

Nationwide prospective audit for the evaluation of appendicitis risk prediction models in adults: right iliac fossa treatment (RIFT)—Turkey

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Abstract

Background: Appendicitis is the most prevalent surgical emergency. The negative appendicectomy rate and diagnostic uncertainty are important concerns. This study aimed to assess the effectiveness of current appendicitis risk prediction models in patients with acute right iliac fossa pain.

Methods: A nationwide prospective observational study was conducted, including all consecutive adult patients who presented with right iliac fossa pain. Diagnostic, clinical and negative appendicectomy rate data were recorded. The Alvarado score, Appendicitis Inflammatory Response (AIR), Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) and Adult Appendicitis Score systems were calculated with collected data to classify patients into risk categories. Diagnostic value and categorization performance were evaluated, with use of risk category-based metrics including 'true positive rate' (percentage of appendicitis patients in the highest risk category), 'failure rate' (percentage of patients with appendicitis in the lowest risk category) and 'categorization resolution' (true positive rate/failure rate).

Results: A total of 3358 patients from 84 centres were included. Female patients were less likely to undergo surgery than men (71.5% versus 82.5% respectively; relative risk 0.866, 95% c.i. 0.834 to 0.901, P < 0.001); with a three-fold higher negative appendicectomy rate (11.3% versus 4.1% respectively; relative risk 2.744, 95% c.i. 2.047 to 3.677, P < 0.001). Ultrasonography was utilized in 56.8% and computed tomography in 75.2% of all patients. The Adult Appendicitis Score had the best diagnostic performance for the whole population; however, only RIPASA was significant in men. All scoring systems were successful in females patients, but Adult Appendicitis Score had the highest area under the receiver operating characteristic curve value. The RIPASA and the Adult Appendicitis Score had the best categorization resolution values, complemented by their exceedingly low failure rates in both male and female patients. Alvarado and AIR had extremely high failure rates in men.

Conclusion: The negative appendicectomy rate was low overall, but women had an almost three-fold higher negative appendicectomy rate despite lower likelihood to undergo surgery. The overuse of imaging tests, best exemplified by the 75.2% frequency of patients undergoing computed tomography, may lead to increased costs. Risk-scoring systems such as RIPASA and Adult Appendicitis Score appear to be superior to Alvarado and AIR.

Introduction

Acute appendicitis is one of the most commonly encountered surgical emergencies^{1,2}. Despite decades of experience and studies, diagnosis remains challenging, particularly in young women for whom acute abdominal pain necessitates the

assessment of a broader range of differential diagnoses^{3,4}. A key concern is overtreatment, which increases unnecessary surgeries (negative appendicectomy) and can be associated with postoperative complications, prolonged hospital stays and unnecessary healthcare costs^{4–6}. Although many international guidelines recommend the routine use of risk prediction models

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in patients with acute abdominal pain, the negative appendicectomy rate (NAR) has been reported to be as high as 28% in female patients and 12% in male patients^{5,7–9}.

To decrease NAR, numerous risk scoring systems that aid in diagnosis have been introduced, including the Alvarado score, Appendicitis Inflammatory Response (AIR), Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) and Adult Appendicitis Score (AAS). However, the positive predictive values (PPV) and negative predictive values (NPV) of these scoring systems are often poor, and inconsistent performance metrics have been demonstrated by many studies 10-12. These limitations have resulted in limited clinical implementation of these scores in patients with right iliac fossa (RIF) pain, and there is an apparent need to establish their utility by comparing outcomes in different populations. Nonetheless, it is crucial to recognize that these scoring systems are particularly limited when assessing female patients, in whom differential diagnoses are various, or while evaluating immigrants, who often experience problems in accessing healthcare and are often affected by a language barrier. Today, around 5-7% of Turkey's population is comprised of immigrants, with the majority being of Syrian origin¹³. Therefore, auditing patients with acute appendicitis and appendicitis scoring systems with respect to sex and immigrant status have become crucial to establish problems in patient management, ensure high-quality healthcare, and reduce the financial burden caused by unnecessary imaging studies and surgeries.

This study presents the first analysis of the Right Iliac Fossa Treatment-Turkey (RIFT-TR) study, which aimed to: identify optimal risk prediction models for acute right iliac fossa (RIF) pain in Turkey's population according to age and sex, to assess whether these scores have similar efficacy in immigrants and to reveal nationwide clinical trends, thereby establishing issues and facilitating debates that may lead to possible improvements.

Methods

Study design

The present study is a continuum of the study conducted by the RIFT study group in the UK and several other European countries⁹. It was designed as a nationwide multicentre prospective observational cohort study to examine risk prediction models used in the assessment of acute appendicitis. Several problems identified in the data collection and analysis processes of the original RIFT study were corrected, and new physical and electronic forms were prepared. The study protocol, including outcome measures and data collection methods, were disseminated through a readily available network of Department Chairs at secondary and tertiary healthcare centres throughout the country (a total of 84 centres).

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethical approval was obtained from the Clinical Research Ethics Committee of Gazi University Faculty of Medicine (7 September, 2020) and the study was registered on clinicaltrials.gov, registration number NCT04614649. All patients received information regarding the study and the use of their data, and written informed consent forms were obtained. The study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies¹⁴.

Eligibility criteria and study groups

All consecutive patients older than 18 years of age who were referred by a general practitioner or emergency physician to the on-call surgical team with acute RIF pain or suspected appendicitis were included in this study. The timeline for the inclusion of patients was from September 2020 to December 2020. Patients who reported they had previously undergone appendicectomy were not included in the analyses. All pregnant women were also excluded from the study because pregnant women usually cannot be assessed with scoring systems and have considerably different clinical needs compared with other patients. Pregnancy was identified by patients' self-reports or urine analysis upon suspicion.

To evaluate scoring systems, patients were divided into two groups: surgical and non-surgical treatment—the latter of which included patients treated with conservative management. Surgical treatment groups were further classified into four subgroups based on their surgical pathology results: those diagnosed with acute appendicitis; those without acute appendicitis but with non-obstetric/gynaecological surgical pathologies; those with obstetric or gynaecological pathologies such as ovarian cyst rupture and pelvic inflammatory disease; and those with negative laparotomy or laparoscopic findings.

Study variables and data collection

All data were collected by use of a standardized case report form and this information was then swiftly transferred to the online database. These data were collected prospectively by the attending physicians at the time of admission, after obtaining the imaging results, completing the care process and at the end of the follow-up interval. Demographic and clinical features including age, sex, symptoms, examination findings, blood tests, and imaging reports obtained from ultrasonography (USG), computed tomography (CT) and magnetic resonance imaging (MRI) were recorded. In addition to these, the operative procedure, operative findings and histopathological results were noted for patients in the surgical treatment group. A supervising consultant surgeon at each hospital oversaw study conduct and was responsible for the overall quality assurance of data submission. Local lead investigators were contacted with specific details of missing data when necessary. Also, ten participating centres were randomly identified to validate their data. Where incorrect data were identified, validators were asked to amend those data points on the study database. If any data points were missing despite aforementioned measures, these data points were excluded from the analysis without excluding the patients themselves. Owing to the exceptionally low level of missing data, this approach was deemed sufficient.

