Predictive values of indirect ultrasound signs for low risk of acute appendicitis in paediatric patients without visualisation of the appendix on ultrasound

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ABSTRACT

Background and objectives The ability to rule appendicitis in or out using ultrasound is limited by studies where the appendix is not visualised. We determined whether the absence of indirect ultrasound signs can rule out appendicitis in children undergoing a radiology-performed ultrasound in which the appendix is not visualised

Methods This was a single-centre retrospective observational study of patients aged 3–13 with a clinical suspicion of acute appendicitis evaluated in a Paediatric Emergency Department in Spain from 1 January 2013 to 31 December 2019. For those patients who had formal ultrasound, direct and indirect findings of ultrasound were abstracted from the ultrasound report. The surgical pathology report was established as the gold standard in patients who underwent an appendectomy. In those who did not, appendicitis was considered not to be present if there was no evidence in their charts that they had undergone an appendectomy or conservative therapy for appendicitis during the episode. The main outcome variable was the diagnosis of acute appendicitis. For patients undergoing ultrasound, the independent association of each indirect ultrasound sign with the diagnosis of appendicitis in patients without a visualised appendix was analysed using logistic regression.

Results We included 1756 encounters from 1609 different episodes. Median age at the first visit of each episode was 10.1 years (IQR, 7.7–11.9) and 921 (57.2%) patients were men. There were 730 (41.6%) encounters with an Alvarado score ≤3, 695 (39.6%) with a score 4–6 and 331 (18.9%) with a score ≥7. Appendicitis was diagnosed in 293 (17.8%) episodes. Ultrasonography was performed in 1115 (61.6%) encounters, with a visualised appendix in 592 (53.1%). The ultrasound findings independently associated with appendicitis in patients without a visualised appendix were the presence of free intra-abdominal fluid in a small quantity (OR:5.0 (95% CI 1.7 to 14.6)) or in an abundant quantity (OR:30.9 (95% CI 3.8 to 252.7)) and inflammation of the peri-appendiceal fat (OR:7.2 (95% CI 1.4 to 38.0)). The absence of free fluid and inflammation of the peri-appendiceal fat ruled out acute appendicitis in patients with an Alvarado score <7 with a sensitivity of 84.6% (95% CI 57.8 to 95.7) and a negative predictive value of 99.4% (95% CI 97.8 to 99.8).

Conclusions Patients with an Alvarado score <7 and without a visualised appendix on ultrasound but who lack free fluid and inflammation of the peri-appendiceal fat are at very low risk of acute appendicitis.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The appendix is not visualised in 10% of abdominal ultrasounds, leading to a delay in the diagnosis of appendicitis and requiring the use of ionising tests, such as an abdominal CT.

WHAT THIS STUDY ADDS

⇒ In this retrospective study of paediatric patient undergoing ultrasound for appendicitis in whom the appendix is not visualised, we found that the absence of free fluid or inflammation of the peri-appendiceal fat in low and intermediate risk patients (based on Alvarado score) makes the diagnosis of acute appendicitis very unlikely.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our results suggest that a more conservative approach may be appropriate for managing low and intermediate risk patients who have suspected appendicitis without a visualised appendix on ultrasound, particularly if they do not exhibit indirect signs on ultrasound. Extending their stay at the emergency department and performing ionising tests, such as abdominal CT, could be avoided for such patients.

INTRODUCTION

Appendicitis is the most common surgical emergency in children.[1 2] It is often difficult to diagnose in its earlier stages. A delay in diagnosis may result in complications including abscesses, peritonitis or even the patient's death; however, it is important to avoid unnecessary surgery, with its inherent morbidity and mortality.[3]

The diagnosis of appendicitis is suspected based on the clinical history and physical examination. The performance of clinical gestalt to rule out appendicitis has shown to be good, with a negative predictive value (NPV) as high as 98.9%, mainly in patients where the physician's gestalt probability is low (<1%).[4] However, emergency physicians often act conservatively, even when their clinical suspicion is low.[4] Also, clinical findings are sometimes inconclusive, making it challenging to exclude appendicitis. To address this situation, clinicians frequently perform blood tests, where various biomarkers, such as white blood cell count, absolute neutrophil count, C reactive protein, procalcitonin or calprotectin, have shown different levels of accuracy.[5] However, the definitive diagnosis at the ED is made by imaging. Imaging tests using ionising radiation such as an abdominal CT have gradually been replaced by abdominal ultrasound, which is less harmful.[6–8] Hence, ultrasound is now the recommended first-line imaging in children with suspected appendicitis.[9]

