



EFFECTIVENESS OF A ROUTINE ULTRASONOGRAPHY AND LIMITED MULTIDETECTOR COMPUTED TOMOGRAPHY IMAGING PROTOCOL FOR EVALUATION OF ADULT PATIENTS WITH CLINICALLY SUSPECTED ACUTE APPENDICITIS

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ABSTRACT

Aim: To study the accuracy of a routine Ultrasonography(US) and limited Multidetector Computed Tomography(MDCT) protocol for imaging patients with suspected acute appendicitis. **Materials And**

Methods: In this observational study approved by the Institutional Review Board (November 2015 to March 2017), 98 adult patients with suspected acute appendicitis(AA) underwent US, which was categorized as positive, negative or equivocal for AA. US positive cases were also categorized as complicated/ uncomplicated appendicitis. MDCT was performed in all US equivocal cases, and a final imaging diagnosis- either positive or negative for AA- was given. Imaging diagnoses were correlated with operative/histopathological findings, or clinical follow-up. **Results:** Among 98 suspected cases, 71(72.4%) were finally diagnosed as AA. 60 cases were US positive, 19 US negative and 19 equivocal on US. CT was performed in all 19 equivocal cases, along with 7 US positive cases (to assess complications) and 1 US negative case (bowel lymphoma). CT was avoided in 71/98 cases. Overall, the imaging protocol (US $\pm$ CT) showed sensitivity of 98.3%, specificity 96.3%, PPV 98.6%, NPV 96.3% for the diagnosis of AA. US identified 60 AA positive cases, with 36 labeled as uncomplicated and 24 complicated AA. Among operated US-positive patients, sensitivity and specificity for complicated AA were 77.8% and 89.3%. Overall imaging accuracy for complicated AA: sensitivity 85.7%, specificity 90.5%, PPV 85.7%, NPV 88.4%. **Conclusion:** An imaging protocol that employs initial US in all suspected cases, followed by CT only in US equivocal cases, shows high sensitivity and specificity for the diagnosis of acute appendicitis, while reducing the number of CT examinations.

KEYWORDS : Acute appendicitis, Ultrasonography, Multidetector Computed Tomography, complicated acute appendicitis, uncomplicated acute appendicitis.

INTRODUCTION

Acute appendicitis (AA) is a frequently encountered clinical condition seen in patients presenting to the emergency with acute abdominal pain. While clinical presentations vary widely, most common signs and symptoms include pain and tenderness in the right iliac fossa (RIF), vomiting and fever. Making an accurate diagnosis is vital for appropriate management of the patient. On one hand, complicated acute appendicitis may result in appendiceal perforation and diffuse peritonitis; while on the other hand, it is important to keep the negative appendectomy rate low. The provisional diagnosis is often suspected on a clinical basis, but imaging has an important role in the diagnostic work-up. Imaging modalities such as ultrasonography (US) and computed tomography (CT) have become standard in the evaluation of suspected appendicitis, and result in lower negative appendectomy rate, compared to clinical evaluation alone [1,2].

The decision whether to operate or not is key in the management of acute appendicitis. Historically, appendectomy has been the gold-standard for the treatment of acute appendicitis, either via an open or a laparoscopic approach. However, this strategy has been challenged in recent years with the advent of antibiotic therapy and studies documenting less morbidity with a nonoperative strategy [3]. It is important to weigh the benefits and potential

disadvantages of both treatment options, keeping in mind that appendectomy itself carries risks including that of mortality [4].

US lacks radiation exposure, has a short acquisition time, is a non-invasive technique (therefore is repeatable), which is readily available in the emergency setting. US can also identify many alternative diagnoses which may mimic acute appendicitis clinically- particularly pathologies of the urogenital tract and female pelvis, like ovarian cysts or torsion, ectopic pregnancy, or ureteric calculi. US is also helpful in differentiating between gangrenous or perforated and uncomplicated appendicitis. Color and power Doppler examination of the appendix is a useful adjunct to improve the sensitivity of US by demonstrating increased flow in an inflamed appendix. However, US is an operator dependent technique and its accuracy is lower in obese individuals. Also, a retrocecal appendix may be obscured on US by overlying bowel gases.

CT has been found to have a higher sensitivity compared to ultrasonography in detecting appendicitis [5, 6]. But CT exposes patients to considerable ionizing radiation. Intravenous iodinated contrast given for abdominal CT may result in contrast-induced nephropathy or allergic reactions. Also, multidetector computed tomography (MDCT) is a costlier investigation, which is less readily available than US in resource limited countries like India.

To reduce the number of CT examinations while maintaining diagnostic accuracy, a strategy of conditional CT has been proposed for acute appendicitis [7]. In this strategy, US is performed in all patients of suspected appendicitis while CT is only done in those patients with inconclusive US findings and in cases of suspected complications. This strategy helps to reduce the number of CT examinations and hence the exposure to radiation. At the same time, performing CT in cases with equivocal US findings helps to increase the accuracy of the imaging diagnosis.