Diagnostic analysis and risk score assessment Negative appendicectomy rate

The NAR value was calculated as the percentage of patients with normal appendix histology who had undergone appendicectomy. Patients with appendix pathology other than appendicitis (such as appendix tumour) were included in the denominator but not the numerator.

Calculation of risk scores

Collected data were also used to calculate the four most commonly used adult risk prediction models: Alvarado¹⁵, AIR¹⁶, RIPASA¹⁷ and AAS¹⁸. If these scores had been calculated by the attending physicians, the values were recorded after being checked for accuracy. However, in the majority of patients, attending physicians had not calculated scores despite data availability. As such, Alvarado, AIR, RIPASA and AAS scores were calculated for each patient by the primary researchers of the RIFT study based on readily recorded information in order to

Table 1 AIR, Alvarado, RIPASA and AAS score characteristics

| | Alvarado | AIR | RIPASA | AAS |
|---|----------|-----|--------|-----|
| Vomiting | | 1 | | |
| Nausea or vomiting | 1 | | 1 | |
| Anorexia | 1 | | 1 | |
| Pain in RIF | | 1 | 0.5 | 2 |
| Migration of pain to the RIF | 1 | | 0.5 | 2 |
| Rovsing's sign | | | 2 | |
| RIF tenderness | 2 | | 1 | |
| Women ≥50 years or men (any age) | | | | 3 |
| Women <50 years | 4 | | 4 0 | 1 |
| Rebound tenderness or muscular | 1 | | 1 + 2 | |
| defence/guarding | | 1 | | 2 |
| Light | | 1 | | 2 |
| Medium | | 2 | | 4 |
| Strong | | 3 | | 4 |
| Body temperature | 1 | | | |
| >37.5°C | 1 | 1 | | |
| ≥38.5°C | | 1 | 1 | |
| >37 to <39°C | | | 1 | |
| White blood cell count >10.0 × 10°/l | 2 | | 1 | |
| 10.0–14.9 × 10 ⁹ /l | 2 | 1 | 1 | |
| 10.0-14.9 x 10·/1 ≥15.0 x 10 ⁹ /l | | 2 | | |
| ≥7.2 and <10.9 × 10% | | 2 | | 1 |
| ≥ 7.2 and $< 10.9 \times 10^{-7}$ ≥ 10.9 and $< 14.0 \times 10^{9}$ /l | | | | 2 |
| ≥10.9 and <14.0 × 10 /1 ≥14.0 × 10 °/1 | | | | 3 |
| Leucocytosis shift | 1 | | |) |
| Polymorphonuclear leucocytes | 1 | | | |
| 70–84% | | 1 | | |
| ≥85% | | 2 | | |
| ≥62% and <75% | | _ | | 2 |
| ≥75% and <83% | | | | 3 |
| ≥83% | | | | 4 |
| CRP concentration | | | | - |
| 10–49 mg/l | | 1 | | |
| ≥50 mg/l | | 2 | | |
| Symptoms <24 h and CRP | | | | |
| (C-reactive protein) concentration | | | | |
| ≥4 and <11 mg/l | | | | 2 |
| ≥11 and <25 mg/l | | | | 3 |
| ≥25 and <83 mg/l | | | | 5 |
| ≥83 mg/l | | | | 1 |
| Symptoms >24 h and CRP | | | | |
| (C-reactive protein) concentration | | | | |
| ≥12 and <53 mg/l | | | | 2 |
| ≥53 and <152 mg/l | | | | 2 |
| ≥152 mg/l | | | | 1 |
| Sex | | | | |
| Male | | | 1 | |
| Female | | | 0.5 | |
| Age | | | | |
| <40 years | | | 1 | |
| ≥40 years | | | 0.5 | |
| Duration of symptoms | | | | |
| <48 h | | | 1 | |
| >48 h | | | 0.5 | |
| | | | | |
| Negative urinalysis | | | 1 | |
| Negative urinalysis Foreign NRIC (national registration | | | 1 1 | |
| Negative urinalysis | 10 | 12 | | 23 |

Alvarado score/acute appendicitis response score (AIR), low risk (<5), intermediate risk (5–8), high risk (>8). Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score, unlikely (<5), low risk (5–7), high risk (7.5–11.5), definite (≥12). Adult Appendicitis Score (AAS), low risk (0-10), intermediate risk (11–15), high risk (≥16). RIF, right iliac fossa; NRIC, national registration identity create a hypothetical clinical scenario for risk prediction models. The information used to calculate these scoring systems was collected prospectively before the results of the imaging studies were available. Of note, the original RIFT study was known to have problems with the calculation of scores and the cut-off values, as well as issues in data collection⁹. These problems were corrected before initiating the present study, both in the printed forms used for bedside data collection and the digital forms/files used for data entry and storage. Scoring systems are summarized in Table 1.

Assessment of diagnostic performance

The diagnostic performance of scores was assessed with two approaches: by examining receiver operating characteristic (ROC) analyses that create a single cut-off value, and by evaluating predictive classification results. For the primary analyses, individuals who had undergone non-surgical treatment were excluded from the ROC analysis. While this approach artificially reduced negative predictive values, it was deemed necessary to simulate real-world scenarios. In the clinical setting, risk stratification systems are useful if they perform well among patients that present with typical RIF pain and are seriously being considered for surgery, not patients who can be excluded by examination or preliminary methods. As such, the primary ROC analyses examined in this study were performed on only the operated on patients (n = 2610). It should be mentioned that non-operated on appendicitis patients were also excluded with this approach, and this may be considered as a limitation. However, this decision aimed to assess the diagnostic accuracy of the scores in situations where they would be most crucial—when surgeons were faced with a challenging decision regarding the necessity of appendicectomy. Nonetheless, ROC analyses with the entire cohort (n = 3358)were also performed in the interest of providing complete outcome evaluations (Supplementary data).

In the second approach, risk prediction models were assessed by evaluating their classification performance by including all subjects enrolled into the study (n = 3358). 'Appendicitis ratio', 'categorization resolution' (CR) and 'failure rate' (the latter widely known as false omission rate) were calculated. The 'appendicitis ratio' was the percentage of patients with acute appendicitis in each category of each risk scoring system. For the highest risk category of each prediction model, this value was accepted to describe the 'true positive rate'. The CR was calculated as a ratio, by dividing the appendicitis ratio in the highest risk category (true positive rate) by the appendicitis ratio in the lowest risk category (the percentage of patients with appendicitis despite being predicted to have the lowest risk = failure rate). This latter value (failure rate) will be used in this study, similar to prior research⁴. The failure rate is defined as the proportion of patients with appendicitis who were stratified into the low-risk group of a given risk score (false negatives/(true negatives + false negatives)). Finally, despite the fact that CR values would be impacted by the uneven distribution of patients into each risk category, this approach was chosen as it would present data for the real-world utility of scoring systems.

Follow-up

Patients were followed up to assess any subsequent hospital admissions within 30 days of initial presentation, and then a further 30 days of follow-up was performed using a combination

of phone calls and electronic hospital records. Thus, all participants were evaluated for a 60-day interval after the initial admission that caused study inclusion.

