Original Article

Bull Emerg Trauma 2025;13(4):2-7.

Bulletin of Emergency And Trauma

The Systemic Inflammatory Response Index as a Novel Diagnostic Tool for Acute Appendicitis

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Received: May 26, 2025
Revised: September 17, 2025
Accepted: September 22, 2025

ABSTRACT

Background: Acute appendicitis (AA) is a leading cause of acute abdominal pain. However, accurately diagnosing AA remains challenging, as a definitive and reliable predictive method has not yet been established. This study aimed to assess the potential of the Systemic Inflammatory Response Index (SIRI) for diagnosing AA, its possible advantages over current methods, and its utility in distinguishing uncomplicated from complicated appendicitis.
Methods: In this cross-sectional study, 240 patients scheduled for appendectomy with a diagnosis of AA were enrolled. Demographic information, clinical and paraclinical findings, including complete blood count (CBC), Alvarado score, SIRI, sonography findings, and pathology results, were documented. Data were analyzed using SPSS software version 26.
Results: Of the 240 patients, 106 (44.2%) were men, and 134 (55.8%) were women, with a mean age of 37.49±15.55 years. Final pathology reports identified 26 (10.8%) cases of a normal appendix, 176 (73.3%) with uncomplicated appendicitis, 23 (9.6%) with complicated appendicitis, and 15 (6.3%) with reactive lymphoid hyperplasia. SIRI demonstrated significant differences across the pathology groups (P<0.0001). It showed notable discrimination between normal and complicated appendicitis (P=0.005), normal and combined appendicitis (P=0.008), and suggestive differences for normal versus uncomplicated (P=0.021) and uncomplicated versus complicated cases (P=0.044). Similarly, Alvarado scores showed significant differences, particularly between the normal and complicated appendicitis groups.
Conclusion: The SIRI and Alvarado scoring systems showed significant potential for diagnosing appendicitis with acceptable sensitivity and specificity. They might also assist in differentiating between uncomplicated and complicated appendicitis.

Keywords: Appendicitis, Appendectomy, Alvarado, Systemic inflammatory response index.

Please cite this paper as:
Ghoncheh B, Taheri MR, Azadmanesh Y, Mostafavian Z, Zandbaf T. The Systemic Inflammatory Response Index as a Novel Diagnostic Tool for Acute Appendicitis. *Bull Emerg Trauma*. 2025;13(4):2-7. doi: 10.30476/beat.2025.107218.1611.

Introduction

Acute appendicitis (AA) is one of the most common causes of acute abdominal pain. However, accurately diagnosing AA remains a challenge, as a definitive and reliable predictive method has not yet been established. Late diagnosis can lead to dangerous complications [1]. The diagnostic process is often complicated by non-specific symptoms and potential overlap with other conditions. Traditionally, diagnosis relies on a combination of clinical presentation, laboratory results, and imaging studies [2]. While several tools and criteria, such as the Alvarado score, aid in diagnosing AA, they often lack sufficient sensitivity and specificity [3, 4]. Similarly, markers such as white blood cell count, serum bilirubin, and CRP are inadequate for accurately predicting or diagnosing AA. Consequently, with sufficient sensitivity and specificity to diagnose AA, differentiating between complicated and uncomplicated cases remains a key discussion point among researchers [5].

In the quest for better diagnostic tools, an innovative inflammatory index termed Systemic Inflammation Response Index (SIRI) was created in 2016. It was first used to predict survival in patients with advanced pancreatic cancer after chemotherapy, demonstrating its practical utility [6]. Subsequent studies indicated that SIRI is associated with oncological diseases and aids in diagnosing disease progression and predicting survival in oncology patients [7]. This study, therefore, aimed to assess the potential of SIRI for diagnosing AA, its possible advantages over current methods, and its usefulness in distinguishing between uncomplicated and complicated appendicitis.

Materials and Methods

This cross-sectional study was conducted from January to December 2023 on 240 patients admitted to the emergency departments of Aria and 22 Bahman Hospitals in Mashhad, Iran, who were scheduled for appendectomy with a preoperative diagnosis of AA. The study was approved by the Research Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.REC.1402.150) and was conducted in accordance with the current (2024) version of the Helsinki Declaration. Written informed consent was obtained from all participants.

