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Comparative evaluation of inflammatory biomarkers and total bilirubin for the early detection of complicated appendicitis in adults

Компаративна евалуација инфламаторних биомаркера и укупног билирубина за рано откривање компликованог апендицитиса код одраслих

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SUMMARY

Introduction/Objective Acute appendicitis (AA) is the most frequent cause of emergency surgical interventions, and numerous biomarkers can be used diagnostically to differentiate patients with AA from those with pain of other etiologies, as well as to predict disease progression.

The aim of this paper is to determine the accuracy of neutrophil-lymphocyte ratio-NLR, procalcitonin (PCT) and total bilirubin (TBil) in the diagnosis of complicated AA (CoAA) and their comparison with the Alvarado score (AS) as well as the histopathological (HP) findings.

Methods AA was diagnosed preoperatively in 67 patients using AS. Examined parameters and AS were determined before surgery and compared postoperatively with HP findings. Depending on the HP findings, the respondents were classified into three groups: gangrenous and gangrenous-perforative appendicitis, which are classified into complicated (CoAA), phlegmonous (PhAA) and catarrhal AA (CAA).

Results The results of the univariate analysis show that a one-unit increase in NLR increased the probability of CoAA by 20% (1.02 to 1.51, $p < 0.05$). PCT ≥ 0.5 ng/ml increases the probability of CoAA by 26.84 times (3.30 to 218.55; $p < 0.001$), while TBil > 21μmol/l increases the probability of CoAA by 4.80 times (1.41 to 16.37, $p < 0.05$). ROC curve showed that PCT was the best predictor of CoAA compared to CAA/PhAA, with a cut-off of 0.56, as well as CAA in relation to PhAA/CoAA with a cut-off of 0.37.

Conclusion PCT, TBil and NLR can be used in daily clinical practice as powerful, easily available, inexpensive parameters in the diagnosis of CoAA in adults.

Keywords: inflammatory biomarkers; total bilirubin; complicated acute appendicitis

САЖЕТАК

Увод/Циљ Акутни апендицитис (АА) је најчешћи узрок хитног хируршког лечења, а бројни биомар-кери се могу користити за предвиђање прогресије болести као и за разликовање пацијената са АА од оних са болом друге етиологије.

Циљ овог рада је да се утврди тачност неутрофил-но-лимфоцитног односа-НЛР, прокалцитонина-ПЦТ и укупног билирубина-ТБил у дијагнози ком-пликованог АА (КоАА) и њихово поређење са Ал-варадо скором (АС), као и са хистопатолошким (ХП) налазима.

Методе АА је дијагностикован преоперативно код 67 пацијената коришћењем АС. Испитивани параметри и АС су одређивани преоперативно и постоперативно упоређивани са ХП налазима. У зависности од ХП налаза, испитаници су били класификовани у три групе: гангренозни и гангренозно-перфоративни апендицитис су сврстани у компликовани (КоАА), затим флегмонозни (ФАА) и катарални АА (КАА).

Резултати Резултати униваријантне анализе показују да повећање НЛР за једну јединицу повећава вероватноћу КоАА за 20% (1,02 на 1,51, $p < 0,05$). ПЦТ ≥ 0,5ng/ml повећава вероватноћу КоАА за 26,84 пута (3,30 на 218,55; $p < 0,001$), док ТБил > 21μmol/l повећава вероватноћу појаве КоАА за 4,80 пута (1,41 на 16,37, $p < 0,05$). *ROC* крива је показала да је ПЦТ најбољи предиктор КоАА у односу на КАА/ФАА, са *cut-off* 0,56, као и за КАА у односу на ФАА/КоАА, са *cut-off* 0,37.

Закључак ПЦТ, ТБил и НЛР могу се користити у свакодневној клиничкој пракси као моћни, лако доступни, јефтини параметри у дијагностици КоАА код одраслих.