In this study, we aimed to study the accuracy of a routine Ultrasonography and limited Multidetector Computed Tomography imaging protocol for evaluation of adult patients with clinically suspected acute appendicitis.

MATERIALS AND METHODS

Study Design And Patient Selection

This was a hospital-based observational study conducted at a tertiary level institute. Institutional review board approval and ethical clearance for this study were obtained. A total of 100 patients of age ≥ 18 years, of either gender, admitted to the hospital with clinical suspicion of acute appendicitis (AA) i.e. acute pain in right iliac fossa were referred for Ultrasonography (US) during the study period. Two women with intrauterine pregnancy were excluded. Patients who required immediate surgical exploration, or had previously diagnosed appendiceal pathology were also excluded.

The final group consisted of 98 patients (55 males, 43 females, mean age 32yrs; age range 18-65yrs). US was performed in 98 patients within 24 hours of admission. MultiDetector Computed Tomography (MDCT) was done only in 27 cases, within 24 hrs of US. In all 98 patients, imaging was done within 2-12 days of symptom onset (Figure 1).

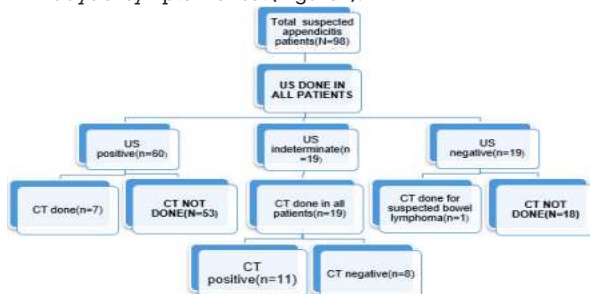


Figure 1. Imaging protocol for the study patients.

Ultrasonography

Imaging Technique

All patients were subjected to ultrasonography examination, on a Philips IU 22 machine with convex (2-5MHz) and linear (3-9 MHz) transducers. First, linear transducer was placed in right upper quadrant and scanning begun at the edge of the right hepatic lobe to locate ascending colon, then it was followed inferiorly into the right iliac fossa to identify cecum and the terminal ileum by using graded compression technique [8]. The ileocecal junction was identified and the appendix was then looked for. The entire abdomen and pelvis was scanned in all patients.

Image Analysis- Definitions

The images obtained were analyzed for the following features/findings (Figure 2)

Maximum outer wall to wall diameter of appendix: measured from echogenic serosa of one side to other, after appropriate magnification, in both short axis and long axis views of appendix in the region of maximum dimension. Average of three measurements (short axis view) was taken. A measurement of ≥ 7 mm was taken as increased outer wall-to-wall diameter.

Maximum Wall Thickness: measured from echogenic serosa to echogenic mucosa of one side of wall in short axis. Average value of three measurements was taken. A measurement of ≥ 3 mm was taken as increased wall thickness.

After optimising the Doppler parameters, increased vascularity on color Doppler was considered if appendiceal wall showed color after applying the color box.

An appendicolith was diagnosed if an echogenic focus with acoustic shadowing was seen in lumen of appendix.

Depth of intraluminal appendiceal fluid was measured as maximum thickness of such material in between echogenic mucosa/submucosa.

Intactness or loss of echogenic submucosal layer was characterized by seeing the entire length of appendix up to its tip and searching for any focal or generalised loss of the echogenic submucosa.

Focal defect in appendiceal wall was recorded if a breach was seen to involve all layers of one side of the wall (transmural defect) at a particular area of appendix.

Raised periappendiceal fat echogenicity was considered if periappendiceal fat (mesoappendix) appeared more echogenic than rest of mesentery.

Any collection near appendix/pericecal region was noted as a periappendiceal/pericecal collection.

Other findings that were recorded included lymph nodes in RIF, ileocaecal (IC) region thickening, free fluid in pelvis, any adnexal pathology and any other finding in abdomen.

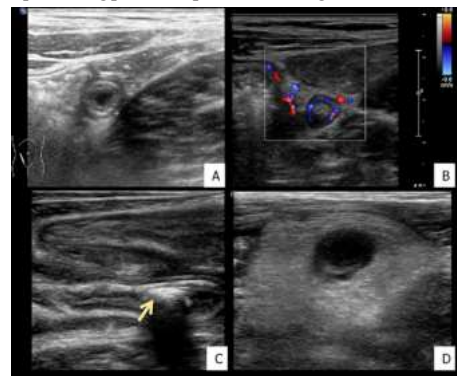


Figure 2: Spectrum of ultrasonographic findings in patients with acute appendicitis (A) Increased outer wall to wall diameter (8mm) (B) Increased vascularity in appendiceal wall on color doppler US. (C) Intraluminal appendicolith (yellow arrow) (D) Raised echogenicity of periappendiceal fat

Image Interpretation

The result of US examination was categorized as positive, negative or equivocal for diagnosis of acute appendicitis.

