Acta Biomed 2021; Vol. 92, N. 4: e2021231 DOI: 10.23750/abm.v92i4.11666 © Mattioli 1885

Review

Diagnosis of acute appendicitis based on clinical scores: is it a myth or reality?

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"An expert is a person who has made all the mistakes that can be made s in a very narrow field" (N. Bohr).

Introduction

Diagnosis of appendicitis is challenging, and some controversies on its management are still present among different settings and practice patterns worldwide. In April 2020, the World Society of Emergency Surgery (WSES) published the first update to the Jerusalem Guidelines on the diagnosis and treatment of acute appendicitis (1).

As common practice patterns vary widely across different settings, the statement concerning the need to perform imaging tests in order to confirm the clinical diagnosis of suspected appendicitis for patients with low or high Alvarado, AIR (Appendicitis Inflammatory Response) and AAS (Adult Appendicitis Score) scores was highly debated during the preliminary phases of the guidelines writing.

The final version of the statements on the topic is as follows:

"Clinical scores alone, e.g. Alvarado, AIR and the new Adult Appendicitis Score are sufficiently sensitive to exclude acute appendicitis, accurately identifying low-risk patients and decreasing the need for imaging and the negative appendectomy rates in such patients. We recommend the use of clinical scores to exclude acute appendicitis and identify intermediate-risk patients needing of imaging diagnostics [QoE: High; Strength of recommendation: Strong; 1A]."

"Patients with strong signs and symptoms and high risk of appendicitis according to AIR score/Alvarado score/AAS and younger than 40 years old may not require cross-sectional pre-operative imaging (i.e. CT scan). We suggest that cross-sectional imaging (i.e. CT scan) for high-risk patients younger than 40 years old (AIR score 9–12, Alvarado score 9–10, and AAS ≥ 16) may be avoided before diagnostic +/- therapeutic laparoscopy [QoE: Moderate; Strength of recommendation: Weak; 2B]."

In this review we have reported a summary of the contemporary evidence from the literature that led to these statements.

Material and Methods

A literature review with a focus on the diagnostic strategies of appendicitis, including the use of clinical scoring systems and diagnostic imaging was conducted. A systematic literature search was performed using MEDLINE (via PubMed), EMBASE, Google Scholar, and the Cochrane Central Register of Controlled Trials databases for studies published on the use of the most common clinical scores (Alvarado score, AIR score, AAS score) and imaging (CT scan, Ultrasound scan, MRI scan) for the diagnosis of appendicitis. Database-specific search terms for "Appendicitis","Alvarado score", "Appendicitis inflammatory response score","Adult appendicitis score", "Computed tomography", "Ultrasound scan", and "Magnetic Resonance Imaging" were combined using the Boolean operators AND, OR, NOT. The detailed search strategy is reported as supplementary material (Suppl. Material Table 1 in Appendix).

A systematic review of the literature was conducted according to the recommendations of the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (2).

Two different systematic search strategies were undertaken; one for articles that investigated the diagnostic strategy for the diagnosis of appendicitis based on clinical scoring systems, and the other for articles that investigate the diagnostic strategy based on imaging.

Literature search was concluded in January 2020, limited to articles in English language published after 2010 and focused on the analysis of previously published systematic reviews and randomized controlled trials assessing the strategies in adult patients. Only for the diagnostic strategies for which systematic reviews and randomized controlled trials were not available, the search was extended to non-randomized observational studies.

Two reviewers (M.P. and S.D.S.) independently screened titles and abstracts to identify appropriate articles for data extraction and discordances were resolved by mutual discussion. Study's first authors and year of publication, study type, target population, performed intervention, type of comparison, outcome and study's conclusion were extracted.

Results

Diagnosis of acute appendicitis based on clinical scores

A total of 199 references were initially identified. One-hundred and thirty-six searches were excluded through title and abstract screening. The remaining 63 publications were considered potentially appropriated to be included in the review and underwent full article review. A further 35 articles were excluded due to the reasons reported in the PRISMA flow-chart (Figure.1).

Ultimately, a total of 28 studies, published between 2008 and 2020 were included in this review (Tab.1 and Tab.2) (3-30).

Imaging is not cost-efficient in patients with low-probability of appendicitis because of high-risk for false positive results. These patients can be safely discharged home from the emergency room, or have their follow-up monitored at the outpatient clinic (11).

The randomized controlled trial by Andersson *et al* demonstrated that, in low-risk patients, the use of an AIR score-based algorithm resulted in less imaging (19.2% vs. 34.5%), fewer hospital admissions (29.5% vs. 42.8%), fewer negative surgical explorations (1.6% vs. 3.2%), and fewer operations for non-perforated appendicitis (6.8% vs. 9.7%) (23).

Although the Alvarado score is not sufficiently specific in diagnosing appendicitis, a cutoff score of <5 is sufficiently sensitive to exclude the disease (sensitivity of 99%). The Alvarado score could, therefore, be used to reduce emergency department length of stay and radiation exposure in patients with suspected appendicitis. This is confirmed by a large retrospective cohort study that found 100% of males with Alvarado score of 9 or greater and 100% of females with an Alvarado score of 10 had appendicitis confirmed by surgical pathology. Conversely, ≤5% of female patients with an Alvarado score of ≤2 and 0% of male patients with an Alvarado score of ≤1 were diagnosed with appendicitis at surgery (9).