Кључне речи: инфламаторни биомаркери; укупни билирубин; компликовани акутни апендицитис

INTRODUCTION

The lifetime prevalence of acute appendicitis (AA), as the most frequent surgical condition, is around 1 in 7 cases, with an incidence of 1.5-1.9 per 1000. The male: female ratio is 1.4. According to literature, there is a correlation between the number of hospitalizations for

appendicitis and atmospheric pressure and temperature [1,2]. Despite the high frequency of AA, correct diagnosis before surgery is a challenge that can tempt even highly experienced surgeons [3]. The literature reports a negative appendectomy rate of 15–25%. In women of reproductive age, this rate has almost doubled due to the prevalence of gynecological diseases, reaching as high as 30–50%. In young male patients, the rate of negative appendectomy is relatively low (5–22%). In children, the diagnosis may be incorrect in 30–46% of cases. Untimely diagnosis and delayed surgical treatment led to perforation and subsequent complications. Therefore, an adequate and easily accessible test that can confirm or rule out complicated forms of appendicitis and can be useful in making decisions about emergency surgical treatment [4].

The modern diagnostic principle aims primarily of confirmation or elimination of the diagnosis of AA and to differentiate complicated from uncomplicated forms of the disease, which also determines the therapeutic modalities [5]. Due to this reason, there is still a research orientation towards finding biomarkers of sufficient specificity and sensitivity that would more clearly suggest the degree of appendicular inflammation and which, are easily available, minimally invasive, cheap and can be repeated if necessary [6, 7]. To reduce the rate of negative appendectomies, i.e. cases of missed AA, the objective of this work was to determine the accuracy of inflammatory biomarkers (NLR, PCT and TBil) and their comparison with AS and HP in adult patients operated on for AA.

METHODS

A prospective study was conducted which included 67 patients older than 18 years in whom appendectomy was performed due to AA during a 6-month period at the Department of Surgery of the Clinical Hospital Center Kosovska Mitrovica. The study was conducted in accordance

with the standards of the institutional ethics committee (number 3482 dated 27.05.2025.). AA was diagnosed using the Alvarado score (AS) (Table 1) [8]. The AS is a clinically validated scoring system. Its validity has been demonstrated in large prospective and retrospective studies, with reported sensitivity ranging from 72% to 88% and area under the ROC curve values exceeding 0.75 in different populations. A cut-off value of ≥6 was used as clinically appropriate for identifying patients with suspected acute appendicitis and for guiding further diagnostic evaluation, and has demonstrated an optimal balance between sensitivity and specificity. After preoperative blood sampling, serum PCT and TBil levels, as well as NLR, were determined. The patients were treated with an open appendectomy. Definitive diagnosis of the removed appendices was established by histopathological analysis of samples. The results of the parameters and AS were compared with the HP findings. According to the HP assessment, the severity of AA was categorized into three groups: gangrenous and gangrenous perforating appendicitis were classified as CoAA in contrast to CAA and PhAA.

Statistical analyses

Continuous variables are presented as means, standard deviations, medians, minimum and maximum values. Student's t-test and Mann-Whitney test were used to compare continuous variables. For comparisons involving three independent groups, ANOVA analysis was used together with appropriate post hoc procedures (Tukey's method and Tamhane's T2 test), as well as Kruskal-Wallis test and Mann-Whitney test for group comparisons. The association between categorical variables was assessed using Pearson's χ^2 test.

Univariate logistic regression was performed to assess the impact of individual independent parameters on changes in the odds ratio for a positive or negative outcome. The diagnostic performance of the parameters in differentiating AA types was examined using ROC curve

analysis and appropriate cut-off values were determined. Statistical significance was set at $p<0.05$. All statistical procedures were performed using SPSS, version 16.0.

RESULTS

The average age of the patients was 38.72±16.46 years, ranging from 18 to 80 years, with 35 (52.24%) male patients and 32 (47.76%) female patients (the male:female ratio is 1.09). CoAA occurred more frequently in older patients, compared to CAA and PhAA ($p<0.05$). Into the first pathohistological group, catarrhal acute appendicitis were classified 16 patients-23.88% (8 men and 8 women), the second group, phlegmonous acute appendicitis consisted of 33 patients-49.25% (17 men and 16 women), while in the third group, gangrenous and gangrenous perforating (complicated) acute appendicitis included 18 patients-26.87% (10 men and 8 women) (Table 2).

The minimum and maximum, as well as the average values of the examined parameters are given in Table 3.

