

Bedside Ultrasonography as an Adjunct to Routine Evaluation of Acute Appendicitis in the Emergency Department

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Introduction: Appendicitis is a common condition presenting to the emergency department (ED). Increasingly emergency physicians (EP) are using bedside ultrasound (BUS) as an adjunct diagnostic tool. Our objective is to investigate the test characteristics of BUS for the diagnosis of appendicitis and identify components of routine ED workup and BUS associated with the presence of appendicitis.

Methods: Patients four years of age and older presenting to the ED with suspected appendicitis were eligible for enrollment. After informed consent was obtained, BUS was performed on the subjects by trained EPs who had undergone a minimum of one-hour didactic training on the use of BUS to diagnose appendicitis. They then recorded elements of clinical history, physical examination, white blood cell count (WBC) with polymorphonuclear percentage (PMN), and BUS findings on a data form. We ascertained subject outcomes by a combination of medical record review and telephone follow-up.

Results: A total of 125 subjects consented for the study, and 116 had adequate image data for final analysis. Prevalence of appendicitis was 40%. Mean age of the subjects was 20.2 years, and 51% were male. BUS was 100% sensitive (95% CI 87-100%) and 32% specific (95% CI 14-57%) for detection of appendicitis, with a positive predictive value of 72% (95% CI 56-84%), and a negative predictive value of 100% (95% CI 52-100%). Assuming all non-diagnostic studies were negative would yield a sensitivity of 72% and specificity of 81%. Subjects with appendicitis had a significantly higher occurrence of anorexia, nausea, vomiting, and a higher WBC and PMN count when compared to those without appendicitis. Their BUS studies were significantly more likely to result in visualization of the appendix, appendix diameter >6mm, appendix wall thickness >2mm, periappendiceal fluid, visualization of the appendix tip, and sonographic Mcburney's sign ($p<0.05$). In subjects with diagnostic BUS studies, WBC, PMN, visualization of appendix, appendix diameter >6mm, appendix wall thickness >2mm, periappendiceal fluid were found to be predictors of appendicitis on logistic regression.

Conclusion: BUS is moderately useful for appendicitis diagnosis. We also identified several components in routine ED workup and BUS that are associated with appendicitis generating hypothesis for future studies. [West J Emerg Med. 2014;15(7):808-815.]

INTRODUCTION

Appendicitis is the most common acute abdominal disorder that requires surgery.¹⁻² The diagnosis is commonly made on the grounds of a combination of history, physical examination, laboratory tests, and diagnostic imaging findings. As these diagnostic steps often take place in a serial fashion in the emergency department (ED), patients suspected of appendicitis tend to stay for prolonged periods of time, requiring considerable staff and physical resources.³⁻⁵

To avoid excessive testing while minimizing missed diagnosis, investigators have derived various appendicitis scores based on components of history, physical examination, and laboratory test results.⁶⁻¹³ Typically these scores are used to rule out appendicitis, yielding a post-test population with moderate to high probability for the condition. While most of these scoring systems have high sensitivities, they cannot be used solely to select patients for surgical intervention because of inadequate specificities. Often further imaging is required to clarify the diagnosis, corresponding to a considerable time and resource burden as patients wait for its completion and interpretation. In addition, the accuracies of these scores tend to worsen when tested by unaffiliated investigators at different sites.^{13,14}

In recent years, studies have been published on the use of beside ultrasound (BUS) to diagnose appendicitis in the ED.¹⁵⁻¹⁷ This is based on the radiology literature, which has shown that ultrasound is moderately to highly sensitive and specific in the diagnosis of appendicitis.¹⁸ Furthermore, BUS emits no ionizing radiation, and can be performed and interpreted rapidly at the bedside, providing obvious advantages to clinicians and patients alike.

The purpose of the study was to determine if emergency physicians (EP) can accurately diagnose appendicitis using BUS, after a brief training in graded-compression abdominal ultrasonography. We also aimed to identify components of ED history, physical examination, laboratory workup, and BUS associated with the diagnosis of appendicitis.

