Systemic inflammatory response index and systemic inflammation index might improve surgical decision making in patients with acute right lower abdominal pain

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Received: 11 December 2022
Revised: 28 December 2022
Accepted: 1 January 2023
Published: 28 April 2023

The Egyptian Journal of Surgery 2023, 41:1666–1674

Objectives
This study tried to assess the distinguishing ability of preoperative clinical scorings and estimated differential leukocytic ratios for patients presenting with acute right lower quadrant (RLQ) pain and requiring surgical intervention.
Patients
A total of 316 patients who had RLQ pain were evaluated clinically and by abdominal ultrasonography, and their blood samples were taken for estimation of total and differential leukocytic count and estimation of serum levels of C-reactive protein. Then, patients received the appropriate surgical procedure. The predictability of the Alvarado score, appendicitis inflammatory score (AIS), Lintula score, the calculated neutrophil/lymphocyte ratio, the systemic inflammatory response index (SIRI), and the systemic inflammation index for operative findings was statistically evaluated.
Results
The Alvarado score showed significantly higher diagnostic performance for appendicitis necessitating appendectomy in comparison with AIS (P=0.049) and Lintula score (P=0.044). For gynecological pathologies requiring surgical intervention, the diagnostic performance of the Alvarado score was significantly higher than that of AIS. The diagnostic performance of the three leukocyte ratios showed nonsignificant differences. Multivariate regression analysis defined a high SIRI ratio and Alvarado clinical score as the variate that can discriminate cases that required appendectomy and high SIRI and neutrophil/lymphocyte ratios as the significant predictors for gynecological cases requiring surgical intervention. Regression analysis confirmed the ability of low SIRI and low AIS scores to indicate canceling of laparotomy.
Conclusion
Surgical decision making for patients who had RLQ pain could be improved by combining the Alvarado score with the determined differential leukocytic indices.

Keywords:
appendectomy, clinical scorings, differential leukocytic ratios, ectopic pregnancy, right lower abdominal quadrant pain

Egyptian J Surgery 41:1666–1674

1110-1121

Introduction

Acute appendicitis (AA) is the most frequent cause of right lower abdominal quadrant (RLQ) pain, is a common reason for hospitalization, and is one of the top indications for emergent surgical intervention worldwide [1]. One of the major concerns with RLQ pain is the decision making for operative intervention that might result in negative laparotomies despite the improved diagnostic facilities [2].

The diagnostic dilemma is more magnified in women owing to the possibilities for the presence of other sources of RLQ pain such as salpingo-oophoritis, pyosalpinx, ruptured ovarian cysts, and endometriosis [3]. Furthermore, RLQ pain in women who had missed periods or were newly pregnant widened the dilemma of decision making for cases presenting with acute RLQ pain [4,5].

Several scoring systems exist to aid decision making for acute RLQ pain; however, the physiological changes may vary according to age, sex, presence of chronic diseases, and patient's immune status, so an applied scoring system may not produce the same score in all patients [6]. Moreover, the available scoring systems did not take pregnancy into account because it is constructed for nonpregnant women [5].

Traditionally, inflammation was clinically manifested by the development of constitutional manifestations and abnormally high total leukocytic count (TLC), high serum C-reactive protein, and radiologically by finding a lesion on routine ultrasound examination [7]. However, these findings may be manifested late or may be misleading, for example, the normal range for TLC is wide and age dependent and C-reactive protein (CRP) despite being a primary phase reactant remains high even after the subsidence of inflammation [8]. This directed attention to the evaluation of the diagnostic indices dependent on the ratios between certain types of leukocytes [9].

Objectives

This study aimed to compare the ability of preoperative clinical scorings and estimated inflammatory markers to distinguish between patients presenting with acute RLQ pain in comparison with the intraoperative findings as the gold standard for comparison and to assess their application to help for surgical decision making.

Design

A prospective multicenter non-randomized comparative study was performed.

Setting

The study was conducted at the Obstetrics and Gynecology and General Surgery Department, Faculty of Medicine, Benha University; Benha Teaching Hospital; and multiple private hospitals.

Patients

All patients attending the emergency department in the participating hospitals with RLQ pain underwent full history taking with special emphasis on pain characteristics, presence of medical disorders, and history of previous surgical interferences and gave blood samples for routine laboratory investigations, including complete blood count with total and differential leukocytic counts. Then, patients underwent abdominal ultrasonography (US) and CT imaging if indicated.

