# The Effectiveness of Appendicitis Inflammatory Response Score in the Evaluation of Acute Appendicitis: A Meta-analysis

## Akut Apandisit Değerlendirmesinde Apandisit Enflamatuvar Yanıt Skorunun Etkinliği: Meta-analiz Çalışması

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**ABSTRACT**

**Background:** One of the most frequent causes of urgent abdominal diseases is appendicitis. Various diagnostic methods are used in the diagnosis of appendicitis, scoring systems are among them. We aimed to meta-analyze the studies evaluating the effectiveness of the appendicitis inflammatory response-score (AIR-S). In light of the studies done on the topic, it was intended to highlight the diagnostic benefits of scoring, which allow for the simultaneous evaluation of clinical, laboratory, and imaging findings as well as the patient's medical history, and to add to the literature.

**Materials and Methods:** All studies published in the last 15 years using the terms "All fields=appendicitis inflammatory response" (AND), "All fields=receiver operating characteristic" (AND) in Web of Science Core Collection, PubMed and Google Scholar databases were searched, systematic review and meta-analysis were performed.

**Results:** Thirteen publications were included in the study according to inclusion and exclusion criteria. It was noted that the studies were conducted on 8.052 patients with a mean age of 30.00 and gender distribution as 48.00% male and 52.00% female. The cut-off point of the studies was found to be 5.00, Sensitivity 85.00%, Specificity 59.00%. The studies were homogeneous ($I^2$=19.830; Cochran Q=14.968; p>0.05). AIR-S diagnostic distinguish ability was statistically significant (total-fixed effects=0.838; 95% confidence interval 0.800-0.875; p<0.001). There was no statistically significant publication bias (p>0.05).

**Conclusion:** In this study, the sum of the values determined for the diagnostic parameters of AIR-S was below 170. This finding result that using AIR-S alone to diagnose acute appendicitis is insufficient, and that it is preferable to utilize it in conjunction with other diagnostic measures.

**Keywords:** Appendicitis, appendicitis inflammatory response score, receiver operating characteristic, bias

**ÖZ**

**Amaç:** Acil karın hastalıklarının en sık nedenlerinden biri apandisittir. Apandisit tanısında çeşitli tanı yöntemleri kullanılmaktadır, skorlama sistemleri de bunlar arasındadır. Apandisit enflamatuvar yanıt-skorunun (AIR-S) etkinliğini değerlendiren çalışmaları meta-analiz tekniği ile değerlendirmek hedefledi. Konuyla ilgili yapılan çalışmalar ışığında, klinik, laboratuvar ve görüntüleme bulgularının yanı sıra hastanın tıbbi öyküsünün de eş zamanlı olarak değerlendirilmesine olanak sağlayan skorlamanın tanısal faydalarını vurgulamak ve literatüre katkıda bulunmak amaçlandı.

**Gereç ve Yöntemler:** Web of Science Core Collection, Pubmed ve Google Scholar veri tabanlarında "All fields=appendicitis inflammatory response" (VE), "All fields=receiver operating characteristic" (VE) terimleri kullanılarak son 15 yılda yayınlanmış tüm çalışmalar taranmış ve sistematik incelemesi ve meta-analizi yapıldı.

**Bulgular:** Çalışmaya dahil etme ve dışlama kriterlerine uygun olarak on üç yayın dahil edildi. Çalışmaların 8,052 hasta üzerinde yapıldığı, yaş ortalamasının 30 olduğu, cinsiyet dağılımının %48 erkek ve %52 kadın olduğu görüldü. Çalışmaların kesim noktası 5, duyarlılık %85, özgüllük %59 olarak bulundu. Çalışmalar homojendi ($I^2$=19,830; Cochran Q=14,968; p>0,05). AIR-S tanısal ayırt etme yeteneği istatistiksel olarak anlamlıydı (toplam-sabit etki=0,838; %95 güven aralığı 0,800-0,875; p<0,001). İstatistiksel olarak anlamlı yayın yanlılığı bulunmadı (p>0,05).