Statistical analysis

All analyses were subject to a significance threshold of P < 0.05 and were performed on SPSS v.25 (IBM, NY, USA). Histogram and Q-Q plots were used to determine whether variables conformed to a normal distribution. Data are given as mean(s.d.) or as median (1st quartile-3rd quartile) for continuous variables according to the normality of distribution, and as an absolute and relative frequency for categorical variables. Normally distributed variables were analysed with the one-way analysis of variance (ANOVA). Non-normally distributed variables were analysed with the Kruskal-Wallis test. Categorical variables were analysed with chi-square tests (Pearson, Yate's correction, Fisher's exact, Fisher-Freeman-Halton). Pairwise comparisons were adjusted by the Bonferroni correction. Risk prediction models were assessed if patients could be scored with the readily available data points, and the prediction performances were evaluated based on sex and immigrant status. The overall ability of the risk prediction models to discriminate between patients with and without acute appendicitis was determined by calculation of the area under the curve (AUC) for ROC analyses, and optimal cut-off points were determined using the Youden J index.

Superscripted letters in tables refer to pairwise comparison results. The letter notation approach was used to describe statistical similarities between columns (groups) that were found to be statistically similar. For each row, the presence of the same letters in different columns indicates that the denoted variables were statistically similar between those groups, as assessed by Bonferroni correction. For example, 'a', 'ab', and 'b' in the same row indicate that there was a significant difference between the first and third groups and that the second group was similar to both the first and third groups.

Results

Clinical characteristics and outcomes

A total of 3358 patients (1911 men and 1447 women) from 84 centres nationwide were included in this study. The median age was 32 (range 18–91) years. A total of 196 (5.8%) immigrant patients were identified. A prior history of RIF pain was reported by 594 (17.8%) patients, while 533 (15.9%) patients had previously undergone abdominal surgery (Table 2).

Table 2 Demographic features and abdominal history of the cohort

| Age (years), median (1st-3rd quartile) | 32 (24–44) |
|--|-------------|
| <45 | 2540 (75.6) |
| ≥45 | 818 (24.4) |
| Sex | |
| Male | 1911 (56.9) |
| Female | 1447 (43.1) |
| Nationality | |
| Turkish | 3162 (94.2) |
| Syrian | 107 (3.2) |
| Other immigrants | 89 (2.7) |
| RIF pain history | |
| Once | 401 (12.0) |
| Twice or more | 193 (5.8) |
| Abdominal surgery history | 533 (15.9) |

Values are n (%) unless otherwise indicated. RIF, right iliac fossa.

At admission, symptom duration was less than or equal to 24 h in 2021 (60.3%) patients, greater than 24–48 h in 596 (17.7%) patients and longer than 48 h in 741 (22%) patients. RIF pain was reported as the primary complaint by 3245 (96.6%) patients, while the other common symptoms of acute appendicitis, nausea and loss of appetite were present in 57.3% and 50.4% of patients respectively. The most common findings on physical examination were 'tenderness without rebound' and 'localized guarding' in 44.8% and 45.2% of patients respectively. USG was utilized in 1906 (56.8%) patients and confirmed appendicitis in 809 of these patients (42.4%), CT was utilized in 2524 (75.2%) patients and confirmed appendicitis in 1766 of these patients

Table 3 Clinical features of the study cohort

| Variables | Overall cohort $(n = 3358)$ |
|---|-----------------------------|
| Duration of symptoms | |
| ≤24 h | 2021 (60.3) |
| 24–48 h | 596 (17.7) |
| >48 h | 741 (22.0) |
| Patient-reported complaints/symptoms | |
| RIF pain | 3245 (96.6) |
| Nausea | 1924 (57.3) |
| Vomiting | 921 (27.4) |
| Loss of appetite | 1686 (50.2) |
| Pain migration to RIF | 1640 (48.8) |
| RIF examination | |
| No tenderness | 171 (5.1) |
| Tenderness without rebound | 1506 (44.8) |
| Localized guarding | 1518 (45.2) |
| Generalized guarding | 163 (4.9) |
| RIF rebound tenderness | 1948 (58.0) |
| Rovsing's sign | 789 (23.5) |
| Urine analysis | 1245 (40.1) |
| No investigation | 1345 (40.1) |
| Negative | 1565 (46.6) |
| Positive Laboratory regults, modian (1st 2rd) | 448 (13.3) |
| Laboratory results, median (1st–3rd | |
| quartiles) White blood cell count (×10³) | 13.05 (9.93–16.11) |
| Neutrophil (×10 ³) | 9.92 (6.85–13.00) |
| CRP | 18.4 (4.2–66.8) |
| USG findings | 10.1 (1.2 00.0) |
| Appendicitis confirmed | 809 (24.1) |
| Appendicitis excluded | 149 (4.4) |
| Appendicitis suspicious | 814 (24.2) |
| Another pathology | 134 (4.0) |
| Not applied | 1452 (43.2) |
| CT findings | ` , |
| Appendicitis confirmed | 1766 (52.6) |
| Appendicitis excluded | 249 (7.4) |
| Appendicitis suspicious | 318 (9.5) |
| Another pathology | 191 (5.7) |
| Not applied | 834 (24.8) |
| MRI findings | |
| Appendicitis confirmed | 7 (0.2) |
| Appendicitis excluded | 8 (0.2) |
| Appendicitis suspicious | 1 (0.0) |
| Another pathology | 12 (0.4) |
| Not applied | 3330 (99.2) |
| Risk prediction scores, mean(s.d.) | |
| Alvarado score | 6.23(1.91) |
| AIR score | 6.38(2.02) |
| RIPASA score | 8.85(2.55) |
| AAS score | 14.63(3.30) |

Values are n (%) unless otherwise indicated. RIF, right iliac fossa; CRP, C-reactive protein; USG, ultrasound; CT, computed tomography; MRI, magnetic resonance imaging; AIR, Appendicitis Inflammatory Response; RIPASA, Raja Isteri Pengiran Anak Saleha Appendicitis; AAS, Adult Appendicitis Score.

(70%), MRI was utilized in only 28 (0.8%) patients and confirmed appendicitis in seven of these patients (25%) (Table 3).

When the whole cohort was assessed with respect to discharge diagnoses (n = 3358), the most frequent were appendicitis in 2614 (77.8%), non-specific pain in 157 (4.7%) and other gastrointestinal pathologies in 111 (3.3%) patients. Among the 2614 patients with appendicitis, 186 (7.1%) had received only conservative treatment (antibiotic therapy). Surgery was performed in 2610 (77.7%) patients and 2428 (93%) of the subjects underwent surgery within 24 h. Discharge diagnoses showed that 2428 (93%) of patients had acute appendicitis, while 182 (7.0%) had normal appendices (NAR: 7%). Despite the fact that female patients with RIF pain were found to be less likely to undergo surgery than men (71.5% versus 82.5% respectively; RR 0.866, 95% c.i. 0.834 to 0.901, P < 0.001), NAR in women was almost three-fold higher than in men (11.3% versus 4.1%; RR 2.744, 95% c.i. 2.047 to 3.677). In the immigrant group, NAR was 7.8%.

A total of 229 surgeries were performed for surgical conditions other than appendicitis. This number included patients in which surgery was begun with a preliminary diagnosis of acute appendicitis, but the surgery was then changed due to intraoperative findings. Open surgery was utilized in 1128 (54.3%) patients, while surgeries were carried out with the laparoscopic approach in 915 (44.1%) patients. In 34 patients (1.6%), the operation was started with the laparoscopic approach but conversion to open surgery was deemed necessary (Table 4).