Exclusion criteria

Exclusion criteria included age younger than 18 and older than 50 years, pregnancy, the presence of autoimmune disorders, liver diseases, history of urinary tract disorders, maintenance on immunosuppressive therapy, malignancy, or refusal of surgical interference if indicated.

Inclusion criteria

Patients aged 18–50 years, presenting with acute RLQ free of exclusion criteria and accepted to be fully investigated and managed were included.

Evaluation tools

(1) Alvarado's score includes three symptoms (migratory lower abdominal pain, the presence of anorexia, and the presence of nausea or vomiting; each was scored by one) three physical signs [lower abdominal tenderness (score=2), rebound tenderness (score=1), and temperature >37.3°C (score=1)] and two laboratory findings [TLC scored by 2 and percentage of neutrophils >75% (score=1)]. The interpretation of the total Alvarado score was as follows: less than 4 indicates low probability, 4–6 indicates intermediate probability, greater than 6 indicates a high probability of inflammatory lesions, and a score of greater than 9 indicates AA.

(2) Appendicitis inflammatory score (AIS) included two symptoms (pain in RLQ and vomiting; each was scored by 1), two signs [rebound tenderness graded as light, medium, and severe (score=1, 2, 3, respectively) and fever with temperature ≥38.5°C scored by 1]; TLC less than 15 (score=1) or greater than or equal to 15 (score=2); percentage of neutrophils less than 85% (score=1) or greater than or equal to 85 (score=2); and serum CRP less than 50 mg/ml (score=1) or greater than or equal to 50 (score=2). AIS of less than 5 indicates a low, 5–8 intermediate, and greater than 8 high probability of appendicitis [10].

(3) Lintula score included nine variables: sex (male, 2 points, and female, 0 points), RLQ pain (Y=4 and N=0), pain intensity (severe=2 and mild–moderate=0), relocation of pain (Y=2 and N=0), vomiting (Y=2 and N=0), temperature (≥37.5°C=3 and <37.5°C=0), guarding (Y=4 and N=0), bowel sounds (absent, tinkling, or high-pitched=4 points, and normal=0), and rebound tenderness (Y=7 and N=0). The maximum score equals 32 points, a cutoff score of greater than or equal to 21 points predicts acute infection that requires emergency surgical interference, whereas a cutoff score of less than or equal to 15 points indicates the absence of acute infection, and a score in the range of 16–20 is an indication for observation [11].

(4) Systemic inflammatory response index (SIRI) was calculated as the number of neutrophils multiplied by the number of monocytes, and the resultant value was divided by the lymphocytic count [12].

(5) The systemic inflammation index (SII) was calculated as a result of multiplying the platelet count by the neutrophil count and dividing the result by the lymphocytic count [13].

Management

All patients received prophylactic broad-spectrum antibiotics and fluid refreshment and underwent surgical interference. The excised specimens were sent for histopathological examination. Patients were managed as 1-day surgery unless a hospital stay was indicated.

Statistical analysis

The obtained results were analyzed using one-way analysis of variance and χ^2 test tests. Regression analysis of the study variate was performed using the stepwise method for multimodal analysis. The receiver operating characteristic (ROC) curve was used to determine the best of the persistently significant predictors as judged by area under the curve (AUC), and its significance was determined in relation to the reference area (AUC=0.5). Test diagnostic performance at the median value of each variable was determined and compared using χ^2-test. All statistical analyses were conducted using IBM SPSS Statistics (Version 22, 2015; Armonk, New York, USA). The significance was evaluated at a cutoff point of *P* less than 0.05.

Results

During the study duration from January 2020 till July 2022, 402 patients presented with acute RLQ pain. Of them, 86 patients were excluded: 51 being out of the defined age range, 17 pregnant women, five had autoimmune disorders, six had liver disorders, and seven were stone passers. Therefore, 316 patients were enrolled in the study. The enrollment data are shown in Table 1.