METHODS

This was a single-site, prospective study on patients treated at the Advocate Christ Medical Center Emergency Department for suspected appendicitis. It was approved by the Advocate Health Care Institutional Review Board. The hospital is a community tertiary referral center with approximately 100,000 ED visits per year. The ED is staffed entirely by board-certified EPs and sponsors a three-year emergency medicine residency training program. On-site staff radiologists provide interpretation of radiologic studies at all hours.

Patients four years of age and older presenting to the ED with abdominal pain concerning for appendicitis (as determined by the ED attending physician after history and physical examination) were eligible for enrollment. Exclusion criteria included previous appendectomy, pregnancy, unstable

vital signs, frank peritonitis, neurological deficits interfering with the ability to localize abdominal pain, wards of the state, and subject/guardian refusal of consent. Potentially eligible subjects were identified by treating EPs, study investigators or the research nurse, by screening of the ED patient tracking board. Enrollment was by convenience sampling, depending on whether a study investigator was available. Investigators were EPs who had undergone a minimum of one-hour didactic training given by the senior investigator (ML) on the use of ultrasound to diagnose appendicitis. Topics discussed during the didactic session included the use of graded compression technique and anatomical landmarks to identify the appendix, appearance of the normal and inflamed appendix, and examples of sonographic findings associated with acute appendicitis as delineated in the data collection sheet. Study investigators were allowed to simultaneously function as treating EPs, and were not blinded to the presentation and clinical history of the subjects.

After informed consent was signed, a focused clinical history and physical examination was obtained from each study subject, followed by a focused BUS of the abdomen performed using a Zonare Z. One (Mountain View, CA) or Sosite M-Turbo (Bothell, WA) machine. Each subject was asked to direct the investigator to the point of maximal pain. The area was then scanned with a high frequency (5-10 Mhz) transducer using graded compression technique. Investigators concluded their BUS when, in their judgment, the best possible images in the subjects were obtained. All BUS studies were completed prior to any radiology department studies or surgical consultations. Study images were recorded and archived at the ED ultrasound office, and were reviewed weekly for quality assurance. Investigators' overall impressions of the BUS, based on real-time sonographic findings as recorded on the data collection sheet, were documented in the patients' medical records. All patients were treated according to the judgment of the ED attending physicians or consultants.

Subject data collected included age, sex, height, weight, body mass index (BMI), time of onset of symptoms, menarche if applicable, ED treatment (pain medication, intravenous fluid, antiemetic) prior to BUS; the presence or absence of anorexia, pyrexia, nausea, vomiting, diarrhea, right lower quadrant (RLQ) pain, migration of pain to right lower quadrant from elsewhere in the abdomen, tenderness to percussion/cough/hopping, leukocyte (WBC) count, and polymorphonuclear neutrophil (PMN) percentage.

Sonographic data collected included visualization and compressibility of the appendix; diameter and wall thickness of the appendix; presence of free fluid, fecalith, or any complex mass in right lower quadrant; and sonographic McBurney's sign (elicitation of pain when concerning structure is compressed with the ultrasound transducer).

Diagnostic test and imaging results, pathological reports, intra-operative findings, and subject hospital course, if

available, were obtained by review of the medical record. A research nurse made follow-up telephone calls at 24 hours and 30 days to subjects who were discharged from the ED or who did not receive operative intervention. Three separate attempts to establish contact were made before subjects were deemed lost to follow-up. One of the investigators (SL) adjudicated final patient outcome based on the information obtained by the above-mentioned means. Diagnosis of appendicitis was based on intraoperative or pathological findings. Diagnosis of "no appendicitis" was based on intraoperative findings, presence of alternate diagnosis, resolved symptoms during inpatient observation or at follow-up telephone calls, lack of appendectomy at subsequent ED visits, or negative abdominal computed tomography results in patients who were otherwise unable to be followed up.