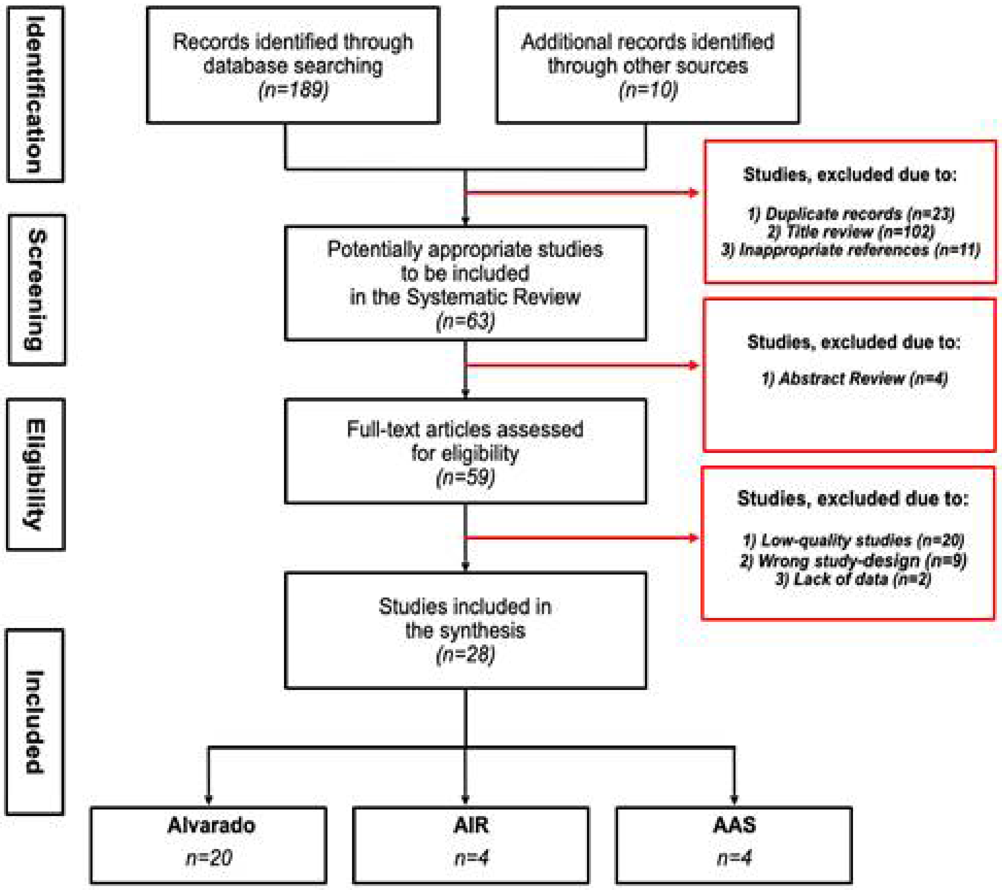

Figure 1. The PRISMA flow diagram for search and selection of articles included in the systematic review of studies that investigated the role of clinical scores in the diagnosis of acute appendicitis.

It is generally reckoned that patients with intermediate probability of appendicitis should undergo diagnostic imaging on a routine basis (1). However, the only randomized trial comparing immediate imaging with clinical reevaluation after a period of observation and selective imaging had better outcome in the observation/selective imaging arm (23).

The prevalence of appendicitis is about 90% in patients with high risk of appendicitis according to the Alvarado score, AAS score and AIR score (22, 26, 27). In the study by Scott *et al*, an AIR score ≥9 was very specific (97%) for appendicitis and the majority of patients with appendicitis in the high-risk group (70%) had perforation or gangrene (24). The study by Kollar *et al* comparing the performance of the AIR Score in predicting risk of appendicitis to both the Alvarado score and the clinical impression of a senior surgeon showed that the AIR score was more accurate at predicting the disease than the Alvarado score in patients deemed high-risk. The three methods of assessment stratified similar proportions of patients to a low-probability of appendicitis, with a false negative rate of <8% that did not differ between the AIR score, Alvarado score or the experienced surgeons clinical assessment. Conversely, the AIR score assigned a smaller proportion of patients to the high-probability zone than the Alvarado score (14 vs. 45%) but it did so with a substantially higher specificity (97%) and positive predictive value (88%) than the Alvarado score (76% and 65%, respectively) (4).

In the validation study by Sammalkorpi *et al*, the AAS was implemented in the diagnostic workup of adult patients suspected of appendicitis, of whom 48% indeed had appendicitis. The AAS score

Table 1. Evidence from the literature: Diagnosis of acute appendicitis based on clinical scores (comparative studies).

Study, year	Study Design	Population	Intervention	Comparison	Outcome	Conclusion
Elsherbiny MW, 2020	Prospective	200 patients with acute appendicitis	Alvarado score + Ultrasound	Ultrasound alone; Alvarado score alone	Alvarado score alone: Sensitivity 56.8%; Specificity 91.7%; Accuracy 61%. Ultrasound alone: Sensitivity 71.6%; Specificity 79.2%; Accuracy 72.5%. Combined Alvarado score + Ultrasound: Sensitivity 68.4%; Specificity 100%; Accuracy 71.9%	Alvarado score is specific in detection of appendicitis and could identify all patients with normal appendix
Kollár D, 2015	Prospective	182 patients with acute right iliac fossa pain	AIR and Alvarado scores; clinical assessment	Final diagnosis of appendicitis	The three methods stratified similar proportion (40%) of patient to a low probability of appendicitis. False negative rate was <8% for the three methods. The AIR score assigned patients to the high probability zone with a higher specificity and positive predictive value than the Alvarado score (97% vs. 76%; 88% vs. 65%)	The AIR score is accurate at excluding appendicitis in patients deemed low risk and more accurate at predicting appendicitis than the Alvarado score in those deemed high risk. Its use as the basis for selective CT imaging in those deemed medium risk should be considered
Mán E, 2014	Prospective, randomized	269 patients with suspected appendicitis	Alvarado score	Clinical judgment	Negative appendectomy rate: Alvarado score 9.15% (specificity 88.9%); Clinical judgment 3.6% (specificity 94.8%)	Clinical judgment is more reliable in the diagnosis of acute appendicitis than the Alvarado score
Damburaci N, 2019	Prospective	100 patients with a clinical diagnosis of appendicitis	Alvarado score	RIPASA score	Modified Alvarado <5.5: Sensitivity 88.09%; Specificity 68.7%; Positive predictive value 93.6%; Negative predictive value 31.2%; Accuracy 73.4%. RIPASA >8.75: Sensitivity 94.04%; Specificity 87.5%; Positive predictive value 97.5%; Negative predictive value 12.5%; Accuracy 85.2%	RIPASA scoring system was found to be superior to modified Alvarado in the prediction of cases with appendicitis
Tan WJ, 2020	Prospective, randomized	160 patients with suspected appendicitis	Alvarado score	Current practice	Overall CT utilization: 93.7% (Alvarado) and 92.5% (current practice). Negative appendectomy rate: 12.5% (Alvarado) and 10% (current practice); Missed diagnosis: 0% in both arms	The Alvarado score-based management algorithm did not reduce the CT utilization rate. Missed diagnoses, negative appendectomy rates, length of stay, and cost of stay were also similar

