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Preoperative predictor laboratory markers for complicated appendicitis: A retrospective analysis of single center experience

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Abstract

In this study, we aimed to investigate the pre-operative predictive role of the serum white blood cell and platelet counts, C-reactive protein (CRP), bilirubin, amylase, lipase, and sodium levels for complicated appendicitis in patients aged≥18 years. We retrospectively evaluated 574 patients (aged≥18 years) who underwent appendectomy due to acute appendicitis (AA) between March 2018 and March 2022 at our clinic. The patient population was divided into two groups as perioperative complicated and uncomplicated appendicitis and the preoperative predictor role of serum white blood cell counts, platelet counts, CRP, bilirubin, amylase, lipase, and sodium levels were compared for complicated versus uncomplicated appendicitis. In multivariate analyses, age>38 years, the timing of Emergency Department (ED) arrival to admission ≥2 days, CRP ≥3.36 mg/dL, and total bilirubin ≥0.76 mg/dL are independent risk factors for detecting complicated AA. Moreover, in the designed scoring system, the AUC: 0.877 (CI: 0.847-0.907) for perforated AA at scores below or above. Estimation of the complications of AA can help clinicians practically with the scoring system designed because of the determined predictive factors.

Keywords: Appendicitis, complication, perforation, diagnostic marker, clinical scoring systems

Introduction

Acute appendicitis (AA) is the most common cause of acute abdomen among young patients who present to the emergency department with abdominal pain. Diagnosis is made by detailed anamnesis, physical examination, and scoring systems taken from the patient. Imaging methods are performed in suspected AA.

One of the most common complications of AA is perforation. Although it differs according to age, its morbidity and mortality are higher than non-perforated AA.

Clinical scoring systems are used in the diagnosis of AA according to the algorithm. In addition, its use alone in diagnosing AA is not sufficient in terms of performance, and it is not useful in differentiating uncomplicated and complicated appendicitis [1]. Even though imaging methods have high specificity, they cannot exclude complicated appendicitis due to their low sensitivity [2].

There are differences in the severity of the disease and treatment approaches of patients with AA, which is related to the level of development of these countries [3]. Recently, randomized controlled trials have demonstrated that treatment with antibiotics is effective for uncomplicated appendicitis [4,5]. Early appendectomy is recommended because of the high morbidity in complicated AA [3]. Therefore, clinicians should distinguish between complicated and uncomplicated appendicitis so that they can manage treatment.

Our study aimed to create a model by determining independent risk factors among biochemical markers, and clinical and imaging

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methods to distinguish between complicated and uncomplicated appendicitis.

Material and Methods

Study design

This was a retrospective analysis and was conducted at Inonu University, 574 patients who underwent appendectomy due to AA between January 2018 and April 2022 were reached from the database. The study was approved by the ethics committee of Inonu University (dated 23.05.2023, and number 2023/4665). The adult patients diagnosed and operated on with AA as a result of clinical and radiological evaluations were included in the study and the exclusion criteria were patients younger than 18 years old and appendectomies performed as a part of another surgical procedure. The patient population was divided into two groups perioperative complicated appendicitis and uncomplicated appendicitis. Demographic (age and gender) data, preoperative white blood cell (WBC) count (10^3/uL), platelet (PLT) count (10^3/uL), C-reactiveprotein (CRP), bilirubin(mg/dL), amylase, lipase, sodium levels, preoperative appendix diameter(mm), the timing of Emergency Department (ED) arrival to admission (days), type of operation (open, laparoscopic, open-converted), length of stay hospital (days) and presence of postoperative complications were obtained from the patient database.

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Statistical analysis and model formation

The normality of distribution was tested using the Kolmogorov-Smirnov test. Equivalent nonparametric tests were used (Mann-Whitney U test). The variables' median, and interquartile range (IQR) values were presented. The ideal cutoff point for age, CRP, the time before hospital admission, and total bilirubin were determined by receiver operating characteristic (ROC) curve analysis. A chi-square analysis was conducted for categorical variables. The frequency and percentage values of these variables were presented. Prospective selective multivariate logistic regression analysis was performed with the variables found to be statistically significant. The Hosmer-Lemeshow test was used to evaluate the goodness of fit. Statistical significance was set at $p<.05$.