We recorded all study information on patient data sheets, and then entered it onto an Excel (2007, Microsoft Corp., Redmond, WA) spreadsheet for analysis. All data entries were double-checked by one of the investigators for accuracy. We analyzed data by SPSS (version 20.0, IBM Corp., Armonk, NY). Student's t test was used for continuous variables and chi square for categorical variables. We calculated the sensitivity, specificity, positive predictive value, negative predictive value of ED BUS studies using the defined outcomes above as the gold standard. We performed univariate analysis on the recorded demographic, history, laboratory, and BUS findings to identify factors associated with appendicitis. Multivariate logistic regression was then performed incorporating significant findings in univariate analysis to determine predictive factors of appendicitis and calculate the degree of association in diagnostic BUS studies.

RESULTS

A total of 125 subjects consented for the study, and 116 had adequate image data for final analysis. Subject demographics are listed in Table 1. Mean age of the subjects was 20.2 years, and 51% were male. Sixty percent were 18 years of age or younger. Prevalence of appendicitis was 40%.

Fifty-two (45%) of the 116 BUS studies were diagnostic. There were 33 true positive, 13 false positive, 6 true negative, and no false negative BUS studies. This corresponds to a sensitivity of 100% (95% CI 87-100%), specificity of 32% (95% CI 14-57%), positive predictive value of 72% (95% CI 56-84%), and negative predictive value of 100% (95% CI 52-100%) of BUS. Alternatively calculated test characteristics assuming all non-diagnostic BUS studies were deemed negative at the bedside are listed in Table 2. Inclusion of subjects with inadequate image data did not worsen these test characteristics. Table 3 lists the BUS findings, final diagnoses, image review comments, and clinical course of subjects with false positive BUS. The majority of these 13 cases had intra-abdominal or pelvic pathology leading to the presence of peritoneal free fluid. Nine of the cases did not have the appendix clearly depicted, or depicted an appendix with a

Table 1. Subject demographic characteristics.

Subject	Number (percentages)
Sex	
Female	57 (49)
Male	59 (51)
Age	
4-8	17 (14.7)
8-12	16 (13.8)
12-18	37 (31.9)
≥19	46 (39.7)
Body mass index	
<18.5	25 (21.6)
18.5-24.9	46 (39.7)
25-29.9	23 (19.8)
30-34.9	12 (10.3)
≥35	10 (8.6)

Table 2. Calculated test characteristics assuming all non-diagnostic bedside ultrasound studies were deemed negatives at the bedside.

Test characteristics	Values (95% CI)
Sensitivity	72% (56-84%)
Specificity	81% (70-89%)
Positive predictive value	72% (56-84%)
Negative predictive value	81% (72-89%)
Positive likelihood ratio	3.86 (2.29-6.51)
Negative likelihood ratio	0.35 (0.22-0.55)

diameter <6mm as determined at the time of image review.

Table 4 compares the demographic, history, laboratory and BUS characteristics of subjects with and without appendicitis. There was a male predominance in subjects with appendicitis. On univariate analysis, subjects with appendicitis had a significantly higher occurrence of anorexia, nausea, vomiting, and a higher WBC count and PMN percentage. BUS of these subjects were also significantly more likely to result in visualization of the appendix, appendix diameter >6mm, appendix wall thickness >2mm, periappendiceal fluid, visualization of the appendix tip, and sonographic Mcburney's sign ($p<0.05$).

In subjects with diagnostic BUS studies, WBC, PMN, visualization of appendix, appendix diameter >6mm, appendix wall thickness >2mm, periappendiceal fluid were found to be predictors of appendicitis on multivariate logistic regression (Table 5).

BUS success and accuracy were independent of operator, parenteral narcotic or antiemetic administration, or scanning time.

DISCUSSION

Apart from individual case reports, currently there have

Table 3. Bedside ultrasound (BUS) findings, final diagnoses, image review comments, and clinical course of false positive BUS.