Study, year	Study Design	Population	Intervention	Comparison	Outcome	Conclusion
Apisarnthanarak P, 2014	Retrospective	158 patients with a clinical diagnosis of appendicitis	Alvarado score	CT scan	Acute appendicitis was confirmed in 13.3% of patients with low probability Alvarado score, 30.8% of patients with equivocal scores, and 60.4% of patients with high probability scores. The accuracy, sensitivity, specificity, positive predictive value and negative predictive value of CT scan were: 97.5%, 98.6%, 96.5%, 96.0% and 98.8%	CT scan had high diagnostic utility for appendicitis. The Alvarado score was not a reliable independent predictive tool for appendicitis and could not replace CT scan
Coleman JJ, 2018	Retrospective	492 patients who underwent CT to rule out appendicitis	Alvarado score	CT scan	Median Alvarado score for appendicitis on CT scan was 7, compared to 3 for negative CT. 100% of female patients with Alvarado score=10 and males with Alvarado score≥9 had appendicitis confirmed by surgical pathology. ≤5% of female patients with ≤2 and 0% of male patients with Alvarado score ≤1 were diagnosed with appendicitis	Males with an AS of ≥ 9 and Females with AS of 10 should be considered for treatment of appendicitis without imaging. Males with AS ≤ 1 and females with AS ≤ 2 can be safely discharged with follow-up
Golden SK, 2017	Prospective	287 patients with abdominal pain who had a CT for suspected appendicitis	Alvarado score	Modified Alvarado score; RIPASA score; Physician-determined likelihood of appendicitis	The Alvarado score had a positive likelihood ratio of 2.2, and a negative likelihood ratio of 0.6. The modified Alvarado score had a positive likelihood ratio of 2.4 and a negative likelihood ratio of 0.7. The RIPASA score had a positive likelihood ratio of 1.3, and a negative likelihood ratio of 0.5. Physician-determined likelihood of appendicitis had a positive value of 1.3, and a negative value of 0.3	Clinical scores do not obviate the need for imaging for possible appendicitis when a surgeon deems it necessary
Jones RP, 2015	Retrospective	119 patients for whom the appendix was not seen on ultrasonography	Alvarado score	CT scan	0% of patients with Alvarado ≤3 had appendicitis, compared with 17.1% of patients with Alvarado scores 4 or higher. CT showed neither appendicitis nor significant alternative findings in 85.7% of patients with Alvarado ≤3	Adults with Alvarado score ≤3 are not likely to benefit from CT

Table 1. (*continued*)

Study, year	Study Design	Population	Intervention	Comparison	Outcome	Conclusion
Karami MY, 2017	Prospective	100 patients with right iliac fossa pain and suspected appendicitis	Alvarado score	AIR score; RIPASA score	Alvarado score >7: Sensitivity 78.4%; Specificity 100%; Positive predictive value 100%; Negative predictive value 38.7%. AIR score >4: Sensitivity 78.4%; Specificity 91.6%; Positive predictive value 98.5%; Negative predictive value: 36.6%. RIPASA score >8: Sensitivity 93.1%; Specificity: 91.6%; Positive predictive value: 98.8%; Negative predictive value: 64.7%	The RIPASA score had higher sensitivity and better negative predictive value for the Iranian population. The Alvarado score was more specific
Meltzer AC, 2013	Prospective	261 patients with suspected appendicitis	Alvarado score	Clinical judgment	The modified Alvarado score showed a sensitivity of 72% and a specificity of 54%. Unstructured clinical judgment demonstrated a sensitivity of 93% and a specificity of 40%	A low modified Alvarado score is less sensitive than clinical judgment in excluding appendicitis
Memon ZA, 2013	Retrospective	110 patients with a preliminary diagnosis of appendicitis	Alvarado score	-	Alvarado score: Sensitivity 93.5%; Specificity 80.6%. Positive and negative predictive values were 92.3% and 83.3%, respectively. Accuracy was 89.8%. Alvarado score ≥9 = 100% Sensitivity; Alvarado score 7-8= 94.1% Sensitivity. Alvarado score 5-6= 60% Sensitivity	Alvarado score can be used to reduce the incidence of negative appendectomies
Nelson DW, 2013	Retrospective	664 patients scheduled for surgery with the presumed diagnosis of appendicitis	Alvarado score	CT scan	Higher Alvarado scores (7-10) were significantly associated with pathologically confirmed appendicitis (96%). The negative appendectomy rate for patients with clinical assessment consistent with appendicitis was 4%, compared with 3% associated with CT	A surgeon's clinical assessment with Alvarado score can reliably diagnose acute appendicitis unaided by CT in highly suspicious cases of appendicitis
Reddy SB, 2017	Retrospective	300 patients with suspected appendicitis	Ultrasound score + Alvarado	-	The combined score demonstrated 98% sensitivity and 82% specificity at 6.5, and 95% sensitivity and 87% specificity at a score of 7.5. The combined Ultrasound and Alvarado score yielded an area under the ROC curve of 97.1	The combined Ultrasound-Alvarado score might replace the need for CT imaging in a majority of patients