In paediatric patients, the overall sensitivity (Sn) of ultrasound for detecting appendicitis ranges from 74% to 100% and from 88% to 99% in the case of specificity (Sp).[7 10 11] Findings suggestive of appendicitis on ultrasound include a non-compressible tubular structure in the right lower quadrant, wall thickness >2 mm, an overall diameter >6 mm, free fluid in the right lower quadrant or thickening of the mesentery.[5 12 13] Moreover, recent studies show that emergency physicians who receive adequate training are capable of performing abdominal ultrasound with reasonable diagnostic accuracy for appendicitis in children.[14]

Unfortunately, ultrasound has the disadvantage of being operator dependent. In addition, patient characteristics such as obesity or unusual anatomical location of the appendix (eg, retrocecal) can make the visualisation of the appendix challenging. Thus, ultrasound fails to visualise the appendix in around 10% of patients.[5 15] In such cases, guidance for a second-line imaging technique is based on local availability and expertise, as there is no strong evidence to support a better diagnostic pathway.[9] One option might be a wait-and-see approach,[16] or performing another imaging test, such as an abdominal CT scan.[7] However, some authors have shown that in cases where the appendix is not visualised, indirect ultrasound findings, such as the inflammation of the peri-appendiceal fat or the presence of peri-appendiceal fluid, can be associated with the diagnosis of acute appendicitis.[17] The aim of our study was to assess whether the absence of such indirect ultrasound signs could reliably rule out the diagnosis of acute appendicitis in children with abdominal pain in whom the appendix is not visualised on ultrasound. As a secondary objective, we sought to derive a predictive model to identify those patients at low risk of appendicitis when the appendix is not visualised on ultrasound.

METHODS

We conducted a single-centre retrospective observational study, including all patients aged between 3 and 13 years of age who attended the Paediatric Emergency Department (ED) of Rio Hortega University Hospital (Valladolid, Spain) from 1 January 2013 to 31 December 2019 with a clinical suspicion of acute appendicitis. 1 January 2013 was chosen as the start date of the study because 2013 was the year in which the electronic medical record was introduced in our hospital, and reviewing charts prior to that date would have had a high risk of missing patients.

Setting

Our ED is a dedicated Paediatric ED with Pediatric Emergency Medicine (PEM) staff in a teaching hospital. Approximately 30 000 patients up to 14 years of age are seen at our ED per year. In accordance with the clinical pathway at our hospital, if the paediatrician suspects acute appendicitis, the patient will first undergo a blood test. When its results are consistent with this diagnosis (mainly leukocytosis or neutrophilia), an abdominal ultrasound is requested from the radiology department. This ultrasound is performed by a board-certified radiologist or a resident physician of radiology, supervised by a radiologist during their first year of residency. Visualisation of an appendix with a diameter ≥7 mm is considered pathological. Since our hospital does not have paediatric surgery, patients requiring surgical assessment are transferred to our referral hospital, the Hospital Clínico de Valladolid.

Participants

As a proxy for suspected appendicitis, we included those patients who were triaged for 'abdominal pain' and who had at least one blood test obtained, regardless of its result. We excluded patients who fulfilled ANY of the following criteria: (a) discharge reports were not found in the hospital's database or the information was not readable, (b) patients with a previous appendectomy or (c) patients finally diagnosed in that episode with a surgical process other than acute appendicitis. In addition, as we intended to calculate the Alvarado score retrospectively, patients who had missing items for the score were excluded.

Since acute appendicitis is often not diagnosed during the first hospital visit,[18] in this study, we defined 'encounters', as each visit of the patient to the ED, and 'episodes' as the period from the onset of symptoms until surgery in cases of appendicitis or until the disappearance of symptoms in patients without acute appendicitis. Encounters that met any of the following criteria were considered to belong to the same episode: (a) consecutive encounters occurring within 7 days of the previous encounter or (b) consecutive encounters where more than 7 days had elapsed, but the patient's clinical chart indicated continuous symptoms throughout the period.

