ORIGINAL ARTICLE

Appendicitis versus non-specific acute abdominal pain: Paediatric Appendicitis Score evaluation

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Received 25 November 2016; accepted 17 January 2017
Available online 21 November 2017

KEYWORDS
Appendicitis; Non-specific acute abdominal pain; Diagnosis; Clinical prediction rule; C-reactive protein; Child

Abstract

Introduction: Non-specific acute abdominal pain is the most common process requiring differential diagnosis with appendicitis in clinical practice. The aim of this study was to assess the Paediatric Appendicitis Score in differentiating between these two entities.

Material and methods: All patients admitted due to suspicion of appendicitis were prospectively evaluated in our hospital over a two-year period. Cases of non-specific acute abdominal pain and appendicitis were enrolled in the study. Several variables were collected, including Score variables and C-reactive protein levels. Descriptive, univariate and multivariate analyses and diagnostic accuracy studies (ROC curves) were performed.

Results: A total of 275 patients were studied, in which there were 143 cases of non-specific acute abdominal pain and 132 cases of appendicitis. Temperature and right iliac fossa tenderness on palpation were the variables without statistically significant differences, and with no discrimination power between groups. Pain on coughing, hopping, and/or percussion tenderness in the right lower quadrant was the variable with greater association with appendicitis.

\*\* Previous presentation: This work will be submitted for consideration as an oral communication in the 65th Congress of the Asociación Española de Pediatría, Santiago, Spain, 2017.

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Appendicitis versus non-specific acute abdominal pain

Introduction

Appendicitis accounts for 10% of the cases of abdominal pain assessed in emergency departments and it is the most common acute surgical disease of the abdomen. Its diagnosis is mostly based on the findings of the history taking and the physical examination, although other tools, such as measurement of inflammatory markers, imaging tests and clinical prediction rules, may help the process. Nevertheless, the rate of misdiagnosis can reach up to 30% due to the low specificity of the symptoms and the broad differential diagnosis of abdominal pain. The Paediatric Appendicitis Score (PAS) (Table 1) is the paediatric clinical prediction rule validated most appropriately and stands out in its ability to stratify patients by risk group. The inflammatory markers included in this prediction rule (total leukocyte and neutrophil counts) and the level of C-reactive protein (CRP) are the most useful markers in the diagnosis of appendicitis. Since non-specific abdominal pain (NSAP) is the most frequent diagnosis at discharge from the emergency department in cases of acute abdominal pain, it is important to differentiate appendicitis from other causes of abdominal pain. This study focused on evaluating the usefulness of PAS in children and adolescents with abdominal pain.

The Score correctly stratified the patients into risk groups. Substitution of temperature for C-reactive protein in the Score increased diagnostic accuracy, although with no statistically significant differences. Conclusions: The Paediatric Appendicitis Score helps in differential diagnosis between appendicitis and non-specific acute abdominal pain. It would be advisable to replace the temperature in the Score, since it has no discrimination power between these groups. C-reactive protein at a cut-off value of 25.5 mg/L value could be used instead.

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pain, and this is the process that most frequently requires differential diagnosis with appendicitis.\(^8\) The objective of this study was to assess the usefulness of the PAS in the differential diagnosis of appendicitis and NSAP.

### Materials and methods

We conducted a prospective study of all patients aged less than 15 years assessed in the emergency department of our hospital (Complexo Hospitalario Universitario de Vigo) for suspected appendicitis between 2013 and 2014, selecting cases of appendicitis and NSAP. The inclusion criteria were: clinical suspicion of appendicitis; documentation of the variables included in the PAS (pain in the right iliac fossa [RIF] on palpation, tenderness in the RIF with coughing, hopping and/or percussion; history of pain migration toward the RIF; anorexia; nausea and/or vomiting; body temperature; total leukocyte count and total neutrophil count); serum CRP level; consent given by a parent or legal guardian of the patient to access patient data for the purpose of research. The exclusion criteria were: age less than 5 years (the PAS is difficult to obtain and has not been validated for this age group); abdominal pain lasting more than 72 h (differential diagnosis of appendicitis and NSAP is rarely needed in such cases) or less than 6 h (diagnostic tests are not usually performed at this point); history of disorder of blood or blood-forming organs, malignancy, liver disease or inflammatory disease, current or diagnosed in the month preceding onset, or antibiotic or anti-inflammatory treatment in the month preceding onset (they could alter the levels of inflammatory markers); interval of more than 12 h between collection of blood sample for analysis and appendectomy (for the adequate correlation between inflammatory markers and the type of appendicitis). The diagnosis of NSAP was made by exclusion when disease was not detected, with nonspecific findings of abdominal ultrasound in all cases, and absence of antibiotic treatment in the month following the diagnosis (to avoid including cases of appendicitis or infectious disease that had not been detected and resolved with treatment). The study was approved by the Clinical Research Ethics Committee of Galicia (2013/361).