Results

Between March 2018 and March 2022, an appendectomy was performed on 574 patients diagnosed with AA at our clinic. Of these, 332 (57.8%) were male. The median age in the population was 34 years(range: 18-92). Intraoperatively, 153 (26.7%) patients had complicated appendicitis. Laparoscopic appendectomy was performed in 386 (67.2%) of the patients. The demographic, type of operation, and postoperative complication data of patients were shown in Table 1.

Among the complicated and uncomplicated appendicitis groups; there was a statistically significant difference in terms of age ($p<.001$), appendix diameter ($p=.006$), the timing of ED arrival to admission ($p<.001$), postoperative complications ($p<.001$), length of hospital stay ($p<.001$), WBC ($p<.001$), CRP ($p<.001$), amylase ($p<.001$), lipase ($p=.043$), sodium ($p<.001$), bilirubin ($p<.001$) values (Tables 2,3).

The scores of the patients from the model were calculated by giving five points for the timing of ED arrival to admission (days) ≥2 days, three points for CRP ≥3.36 mg/dL, one point for age>38, and one point for total bilirubin ≥0.76 mg/dL (Table 4). According to the model, the median score of the patients was 9 (6-10) in complicated AA and 2 (1-6) in uncomplicated AA.

Table 1. Demographic, type of operation, and complication data

Variables		Count (%)	Median (IQR)
Gender	Female	242 (42.2%)	
	Male	332 (57.8%)	
Age (years)			34 (25-50)
Complication situation	Uncomplicated	421 (73.3%)	
	Complicated	153 (26.7%)	
Type of operation	Open	184 (32.1%)	
	Laparoscopic	386 (67.2%)	
	Open-converted	4 (0.7%)	
Postoperative complication	Absent	524 (91.3%)	
	Paralytic ileus	22 (3.8%)	
	Superficial SSI	8 (1.4%)	
	Deep SSI	11 (1.9%)	
	Pneumonia	4 (0.7%)	
	Cardiac complication	3 (0.5%)	
	Postoperative hemorrhage	1 (0.2%)	
	Acute kidney failure	1 (0.2%)	

IQR: interquartile range, SSI: surgical site infection

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Table 2. Analysis of continuous variables and categorical data

Variables		Complication situation				
		Uncomplicated		Complicated		
		Count (%)	Median (IQR)	Count (%)	Median (IQR)	p
Gender	**Female**	174 (41.3%)		68 (44.4%)		.504
	Male	247 (58.7%)		85 (55.6%)		
Age (years)			31 (23-44)		45 (31-63)	**<.001***
Timing of ED arrival to admission (day)			1 (1-2)		3 (2-3)	**<.001***
Diameter of appendix (mm)			10 (7-12)		10 (8-14)	**.006***
Operation type	**Open**	119 (28.3%)		65 (42.5%)		**<.001**
	Laparoscopic	302 (71.7%)		84 (54.9%)		
	Open-converted	0 (0%)		4 (2.6%)		
Postoperative complication	**Absent**	408 (96.9%)		116 (75.8%)		**<.001**
	Paralytic ileus	7 (1.7%)		15 (9.8%)		
	Superficial SSI	1 (0.2%)		7 (4.6%)		
	Deep SSI	2 (0.5%)		9 (5.9%)		
	Pneumonia	1 (0.2%)		3 (2.0%)		
	Cardiac complication	1 (0.2%)		2 (1.3%)		
	Postoperative hemorrhage	1 (0.2%)		0 (0%)		
	Acute kidney failure	0 (0%)		1 (0.7%)		
Length of stay hospital(days)			1 (1-2)		4 (2-5)	**<.001***
Model Score	**≥6 point**		110 (26.1%)		128 (83.7%)	**<.001**
	<6 point		311 (73.9%)		25 (16.3%)	

IQR: interquartile range, ED: emergency department, SSI: surgical site infection, Pearson chi-square test, * Mann-Whitney U test results were considered significant at p<.05.