The most authoritative criteria for the definitive diagnosis of AA were positive AS value ($AS\geq6$) and the HP finding. In table 4 are given the average values of the tested parameter compared to the AS. All three parameters, NLR and PCT($p<0.001$) and TBil ($p<0.01$), had significantly higher values in positive AS. The average values of the investigated parameters compared to the HP finding of AA are given in Table 5. AS was statistically significant in CoAA compared to CAA and PhAA ($p<0.001$), as well as in PhAA compared to CAA($p<0.01$). NLR values were statistically higher in CoAA ($p<0.01$) and PhAA ($p<0.05$) compared to CAA. PCT values were higher in CoAA in relation to PhAA and CAA and in PhAA in relation to

CAA ($p<0.001$). TBil was elevated in CoAA compared to PhAA and CAA at a statistical significance level of $p<0.05$.

Table 6 shows the frequency of elevated values of the tested parameters compared to AS. In patients with AS ≥ 6, PCT and TBil values were higher, as well as more frequent HP findings of CoAA ($p<0.001$).

Compared to HP, the AS finding in CoAA was statistically more significant than in PhAA and CAA ($p<0.001$). PCT was elevated in CoAA compared to CAA ($p<0.001$), as well as in PhAA($p<0.05$). This parameter was elevated in PhAA compared to CAA($p<0.001$). TBil had elevated values in CoAA compared to CAA($p<0.05$). Table 7.

In order to determine the importance of each of the examined parameters in predicting the degree of appendicitis definitively established by HP finding, univariate logistic regression analysis was conducted. NLR, PCT and TBil were correlated with AS values of 6 or more: a one-unit increase in NLR values led to an increase in the probability AS≥6 by 44%, while the value of PCT≥0.5ng/ml increases 9.20 and TBil 9.00 times the probability of AS≥6 (Table 8). The examined parameters as factors of interest for the HP finding of CoAA are shown in Table 9. A positive AS value increases the probability of occurrence of CoAA24.67 times. The probability of CoAA occurrence increases by 20% with a unit increase in NLR (1,02 to 1,51, $p<0,05$).

TBil>21μmol/l increases the probability of CoAA 4,80 times (1,41 - 16,37, $p<0,05$), while PCT≥0.5nng/ml - 26.84 times (3,30 - 218,55; $p<0,01$).

For NLR, PCT, TBil and AS, which were shown by univariate logistic regression analysis to be factors of interest for the HP findings, as the gold standard for establishing the type of AA, their diagnostic potential (sensitivity and specificity) was determined by analysing ROC

curves. Two cut-off values were calculated for each parameter, the first separating catarrhal from phlegmonous or complicated AA and the second separating complicated from catarrhal or phlegmonous AA. Based on the parameter values, it is evident that PCT showed the best diagnostic characteristics for differentiating CAA from PhAA/CoAA and for CoAA compared to CAA/PhAA. In the first case, the AUC is 1.000 with a statistical significance of $p<0.001$. The cut-off is 0.37, confidence interval 0.946-1,000, it has the highest sensitivity and specificity and highest overall accuracy (Figure 1, Table 10). In the second case, PCT was also shown to have the best predictive characteristics for CoAA compared to CAA/PhAA. The AUC is 0.963, and the statistical significance of $p<0.001$. The cut-off value is 0.56 with a confidence interval of 0.885-0.994, with sensitivity and specificity of 94.44% and 91.84%, as well as the highest values of PPV, NPV and overall accuracy. AS has been shown to have good predictive characteristics for CoAA compared to CAA/PhAA. The AUC is 0.823, with a cut-off value >8, sensitivity 88.89% and specificity 75.51%, high overall accuracy, PPV and NPV (Figure 2, Table 11).

DISCUSSION

Despite the increased use of laboratory tests, radiological diagnostic methods and clinical scoring systems for timely diagnosis, AA remains the most common dilemma of the surgical team. In recent years, laparoscopic appendectomy (LA) has been the gold standard for surgical treatment of appendicitis. Numerous studies have shown the advantages of LA over open appendectomy: reduced pain intensity, lower complication rates, shorter hospitalization, and better quality of life postoperatively [9]. In order to avoid unnecessary operative explorations, as well as overlooked AAs in everyday surgical practice, there is a constant effort to find more reliable and precise diagnostic tools. Therefore, the search for an ideal biomarker that would

be used exclusively or combined with other parameters or as part of the stratification results has been ongoing for a long time [6,7].

Neutrophils represent the first line of defense against infection agents, primarily bacteria. Lymphocytes are immunocompetent cells that coordinate the immune response and assist neutrophil activity. Neutrophilia and lymphocytopenia are components of the cellular response in systemic inflammation [10,11]. In a study by Omari et al. investigating risk factors for appendicitis in the elderly, 94% of the perforated group had a left shift compared with 61% of the nonperforated group [12].