The study included patients aged 16 to 75 years with a primary diagnosis of AA. Exclusion criteria were known hematologic disorders, pregnancy, known autoimmune disorders, concurrent febrile or infectious diseases, chronic kidney or liver disease, or a history of malignancy.

A checklist was completed for each patient to document demographic information and clinical and paraclinical findings, including complete blood count (CBC), Alvarado score, SIRI, sonography findings, and pathology results. Postoperative pathology reports categorized the appendix specimens into four groups: normal appendix, uncomplicated appendicitis (focal, or suppurative appendicitis), complicated appendicitis (gangrenous or perforated appendicitis and periappendiceal abscess formation), and reactive lymphoid hyperplasia (non-neoplastic enlargement of the lymph nodes).

The Alvarado score was calculated based on eight criteria (six clinical and two laboratory), yielding a total score between 0 and 10. SIRI was calculated by the formula: (Neutrophil count×Monocyte count)/ Lymphocyte count. The CBC results were obtained using a Sysmex KX-21N analyzer.

The quantitative data were expressed as mean±standard deviation (SD) or median and interquartile range. The Shapiro-Wilk test was used to assess normality. Due to non-normal distribution, the Kruskal-Wallis test was used for comparisons between groups. The Chi square test was used to analyze relationships between categorical variables. The sensitivity and specificity of the SIRI index were assessed using receiver operating characteristic (ROC) curve analysis. All statistical analyses were performed using SPSS software (version 26), with a significance level set at $p<0.05$.

Results

This study enrolled 240 patients, comprising 106 (44.2%) men and 134 (55.8%) women. The age range was 16 to 75 years, with a mean age of 37.49±15.55 years. Based on postoperative pathology, the diagnoses were distributed as follows: 26 (10.8%) patients had a normal appendix (negative appendicitis), 176 (73.3%) had uncomplicated appendicitis, 23 (9.6%) had complicated appendicitis, and 15 (6.3%) had reactive lymphoid hyperplasia.

Table 1 presents the frequency distribution of age according to pathology results. No significant difference in age was found across the diagnostic groups ($p=0.07$). In contrast, Table 2 presents the distribution of sex based on pathology results, where a significant difference was observed between the two groups according to their pathology findings ($p=0.04$).

The SIRI and Alvarado scores for each patient were assessed. The distribution of these indices across pathology groups is detailed in Table 3. The SIRI demonstrated significant variation among the four pathology groups. Post-hoc analysis revealed a particularly notable difference between the normal appendix and complicated appendicitis groups. Similarly, the mean Alvarado scores varied significantly across the groups, with a marked distinction between the normal appendix group and the complicated appendicitis group.

Group 1 (normal appendix) exhibited the lowest mean SIRI and Alvarado scores, while group 3 (complicated appendicitis) had the highest.

Table 1. The frequency distribution of age (years) according to pathology results in patients with suspected appendicitis

Pathology results	Lowest	Highest	Number	Mean±SD	*p*-value
Normal	17	75	26	37.19±17.57	0.07
Uncomplicated appendicitis	16	75	176	36.87±15.21	
Complicated appendicitis	19	68	23	45.17±15.27	
Reactive lymphoid hyperplasia	19	68	15	33.47±14.18	

Table 2. The distribution of sex based on pathology results

Pathology		Normal n (%)	Uncomplicated Appendicitis n (%)	Complicated Appendicitis n (%)	RLH n (%)	*p*-value
Sex	Man	6 (23.1)	84 (47.7)	12 (52.2)	4 (26.7)	0.04
	Woman	20 (76.9)	92 (52.3)	11 (47.8)	11 (73.3)	
Total		26 (100)	176 (100)	23 (100)	15 (100)	

RLH: Reactive Lymphoid Hyperplasia

Table 3. The distribution of measured indicators according to pathology results in suspected appendicitis.