Table 4 Operative features of the surgical cohort

| Variables | Surgical cohort (n = 2610) |
|--|-------------------------------|
| Time between admission and surgery | |
| <24 h | 2428 (93.0) |
| 24–48 h | 148 (5.7) |
| 48–72 h | 16 (Ò.6) |
| 72–96 h | 8 (0.3) |
| 96–168 h | 3 (0.1) |
| >168 h | 7 (0.3) |
| Discharge diagnosis with respect to | , , |
| subgroups | |
| Acute appendicitis | 2428 (93) |
| Patients with normal appendicectomy | 182 (7) |
| (NAR) | . , |
| Surgical pathology except OB/GYN | 61 (2.3) |
| OB/GYN pathologies | 51 (2.0) |
| No pathology detected | 70 (2.7) |
| Operative approach (reported in 2077 | |
| patients) | |
| Open—RIF incision | 1042 (50.2) |
| Open—midline incision | 86 (4.1) |
| Laparoscopic | 915 (44.1) |
| Conversion to open surgery | 34 (1.6) |
| Procedure(s) other than appendicectomy | |
| (performed in 229 patients) | |
| Diagnostic | 32 (14.0) |
| Right hemicolectomy | 17 (7.5) |
| Meckel's diverticulum resection | 3 (1.3) |
| Small intestine resection | 4 (1.7) |
| Other intestinal surgery | 22 (9.7) |
| Gynaecological | 48 (20.9) |
| Urological | 2 (0.8) |
| Other | 101 (44.1) |
| Duration of hospital stay in days, median (1st-3rd quartile) | 1 (1–2) |

Values are n (%) unless otherwise indicated. RIF, right iliac fossa, NAR, normal appendicectomy rate, OB/GYN, obstetric/gynaecological.

Patient characteristics compared across groups

Among the 2610 patients who underwent surgery, 2428 (93.0%) patients had received surgical treatment for acute appendicitis, with the majority being men (62.2%). In this group, surgical intervention was performed in 2370 (97.6%) patients at first admission, while 58 (2.4%) underwent surgery at readmission. Simple appendicitis was diagnosed in 1768 and complex appendicitis in 596, while definitive results were not reported in 51 patients. Surgical patients with acute appendicitis had the highest white blood cell (WBC) values (13.89 (11.00-16.66)), whereas the mean C-reactive protein (CRP) values (75.8 (14–172)) were found to be highest in patients with other surgical abnormalities (except obstetric and gynaecological). Interestingly, mean CRP values were similar between surgically treated acute appendicitis patients (21.82 (5.2-71.6)) and those with negative laparotomy/laparoscopy findings (21.74 (4.9-63.9)). The mean Alvarado, RIPASA and AAS scores were significantly higher in patients with surgically treated acute appendicitis, whereas the mean AIR score was found to be higher in patients with other surgical abnormalities (Table 5).

Diagnostic performance of risk scoring systems

A total of 1125 (33.5%) patients were recorded as having been formally risk scored at admission by their clinical/surgical team. The Alvarado score was by far the most frequently used scoring system by attending physicians (1106 of 1125, 98.3%), while AIR scoring was performed in the remaining 19 patients. For the remaining 66.5% of patients, physicians did not formally utilize any of the scores in the initial patient management process, despite availability of data. These scores were calculated by RIFT researchers with use of the data collected as part of the study, given that all data allowing calculation were available. In the comparison of the risk scoring systems, it was found that the AAS score had the highest AUC and demonstrated 76.4% sensitivity and 49.4% specificity for its optimal cut-off point (more than 13 points). All scoring systems had significance for prediction, but AUC values were somewhat poor (<0.700) (Table 6). The primary analyses reported in Table 6 only included the surgical cohort (n = 2610). This approach was preferred as these patients represent the subgroup in which risk scoring would be most useful in a real-world scenario. However, in the interests of providing comprehensive data, ROC analysis results including the entire cohort (n = 3358; Table S1) have also been reported. ROC curves for all four risk scoring systems were created by the analysis of the surgical subgroup and the entire cohort (Figs. S1, S2).

Among the 1576 men who underwent surgery, 1511 (95.9%) had acute appendicitis and 65 (4.1%) had normal appendices. Only RIPASA score performance was significant to predict acute appendicitis in men (cut-off: more than 6.5, AUC: 0.580, P = 0.036). On the other hand, despite being marginally non-significant, AAS achieved the highest specificity (77.8%) in men (Table 7). Data including non-surgical men are detailed in Table S2.

A total of 1034 women had undergone surgery and 917 (88.7%) of these were diagnosed with acute appendicitis, while 117 (11.3%) had normal appendices. All scoring systems were successful in predicting acute appendicitis in women. AAS had the highest AUC (0.707) and a cut-off value of more than 13 points, whereas Alvarado achieved the highest specificity (72.4%) (Table 8). Data including non-surgical women are detailed in Table S3.

Finally, a total of 154 immigrants underwent surgery and 142 (92.2%) of these were ultimately discharged with a diagnosis of

Table 5 Clinical and operative features stratified according to pathology results