Study, year	Study Design	Population	Intervention	Comparison	Outcome	Conclusion
Singla A, 2016	Prospective	50 patients presenting with right iliac fossa pain	Alvarado score	RIPASA score	Alvarado: sensitivity of approximately 53% at the specificity of 100% (the cut-off score having maximum sensitivity and specificity came to be 4.5); RIPASA: sensitivity of 95.6% at the specificity of 80% (the cut-off score having maximum sensitivity and specificity came to be 8.0)	The RIPASA score correctly classified 88% of patients with histologically confirmed appendicitis, compared with 48% with Alvarado score
Tan WJ, 2013	Retrospective	358 patients with suspected appendicitis	Alvarado score	CT scan	Patients who underwent CT evaluation had a negative appendectomy rate of 5.7% compared to 17.9% in those without CT evaluation. CT scan had a sensitivity and specificity of 92.6% and 96.9%, respectively. An Alvarado score >3 had a sensitivity superior to CT (95.5%), while an Alvarado score ≥9 had a specificity superior to CT (100%)	In suspected appendicitis, patients who benefit from CT evaluation are those with an Alvarado score ranging from 4 to 8
Tan WJ, 2015	Prospective	350 patients with suspected appendicitis who were evaluated with CT scan	Alvarado score	CT scan	Alvarado scores ≥7 in males (AS >7, p=0.513; AS ≥8, p=0.442; AS ≥9, p=0.398; AS ≥10, p=0.896) and ≥9 in females (AS ≥9, p=0.513; AS ≥10, p=0.638) have a positive likelihood rations comparable to those of CT scan	Evaluation by CT is beneficial mainly in patients with Alvarado score of ≤6 in males and ≤8 in females
Wang SY, 2012	Prospective	60 patients with suspected appendicitis and an Alvarado score of 4-7	Alvarado score	CT scan	There were statistically significant difference in WBC count and neutrophilia between patients with Alvarado score 4-7 with histologically proven appendicitis vs. non-appendicitis	CT is necessary for patients with Alvarado score 4-7 when leukocytosis is noted

Table 1. (*continued*)

Study, year	Study Design	Population	Intervention	Comparison	Outcome	Conclusion
Shuaib A, 2017	Retrospective	136 patients who underwent appendectomies	Alvarado score	RIPASA	A cut-off threshold point of the Alvarado score set at 7.0 yielded a sensitivity of 82.8% and a specificity of 56%. The positive predictive value was 89.3% and the negative predictive value was 42.4%. A cut-off threshold point of the RIPASA score set at 7.5 yielded a 94.5% sensitivity and 88% specificity. The positive predictive value was 97.2% and the negative predictive value was 78.5%. The negative appendectomy rate was 10.7% for the modified Alvarado score and 2.2% for the RIPASA score	The RIPASA score has a better sensitivity and specificity than the modified Alvarado scoring system in Asian populations
Andersson M, 2008	Prospective	545 patients with suspected appendicitis	AIR score	Alvarado score	The ROC area of the AIR score was 0.97 for advanced appendicitis and 0.93 for all appendicitis, compared with 0.92 (p=0.0027) and 0.88 (p=0.0007), respectively, for the Alvarado score. 63% of the patients were classified into the low- or high- probability groups with an accuracy of 97.2%. 73% of the non-appendicitis patients, 67% of the advanced appendicitis, and 37% of all appendicitis patients were correctly classified into the low- and high-probability zone, respectively	The AIR score can correctly classify the majority of patients with suspected appendicitis, leaving the need for diagnostic imaging or laparoscopy to the smaller group of patients with an indeterminate scoring result
Andersson M, 2017	Prospective, randomized	2639 patients with suspected appendicitis in the intervention period	AIR score	Routine imaging – intermediate risk zone -	In low-risk patients, use of the AIR score-based algorithm resulted in less imaging (19.2% vs. 34.5%, p< 0.001), fewer admissions (29.5% vs. 42.8%, p< 0.001), fewer negative explorations (1.6% vs. 3.2%, p= 0.030) and operations for non-perforated appendicitis (6.8% vs. 9.7%, p= 0.034). Intermediate-risk patients randomized to imaging and observation had the same proportion of negative appendectomies (6.4% vs. 6.7%, p= 0.884), but routine imaging was associated with an increased proportion of patients treated for appendicitis (53.4% vs. 46.3%, p= 0.020)	The AIR score-based risk classification can safely reduce the use of diagnostic imaging and hospital admission in patients with suspicion of appendicitis

Study, year	Study Design	Population	Intervention	Comparison	Outcome	Conclusion
Scott AJ, 2015	Prospective	464 patients with suspected appendicitis	AIR score	Ultrasound/CT scan	63.3% of patients with non-appendicitis were correctly classified as low risk. Low-risk patients accounted for 57% of negative explorations and 50.7% of imaging requests. An AIR score ≥5 (intermediate and high risk) had high sensitivity for all severities of appendicitis (90%) and also for advanced appendicitis (98%). An AIR score ≥9 (high risk) was very specific (97%) for appendicitis, and the majority of patients with appendicitis in the high-risk group (70%) had perforation or gangrene. Ultrasound imaging could not exclude appendicitis in low-risk patients, but could rule-in the diagnosis in intermediate-risk patients. CT could exclude appendicitis in low-risk patients and rule-in appendicitis in the intermediate group	Risk stratification of patients with suspected appendicitis by the AIR score could guide decision-making to reduce admissions, optimize utility of diagnostic imaging and prevent negative explorations.
Sammalkorpi HE, 2014	Prospective	829 with clinical suspicion of appendicitis	AAS score	Alvarado score; AIR score	58% of patients had score value ≥16 and were classified as high probability group with 93% specificity. Only 4% of patients had a score <11, and non of them had complicated appendicitis. 54% of non-appendicitis patients had score <11. There were no cases with complicated appendicitis in the low probability group. The area under ROC curve was significantly larger with the AAS (0.882) compared with that of Alvarado score (0.790) and AIR score (0.810)	The AAS score identifies a relatively small (38%) group of patients that would benefit from further diagnostic imaging
Sammalkorpi HE, 2017	Prospective	908 patients with suspected appendicitis	AAS score	-	The AAS stratified 49% of all appendicitis patients into high-risk group, with specificity of 93.3%. In the low-risk group, prevalence of appendicitis was 7%. The histologically confirmed negative appendectomy rate decreased from 18.2% to 8.7% ($p < 0.001$)	The AAS score results in low negative appendectomy rate