- Positive US:** US was reported as positive for diagnosis of AA if an increased (≥ 7 mm) outer wall-to-wall diameter of the appendix was found, along with other findings suggestive of acute appendicitis. Findings suggestive of complicated AA were loss of echogenic submucosal layer, focal defect in wall, periappendiceal fluid collection and raised periappendiceal/pericecal fat echogenicity.
- Negative US:** US was considered negative for diagnosis of AA on complete visualization of a compressible appendix measuring < 6.0 mm in diameter, or if an alternate diagnosis was identified on US.
- Equivocal:** Equivocal or indeterminate on US was given if an inflamed appendix was not visualized and no alternate

diagnosis was rendered.

Computed Tomography Imaging Technique

Multidetector computed tomography of the abdomen was performed in patients on a Philips Brilliance 40 slice MDCT scanner. Serum creatinine values were checked before intravenous contrast administration.

Contrast enhanced (CE) CT was done using non-ionic, iodinated contrast (Iopamide-Ultravist 370) and 60-100 ml contrast material at a dose of 1.5 ml/kg was administered intravenously followed by a saline chase of 20ml normal saline. Post contrast scanning of the whole abdomen was done in the porto-venous (70 sec after contrast injection). Out of 27 patients who underwent CT, Non Contrast CT(NCCT) was done in one patient and CECT in 26 patients.

Image Analysis- Definitions

Outer wall to wall diameter of appendix was measured in axial sections of appendix after sufficient magnification, in the area of maximum dimension. We took the average of three measurements. A measurement of $\geq 10\text{mm}$ was taken as increased outer wall to wall diameter. Diameter $< 6\text{mm}$ was taken as normal. Values between 6 to 10mm were considered equivocal and correlated with other CT findings. (Figure3)

Mural Thickness: measured in longitudinal section of appendix after magnification, measurement of $\geq 3\text{mm}$ taken as increased.

Maximum Depth Of Intraluminal Fluid: measured at the region where no appendicolith or air foci were noted in the lumen.

Appendiceal Wall Hyper Enhancement: considered if it enhanced more than the rest of bowel wall after intravenous contrast administration.

Transmural Defect: diagnosed if a focal enhancement defect was seen in the appendiceal wall.

Appendicolith: diagnosed if a well-defined hyperdense focus was noted in the lumen of appendix.

Periappendiceal inflammation: diagnosed if stranding of the periappendiceal fat and thickening of the lateroconal fascia was noted.

Any Collections Near The Appendix And Cecum: determined as periappendiceal/pericecal collections.

Other findings that were recorded included lymphnodes in RIF, IC region thickening, free fluid in pelvis, any adnexal pathology and any other finding in abdomen.

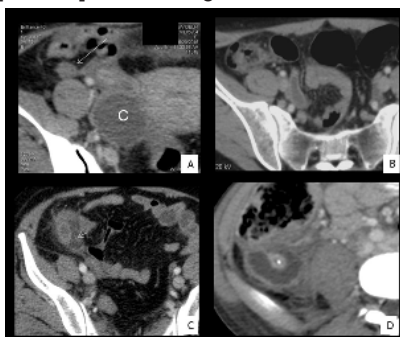


Figure 3: Spectrum of CT findings in patients with acute appendicitis (A) Increased outer wall to wall diameter of appendix (white arrow) with increased mural thickness (C – right adnexal cyst) (B) Increased depth of intraluminal fluid

with periappendiceal fat stranding (C) Appendiceal wall hyperenhancement, with periappendiceal collection (small white arrow) and periappendiceal fat stranding. (D) Intraluminal appendicolith with periappendiceal fluid collection

Image Interpretation

Positive And Negative Diagnoses On MDCT Were Defined As:

- **Positive:** Visualization of a thickened appendix with associated findings of inflammation (details mentioned under image analysis).
- **Negative:** Visualization of normal appendix and/ or, if an alternate diagnosis was identified

Each patient was given a final imaging diagnosis either positive for acute appendicitis or negative for acute appendicitis.

All US examinations were performed by a single radiology trainee resident, who was specially trained in the US technique prior to starting the study. All US and CT images were interpreted by a single radiologist with more than ten years' experience in abdominal imaging.

The final imaging diagnosis (Positive or negative for acute appendicitis) was correlated with per-operative/ histopathological diagnosis and/or the clinical follow up of these patients (Figure4). The final diagnosis of appendicitis or no appendicitis was made either on basis of operative and histopathological findings (in those cases that were operated) or on the basis of clinical follow up (in those cases that underwent non-surgical management).