The NLR is derived directly from the differential blood count. The fact is that from previous studies, NLR is a more sensitive parameter than leukocyte count, and the NLR value can be used to identify those patients who have a higher risk of complications and a more careful observation must be considered. Numerous studies have shown that NLR are increased in AA and are correlated with the severity of inflammation. NLR has been suggested as a valuable predictor of gangrenous appendicitis in patients undergoing surgery for AA [13,14]. In 2014, Kahramanca et al. published a study comparing normal and inflamed appendices and found an NLR cut-off value of 4.68. In complicated appendicitis, the NLR cut-off value was estimated to be 5.74, with 70.8% sensitivity and 48.5% specificity. In a limited number of published studies, the diagnostic value of NLR was higher than that of conventional laboratory assessments (leucocyte count, CRP) [15]. Godinez-Vidal compared NLR with other biomarkers to assess disease severity. It was shown that NLR>12 may be associated with generalized peritonitis and perforated appendicitis [16]. The results of our study show good performance of NLR, which can be accepted as an easily applicable, inexpensive and available additional parameter contributing to the diagnosis of appendicitis. The odds ratio for AS≥6 and AS<5 increased by 44% with a unit increase in NLR (1.17-1.79, $p<0.001$), and the probability

of PH findings of CoAA and PhAA/CAA increases by 20% with a unit increase in NLR (1.02-1.51, p<0.05) (Tables 8 and 9). The cut-off value between CAA and PhAA/CoAA was 3.29, with statistical significance of p<0.05 (Table 10). The cut-off value between CoAA and CAA/PhAA was >4,52, the AUC is 0.728 with a statistical significance of p<0.01 (Table 11). These findings are in concordance with available data from the literature and indicate that NLR can be accepted as an additional parameter that contributes to the diagnosis of appendicitis.

Hyperbilirubinemia results from an imbalance between bilirubin production and excretion. Some studies have shown that bacterial endotoxins, such as toxins produced by Escherichia coli, reduce liver cell secretion, contributing to intrahepatic cholestasis and sinusoidal damage [17,18]. Emanuel et al. found in their study that the specificities of white cell count and C-reactive protein were less than hyperbilirubinaemia for simple appendicitis (60% and 72%) and perforated or gangrenous appendicitis (19% and 36%) [19]. The results of Nevler et al. suggest that bilirubin levels may be an important diagnostic factor, similar to LE, CRP, and AS [20]. The sensitivity of total serum bilirubin in predicting complicated appendicitis was found 91.43% (76.94% to 98.20%), whereas the specificity of this test was 88.00% (78.44% to 94.36%), PPV and NPV were 78.03% and 95.65%, respectively, in the study of Bakshi et al. [21]. In our work, TBil>21 μmol/l increases the probability of CoAA by 4.80 times (1.41-16.37, p<0.05) (Table 9). The result of ROC analysis for bilirubin showed AUC=0.70 (95%CI:0.58–0.81, p<0.05), with specificity and sensitivity of 95.9% and 38.9%, PPV-70% and NPV-81%, indicating acceptable/good discrimination of complicated from uncomplicated appendicitis (Table 11).

PCT is a prohormone of calcitonin, and the main site of synthesis is the liver, but also the neuroendocrine cells of the lungs and small intestine. Under physiological conditions, PCT is not released into the circulation. PCT is initially detected in plasma 6 to 12 hours after intake,

increases and reaches a peak after 12 to 24 hours, and remains in the form of a plateau in the following 2-3 days. Numerous studies have addressed the role of PCT in the diagnosis of complicated AA, all with the aim of implementing proper treatment and preventing unnecessary appendectomy [22]. Reviewing the literature, there is no firm consensus regarding the role of PCT in the diagnosis of appendicitis. Wu J. et al. found that PCT was statistically more significant in patients with CoAA, with an AUC of 0.69 compared to 0.61 for CRP. Prediction of disease severity can be made depending on the quantitative values of PCT [23]. The aim of the study conducted by Sand et al. was to examine the diagnostic significance of PCT in AA. They concluded that PCT is elevated, especially after gangrene and perforation of the appendix. Extremely small sensitivity does not recommend its routine use for AA [24]. Research by Hagi et al. suggests that PCT and IL-6 together may provide useful evidence for decision-making. Negative results for either of these biomarkers may help to exclude AA and reduce the number of negative appendectomies [25]. In our research compared to AS the level of PCT≥0.5 ng/ml was shown to increase the odds ratio for positive and negative AS value by 9.20 times (2.84-29.77; $p<0.001$) and increases the probability of occurrence of CoAA by 26.84 times (3.30-218.55; $p<0.01$) (Tables 8 and 9). These data demonstrate that PCT values can influence the accuracy of AA diagnosis, predict the severity of inflammation, and may serve as independent markers for CoAA.

