CHAPTER 5

A scoring system to predict the severity of appendicitis in children

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Abstract

Background

It appears that two forms of appendicitis exist. Preoperative distinction between the two is essential to optimise treatment outcome. This study aims to develop a scoring system to accurately determine the severity of appendicitis in children.

Methods

Historical cohort study of paediatric patients (aged 0-17 years old) with appendicitis treated between January 2010 and December 2012. Division into simple, complex appendicitis or another condition based on pre-set criteria. Multiple logistic regression analysis was used to build the prediction model with subsequent validation.

Results

There were 64 patients with simple and 66 with complex appendicitis. Five variables explained 64% of the variation. Independent validation of the derived prediction model in a second cohort (55 simple and 10 complex appendicitis patients) demonstrated 90 [54-99] % sensitivity, 91 [79-97] % specificity, a PPV of 64 [36-86] % and a NPV of 98 [88-100] %. The LR + was 10 [4.19-23.42] and LR- was 0.11 [0.02-0.71]. Diagnostic accuracy was 91 [84-98]%.

Conclusions

Our scoring system consisting of five variables can be used to exclude complex appendicitis in clinical practice if the score is < 4.

Introduction

Since Fitz's report in 1886, appendicitis has been considered an irreversibly progressive disease that should be treated with an appendectomy.[1] Presently appendicitis is classified into two distinct types: simple (nonperforated) and complex appendicitis (gangrene, perforation and abscess or phlegmon formation).[2-4] Appendectomy is still considered as the gold standard and although it is highly effective, it has become subject of debate recently. Both non-operative treatment (i.e. with antibiotics and/or percutaneous drainage) and surgical treatment have been widely accepted for children with an appendicular mass or abscess, although in these children appendectomy is associated with increased morbidity.[5,6] On the other hand, children with perforated appendicitis with localised or generalised purulent/faecal peritonitis are treated with an appendectomy. New insights also suggest that initial non-operative treatment is safe and effective for adults with simple appendicitis.[7-9] Recently, limited data on this strategy in children also suggests it to be safe in well-selected patients, although hard data regarding its effectiveness on the long term till date is lacking.[10-11] Therefore the optimal treatment strategy for each type of appendicitis is yet to be determined.

When the type of appendicitis dictates the choice of treatment, a correct preoperative diagnosis is crucial. However, current reports regarding preoperative markers of complex appendicitis are inconsistent. In a recent systematic review, inflammatory markers (CRP and leucocytes) were found to be more elevated in the presence of complex appendicitis.[12] To predict complex appendicitis preoperatively, several studies have developed a scoring system which have included a wide variety of clinical and biochemical variables.[13-17] Our national guideline suggests that all children with the suspicion of appendicitis should undergo ultrasound examination, in order to reduce our high negative appendectomy rate.[18] Therefore information from ultrasound might aid in the preoperative discrimination between simple and complex appendicitis. To our knowledge none of the abovementioned studies have included results from ultrasound examination in their scoring system. One study has included a variable from CT-scan in its scoring system.[13] However this scoring system is not applicable in settings where CT is not routinely used in diagnosing (or distinguishing between simple and complex) appendicitis in children.

This study aims to develop and validate a prediction model based on clinical, laboratory and ultrasound variables to distinguish simple from complex appendicitis in children with a high index of suspicion of appendicitis preoperatively. We chose to follow the common practice in Europe. This scoring system can aid in selecting those patients with simple appendicitis suitable for non-operative treatment.

Materials and Methods

Patients

Retrospectively, we have identified patients treated for acute appendicitis in our tertiary referral centre. Patients eligible for inclusion were 0-17 years old, admitted with suspicion of acute appendicitis and treated with appendectomy between January 2010 and December 2012. We excluded patients treated non-operatively and those who underwent routine appendectomy (either as an elective procedure after initial treatment of complex appendicitis or, for example, as a standard procedure during correction of an intestinal rotation disorder of the bowel). Patients with a noninflamed appendix (histologically proven in retrospect), malignancy of the appendix or parasitic infection (such as *Enterobius vermicularis*) and in addition those with missing data regarding both additional radiological imaging studies and laboratory investigations were also excluded from further analysis. This way we obtained a group of patients with proven appendicitis - all had been operated on and shown to have appendicitis - and a complete set of potential predictors. Approval was obtained from the medical ethics committee of our hospital. Patients were divided into simple or complex appendicitis according to the following definitions:

- Simple:
    - An intraoperative diagnosis made by the surgeon based on signs of an inflamed appendix without signs of perforation, purulent fluid, contained phlegmon or IAA. There is no need for additional postoperative antibiotics (exception: indication for perioperative spillage), *and*:
    - Histopathology: confirmation of the diagnosis of appendicitis without necrosis or perforation.
- Complex:
    - A perioperative diagnosis made by the surgeon based on signs of a gangrenous appendix with or without perforation, intra-abdominal abscess, periappendicular contained phlegmon or purulent free fluid and the need for additional postoperative antibiotics directly after appendectomy, *or*:
    - Histopathology: findings of extensive necrotic tissue in the outer layer of the appendix or signs of perforation.

Development of the prediction model

A standardised data extraction form, based upon previous studies, with both potential predictors and outcome variables was used to review the medical charts.[13-17] Potential predictors were divided into the 5 categories mentioned below. The following variables were recorded within each category and considered as potential predictors:

- Baseline: age, sex
- Medical history: duration of abdominal pain (from time of onset to presentation at the emergency department, in days), presence of nausea, vomiting, loss of appetite, diarrhoea, constipation, and reported fever measured at home (body temperature more than 38.5 degrees Celsius);
- Physical examination: body temperature (degrees Celsius), heart rate (beats per minute), tachycardia at the time of presentation adjusted for age (yes or no) [19], diffuse abdominal guarding or tenderness;
- Laboratory data: C-reactive protein (CRP) (mg/l), white blood cell count (WBC; x 10^9/l), creatinine (μmol/l);
- Ultrasound findings: appendix diameter, compressibility, faecalith, abscess, fatty infiltration, lymphadenopathy, appendicular contained phlegmon, free intraperitoneal fluid. Reported suspicion of complex appendicitis (see below)

Regarding the ultrasound, if an abscess, contained phlegmon, dilated bowel (ileus) was noted or when the radiologist had reported the ultrasound to be suspicious for complex appendicitis, it was decided that the ultrasound was indicative of complex appendicitis. Ultrasound coverage was available 24/7 and it was performed by radiologists and trainees (under supervision), not always with specific paediatric expertise. Due to the size of our referral centre, numerous radiologists and radiology residents made the ultrasounds.

Treatment variables were type of surgery, findings during surgery (e.g., perforation, purulent fluid), surgeon's intraoperative diagnosis (i.e., simple or complex appendicitis) and need for additional antibiotic treatment after appendectomy. Finally, the pathological diagnosis was recorded as noninflamed appendix, inflamed appendix, perforated appendix, or other (non-infectious) disease.

Data analysis for the predictive model

Statistical analysis was performed using SPSS version 20 (SPSS, Chicago, IL, USA). First, all potential predictors were analysed separately to assess their association with complex appendicitis. For continuous variables, Student's t-test or the Mann-Whitney U test was used, as appropriate. For categorical variables, the Chi square test was used. Statistical significance was defined as a P value < 0.05.

The predictors that were significantly associated with complex appendicitis were considered for the multivariable logistic regression model. For numerical variables, a receiver operating characteristic (ROC) curve was obtained from which the appropriate (optimal combination of sensitivity and specificity) cut-off value was identified for dichotomisation. Predictors were grouped into: 1. Medical history, 2. Physical examination, 3. Laboratory data, and 4. Ultrasound findings. These categories were analysed separately to identify the most important determinants within each category before building the final model. Per category, each variable

was entered manually into the model. Only if the addition of a variable to the model led to an increase in the explained variance of at least 10%, this variable was kept in the model. The variable with the highest F value was kept in the model as the best predictor and the other variables were added to the model until the increase in the explained variance by adding a variable was less than 10%. This procedure was repeated for each category, thus yielding a limited number of determinants for consideration in the final model.
Secondly, all identified independent predictors meeting the previously mentioned criteria were put into the final logistic model. Rounded weights were added to the final model based on the Odds Ratios in the prediction model. Subsequently, a ROC curve was obtained to identify the optimal threshold value. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for this model with 95% confidence intervals.

