Value of total leucocytic count and pelvic-abdominal ultrasound in distinguishing complicated from noncomplicated acute appendicitis

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Background
Complicated appendicitis is associated with elevated rates of morbidity and mortality compared with noncomplicated appendicitis. In this study, we aimed to investigate the role of combining total leucocytic count (TLC) and abdominal ultrasound (US) in distinguishing simple from complicated appendicitis.
Patients and methods
This is a prospective study that included patients with acute appendicitis who underwent appendectomy. The patients' data regarding demographic characteristics, clinical, laboratory, and US findings, as well as intraoperative findings and postoperative complications, were recorded and analyzed.
Results
This study included 80 patients. Overall, 48 (60%) patients had noncomplicated appendicitis, and 32 (40%) had complicated appendicitis. Patients with complicated appendicitis had significantly higher ages and TLC. Concerning the US findings, significantly higher cases of visualized blind-ended loop ($P = 0.042$), right iliac fossa fluid ($P = 0.006$), and pelvic collection ($P < 0.001$) were shown in the complicated group. Multiple regression analysis revealed that TLC and the presence of pelvic collection by the US were the only variables significantly predicting complicated appendicitis. Adopting either a TLC cut-off value of 12.95×10^9/l and/or the presence of pelvic collection for the diagnosis yielded a sensitivity of 90.6%, a specificity of 77.1%, and an accuracy of 82.5%.
Conclusion
The presence of a TLC cut-off value of 12.95×10^9/l and/or a pelvic collection in abdominal ultrasound seems to be reproducible for the preoperative prediction of complicated acute appendicitis.

Keywords:
abdominal ultrasound, acute appendicitis, simple versus complicated, total leucocytic count

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Introduction

An ~10% of patients attending the emergency department have acute abdominal pain [1]. Acute appendicitis is described as one of the commonest causes of acute abdomen in young adults who present to the emergency department [2].

A major concern for surgeons is the development of appendicitis complications. Complicated appendicitis is associated with elevated rates of morbidity and mortality compared with noncomplicated appendicitis [3].

There is a tendency to obtain a preoperative conclusion about whether the appendiceal inflammation is simple or complicated. This would help to decide the proper treatment for each patient [4].

Acute appendicitis is clinically diagnosed when typical symptoms such as anorexia, nausea, low-grade fever, and abdominal pain that begins around the umbilicus and then migrates to the right iliac fossa are present, along with classic signs including right iliac fossa tenderness and rebound tenderness [5].

The role of laboratory markers in the depiction of complicated cases was described. Some markers such as total leucocytic count (TLC), C-reactive protein (CRP), and mean platelet volume (MPV) [6,7]. Imaging modalities like abdominal ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) could also be helpful to discriminate complicated cases [8].

In this study, we aimed to investigate the role of combining TLC and abdominal US in distinguishing simple from complicated appendicitis.

Patients and methods

This is a prospective study that included consecutive patients presenting to the emergency unit of our institution with acute lower abdominal pain during the period from March 2021 to October 2021. The study was initiated after approval by the Research Ethics Committee and adhered to the declaration of Helsinki.

Patients with symptoms and signs typical of acute appendicitis were eligible for the study. Patients with blood disorders, immunocompromised patients, and pregnant women were excluded from the study.

Sample size

The power of the study was estimated using the G * power 3.1.9.4 software (Universities Kiel, Germany). The sample size was computed based on the difference in TLC count between patients with simple and complicated acute appendicitis, as obtained from a similar study [9]. After setting the study power at 95% and α at 0.05, a minimum of 78 participants were required. We included 80 patients in this study.

The included patients were subjected to full history taking, routine general physical assessment, abdominal examination, laboratory investigations including TLC, and abdominal US. Written informed consent was obtained from the included patients before surgery.

Because of the coronavirus disease 2019 (COVID-19) pandemic and the nonfunctioning laparoscopic setup in the emergency department, the study patients underwent a conventional open appendectomy. The surgery was performed as previously standardized. A postoperative histopathologic examination of the removed appendix was performed.

The patients' data regarding demographic characteristics, clinical, laboratory, and US findings, as well as intraoperative findings and postoperative complications, were recorded and analyzed.