Patient	Age, Sex	BUS Findings	Additional comments on image review	Final diagnosis	Clinical course
1	15, male	D, NC, F, TV, MB	N/A	Abdominal pain	CT no appendicitis. Returned one week later for same complaint, and was discharged with symptomatic care. On 30-day followup no surgery was performed
2	56, male	NC, MB	Appendix not visualized	Sigmoid diverticulitis with phlegmon	Taken to surgery based on BUS and clinical findings. Underwent sigmoid colectomy/ colon anastomosis, and was eventually discharged home.
3	8, female	D, T, NC, FF, TV, MB	Appendix diameter <6mm	Abdominal pain	CT no appendicitis. Patient discharged home. Lost to phone followup. No further emergency department visit.
4	21, female	D, T, F, FF, TV, MB	N/A	Pelvic inflammatory disease	CT no appendicitis. Hospitalized for observation. Cervical swab tested positive for gonorrhea. Patient treated and discharged.
5	20, female	D,T, NC, MB	Appendix wall thickness <2mm	Abdominal pain	CT and US non-diagnostic. Admitted for observation. Pain improved while hospitalized and patient discharged home. Did well on 30-day followup.
6	6, female	D, NC, FF, TV, MB	N/A	Ovarian torsion	Taken to surgery based on BUS findings. Found to have ovarian torsion secondary to dermoid cyst. Resection performed.
7	47, female	D, NC, F, CM, FF, MB	Appendix not visualized	Colonic diverticulitis	CT showed inflammation around distal cecum/ proximal ascending colon but no appendicitis. Admitted for observation and discharged on oral antibiotics.
8	37, female	D, NC, TV, MB	Appendix not visualized	Abdominal pain	US non-diagnostic. CT no appendicitis. Patient discharged home and had no further intervention on 30-day followup.
9	29, female	D, NC, CM, TV, MB	Appendix not visualized	Diverticulitis	CT showed ascending colon inflammation/ diverticulitis. Admitted for observation and discharged home on oral antibiotics.
10	24, female	NC, F, CM, FF, TV, MB	Appendix 4.7mm	Ruptured ovarian cyst	CT no appendicitis. Final diagnosis made on pelvic US. Patient discharged home. On followup still had intermittent pain but no appendectomy.
11	31, female	D, NC, FF, TV, MB	Appendix not visualized	Mesenteric adenitis	Discharged and returned 1 day later. Admitted for observation. No surgery performed. Asymptomatic on followup.
12	11, male	D, NC, F, CM, FF, TV, MB	Appendix not visualized	Terminal ileitis	US non-diagnostic. Diagnosis made by CT. Unremarkable colonoscopy. Discharged home with symptomatic care.
13	18, male	NC, FF, MB	Appendix not visualized	Abdominal pain/ pancreatitis	Lipase elevated. US non-diagnostic. CT no appendicitis. Admitted for observation. No further symptoms on followup.

CT, computed tomography; US, ultrasound study performed by the radiology department; D, appendix diameter > 6mm; T, appendix wall thickness > 2mm; NC, appendix non-compressible on BUS; F, Fecalith within appendix; CT, computed tomography of abdomen and pelvis; CM, complex mass in right lower quadrant; FF, Periappendiceal free fluid collection; TV, appendiceal tip visualized; MB, sonographic McBurney's sign

been three published clinical trials on EP-performed BUS for the diagnosis of appendicitis. Chen et al. found that BUS had a sensitivity of 96.4% and a specificity of 67.6% for diagnosis of appendicitis, compared to 86.2% sensitivity and 37% specificity based on surgeons' clinical judgment.¹⁵ However, prevalence of appendicitis was 75% in their study, and all physician sonographers had extensive BUS experience, reflecting a setting atypical for most EDs in the United States

Fox et al. published two studies on the topic. Their first study was a retrospective registry review, which revealed that EPs without focused training on the use of BUS to diagnose appendicitis had a sensitivity of 39% and specificity of 90%.¹⁶ This was followed by a prospective study (in which all physician investigators received standardized training), which concluded that BUS was 65% sensitive and 90% specific in diagnosing appendicitis.¹⁷ This latter study was conducted

Table 4. Univariate analysis of demographic, history, laboratory and bedside ultrasound (BUS) characteristics of subjects with and without appendicitis.