The AS is a scoring system used to determine the risk of AA in patients with abdominal complaints. Data from the literature indicate that AS is used to diagnose AA [8]. We selected a cut-off value of ≥6 for the AS based on previously published validation studies showing that this cut-off provides an optimal balance between sensitivity and specificity for the diagnosis of acute appendicitis. Lower cut-offs increase sensitivity at the expense of specificity, whereas higher cut-offs (≥7) may lead to missed diagnoses. Therefore, a cut-off value of ≥6 was considered clinically appropriate for identifying patients with suspected acute appendicitis and

for further diagnostic evaluation [26, 27]. In our work, the ROC curve showed that AS with a cut-off value of >8 was a good predictor of CoAA compared to CAA/PhAA, with AUC=0.823(0.719-0.927), which is lower only compared to PCT (Figure 2, Tables 11). All this indicates a high predictive ability of AS, especially for estimating the probability of CoAA. This is in line with the findings of other studies that report AS as a superior diagnostic aid [28].

CONCLUSION

This study demonstrated very good diagnostic properties of NLR, AS and especially PCT and their ability to predict CoAA. Elevated TBil may be one of the markers of a complicated course of the disease, especially when combined with other parameters. These parameters are inexpensive for patients, easily accessible, minimally invasive and can be repeated if necessary and do not require any special apparatus or training. Results are acquired quickly, unnecessary additional diagnostics can be reduced, the rate of negative appendectomies is reduced, as is the rate of AA complications. NLR, TBil, PCT together with the Alvarado score should be used in daily practice, preferably in combination, as powerful diagnostic parameters and predictors of CoAA. It is certainly necessary to conduct further research in this area in the near future. Further multicenter prospective studies with larger samples and longer study periods are needed to confirm the significance of NLR, TBil, and PCT in the diagnosis of AA in adults, especially its complicated form.

Conflict of interest: None declared.

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Table 1. Alvarado score

Symptoms	**Alvarado score**
Pain migration	1
Anorexia	1
Nausea/vomiting	1
Signs	
Tenderness in right iliac fossa	2
Bloomberg's sign	1
Elevated temperature (> 37.2 °C)	1
Laboratory	
Leukocytosis (> 10×10^9)	2
Neutrophils > 75%	1
Total	10

Table 2. Histopathological forms of acute appendicitis in relation to gender and average age of patients

Histopathology	Number (%)	Sex		Age (years)
		Male	Female	
CAA	16 (23.88%)	8	8	35 ± 17.91 (29)
PhAA	33 (49.25%)	17	16	36.94 ± 15.94 (35)
CoAA	18 (26.87%)	10	8	45.28 ± 15.12^{ab*} (46)
Σ	**67 (100%)**	**35**	**32**	**38.72 ± 16.46 (36)**

CAA – catarrhal acute appendicitis; PhAA – phlegmonouse acute appendicitis; CoAA – complicated acute appendicitis; parameters are given as numbers, mean value, standard deviation, median;

*-$p < 0.05$;

a–*vs* CAA;

b–*vs* PhAA

Table 3. Average values of the tested parameters

Parameter	X ± SD	Med	Min	Max
AS	7.94 ± 1.82	8	2	10
NLR	6.24 ± 3.4	5.34	1.53	16.67
PCT (ng/ml)	0.50 ± 0.19	0.51	0.19	0.97
TBil (μmol/L)	17.05 ± 12.16	14.50	2.40	94.30

AS – Alvarado score; NLR – neutrophil-lymphocyte ratio; PCT – procalcitonin; TBil – total bilirubin; parameters are given as mean value (X), standard deviation (SD), median (Me), minimum (Min) and maximum (Max) value

Table 4. Average values of the tested parameters compared to Alvarado score (AS)