Study outcomes

The primary outcome of the study was the difference in TLC and abdominal US findings between simple and complicated appendicitis. The secondary outcome was their value for the prediction of complicated cases.

Statistical analysis

The obtained data were analyzed using SPSS statistical software (IBM Corp., Armonk, NY, USA), version 28. The comparison of numerical values was done by the independent t-test. The χ^2 test or z test for proportion was used to compare categorical variables as appropriate. Univariate and multiple binary logistic regression analyses were performed to identify the predictors of complicated appendicitis. Factors found to be statistically significant in the univariate analysis were incorporated into a multiple regression model. Variables found to be significant in the multiple regression test were used in the receiver operating characteristic (ROC) analysis. A P value less than 0.05 was considered statistically significant.

Results

This study included 80 patients who were eligible for the study. The patients' ages ranged from 15 to 60 years, with a mean of 31.04±12.46 years. There was a sex predilection towards males (n=52, 65%) (Table 1).

The preoperative TLC (x 10^9/l) ranged from 4.37 to 38.5, with a mean of 15.31±7.91. The pelviabdominal US findings were a blind-ended loop (n=34, 42.5%), tenderness on probing (n=40, 50%), right iliac fossa-free fluid (n=40, 50%), and pelvic collection (n=18, 22.5%) (Table 1).

Intraoperatively, acute inflammation of the appendix was found in 33 (41.3%) patients, acute suppurative

Table 1 Baseline and operative data of the study patients

	Study patients (n=892)	
	Mean±SD	Range
Age (y)	31.04±12.46	15–60
TLC (x 10^9/l)	15.31±7.91	4.37–38.5%
	Count	**%**
Sex		
Male	52	65%
Female	28	35%
Abdominal ultrasound findings		
Blind ended loop	34	42.5%
Tender on probing	40	50.0%
RIF free fluid	40	50.0%
Pelvic collection	18	22.5%
Intraoperative findings		
Acute catarrhal	33	41.3%
Acute suppurative	15	18.8%
Acute perforated	17	21.3%
Acute mass	6	7.5%
Acute Abscess	9	11.3%
Complicated appendicitis		
Yes	Yes	Yes
No	No	No

Table 2 Baseline demographic data and weight loss outcome of the study patients

	Study patients (*n*=80)		
	Not complicated *N*=48 Mean±SD/Count (%)	complicated *N*=32 Mean±SD/Count (%)	*P* value
Age (y)	36.5±13.67	27.4±10.18	0.002*[a]
TLC (x 10^9/l)	11.29±3.58	21.33±8.81	<0.001*[a]
Sex			
Male	31 (64.6)	21 (65.6)	0.924 [b]
Female	17 (35.4)	11 (34.4)	
Abdominal ultrasound findings			
Blind ended loop	16 (47.1)	18 (52.9)	0.042*[c]
Tender on probing	26 (65)	14 (35)	0.361 [c]
RIF free fluid	18 (45)	22 (55)	0.006*[c]
Pelvic collection	2 (11.1)	16 (88.9)	<0.001*[c]

[a]independent *t*-test. [b]χ^2 Chi-square test. [c] z test for proportion. * Statistically significant at 0.05.

inflammation in 15 (18.8%) patients, acute perforated appendicitis in 17 (21.3%) patients, acute appendicular mass in 6 (7.5%) patients, and acute abscess in 9 (11.3%) patients. Overall, 48 (60%) patients had noncomplicated appendicitis, and 32 (40%) had complicated appendicitis (Table 1).

Comparison between noncomplicated and complicated cases

Comparison between noncomplicated and complicated cases revealed that there was a statistically significant difference in age, with older age in the complicated group (36.5±13.67 vs. 27.4±10.18; $P=0.002$). The sex distribution was comparable in the two groups ($P=0.924$) (Table 2).

A statistically significant increased mean TLC (x 10^9/l) was shown in the complicated group (21.33±8.81) compared with the noncomplicated group (11.29 ±3.58), with a *P* value of <0.001 (Table 2).

