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NON-ENHANCED CT FINDINGS IN PATIENTS SUSPECTED OF ACUTE APPENDICITIS WITH NON-DIAGNOSTIC ULTRASONOGRAPHY

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Abstract

Introduction: *In this study, we aimed to investigate the finding of non-enhanced CT assessment in a group of patients with non-diagnostic ultrasonography.*

Material and Method: *This cross-sectional study prospectively recruited patients with clinical symptoms and ultrasonographfindings suspicious of acute appendicitis but the appendix loop was not seen in the ultrasonograph evaluation by the radiologist, during a one-year interval. The main study variables were radiologic findings in the CT evaluation including diagnosis of appendicitis, diameter of appendix loop, appendix wall thickness, peri-appendix fat stranding, cecum wall thickness in comparison with the hepatic flexure wall, phlegmon, appendicolith, and other possible pathologies in the imaging. Various descriptive and analytic evaluations were done on the study variables.*

Results: *A total number of 129 patients with a mean age of 36.8 ± 15.7 were included in this study. Among these patients, appendicitis diagnosis via the CT evaluation was made in 12 (9.3%) of the patients. Also, 7 (5.4%) patients had appendix loop diameter ≥6 mm. The assessed appendix wall thickness was ≥3 mm in 6 (4.7%) of the cases and peri-appendix fat stranding was positive in only 6 (4.7%) of the cases. Eighty (62.0%) patients had other pathologies in the non-enhanced CT imaging. The appendix loop diameter ≥6 mm, appendix wall thickness ≥3 mm, peri-appendix fat stranding, presence of phlegmon, and thicker cecal wall were significantly associated with the diagnosis of appendicitis in the included sample of patients (P-values<0.001).*

Conclusion: *This study presented the CT findings of patients suspected to have acute appendicitis with non-diagnostic ultrasonograph.*

Keywords: *appendicitis, computed tomography, ultrasonography, acute abdomen, aiagnosis*

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Introduction

Acute appendicitis as the most common cause of acute abdomen leading to surgical management is a major health concern and carries a high burden [*Téoule et al., 2020*]. According to the latest estimations by the Global Burden of Disease study, about 17.7 million new cases of appendicitis happened globally in 2019 with an age-standardized incidence rate of 229.9 new cases per 100,000 population. Also, globally this condition caused about 1.5 million disability-adjusted life years (DALYs) and lead to 33,400 deaths worldwide in 2019 [*Vos T, et al.,2020, Wickramasinghe et al., 2021*]. Due to high burden of acute appendicitis, besides the vague clinical presentation of the condition leading to difficulties in timely diagnosis and management of the pathology [*Kosaka et al., 2007*], incorporating appropriate approaches and measures in diagnosis of appendicitis is essential and one of the best known and practiced tools is the imaging evaluations [*Mostbeck et al., 2016*].

Regarding the radiologic evaluation and diagnosis of acute appendicitis, controversies have existed and still go on, especially in the past two decades with the development of several imaging techniques and protocols [*Sivit 2004; Swenson et al., 2018*]. Ultrasonography as one of the major initial imaging methods in further evaluation of appendicitis, is still extensively used since it is widely available, easy to use, does not need specific preparation, and does not have side effects; therefore, it is highly suggested as the first line radiologic assessment in patients suspected with acute appendicitis [*Mostbeck et al., 2016; Pinto et al., 2013; Tomizawa et al., 2017*]. A recent meta-analysis found the overall sensitivity of 77.2% (95% confidence interval (CI): 75.4-78.9) and specificity of 60% (95% CI: 58-62) for abdominal ultrasonography in patients with suspected acute appendicitis [*Fu et al., 2021*]. However, due to many drawbacks including the operator-based nature of this modality and limited accuracy and power of ultrasonography [*Pinto et al., 2013*], this evaluation could be non-diagnostic; thus complementary evaluations with advanced modalities like computed tomography (CT) imaging is suggested in selective cases to improve the diagnostic accuracy in detecting acute appendicitis [*Tomizawa et al., 2017*]. Contrast-enhanced and non-enhanced Computed tomography scan are the two major methods of this imaging with different indications and although the contrast-enhanced Computed tomography evaluation is more used in acute abdominal events, it is shown that in case of acute appendicitis, non-enhanced imaging has been significantly successful in detection of pathology by a rapid evaluation and saving patients via early-stage intervention before any complications happen [*Agarwal et al., 2015; Eurboonyanun et al., 2021*].