Data collection and variables

In order to stratify the patients' risk for appendicitis, for those with sufficient information, we retrospectively calculated the Alvarado score as this score is not routinely calculated by the staff. We considered patients with a score ≤3 as having a low risk of appendicitis, patients between 4 and 6 as having an intermediate risk and ≥7 as having a high risk of acute appendicitis.[19]

Six researchers reviewed both the discharge reports of all patients and the radiological reports of those on whom ultrasound had been performed. They extracted the patient's demographic data, the symptoms described by the patient, the duration of the symptoms, physical examination findings and blood test results. The presence or absence of the following findings was abstracted from the radiology reports: peri-appendiceal fat inflammation as indicated by increased echogenicity of the peri-appendiceal fat, peri-appendiceal fluid (little or profuse), the presence of an appendicular phlegmon, the presence of adenopathy, the maximum diameter of any nodes and whether the radiologist considered them to be reactive. Maximum appendiceal diameter, when observed, was also recorded.

The surgical pathology report was established as the gold standard in patients who underwent an appendectomy. In patients who did not undergo surgery, medical charts from both Río Hortega and Clínico hospitals were reviewed. If there was no record of having had an appendectomy within 7 days of the last encounter of that episode, that patient was considered not to have suffered from appendicitis (conservative therapy for appendicitis using antibiotics was not done during this period.)

Since each patient was reviewed by a single researcher, no interobserver agreement analysis was performed. However, the researchers received brief training to achieve as much homogeneity as possible in the data extraction process.

Outcomes

The main outcome variable was the diagnosis of acute appendicitis.

Analysis

The relationship of each of the indirect ultrasound signs with the diagnosis of appendicitis was first analysed by univariate analysis. The χ^2 test was used for categorical variables and Student's t-test for continuous variables. To determine the independent association of each of these signs with appendicitis, logistic regression was used. For this purpose, a first model was built including the variables with a p value <0.1 in the univariate analysis, in addition to the variables considered *a priori* as confounding factors (age, sex, duration of symptomatology and Alvarado score), which were included independently of their p value in the univariate analysis. Starting from this initial model, and using the backward stepwise method, the final prediction model was derived. Finally, the diagnostic values (Sn, Sp, NPV and positive predictive values and likelihood ratio) of the combination of indirect signs included in the model were analysed.

Patient and public involvement

No patients were involved.

RESULTS

We reviewed charts of 1940 encounters. We excluded 114 (5.9%) due to a missing or an illegible report, 3 (0.2%) who had a previous appendectomy and 14 (0.7%) who had a final surgical diagnosis other than appendicitis. Another 53 (2.7%) patients were excluded because not all the items of the Alvarado score were recorded. Therefore, 1756 (90.5%) encounters were included, corresponding to 1609 episodes of 1438 different patients.

Figure 1 shows the flowchart of patients. The median age of patients at the first visit of each episode was 10.1 years (IQR, 7.7–11.9), and 921 (57.2%) of the patients were men (table 1). The median Alvarado score was 4 (IQR, 2–6). The median was one visit per episode (IQR, 1–1). There were 105 (6.5%) episodes with two encounters, 19 (1.2%) with 3 and 1 (0.1%) episode with four encounters. Of the 1609 episodes, 342 (21.3%) patients were referred to paediatric surgery consultation. Among them, 308 (90.1%) underwent surgery. There were no patients with appendicitis managed conservatively with antibiotics and observation. The final diagnosis was a normal appendix in 19 (6.2%) episodes, phlegmonous appendicitis in 215 (69.8%), gangrenous appendicitis in 49 (15.9%), perforated appendicitis in 19 (6.2%) and peritonitis or abscess in 6 (2.0%).

Ultrasonography was performed in 1075 (61.2%) encounters. Ultrasound was requested more frequently in those patients with an Alvarado Score >3 (38.7% vs 77.2%; p<0.01). The appendix was visualised on 579 (53.9%) of ultrasounds (table 2). The appendix was less frequently visualised in patients with an Alvarado Score ≤3 than in those with a higher score (29.0% vs 62.8%; p<0.01). The prevalence of appendicitis was higher in patients in whom the appendix was visualised on ultrasound than in those in whom it was not (48.9% vs 5.0%; p<0.01).

Table 3 shows the association of each of the indirect signs on ultrasound with the final diagnosis of appendicitis regardless of whether the appendix was visualised or not. Among the 25 (5.0%) patients in whom the appendix was not visualised and were ultimately diagnosed with appendicitis, there were three patients who did not have any indirect signs on ultrasound.

Among the 471 patients without a visualised appendix and who did not have appendicitis, 202 (42.9%) had one or more indirect signs.