Variable	Normal Appendix[a]	Uncomplicated Appendiciti[s]b	Complicated Appendicitis[c]	RLH[d]	Test Statistic
SIRI	2.73±3.63	5.28±5.72	8.35±8.87	3.80±2.82	Kruskal-Wallis=19.75 $p<0.0001$ $p^{a}p^{c}=0.005$ $p^{a}p^{c,b}=0.008$ $p^{b}p^{c}=0.044$
	1.84 (0.72–2.77)	3.57 (1.62–6.08)	5.75 (3.24–9.43)	2.55 (1.23–7.13)	
Alvarado	5.92±2.04	7.1±1.88	7.26±1.62	6.93±1.43	Kruskal-Wallis=8.37 $p=0.039$ $p^{a}p^{c}=0.002$ $p^{a}p^{c,b}=0.004$ $p^{b}p^{c}=0.63$
	6 (4–8)	8 (6–9)	8 (6–9)	7 (6–8)	

SIRI: Systemic Inflammatory Response Index; RLH: Reactive lymphoid hyperplasia; Values are presented as mean±SD and median (interquartile range)

This difference was statistically significant. Conversely, no significant differences in the mean scores of either marker were found between group 4 (reactive lymphoid hyperplasia) and group 1 (normal appendix), with *p*-values of 0.83 for SIRI and 0.127 for the Alvarado score.

This study assessed the sensitivity and specificity of the Alvarado score and the SIRI for diagnosing AA and their effectiveness in differentiating between complicated and uncomplicated cases.

The Alvarado score, at a cut-off value of >6.5, demonstrated a sensitivity of 67.3% and a specificity of 57.7% for diagnosing AA. For distinguishing between uncomplicated from complicated appendicitis at a cut-off of >5.5, it demonstrated a sensitivity of 84.3% and a specificity of 26%. The positive predictive value (PPV) was 93%, the negative predictive value (NPV) was 18%, the positive likelihood ratio (LR+) was 1.59, and the negative likelihood ratio (LR-) was 0.57.

In contrast, the SIRI, at a cut-off value of >2.89 for diagnosing AA, exhibited a sensitivity of 59.3% and a specificity of 84.6%. For differentiating between uncomplicated and complicated appendicitis at the same cut-off (>2.89), SIRI demonstrated a sensitivity of 84.3% and a specificity of 48%. The PPV was 97%, the NPV was 20%, the LR+ was 3.85, and the LR- was 0.48.

These results indicated that while there was no statistically significant difference between the two indicators in diagnosing AA, a significant difference was observed in their ability to distinguish between uncomplicated and complicated appendicitis. Detailed results are presented in Figures 1 and 2.

Discussion

This study aimed to evaluate the utility of the SIRI as a diagnostic tool for appendicitis and its ability to differentiate between complicated and uncomplicated cases, with comparisons drawn to the Alvarado score. Our results indicated that both the SIRI and Alvarado scores indicated significant potential for diagnosing acute appendicitis (AA) with acceptable sensitivity and specificity. Notably, a positive SIRI result was 3.85 times more likely in patients with AA than in those without. Furthermore, both tools might be valuable in differentiating between uncomplicated and complicated appendicitis.

AA is a leading cause of acute abdominal pain presenting to the emergency departments. Despite the availability of various diagnostic tools, including

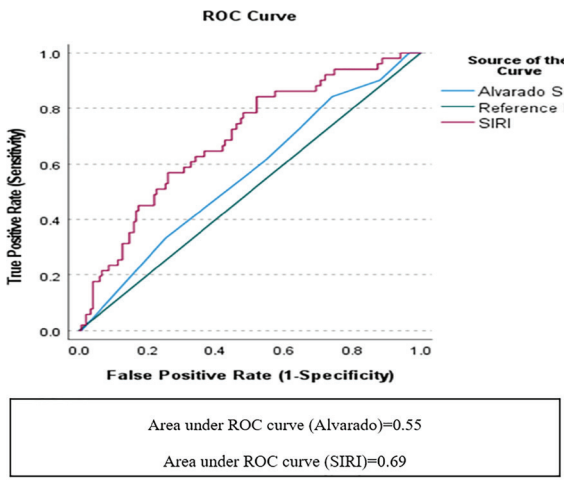

Fig. 1. Comparison of the area under the ROC curve between the SIRI and Alvarado indices in diagnosing complicated appendicitis from Uncomplicated appendicitis