Objectives: Considering the controversies on the use of various imaging modalities in evaluation of acute abdomen cases suspected to appendicitis, further studies are necessary to reveal the efficacy and power of the available methods. In this regard, we aimed to present our experience on a sample of patients suspected to acute appendicitis with non-diagnostic ultrasonography, which undergone non-enhanced Computed tomography imaging, to add to evidence in the field and help clinicians in management of this condition.

Materials and Methods

Study design and population: We designed a cross-sectional study to investigate the aim in this manuscript. Patients with clinical symptoms and ultrasonography findings suspicious of acute appendicitis but the appendix loop was not seen in the ultrasonography evaluation by the radiologist, were prospectively recruited in this study, during a one-year interval of 2020, in the Golestan hospitals of the Ahvaz City, Iran. Criteria for inclusion in this study were (#1) age between 5-90 years-old, (#2) history, physical examination, and laboratory findings compatible with acute appendicitis, and (#3) equivocal findings in ultrasonography examination of the right lower quadrant (RLQ) of abdomen, specifically absence of inflamed appendix loop in spite of increases subcutaneous fat echogenicity, enlargement and inflammation in regional lymph node, free fluid in abdomen, and decreased peristalsis of the intestines. Exclusion criteria from this study were (#1) age <5 or >90 years-old, (#2) presence of appendix loop in ultrasonography, (#3) previous surgical history in the Right lower quadra region, and (#4) patient's preference to not participating in study for any reason.

Radiologic evaluation: ultrasonography evaluation was done by a high-resolution ultrasonography device and with the linear probe. Cases with appendix thicker than 6 mm, appendix wall thickness more than 3 *mm*, and non-compressible appendix in ultrasonography were assumed as appendix positive and cases with clear and complete observation of the appendix in ultrasonography while having a diameter less than 6 mm, were assumed negative regarding acute appendicitis and both mentioned groups were excluded from study. Otherwise, cases were non-diagnostic and underwent non-enhanced CT evaluation after obtaining the approval from the corresponding surgeon. The Computed tomography imaging was done by a 16-slice device and images were reported by an experienced radiologist. Enlarged and inflamed appendix with diameter >6 *mm* and wall thickness >3 *mm*, peri-appendix inflammation with fat stranding, thickened mesoappendix, increased thickness of cecum wall, presence of phlegmon in the region, and observation of appendicolith were the criteria for diagnosis of the acute appendicitis in Computed tomography

Study variables: Patients' age and sex were the demographic variables reported in this study. The main study variables were radiologic findings in the CT evaluation including diagnosis of appendicitis (positive/negative), diameter of appendix loop (<6/≥6 *mm*), appendix wall thickness (<3/≥3 *mm*), peri-appendix fat stranding (positive/negative), cecum wall thickness in comparison with the hepatic flexure wall (equal/thicker), phlegmon (positive/negative), appendicolith (positive/negative), and other possible pathologies in the imaging (renal stone, urinary tract stone, and other).

Statistical analysis: The descriptive presentation of the results included the mean and standard deviation (SD) of the quantitative variables and frequency and percentage of the qualitative variables. The Chi-squared test and independent student t-test were used to statistically compare the findings between study variables. Fisher's exact test was used as the statistical significance test in analyzing contingency tables with small sample sizes. P-values <0.05 were assumed statistically significant. All statistical analyses were conducted by the IBM SPSS Statistics package (SPSS for Windows, Version 22.0. Chicago, SPSS Inc.).