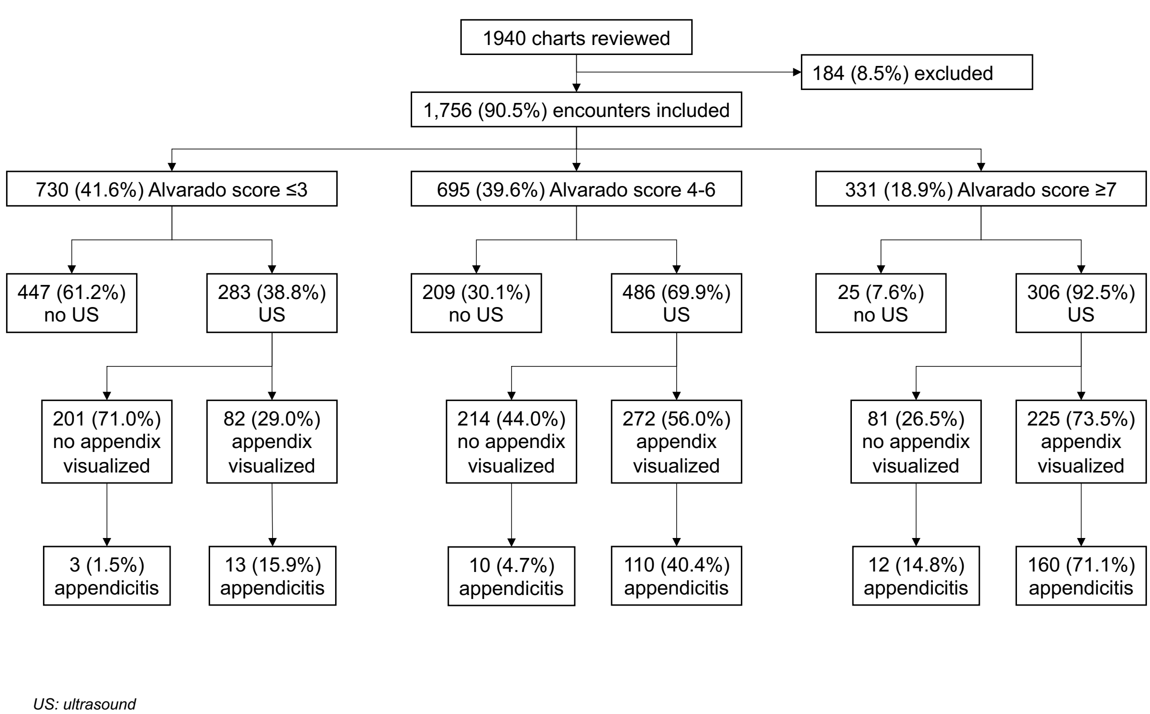

Figure 1 Flowchart of patients. US, ultrasound.

Table 1 Characteristics of the 1756 included encounters

	N (%)
Age (median, IQR) years	10.1 (7.7–11.9)
Sex—male	921 (57.2%)
Encounters	
One	1484 (92.2%)
Two	105 (6.5%)
Three or more	20 (1.3%)
Length of symptoms (median, IQR) hours	24 (7–48)
Symptoms	
Right lower quadrant pain	1068 (60.8%)
Migration of pain	424 (24.2%)
Nausea or vomiting	846 (48.2%)
Signs	
Hyporexia	386 (22.0%)
Fever	517 (29.4%)
Pain with cough or percussion	172 (9.8%)
Positive Blumberg sign*	811 (46.2%)
Positive iliopsoas sign	259 (14.8%)
Positive Rovsing sign†	60 (3.4%)
Alvarado score	
0–3	730 (41.6%)
4–6	695 (39.6%)
7–10	331 (18.9%)
Appendix visualised on ultrasound‡	579 (53.9%)
Diagnosed with appendicitis‡	311 (17.7%)

*Pain on removal of pressure rather than application of pressure to the abdomen.
†Pain elicited in the right lower quadrant with palpation pressure in the left lower quadrant.
‡Ultrasound obtained in 1075 encounters.