Validation of the model
The final model was validated in a separate cohort obtained independently from a large general peripheral hospital. Data extraction was done by one of the authors, who was not involved in the development of the prediction model and therefore was yet unfamiliar with the model. Children (0-17 years old) treated surgically for acute appendicitis between January 2013 and December 2014 were eligible for inclusion. The same inclusion and exclusion criteria were used. Ultrasound coverage in this hospital was 24/7 by seven senior radiologists. Patients with missing values, who therefore were unclassifiable, were left out of the analysis. Sensitivity, specificity, PPV, NPV and likelihood ratio of our prediction model were calculated from this cohort with 95% confidence intervals.

Results

Between January 2010 and December 2012, 145 consecutive children were treated for suspected acute appendicitis. The majority underwent appendectomy; only five patients were treated non-operatively with antibiotics and drainage procedures because of the formation of a well-defined abscess. In five patients no appendicitis was found during surgery (three with noninflamed appendix, one with a mucocele and one with parasitic invasion). An additional five were excluded due to lack of data in one, interval appendectomy in three and surgery in another centre in one. Of the remaining 130 patients, 64 (49%) were diagnosed with simple appendicitis and 66 (51%) with complex appendicitis.
The clinical, laboratory and ultrasound findings per group are displayed in table 1a and 1b. Patients with complex appendicitis were significantly younger, had longer duration of symptoms and more frequently reported vomiting and fever. In addition, on physical examination they were found to have significantly higher body temperature, higher heart rate, presented more

often with a tachycardia, while a larger percentage was found to have diffuse abdominal guarding (Table 1a).

CRP and WBC were both significantly higher in the complex compared to the simple appendicitis group; 105 mg/L versus 10 mg/L and 18.0 x 10^9/L versus 14.1 x 10^9/L, respectively. On ultrasound, free fluid, distended bowels, abscess and contained phlegmon were seen significantly more frequently in the complex appendicitis group (Table 1b).

Table 1a. Baseline characteristics, medical history and physical examination of patient groups with simple and complex appendicitis

	Missing**	Simple appendicitis N=64 N (%)	Missing**	- Complex appendicitis N=66 N (%)	P value
Baseline characteristics					
Male	0	35 (55)	0	34 (52)	0.73
Age (years)*	0	11 (2-17)	0	9 (1-17)	0.003
Medical history					
Duration of pain (days)*	0	1 (0-14)	0	2 (1-14)	< 0.001
Nausea	0	43 (67)	0	51 (77)	0.24
Vomiting	0	32 (50)	0	47 (71)	0.02
Diarrhoea	0	4 (6)	0	16 (24)	0.06
Constipation	0	4 (6)	0	4 (6)	1.000
Anorexia	0	44 (69)	0	55 (83)	0.06
Reported fever	0	14 (22)	0	38 (58)	< 0.001
Physical examination					
Body temperature (^{0}C)*	1	37.0 (35.0-39.4)	2	38.0 (36.0–39.9)	< 0.001
Heart rate (Beats/min)*	6	90 (58-134)	5	120 (52-156)	< 0.001
Tachycardia at time of presentation (adjusted for age)	6	4 (7)	5	20 (33)	< 0.001
Diffuse abdominal guarding	0	5 (8)	0	26 (39)	< 0.001

Data are reported as N (%), unless stated otherwise

- * = Median (min - max)
- ** = Count

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Table 1b. Laboratory and ultrasound variables of patient groups with simple and complex appendicitis