### Variables under study

We collected data for the following variables: age, sex, time elapsed between onset of abdominal pain and performance of blood tests, PAS variables, serum CRP levels and type of appendicitis (suppurative, gangrenous or perforated). Suppurative appendicitis was defined by the presence of neutrophilic infiltrate in the muscularis propria and gangrenous appendicitis by the presence of necrosis in the appendiceal wall.\(^10\) Perforated appendicitis was diagnosed based on the presence of a hole in the appendiceal wall or of a free appendicolith in the peritoneal cavity.\(^11\) We considered suppurative appendicitis uncomplicated appendicitis, and gangrenous and perforated appendicitis complicated appendicitis. We followed up cases of NSAP through outpatient visits or by phone in the first month from the diagnosis with the purpose of assessing the exclusion criteria.

All laboratory tests were performed in the haematology emergency laboratory (total leukocyte and neutrophil count) and clinical analysis laboratory (CRP) of our hospital, following routine procedure and always using the same method for each variable.

### Statistical analysis

We conducted the statistical analysis with the package SPSS 19.0 for Windows (SPSS Inc; Chicago, IL, USA; 2010). We performed a descriptive analysis of all the variables under study, univariate analyses of quantitative variables with the Student t test and of qualitative variables with the \(\chi^2\) test, and multivariate logistic regression to detect the variables most strongly correlated with appendicitis. We also assessed the diagnostic yield of different quantitative variables and the PAS by measuring the area under the ROC curve (AUC), identifying the cut-off points with the highest discriminatory power for the diagnosis of appendicitis. Lastly, we developed a modified PAS by adding the CRP level, categorised based on the cut-off point, to the original score. We defined statistical significance as a P-value of less than .05 for all tests.

### Results

During the period under study, 764 patients underwent evaluation for suspected appendicitis, and the most frequent diagnoses were NSAP, with 327 cases (42%), and appendicitis, with 273 (36%) (Table 2). The total number of patients included after applying the inclusion and exclusion criteria were 275, of whom 143 were in the NSAP group and 132 in the appendicitis group (100 cases of uncomplicated appendicitis and 32 of complicated appendicitis [9 gangrenous and 23 perforated]).

Table 3 shows the descriptive analysis of the variables under study. The univariate analysis showed statistically significant differences between the NSAP and appendicitis groups in sex, but not in age or duration of symptoms. We ended up removing the variable of pain in the RIF on palpation from the analysis because it was present in all cases. There were statistically significant differences in the rest of the qualitative variables included in the PAS between the NSAP and the appendicitis groups (Table 3). The analysis of these qualitative variables by type of appendicitis also found statistically significant differences in every instance, except for nausea and/or vomiting between the NSAP and uncomplicated appendicitis groups (\(P=.830\) (Table 4).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Cases of suspected appendicitis (2013–2014).</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAP</td>
<td>327 (42.8%)</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>273 (35.7%)</td>
</tr>
<tr>
<td>Mesenteric lymphadenitis</td>
<td>35 (4.5%)</td>
</tr>
<tr>
<td>Acute gastroenteritis</td>
<td>24 (3.1%)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>17 (2.2%)</td>
</tr>
<tr>
<td>Ovarian cyst</td>
<td>14 (1.8%)</td>
</tr>
<tr>
<td>Respiratory tract infection</td>
<td>11 (1.4%)</td>
</tr>
<tr>
<td>Other</td>
<td>63 (8.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>764 (100%)</td>
</tr>
</tbody>
</table>