**Sonuç:** Bu çalışmada, AIR-S'nin tanısal parametreleri için belirlenen değerlerin toplamı 170'in altındadır. Bu bulgu, AIR-S'nin akut apandisit tanısında tek başına kullanılmasının yetersiz olduğunu ve diğer tanısal ölçümlerle birlikte kullanılmasının daha uygun olduğunu ifade etmektedir.

**Anahtar Kelimeler:** Apendisit, apandisit enflamatuvar yanıt skoru, alıcı işlem karakteristiği, yanlılık

## Introduction

One of the most frequent causes of urgent abdominal diseases is appendicitis. It is known that acute appendicitis (AA) affects 90-100/100,000 people in developed countries (1). If appendicitis is suspected in a patient presenting with acute abdominal symptoms, the diagnosis should be confirmed before performing emergency surgery. Rapid and accurate diagnosis is of great importance to reduce the complications of AA and even to decrease the mortality rates that may occur due to complications. For many other reasons (pregnancy, hematologic origin etc.), obtaining a reliable preoperative diagnosis may be difficult even for physicians and/or experienced surgeons (2,3).

Clinicians have developed various scoring tools with prognostic value based on the principle of evaluating many clinical findings together in order to minimize the margin of error in the diagnosis of AA and to confirm the preliminary diagnosis. Among these scores, Alvarado, Modified Alvarado, Lintula, Tzanakis, appendicitis inflammatory response score (AIRS), Ohmann, Fenyo-Lindberg and Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) aim to improve diagnostic ability and reduce the rate of negative appendicectomy (4). Recently, scoring models have been reported to predict complicated acute appendicitis. Scoring systems that combine clinical and imaging features and scoring models that can be calculated using predictive equations have been proposed (5,6,7,8).

Important clues for AA can be obtained through tools that assess risk according to a score obtained by combining patients' symptoms, clinical findings and laboratory results, and even calculating according to their severity and level. The appendicitis inflammatory response-score (AIR-S), one of these instruments, was created in 2008 and is currently the most used pre-operative tool. The World Society for Emergency Surgery's 2020 clinical practice suggests using AIR-S for the diagnosis and management of AA (9).

In this study, we aimed to meta-analyze the studies evaluating the effectiveness of the AIR-S. In the light of these studies, it was aimed to draw attention to the diagnostic values of scoring, which enables the evaluation of clinical, laboratory and imaging methods together as well as the history obtained from the patient, to emphasize the importance of its use in daily practice and to contribute to the literature.

## Material and Methods

The preferred PRISMA reporting elements for systematic reviews and meta-analyses were followed when conducting this investigation. This study's execution did not require ethical approval.

### Keywords and Search Strategy

In this study, studies using AIR-S in patients with AA and evaluating the diagnostic value of this score according to receiver operating characteristic (ROC) were analyzed. All studies published in the last 15 years using the terms "All fields=appendicitis inflammatory response" (AND), "All fields= ROC" (AND) in Web of Science Core Collection, PubMed and Google Scholar databases (accessed March, April and May 2023) were searched and systematic review and meta-analysis were performed.

### AIRS

Vomiting, right iliac fosse-migrating abdomen pain, rebound tenderness, fever (°C), leukocyte count (PML), white blood cell count (WBC $10^9$/L), and C-reactive protein (CRP) (mg/L) concentration are all considered indications for AIR-S. Each evaluation criterion has a score determined for the severity of the evaluation. Accordingly; vomiting (score: 1), abdominal pain that migrates to the right iliac fossa (score: 1), rebound tenderness or muscular defense (Light: 1, Moderate: 2, Strong: 3), fever of 38. 5 °C or more (score: 1), PML (70-84%: 1, ≥85%: 2), WBC (10.0-14.9 x $10^9$/L: 1, ≥15.0x$10^9$/L: 2), CRP (10-49 g/L: 1, ≥50 g/L: 2). The assessment results in a final score ranging from 0 to 12. A total score between "0-4" means "low probability follow-up", "5-11" means "re-evaluation/outpatient follow-up" and "9-12" means "high probability/surgical exploration" (9).