	Missing**	Simple appendicitis (N=64)	Missing**	Complex appendicitis N=66	P-value
Laboratory results					
CRP (mg/l)*	0	10.0 (0.3–133.0)	1	105.5 (1.0–412.0)	< 0.001
WBC (x10^9/l)*	0	14.1 (2.2–37.0)	1	18.0 (5.8–42.0)	< 0.001
Creatinine (µmol/l)*	11	46.0 (14.0–74.0)	15	46.0 (9.0–92.0)	0.90
Ultrasound					
Appendix visible	0	55 (83)	4	34 (52)	< 0.001
Diameter (mm)*	10	8.0 (6.0–22.0)	34	9.5 (5.0-17.0)	0.45
Compressible	10	2 (4)	33	0 (0)	0.52
Faecalith present	10	11 (20)	32	9 (27)	0.60
Free fluid	10	25 (39)	5	36 (59)	0.03
Abscess	0	2 (3)	4	15 (24)	0.001
Contained phlegmone	0	5 (8)	4	27 (43)	<0.001
Distended bowel	1	2 (3)	6	18 (30)	< 0.001
Ultrasound indicative for complex appendicitis	0	7 (11)	3	42 (64)	< 0.001

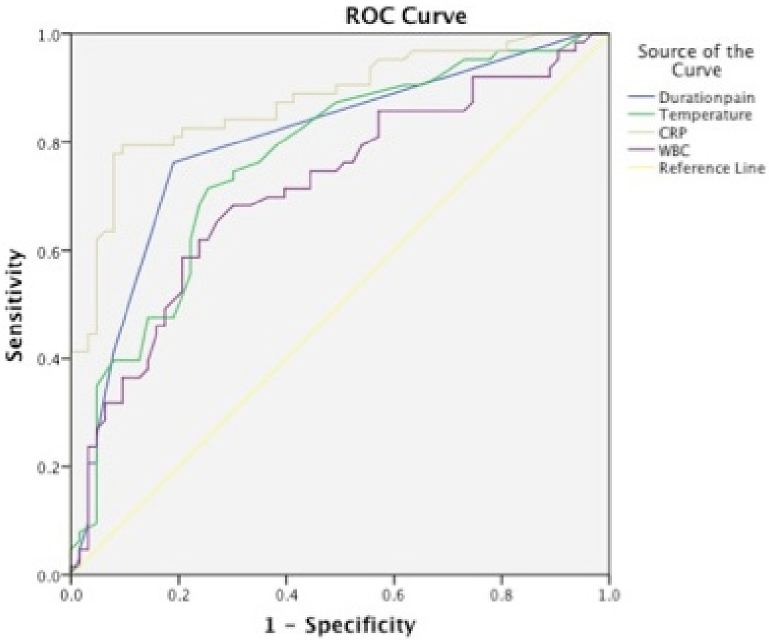
Data are reported as N (%), unless stated otherwise

- * = Median (min - max)
- ** = Count

Dichotomisation

All the numerical variables associated with complex appendicitis were dichotomised based upon the ROC curve, which is displayed in figure 1. The appropriate cut-off value was determined based upon the maximum combination of sensitivity and specificity. This led to the following cut-off values: abdominal pain duration: 1 day, body temperature: 37.5 degrees Celsius, CRP level: 38 mg/L, white blood cell count: 16 x 10^9/L.

Figure 1. ROC curves of all numerical variables



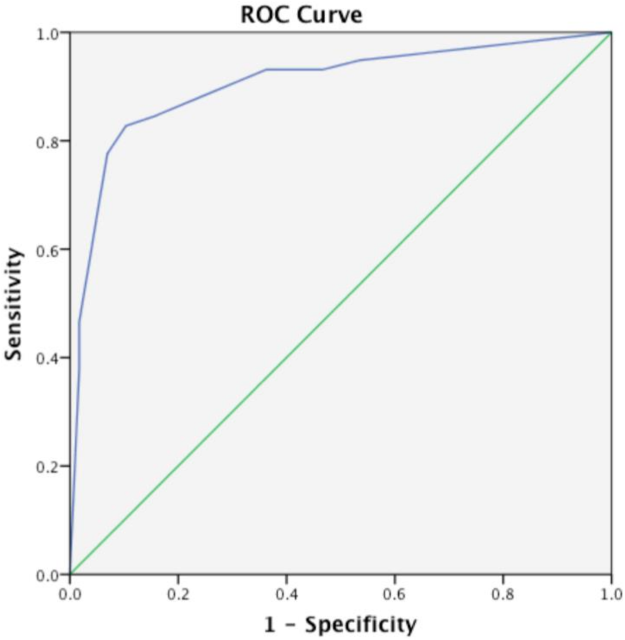
	Area under the curve [95%CI]	P-value
Duration of abdominal pain (days)	0.80 [0.72 - 0.88]	<0.001
Temperature (degree Celsius)	0.77 [0.68 – 0.85]	<0.001
Level of CRP (mg/L)	0.88 [0.82 - 0.94]	<0.001
WBC (x10^9/L)	0.71 [0.62 – 0.80]	<0.001

