Diagnosing Ruptured Appendicitis Preoperatively in Pediatric Patients

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BACKGROUND: Over the past decade, pediatric patients with ruptured appendicitis (RA) have been successfully treated with IV antibiotics and an interval appendectomy. Because the treatment of acute appendicitis (AA) and RA in children is now diverging, distinguishing between these two conditions preoperatively is critical.

STUDY DESIGN: A prospective cohort study was conducted. Clinical data were collected, and the attending surgeon's preoperative diagnosis was recorded. Accuracy of the pediatric surgeon's diagnosis was determined. Univariable and multivariable logistic regression were then used to determine independent clinical predictors of RA. Using the relative beta coefficients of these predictors, a scoring system was constructed to aid in the diagnosis of RA.

RESULTS: Two hundred forty-seven patients were evaluated: 98 AA (40%), 53 RA (21%), and 97 not appendicitis (39%). Median age was 10 years old. The overall accuracy of the pediatric surgeon's preoperative diagnosis was 92%. Sensitivity and specificity for the diagnosis of RA were 96% and 83%, respectively. Multivariable regression analysis identified generalized tenderness on examination, duration of symptoms longer than 48 hours, WBC $>$ 19,400 cells/μL, abscess, and fecalith on CT scan as independent predictors for RA. A novel scoring system was developed with these variables, and, when applied to the study population, the specificity for the diagnosis of RA improved to 98%.

CONCLUSIONS: Pediatric surgeons differentiate AA from RA and not appendicitis preoperatively with high accuracy and sensitivity, but the specificity for diagnosing ruptured appendicitis is lower. The scoring system improved the specificity of the preoperative diagnosis. The validity and utility of this scoring system should be examined in future studies in larger patient populations. (J Am Coll Surg 2009;208:819–828. © 2009 by the American College of Surgeons)

Appendicitis is the most common abdominal condition leading to urgent operation in children. There were more than 100,000 children with appendicitis discharged from children's hospitals in 2006 in the US.[1] The rate of ruptured appendicitis (RA) is higher in children than in adults and has varied in the literature from 30% to 74% depending on the study population.[2]

Treatment for acute appendicitis (AA) consists predominantly of urgent appendectomy, although occasionally this dogma is questioned. Treatment for RA has much greater variation between pediatric surgeons, medical centers, and for individual patients.[3-6] Whether urgent appendectomy or initial antibiotics with interval appendectomy should be the preferred treatment for children with RA remains controversial. Various groups have reported that interval appendectomy may be associated with decreased hospital length of stay and decreased postoperative morbidity.[7-11] Others argue that interval appendectomy may not be needed after resolution of the acute illness with antibiotics and other supportive measures.[12,13] Our group is currently conducting a prospective randomized trial comparing early versus interval appendectomy in patients younger than 18 years of age with RA.[14]

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Abbreviations and Acronyms

AA = acute appendicitis
LR = likelihood ratio
NA = not appendicitis
RA = ruptured appendicitis

Distinguishing ruptured from acute appendicitis is very important if the treatment differs for the two conditions. Various publications have retrospectively compared patients found to have acute versus ruptured appendicitis at operation and measured differences between the groups.[15-20] Characteristics reported to increase the risk for RA, compared with AA, have included longer duration of symptoms (2 to 3 days), diffuse abdominal pain as opposed to localized right lower quadrant pain, younger age, more significant fever, and a variety of laboratory findings that are inconsistent between studies. Other studies have focused on the impact of race, insurance status, and hospital volume on the risk for RA.[2] The pediatric surgeon's ability to distinguish these two conditions preoperatively has not been prospectively studied. If treatment recommendations continue to differ for the two diagnoses, and clinical trials are conducted in RA patients, we propose that the distinction between AA and RA is critically important. The goals of this study were to determine the current accuracy of the pediatric surgeon's preoperative diagnosis of AA versus RA (and versus nonappendicitis abdominal pain), to prospectively identify and rank patient characteristics that increase the risk of having ruptured appendicitis, and to investigate potential improved methods of distinguishing AA from RA preoperatively.

METHODS

We tested two hypotheses in this study: the surgeon's preoperative diagnosis would have a higher accuracy than any single objective characteristic available preoperatively (we estimated that the accuracy would be approximately 90% as measured by agreement with final diagnosis), and the use of a combination of objective variables may improve accuracy over that found with the surgeon's preoperative diagnosis.