Table 1 Preoperative data of the enrolled patients

Data	*N* (%)	Mean (SD)
Age (years)		
<30	148 (46.9)	25±2.6
31–40	100 (31.6)	34.5±2.5
41–50	68 (21.5)	45.8±2
	316 (100)	32.5±8.5
Sex		
Males	119 (37.7)	
Females	197 (62.3)	
Weight (kg)		
60–69	316 (100)	81.5±6.3
Pain characteristics		
Time-lapse	4 (3–5)	
Type of pain		
Stabbing	164 (51.9)	
Colicky	61 (19.3)	
Stitching	91 (28.8)	
Radiation to		
Umbilicus	126 (39.9)	
Vulva	102 (32.3)	
Renal angle	15 (4.7)	
No radiation	73 (23.1)	
Gynecological manifestations		
Amenorrhea	83 (42.1)	
Missed period	26 (13.2)	
Vaginal discharge	31 (15.7)	
No	57 (29)	
Total	197 (100)	

According to intraoperative findings, 219 (69.3%) patients had appendicitis, comprising 94 patients with catarrhal, 72 with a suppurative infection, 34 patients with an appendicular abscess, and 19 patients with an appendicular mass. A total of 27 (8.2%) patients had an ectopic pregnancy and 71 patients had salpingo-oophoritis, comprising 49 (15.5%) had a simple infection and 22 (7%) had pyosalpinex. Abdominal US could accurately diagnose only 173 patients (54.8%). In comparison with operative findings as a gold standard for comparison, the US showed varied diagnostic accuracy, which was highest for the presence of pyosalpinex, ectopic pregnancy, and appendicular mass, as shown in Table 2.

The median values of Alvarado score, AIS, and Lintula scores are 6 [interquartile range (IQR): 5–8], 6 (IQR: 5–7), and 16 (13–19). Considering the median value for each scoring system as the cutoff point for the determination of the scoring system diagnostic performance versus operative findings, the Alvarado score showed significantly higher diagnostic performance for diagnosis of appendicitis necessitating surgical interference in comparison with AIS (*P*=0.049) and Lintula score (*P*=0.044), with nonsignificant difference among these scores. Regarding the diagnosis of gynecological pathologies requiring surgical interference, the diagnostic performance of the Alvarado score was significantly higher than that of AIS but were nonsignificantly higher than that of the Lintula score, and there was an insignificant difference between AIS and Lintula scores (Table 3).

Median values of neutrophil/lymphocyte (N/L), SIRI, and SII ratios are 5 (IQR: 4.01–7.95), 1471 (IQR: 1023–2247), and 1420 (1152–2270). The diagnostic performance of the three ratios showed nonsignificant

Table 2 Preoperative US findings in comparison with operative findings as the gold standard for comparison

Diagnosis	Operative findings, n (%)	US findings, *n* (%)	
		Positive	Negative
Appendicitis			
Catarrhal	94 (29.8)	30 (31.9)	64 (68.1)
Suppurative	72 (22.8)	31 (43)	41 (57)
Abscess	34 (10.8)	10 (29.4)	24(70.6)
Mass	19 (5.9)	13 (68.4)	6 (31.6)
Ectopic pregnancy	26 (8.2)	21 (80.8)	5 (19.2)
Tubo-ovarian			
Salpingo-oophoritis	49 (15.5)	11 (22.4)	38 (77.6)
Pyosalpinx	22 (7)	19 (86.4)	3 (13.6)
Negative	316 (100)	135 (42.7)	181 (57.3)

US, ultrasound.

Table 3 Patient distribution according to the grades of RLQ pain scorings and performance of these scores

Alvarado score			AIS		Lintula score	
Score	*N* (%)		Score	*N* (%)	Score	*N* (%)
<4	51 (16.2)		<5	84 (26.6)	≤15	146 (46.2)
4–6	124 (39.2)		6-8	222 (70.3)	16–20	131 (41.5)
7–8	120 (38)		>8	10 (3.1)	≥21	39 (12.3)
9–10	21 (6.6)					
Median [IQR]	6 [5–8]		6 [5–7]		16 [13–19]	
	Appendicitis	Gynecological problems	Appendicitis	Gynecological problems	Appendicitis	Gynecological problems
Sensitivity (%)	80 (72–87)	73.7 (57–87)	67.2 (58–75)	39.6 (26–55)	53.6 (44–63)	43 (28–58)
Specificity (%)	31.2 (21–43)	51.7 (38–65)	61 (49–72)	60 (45–74)	49.4 (38–61)	35 (22–50)
PPV (%)	65.4 (61–69)	50 (42–58)	73.7 (67–79)	50 (38–62)	63.2 (57–69)	38.5 (29–48)
NPV (%)	49 (37.2–61)	75 (62.5–84.4)	53 (45.7–61)	50 (42–58)	40 (33–47)	38.6 (28.5–50)
+LR	1.16 (1–1.4)	1.53 (1.1–2.1)	1.72 (1.3–2.3)	1 (0.61–1.64)	1.1 (0.8–1.4)	0.65 (0.4–1)
Accuracy (%)	61.4 (54–68)	60.4 (50–70)	64.9 (58–71)	50 (39.6–60.4)	52 (45–59)	38.5 (28.8–49)