NSAP: nonspecific abdominal pain.
Appendicitis versus non-specific acute abdominal pain

### Table 3: Descriptive and univariate analysis of NSAP and appendicitis groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>NSAP</th>
<th>Appendicitis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male/female (ratio)</td>
<td>60/83</td>
<td>93/39</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Age, mean (years) ± SD</td>
<td>10.4 ± 2.5</td>
<td>9.9 ± 2.5</td>
<td>.152&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Duration of symptoms (h) ± SD</td>
<td>25.8 ± 16.9</td>
<td>24.2 ± 15.9</td>
<td>.406&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Tenderness with coughing, hopp. and/or perc., n (%)</td>
<td>20 (14.0)</td>
<td>84 (63.6)</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Migration of pain to RIF, n (%)</td>
<td>18 (12.6)</td>
<td>70 (53.0)</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Anorexia, n (%)</td>
<td>37 (25.9)</td>
<td>88 (66.7)</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Nausea and/or vomiting, n (%)</td>
<td>80 (55.9)</td>
<td>94 (71.2)</td>
<td>.009&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Body temperature (°C), mean ± SD</td>
<td>37.2 ± 0.9</td>
<td>37.1 ± 0.8</td>
<td>.871&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Leukocytes (×10&lt;sup&gt;9&lt;/sup&gt;/L), mean ± SD</td>
<td>10.94 ± 5.26</td>
<td>15.47 ± 3.99</td>
<td>&lt;.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Neutrophils (×10&lt;sup&gt;9&lt;/sup&gt;/L), mean ± SD</td>
<td>7.97 ± 5.25</td>
<td>12.51 ± 3.93</td>
<td>&lt;.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>CRP (mg/L), mean ± SD</td>
<td>15.8 ± 22.0</td>
<td>37.1 ± 52.1</td>
<td>&lt;.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

CRP, C-reactive protein; NSAP, nonspecific abdominal pain; RIF, right iliac fossa; SD, standard deviation.
<sup>a</sup> χ<sup>2</sup> test.  
<sup>b</sup> Student t test.

### Table 4: Univariate analysis of variables in the NSAP, UA and CA groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>NSAP vs UA, P</th>
<th>NSAP vs CA, P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenderness with coughing, hopp. and/or perc.</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Migration of pain to RIF</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Anorexia</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Nausea and/or vomiting</td>
<td>.83&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.003&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Body temperature</td>
<td>.05&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.002&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>&lt;.001&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>&lt;.001&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>.335&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

CA, complicated appendicitis; NSAP, nonspecific abdominal pain; RIF, right iliac fossa; UA, uncomplicated appendicitis.
<sup>a</sup> χ<sup>2</sup> test.  
<sup>b</sup> Student t test.

Body temperature was the only quantitative variable for which there were no differences between the NSAP and appendicitis groups (P = .871); while differences were found for the rest (total leukocyte count, total neutrophil count, and serum CRP level; P < .001) (Table 3). The analysis of these variables by type of appendicitis revealed significant differences in every instance (P < .05) except in body temperature between the NSAP and uncomplicated appendicitis groups (P = .05) and in CRP levels between the NSAP and uncomplicated appendicitis groups (P = .335) (Table 4).

Following the multivariate regression analysis, the only variables that remained in the model were tenderness with coughing, hopping and/or percussion, migration of pain, anorexia, the neutrophil count and the leukocyte count, although the differences were no longer statistically significant for the last one. The variables that exhibited the strongest association with appendicitis were tenderness with coughing, hopping and/or percussion (odds ratio, 20.0) and migration of pain (odds ratio, 11.4) (Table 5).