| | | Surgical coh | ort (n = 2610) | | Non-surgical | P |
|----------------------------|-------------------------------|---|------------------------------------|--|----------------------------|---------|
| | Acute appendicitis (n = 2428) | Other surgical abnormality except for OB/GYN (n = 61) | OB/GYN surgical pathology (n = 51) | Negative laparotomy/ laparoscopy (n = 70) | treatment (n = 748) | |
| Age | 32 (24–44) ^a | 44 (30–59) ^b | 32 (26–38) ^a | 30.5 (24–41) ^a | 33 (25–45) ^a | <0.001 |
| <45 | 1850 (76.2) | 32 (52.5) | 44 (86.3) | 55 (78.6) | 559 (74.7) | < 0.001 |
| ≥45 | 578 (23.8) ^á | 29 (47.5) ^b | 7 (13.7) ^á | 15 (21.4) ^a | 189 (25.3) ^a | |
| Sex | , , | , , | , , | , , | , | |
| Male | 1511 (62.2) ^a | 33 (54.1) ^{a,b} | 0 (0.0) ^c | 32 (45.7) ^{a,b} | 335 (44.8) ^b | <0.001 |
| Female | 917 (37.8) | 28 (45.9) | 51 (100.0) | 38 (54.3) | 413 (55.2) | |
| Nationality | , , | , , | , , | , , | , , | |
| Turkish | 2286 (94.2) | 57 (93.4) | 45 (88.2) | 68 (97.1) | 706 (94.4) | 0.041 |
| Syrian | 77 (3.2) | 4 (6.6) | 1 (2.0) | 2 (2.9) | 23 (3.1) | |
| Other immigrants | 65 (2.7) ^a | 0 (0.0) ^a | 5 (9.8) ^b | 0 (0.0) ^a | 19 (2.5) ^a | |
| RIF pain history | , | , , | , | , | , | |
| One | 275 (11.4) | 7 (11.5) | 6 (12.2) | 12 (17.1) | 101 (13.5) | < 0.001 |
| Two or more | 105 (4.3) ^á | 6 (9.8) ^b | 2 (4.1) ^á | 7 (10.0) ⁶ | 73 (9.8) ^{b′} | |
| Abdominal surgery | 333 (13.7) ^a | 14 (23.0) ^b | 9 (17.6) ^{ab} | 15 (21.4) ^b | 162 (21.7) ^b | <0.001 |
| history | () | , | () | , | , | |
| White blood cell count | 13.89 | 11.70 (8.70–15.21) ^{a,b} | 9.34 (7.45-12.29) ^b | 11.45 (8.58–15.09) ^b | 10.52 | < 0.001 |
| $(\times 10^3)$, median | (11.00-16.66) ^a | , | , | , | (8.05-13.87) ^b | |
| (1st-3rd quartile) | , | | | | , | |
| Neutrophil (x103), median | 10.80 | 8.80 (6.84–12.20) ^{a,b} | 6.15 (4.82-9.73) ^c | 8.38 (5.00–11.48) ^{b,c} | 7.20 | <0.001 |
| (1st-3rd quartile) | (8.00-13.55) ^a | , | , | , | (4.80-10.50) ^c | |
| CRP, median | 21.82 | 75.8 (14–172) ^b | 21.5 (5.45-64.7) ^a | 21.74 (4.9-63.9) ^a | 9.5 (2.48–40) ^c | <0.001 |
| (1st-3rd quartile) | (5.2-71.6) ^a | , | , | , | , | |
| Surgery performed at | , | | | | | |
| First admission | 2370 (97.6) ^a | 54 (88.5) ^b | 45 (88.2) ^b | 66 (94.3) ^{a,b} | _ | <0.001 |
| Re-admission | 58 (2.4) | 7 (11.5) | 6 (11.8) | 4 (5.7) | _ | |
| Operative approach | \ | , | (/ | , | | |
| Open—RIF incision | 996 (52.0) ^a | 19 (35.2) ^a | 4 (8.3) ^b | 23 (39.7) ^a | _ | <0.001 |
| Open—midline incision | 69 (3.6) | 11 (20.4) | 2 (4.2) | 4 (6.9) | _ | |
| Laparoscopic | 825 (43.0) ^a | 19 (35.2) ^a | 42 (87.5) ^b | 29 (50.0) ^a | _ | |
| Conversion to open | 27 (1.4) | 5 (9.3) | 0 (0.0) | 2 (3.4) | _ | |
| Duration of hospital stay, | 2 (1-2) ^a | 3 (2–6) ^b | 3 (2–3) ^b | 1 (1–3) ^a | 1 (0-1) ^c | <0.001 |
| median (1st-3rd quartile) | - (+ -) | 3 (= 3) | J (= J) | - () | + (~ +) | 10.001 |
| Alvarado score, mean(s.d.) | 6.63(1.75) ^a | 6.30(1.68) ^{a,b} | 4.82(1.58) ^c | 5.85(1.85) ^b | 5.07(1.92) ^c | < 0.001 |
| AIR score, mean(s.d.) | 6.75(1.88) ^a | 7.09(2.09) ^a | 4.75(2.11) ^b | 6.07(1.88) ^c | 5.24(2.01) ^b | <0.001 |
| RIPASA score, mean(s.d.) | 9.47(2.34) ^a | 8.52(2.68) ^b | 7.15(2.07) ^{c,d} | 8.24(2.30) ^{b,c} | 7.02(2.27) ^d | <0.001 |
| | | 14 75(2 84) ^{a,b} | | | | <0.001 |
| AAS, mean(s.d.) | 15.46(2.90) ^a | 14.75(2.84) ^{a,b} | 10.78(2.46) ^c | 13.84(3.00) ^b | 12.31(3.34) ^d | <0.0 |

Values are n (%) unless otherwise stated. Superscripted letters refer to pairwise comparison results, same letters indicate statistically similar values in the denoted groups. Bold values indicate statistically significant results. RIF, right iliac fossa; WBC, white blood cell count; CRP, C-reactive protein; AIR, Appendicitis Inflammatory Response; RIPASA, Raja Isteri Pengiran Anak Saleha Appendicitis; AAS, Adult Appendicitis Score; OB/GYN, obstetrics and gynecology.

Table 6 Performance of the scores to predict acute appendicitis in all operated on patients

| | Alvarado | AIR | RIPASA | AAS |
|----------------|---------------------|---------------------|---------------------|---------------------|
| Cut-off | >5 | >5 | >7 | >13 |
| Sensitivity | 74.5% | 74.6% | 81.0% | 76.4% |
| Specificity | 46.1% | 44.3% | 43.7% | 49.4% |
| Accuracy | 72.5% | 72.4% | 78.4% | 74.4% |
| PPV | 94.8% | 94.4% | 95.0% | 95.0% |
| NPV | 12.0% | 12.2% | 14.7% | 14.3% |
| AUC (95% c.i.) | 0.645 (0.603,0.686) | 0.602 (0.555,0.650) | 0.669 (0.626,0.712) | 0.686 (0.645,0.727) |
| P | <0.001 | <0.001 | <0.001 | < 0.001 |

Bold values indicate statistically significant results. PPV, positive predictive value; NPV, negative predictive value; AUC, area under receiver operating characteristic (ROC) curve; c.i., confidence intervals; AIR, Appendicitis Inflammatory Response; RIPASA, Raja Isteri Pengiran Anak Saleha Appendicitis; AAS, Adult Appendicitis Score.

acute appendicitis. Twelve (7.8%) immigrants had normal appendices, yielding a NAR value of 7.8%. AAS was the only scoring system that demonstrated predictive significance among immigrants, with an AUC of 0.826 and a cut-off value of more than 13 points (*Table 9*). Analyses including non-surgical immigrants are reported in *Table S4*.

Analysis of risk categories

In addition to diagnostic performance analyses that were based on ROC results in operated on patients, each scoring system was evaluated according to the distribution of the entire population into risk categories based on literature-defined cut-off values. In overall analysis, it was found that being categorized as 'high

Table 7 Performance of the scores to predict acute appendicitis in operated on male patients

| | Alvarado | AIR | RIPASA | AAS |
|----------------|---------------------|---------------------|---------------------|---------------------|
| Cut-off | >5 | >6 | >6.5 | >17 |
| Sensitivity | 73.4% | 54.2% | 87.3% | 33.3% |
| Specificity | 35.9% | 54.1% | 30.0% | 77.8% |
| Accuracy | 71.9% | 54.2% | 85.0% | 35.2% |
| PPV | 96.4% | 96.3% | 96.8% | 97.1% |
| NPV | 5.5% | 5.0% | 8.9% | 5.0% |
| AUC (95% c.i.) | 0.562 (0.491,0.634) | 0.536 (0.460,0.612) | 0.580 (0.501,0.659) | 0.567 (0.499,0.635) |
| P | 0.092 | 0.345 | 0.036 | 0.072 |

Bold value indicate statistically significant results. PPV, positive predictive value; NPV, negative predictive value; AUC, area under receiver operating characteristic (ROC) curve; c.i., confidence intervals; AIR, Appendicitis Inflammatory Response; RIPASA, Raja Isteri Pengiran Anak Saleha Appendicitis; AAS, Adult Appendicitis Score.