+LR, positive likelihood ratio; AIS, appendicitis inflammatory score; IQR, interquartile range; NPV, negative predictive value; PPV, positive predictive value.

differences despite being higher for SIRI for the prediction of gynecological problems requiring surgical interference and for SII for the prediction of appendicitis requiring laparotomy (Tables 4 and 5).

ROC curve analysis for the studied variables defined high SII and SIRI ratios, AIS clinical scoring, N/L ratio, and Alvarado clinical score as the discriminators for cases requiring laparotomy for pathological appendix, in decreasing order of significance (Fig. 1). Multivariate regression analysis excluded the AIS and Lintula clinical scorings and N/L and SII ratios and defined high SIRI ratio and high Alvarado clinical score as the variables that can discriminate cases requiring appendectomy.

High SII, SIRI, and N/L ratios and Alvarado score could define women with RLQ pain who require laparotomy for either ectopic pregnancy or drainage of pyosalpinx (Fig. 2). Regression analysis defined high SIRI and N/L ratios as the significant predictors while excluding the remaining variables.

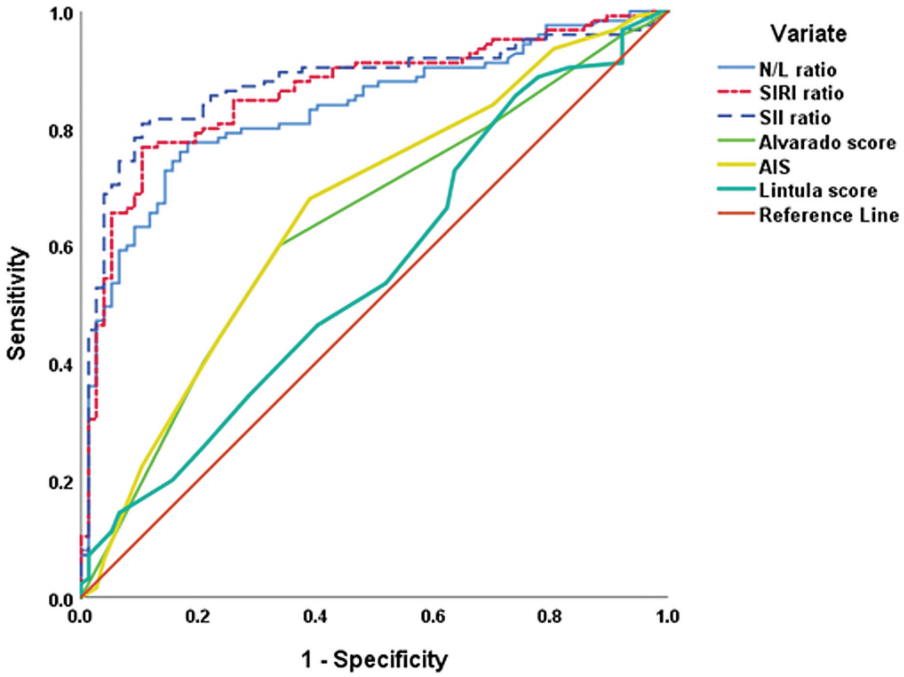
Variables that might help surgical decision for canceling laparotomy for any case presenting RLQ pain included low SII, SIRI, and N/L ratios and low AIS clinical score in decreasing order of significance as judged by the area under the ROC curve (Fig. 3). Regression analysis excluded low N/L and SII ratios and ensured the ability of low SIRI and low AIS scores to indicate canceling of laparotomy.