Variable (Mean/percentage)	Subjects with appendicitis	Subjects without appendicitis	p-value
Demographics			
Age (years)	20.4	20.1	0.749
Sex (percentage male)	71.1	38.0	0.001
BMI	24.0	24.3	0.523
Duration of symptoms (hours)	30.6	39.9	0.289
Presenting symptoms			
Anorexia	86.7	62.9	0.005
Fever > 100.4°F	21.4	14.3	0.330
Nausea	81.8	61.8	0.024
Vomiting	60.0	41.4	0.052
Diarrhea	13.3	18.6	0.460
Pain in RLQ	97.8	91.4	0.243
Migration of pain to RLQ	62.2	48.5	0.154
Laboratory results			
WBC count (10 ³ /mm ³)	15.6	9.7	<0.001
PMN percentage	82.6	67.3	<0.001
BUS findings			
Visualization of appendix	80.0	37.7	<0.001
Appendix diameter > 6mm	91.9	48.5	<0.001
Appendix wall thickness > 2mm	50.0	20.0	0.018
Appendix non-compressible	94.1	75.9	0.068
Fecalith within appendix	24.3	17.6	0.491
Complex mass in RLQ	30.6	12.8	0.061
Periappendiceal free fluid collection	77.8	33.3	<0.001
Appendiceal tip visualized	55.6	91.9	<0.001
Sonographic McBurney's sign	54.7	45.3	0.016

BMI, body mass index; RLQ, right lower quadrant; WBC, white blood cell; PMN, polymorphonuclear percentage

Table 5. Appendicitis predictor variables and their odds ratios on logistic regression of diagnostic bedside ultrasound (BUS) studies.

Variable	Odds ratio (95% CI)
WBC	1.42 (1.18-1.72)
PMN	1.10 (1.04-1.17)
Visualization of appendix on BUS	6.62 (2.75-15.92)
Appendix diameter > 6mm on BUS	13.95 (2.57-75.59)
Appendix wall thickness > 2mm on BUS	4.73 (1.06-21.15)
Periappendiceal free fluid collection on BUS	6.19 (1.74-22.02)

WBC, white blood cell; PMN, polymorphonuclear percentage

in a similar setting to ours (teaching hospital, moderate appendicitis prevalence, brief training of sonographers). The major difference between our study and theirs was the diagnosis criteria for appendicitis. In the Fox study, diagnosis was based on three chosen criteria after visualization of the appendix on BUS (internal diameter > 6mm, lack of

peristalsis, noncompressibility in the transverse plane), and absence of any of these findings or inability to visualize the appendix was considered a negative BUS study. In our study, diagnosis of appendicitis was based on overall bedside impression of the BUS, and investigators were allowed to deem their BUS as non-diagnostic. As a result, there were only a few negatives, but many non-diagnostic BUS studies. This likely accounted for the unusually low calculated specificity in our results. Indeed, when the test characteristics were calculated assuming all non-diagnostic BUS were negative studies, the results fell within the same range as the Fox study. Additionally, as far as the authors are aware, our study was also the first to examine the association of appendicitis with specific BUS findings.

On multivariate logistic regression BUS findings, we found that appendix diameter of > 6mm was the strongest predictor of appendicitis, followed by visualization of appendix, periappendiceal free fluid collection, and