Data were prospectively collected over a 9-month period (February 2007 to October 2007) on all patients younger than18 years of age referred for surgical consultation for abdominal pain at a regional children's hospital. Patient demographics, elements of the history and physical examination, laboratory values, and diagnostic imaging reports were collected. The pediatric surgical team, including an attending pediatric surgeon, a fellow in pediatric surgery, and a general surgery resident, recorded an agreed initial (preoperative) diagnosis using all data available. Establishing the preoperative diagnosis was a dedicated part of this study and typically involved repeated history and physical examinations by multiple team members (over a brief period, usually in the emergency department), independent reviews of the available data, and consultation with pediatric radiologists when needed for detailed review of the imaging studies. The use of advanced imaging (CT or ultrasonography) was decided by emergency department physicians, referral physicians, or pediatric surgeons. When there was disagreement between team members about the initial diagnosis, the attending pediatric surgeon made the final decision. Final diagnosis was determined using operative findings, pathology reports, or discharge diagnosis in those not undergoing operation. Final diagnosis in patients who did not undergo an operation was confirmed with followup telephone contact and followup review of the electronic medical record aimed at identifying care received after the initial discharge. The Institutional Review Board at the University of Tennessee Health Science Center and Le Bonheur Children's Medical Center approved this study.

Accuracy of the pediatric surgeon's preoperative diagnosis was calculated by comparing the initial diagnosis with the discharge diagnosis for the entire dataset. This discharge diagnosis was used as the gold standard for comparing each test, because pathology was not available on patients treated nonoperatively.

Analyses were performed to determine independent predictors of RA among patients determined to have a diagnosis related to the appendix (excluding nonappendicitis patients). Accuracy, sensitivity, specificity, positive likelihood ratios (LR+), and negative likelihood ratios (LR−) used to distinguish acute from RA were calculated with 95% confidence intervals using the methods described by Simel and colleagues.[21]

Univariable analysis was also performed on all preoperative variables comparing patients with a discharge diagnosis of RA to those with AA. Continuous variables were converted to categorical variables by using a cut point that maximized the Youden's index.[22] The Youden's index is the value that maximizes the sensitivity and specificity of any continuous variable, helping to choose an appropriate cut point for dichotomization. Any variables with a p value ≤ 0.2 on univariate analysis were placed into the multivariable model. The final multivariable model of RA was completed in a manual, backward, stepwise fashion to determine preoperative variables independently associated with RA.

Using the predictors identified with multivariable analysis, a scoring system was constructed to evaluate whether an objective score based on available data might improve the ability to accurately diagnose RA. Points were assigned to each preoperative variable based on the beta coefficients

Table 1. Patient Characteristics

Characteristic	Acute (n = 98)	Ruptured (n = 53)	Not appendicitis (n = 96)
Age, y, median (range)	11.2 (2–17)	9.2 (1–16)*	9.8 (0.25–17)*
Female, n (%)	34 (35)	18 (34)	45 (47)
Duration of symptoms, h, median (range)	34.4 (4–360)	86.7 (20–384)*	86.4 (2–720)*
Localized RLQ tenderness, n (%)	89 (91)	19 (36)*	27 (30)*
Diffuse tenderness, n (%)	9 (9)	33 (62)*	16 (17)
WBC $\times$ $10^3/\mu$L, median (range)	15.4 (6–28)	17.9 (5–29)*	12 (3–39)*
Bands, %, median (range)	9.6 (0–22)	7.9 (0–27)	7.8 (0–42)
CT, n (%)	71 (72)	50 (94)	75 (78)
Ultrasound, n (%)	10 (10)	7 (13)	36 (38)

*$p < 0.05$.
RLQ, right lower quadrant.

from the multivariable final model. The patient's score was calculated by adding the appropriate points based on the number of significant preoperative variables present. Positive and negative likelihood ratios (LR) were calculated for the pediatric surgeon's preoperative diagnosis and the score according to the scoring system.

RESULTS

Overall study cohort

Two hundred forty-seven patients were evaluated over a 9-month study period. Ninety-eight had AA, 53 had RA, and 96 did not have appendicitis. The median age was 10 years (range 1 to 17 years), 39% were female, and the median duration of symptoms at the time of surgery consultation was 2.8 days. The majority of the patients were Caucasian (52%); smaller percentages were African American (34%) or Hispanic (9%). Fifty-five percent of the patients had localized right lower quadrant pain; 9% presented with generalized peritonitis. Most patients underwent some form of diagnostic imaging, with 79% of patients having a CT scan, 21% receiving an abdominal ultrasound, and 15% undergoing both. The perforation rate among all patients with appendicitis was 35%.

Acute appendicitis

The 98 children with a discharge diagnosis of AA based on intraoperative findings were older and had a shorter duration of symptoms than patients with ruptured or no appendicitis (Table 1). These children had a median duration of symptoms of 24 hours, with 73% presenting with emesis and 75% complaining of anorexia. Ninety-one percent of patients with AA had localized right lower quadrant pain; only 30% had rebound tenderness. The median WBC count was lower in patients with AA, although there was no difference in the percentage of bands among the three diagnostic groups. Seventy-two percent of these patients had a CT scan performed and 10% underwent abdominal ultrasonography. All patients with a preoperative diagnosis of AA underwent an operation, with a negative appendectomy rate of 4.4%.