A multivariate analysis was performed in those patients in whom the appendix was not visualised (n=483), using the backward stepwise strategy, including indirect ultrasound signs with a p value <0.1 in the univariate analysis included in table 3, and sex, age, duration of symptomatology and Alvarado score as confounding factors (table 4). After the analysis, a prediction model was built including those signs that showed an independent association with the diagnosis of appendicitis: the presence of free intra-abdominal fluid in a small quantity (OR 5.0 (95% CI 1.7 to 14.6)) or in an abundant quantity (OR 30.9 (95% CI 3.8 to 252.7)) and inflammation of the peri-appendiceal fat (OR 7.2 (95% CI 1.4 to 38.0)).

Table 2 Findings of the 1075 performed ultrasonography

	Non-visualised appendix	Visualised appendix	P value
N	496 (46.1)	579 (53.9%)	–
Age (in years old)*	10.2 (7.6–11.9)	10.3 (7.9–12.1)	0.54
Male—sex	262 (52.8%)	338 (58.4%)	0.07
Appendix diameter (mm)*	–	7 (5–9)	–
Free fluid			<0.01
No	376 (75.8)	280 (48.4%)	
Little	112 (22.6%)	270 (46.6%)	
Profuse	8 (1.6%)	29 (5.0%)	
Adenopathies	165 (33.3%)	275 (47.5%)	<0.01
Diameter (mm)*	7.5 (6–10)	7 (5–10)	0.04
Reactive adenopathies	78 (15.7%)	167 (28.8%)	<0.01
Appendicular phlegmon	5 (1.0%)	24 (4.2%)	<0.01
Peri-appendiceal fat inflammation	12 (2.4%)	241 (41.6%)	<0.01

Data expressed as absolute frequencies and percentages.
*Variable expressed in median and interquartile range.

Table 5 shows the diagnostic values of the prediction model. The absence of free fluid and inflammation of the peri-appendiceal fat ruled out the diagnosis of acute appendicitis in patients with an Alvarado score <7 with an Sn of 84.6% (95% CI 57.8 to 95.7), an Sp of 80.6% (95% CI 76.4 to 84.2) and an NPV of 99.4% (95% CI 97.8 to 99.8).

There were six encounters in which neither the appendix nor free fluid or inflammation of the peri-appendiceal fat was visualised and in which the patient was finally diagnosed with acute appendicitis. All of the patients reported symptoms lasting 12 hours or less, and four had an Alvarado score ≥7. Of the other two, one patient had abdominal pain lasting 12 hours and an Alvarado score of 4; an ultrasound was repeated 30 hours later in which the appendix was seen. The other one had been in pain for 3 hours and had an Alvarado score of 3; the ultrasound was repeated 20 hours later but again the appendix was not seen, and he underwent surgery. In both cases, the diagnosis was uncomplicated phlegmonous appendicitis.

DISCUSSION

Our study found that the absence of certain indirect signs of inflammation on ultrasound, which are free fluid and swelling of the peri-appendicular fat, may be useful in determining whether expectant management of acute appendicitis in children is appropriate.

Our results suggest that even without visualisation of the appendix, several ultrasound findings are strongly associated with the diagnosis of acute appendicitis. The presence of free fluid, lymphadenopathies, phlegmon in the area of the appendix or inflammation of the peri-appendiceal fat was the most frequent findings in patients with acute appendicitis. These results are similar to those found by Telesmanich *et al*.[17] However, in that study, the appendix was not visualised on ultrasound in only six patients, while our sample includes more than 500 ultrasound scans in which the appendix was not visualised. This allowed us to thoroughly analyse the association of each of the indirect signs adjusting for potential confounding factors that have been shown to influence ultrasound performance, such as age and duration of symptoms.[11] Thus, we were able to determine a number of items that might help to select patients at low risk of appendicitis.[5] Malia *et al* also developed a rule to predict appendicitis in patients where the ultrasound does not visualise the appendix; however, our prediction model contains fewer variables and would also be more efficient, as we only include ultrasound findings and not laboratory tests.[5]

Using our predictive model, we found that for patients suspected of appendicitis where the appendix is not visualised on ultrasound, if the Alvarado score is <7, and free fluid and swelling of the periappendicular fat are both absent, the NPV is 99.4% (95% CI 97.8 to 99.8). However, the NPV is dependent on the prevalence of the condition under consideration and thus is less important than Sn, which was only 84.6% (95% CI 57.8 to 95.7). However, in our cohort, using this rule, only two patients would have been misdiagnosed. Neither of them had complicated appendicitis and both reported a relatively short duration of symptoms, which potentially meant less time for the secondary signs to develop. Furthermore, we believe it is important to point out that the model, in addition to a good Sn,