The analysis of the diagnostic yield based on the AUCs of ROC curves for body temperature and inflammatory markers in the appendicitis vs NSAP groups (Table 6) showed that the yield of body temperature was all but negligible (AUC, 0.51), the yield of CRP was low (AUC, 0.64) (Fig. 1) and the yield of leukocyte and neutrophil counts was moderate (AUC, 0.79). In this analysis, the PAS exhibited a high yield (AUC, 0.90), with 3 and 7 being the best cut-off points for the differentiation of low-, intermediate- and high-risk groups. The analysis of the modified PAS where body temperature was replaced by CRP category based on the cut-off point (CRP < 25.5 mg/L: 0 points; CRP > 25.5 mg/L: 1 point) showed that it had a higher diagnostic yield compared to the PAS (ROC, 0.92), although the difference was not statistically significant (P = .552) (Table 6) (Fig. 1). The modified PAS improved patient stratification, placing a greater number of NSAP cases in the low-risk group and of complicated appendicitis cases in the high-risk group (Table 7).

### Discussion

Non-specific abdominal pain refers to an acute abdominal pain process without a suspected organic cause that is self-limiting and does not recur. It is a diagnosis of exclusion that is safe in children, as a specific disease is subsequently found in only 1.6% to 5.8% of diagnosed cases with a low associated risk of undetected appendicitis. It is the most frequent discharge diagnosis in cases of acute abdominal pain in pediatric emergency departments, and the process that most frequently requires a differential diagnosis with appendicitis in clinical practice. In our study, NSAP was the most frequent diagnosis (42%) in cases of suspected appendicitis. Non-specific abdominal pain is distributed fairly evenly between the two sexes, but appendicitis is more frequent in males, with a male: female ratio of 1.5–1.9:1, a fact
Table 6  Area under ROC curve and cut-off points for variables and the PAS in the differentiation of appendicitis and NSAP.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Appendicitis vs NSAP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AUC</td>
</tr>
<tr>
<td>Body temperature (°C)</td>
<td>0.51</td>
</tr>
<tr>
<td>Leucocytes (&gt;10^7/L)</td>
<td>0.79</td>
</tr>
<tr>
<td>Neutrophils (&gt;10^9/L)</td>
<td>0.79</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>0.64</td>
</tr>
<tr>
<td>PAS (1–10)</td>
<td>0.90</td>
</tr>
<tr>
<td>PAS-CRP (1–10)</td>
<td>0.92</td>
</tr>
</tbody>
</table>

AUC, area under the curve; CI, confidence interval; CRP, C-reactive protein; COP, cut-off point with highest discriminatory power; NSAP: nonspecific abdominal pain; PAS, *Paediatric Appendicitis Score*; PAS-CRP, modified PAS including CRP; Sen, sensitivity; Spe, specificity.

Figure 1  Receiver operating characteristic curves for body temperature and CRP (A) and for the PAS and the PAS modified with addition of the CRP (B) for differentiation of appendicitis and NSAP.

Table 7  PAS and modified PAS in NSAP and different types of appendicitis.

<table>
<thead>
<tr>
<th></th>
<th>NSAP</th>
<th>UA</th>
<th>CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–3</td>
<td>41 (28.7%)</td>
<td>1 (1.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>4–7</td>
<td>101 (70.6%)</td>
<td>61 (61.0%)</td>
<td>7 (21.9%)</td>
</tr>
<tr>
<td>8–10</td>
<td>1 (0.7%)</td>
<td>38 (38.0%)</td>
<td>25 (78.1%)</td>
</tr>
<tr>
<td>PAS-CRP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–3</td>
<td>46 (32.2%)</td>
<td>1 (1.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>4–7</td>
<td>95 (66.4%)</td>
<td>64 (64.0%)</td>
<td>4 (12.5%)</td>
</tr>
<tr>
<td>8–10</td>
<td>2 (1.4%)</td>
<td>35 (35.0%)</td>
<td>28 (87.5%)</td>
</tr>
</tbody>
</table>

CA, complicated appendicitis; NSAP: nonspecific abdominal pain; PAS: *Paediatric Appendicitis Score*; PAS-CRP, *Paediatric Appendicitis Score* modified to include C-reactive protein; UC, uncomplicated appendicitis.

In our study, we found statistically significant differences between cases of appendicitis and cases of NSAP in all the signs and symptoms under study except for body temperature and pain in RIF on palpation, although a considerable percentage of patients did not exhibit a classic presentation.