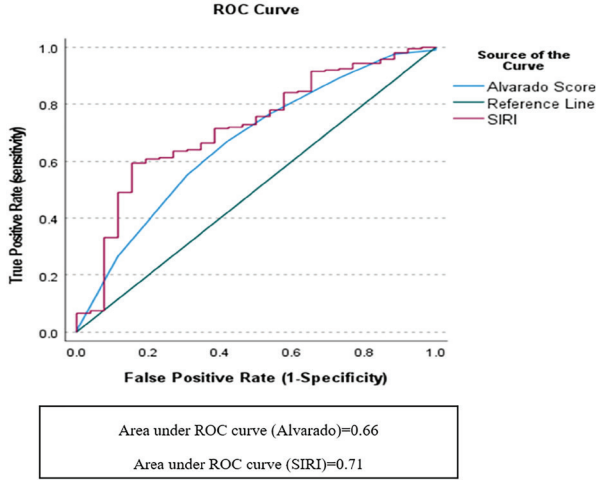

Fig. 2. Comparison of the area under the ROC curve between the SIRI and Alvarado indices in diagnosing acute appendicitis

patient history, clinical evaluation, and physical examinations, a definitive preoperative method for diagnosing appendicitis and its complications remains elusive, with histopathological examination still serving as the gold standard [8]. Inflammatory markers, such as white blood cell (WBC) count, C-reactive protein (CRP) levels, and mean platelet volume, are valuable non-invasive aids for diagnosing AA and assessing its complications. However, these markers alone lack sufficient accuracy for a definitive diagnosis [9].

Recent studies have introduced innovative methods utilizing ratios of inflammatory markers, which have proven effective in predicting prognosis in oncological conditions [6, 10] and cardiovascular diseases [11]. The Alvarado score, a widely used clinical tool that combines symptoms, signs, and laboratory findings to stratify AA risk, is a similar composite measure. Nevertheless, its diagnostic accuracy is debated, with studies highlighting its inadequate specificity and high false-positive rates [12, 13].

A study by Cakcak and Türkyılmaz involving 161 patients with right lower quadrant (RLQ) pain investigated the relationship between SIRI, the Systemic Inflammation Index (SII), and the Alvarado score in relation to AA. Their findings suggested that the Alvarado score, SIRI, and SII could be helpful markers in determining the occurrence of complications, either preoperatively or postoperatively. However, that study did not establish specific cutoff values for SIRI or the Alvarado score [14]. These results were in line with our findings. Furthermore, our research indicated that the optimal cutoff points for SIRI and the Alvarado score in diagnosing AA were 2.89 and 6.5, respectively.

In another study, Yildiz and Selvi examined 220 patients with abdominal pain who subsequently underwent surgery for AA. They assessed the effectiveness of SIRI and SII in predicting AA and its complications, finding both to be reliable tools with superior predictive value compared to WBC count and CRP levels. Their study established a SIRI cut-off point of 4.65 for differentiating complicated from uncomplicated appendicitis, with 68.2% and a specificity of 60.5% [7]. The present study corroborated the utility of SIRI; however, it identified a lower cut-off point of 2.89, which yielded a higher sensitivity of 84.3% and a lower specificity of 48% for this differentiation.

In our study, the Alvarado score demonstrated moderate diagnostic capability for AA, with a sensitivity of 67.3% and specificity of 57.7% at a cut-off of >6.5. For differentiating complicated from uncomplicated appendicitis (cut-off >5.5), it showed high sensitivity (84.3%) but low specificity (26%). These results contrast with studies that question the score's reliability. For instance, Ohle and O'Reilly (2011) reported poor specificity (57% in men, 73% in women at a cut-off of 7) and significant over-prediction in females (relative risk 5.35 for low risk), concluding that it was not a reliable standalone tool [12]. Similarly, Memon *et al.,* found a high negative appendectomy rate (28.7%), despite a high sensitivity of 93.5%, indicating frequent false positives [13].

