed that a substantial proportion of appendixes that were not visualized sonographically were located above the iliac crests (19.8%), a region not routinely emphasized in our typical graded compression sonography examination or in much of the previous literature [7, 11, 26–31]. These results parallel those of previous studies. For example, appendixes were found above the iliac crests in 21.4% of patients with abdominal pain who underwent noncompressive sonography [33], in 14.3% of patients with appendicitis, and in 6.8% of patients without appendicitis who underwent compressive and noncompressive sonography [32].

To evaluate appendiceal depth during graded compression sonography and compare it with transducer penetration, we first generated a regression model associating depth on CT with depth on graded compression sonography. Because appendixes were not visible on graded compression sonography in our patient sample, we evaluated the depth of vascular structures visible on both CT and graded compression sonography, performed regression analysis on these data, and then applied the results to appendixes. This analysis revealed that 38 of 197 appendixes (19.3%) were located at depths exceeding the penetration expected of the transducers of at least 10 MHz that we typically use in our laboratory, with a statistically significant majority of these located in the posteromedial quadrant. Importantly, parallel analysis indicates that 6-MHz transducers would reach all the appendixes of our 197 patients. Accordingly, although modern scanning benefits from high-frequency high-resolution images that show features such as mural hyperemia, hyperechoic periappendiceal fat, and fine mural anatomy, findings that are essential in the sonographic evaluation of appendicitis [6–8, 25, 26, 29, 37, 38], a role clearly exists for lower-frequency scanning as well.

On the basis of our findings, we encourage specific practical modifications to recent graded compression sonography protocols, such as the three-step algorithm reported by Chang et al. [9]. First, we propose having both higher-frequency (at least 10 MHz) and lower-frequency (6 MHz) transducers connected at the outset of each examination. Should the appendix not be visualized with typical scanning performed with transducers of at least 10 MHz, we suggest, first, targeted scanning of the posteromedial quadrant and, second, palpation of the iliac crests and targeted scanning of the region above them. Should the appendix still remain unseen, we suggest toggling to the lower-frequency transducer already connected and again addressing the posteromedial quadrant and the region above the iliac crests. Once the appendix is visualized at lower frequency, the sonographer can toggle back and use the higher-frequency transducer; the sonographer may then find it possible to visualize the appendix and generate higher-resolution images. These maneuvers specifically address the 62.4%, 19.8%, and 19.3% of the nonvisualized appendixes found in the posteromedial quadrant, above the iliac crests, and at depths exceeding the typical range of transducers of at least 10 MHz, respectively. Figures 4 and 5 show the value of scanning the posteromedial quadrant with a 6-MHz transducer after nonvisualization of the appendix with a 10-MHz transducer, and Figures 6 and 7 show the value of scanning above the iliac crests when the appendix is not visualized in a typical pelvic position.

Several limitations deserve mention. We used the appendiceal tip to localize the appendix because the tip must be seen to confidently identify the appendix as a blind-ending structure [2, 7, 14, 29, 31] and because the tip constitutes a unique point in space. We chose to permit a 48-hour period between graded compression sonography and CT, to include patients with more straightforward and less straightforward clinical courses, as has been done in previous studies [19, 30, 39]; other periods could have been chosen. This is a single-institution, retrospective study; therefore, it is possible that patients could have presented elsewhere with recurrent symptoms without our being able to tabulate these individuals. The sample in this study was not adequate to permit meaningful stratification by sex and age, characteristics that will await later investigation. Our evaluation of transducer penetration uses a relationship between frequency and penetration that is likely approximate [34], and we thus consider our depth analysis helpful yet approximate. Also, a variety of factors can affect appendiceal sonography, in addition to the factors that we specifically address. Scanning at 6 MHz provides greater penetration than does scanning at at least 10 MHz, although penetration may be limited by increased numbers of intervening bowel loops, bowel gas, and decreased spatial resolution. At our institution, clinical decisions regarding management and referral for imaging are made by clinical colleagues; different decisions could have been made at other institutions. Finally, we did not address the additional costs of the maneuvers that we suggest for use when the appendix is not initially visualized.

In conclusion, appendixes not visualized on graded compression sonography are located in the posteromedial quadrant in a statistically significant majority of patients, are superior to the iliac crests in nearly 20% of patients, and are located at depths exceeding the range of transducers of at least 10 MHz in 19.3% of patients. Accordingly, more intensive scanning of the posteromedial quadrant and the region above the iliac crests, and with lower frequency (e.g., 6 MHz) transducers, may reveal appendixes that are otherwise nonvisualized on graded compression sonography, potentially leading to improved diagnosis by graded compression sonography and correspondingly less exposure to CT. Prospective studies will be needed to corroborate these findings and to evaluate the costs and benefits of the maneuvers suggested for addressing them.

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