Parameter	AS negative (≤ 5)	AS positive (≥ 6)	p
NLR	4. 85 ± 2.70 (4.52)	**8. 17 ± 3.47 (7.16)**	**0. 0000*****
PCT (ng/ml)	0.40 ± 0.14 (0.42)	**0.63 ± 0.17 (0.61)**	**0.0000*****
TBil (µmol/L)	15.16 ± 14.14 (12.51)	**19.69 ± 8.22 (19.20)**	**0.0019****

NLR – neutrophil-lymphocyte ratio; PCT – procalcitonin; TBil – total bilirubin; parameters are given as mean value (X)±standard deviation (SD), median (Me);

-p < 0.01*-p < 0.001 (Student t-test or Mann–Whitney U-test)

Table 5. Average values of the tested parameters compared to histopathological findings

Parameter	CAA (n = 16)	PhAA (n = 33)	CoAA (n = 18)	p
AS	6.94 ± 1.18 (7)	**7.70 ± 2.05^{a*} (7)**	**9.28 ± 0.83^{a***b**} (9.00)**	**0.0000*** **
NLR	4.71 ± 2.65 (4.62)	6.09 ± 3.65 (5.19)	**7.88 ± 3.11^{a***b*} (7.01)**	**0.0083****
PCT (ng/ml)	0.25 ± 0.05 (0.25)	**0.50 ± 0.06^{a***} (0.51)**	**0.72 ± 0.15^{ab***} (0.69)**	**0.0000*** **
TBil (µmol/L)	17.64 ± 20.94 (12.8)	14.95 ± 6.48 (14.20)	**20.37 ± 9.32ab* (19.50)**	**0.0600**

CAA – catarrhal acute appendicitis; PhAA – phlegmonouse acute appendicitis; CoAA – complicated acute appendicitis; AS – Alvarado score; NLR – neutrophil-lymphocyte ratio; PCT – procalcitonin; TBil – total bilirubin; parameters are given as mean value (X) ± standard deviation (SD) and median (Me)a–*vs* CAA, b–*vs*PhAA, c–*vs*CoAA;

*-$p < 0.05$;

**-$p < 0.01$;

***-$p < 0.001$ (ANOVA, Kruskal–Wallis test Student t-test, Mann–Whitney U-test)

Table 6. Frequency of elevated values of the tested parameters compared to Alvarado score (AS)

Parameter	Value	AS		p
		≤ 5	≥ 6	
PCT (ng/ml)	< 0.5	58.97%	10.71%	**0.0001*****
	≥ 0.5	41.03%	**89.29%**	
TBil (µmol/L)	≤ 21	92.31%	57.14%	**0.0007*****
	> 21	7.69%	**42.86%**	
Histopathology	CAA and PhAA	94.87%	42.86%	**0.0000*****
	CoAA	5.13%	**57.14%**	

PCT – procalcitonin; TBil – total bilirubin; CAA – catarrhal acute appendicitis; PhAA – phlegmonouse acute appendicitis; CoAA – complicated acute appendicitis;
*** -$p < 0.001$ (χ^2 test)

Table 7. Frequency of elevated values of the tested parameters compared to histopathological findings

Parameter	Value	Histopathology			p
		CAA	PhAA	CoAA	
AS	**≤ 5**	93.75%	66.67%	11.11%	**0.0000*****
	≥ 6	6.25%	33.33%	**88.89%**^{ab***}	
PCT (ng/ml)	< 0.5	100 %	42.42%	5.56%	**0,0000*****
	≥ 0.5	0%	**57.58%** ^{a***}	**94.44%** ^{a***b*}	
TBil (µmol/L)	≤ 21	93.75%	81.82%	55.56%	**0.0205***
	> 21	6.25%	18.18%	**44.44%**^{a*}	

AS – Alvarado score; CAA – catarrhal acute appendicitis; PhAA – phlegmonous acute appendicitis; CoAA – complicated acute appendicitis;

a–*vs* CAA;

b–*vs* PhAA;

c–*vs* CoAA;

*-$p < 0.05$;

**-$p < 0.01$;

***-$p < 0.001$ (χ^2 test)

Table 8. Univariate logistic regression analysis estimating the probability of predicting Alvarado score

Parameter	OR	Limits 95%CI		p
		Lower	Upper	
NLR	**1.44**	1.17	1.79	**0.0007*****
PCT ≥ 0.5ng/ml	**9.20**	2.84	29.77	**0.0002*****
TBil > 21µmol/l	**9.00**	2.23	36.33	**0,0020****