Table 1. (*continued*)

Study, year	Study Design	Population	Intervention	Comparison	Outcome	Conclusion
Sammalkorpi HE, 2017	Prospective	822 patients who underwent diagnostic imaging for suspected appendicitis	AAS score	Ultrasound/CT scan	Probability of appendicitis for patients in the high-risk group was 92.6% without any imaging, 78.9% with CT scan, 78.8% with ultrasound scan; Probability of appendicitis for patients in the intermediate-risk group was 51.7% without any imaging, 50% with CT scan, 47.3% with ultrasound scan; Probability of appendicitis for patients in the low-risk group was 2.2% without any imaging, 16.2% with CT scan, 9.1% with ultrasound scan	Diagnostic imaging has limited value in patients with low probability of appendicitis according to AAS
RIFT study group, 2020	Prospective – Systematic Review	5345 patients with right iliac fossa pain	15 different scores	-	The AAS performed best (cut-off score ≤8, specificity 63.1%, failure rate 3.7%). The AIR score performed best for men (cut-off score ≤2, specificity 24.7%, failure rate 2.4%)	Risk prediction models may act as adjuncts to serial clinical assessment of patients, rationalizing exposure to ionizing radiation to those patients most likely to benefit from CT

AIR= Appendicitis Inflammatory Response (score); **AAS**= Adult Appendicitis Score; **RIPASA**= Raja Isteri Pengiran Anak Saleha Appendicitis (score); **ROC**= Receiver Operator Curve.

Table 2. Evidence from the literature: Diagnosis of acute appendicitis based on clinical scores (systematic reviews).

Study, year	Study Design	Population	Intervention	Comparison	Outcome	Conclusion
Frountzas M, 2018	Meta-analysis	20 studies, 2.161 patients	Alvarado score	RIPASA score	The sensitivity of RIPASA score was 94%, and the specificity was 55%. The area under the ROC curve was 0.9431 and the diagnostic Odds Ratio was 24.66. The sensitivity of Alvarado score was 69% and the specificity was 77%. The area under the ROC curve was 0.7944 and the diagnostic Odds Ratio was 7.99	RIPASA scoring system is more sensitive than Alvarado. The use of both tests is recommended in health systems that lack imaging tests, such as developing countries and rural hospitals
Kularatna M, 2017	Systematic review	34 studies	AIR score	Alvarado score, RIPASA score	The overall best performer in terms of sensitivity (92%), specificity (63%) and area under the ROC curve values (0.84-0.97) was the AIR score, but only a limited number of studies investigated at this score	There are 12 clinical scores available for diagnosis of appendicitis in adults. The AIR score appeared to be the best performer

AIR= Appendicitis Inflammatory Response (score); **RIPASA=** Raja Isteri Pengiran Anak Saleha Appendicitis (score); **ROC=** Receiver Operator Curve.

high-probability group (AAS ≥16) comprised 439 patients of whom 386 (87.9%) indeed had an appendicitis at surgery. Using only the AAS score and no imaging the post-test probability for appendicitis increased to 92.6%, equivalent to a negative appendectomy rate of 7.3%. In the high probability group, CT was performed in only 26% of patients, and CT pretest probability of appendicitis increased from 78.9% to a 98.9% post-test probability for a positive CT and 0% for a negative CT, equivalent to a negative appendectomy rate of 1.1% (28).

Previous decision models demonstrated that the most cost-effective diagnostic strategy is dependent on risk-stratification carried out by clinical scores. At a prevalence <16% and >95% patients may forego imaging completely. For patients with a risk of acute appendicitis between 16% and 67%, it is cost-effective to perform an initial US and forego additional imaging if the US does not visualize the appendix but shows no secondary signs of inflammation. Conversely, when the pretest probability of acute appendicitis is >67% but <95%, it is cost-effective to follow-up all non-visualized US with a CT even without secondary signs of inflammation on US (31).

Diagnosis of acute appendicitis based on imaging

A total of 97 references were initially identified. Sixteen searches were excluded through title and abstract screening. The remaining 81 publications were considered potentially appropriated to be included in the review and underwent full article review. A further 67 articles were excluded due to the reasons reported in the PRISMA flow-chart (Figure.2).