Table 4 Median values of N/L, RISI, and SII ratios and their diagnostic performance

Characters	N/L		SIRI		SII	
	5 [4.01–7.95]		1471 [1023–2247]		1420 [1152–2270]	
Median [IQR]	Appendicitis	Ob/gyna problem	Appendicitis	Ob/gyna problem	Appendicitis	Ob/gyna problem
Sensitivity (%)	76 (67–83)	64 (48.5–77)	78.4 (70–85)	88 (75–95)	82 (75–89)	75 (60–86)
Specificity (%)	83.1 (73–91)	76.5 (63–87)	88.3 (79–95)	82 (68–91)	88.5 (79–95)	88 (76–95)
PPV (%)	88 (81.5–92)	71.4 (59–81)	91.6 (85–95)	83 (72–90)	92 (86–96)	86 (74–93)
NPV (%)	68 (60.6–75)	70 (60–77)	71.6 (64–78)	87 (76–93)	76 (68–82)	79 (69–86)
+LR	4.5 (2.7–7.5)	2.7 (1.6–4.7)	6.7 (3.6–12.5)	4.8 (2.6–8.7)	7.1 (3.8–13)	6.2 (2.9–13.5)
Accuracy (%)	78.7 (72–84)	70 (60–79)	82.2 (76–87)	84.7 (76–91)	84.7 (79–89)	82 (73–89)

+LR, positive likelihood ratio; IQR, interquartile range; N/L, neutrophil/lymphocyte ratio; NPV, negative predictive value; PPV, positive predictive value; SII, systemic inflammation index; SIRI, systemic inflammatory response index.

Figure 1



Receiver operating characteristic curve for the studied variables as a support for surgical decision making for appendectomy for patients who had right lower quadrant pain.

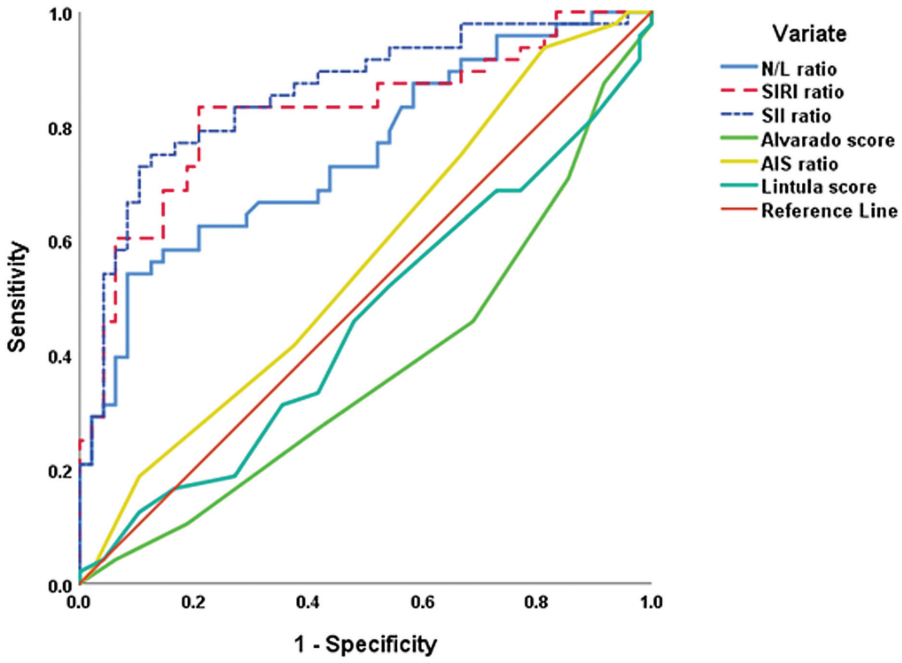
Discussion

Surgical interference for patients presenting with RLQ pain is the most frequent surgical decision worldwide and is the commonest cause of hospitalization and consumption of resources, and higher days off from work [14]. Improvement of surgical decision making and reduction of false laparotomy rate is mandatory to reduce the health and financial burdens [15].

Surgical decision making for RLQ pain depends on certain scores that evaluate patients' symptoms, findings on examination, and TLC with or without estimation of serum CRP levels. The current study compared the diagnostic performance of three of the commonly used scoring systems for RLQ pain versus the operative findings and detected weak significantly higher diagnostic performance for the Alvarado scoring system versus the AIS and Lintula score, which showed nonsignificant difference. Moreover, no scoring system showed high specificity or positive predictive value for the necessity for surgical interference for AA higher than 60%. Thus, the false laparotomy rate is high on the dependence of any of these scores.