Results

A total number of 129 patients with a mean age of 36.8 (SD: 15.7, range: 10-90) were included in this study (Table 1). Among these patients, appendicitis diagnosis via the CT evaluation was made in 12 (9.3%) of the patients. Also, 122 (94.6%) patients had appendix loop diameter less than 6*mm* and only 7 (5.4%) had diameter ≥6 *mm*. The assessed appendix wall thickness was ≥3 *mm* in 6 (4.7%) of the cases and less than 3 *mm* in the 123 (95.3%) of them. Peri-appendix fat stranding was positive in only 6 (4.7%) of the cases. Also, phlegmon was seen in 3 (2.3%) cases and appendicolith was positive in only one (0.8%) case. The cecal wall thickness in 5 (3.9%) of the cases were thicker than the hepatic flexure wall and in the other 124 (96.1%) patients they had almost the same wall thickness in the computed tomography assessment. Regarding the other pathologies, 49 (38.0%) patients had no pathology, 42 (32.6%) had urinary tract stone, 7 (5.4%) had renal stone, and the other 27 (20.9%) individuals had other miscellaneous pathologies (table 1).

The appendix wall diameter ≥6 *mm* was significantly associated with the diagnosis of appendicitis in the included sample of patients (P-value<0.001). Also, the appendix wall thickness ≥3 *mm*, peri-appendix fat stranding, presence of phlegmon, and thicker cecal wall had the same strong association with the appendicitis diagnosis (P-values<0.001). Although the only case with appendicolith was finally positive for appendicitis, the examination showed no statistically significant association between these two variables (P-value=0.93). Patients with other pathologies were significantly negative for the appendicitis (P-value=0.001). Moreover, there was a positive correlation between appendicitis and other variables except pathologies (Table 2).

Discussion

The main findings of this study were the significant number of patients diagnosed with appendicitis by the non-enhanced Computed tomography imaging, the diagnosis of other abdominal pathologies in the major proportion of the patients that could be the etiology of the acute abdomen, and the strong association of related radiologic features including appendix loop diameter ≥6 mm, appendix wall thickness ≥3 mm, peri-appendix fat

Table 1.

Basic characteristics of patients.

Variables	Patients (N = 129)
Age (year), Mean ± SD (Range)	36.8 ± 15.7 (10-90)
Gender (Male), N (%)	59 (46)
Appendicitis, N (%)	
Negative	117 (90.7)
Positive	12 (9.3)
Appendix loop diameter, N (%)	
< 6 mm	122 (94.6)
≥ 6 mm	7 (5.4)
Appendix wall thickness, N (%)	
≥ 3 mm	6 (4.7)
< 3 mm	123 (95.3)
Peri-appendix fat stranding, N (%)	
Negative	123 (95.3)
Positive	6 (4.7)
Phlegmon, N (%)	
Negative	126 (97.7)
Positive	3 (2.3)
Appendicolith, N (%)	
Negative	128 (99.2)
Positive	1 (0.8)
Cecal wall/ the hepatic flexure wall thickness, N (%)	
Thicker	5 (3.9)
Same	124 (96.1)
Pathologies, N (%)	
No pathology	49 (38.0)
Urinary tract stone	42 (32.6)
Renal stone	7 (5.4)
Other miscellaneous pathologies	27 (20.9)

stranding, presence of phlegmon, and thicker cecal wall with the final diagnosis of appendicitis.