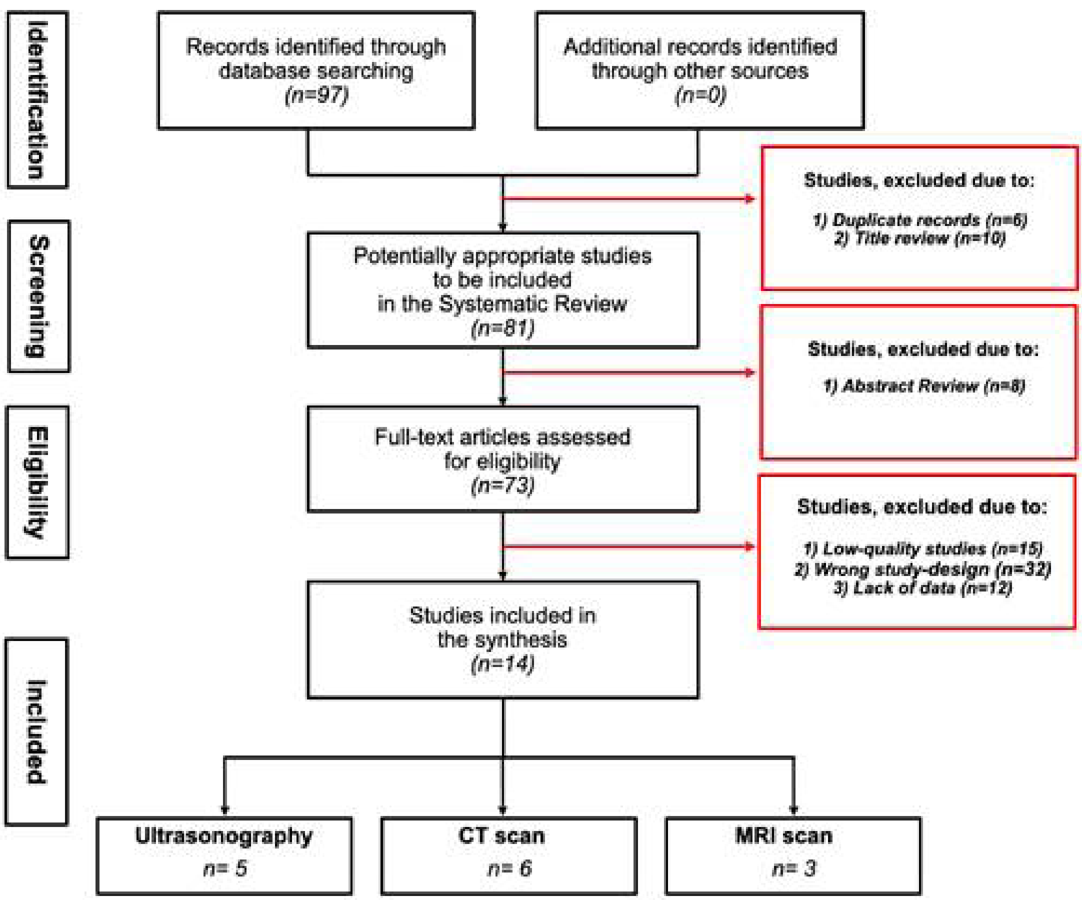

Figure 2. The PRISMA flow diagram for search and selection of articles included in the systematic review of studies that investigated the role of diagnostic imaging for acute appendicitis.

Ultimately, a total of 14 studies, published between 2011 and 2019 were included in this review (Tab.3 and Tab.4) (32-45).

Before CT was used for the diagnosis of appendicitis, 20% of patients taken to surgery had a normal appendix. Only after CT availability, negative appendectomy rate has lowered overall (20% to 7%), in men (11% to 5%), in women (35% to 11%), in boys (10% to 5%), and in girls (18% to 12%) (46).

The sensitivity and specificity of CT is reported at 0.91-0.94 and 0.90-0.95 in systematic reviews. The corresponding results for US are 0.78-0.88 and 0.81-0.94, respectively (41, 47).

Two approaches have been proposed to reduce the radiation exposure that is associated with CT scans. A low dose CT scan can give almost identical sensitivity and specificity as conventional standard dose CT scan (0.945 and 0.933 vs 0.95 and 0.938, respectively). Kim *et al* in 2012 demonstrated that low-dose CT scan has become the gold standard preoperative test for diagnosing acute appendicitis in young adults. The reported negative appendectomy rate in this study is 3.5% in the low-dose CT group and 3.2% in the standard-dose CT group. The two groups do not differ significantly in terms of the appendiceal perforation rate (26.5% with low-dose CT and 23.3% with standard-dose CT) or the proportion of patients who needed additional imaging tests (3.2% and 1.6%) (34). The alternative is represented by conditional (or staged) imaging strategies, starting with US in all patients followed by CT scan in patients with a negative or inconclusive US examination. The diagnostic potential of this strategy has been evaluated in simulation models from data in patients having both US examination and CT scan, with sensitivity 0.94-0.97 and specificity 0.68-0.91 (48). The recently published Cochrane systematic review on CT scan for diagnosis of appendicitis in adults identifies, in subgroup analyses according to contrast enhancement, that summary sensitivity for low-dose CT (0.94) is similar to summary sensitivity for standard-dose or unspecified-dose CT (0.95) and specificity does not differ between low-dose and standard-dose or unspecified-dose CT (36).

MRI has at least the same sensitivity and specificity as CT and, although has higher costs and issues around availability in many centers, should be preferred over CT as a first-line imaging study in pregnant women. In fact, the sensitivity and specificity of MRI for the diagnosis of acute appendicitis are 96% and 96%, respectively. In pregnant patients, the sensitivity and specificity of MRI are 94% and 97%, respectively, whereas in children, sensitivity and specificity are 96% and 96%, respectively.

Based on the mean of the sensitivity and specificity cited above, the posterior probability of a positive test (the probability a patient will have an appendicitis after all information from an US, CT, or MRI scan has been taken into account) would be 0.98-0.99 in all the imaging strategies. Thus, a positive diagnostic imaging can confirm the diagnosis with very high certainty. Conversely, the posterior probability after a negative imaging test would be from 0.35 in the best scenario, to negative 0.64 in the worst. A CT scan or a conditional US/CT strategy in patients with high probability of appendicitis thus cannot rule out appendicitis with sufficiently high accuracy. Therefore, routine imaging will give an important proportion of patients with false negatives and the surgeon is still left with an important proportion of patients with continuing symptoms indicating a need for intervention. For the majority of patients in the high-risk group an abdominal exploration, starting with diagnostic laparoscopy, could be indicated. For this subgroup of patients, in fact, imaging could be avoided starting from the assumption that such patients suffer from intra-abdominal sepsis of any origin. CT may be motivated to detect alternative causes, but those are rare in young male patients with right iliac fossa pain, and it may not add any useful information for avoiding exploration. However, when the surgeon deems diagnostic imaging is still needed to confirm appendicitis despite the patient has been scored at high-risk, a conditional CT scan strategy may be advised, with CT scan performed only after a negative or equivocal US (1).