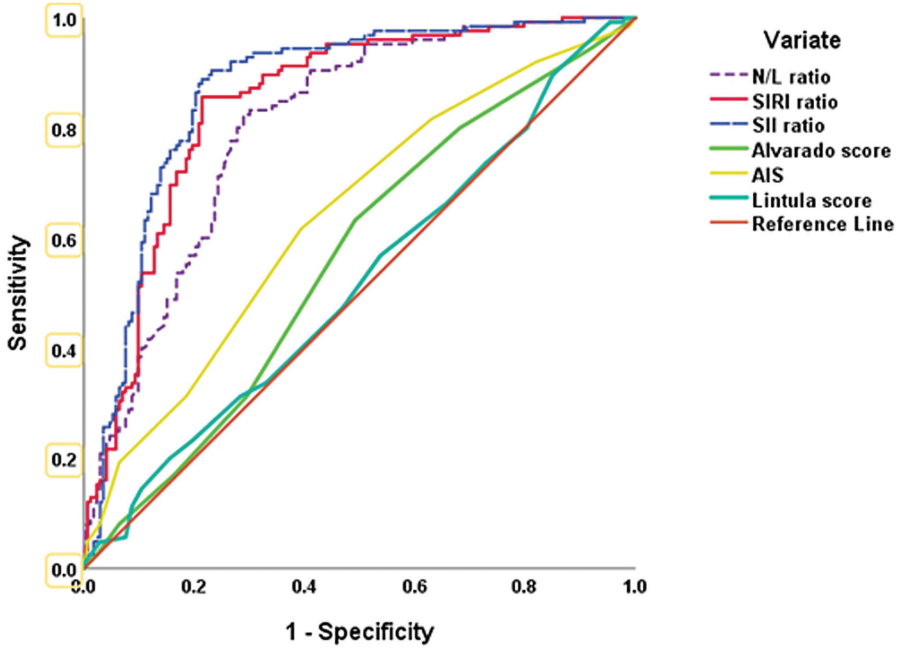
In line with these results, Prapruttam *et al.* [16] documented that for patients with AA, the Alvarado score is not a predictive factor of nondiagnostic US, especially in the absence of migratory pain and/or leukocytosis, and low pain score. Moreover, Gonullu *et al.* [6] found the diagnostic performance of the

Figure 2



Receiver operating characteristic curve for the studied variables as a support for surgical decision making for laparotomy for obstetrician/gynecologist. problems in patients who had right lower quadrant pain.

Figure 3



Receiver operating characteristic curve for the studied variables as a support for canceling a surgical decision for patients who had right lower quadrant pain.

Alvarado, the Fenyo-Linberg, and the Eskelinen scoring systems for AA is age dependent and concluded that no scoring system could be applied to all patients. Furthermore, Pifeleti *et al.* [17] documented that despite the high sensitivity of the Alvarado Score (≥5) for AA and the significant relation with the US scan, it showed a specificity of 50%.

Multiple recent studies tried to improve the diagnostic performance of these scores and to reduce their fallacies, wherein Frankcombe *et al.* [18] found the

Table 5 Receiver operating characteristic curve and regression analyses for the studied variables as supportive for surgical decision making for patients who had RLQ pain

Surgical decision	Alvarado score	AIS	Lintula score	N/L ratio	SIRI ratio	SII ratio
Appendectomy						
ROC curve						
AUC	0.633	0.658	0.556	0.832	0.862	0.875
SE	0.040	0.040	0.042	0.029	0.027	0.026
P value	0.001	<0.001	0.184	<0.001	<0.001	<0.001
95% CI	0.555–0.712	0.580–0.736	0.474–0.637	0.775–0.888	0.810–0.914	0.824–0.926
Regression						
β	0.211	0.165	Excluded by ROC	0.044	0.418	0.067
P value	0.001	0.010		0.652	<0.001	0.495
Laparotomy for OB/Gyn problem						
ROC curve						
AUC	0.376	0.566	0.458	0.752	0.823	0.857
SE	0.057	0.059	0.059	0.049	0.044	0.039
P value	0.036	0.265	0.482	<0.001	<0.001	<0.001
95% CI	0.264–0.488	0.451–0.681	0.342–0.574	0.656–0.849	0.737–0.909	0.781–0.934
Regression						
β	0.139	Excluded by ROC		0.209	0.374	0.102
P value	0.122			0.048	0.001	0.535
Canceling of surgery						
ROC curve						
AUC	0.561	0.640	0.519	0.804	0.846	0.868
SE	0.033	0.032	0.034	0.025	0.023	0.022
P value	0.072	<0.001	0.570	<0.001	<0.001	<0.001
95% CI	0.496–0.627	0.576–0.703	0.453–0.586	0.754–0.853	0.801–0.891	0.826–0.911
Regression						
β	Excluded by ROC	0.172	Excluded by ROC	0.110	0.407	0.082
P value		0.001		0.322	<0.001	0.124