Concerning the US findings, significantly higher cases of visualized blind-ended loop (53.3% vs. 33.3%, $P=0.042$), right iliac fossa fluid (68.8% vs. 37.5%, $P=0.006$), and pelvic collection (50% vs. 4.2%, $P<0.001$) were shown in the complicated group. No statistically significant difference was shown regarding tenderness on probing ($P=0.361$) (Table 2).

Predictors for complicated appendicitis

Univariate binary logistic analysis showed that age, TLC, US visualization of a blind-ended edematous loop, right iliac fossa free fluid, and pelvic collection were significant predictors for complicated appendicitis (Table 3). Multiple regression analysis revealed that TLC and the presence of pelvic collection by US were the only variables significantly predicting complicated appendicitis. A unit increase in TLC (10^9/l) was associated with a 1.37 times higher risk of complicated appendicitis (OR: 1.37, 95% CI: 1.15, 1.62), and the presence of pelvic collection was associated with a 17.48 times higher risk of having complicated appendicitis (OR: 17.48, 95% CI: 2.34, 130.6) (Table 3).

Table 3 Univariate and multiple logistic regression analysis for the prediction of complicated appendicitis

			95% C.I. for OR	
	OR	*P* value	Lower	Upper
Univariate analysis				
Age	1.07	0.002*	1.023	1.111
Sex	1.05	0.924	0.409	2.678
TLC	1.34	<0.001*	1.165	1.537
Blind ended loop	0.389	0.004*	0.155	0.977
Tender on probing	1.52	0.362	0.618	3.738
RIF free fluid	0.273	0.007*	0.106	0.704
Pelvic collection	20.21	<0.001*	3.19	135.41
Multiple analysis				
Age	1.07	0.06	.9970	1.142
TLC	1.33	<0.001*	1.152	1.619
Blind ended loop	2.05	0.383	0.410	10.206
RIF free fluid	0.589	0.536	0.110	3.148
Pelvic collection	17.48	0.005*	2.339	130.600

ROC curve analysis showed that a TLC cutoff point of 12.95×10^9/l was able to distinguish between complicated and non-complicated cases with a sensitivity of 81.3%, a specificity of 79.8%, and an accuracy of 78.75% ($P<0.001$) (Fig. 1).

When the presence of pelvic collection was used alone for the diagnosis of complications, it gave a sensitivity of 50%, a specificity of 95.8%, and an accuracy of 77.5% (Fig. 2). Adopting either a TLC cut-off value of 12.95×10^9/l and/or the presence of pelvic collection for the diagnosis yielded a sensitivity of 90.6%, a specificity of 77.1%, and an accuracy of 82.5% (Fig. 3).

Discussion

The extent of inflammation in appendicitis dictates the manifestation of symptoms, signs, and complications. Increasing edema and ischemia can lead to blood vessel thrombosis, weakening of the epithelial wall, and necrosis, culminating in perforation and potentially life-threatening peritonitis. Occasionally, the momentum might form a peri-appendiceal abscess or phlegmon. Complicated appendicitis refers to cases where inflammation of the appendix is accompanied by additional complications, such as perforation, abscess formation, or localized peritonitis [10].

The aim of nonoperative management (NOM) is to avoid surgery by employing antibiotics [11]. Initial studies in the 1950s demonstrated successful treatment of acute appendicitis solely with antibiotics, particularly for cases with symptoms lasting under 24 h [12,13]. Recently, there has been a renewed focus on NOM for uncomplicated acute that has been suggested to resolve with antibiotic therapy alone [14]. Reports indicate a 91% short-term success rate and 71% becoming appendectomy-free within a year when treating appendicitis with antibiotics [15]. In the United States, conservative antibiotic-based management before surgery has shown favorable outcomes [16]. On the other hand, emergency appendectomy is required in patients with complicated appendicitis [17,18].

Despite the stated guidelines that simple appendicitis could be controlled with medical treatment while complicated appendicitis should be managed urgently, no clear distinguishing criteria were explicitly proposed [17,18].