Table 3. Analysis of hematological and biochemical data

Variables	Complication situation		
	Uncomplicated	Complicated	
	Median (IQR)	Median (IQR)	p
WBC (10^3/uL)	12.2 (9.6-15.3)	13.6 (11.2-17.4)	**<.001**
Platelet (10^3/uL)	238 (202-286)	237 (193-284)	.719
CRP (mg/dL)	1 (0.3-3.2)	9.7 (3.7-15)	**<.001**
Total bilirubin (mg/dL)	0.7 (0.4-1)	0.9 (0.6-1.4)	**<.001**
Direct bilirubin (mg/dL)	0.2 (0.1-0.3)	0.3 (0.2-0.5)	**<.001**
Amylase (U/L)	57 (44-70)	48 (34-62)	**<.001**
Lipase (U/L)	16 (11-23)	14 (8-25)	**.043**
Sodium (mmol/L)	138 (136-139)	137 (135-138)	**<.001**
Model score (point)	2 (1-6)	9 (6-10)	**<.001**

WBC: white blood cell, CRP: C-reactive protein, IQR: interquartile range. Mann-Whitney U test results were considered significant at p<.05.

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Table 4. Scoring of variables used to predict uncomplicated appendicitis

Age(years)	≤38	0 point
	>38	1 point
CRP(mg/dL)	<3.36	0 point
	≥3.36	3 point
Bilirubin(mg/dL)	<0.76	0 point
	≥0.76	1 point
Timing of ED arrival to admission (days)	<2	0 point
	≥2	5 point

CRP: C-reactive protein, ED: emergency department

However, in multivariate analyzes age>38 years (OR: 2.156 CI 95%: 1.336-3.479, p=.002), total bilirubin ≥0.76 mg/dL (OR: 1.764 CI 95%: 1.088- 2.861, p=.021), CRP≥3.36 mg/dL(OR: 6.140 CI 95%: 3.770- 10.001, p<.001), timing of ED arrival to admission ≥2 days (OR: 10.604 CI 95%: 5.946-18.911, p<.001) variables were found to be independent risk factors in complicated appendicitis (Table 5).

The cut-off values of the variables were analyzed by ROC (five points for timing of ED arrival to admission ≥2 days, three points for CRP ≥3.36 mg/dL, one point for age>38, and one point for total bilirubin ≥0.76 mg/dL, Model Score ≥6 points). According to the model, the median score of the patients was 9 (6-10) in complicated AA and 2 (1-6) in uncomplicated AA (p<.001) (Table 6). With ROC analysis, the power of the model to predict complicated AA was found to be AUC 0.877 (0.847-0.907). The sensitivity of the model was 83.66% and the specificity was 73.87%.

Table 5. Univariate and multivariate logistic regression analysis results

	Univariate	**Logistic**	**Regression**	**Multivariate**	**Logistic**	**Regression**
Variables	OR	95.0% CI	p	OR	95.0% CI	p
Age >38 years	2.906	2.039-4.402	**<.001**	2.156	1.336-3.479	**.002**
Timing of ED arrival to admission ≥2 days	15.389	8.942-26.485	**<.001**	10.604	5.946-18.911	**<.001**
Diameter of appendix (mm)	1.030	1.002-1.059	**.036**			
WBC (10^3/uL)	1.093	1.049-1.139	**<.001**			
CRP ≥3.36 mg/dL	10.297	6.662-15.915	**<.001**	6.140	3.770-10.001	**<.001**
Total bilirubin ≥0.76 mg/dL	2.576	1.753-3.786	**<.001**	1.764	1.088-2.861	**.021**
Amylase (U/L)	1.013	1.005-1.022	**.001**			
Sodium (mmol/L)	1.221	1.135-1.315	**<.001**			