Statistical Evaluation

Quantitative data was expressed as mean $\pm$ standard deviation (sd). For Qualitative data, proportions were calculated and chi square test or Fischer's test was used, as appropriate to find out statistical significance. Statistical analysis was carried out by SPSS software (version 25, SPSS Inc. Chicago, IL).



Figure 4. Final diagnosis in all study patients (N=98)

RESULTS AND OBSERVATIONS

Demographic Characteristics And Clinical Features

The study included 98 patients in age group 18 to 65 years, with maximum patients (n=55) between 18 to 30 years. There were 55 males and 43 females (male to female ratio 1.3:1) Details of the demographic characteristics, clinical features, Alvarado score, categorization on US and CT are shown in Table 1. Out of 98, 71 patients were finally diagnosed as AA.

Final Diagnosis

Cases Who Underwent Surgery

Of all 98 patients, 55(56.1%) were operated and 43(43.9%) were not. All patients underwent surgery within 48 hours of admission, except one patient who underwent interval appendectomy (after 6 weeks).

Among the operated patients, 52/55 (94.5%) were imaging positive for AA, with 33 (63.5%) diagnosed finally as uncomplicated AA and 18 (34.6%) complicated AA; 1 had no appendicitis. Of the 3 (5.5%) imaging-negative cases who underwent surgery, 2 had right adnexal ectopic pregnancy and the third, who underwent CT after 14 days followed by right hemicolectomy, was diagnosed as ileal stricture with healed appendicitis. Table 2 lists the final diagnosis in the operated cases of acute appendicitis.

Among the 43 non-operated patients, 9 (20.9%) were diagnosed with uncomplicated AA, 10 complicated appendicitis (23.3%), and 24 (55.8%) had no appendicitis.

Table 1. Demographic characteristics, clinical features, Alvarado score, categorization on US and CT for all cases (N=98).

	N (%)
Males: Females	55(56.1%): 43 (43.9%)
Age, years (mean $\pm$ SD)	32 (32.0 $\pm$ 12.1)
Clinical features	
Pain in Right Iliac Fossa	98 (100%)
Tenderness	94 (95.6%)
Anorexia	57 (58.2%)
Vomiting	82 (83.7%)
Fever	41 (41.8%)
Leukocytosis ($> 11,000/\mu\text{L}$)	43 (43.9%)
Alvarado score	
Score ≤ 4	17 (17.3%)
Score 5-6	32 (32.7%)
Score ≥ 7	49 (50%)
Categorization on Ultrasound (US)	
US positive	60 (61.2%)
Complicated Acute appendicitis	24 (24.4%)
Uncomplicated Acute appendicitis	36 (36.7%)
US indeterminate	19 (19.3%)
US negative	19 (19.3%)
Categorization on Computed Tomography (CT)	
Total CT done	27 (27.5%)
CT done in US indeterminate category	19 (19.3%)
CT done in US positive category (for assessment of complications)	7 (7.1%)
CT done in US negative category (suspected lymphoma)	1 (1.0%)
Total CT avoided	71 (72.4%)
CT positive	18 (18.3%)
CT negative	8 (8.1%)

Table 2. Final histopathological/surgical diagnosis in operated cases of acute appendicitis (N=52)

Final diagnosis	N (%)
Uncomplicated AA	33 (63.4%)
Acute appendicitis	4 (7.6%)
Acute appendicitis with periappendicitis	12 (23.0%)
Healed appendicitis	17 (32.6%)
Complicated AA	18 (34.6%)
Ulcerative appendicitis with perforation	3 (5.7%)
Gangrenous appendicitis with perforation	2 (3.8%)
Suppurative appendicitis with periappendicitis	1 (1.9%)
Acute appendicitis with perforation	10 (19.2%)
Healed appendicitis with healed perforation	2 (3.8%)
Ileal stricture with healed appendicitis (This was False negative on imaging)	1 (1.9%)

Ultrasound Imaging Features

'US Positive' Cases (n=60)

Sonographic findings in 'Ultrasound positive' patients are shown in Table 3. The outer wall-to-wall diameter ranged from 7mm to 14mm. The observed mural thickness of an inflamed appendix wall ranged from 1.6mm to 6.2mm. Mural thickness of appendiceal wall $\geq 3\text{mm}$ was seen in 50 (83.3%) patients, while increased vascularity on color Doppler in appendiceal wall was seen in 31 (51.7%) patients.

Out of 60 patients who were 'US positive', presence of complicated AA was suspected on US in 24(40%) patients, based on the findings of loss of echogenic submucosal layer (Figure 5), raised periappendiceal echogenicity, appendicolith, and periappendiceal /pericecal collection seen in 24/24(100%), 24/24(100%), 3/24(12.5%), and 19/24 (79.1%) respectively.