Prediction model

The results of our final logistic regression models for each category of determinants are shown in table 2a. These five independent predictors for complex appendicitis were selected for our final model and were entered into the final regression model, which explained 64% of the variance (table 2b). Based upon the adjusted odds ratios we awarded 1 point to temperature more than 37.5 degree Celsius, 2 points to more than one day of abdominal pain, to CRP level of more than 38 mg/L and to signs on ultrasound indicative of complex appendicitis. Diffuse abdominal guarding was awarded 3 points. The maximum possible score of our model is 10 points (Table 2b).

The area under the ROC curve (figure 2) was 0.91 [0.86-0.97]. The threshold was set on a value of equal to or larger than 4, as this was the value with the highest sensitivity and associated highest specificity: 89% and 88%, respectively.

Figure 2. ROC curves of our final model



	Area under the curve [95%CI]	P-value
Scoring system	0.91 [0.86 - 0.97]	<0.001

Table 2a. Final logistic regression models for each category.

	N	OR [95% CI]	*P* value	Nagelkerke R Square of the model containing one determinant
1.Medical History				
>1 day of abdominal pain	130	14.7 [6.3-34.5]	<0.001	0.41
2. Physical examination				
Temperature > 37.5 degree Celsius	127	5.9 [2.7–12.7]	<0.001	0.22
Diffuse abdominal guarding	130	7.7 [2.7–21.7]	<0.001	0.18
3. Laboratory results				
CRP level > 38 mg/L	129	19.3 [7.9–46.9]	<0.001	0.46
4. Ultrasound findings				
Signs indicative of complex appendicitis	127	16.3 [6.3-41.8]	<0.001	0.40

Table 2b. Final multivariable logistic regression model to predict complex appendicitis (n=123) with 64% explained variance

Determinants	*Adjusted OR [95% CI]*	*p value*	*Awarded points*
Final model			
Diffuse abdominal guarding	5.4 [1.4-21.1]	0.01	3
CRP level more than 38 mg/L	4.4 [1.4-14.6]	0.009	2
“Signs indicative of complex appendicitis”	4.2 [1.3-13.5]	0.02	2
>1 day of abdominal pain	3.9 [1.3–12.0]	0.02	2
Temperature > 37.5 degree Celsius	2.6 [0.9–7.7]	0.09	1

Validation

The second cohort consisted of 65 children. Ten patients (15%) had complex appendicitis. The 2 by 2 table is shown in table 3. Our prediction model was shown to have a sensitivity of 90 [54-99]%, a specificity of 91 [79-97]% a PPV of 64 [36-86]% and a NPV of 98 [88-100]%. The positive and negative likelihood ratios were 10 [4.19-23.42] and 0.11 [0.02-0.71], respectively. The diagnostic accuracy of our model in this cohort was 91 [84-98]%.

Table 3. Performance of scoring system in second cohort

	Complex appendicitis	Simple appendicitis	Total
Score ≥ 4	9	5	14
Score < 4	1	50	55
Total	10	55	65

Data are displayed as N

Discussion

In this study we developed a scoring system based upon preoperative variables, aiming to make a distinction between simple and complex appendicitis in children. It is highly accurate to rule out complex appendicitis in case the test is negative. It is applicable in patients with a high index of suspicion of appendicitis and is in line with our national guideline.[18] It is, to our knowledge, the first model to integrate clinical findings, laboratory results and results from ultrasound in the analysis. This model might be used to exclude children with complex appendicitis in studies on the non-operative treatment for simple appendicitis.