### Inclusion and Exclusion Criteria

The inclusion criteria were that the studies were conducted in adult patients, published in the last fifteen years, the diagnosis was acute appendicitis, the AIR Score efficiency was performed by applying ROC analysis, the area

under the curve (AUC) value and the standard error/95% confidence interval were calculated accordingly.

Exclusion criteria were defined as not including one or more of the inclusion criteria, studies in pediatric patients, case reports, systematic reviews, conference reports, animal experiments and missing data in ROC analysis results.

**Outcome Measures**

For the effectiveness of AIR scores on clinical decision-making, we used all calculated and reported ROC analysis results within the total number of cases in the studies.

**Data Extraction and Assessment of Quality**

A total of 315 studies were accessed in line with the search strategies. The researchers who planned the study (four independent researchers with academic qualifications in general surgery, emergency medicine, and family physician specialists) checked the "Title" and "Abstract" parts of the retrieved articles for compliance with the study strategies. At the end of all search and control processes, all data were recorded by the researchers on the designed data collection forms and all records were collected under a common file. The findings of a total of 13 studies that met the inclusion criteria were statistically evaluated. Figure 1A displays the study's PRISMA flow diagram.

**Statistical Analysis**

Studies obtained through this systematic review were considered meta-analysis. Heterogeneity between studies $I^2$ and the risk of publication bias were investigated with Funnel Chart and Egger's Regression. In the included studies, the Cochrane Risk of Bias technique, which evaluates the presence of bias with seven criteria, was used. According to this technique, each study was evaluated according to the "low, unclear, high" bias criteria (10). The threshold value of 0.25 for the $I^2$ value and 0.05 for statistical significance was accepted to determine whether heterogeneity was present. Calculations were performed with Medcalc (version 20.218 Free-Trial) and Meta-DISC (version 1.4) program.

**Results**

After a database search, a total of 315 articles containing patient data related to AIR-S were found. Thirteen publications in total were included in the study for evaluation after taking the inclusion and exclusion criteria into account. The articles' titles and abstracts were read, and it was determined whether they were pertinent to the topic. The PRISMA flow chart of the study is shown in Figure 1A. Seven criteria were used to assess the risk of bias. Each study was assessed as low risk, high risk or unclear risk of bias. The highest risk was "blinding of participants and personnel" and the lowest risk was "allocation concealment" (Figure 1B).

It was seen that 13 studies using ROC curve, a statistical technique for performance measurement of AIR-S, were conducted with a total of 8.052 patients, 48% were male, 52% were female, and the mean age of all patients was 30 years. When the common features of the studies were analyzed, the cutoff point was found to be 5, sensitivity
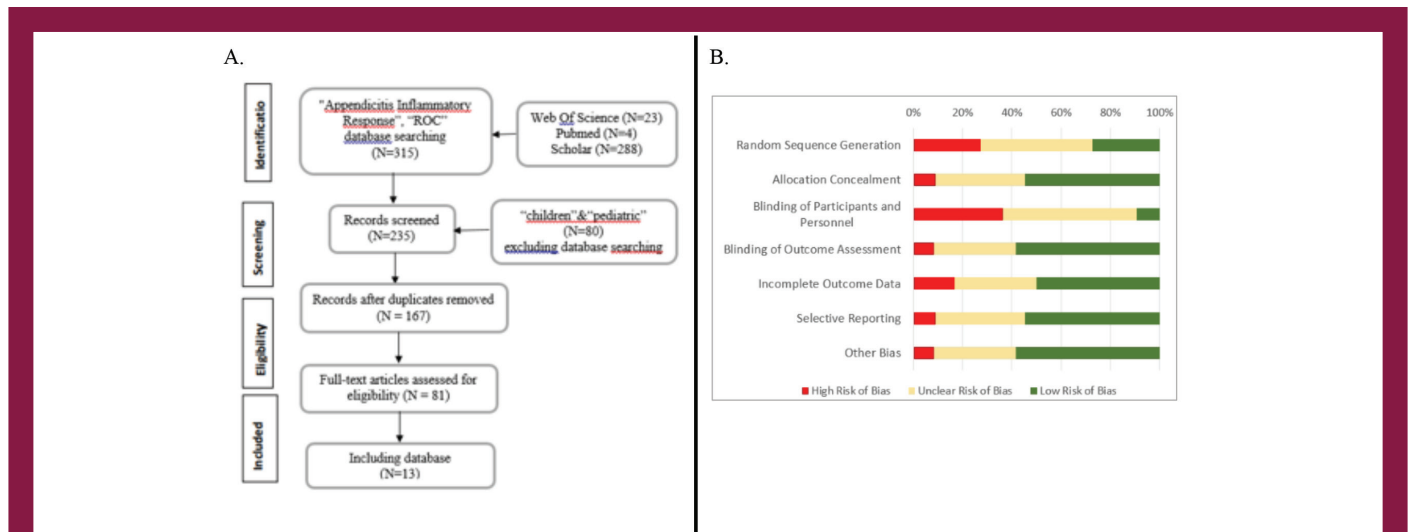