OR – odd ratio (probability ratio positive Alvarado score and negative Alvarado score); CI – confidence interval;
**-p < 0.01;
***-p < 0.001

Table 9. Univariate logistic regression analysis estimating the probability of predicting acute appendicitis histopathology

Parameter	OR	Limits 95%CI		p
		Lower	Upper	
Alvarado score ≥ 6	**24.67**	4.94	123.12	**0.0001*****
NLR	**1.20**	1.02	1.51	**0.0249***
PCT ≥ 0.5ng/ml	**26.84**	3.30	218.55	**0.0021****
TBil > 21 µmol/l	**4.80**	1.41	16.37	**0.0122***

NLR – neutrophil-lymphocyte ratio; PCT – procalcitonin; TBil – total bilirubin; OR – odds ratio (between catarrhal acute appendicitis and phlegmonous acute appendicitis on one side and complicated acute appendicitis on the other), CI–confidence interval;

*-$p < 0.05$;

**-$p < 0.01$;

***-$p < 0.001$

Table 10. Diagnostic characteristics of Alvarado score (AS), neutrophil-lymphocyte ratio (NLR), neutrophil and procalcitonin (PCT) for distinguishing catarrhal acute appendicitis from phlegmonous acute appendicitis / complicated acute appendicitis

Parameter	Area below ROC curve (95% CI)	SE	p	Cut-off	Se (%)	Sp (%)	PPV (%)	NPV (%)	OA (%)
AS	0.775 (0.662–0.889)	0.053	0.0001***	8.5	52.94	93.75	96.43	37.50	62.69
NLR	0.676 (0.520–0.832)	0.080	0.0342*	3.29	86.27	43.75	83.02	30.43	30.43
PCT	**1.000 (0.946–1.000)**	**0.000**	**0.000*** **	**0.37**	**100**	**100**	**100**	**100**	**100**
TBil	0.611 (0.456–0.759)	0.079	0.161	16.5	81.3	45.1	88.46	31.71	53.73

*-$p < 0.05$;

***-$p < 0.001$;

TBil – total bilirubin; CI – confidence interval; SE – standard error; Se – sensitivity; Sp – specificity; PPV – positive predictive value; NPV – negative predictive value; OA – overall accuracy

Table 11. Diagnostic characteristics of Alvarado score (AS), neutrophil-lymphocyte ratio (NLR), and procalcitonin (PCT) for distinguishing complicated acute appendicitis from catarrhal acute appendicitis/phlegmonous acute appendicitis

Parameter	Area below ROC curve (95% CI)	SE	p	Cut-off	Se (%)	Sp (%)	PPV (%)	NPV (%)	OA (%)
AS	0.823 (0.719–0.927)	0.053	0.0001***	> 8	88.89	75.51	57.14	72.55	79.10
NLR	0.728 (0.608–0.848)	0.061	0.0045**	> 4.52	100	44.90	40	44.90	59.70
PCT	**0.963 (0.885–0.994)**	**0.029**	**0.000*** **	**> 0.56**	**94.44**	**91.84**	**80.95**	**97.83**	**92.54**
TBil	0.70 (0.58–0.81)	0.079	0.011*	> 23.2	38.9	95.9	70	81	79

*-p < 0.05;

**-p < 0.01;

***-p < 0.001;

TBil – total bilirubin; CI – confidence interval; SE – standard error; Se – sensitivity; Sp – specificity; PPV – positive predictive value; NPV – negative predictive value; OA – overall accuracy