Table 3 Association of each of the indirect signs on ultrasound with the final diagnosis of appendicitis

	Whole sample			Non-visualised appendix		
	No appendicitis (n=767)	Appendicitis (n=308)	P value	No appendicitis (n=471)	Appendicitis (n=25)	P value
Free fluid			<0.01			<0.01
No	550 (71.7%)	106 (34.4%)		370 (78.6%)	6 (24.0%)	
Little	205 (26.7%)	177 (57.5%)		97 (20.6%)	15 (60.0%)	
Profuse	12 (1.6%)	25 (8.1%)		4 (0.9%)	4 (16.0%)	
Adenopathies	305 (39.8%)	135 (43.8%)	0.22	151 (32.1%)	14 (56.0%)	<0.01
Diameter (mm)*	7 (5–11)	6.5 (1–9)	0.48	7 (6–10)	7 (6–10)	0.97
Reactive adenopathies	164 (21.4%)	81 (26.3%)	0.08	72 (15.3%)	6 (24.0%)	0.24
Appendicular phlegmon	5 (0.7%)	24 (7.8%)	<0.01	1 (0.2%)	4 (16.0%)	<0.01
Peri-appendiceal fat inflammation	54 (7.0%)	199 (64.6%)	<0.01	6 (1.3%)	6 (24.0%)	<0.01

Data expressed as absolute frequencies and percentages.
*Variable expressed in median and interquartile range.

has an Sp of 80%, so it is not expected to pose a significant risk of performing surgery on healthy patients.

On the other hand, in patients with a score of Alvarado >7, the Sn of indirect signs to predict appendicitis was only 66%. The six potentially misdiagnosed cases all had a duration of symptoms equal to or less than 12 hours, so this is consistent with a theory that the indirect signs may only be useful after a certain duration of symptoms. However, our results do not allow us to confirm or rule out this hypothesis.

We believe that our results support discharging low-risk patients with an Alvarado Score <7 and no ultrasound findings suggestive of appendicitis,[19 20] while those with higher scores might be managed with a wait-and-see approach and repeat ultrasonography in 12–24 hours. This recommendation is further supported by previous research demonstrating that the likelihood of complicated appendicitis is minimal among patients in whom the appendix is not visualised on ultrasound.[21] Furthermore, our results would not support the use of ultrasound as the only means of diagnostic decision-making, but that our findings should be integrated with a clinical decision aid, such as the Alvarado score or similar.

There are limitations to our study. First, this research was performed at a single paediatric emergency department and, thus, may not be reproducible in other practice settings. We relied on chart data to determine if appendicitis was subsequently diagnosed. It is possible the patient went to another hospital, but our hospital is one of the two hospitals of the public health system in our city and the database is shared, so it is not possible for the patient to have been lost unless he or she was treated in another city, which would be rare and unlikely to jeopardise the validity of our results. The retrospective nature of the study means that some patient data could not be retrieved. However, less than 6% of patients were excluded for this reason. In addition, since it is retrospective, the decision whether or not to perform ultrasound was made by the paediatrician who attended the patient at each visit during the episode, and it is reasonable to suppose that the imaging test was performed in those patients in whom the clinical and laboratory tests were more suggestive of acute appendicitis, so a selection bias could not be totally ruled out.

A pathological diagnosis was chosen as the gold standard for appendicitis. Although it is impossible to ensure that no patient discharged without surgery had appendicitis that resolved spontaneously, we do know that no patient in our study was discharged with antibiotics and, thus, resolution without surgery is unlikely.

The study was conducted using a sample of patients seen in the ED since the implementation of electronic record was introduced in the hospital, so no a priori sample size calculation was made. This meant that the number of appendicitis included was low, and some indirect signs were present in few patients, resulting in wide CIs.