**Figure 1.** **(A)** PRISMA methodological quality summary study flow diagram with AIR-S. **(B)** Risk of bias graph: risk of bias item presented across all included studies

*ROC: Receiver operating characteristic*

86.90%, specificity 53.80% (n=10). While the 3 studies aimed to show the clinical efficacy of the AIR-S with ROC analysis results, they did not share the cutoff point and the sensitivity analysis results related to this point (Table 1).

The clinical efficacy of AIR-S was evaluated in 13 included studies. For the calculation of the standard error, it was extended with five to all cell counts in all runs to avoid division with zero error. Homogeneity was observed in the studies ($I^2$=19.830; Cochran Q=14.968; p=0.243). According to the results, the area under the curve of AIR-S was statistically significant (total-fixed effects=0.838; 95% confidence interval 0.800-0.875; p<0.001; Figure 2A). The summary receiver operating characteristic (sROC) curve, which is shaped according to the common results of the studies and includes the sensitivity analysis values, is presented in Figure 2B. AIR-S diagnostic distinguishability was statistically significant (p<0.001).

There was no statistically significant publication bias (p=0.191). Funnel graps shows the symmetrical, the likely it is not that of bias will be substantial (Figure 3).

## Discussion

Today, patients can present with symptoms of AA at any time of the day to the emergency department, general surgery outpatient clinic or family medicine centers of healthcare facilities. It is important for physicians to rely on clinical scoring systems during off-hours (nights, weekends, holidays) when access to imaging services (especially ultrasonography) is difficult. In this study, we aimed to examine the diagnostic efficacy of the AIR-S developed for the combined evaluation of clinical and laboratory parameters in the diagnosis of AA by meta-analysis.

The AIR-S has been accepted as one of the best-performing scores for the diagnosis of AA among the various clinical prediction tools available. AIR-S with other scoring systems can significantly reduce the risk of overdiagnosis of AA and thus provide a reliable diagnostic performance, while at the same time enabling treating surgeons to avoid the routine use of computed tomography (24).

The results obtained from validation studies were summarized and it was shown that the AIR-S had an area under the ROC curve (AUC) of 0.84, sensitivity (92%), specificity (63%), The AIR score performed best performance compared to other scoring systems (Alvarado, PIRASA, Ohmann, Eskelinen, Lintula, Modified Alvarado) in terms of sensitivity, specificity AUC values and usability (25). However, it is recommended that the sum of the sensitivity and specificity of the tests that should be used for diagnosis should be above 170 (26). In our study, the sum of the values determined for the diagnostic parameters of the AIR-S was below 170. This result indicates that the use of the AIR-S alone in the diagnosis of AA is not a sufficient diagnostic tool and that it is more appropriate to use it together with other parameters that help the diagnosis.

The AIR-S is a valid decision support system for clinical diagnosis and has high sensitivity for complicated appendicitis. In addition, it was emphasized that the AIR-S had a high discrimination capacity in children and patients with long-term symptoms and performed equally well in both sexes (13).