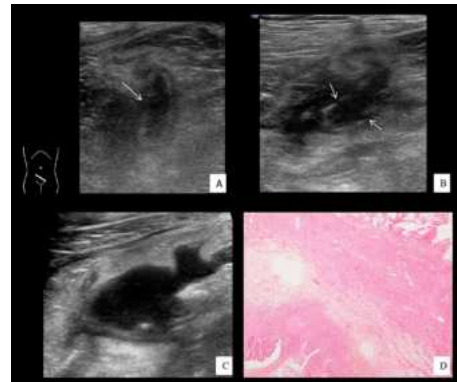


Figure 5: A 30 yr old male with RIF pain for 1 day with vomiting, TLC – 17500 and Alvarado score – 7, with US suggestive of complicated appendicitis, final diagnosis - Acute ulcerative appendicitis with perforation. (A) USG with high frequency transducer shows focal defect in appendiceal wall (large white arrow). (B) Loss of echogenic submucosa at multiple areas (small white arrows) with periappendiceal collection noted. (C) Free fluid in RIF (D) Acute ulcerative appendicitis with transmural inflammation and perforation, H&E, 40x.

'US Negative' Cases(n=19)

In 19(19.4%) out of 98 patients, US was able to find other non-appendiceal causes of RIF pain ('US negative' cases), which constituted of right adnexal cyst- 6(31.5%), right ureteric calculus- 4(21%), right adnexal ruptured ectopic- 2(10.5%), IC thickening- 4(21%), other causes (including worm infestation in small bowel, terminal ileum thickening, bowel lymphoma (corroborated with CT) in 1 patient each.

Normal appendix was seen in 14(73.7%) patients of US negative category whereas in 5(26.3%) normal appendix was not seen on US.

Probe tenderness and RIF Collection: Among US-positive cases (n=60), 57 (95%) had probe tenderness and 29 (48.3%) had RIF collection. In US-indeterminate cases, 15/19 (78.9%) had probe tenderness and 2 (10.5%) had RIF collection. In US-negative cases, 11/19 (57.9%) had probe tenderness and 3 (15.8%) had RIF collection.

CT Imaging Findings

CT was done in all 19 US-indeterminate cases as part of our study imaging protocol. In addition, 7/60 US-positive cases underwent CT for evaluation of suspected complications, and 1 US-negative case, had a CT for staging of suspected bowel lymphoma.

CT Positive Cases (n=18): Various CT findings in patients with a positive CT diagnosis of AA (in US indeterminate and US positive patients) are described in Table 4. Outer wall-to-wall diameter $\geq 10\text{mm}$ was seen in all patients (except one

patients in whom appendix was not visualized on CT). The observed appendiceal outer wall to wall diameter ranged from 10.2 to 12.3mm, while the mural thickness ranged from 2.0 to 5.4mm.

Table 3. Sonographic findings in 'Ultrasound positive' patients (n=60).

US findings	N (%)
Probe tenderness	57 (95%)
Increased outer wall to wall diameter [≥ 7 mm]	60 (100%)
Increased wall thickness [≥ 3 mm]	50 (83.3%)
Loss of submucosal layer	24 (40%)
Increased vascularity on color Doppler	31 (51.7%)
Appendicolith	7 (11.7%)
Periappendiceal raised echogenicity	46 (76.7%)
Periappendiceal fluid collection/fluid in RIF	29 (48.3%)
Intraluminal fluid	21 (35%)

Table 4. CT Findings In Patients With A Positive CT Diagnosis Of Acute Appendicitis

Findings	CT in US Indeterminate patients (N=11)	CT in US Positive patients (N=7) for evaluation of complications	CT in positive and indeterminate US (n=18)
Increased outer wall to wall diameter [≥ 10 mm]	10 (90.9%)	7 (100%)	17 (94.4%)
Increased wall thickness [≥ 3 mm]	8 (72.2%)	5 (71.4%)	13 (72.2%)
Mural stratification present	8 (72.2%)	4 (57.1%)	12 (66.7%)
Wall hyperenhancement (Increased vascularity (US) versus wall hyperenhancement (CT))	5 (45.5%)	(42.9%)(NC CT was done in one case)*	8 (44.4%)
Intraluminal air	1 (9.0%)	1 (14.3%)	2(11.1%)
Appendicolith	-	2 (28.6%)	2(11.1%)
Periappendiceal fat stranding (Periappendiceal raised echogenicity (US) versus periappendiceal fat stranding (CT))	7 (63.6%)	6 (85.7%)	13 (72.2%)
Periappendiceal/pericecal/pelvic collection	1 (9.0%)	7 (100%)	8 (44.4%)

*In one case NCCT was done because of raised serum creatinine therefore wall hyperenhancement could not be assessed.