The most important finding of this study was the prevalence of the final appendicitis diagnosis after the CT evaluation following a non-diagnostic ultrasonography examination, that was about one tenth of the included sample in study. The importance of this finding is the contribution of the CT evaluation to the accurate diagnosis of the acute appendicitis and prevention of surgical intervention in patients who might have pathologies other than appendicitis. A recent study found that pre-operative examination of suspected appendicitis cases with computed tomography imaging could effectively reduce the negative appendectomy rates in the studied samples and therefore lead to save costs and resources [*Chan et al., 2020*]. This point was supported by the other similar literature, too [*Boonstra, et al.,, 2015; Cobben et al., 2009*]. Also, in specific populations like the pregnant women, the cost effectiveness of additional imaging modalities including computed tomography and magnetic resonance imaging (MRI) in cases with indeterminate ultrasonography is proved [*Kastenberg et al., 2013*]. However, this evidence is against a previous investigation that showed the increased pre-operative imaging had no significant impact on clinical outcomes of acute appendicitis including negative appendectomy, perforation, and complication rates [*Markar et al., 2011*]. Additionally, a recent large-scale cohort found no significant difference regarding negative appendectomy rate between clinical diagnosis and CT evaluation and proposed the appropriate utilization of the pre-operative imaging tools only in necessary cases to reduce potential burden on the health system and surgical departments [*Rait et al., 2020*]. From the economic perspective, a study showed that patients with moderate risk for appendicitis were the most cost-effective to conduct imaging and among the modalities, ultrasonography was proposed as the initial evaluation followed by Computed tomography in indeterminate cases [*Jennings et al., 2020*].

In the current investigation we examined all patients with both ultrasonography and computed tomography modalities; however, due to the study design we were unable to compare the detailed features and findings of the two tools on the patients with suspected acute appendicitis and only CT findings were reported. Controversies in the literature still exist on the best radiologic approach to accurate and timely diagnosis of appendicitis. Three meta-analyses on literature, found computed

Table 2.

Correlation between Appendicitis and other variables.

Variables	Appendicitis	
	Correlation Coefficient	P-Value
Appendix loop diameter	0.748	0.000
Appendix wall thickness	0.690	0.000
Peri-appendix fat stranding	0.690	0.000
Phlegmon	0.482	0.000
Cecal wall/ the hepatic flexure wall thickness	0.276	0.002
Appendicolith	0.627	0.000
Pathologies	-0.256	0.003

tomography the modality with significantly higher sensitivity, specificity, and accuracy than ultrasonography in diagnosis of acute appendicitis in both children and adults [*Doria et al., 2006; Terasawa et al., 2004; Weston, et al., 2005*]; however, considering the safety precautions deteriorates the position of CT imaging especially in children since the radiation could be harmful [*Doria et al., 2006*]. From different perspectives, the decision on choosing the imaging modality in evaluation of appendicitis in children have been diverse and no unique suggestion could be made and the decision have been assigned to the clinicians to make the best choice based on each case [*Frush, et al., 2009; Holscher, Heij 2009*].

In this study we evaluated the computed tomography findings followed by an initial non-diagnostic ultrasonography examination. The order of imaging modalities in management of appendicitis has been routinely proposed the ultrasonography as the initial first-line diagnostic radiologic evaluation [*Tomizawa et al., 2017; Mostbeck et al., 2016*], as done in the current study. A previous study found that conditional Computed tomography when initial ultrasonography findings are negative and inconclusive in cases with suspected appendicitis is more useful than immediate CT imaging and this approach could have the number of Computed tomographys needed [*Atema et al., 2015*]. On the other hand, a study investigated the role of ultrasonography re-evaluation in patients with non-diagnostic and equivocal CT assessment and found this approach useful in diagnosis of acute appendicitis [*Kim et al., 2018*]. It seems that a first-line ultrasonography examination followed by Computed tomography imaging, is the best diagnostic radiologic approach in these patients. Further, the recent studies proposed MRI as a feasible alternative to CT in cases with equivocal ultrasonography and suspected acute appendicitis, with comparable diagnostic accuracy and additional benefit of lesser radiation and absence of intravenous contrast [*Martin et al., 2018*].