Table 8 Performance of the scores to predict acute appendicitis in operated on female patients

| | Alvarado | AIR | RIPASA | AAS |
|----------------|---------------------|---------------------|---------------------|---------------------|
| Cut-off | >6 | >5 | >7 | >13 |
| Sensitivity | 55.8% | 75.1% | 77.1% | 64.0% |
| Specificity | 72.4% | 50.4% | 50.0% | 66.1% |
| Accuracy | 57.7% | 72.1% | 74.0% | 64.2% |
| PPV | 94.0% | 91.7% | 92.2% | 93.3% |
| NPV | 17.4% | 21.7% | 22.3% | 19.8% |
| AUC (95% c.i.) | 0.695 (0.645,0.744) | 0.640 (0.580,0.700) | 0.692 (0.642,0.742) | 0.707 (0.657,0.756) |
| P | <0.001 | <0.001 | <0.001 | <0.001 |

Bold values indicate statistically significant results. PPV, positive predictive value; NPV, negative predictive value; AUC, area under receiver operating characteristic (ROC) curve; c.i., confidence intervals; AIR, Appendicitis Inflammatory Response; RIPASA, Raja Isteri Pengiran Anak Saleha Appendicitis; AAS, Adult Appendicitis Score.

Table 9 Performance of the scores to predict acute appendicitis in operated on immigrants

| | Alvarado | AIR | RIPASA | AAS |
|----------------|---------------------|---------------------|---------------------|---------------------|
| Cut-off | >5 | >5 | >7 | >13 |
| Sensitivity | 82.4% | 82.3% | 87.4% | 85.0% |
| Specificity | 50.0% | 50.0% | 41.7% | 63.6% |
| Accuracy | 79.9% | 79.9% | 83.7% | 83.2% |
| PPV | 95.1% | 95.3% | 94.4% | 96.2% |
| NPV | 19.4% | 18.5% | 22.7% | 28.0% |
| AUC (95% c.i.) | 0.655 (0.504,0.806) | 0.585 (0.375,0.795) | 0.613 (0.434,0.792) | 0.826 (0.714,0.937) |
| P | 0.076 | 0.372 | 0.195 | <0.001 |

Bold value indicate statistically significant results. PPV, positive predictive value; NPV, negative predictive value; AUC, area under receiver operating characteristic (ROC) curve; c.i., confidence intervals; AIR, Appendicitis Inflammatory Response; RIPASA, Raja Isteri Pengiran Anak Saleha Appendicitis; AAS, Adult Appendicitis Score

Table 10 The frequencies of acute appendicitis diagnoses according to risk category in the whole study group

| | Acute appendicitis | | True appendicitis | CR |
|----------------------|--------------------|------------|-------------------|--------|
| | Yes | No | % | (fold) |
| Alvarado (n) | 2395 | 915 | | |
| High (>8) | 336 (14.0) | 32 (3.5) | 91.3 | 1.93 |
| Intermediate (5–8) | 1787 (74.6) | 580 (63.3) | 75.5 | |
| Low (<5) | 272 (11.3) | 303 (33.1) | 47.3* | |
| AIR (n) | 2182 | 831 | | |
| High (>8) | 383 (17.5) | 57 (6.8) | 87.0 | 1.87 |
| Intermediate (5–8) | 1542 (70.6) | 480 (57.7) | 76.3 | |
| Low (<5) | 257 (11.7) | 294 (35.3) | 46.6* | |
| RIPASA (n) | 2314 | 887 | | |
| Definite (≥12) | 419 (18.1) | 41 (4.6) | 91.1 | 3.88 |
| High (7.5–11.5) | 1456 (62.9) | 338 (38.1) | 81.2 | |
| Low (5–7) | 408 (17.6) | 407 (45.8) | 50.1 | |
| Unlikely (<5) | 31 (1.3) | 101 (11.3) | 23.5* | |
| AAS (n) | 2236 | 874 | | |
| High (≥16) | 1161 (51.9) | 178 (20.3) | 86.7 | 2.61 |
| Intermediate (11–15) | 950 (42.4) | 444 (50.8) | 68.1 | |
| Low (0-10) | 125 (5.6) | 252 (28.8) | 33.2* | |

Values are n (%) unless otherwise indicated. CR was calculated by dividing the appendicitis percentage in the highest risk category by the percentage in the lowest risk category (true positive rate/failure rate). Percentages in parentheses are row percentages, showing the distribution of patients in each risk category. *Corresponds to failure rate. CR, categorization resolution; AIR, Appendicitis Inflammatory Response; RIPASA, Raja Isteri Pengiran Anak Saleha Appendicitis; AAS, Adult Appendicitis Score.

Table 11 The frequencies of acute appendicitis diagnoses according to risk category, divided by sex

| | | Acute app | pendicitis | True appendicitis % | CR (fold) |
|--------|----------------------|-------------|------------|------------------------|--------------|
| Sex | Scoring system | Yes | No | 76 | (IOIU) |
| Male | Alvarado (n) | 1490 | 392 | | |
| | High (>8) | 203 (13.6) | 16 (4.0) | 92.7 | 1.58 |
| | Intermediate (5–8) | 1112 (74.6) | 253 (64.5) | 81.5 | |
| | Low (<5) | 175 (11.7) | 123 (31.3) | 58.7* | |
| | AIR (n) | 1355 | 355 | | |
| | High (>8) | 239 (17.6) | 29 (8.1) | 89.2 | 1.54 |
| | Intermediate (5–8) | 956 (70.5) | 210 (59.1) | 82.0 | |
| | Low (<5) | 160 (11.8) | 116 (32.6) | 58.0* | |
| | RIPASA (n) | 1445 | 377 | | |
| | Definite (≥12) | 279 (19.3) | 28 (7.4) | 90.9 | 3.89 |
| | High (7.5–11.5) | 926 (64.0) | 158 (41.9) | 85.4 | |
| | Low (5–7) | 229 (15.8) | 155 (41.1) | 59.6 | |
| | Unlikely (<5) | 11 (0.7) | 36 (9.5) | 23.4* | |
| | AAS (n) | 1384 | 377 | | |
| | High (≥16) | 848 (61.2) | 120 (31.8) | 87.6 | 2.76 |
| | Intermediate (11–15) | 498 (35.9) | 175 (46.4) | 74.0 | |
| | Low (0–10) | 38 (2.7) | 82 (21.7) | 31.7* | |
| Female | Alvarado (n) | 905 | 523 | | |
| | High (>8) | 133 (14.6) | 16 (3.1) | 89.3 | 2.55 |
| | Intermediate (5–8) | 675 (74.5) | 327 (62.5) | 67.4 | |
| | Low (<5) | 97 (10.7) | 180 (34.4) | 35.0* | |
| | AIR (n) | 827 | 476 | | |
| | High (>8) | 144 (17.4) | 28 (5.8) | 83.7 | 2.37 |
| | Intermediate (5–8) | 586 (70.8) | 270 (56.7) | 68.5 | |
| | Low (<5) | 97 (11.7) | 178 (37.3) | 35.3* | |
| | RIPASA (n) | 869 | 5Ì0 ´ | | |
| | Definite (≥12) | 140 (16.1) | 13 (2.5) | 91.5 | 3.89 |
| | High (7.5–11.5) | 530 (60.9) | 180 (35.3) | 74.6 | |
| | Low (5–7) | 179 (20.5) | 252 (49.4) | 41.5 | |
| | Unlikely (<5) | 20 (2.3) | 65 (12.7) | 23.5* | |
| | AAS (n) | 852 | 497 | | |
| | High (≥16) | 313 (36.7) | 58 (11.6) | 84.4 | 2.49 |
| | Intermediate (11–15) | 452 (53.0) | 269 (54.1) | 62.7 | |
| | Low (0-10) | 87 (10.2) | 170 (34.2) | 33.9* | |