Future perspectives: artificial intelligence

Recently, many studies presented different methods for automatic diagnosis of appendicitis, as well as the differentiation between complicated and uncomplicated forms using values/parameters which are

Table 3. Evidence from the literature: Imaging-guided diagnosis of acute appendicitis (comparative studies).

Study, year	Study Design	Population	Intervention	Comparison	Outcome	Conclusion
Lietzén E, 2017	Prospective, randomized	1.065 patients with suspected acute appendicitis	CT scan performed by consultants	CT scan performed by residents	The sensitivity and the specificity of CT scan were 96.7% and 95.9%, respectively. The rate of false CT diagnosis was 4.2% for experienced consultant radiologists and 2.2% for inexperienced resident radiologists (p=0.071)	The experience of the radiologist had no effect on the accuracy of CT diagnosis. The results emphasize the role of CT as an accurate modality in daily routine diagnostics for appendicitis in all clinical emergency settings.
Jones R, 2019	Prospective, randomized	68 patients with atypical right iliac fossa pain	CT scan (unenhanced)	Serial physical examination with/without Ultrasound scan	CT was associated with superior diagnostic accuracy, with 100% positive and negative predictive value. In the CT arm, there was a lower negative laparoscopy rate	Patients with atypical right iliac fossa pain may benefit from CT
Kim K, 2012	Prospective, randomized	891 patients with suspected appendicitis. 444 patients were randomly assigned to low-dose CT, and 447 to standard-dose CT	Low-dose CT scan	Standard-dose CT scan	The negative appendectomy rate was 3.5% in the low-dose CT group and 3.2% in the standard-dose CT group. The two groups did not differ significantly in terms of the appendiceal perforation rate (26.5% with low-dose CT and 23.3% with standard-dose CT) or the proportion of patients who needed additional imaging tests (3.2% and 1.6%, respectively)	Low-dose CT was non-inferior to standard-dose CT with respect to negative appendectomy rates in young adults with suspected appendicitis
Sippola S, 2020	Prospective, randomized	60 patients with suspected appendicitis and BMI <30 Kg/M^2 were enrolled to undergo both standard and low-dose contrast enhanced CT scan	Low-dose CT scan	Standard-dose CT scan	The low-dose protocol was not inferior to standard protocol in terms of diagnostic accuracy: 79% accurate diagnosis in low-dose and 80% in standard CT. Accuracy to categorize appendicitis severity was 79% for both protocols. The mean radiation dose of low-dose CT was significantly lower compared with standard CT (3.33 and 4.44 mSv, respectively)	Diagnostic accuracy of contrast enhanced low-dose CT was not inferior to standard CT in diagnosing acute appendicitis or distinguishing between uncomplicated and complicated acute appendicitis in patients with a high likelihood of acute appendicitis. Low-dose CT enabled significant radiation dose reduction

BMI= Body Mass Index; **mSv=** milliSievert.

Table 4. Evidence from the literature: Imaging-guided diagnosis of acute appendicitis (systematic reviews).

Study, year	Study Design	Population	Intervention	Comparison	Outcome	Conclusion
Carroll PJ, 2013	Systematic review and Meta-analysis	8 studies, with a total of 1.268 patients	Ultrasound scan	-	Surgeon-performed Ultrasound scan had a pooled sensitivity of 0.92 and a pooled specificity of 0.96	Surgeon-performed Ultrasound offers promise as a sensitive and specific modality for the detection of appendicitis, potentially obviating the need for Radiologist-performed Ultrasound
Eng KA, 2018	Systematic review and Meta-analysis	Adults: Ultrasound (3 studies, 169 patients); CT (11 studies, 1027 patients); MRI (6 studies, 427 patients). Second-line imaging after initial Ultrasound for assessing appendicitis	Ultrasound scan	CT scan; MRI scan	Ultrasound: the pooled sensitivity and specificity were 83.1% and 90.9%, respectively; CT scan: pooled sensitivity and specificity were 89.9% and 93.6%, respectively; MRI scan: pooled sensitivity and specificity were 89.9% and 93.6%, respectively	Second-line US, CT, and MRI have high accuracy in helping to diagnose appendicitis in children and adults, including pregnant women
Fields JM, 2017	Systematic review and Meta-analysis	21 studies, with a total of 6.636 patients	Point-of-care Ultrasound scan (POCUS)	-	The sensitivity and specificity for POCUS in diagnosing appendicitis were 91% and 97%, respectively. The positive and negative predictive values were 91% and 94%, respectively. Studies performed by emergency physicians had slightly lower test characteristics (sensitivity= 80%, specificity= 92%)	POCUS is an appropriate initial imaging modality for diagnosing appendicitis
Giljaca V, 2016	Systematic review and Meta-analysis	17 studies, with 2.841 included patients	Ultrasound	-	The summary sensitivity and specificity of Ultrasound for diagnosis of appendicitis were 69% and 81%, respectively. At the median pretest probability of appendicitis of 76.4%, the post-test probability for a positive and negative result of Ultrasound was 92% and 55%, respectively	Ultrasound does not seem to have a role in the diagnostic pathway for diagnosis of appendicitis Patients that require additional diagnostic workup should be referred to CT scan

Table 4. (*continued*)