appendix wall thickness $> 2\text{mm}$. In addition, visualization of the appendix tip on BUS and sonographic McBurney's sign were found to be significant on univariate analysis. This is largely in concordance with the current radiology literature. Goldin et al. found that classifying studies based on findings of appendix diameter $\geq 7\text{mm}$ or appendix wall thickness $> 1.7\text{mm}$ would have accomplished 97% diagnostic accuracy in a retrospective review of pediatric ultrasound studies performed at their institution.¹⁹ This is similar to the study by Kessler et al., which found that appendix diameter $\geq 6\text{mm}$ on ultrasound had both sensitivity and specificity of 98%.²⁰ Likewise, Je et al. determined that the optimal appendix diameter and wall thickness cutoff for diagnosis of pediatric appendicitis were 5.7mm and 2.2mm respectively.²¹ In another study, Van Randen et al found that thickened appendix ($> 6\text{mm}$), transducer tenderness, and periappendiceal fat infiltration to be significant variables predicting ultrasound diagnostic accuracy.²² Pinpoint tenderness under ultrasonography was also found by Soda et al. to be 87% sensitive and 90% specific for appendicitis diagnosis.²³ Both Goldin and Franke found periappendiceal fluid collection to be highly specific (99%) but insensitive (20%, 14% respectively) for appendicitis diagnosis, yielding a moderate accuracy (77%).^{19,24} Due to the design of most bedside ultrasound machines and abbreviated scanning time of most BUS studies, findings such as periappendiceal fat infiltration might be difficult to discern, and it is possible that some of the significant findings in BUS might be different from those derived from radiology department ultrasound studies. Hence, further studies with a larger sample size might be required to confirm our study findings.

Our BUS had a lower sensitivity and specificity than that generally reported in the radiology literature.²⁵⁻²⁷ We also had a significant number of false positive BUS studies. We speculate this might be related to the limited application-specific training and experience of our sonographers. Appendiceal sonography can be hard to master given the difficulty in visualizing the uninflamed appendix, frequent anatomical variation, common interference from the surrounding structures, and mimics from other intra-abdominal pathologies. Though all of our investigators were relatively experienced sonographers (fellow or attending credentialed in emergency ultrasound in our ED), many were new to the application at the time of the study, with limited hands-on experience beyond the one-hour didactic training. On image review by expert sonographers, many of the false positives were deemed not to have the appendix clearly depicted. If all such cases were excluded, specificity would have improved to 91%, making BUS quite useful for ruling in appendicitis. It might also be helpful to acquire dedicated pelvic BUS views in females, given the prevalence of gynecological pathology. In addition to more in-depth education and hand-on experience prior to implementation of appendix BUS protocol, we would recommend low threshold for confirmatory studies

on inconclusive or difficult bedside studies based on our anecdotal experience.

Based on a combination of presenting symptoms, signs, laboratory findings, as well as radiologist-performed sonography, Tzanakis et al. developed an acute appendicitis scoring system and found it to be highly sensitive and specific in diagnosing appendicitis, with an overall accuracy of 96.5%.²⁸ Ultrasound result carried a much heavier weight than the other components (RLQ tenderness, rebound tenderness, WBC $> 12,000/\mu\text{L}$), though specific sonographic findings were not mentioned. Similarly, we also found significant associations between appendicitis and certain components of history, laboratory workup, and BUS. However, due to limited appendicitis cases and the large number of variables examined, we were unable to derive a predictive model. Future potential trials based on our results may include derivation of a "BUS appendicitis score" comprised of the above-mentioned components, possibly leading to better accuracy than BUS alone. If found to be highly accurate as in Tzanakis' case, BUS may be used as an adjunct to streamline appendicitis workup, and lead to more effective resource allocation in the ED.

Limitations

A major limitation of the study was convenience sampling of the subjects, leading to selection bias. Nevertheless, our prevalence of appendicitis and demographic characteristics were similar to other published studies on the topic, and BMI of our subjects appeared to follow a normal distribution. Investigators were also unblinded to the history and clinical examination findings of the subjects. Awareness of these findings, however, is exactly what distinguishes BUS from ultrasound performed by non-clinicians, and thus we do not consider this a weakness of our study. Our sample size was relatively small, leading to large confidence intervals in some of our calculated test characteristics. Future large-scale studies would be necessary to confirm our findings. All investigators who performed BUS in our study were ED ultrasound fellows or faculty, with ultrasound experience exceeding that recommended by the American College of Emergency Physicians.²⁹ Hence, our study findings may not be applicable to operators with different BUS skill levels.

CONCLUSION

Bedside ultrasound performed by emergency physicians with limited training is moderately useful for the diagnosis of appendicitis. We have identified several history, laboratory and BUS components predictive of appendicitis in our study, which might be helpful in generating hypotheses for future studies.

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