It has been stated that the diagnostic accuracy of the RIPASA system, which is used in the literature as one of the

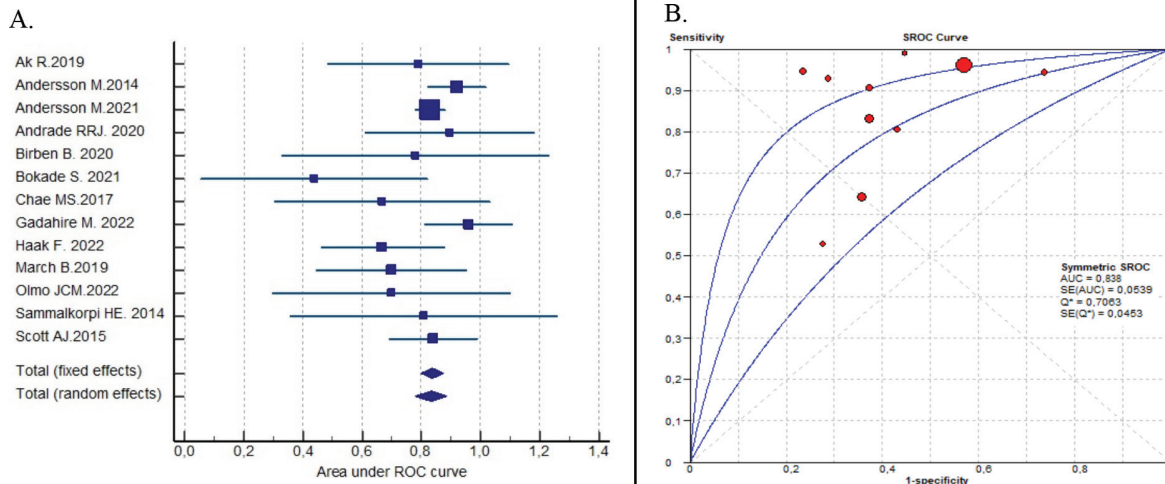| Table 1. Statistical characteristics of AIR-S studies | | | | | | |
|---|---|---|---|---|---|---|
| Study | n | M/F | Age | Cut-off | Sensitivity (95% CI) | Specificity (95% CI) |
| Ak et al. (11) | 232 | 105/127 | Median: 33 | ≥5 | 94.39 (88.19-97.92) | 26.13 (18.25-35.32) |
| Andersson et al. (12) | 229 | 105/124 | Mean: 23.40 | >4 | 93.00 (89.00-97.00) | 71.00 (65.00-77.00) |
| Andersson et al. (13) | 3878 | 1802/2076 | Median: 26.10 | <6 | 96.10 | 43.00 |
| Andrade et al. (14) | 292 | 183/109 | - | <6 | 94.70 (80.40-98.3) | 76.50 (74.2-90.30) |
| Birben et al. (15) | 237 | 126/111 | Mean: 34.00 | >4 | 80.62 (72.74-87.05) | 57.14 (28.86-82.34) |
| Bokade et al. (16) | 90 | 62/28 | Mean: 32.14 | - | - | - |
| Chae et al. (17) | 189 | 63/126 | Mean: 33.00 | >4 | 52.50 (39.30-65.40) | 72.70 (64.10-80.20) |
| Gadahire et al. (18) | 100 | 55/45 | Mean: 25.89 | ≥5 | 100.00 | 55.00 |
| Haak et al. (19) | 956 | 486/470 | Mean: 28.00 | ≥5 | 64.50 | 63.67 |
| March et al. (20) | 98 | 41/57 | Median: 30.00 | - | - | - |
| Martín-Del Olmo et al. (21) | 458 | 266/192 | Median: 31.00 | - | - | - |
| Sammalkorpi et al. (22) | 829 | - | Median: 32.00 | ≥5 | 83.10 | 63.10 |
| Scott et al. (23) | 464 | 172/292 | Mean: 27.00 | ≥5 | 90.00 (84.00-95.00) | 63.00 (58.00-68.00) |
| CI: Confidence interval, AIR-S: Appendicitis inflammatory response-score | | | | | | |