CT Negative Cases (n=8): The most common diagnosis of 'CT negative' patients was ileocecal Koch's (5/8,62.5%), followed by typhilitis (1/8,12.5%). Two cases had a normal CT study. Amongst these one case later underwent a right hemicolectomy for bowel obstruction, and histopathology showed healed appendicitis along with fibrous ileal stricture (i.e. false negative on imaging).

Correlation of US diagnosis and final diagnosis of acute appendicitis

Among 60 US-positive AA cases, 36 (60%) were labelled on US as uncomplicated AA and 24 (40%) as complicated AA. The correlation of the US diagnosis with final diagnosis is shown in Table 5.

Sensitivity and specificity of US diagnosis of complicated AA were 84% and 91.2%, respectively. Positive predictive value (PPV) and negative predictive value (NPV), likelihood ratio (LR) + and LR- of US diagnosis of complicated AA were 87.5%

and 88.6%, 9.52 and 0.18, respectively.

Table 5. Correlation of US positive diagnosis and final/histopathological diagnosis of complicated/uncomplicated AA

All patients	Final diagnosis	
	Complicated appendicitis	Uncomplicated appendicitis
US positive appendicitis (n=60)		
US s/o complicated appendicitis (n=24)	21 (87.5%)	3 (12.5%)
US s/o uncomplicated appendicitis (n=36)*	4 (11.1%)	31 (86.1%)
Operated patients		
	Complicated appendicitis	Uncomplicated appendicitis
US positive appendicitis (n=47)		
US s/o complicated appendicitis (n=17)	14 (82.4%)	3 (17.6%)
US s/o uncomplicated appendicitis (n=30)*	4 (13.3%)	25 (83.3%)

*In one patient, suspected as uncomplicated AA on US, final diagnosis was no appendicitis.

Correlation Of US Diagnosis And Histopathological Diagnosis Of Acute Appendicitis

Out of 47 operated US-positive AA cases, 30 were labelled as uncomplicated AA and 17 as complicated AA on US. Correlation with histopathological diagnosis is shown in Table 5. The sensitivity and specificity of US diagnosis of complicated appendicitis were 77.8% and 89.3%, respectively, in operated patients.

Comparison of US imaging features of patients with a final diagnosis of complicated and uncomplicated AA is summarized in Table 6, while comparison of US imaging features of patients with a histopathological diagnosis of complicated and uncomplicated AA is shown in Table 7.

Table 6. Comparison of US features of patients with a final diagnosis of complicated versus uncomplicated appendicitis (N=59)

US findings	Final diagnosis as complicated AA (n=25)	Final diagnosis as uncomplicated AA cases (n=34)	P value
Loss of submucosal layer	21 (84%)	3 (8.8%)	<0.001
Appendicolith	3 (12%)	4 (11.8%)	0.978
Intraluminal fluid	8 (32%)	12 (35.3%)	0.792
Periappendiceal/pericecal collection	17 (68%)	11 (32.4%)	0.007
Periappendiceal raised echogenicity	25 (100%)	21 (61.8%)	<0.001

*In one patient, suspected as uncomplicated AA on US, final diagnosis was no appendicitis.

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Comparison of CT features with final diagnosis of acute appendicitis

In total 18 CT positive AA cases, 8(44.4%) patients were finally diagnosed as a complicated AA and 10(55.6%) as uncomplicated AA.

Among cases of complicated AA (n=8), all had periappendiceal collection, with periappendiceal fat stranding, focal defect in appendiceal wall, appendicolith seen in 7, 4, and 2 cases, respectively. None of the patients showed extraluminal air. In uncomplicated AA cases (n=10), fat stranding was seen in 6 patients, wall defect and collection

in 1 case each; none had appendicolith or extraluminal air.

Table 7. Comparison of US features of patients with a histopathological diagnosis of complicated versus uncomplicated appendicitis (N=46)

US findings	Histopathological diagnosis as complicated AA (n=17)	Histopathological diagnosis as uncomplicated AA cases (n=29)	P value
Loss of submucosal layer	14 (77.8%)	3 (10.7%)	<0.001
Appendicolith	-	4 (14.3%)	0.281
Intraluminal fluid	6 (37.5%)	11 (39.3%)	1.000
Periappendiceal /pericecal collection	11 (61.1%)	9 (32.1%)	0.026
Periappendiceal raised echogenicity	17 (100%)	19 (67.9%)	0.008

Correlation of imaging diagnosis and final diagnosis of acute appendicitis

Among 71 imaging-positive cases, 28(39.4%) were suspected complicated AA on imaging; out of which 24 (85.7%) were confirmed as complicated AA, and 4 as uncomplicated AA on final diagnosis.

Of 43 cases labelled as uncomplicated AA on imaging; 38 were later confirmed, 4 were complicated AA, and 1 had no appendicitis on final diagnosis.