In this context, clinical scoring systems and biochemical markers were proposed to provide some predictive value for distinguishing complicated appendicitis [19–21]. Although computed tomography scan findings such as extraluminal appendicolith, abscess, and enhancement defects indicate complicated appendicitis, their sensitivity is limited. The presence of appendicolith has been linked to the lack of success in NOM [22]. Moreover, a combination of C-reactive protein greater than 60 g/l, WCC greater than 12×109/l, and age greater than 60 years has been correlated with complicated appendicitis [23].

Several clinical, laboratory, and imaging criteria were proposed to discriminate between simple and complicated cases [24,25]. In this study, we chose to investigate the role of TLC assessment and abdominal US in this concern. Both methods are simple and easily accessible in almost all healthcare settings.

This study showed that patients with complicated appendicitis were significantly older. Similar findings were reported by Zhang *et al.* [26] This could be attributed to the fact that older individuals may be more likely to ignore early symptoms of acute appendicitis or may have comorbidities that mask the signs of appendicitis, leading to a delayed diagnosis and progression to complicated appendicitis.

In the present study, the complicated group showed significantly increased mean TLC compared with the noncomplicated group. This association was confirmed by the regression analysis which showed TLC to be a predictor of complicated appendicitis. A cut-off value of 12.95 was able to discriminate complicated cases with a sensitivity of 81.3% and a specificity of 79.8%.

In accordance with our results, previous studies reported the validity of TLC in distinguishing cases of complicated appendicitis from those with simple appendicitis. This could be easily realized since complicated appendicitis entails a more severe inflammatory process that triggers a more robust immune response compared with uncomplicated cases. The cut-off value obtained in the current study lies within the range of values described previously. Jung *et al.* [27] reported a cut-off value of 10.6×10^9/l (71.2% sensitivity and 68.2% specificity), Sengul *et al.* [9] found a cut-off value of 11.5×10^9/l (88% sensitivity and 70% specificity), while Ünal *et al.* [28] reported a cut-off value of 15.8×10^9/l (75% sensitivity and 70% specificity).

As for the US findings, the significantly higher rates of right iliac fossa fluid and pelvic collection in complicated cases are supported by the previously established sonographic criteria for complicated appendicitis [25]. The significantly higher rate of visualizing the blind-ended appendix loop is likely attributed to the fact that the presence of fluid around the complicated appendix enhances the visualization by US and enables the easy detection of the blind-ended inflamed appendix. Among the US features, this study showed that only the presence of pelvic collection was a significant predictor for complicated appendicitis in the multiple regression test. It gave a sensitivity of 50% and a specificity of 95.8% to distinguish these cases. This low sensitivity indicates that we cannot exclude the diagnosis of

complicated appendicitis based on the US diagnosis. In agreement with our findings, a previous review study displayed that the sensitivity of US in the diagnosis of acute appendicitis ranged from 44 to 100% and the specificity ranged from 47 to 100% [29]. Therefore, for the diagnosis of complicated appendicitis, US was predominantly implemented in scoring systems that include clinical and laboratory findings beside the US diagnosis [15,30].

In this concern, we found that adopting either a TLC cut-off value of 12.95×10^9/l or the presence of pelvic collection for the diagnosis yielded a sensitivity of 90.6%, a specificity of 77.1%, and an accuracy of 82.5%, which was better than that of each of them separately (78.75 and 77.5%, respectively). It is worth noting that the high sensitivity achieved in our tool (90.6%) indicates remarkable reproducibility in ruling out complicated cases.

This work presented a simple, easy, and readily accessible tool for the preoperative prediction of complicated appendicitis. The study is, however, limited by being a single-centered work and the relatively small sample size.

Conclusion

The presence of a TLC cutoff value of 12.95×10^9/l and/or a pelvic collection in abdominal US seems to be reproducible for the preoperative prediction of complicated acute appendicitis. Application of our tool to a larger cohort is recommended to obtain validity for its routine use.