AIS, appendicitis inflammatory score; AUC, area under the curve; N/L, neutrophil/lymphocyte; OB/Gyn, obstetrician/gynecologist; RLQ, right lower quadrant; ROC, receiver operating characteristic; SII, systemic inflammation index; SIRI; systemic inflammatory response index.

reliance on preoperative imaging resulted in a significant reduction in negative appendectomy, complications, readmissions, and interval appendicectomy rates. Moreover, Haentjens *et al.* [19] documented that low negative appendectomy rates can be achieved by a combination of radiological and clinical examinations with laboratory tests. Moreover, Shikha and Kasem [20] using an artificial intelligence pediatric appendicitis decision tree detected high accuracy in diagnosing AA in children without the need for imaging with significantly improved outcomes, and reduced costs and recommended its application for adults. Furthermore, Arredondo Montero *et al.* [21] detected good performance of preoperative estimation of interleukin-6 for discerning between complicated and uncomplicated AA and recommended its application in addition to scores including clinical and radiological variables to increase the diagnostic performance.

On the contrary, the dependence of differential leukocytic count indices for discrimination of complicated appendicitis showed high PPV, which ranged between 88% for N/L and 92% for SII and SIRI, with a high positive likelihood ratio and accuracy of diagnosis. In line with these findings, Delgado-Miguel *et al.* [22] found N/L ratio showed the highest AUC for the diagnosis of negative appendicitis in comparison with TLC and neutrophil count, and CRP levels, with sensitivity and specificity rates of 84.2 and 83.8%, respectively, and concluded that preoperative N/L ratio is the best preoperative parameter that can discriminate patients with RLQ pain without AA. Moreover, statistical analyses defined high SIRI ratio and Alvarado clinical score as the variables that can discriminate AA cases requiring appendectomy. Similarly, Cakcak *et al.* [23] reported that Alvarado score, SIRI, and SII are directly proportional to the presence of complicated AA and can be used as markers to differentiate cases with complicated AA.

Regarding the operative decision making for women presenting with RLQ pain, the evaluated clinical scorings showed a low diagnostic performance,

which made the surgical decision unreliable. On the contrary, the differential leukocytic ratios showed high diagnostic performance, and statistical analyses defined high N/L and RISI ratios as highly diagnostic variables for laparotomy decision making. These results support a previous reported by Kan *et al.* [24] that both N/L and platelet/lymphocyte (P/L) ratios were significantly higher in women who had ruptured tubal pregnancy, and ROC curve analysis defined high β-human chorionic gonadotropin, and these ratios were significantly associated with pathologically confirmed tubal rupture. Recently, Saçıntı *et al.* [25] found serum CRP and TLC and N/L ratio increase and peak within the 48 hours after surgery for tubo-ovarian abscess, but TLC and N/L ratio are the fastest to normalize after successful surgery, whereas CRP is the slowest to normalize, so TLC and N/L ratios are the best for postoperative follow-up for these women. Moreover, Cicek and Doger [26] reported that a higher N/L ratio after artificially frozen embryo transfer cycles could predict biochemical miscarriage. Furthermore, Muangto *et al.* [27] detected an association between high preoperative N/L and P/L ratios and myometrial invasion in women who had endometrial cancer.

Conclusion

The surgical decision making for patients who had RLQ pain could be improved by combining the Alvarado score with the determination of differential leukocytic indices such as N/L, SIRI, and SII ratios.

Recommendations

The diagnostic performance of these indices needs to be evaluated for cases presenting with generalized acute abdominal pain.

Acknowledgment

The authors are thankful to the staff of the Clinical Pathology Departments for their great help.

Financial support and sponsorship

Nil.

Conflicts of interest

No conflict of interest to be declared.

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