Accurate differentiation between simple and complex appendicitis is emerging as a potentially key issue as the historical standard of care, i.e. prompt appendectomy, is increasingly questioned in paediatric patients.[13-17,20,21] Both clinical, laboratory and radiological variables have been reported to be of value in diagnosing complex appendicitis, but the results are equivocal.[12-17,22-29] In children, complex appendicitis is seen more often in younger children, whereas in adults it is seen more often in patients >50 years old, confirming the general idea that complex appendicitis occurs in the extreme ages.[16,24,26] Even though clinical variables such as duration of abdominal pain were integrated in previous models as well as in ours, we need to keep in mind that these variables are of subjective nature and their reproducibility is low.[13,16] In addition we need to realise that some variables from physical examination are also subjective and depend on age and each other. Objective variables obtained from blood samples and imaging studies are usually better reproducible and therefore of higher value. As supported by many other studies, CRP was found to contribute significantly to the prediction of complex appendicitis.[12,14,15,23,24,26,28,29] A meta-analysis in 2004, focussing on the diagnosis of acute appendicitis in children as well as adults, reported that high WBC, high granulocyte count and elevated CRP are strong predictors of complex appendicitis.[12] In our study in children, WBC was found to be a predictor of complex appendicitis, but CRP appeared to be the best discriminator between simple and complex appendicitis. As an acute inflammatory protein, however, CRP is elevated in virtually all inflammatory processes and it should therefore be seen in the context of the clinical symptoms. Bilirubin has also been demonstrated to be of value in predicting complex appendicitis.[30] Although it has reasonable value on its own, its value might be useful in scoring systems.[30] In our country however, bilirubin is not part of the routine work-up in children with a suspected appendicitis and could therefore not be analysed in our cohort. New biomarkers such as lactoferrin, calprotectin and interleukin 6 and 8 have recently been reported to be associated with complex appendicitis, although they are not yet part of routine workup.[31-33]

Although it is not surprising that abscess and appendicular contained phlegmon are indicative of complex appendicitis, information on the value of ultrasound in differentiating simple from complex appendicitis in children is scarce.[15] For the diagnosis of acute appendicitis, ultrasound is the diagnostic modality of choice in children; it has higher sensitivity (99%), specificity (95%) and positive predictive value (97%) than in adults.[34-36] Some earlier publications have discussed the use of ultrasound in order to differentiate simple from complex appendicitis. Recently a retrospective study in 161 paediatric patients, evaluating the value of ultrasound in distinguishing simple from complex appendicitis, identified signs of an abscess, intraluminal appendicalith and loss of submucosal echogenic layer of the appendix to be associated with appendicular perforation.[37] Another study reported a specificity of 98% and a positive predictive value of 95%, but with a sensitivity of 35% and a negative predictive value of 55%, with an overall diagnostic accuracy of 62-64% for ultrasound to differentiate simple from complex appendicitis.[15] The interpretation of ultrasound is operator dependent. In our centre, all ultrasound examinations were performed under the responsibility of an experienced (paediatric) radiologist. Although the value of CT in detecting complex appendicitis in adults has been well evaluated and appreciated, in children CT should preferably be avoided because of the radiation risk.[18,19,24,27] We have not performed a CT-scan routinely in children suspected of appendicitis, as this is not supported by our national guideline.[18] MRI has comparable sensitivity and specificity value as CT-scan without the radiation exposure.[38] However this modality is also operator dependent (i.e. level of experience of interpreter) and it is not available 24/7 in all hospitals in our country.