Values are n (%) unless otherwise indicated. CR was calculated by dividing the appendicitis percentage in the highest risk category by the percentage in the lowest risk category (true positive rate/failure rate). Percentages in parentheses are row percentages, showing the distribution of patients in each risk category. *Corresponds to failure rate. CR, categorization resolution; AIR, Appendicitis Inflammatory Response; RIPASA, Raja Isteri Pengiran Anak Saleha Appendicitis; AAS, Adult Appendicitis

risk' by the Alvarado score resulted in the highest true positive rate (91.3%), followed by the 'definite risk' category of RIPASA (91.1%). When the lowest risk categories were examined, it was found that the RIPASA and the AAS had the lowest (best) failure rates (23.5% and 33.2% respectively). RIPASA and AAS also had the highest CR (3.88 and 2.61) values, indicating better performance in differentiating the likelihood of appendicitis in the highest and lowest risk groups (Table 10).

When assessed in only male patients, the 'high risk' category of Alvarado again proved to have the highest true positive rate (92.7%), whereas in female patients, the 'definite' category of RIPASA had the highest true positive rate (91.5%). Interestingly, for men, failure rates of the Alvarado and AIR scoring systems were 58.7% and 58.0% respectively (both were non-significant in ROC analyses), whereas the corresponding values in women were 35% and 35.3% respectively. Notwithstanding the fact that AAS was non-significant in the ROC analysis for men, the RIPASA and AAS systems again had the highest CR values in men (3.89 and 2.76). In women, RIPASA was also leading in this respect (3.89); however, Alvarado (2.55) had a greater CR compared with AAS (2.49) (Table 11).

Finally, in immigrants, all patients (100%) in the 'high risk' category of Alvarado were ultimately diagnosed with acute appendicitis, showing perfect true positive performance. RIPASA had 100% rule-out accuracy (0% failure rate) among patients in

the 'unlikely' category, and therefore, the best CR. However, due to the limited number of patients in categories and the 0% failure rate for RIPASA, the CR value was calculated by combining the 'low' and 'unlikely' categories to determine failure rate. As described previously, AAS was the only scoring system that demonstrated diagnostic significance among immigrants. AAS also proved to be successful in terms of CR, as demonstrated by the fact that CR values were higher in immigrants compared with overall analysis (3.38 versus 2.61) (Table 12).

Discussion

This study found that women with acute RIF pain in Turkey had a lower likelihood of undergoing surgery than men (71.5% versus 82.5%); however, NAR in women was almost three-fold higher than in men (11.3% versus 4.1%). In the immigrant group, NAR was found to be slightly higher compared with NAR in the entire population (7.8% versus 7%). All scoring systems had successful prediction performance in overall analyses with variations based on sex and immigrant status; however, performance metrics, particularly sensitivity values, were notably low. In ROC analyses, RIPASA score was the only scoring system that was significant for men. In the immigrant group, AAS was the only significant predictor of acute appendicitis (cut-off point of more than 13) and had relatively high CR compared with the overall

Table 12 The frequencies of acute appendicitis diagnoses according to risk category among immigrants

| | Acute appendicitis | | True appendicitis | CR (6-14) |
|----------------------|--------------------|-----------|-------------------|--------------|
| | Yes | No | % | (fold) |
| Alvarado (n) | 142 | 53 | | |
| High (>8) | 17 (11.9) | 0 (0.0) | 100.0 | 1.89 |
| Intermediate (5–8) | 107 (75.3) | 37 (69.8) | 74.3 | |
| Low (<5) | 18 (12.6) | 16 (30.2) | 52.9* | |
| AIR (n) | 124 | 43 | | |
| High (>8) | 31 (25.0) | 4 (9.3) | 88.6 | 1.94 |
| Intermediate (5–8) | 82 (66.1) | 26 (60.4) | 75.9 | |
| Low (<5) | 11 (8.87) | 13 (30.2) | 45.8* | |
| RIPASA (n) | 135 | 53 | | |
| Definite (≥12) | 31 (22.9) | 2 (3.7) | 93.9 | 2.71† |
| High (7.5–11.5) | 87 (64.4) | 19 (35.8) | 82.1 | |
| Low (5–7) | 17 (12.5) | 28 (52.8) | 37.8 | |
| Unlikely (<5) | 0 (0.0) | 4 (7.5) | 0.0* | |
| AAS (n) | 120 | 48 | | |
| High (≥16) | 73 (60.8) | 8 (16.6) | 90.1 | 3.38 |
| Intermediate (11–15) | 43 (35.8) | 29 (60.4) | 59.7 | |
| Low (0–10) | 4 (3.33) | 11 (22.9) | 26.7* | |

Values are n (%) unless otherwise indicated. CR was calculated by dividing the appendicitis percentage in the highest risk category by the percentage in the lowest risk category (true positive rate/failure rate). Percentages in parentheses are row percentages, showing the distribution of patients into each risk category. *Corresponds to failure rate. †Calculated by combining the 'low' and 'unlikely' categories due to 0% failure rate in the 'unlikely' category. CR, categorization resolution; AİR, Appendicitis Inflammatory Response; RIPASA, Raja Isteri Pengiran Anak Saleha Appendicitis; AAS, Adult Appendicitis Score.

results, indicating an important advantage in this population. The poor performance of Alvarado and AIR in this respect was associated with the high failure rates of these scoring systems among men (over 50% for both), which showed high failure and very low CR.

The first RIFT study was a dramatic example of different clinical trends regarding NAR, which was found to be 20% (392 of 1957) in the UK and 6.2% (54 of 868) in other participating countries⁴. One of the major factors with an impact on NAR is the use of diagnostic imaging 19,20, as exemplified by a study showing that NAR was reduced from 19% to 3.5% when preoperative imaging was employed²¹. Another nationwide audit reported a NAR value as low as 3.2% when cross-sectional imaging was employed in 99.7% of subjects²². The literature also exhibits the effect of female sex on NAR, which ranges from 4 to 35% throughout the world^{21,23-30}. Studies from Turkey report NARs of 15.8% to 43.9%, and also demonstrate the higher frequencies among women and the positive impact of imaging^{31–35}. In this study, USG (with or without CT) was used in 98.6% of patients who underwent surgery and overall NAR was found to be 7%.