OR: odds ratio, CI: confidence interval, ED: emergency department, WBC: white blood cell, CRP: C-reactive protein. p<.05 was considered statistically significant

Table 6. The power of predictive factors in detecting complicated appendicitis

Variables	**Cut-off**	**Sensitivity**	**Specificity**	**AUC**	**%95CI**	**p**
Age	>38	64.05%	62.71%	0.687	0.637-0.738	**<.001**
CRP (mg/dL)	≥3.36	76.47%	76.01%	0.835	0.796-0.874	**<.001**
Bilirubin (mg/dL)	≥0.76	65.36%	57.72%	0.652	0.602-0.703	**<.001**
Timing of ED arrival to admission (day)	≥2day	88.89%	65.80%	0.833	0.795-0.877	**<.001**
Model score	≥6 point	83.66%	73.87%	0.877	0.847-0.907	**<.001**

AUC: area under the curve, CI: confidence interval, ED: emergency department, CRP: C-reactive protein. p<.05 was considered statistically significant

Discussion

Currently, scoring systems are used in patient management in many diseases that cause acute abdomen [6,7]. Many scoring systems are used in the diagnosis and patient management of AA. However, they were not demonstrated to be beneficial among complicated and uncomplicated appendicitis.

In our study, age >38 years, the timing of ED arrival to admission ≥2 days, the diameter of the appendix(mm), WBC, CRP≥3.36 mg/dL, total bilirubin ≥0.76 mg/dL, hyperamylasemia, and sodium were statistically significant in univariate regression analyzes. However, in multivariate analyses, age >38 years, the timing of ED arrival to admission ≥2 days, CRP≥3.36 mg/dL, and total bilirubin ≥0.76 mg/dL are independent risk factors for detecting complicated AA. In addition, the created scoring system has a sensitivity of 83.66% and a specificity of 73.87% in terms of complicated AA. The complicated acute appendicitis group had longer hospital stays (median 4 (2-5) days vs 1 (1-2) days) and more postoperative complications (24.1% vs 3.1%).

A meta-analysis performed at the time of admission to the emergency department showed that it was associated with increases in rates of complications [8]. Delayed appendectomy (>8 hours) is performed in AA. In a retrospective study, no difference was found between delayed appendectomy and early appendectomy in terms of postoperative morbidity [9]. During the COVID-19 pandemic period, the time to apply to the

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emergency room due to corona phobia has extended. Therefore, it has been shown that complication rates increase in AA [10]. In our study, the risk of perforation increased approximately tenfold in patients with a duration of admission to the emergency department longer than 48 hours. It is also an independent risk factor for the duration of admission to the emergency department in complicated appendicitis. A delayed appendectomy is performed in AA. Therefore, it should be applied with caution in patients whose hospital admission time is longer than 48 hours, and more care should be taken in terms of complications.

Bilirubin may be elevated due to intra-abdominal infections. Transient portal pyrexia and inflammatory-mediated cholestasis cause this condition [11]. Therefore, total bilirubin is elevated in complicated AA, especially perforation [12,13]. In another study, total bilirubin >0.45 mg/dL increased the likelihood of complicated appendicitis approximately threefold [14]. In our study, total bilirubin ≥0.76 mg/dL increases the risk of complications approximately twofold.

It is known as the acute phase reactant of CRP synthesized from the liver. It usually rises in response after leukocytosis and is associated with the severity of inflammatory processes. It is used in scoring systems in the diagnosis of AA, as well as in the differentiation of complicated and non-complicated AA cases. In a study, its sensitivity was 92% and specificity 72.5% in terms of detecting complications in AA with CRP>25.5 mg/dL [14].In another study, it was shown that CRP and WBC were ineffective in distinguishing between complicated and non-complicated AA [15]. In our study, CRP ≥3.36 mg/dL increases the probability of complications in AA approximately six times.