**Figure 2.** **(A)** Forest graph of ROC analyses of AIR-S studies. **(B)** sROC curve of studies included in the systematic review on AIR-S

*AIR-S: Appendicitis inflammatory response-score, ROC: Receiver operating characteristic, SROC: Summary receiver operating characteristic, AUC: Area under the curve*
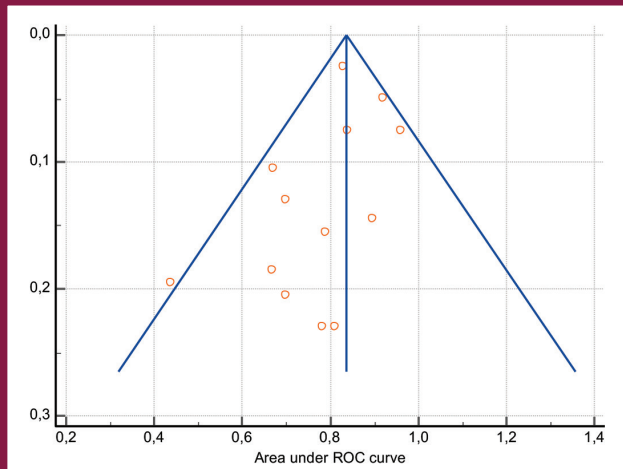


**Figure 3.** Funnel graph for ROC analysis of AIR-S studies

*AIR-S: Appendicitis inflammatory response-score, ROC: Receiver operating characteristic*

scoring systems, is better than the Alvarado and AIR scores, but the single-center study is a disadvantage because the results differ for region and ethnicity (20).

It was determined that Alvarado and AIR-S, which are most commonly used in the diagnosis of AAin pregnant women, are effective methods in the diagnosis of AA. However, the higher accuracy of AIRS, which includes CRP value, suggests that this system is an advantage (27).

In line with the results of this meta-analysis, it can be said that patients evaluated with the AIR-S can be discharged with detailed information (if the complaints of pain, nausea, vomiting, etc. do not go away and worsen, they should apply to the emergency department again) if the total score of the patients evaluated with the AIR-S is below 5, knowing that re-evaluation and careful follow-up are essential in case of change and/or worsening of symptoms. Recent studies have also shown that antibiotics as a non-operative treatment method have a low morbidity and treatment success rate after 30 days of follow-up (28,29).

AIR-S can be particularly useful in environments and situations where imaging methods are limited or unavailable and resources are scarce. The risk stratification of patients with suspected AIR-S AA can guide the decision-making process to optimize the utility of diagnostic imaging and avoid negative and unnecessary investigations.

## Conclusion

The AIR-S has significant diagnostic efficacy in the diagnosis of AA. Risk stratification of patients with suspected AA according to the AIR-S can guide decision-making to reduce admissions, optimize the utility of diagnostic imaging, and avoid adverse and unnecessary explorations. Physician confidence in clinical scoring systems is also important.

However, in this study, the sum of the values determined for the diagnostic parameters of AIR-S was below 170. This result indicates to clinicians that the AIR-S alone is not an adequate diagnostic tool in the diagnosis of AA and that it is more appropriate to use it in conjunction with other diagnostic parameters.

## Ethics

**Ethics Committee Approval:** Ethics committee approval was not required as it was a meta-analysis study.

**Informed Consent:** Not required as it was a meta-analysis study.

**Peer-review:** Externally and internally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: İ.G., D.S., S.Ö., N.B., Concept: İ.G., D.S., Design: İ.G., D.S., Data Collection or Processing: İ.G., D.S., N.B., Analysis or Interpretation: İ.G., D.S., N.B., Literature Search: İ.G., D.S., N.B., Writing: İ.G., D.S., S.Ö., N.B.

**Conflict of Interest:** There is no conflict of interest between the authors.

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