Sensitivity and specificity of imaging for the diagnosis of complicated appendicitis were 85.7% and 90.5% respectively. PPV and NPV, LR(+) and LR(-) for the diagnosis of complicated appendicitis were 85.7% and 88.4%, 8.99 and 0.158, respectively.

Sensitivity And Specificity Of Imaging Protocol In Diagnosis Of Acute Appendicitis

In this study, imaging (US±CT) was positive for AA in 71 (72.4%) patients, with 70 true positives and 1 false positive. Imaging was negative in 27 (27.6%) patients, with 26 (96.7%) true negatives and 1 (3.7%) false negative.

Sensitivity and specificity of imaging (US±CT) for the diagnosis of AA were 98.3% and 96.3% respectively. PPV and NPV, LR(+) and LR(-) of imaging were 98.6% and 96.3%, 28.91 and 0.014, respectively.

DISCUSSION

This study aimed to assess the diagnostic accuracy of a routine ultrasonography and limited multidetector computed tomography imaging protocol in diagnosis of acute appendicitis in adult patients - that is, performing only Ultrasonography (US) in cases with a clear-cut positive or negative diagnosis based on the sonographic findings, and performing US followed by Computed Tomography (CT) in cases with indeterminate findings on US. We found that such an imaging protocol had good sensitivity (98.3%) and specificity (96.3%) for the diagnosis of acute appendicitis in adults. Also, CT could be avoided in 71/98 (72.4%) of our cases.

Findings In US Positive Acute Appendicitis Group

In our study population of 98 patients, 60 patients were labelled as 'US positive' appendicitis group (59/60 were finally diagnosed as appendicitis). Increased outer wall to wall diameter ≥ 7mm was seen in all patients. Various studies have shown that increased outer wall-to-wall diameter on US has a high sensitivity in diagnosis of AA. [9,10]

US findings in complicated versus uncomplicated appendicitis

We examined five sonographic variables to differentiate

complicated appendicitis to uncomplicated on US- loss of echogenic sub mucosal layer, appendicolith, intraluminal fluid, periappendiceal/pericecal collection and raised periappendiceal echogenicity. We found that loss of echogenic submucosal layer, presence of periappendiceal/pericecal collection and periappendiceal raised echogenicity showed statistically significant differences between the two groups.

Loss of echogenic submucosal layer was significantly associated with complicated appendicitis- seen in 21(84%) patients of finally diagnosed complicated appendicitis but only in 3 patients of uncomplicated appendicitis. There were 4 patients who were labelled as uncomplicated AA on US, and final diagnosis was complicated AA. Three of these patients showed focal perforation on histopathology, thus this focal abnormality was likely missed on US. On the other hand, there were 3 patients in which we gave the possibility of complicated appendicitis based on apparent loss of submucosal layer, but all these patients were finally diagnosed as uncomplicated appendicitis on histopathology. In our study, sensitivity and specificity of US diagnosis of complicated appendicitis were 77.8% and 89.3% respectively in operated patients. Yingding Xu et al [11] found in their study that loss of the submucosal layer was the only independent significant indicator of complicated appendicitis in multivariate regression, with sensitivity and specificity of 100.0% and 92.0%, respectively.

In complicated appendicitis group, 68% patients showed periappendiceal /pericecal collection, while 32.4% patients of uncomplicated appendicitis group also had periappendiceal /pericecal collection. Periappendiceal raised echogenicity was seen in all 25 patients with complicated appendicitis, while in uncomplicated appendicitis periappendiceal raised echogenicity was seen in 61.8% patients. In our study, we did not take measurement criteria of raised periappendiceal fat echogenicity of > 1cm in thickness, as given by Yingding Xu et al [11]. If we had, this finding would possibly have been more specific for complicated appendicitis.

Findings In CT Positive Appendicitis

We examined five variables to differentiate complicated and uncomplicated appendicitis on the basis of CT findings - defect in appendiceal wall, appendicolith, extraluminal air, periappendiceal fat stranding and periappendiceal/pericecal collection. A total of 18 cases were CT positive appendicitis, out of whom 8 had a final diagnosis of complicated AA. We found that defect in appendiceal wall, appendicoliths and periappendiceal/pericecal collection were significantly noted more often in complicated appendicitis patients compared to uncomplicated appendicitis. Periappendiceal fat stranding was seen in cases of both complicated and uncomplicated appendicitis. None of the patients had extraluminal air foci on CT.

Imaging Negative Appendicitis Group

In our study, the most common non-appendiceal causes of RIF pain were ileo-cecal/ terminal ileal thickening, right ureteric calculi, right ovarian cysts and right adnexal ruptured ectopic pregnancy. Notably, we were able to identify the normal appendix in 14(73.7%) patients out of 19 US negative scans. Previous studies [12] have reported identification of normal appendix in upto 81% of US negative scans performed in children. However, the visualization of normal appendix on US in adults is more challenging than in children.