Because some included patients were seen in one more than one encounter and had more than ultrasound, collinearity between some variables cannot be entirely excluded. However, there are only 15 episodes out of 496 in which the patient underwent two ultrasounds in which the appendix was not seen. Thus, even if there could be some degree of collinearity between the variables of these patients, it is unlikely that it has contributed significantly to overestimating our results. Sixth, and probably the most important limitation is that it is impossible to know retrospectively whether or not patients included were suspected of having appendicitis. The protocol for the management of acute abdomen at our centre recommends requesting a blood test for all patients with suspected appendicitis and thus we considered a patient whose main symptom at triage was abdominal pain and who had at least a leucocyte count to be suspected of having appendicitis. We also excluded those under 3 years of age, who may have had abdominal pain and had labs drawn, since gastrointestinal infections are more frequent in this age group than appendicitis. The prevalence of appendicitis in our sample resembles that of other prospective studies, so we believe that our criteria captured the appropriate cohort. Although we did not determine the identity of the radiologist conducting the ultrasound, any interobserver variability that may be reflected in our results is similar to that found in

Table 4 Indirect signs independently associated with a pathological diagnosis of appendicitis in patients without a visualised appendix

N=483	OR	95% CI
Free fluid		
No	1	–
Little	5.0	1.7 to 14.6
Profuse	30.9	3.8 to 252.7
Adenopathies	1.7	0.6 to 4.8
Reactive adenopathies	0.6	0.2 to 1.9
Appendicular phlegmon	8.5	0.5 to 136.3
Peri-appendiceal fat inflammation	7.2	1.4 to 38.0
Alvarado score	1.4	1.1 to 1.7
Length of symptoms (hours)	1.0	1.0 to 1.0
Age (years old)	1.0	0.8 to 1.2
Female—sex	1.1	0.4 to 2.9

Age, sex, length of symptomatology and Alvarado score were included in the analysis as potential confounders.

Table 5 Diagnostic performance of the absence of free fluid and inflammation of the peri-appendiceal fat

	Whole sample (n=496)	Alvarado score ≤3 (n=201)	Alvarado score 4–6 (n=214)	Alvarado score ≥7 (n=81)
Appendicitis (n, %)	25 (5.0)	3 (1.5)	10 (4.7)	12 (14.8)
Sensitivity	76.0 (56.6–88.5)	66.7 (20.8–93.9)	90.0 (59.6–98.2)	66.7 (39.1–86.2)
Specificity	77.9 (74.0–81.4)	87.9 (82.6–91.7)	73.5 (67.1–79.1)	62.3 (50.5–72.8)
Positive predictive value	15.4 (10.1–22.9)	7. 7 (2.1–24.1)	14. 3 (7.7–25.0)	23.5 (12.4–40.0)
Negative predictive value	98.4 (96.5–99.3)	99.4 (96.8–99.9)	99.3 (96.3–99.9)	91.5 (80.1–96.6)
Positive likelihood ratio	3.4 (2.6–4.6)	5.5 (2.3–13.3)	3.4 (2.5–4.6)	1.8 (1.1–2.9)
Negative likelihood ratio	0.34 (0.19–0.62)	0.38 (0.08–1)	0.14 (0.02–0.88)	0.54 (0.24–1)

Data are expressed in percentages and 95% CI.

daily clinical practice. On the other hand, we did not use ultrasounds obtained by emergency physicians. While prior research suggests good performance of point-of-care ultrasound performed by emergency physicians for the diagnosis of acute appendicitis,[22] we cannot apply the results of our study to emergency physician-performed ultrasound. Another limitation was that a predicted probability threshold to detect Sn/Sp was not chosen. Although Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) guidelines suggest doing that[23] the intention of the authors is to validate the findings of this work after publication, for which a prospective, and probably multicentre, study will be designed to develop the complete analysis. Finally, the low prevalence of appendicitis in patients with low Alvarado scores may have overestimated the NPV value. This should be considered when interpreting data from our study.

In conclusion, our data provide evidence that paediatric patients with suspected acute appendicitis and an Alvarado score <7, in whom the appendix is not visualised on ultrasound but who do not have free fluid and inflammation of the peri-appendiceal fat might be managed with an expectant approach, without further ionising imaging tests. Our results should be confirmed in a prospective study before incorporating them into clinical practice.

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Contributors RV designed the study, analysed the data, wrote the initial draft of the manuscript and approved the final manuscript as submitted. JP conceptualised and designed the study, collaborated in data collection, revised multiple drafts of the manuscript and critically revised the final submitted manuscript. TC, IS, PdP and EG collaborated in the design of the study and in data collection, revised multiple manuscript drafts and critically revised the final submitted manuscript. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work. RV acts as guarantor, and accepts full responsibility for the finished work and the conduct of the study, had access to the data and controlled the decision to publish.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by Valladolid Oeste Ethical Committee (22-PI106). It was a retrospective study, with de-anomysed data, and IRB gave us permission to avoid contacting all the families to ask for informed consent.

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Data availability statement Data are available upon reasonable request.

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