Our study investigated the non-enhanced CT findings in patients with suspected acute appendicitis. Although the Computed tomography imaging has its own side effects regarding the radiation, it is shown that the use of non-enhanced CT is sensitive and specific enough in detection of appendicitis and this approach could be used to decrease the complications of the various oral and intravenous contrasts, particularly in vulnerable populations like pediatric patients and those with nephrology limitations [*Lowe et al., 2001*]. A previous study showed the limited added value of contrast-enhanced Computed tomography in patients undergoing non-enhanced Computed tomography for evaluation of flank pain, which among their acute appendicitis patients only one patient with was diagnosed in the contrast-enhanced phase [*Agarwal et al., 2015*]. A recent publication also compared the two tomography techniques in patients with acute appendicitis and showed they almost the same ability and accuracy in diagnosis of the condition and suggested the non-enhanced tomography since it has lower risk of severe adverse reactions [*Eurboonyanun et al., 2021*]. It could be concluded that use of non-enhanced tomography in diagnosis of acute appendicitis is accurate and safe enough in the management of these patients.

By the utilization of non-enhanced CT evaluation in a sample of patients with non-diagnostic ultrasonography suspected to acute appendicitis in this study, the investigators were able to diagnose an additional number of 12 patients with the appendicitis diagnosis and help to saving the patients by a faster detection of the pathology. Also, it is important to mention that the implemented non-enhanced computed tomography imaging on this sample of patients could reveal the etiology of acute abdominal pain in a majority of cases by detecting the pathologies other than acute appendicitis and could avert the unnecessary need for surgical intervention in these patients. These two major findings distinguish this study with similar literature in the field and highlight the role of non-enhanced CT imaging in the management of patients with suspected appendicitis. Putting together the available previous evidence on the use of non-enhanced tomography in these patients and the findings of this study, the non-enhanced tomography is a safe and rapid choice for evaluation of patients with suspected acute appendicitis. This point is added to the reduced risk of severe reaction to contrast and nephropathy in patients with various nephropathies including some prevalent examples like diabetic nephropathy, by the use of non-enhanced CT evaluation [*Andreucci et al.,*

2014; Hasebroock, Serkova 2009]; besides, the reduced time for diagnosis of acute appendicitis and being more cost effective make the non-enhanced imaging a more suitable and feasible option in the management of these patients.

This study had some limitations. The limited sample size was the main limitation needed to be stated. Expanding the study for greater sample sizes to include more diverse patterns in the imaging is suggested for future researches in this field. The other major limitation of this study was the incompetency in comparison of the ultrasonography and CT findings since the data was only on the CT examinations and it made the effective comparison of these two modalities impossible in this study. Also, incorporating other imaging modalities like MRI is highly suggested. Furthermore, the pathologic evaluation of the cases undergoing surgical excision of the inflamed appendix could add to the evidence in this regard.

CONCLUSION

This study described and analyzed findings of non-enhanced CT evaluation of patients with acute abdomen suspected to appendicitis who were non-diagnostic in the ultrasonography examination. The findings of this investigation revealed a significant number of the included patients were finally diagnosed with appendicitis by the use of rapid evaluation of non-enhanced tomography scan. The most radiologic features in computed tomography imaging helping to diagnosis of acute appendicitis in this study were the diameter of the appendix loop and the appendix wall thickness which need to be considered by radiologists evaluating the suspected patients. The rapid, available, and safe utilization of non-enhanced tomography imaging are the features which make this method an appropriate option in the timely management of patients with acute appendicitis. The added value of non-enhanced tomography evaluation in finalizing the diagnosis in a substantial number of patients leading to timely surgery and intervention, and also the detection of other pathologies that could be the etiology of acute abdomen by this imaging leading to preventing unnecessary appendectomy in this group of patients with a significant proportion of the samples in this study, highlight the beneficiaries of use of non-enhanced CT and could promote this radiologic technique in further clinical and para-clinical approaches on this very critical type of patients with acute abdomen. Lowering the risk of various contrast-mediated reactions and side effects, and the time- and cost-effectiveness features of the non-enhanced imaging, place this method at priority in the management of suspected acute appendicitis cases. The findings of this study expand the knowledge on the pre-operative management of patients with appendicitis and could help in reaching a timely approach on the suspected individuals and preventing the adverse outcomes due to late surgical intervention.

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