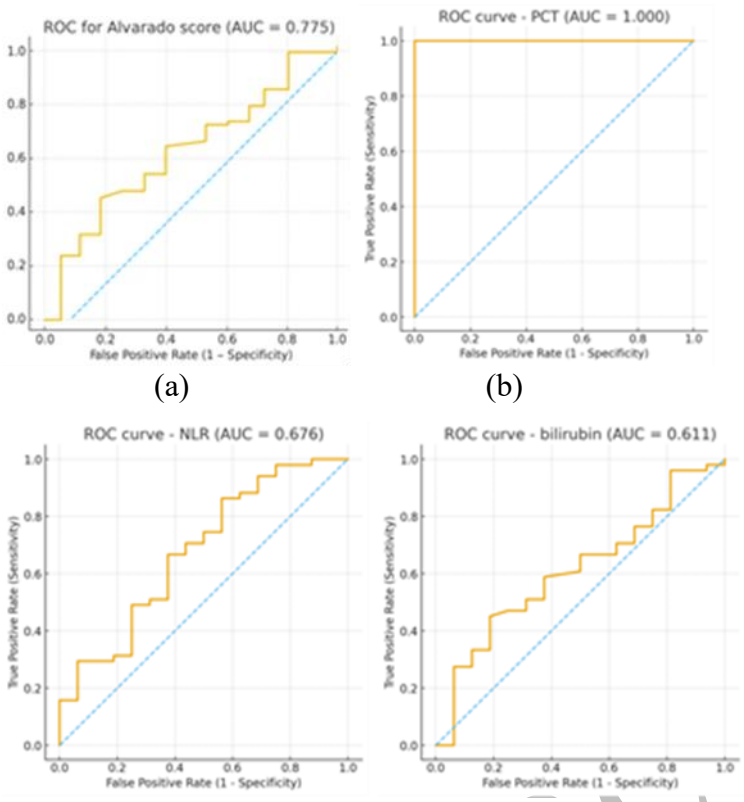

Figure 1. ROC curve and predictive characteristics of a) Alvarado score (AS); b) procalcitonin (PCT); c) neutrophil-lymphocyte ratio (NLR); d) total bilirubin (TBil) for distinguishing catarrhal acute appendicitis from phlegmonous acute appendicitis / complicated acute appendicitis

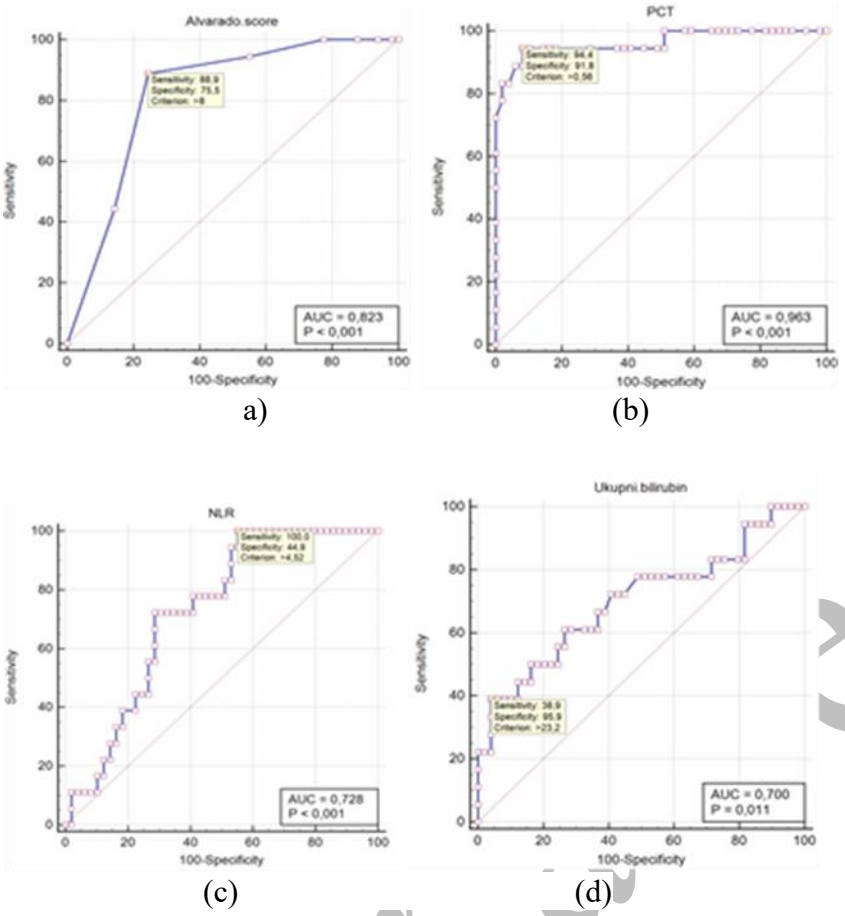

Figure 2. ROC curve and predictive characteristics of a) Alvarado score (AS); b) procalcitonin (PCT); c) neutrophil-lymphocyte ratio (NLR); d) total bilirubin (TBil) for distinguishing complicated acute appendicitis from catarrhal acute appendicitis/phlegmonous acute appendicitis