Study, year	Study Design	Population	Intervention	Comparison	Outcome	Conclusion
Shen G, 2019	Systematic review and Meta-analysis	27 studies, with 7.403 included patients	Ultrasound scan (Bedside)	-	Bivariate analysis yielded a mean sensitivity of 90% and specificity of 95%. The area under the ROC curve was 0.97	Bedside Ultrasound scan provides superior diagnostic performance in the diagnosis of appendicitis
Rud B, 2019	Systematic Review and Meta-analysis	64 studies including 71 separate study populations, with a total of 10.280 patients	CT scan	-	Sensitivity ranged from 0.72 to 1.0 and specificity ranged from 0.5 to 1.0. Summary sensitivity was 0.95, and summary specificity was 0.94. At the median prevalence of appendicitis (0.43), the probability of having appendicitis following a positive CT result was 0.92, and the probability of having appendicitis following a negative CT result was 0.04. Sensitivity was higher for CT with intravenous contrast (0.96), CT with rectal contrast (0.97), and CT with intravenous and oral contrast enhancement (0.96) than for unenhanced CT (0.91). Summary sensitivity of CT with oral contrast enhancement (0.89) and unenhanced CT was similar. Summary sensitivity for low-dose CT (0.94) was similar to summary sensitivity for standard-dose or unspecified-dose CT (0.95). Summary specificity did not differ between low-dose and standard-dose or unspecified-dose CT	The sensitivity and specificity of CT for diagnosing appendicitis in adults are high. Use of different types of contrast enhancement or no enhancement does not appear to affect specificity. Differences in sensitivity and specificity between low-dose and standard-dose CT appear to be negligible
Krajewski S, 2011	Systematic review and Meta-analysis	28 studies, with 9.330 included patients	CT scan	Clinical evaluation	The negative appendectomy rate was 8.7% when using CT compared with 16.7% when using clinical evaluation alone ($p < 0.001$). Appendiceal perforation rates were unchanged by the use of CT (23.4% in the CT group vs. 16.7% in the clinical evaluation group, $p = 0.15$)	The use of preoperative abdominal CT is associated with lower negative appendectomy rates. Routine CT in all patients presenting with suspected appendicitis could reduce the rate of unnecessary surgery without increasing morbidity

Table 4. (*continued*)

Study, year	Study Design	Population	Intervention	Comparison	Outcome	Conclusion
Repplinger MD, 2016	Systematic review and Meta-analysis	10 studies, with 838 included patients	MRI scan	-	The summary sensitivity of MRI was 96.6%, and summary specificity was 95.9%	MRI has a high sensitivity and specificity for the diagnosis of appendicitis, similar to that reported previously for CT scan
Kave M, 2019	Systematic review and Meta-analysis	19 studies, with 2.400 pregnant women suspected of appendicitis	MRI scan	-	MRI sensitivity was 91.8%. The specificity was 97.9%	MRI is an excellent imaging technique in pregnant patients with suspected appendicitis. It does not expose a fetus, or the mother, to ionizing radiation
Duke E, 2016	Systematic review and Meta-analysis	30 studies, that comprised 2.665 patients	MRI scan	-	The sensitivity and specificity of MRI for the diagnosis of acute appendicitis are 96% and 96%, respectively. In pregnant patients, the sensitivity and specificity of MRI were 94% and 97%, respectively. In children, sensitivity and specificity were found to be 96% and 96%, respectively	MRI has a high accuracy for the diagnosis of acute appendicitis, including subgroup populations of children and pregnant patients. It may be considered as a first-line imaging test that avoids the potential risk for exposure to ionizing radiation

MRI= Magnetic Resonance Imaging; **ROC=** Receiver Operating Characteristic; **POCUS=** Point-of-care Ultrasound scan.

routinely and unbiasedly obtained for each patient with suspected acute appendicitis (49).

The study by Park *et al* showed that models using artificial neural networks performed significantly better than the Alvarado clinical scoring system. The accuracy of the models ranged from 99.80% to 97.84%, whereas that of Alvarado was 72.19%. The area under the ROC curve of these artificial models and Alvarado was 0.998 and 0.633, respectively (50). Artificial intelligence in this field has shown comparable performance to physician chart reviewers as measured by their inter-annotator agreement and represents a promising new approach for computerized decision support to promote application of evidence-based medicine.

Conclusions

Alvarado score, AIR score, and the new AAS score are sensitive enough to exclude appendicitis, accurately identifying low-risk patients and decreasing the need for imaging and the negative appendectomy rate in these patients. Controversy exists regarding the role of imaging in patients with high-probability of appendicitis. Because of the high prevalence of the disease in this group of patients (~90%) a negative imaging scan cannot rule out appendicitis.

Based on this evidence, laparoscopic abdominal exploration without imaging may be an option in young patients who have been scored as having high probability for appendicitis.

Contributions of authors. All Authors contributed equally in the study conception and design, literature search, drafting and critically revising the article for important intellectual content, and final approval of the version to be published.

Conflicts of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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Received: 1 April 2021
Accepted: 26 April 2021
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APPENDIX

Suppl. Material Table 1.

Search strategy.
Search:((CT scan[Title/Abstract] OR (Computed tomography[Title/Abstract])) AND (Appendicitis[Title/Abstract]) Filters: Meta-Analysis, Randomized Controlled Trial, in the last 10 years Sort by: Most Recent
Search:((Ultrasound[Title/Abstract]) OR (Ultrasonography[Title/Abstract]) AND (Appendicitis[Title/Abstract]) Filters: Meta-Analysis, Randomized Controlled Trial, in the last 10 years Sort by: Most Recent
Search:((MRI) OR (magnetic resonance)) AND (appendicitis) Filters: Meta-Analysis, Randomized Controlled Trial, Systematic Review, in the last 10 years Sort by: Most Recent ("magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields] OR "MRI"[All Fields] OR ("magnetic resonance spectroscopy"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "spectroscopy"[All Fields]) OR "magnetic resonance spectroscopy"[All Fields] OR ("magnetic"[All Fields] AND "resonance"[All Fields]) OR "magnetic resonance"[All Fields])) AND ("appendiceal"[All Fields] OR "appendicitis"[MeSH Terms] OR "appendicitis"[All Fields])
Search:((Appendicitis inflammatory response score[Title/Abstract] AND (Appendicitis[Title/Abstract])) NOT (children[Title/Abstract]) Sort by: Most Recent
Search:((Adult appendicitis score[Title/Abstract] AND (Appendicitis[Title/Abstract])) NOT (children[Title/Abstract]) Sort by: Most Recent
Search:((Alvarado[Title/Abstract]) AND (appendicitis[Title/Abstract])) NOT (children)[Title/Abstract]) Filters: in the last 10 years Sort by: Most Recent