The reasonable performance of the Alvarado score in the present study might be attributed to several factors. This study, with 240 patients (44.2% men, 55.8% women, mean age 37.49 years), had a balanced demographic, which might have mitigated the sex-specific biases reported in other studies [12, 13]. The use of pathology as the gold standard and consistent clinical assessments in a single-center setting likely reduced diagnostic variability, thereby enhancing the score's apparent accuracy. Furthermore, the optimized cut-off of >6.5, derived from ROC analysis, probably provides a better balance of sensitivity and specificity than standard cut-offs of 5 or 7. These findings suggested that, within our clinical context, the Alvarado score remained a practical screening tool, particularly for initial risk stratification in resource-constrained environments.

In contrast, SIRI demonstrated a sensitivity of

59.3% and a specificity of 84.6% for diagnosing AA (cut-off >2.89), and a sensitivity of 84.3% with a specificity of 48% for distinguishing complicated from uncomplicated cases (cut-off >2.89). Its higher specificity compared to the Alvarado score (84.6% vs. 57.7% for diagnosis; 48% vs. 26% for complications) suggested a superior ability to rule out non-appendicitis cases and to identify true positives among complicated appendicitis cases. The significant *p*-values for SIRI underscored its discriminatory power, particularly for severe pathology, where elevated neutrophil and monocyte activity likely elevated the index.

SIRI's strengths include its objectivity and accessibility. As it is derived from routine CBC data, it avoids the subjectivity inherent in clinical criteria, such as tenderness or nausea, that contribute to the variability of the Alvarado score. Its cost-effectiveness also makes it particularly feasible in low-resource settings, unlike imaging modalities such as ultrasound or CT, which require specialized expertise and infrastructure. However, SIRI's moderate sensitivity (59.3%) for diagnosing AA suggested that it should be used to complement clinical judgment and imaging, rather than as a replacement.

The clinical implications of these findings are significant. The reasonable performance of the Alvarado score in our cohort supported its continued use as an initial screening tool, particularly in settings where rapid decisions are required. However, its limited ability to distinguish between complicated and uncomplicated AA restricted its utility in determining surgical urgency. SIRI offers a valuable complementary approach, as it demonstrated significant differences across pathology groups. A high SIRI value (>2.89) could help prioritize patients for urgent surgery when complications are suspected, while a low score might support a period of observation or the use of further diagnostics. This approach could potentially reduce the negative appendectomy rates associated with reliance on the Alvarado score alone [14].

Future research should focus on validating these SIRI and Alvarado cut-offs in larger multicenter cohorts. Studies should also examine their diagnostic performance across various demographic subgroups (e.g., females and children) and investigate whether hybrid models combining SIRI, the Alvarado score, and imaging techniques can further enhance diagnostic accuracy.

Conclusion

This study demonstrated that the Alvarado score could be a practical tool for diagnosing appendicitis, challenging previous literature that reported low specificity. In contrast, the SIRI score demonstrated superior specificity and discriminatory power, showing promise as a tool for identifying complicated cases. Integrating both scores with clinical assessment could enhance diagnostic precision and improve patient outcomes.

Declaration

Ethics approval and consent to participate: This study was approved by the Research Ethics Committee of Mashhad University of Medical Sciences (code: IR.MUMS.REC.1402.150). Written informed consent was obtained from all participants included in the study.

Consent for Publication: All authors have read and approved the final manuscript and consent to its publication.

Conflict of Interest: None declared.

Funding: None.

Authors' Contribution: BG: Conceptualization, investigation, data curation, and writing original draft; MRT: Investigation and data curation; YA: Investigation and data curation; ZM: Methodology and formal analysis, investigation, and data curation; TZ: Conceptualization, writing, review and editing, and supervision.

Acknowledgment: This article is derived from Dr. Behrad Ghoncheh's thesis, entitled " Evaluation of the diagnostic value of Systemic Inflammation Response Index in acute appendicitis". This thesis was conducted as part of the general medicine program and was approved by the Islamic Azad University, Mashhad Medical Sciences Unit.

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