There is evidence that peritoneal irritation, such as abdominal pain on percussion, and a history of migration of abdominal pain toward the RIF are the strongest predictors of appendicitis. In our multivariate analysis, these two variables exhibited the strongest associations with appendicitis, with odds ratios of 20 and 11, respectively. The strong association of coughing, hopping and/or percussion tenderness, which assesses the presence of peritoneal irritation in the PAS, explains the higher weight it is given in the score.

Some studies have already suggested that body temperature is of limited use in the diagnosis of appendicitis. In our study, body temperature was not useful in differentiating between appendicitis and NSAP.

The inflammatory markers used most commonly in the diagnosis of appendicitis are the total leukocyte count, the

Reflected in the larger proportion of this sex in our group of patients (2.4:1 ratio).

Up to 40% to 50% of appendicitis cases may present without one or more of the classic signs or symptoms, such as migration of abdominal pain toward the RIF, signs of peritoneal irritation or anorexia. In our study, we found
total neutrophil count and the serum level of CRP, and to
date no other markers have been found that offer better
results. There is considerable variability in the sensitivity
and specificity of leukocyte and neutrophil counts reported
in the literature, with values ranging from 55% to 89% and
from 43% to 66%, respectively. Their low specificity is
due to the elevation of these counts in many other pro-
cesses that manifest with pain in the RIF. They are more
useful in the first 24 h from onset, as inflammatory and infec-
tious processes are associated to neutrophil activation in
the first 3–6 h from onset. For the purpose of diagnosing
appendicitis, leukocytes and neutrophils are considered to
be elevated when their total counts exceed $10.0 \times 10^9$/L
and $7.5 \times 10^9$/L, respectively. The cut-off points with
the most discriminatory power and the sensitivity and speci-
city found in our study were consistent with the existing
literature.

There is also considerable variability in the values
reported in the literature for the sensitivity and speci-
city of CRP in the diagnosis of appendicitis, which range
from 58% to 100% and from 28% to 93%, respectively. C-
reactive protein is a nonspecific biomarker of inflamma-
tion whose synthesis starts 4–6 h after the stimulus, with
its concentration doubling every 8 h, so that serum levels are
significantly elevated starting at 12–24 h. The discrimina-
tory power of CRP for the diagnosis of appendicitis is not
high, especially in the early stages, where its value is within
ranges compatible with other processes, but CRP levels are
useful for differentiating between uncomplicated and com-
plicated appendicitis. Several studies have shown that
CRP concentrations between 10 and 50 mg/L are associated
with uncomplicated appendicitis, with a greater probabili-
ty of complications (gangrene or perforation) at higher
concentrations. In our study, CRP was moderately use-
ful for differentiating between appendicitis and NSAP. The
assessment of its diagnostic yield through the analysis of ROC
curves identified a cut-off point for discriminating appe-
ndicitis that was similar to those reported in the literature
(25.5 mg/L).

There is evidence that the combination of different
inflammatory markers increases their discriminatory and
predictive power in the diagnosis of appendicitis. The com-

bination of the total leukocyte count and the CRP level
reaches sensitivity and specificity values of 90%–95% for
the prediction of appendicitis, with a stronger correla-
tion between elevation of both values and the severity
of disease. This increase in discriminatory and predictive
power obtained through the combination of the leukocyte
count and CRP level makes the addition of the CRP con-
centration to the PAS variables particularly attractive.

In recent decades, several clinical prediction rules have
been developed for the diagnosis of appendicitis in chil-
dren, and their use in clinical practice has been associated
with an increase in diagnostic accuracy and a decreased
rate of perforation. The PAS prediction rule, published in
2000, is the rule that has been most thoroughly evaluated
in the paediatric age group. It was developed through a
multiple linear logistic regression analysis of clinical and
laboratory parameters after the prospective evaluation of
1170 children with suspected appendicitis aged 4–15 years.
It comprises 8 variables with a statistically significant asso-
ciation that were assigned values based on their sensitivity,
its place, for while it exhibits only a moderate ability to differ-
entiate between appendicitis and NSAP, when combined
with the leukocyte and neutrophil counts, its value can be
particularly useful in the diagnosis of appendicitis.

Conflicts of interest

The authors have no conflicts of interest to declare.

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