We did not attempt to validate the four scoring systems developed earlier, because they included CT results or laboratory values not obtained by us. Table 4 summarises these prediction models and the model resulting from our study.[13-17] The goals of the scoring systems vary. Some determine the necessity of additional imaging studies,[15,16] while others use it for therapeutical goals.[13,14] The reason for us to develop a scoring system was to assess the type of acute appendicitis so that in the future we can choose the optimal treatment strategy for each type. This is based upon the idea that it might be of value to initially treat simple appendicitis with antibiotics, avoiding surgery in a substantial proportion. We want to point out that our scoring system is only applicable when the diagnosis of appendicitis has already been made. It has not been tested in the general population or in children with abdominal pain presenting at the emergency department. Our scoring system outperforms the previous models especially in terms of sensitivity, negative predictive value and negative likelihood ratio. To our knowledge, we are the first to validate the prediction model in a separate cohort of patients. All earlier studies validated their models in the same cohort from which the scoring system was derived, which is bound to lead to overestimation of the diagnostic accuracy.[13-17]

Our model is of value in cases of a negative result. The false negative rate was only 3%, meaning that only 1 out of 33 children with complex appendicitis will be classified as simple appendicitis, possibly delaying optimal treatment. Information about the consequences of non-operative management of complex appendicitis (gangrenous, perforated, abscess, phlegmon) in children is scarce, although there is some support that this strategy will not negatively influence the outcome of complex appendicitis, or should even be recommended in cases of an appendicular abscess or phlegmon.[5,6] Obviously, patients with assumed simple appendicitis on initial antibiotic treatment must be monitored intensively in order to detect clinical deterioration in an early stage. This ensures that those (false negative) patients will receive the optimal treatment as soon as possible.

Table 4. Summary of the prediction models from the literature including this study.[13-17]

Reference	Age category	Simple vs complex appendicitis	Predictors in model	Diagnostic accuracy	Sensitivity / specificity	PPV / NPV	Validation in second cohort
Williams, 2009 [13]	Children < 18 years	S= 98 C= 53	- Generalised tenderness - Abscess on CT - Duration > 48 hours - WBC >19400 cells/microlitre - Faecalith on CT	NA	47% / 98%	Likelihood ratio: Positive: 27 Negative: 0.53	No
Adibe 2011[17]	Children < 18 years	S= 44 C= 18	PAS >9	NA	NA	66% / 33%	No
Broker, 2012 [14]	Children + Adults	S= 393 C= 105	- CRP - Days of abdominal pain	82%	- / 96%	67% / 84%	No
Peng, 2006 [15]	Children < 18years	S= 45 C= 229	- Duration > 2 days - Peritoneal signs - Temperature > 37.9^{o}C - Neutrophil >12 (10^{-6}L) - ESR > 25mm/h - Age <9 year	NA	87% / 49%	-	No
Oliak, 2000 [16]	Adults	S= 244 C= 76	- Duration > 2 days - Temperature > 38.3^{o}C - Localised tenderness other than RLQ	NA	86% / 58%	39% / 93%	No
Gorter, 2015 (Current study)	Children < 18 years	S= 64 C= 66	- Diffuse abdominal guarding - CRP > 38mg/L - Ultrasound indicative of complex - Duration > 1 day - Temperature > 37.5 ^{0}C	91%	86% / 91%	67% / 97% LR+:10 LR-:0.15	Yes

Limitations

Our study has some limitations. Firstly, the information on determinants and outcomes was extracted retrospectively from patient files by one observer in the validation phase, which may have led to information bias and inflated results. Secondly, the definitions of simple and complex appendicitis are still subject of debate. Our definitions (based upon surgical and histological reports), are supported by previous studies.[13,14,23,26] Patients with complex appendicitis treated non-operatively were excluded. Even though these patients are of interest; the intraoperative and histopathological confirmation of appendicitis was lacking, as in our hospital interval appendectomy is not performed routinely. Thirdly, the prediction model was derived from our tertiary referral centre, which might have led to selection of more severely affected patients, although we validated our model in a subsequent cohort of patients from a large general hospital. Fourthly, ultrasound is an operator dependent modality. Therefore, the reliability of this scoring system depends at least in part on the skills of the radiologist.

Conclusions

In conclusion, our study shows that a model containing five variables explains 64% of the variance between complex and simple appendicitis. The model has been successfully validated on subsequent patients from a large general hospital with a diagnostic accuracy of 91%. We welcome additional prospective validation studies by other research teams. Due to the simplicity of the model, this should be feasible.

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