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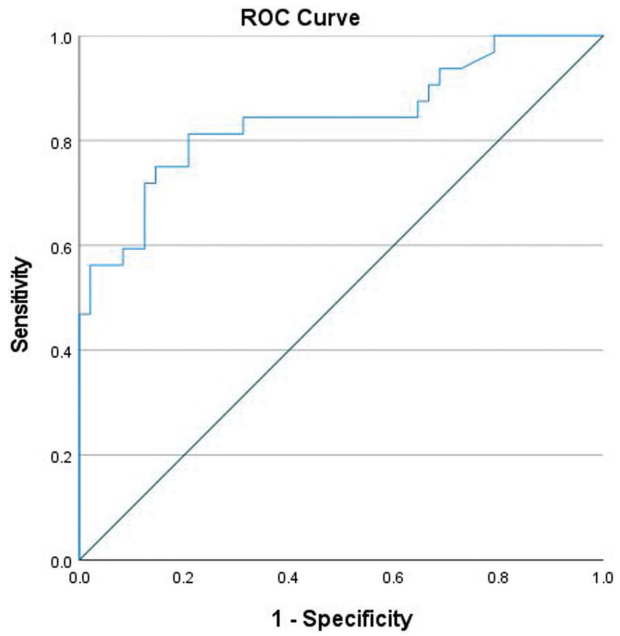
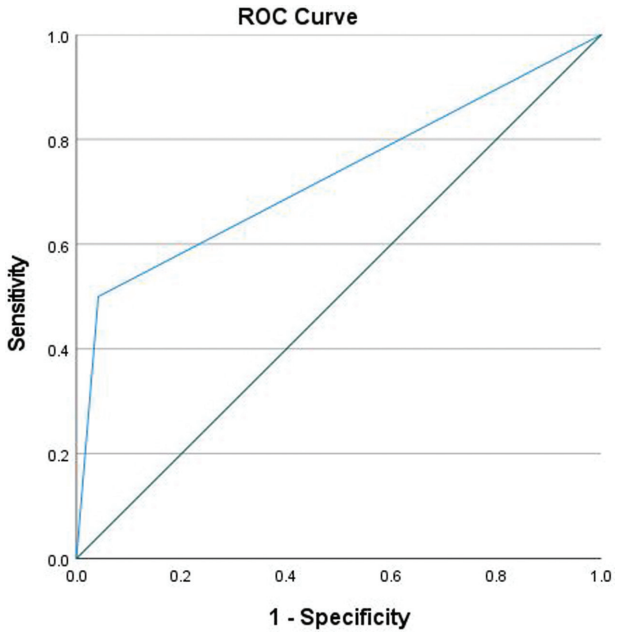
None.

Fig. 1



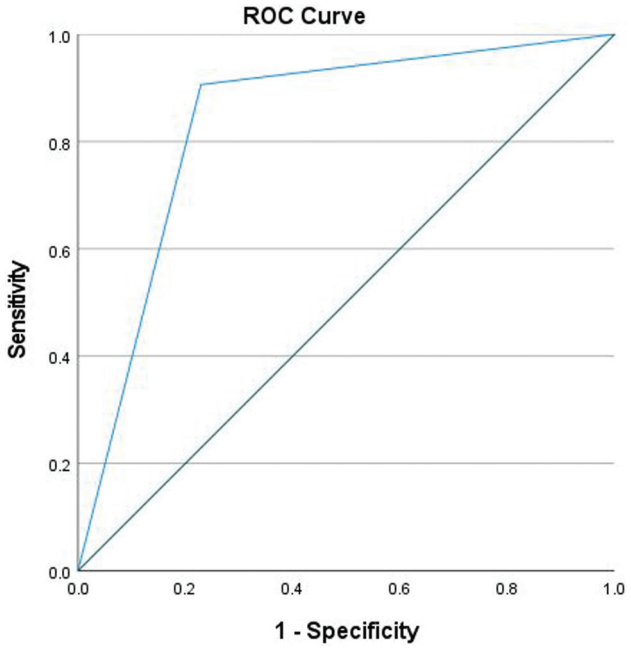
Receiver operating characteristic curve using total leucocytic count for the prediction of complicated appendicitis.

Fig. 2



Receiver operating characteristic curve using pelvic collection in ultrasound for the prediction of complicated appendicitis.

Fig. 3



Receiver operating characteristic curve using total leucocytic count and/or pelvic collection in ultrasound for the prediction of complicated appendicitis.

Statements and declarations

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