Routine ultrasonography and limited multidetector computed tomography imaging protocol

To combine the radiation-free advantage of US with increased sensitivity of MDCT, we used a routine ultrasonography and limited multidetector computed tomography imaging protocol to diagnose acute appendicitis in adult patients.

Previous literature reports extremely variable diagnostic accuracy of US for acute appendicitis, with sensitivity ranging from 21% to 95.7%, and specificity from 71.4% to 97.9%. [13-17] A recent study of 790 patients aimed to determine the accuracy of US and CT in diagnosing acute appendicitis, while taking into account the number of indeterminate examinations, in accordance with the Standards for Reporting Diagnostic accuracy (STARD) guidelines [18]. They found that a large proportion of US studies were indeterminate for appendicitis, and reported an accuracy of 13.7% for US and 95.6% for CT, taking indeterminate studies into account. They recommended CT as the first-line imaging modality for evaluating appendicitis in non-obstetric adult patients.

Various studies have been published which have examined the diagnostic accuracy of a staged imaging protocol- US followed by CT, if required- for diagnosis of acute appendicitis. Many of these have been conducted on patients in the pediatric age group, and found that CT could be avoided in many children [19,20,21] while the sensitivity and specificity for diagnosis of acute appendicitis remained high- sensitivity and specificity of the staged protocol were 98.6% and 90.6%, respectively in the study by Rajesh Krishnamoorthi et al [12].

A similar study conducted in adults [22] compared the diagnostic accuracy of conditional CT, i.e. CT when initial ultrasound findings were negative or inconclusive, and immediate CT for acute appendicitis in 422 adult patients with suspected appendicitis (with a final diagnosis of appendicitis in 251). They found that the number of CT examinations could be reduced by half by using a conditional strategy. Conditional CT correctly identified as many cases as immediate CT, although the specificity was lower with conditional CT, which had more false positives. Another study in 420 adult patients who underwent US as the first imaging technique for suspected acute appendicitis reported that sonography and CT correctly diagnosed acute appendicitis in 66 of 75 patients and in 38 of 39 patients, respectively, and correctly denied acute appendicitis in 312 of 326 and in 92 of 92 patients. Sonography was inconclusive only in 17 of 418 cases. Sensitivity, specificity, and accuracy for sonography were 74.2%, 97%, and 92%, respectively, and for CT, 100%, 98.9%, and 99%. The authors recommended that Doppler-US should be the first imaging modality in adult patients with suspected appendicitis, and CT should be performed in selected cases [23].

Wan et al [24], with use of a Markov decision analytic model, compared the cost effectiveness of US alone, CT alone, and US followed by CT if the initial US findings were negative in children with suspected appendicitis. In their analysis, US followed by CT was found to be the most costly and most effective. We did not calculate cost parameter in our study. MDCT scans are more expensive than US scans. We performed CT only in a limited number of cases (27/ 98; 27.6%). It is reasonable to assume that using a staged protocol is less expensive than CT alone.

It is noteworthy that the better diagnostic accuracy of our US-first staged imaging protocol for acute appendicitis, with lesser numbers of US indeterminate cases as compared to studies from the West [18]- was likely to have been affected by factors such as the patients' body habitus. On average, the body weight and body mass index of our adult patients is less as compared to patients from western countries, and this may explain better overall performance of US in diagnosis of acute appendicitis.

The performance of US in diagnosis of AA is also operator dependent. One of the strengths of our study is that all US

examinations were performed by a single resident, who was trained in the technique of examination prior to the study. Unavailability of trained radiologists or sonologists outside of routine working hours may be another potential reason for surgeons to refer suspected cases of acute appendicitis directly for a CT examination.

Our study has certain limitations. The total sample size was relatively small. The number of our US negative and US indeterminate/ equivocal cases were less, and thus, number of patients who underwent CT was also less. Also, many of our patients of acute appendicitis were managed conservatively, with or without abscess drainage. Therefore, surgical/ histopathological confirmation of diagnosis was available only in a subset of our cases. However, this is as per the standard of care and routine protocols of clinical management. Imaging was limited by interpretation from a single trained resident for USG and one radiologist for CT, potentially to avoid greater interobserver variability.

Overall, in our study, we found a sensitivity of 98.3% and specificity of 96.3% of our imaging protocol for the diagnosis of acute appendicitis in adults. Positive predictive value and negative predictive value were 98.6% and 96.3% respectively. We found that the performance of our protocol was as good as that reported in the literature for CT alone in terms of sensitivity and specificity. [16,18,25,26,27]

CONCLUSION

An imaging protocol in which initial US is performed in all adult patients with clinically suspected appendicitis, but CT is performed only in cases with equivocal findings on US is effective as it achieves a high sensitivity and specificity, while at the same time avoids unnecessary CT and thus reduces the radiation exposure.

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