Routine risk scoring has been found to be associated with reduced need for imaging and hospital admission, as well as reduced NAR^{4,18,36}. This study revealed that the attending surgeons/clinical teams had used these models in only 33.8% of patients, despite the fact that necessary clinical data for each scoring system had been gathered. The most frequently used scoring system in clinical practice was Alvarado, followed by AIR in a very small number of subjects; however, based on the results, RIPASA and AAS outperformed these models in almost every metric. Since ROC analyses were employed to determine optimal cut-off values in the assessment of diagnostic performance, it must be kept in mind that these singular cut-off values should not be used to classify risk^{7,17,18}. Further analysis of data with a purposefully selected study group is necessary to create risk categories, which will also necessitate the input of experts in the field. The current results, however, show that specific improvements are required to address the limitations of these models in the Turkish population. These efforts can enhance the value of risk prediction models and increase their utilization in clinical practice, thereby improving patient management and reducing costs.

In addition to determining cut-off values via ROC analyses, risk categories and calculated CR were assessed to further examine classification performances. Overall, the 'high risk' category of Alvarado resulted in the highest true positive rate (91.3%), while RIPASA, likely owing to its four-category classification approach, had the best CR values in all analyses. AAS also exhibited better CR compared with Alvarado and AIR, despite all three systems having three risk categories—revealing an important superiority. Therefore, utilizing RIPASA or AAS (and preferring AAS for immigrants) could be beneficial in the clinical setting, especially in high-volume centres where risk stratification can simplify and expedite patient management. It is also critical to note that the Alvarado and AIR systems, which were utilized by attending physicians, had the highest (worst) failure rates in overall analysis (47.3% and 46.6% respectively). These poor performances were largely associated with the exceptionally high failure rates in men (58.7 and 58% respectively).

An important factor to consider in this study was the restrictions on laparoscopic surgery due to the coronavirus disease (COVID)-19 pandemic³⁷. The impact is evident through the substantial high frequency of open surgeries (54.3%) when compared with the recommended laparoscopic approach⁷. During the initial waves of the pandemic, open surgery was prioritized in an attempt to ensure the safety of healthcare workers³⁷. Compared with the Prospective Observational Study on acute Appendicitis Worldwide (POSAW) study published in the pre-COVID era (116 surgical departments from 44 countries), the present study demonstrated a 10-12% shift towards open surgery preference. The RIFT Turkey data shows that 44.1% of the appendicectomies were performed laparoscopically (51.7% in POSAW), and 55.4% of the appendicectomies were open $(42.2\% \text{ in POSAW})^{38}$.

Diagnostic imaging data shows that 56.8% of patients admitted for RIF pain had undergone USG and 75.2% had undergone CT. Overuse of imaging could lead to long-term issues with regard to healthcare costs. A high proportion of USG examinations is relatively acceptable in RIF pain, due to patient-related needs and also the interobserver variability of USG in different centres and in the hands of different operators (radiologists, emergency physicians or surgeons). Nevertheless, it is rather evident that CT should not be the first choice to rule out acute appendicitis; it should be reserved only for select patients, particularly when USG results are uncertain. The present study demonstrates an extremely high frequency of CT use in Turkey, but this could again be associated with the reluctance to perform USG examinations during the pandemic. Indeed, another UK-based study has drawn attention to the increased use of CT during the COVID-19 pandemic (from 36.3% to 85.9%), which resulted in a significant decrease in NAR (from 21.7% to 7.1%)³⁹. Therefore, the overuse of CT may be another factor that reduced NAR in the present study.

Ultimately, the utilization of risk prediction models has been well documented to have positive effects in reducing unnecessary imaging tests, hospital admissions and surgeries^{4,36}. Therefore, the authors recommend implementation of appropriate risk prediction models in routine clinical practice for patients presenting with acute RIF pain or suspected acute appendicitis. A careful/sparing incorporation of imaging tests is necessary, and it appears that the RIPASA and AAS systems could yield considerable benefits in this regard if they were to be utilized more widely. The fact that the Alvarado and AIR systems had greater than 50% failure rates in men is a critical concern, given that these models are quite clearly the only models that have been formally applied to patients. It is worth noting that AAS was the only system that showed significance in ROC analysis for immigrants, which is a critical finding with potential implications for risk assessment and management strategies in diverse healthcare settings.

A total of 84 hospitals contributed to data collection, almost all of them being the highest volume centres from the largest cities of Turkey. The findings are therefore broadly generalizable across Turkey. Nonetheless, there are several limitations that deserve mention. The present study aimed to include all patients admitted with RIF pain, but inclusion was not done at triage. This creates potential for selection bias towards relatively typical RIF pain and could explain the high rate of surgical intervention (77.7%) and the failure of scoring systems in terms of ruling out appendicitis. Triage may also lead to the underrepresentation of women, as they may have been diverted for obstetric/ gynaecological assessment. However, it is critical to reiterate that all centres were secondary or tertiary healthcare institutions, ensuring uninterrupted availability of surgical teams. Second, epidemiological evidence suggests a weak but notable seasonal variation in appendicitis incidence⁴⁰. Collecting year-long data could improve generalizability, but maintaining high-quality data collection for extended intervals may prove challenging. Third, the primary ROC analyses were restricted to the surgical cohort (n = 2610) to create a single cut-off for testing the utility of scores in a real-world scenario, and thus, patients excluded based on clinical examination and those who received non-surgical appendicitis treatment were not included in this analysis. ROC data concerning the entire population has been provided in the Supplementary data. Finally, it is essential to acknowledge that the classification analyses may have obscured the utility of intermediary risk categories, because CR was calculated based on the highest and lowest risk groups. However, this approach creates a reliable ratio to assess the discriminatory capabilities of each system, particularly since it is feasible to suggest that the intermediary groups may not alleviate diagnostic uncertainty.

The present nationwide audit offers valuable insights regarding the characteristics of patients with RIF pain in Turkey, as well as the importance of using appendicitis risk scoring systems. This information can assist clinicians in making informed decisions, improving diagnostic accuracy and optimizing patient care. NAR was low overall (7%) with a similar result in immigrants (7.8%); however, NAR was around three-fold greater in women compared with men (11.3% versus 4.1%), indicating the need for improvement in the evaluation of women. Clinicians in Turkey may be overutilizing imaging tests, particularly CT, leading to increased healthcare costs. Follow-up studies are needed to determine whether the increased use of CT due to the COVID-19 pandemic is becoming an unnecessary trend. Based on the results, risk scoring systems could alleviate the financial burden associated with imaging tests, particularly if the superior RIPASA and AAS scoring systems are adopted. Moreover, AAS may serve as the best risk stratification tool for immigrants; however, further evidence is necessary before drawing generalizable conclusions for diverse populations.

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Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at BJS Open online.

Data availability

All data are available from the corresponding author upon reasonable request.

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Ali Yalcinkaya (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Writing-original draft, Writingreview & editing), Ahmet Yalcinkaya (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing-original draft, Writing-review & editing), Bengi Balci (Conceptualization, Data curation, Methodology, Writing-original draft, Writing-review & editing), Can Keskin (Data curation, Formal analysis, Investigation, Validation, Visualization, Writing—original draft, Writing—review & editing), Ibrahim Erkan (Data curation, Formal analysis, Investigation, Software, Validation, Writingoriginal draft, Writing—review & editing), Alp Yildiz (Data curation, Validation, Writing-review & editing), Erdinc Kamer (Conceptualization, Project administration, Supervision, Writing-review & editing) and Sezai Leventoglu (Conceptualization, Project administration, Resources, Supervision, Writing—review & editing).

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