Although it is helpful in the diagnosis of complicated AA and negative cases, it does not recommend the use of biochemical markers (without serum inflammatory markers) in the diagnosis of AA in the current guideline [3].

In the designed scoring system, the AUC: 0.877 (CI: 0.847-0.907) for perforated AA at scores below or above, with a sensitivity of 83.66% and a specificity of 73.87%. However, this scoring system needs to be validated with randomized controlled studies.

Conclusion

In addition to the fact that the time of admission to the emergency department is more than 48 hours, simple and easily accessible serum biochemical markers (Total bilirubin and CRP) can help predict perforated AA. In addition, with the scoring system created, can enable clinicians in the emergency department to make quick decisions about patient management.

Conflict of Interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical Approval

Permission for the study, dated 23/05/2023 and numbered 2023/4665, was obtained from the Local Ethics Committee.

References

1. Bhangu A; RIFT Study Group on behalf of the West Midlands Research Collaborative. Evaluation of appendicitis risk prediction models in adults with suspected appendicitis. Br J Surg. 2020;107:73-86.
2. Kim HY, Park JH, Lee YJ, et al. Systematic review and meta-analysis of CT features for differentiating complicated and uncomplicated appendicitis. Radiology. 2018;287:104-15.
3. Gomes CA, Abu-Zidan FM, Sartelli M, et al. Management of appendicitis globally based on income of countries (MAGIC) study. World J Surg. 2018;42:3903-10.
4. Salminen P, Paajanen H, Rautio T, et al. Antibiotic therapy vs appendectomy for treatment of uncomplicated acute appendicitis: the APPAC randomized clinical trial. JAMA. 2015;313:2340-8.
5. CODA Collaborative; Flum DR, Davidson GH, Monsell SE, et al. A randomized trial comparing antibiotics with appendectomy for appendicitis. N Engl J Med. 2020;383:1907-19.
6. Ceylan C, Baran NT, Kocaaslan H, et al. A new model for prediction of bowel gangrene in sigmoid volvulus. Ulus Travma Acil Cerrahi Derg. 2023;29:471-6.
7. Alvarado A. A practical score for the early diagnosis of acute appendicitis. Ann Emerg Med. 1986;15:557-64.
8. Al Busaidi O, Lee S, Kortbeek JB, et al. Complications of appendectomy and cholecystectomy in acute care surgery: a systematic review and meta-analysis. J Trauma Acute Care Surg. 2020;89:576-84.
9. Terrón-Arriaga RM, Luna Tovar A, Ramírez BuenSuceso Conde NA, et al. Perioperative morbidity in acute appendicitis: is delayed appendectomy still an option?. J Laparoendosc Adv Surg Tech A. 2021. doi:10.1089/lap.2021.0614
10. Taşçı A, Gürünlüoğlu K, Yıldız T, et al. Impact of COVID-19 pandemic on pediatric appendicitis hospital admission time and length of hospital stay. Ulus Travma Acil Cerrahi Derg. 2022;28:1095-9.
11. Bhogal HK, Sanyal AJ. The molecular pathogenesis of cholestasis in sepsis. Front Biosci (Elite Ed). 2013;5:87-96.
12. Hong YR, Chung CW, Kim JW, et al. Hyperbilirubinemia is a significant indicator for the severity of acute appendicitis. J Korean Soc Coloproctol. 2012;28:247-52.
13. Chambers AC, Bismohun SL, Davies H, et al. Predictive value of abnormally raised serum bilirubin in acute appendicitis: a cohort study. Int J Surg. 2015;13:207-10.
14. Patmano M, Çetin DA, Gümüş T. Laboratory markers used in the prediction of perforation in acute appendicitis. Ulus Travma Acil Cerrahi Derg. 2022;28:960-6.
15. Lietzén E, Mällinen J, Grönroos JM, et al. Is preoperative distinction between complicated and uncomplicated acute appendicitis feasible without imaging?. Surgery. 2016;160:789-95.