Ruptured appendicitis

The RA group consisted of 53 patients, with a median age of 9.2 years; 34% were female (Table 1). Patients with RA had symptoms for a median of 86.7 hours, similar to the not appendicitis (NA) group, and had a higher WBC count (median 17,900 cells/μL). The majority of patients with RA had diffuse abdominal pain (62%) and CT scans performed (94%). Of the 53 patients, 35 underwent immediate appendectomy, 17 had an interval appendectomy 7 to 21 weeks after initial presentation with RA, and 1 patient was managed with IV antibiotics but did not return for interval appendectomy.

Not appendicitis

Ninety-six patients in the study cohort did not have appendicitis. These patients were similar to patients in the RA group in age and duration of symptoms (Table 1). But the NA group had a larger percentage of females and a lower median WBC count than the AA or RA groups. Eight patients with diagnoses other than appendicitis underwent exploratory laparotomy. Two of these patients had RA identified at the time of exploration. Discharge diagnoses are listed in Table 2. Followup was conducted on all patients who did not undergo an operation (11 to 20 months after discharge): either by telephone followup questionnaire (76%), review of the hospital medical record system, or both. No patient reported a subsequent diagnosis of appendicitis during this followup period.

Accuracy of pediatric surgeons' preoperative diagnosis

Pediatric surgeons at our institution diagnosed acute, ruptured, and not appendicitis with an accuracy of 93.5%,

Table 2. Diagnoses of Not Appendicitis Cohort

Acute gastroenteritis (40)
Mesenteric adenitis (9)
Constipation (5)
Colitis (4)
Pyelonephritis (3)
Pelvic inflammatory disease (3)
Urinary tract infection (2)
Small bowel obstruction (2)
Ruptured ovarian cyst (2)
Functional abdominal pain
Anterior superior iliac spine fracture
Epiploic appendagitis
Pneumonia
Intussusception
Retroperitoneal lymphangioma
Acetaminophen toxicity
Gluteal myositis
Urinary retention
Crohn's ileitis
Gastroesophageal reflux disease
Tubal torsion

93.5%, and 96.8%, respectively (Table 3). Although pediatric surgeons were able to diagnose AA with high sensitivity (92.6%) and specificity (94.9%), these figures for the diagnosis of RA were mixed. RA was correctly diagnosed preoperatively with a sensitivity of 96.4% and a specificity of 83%. Appendicitis was excluded with high sensitivity (98.7%) and specificity (93.8%). Although the overall surgeon's preoperative diagnostic accuracy was 92%, there was variability among the 5 attending pediatric surgeons participating in this study. Accuracy rates varied from 97% (36 patients) to 83% (30 patients) among the pediatric surgeons, for an absolute difference of approximately 14%.

Table 3. Pediatric Surgeon Preoperative Diagnosis

Variable	Acute	Ruptured	Not appendicitis
Accuracy, %	93.5	93.5	96.8
Sensitivity, %	92.6	96.4	98.7
Specificity, %	94.9	83	93.8
Positive likelihood ratio	12.8	23	72
Negative likelihood ratio	0.05	0.21	0.06

The univariable predictive value of all recorded data variables in diagnosing ruptured appendicitis is shown in Table 4. No single variable accurately predicted the final diagnosis. Decreased age and African-American race were significantly more common in RA patients. Gender had no association with final diagnosis. Elements of the history significantly associated with RA included anorexia, emesis, and duration of symptoms greater than 48 hours (Table 4). Signs of ruptured appendicitis included fever (temperature $> 38°$ C), right lower quadrant tenderness to palpation, diffuse abdominal tenderness, generalized peritonitis, and high white blood cell count (WBC $>$ 19,400 cells/μL), though the presence of diffuse abdominal pain and generalized peritonitis was positively correlated with each other and negatively correlated with right lower quadrant tenderness to palpation. Extraluminal air, fecalith, and abscess on CT scan were also associated with RA. All variables from the univariable analysis with a p value ≤ 0.2 were placed into the multivariable analysis.

The final model identified 5 preoperative variables that were independently associated with the diagnosis of RA: duration of symptoms greater than 48 hours, pain not localized to the right lower quadrant, WBC $>$ 19,400 cells/μL, and fecalith and abscess on CT scan (Table 5).

Table 4. Univariate Analysis for Ruptured Appendicitis

Variable	Odds ratio	95% CI	p Value
Patient demographics			
Age $>$ 6 y	0.848	0.386–1.864	0.6812
Female gender	0.945	0.465–1.919	0.8748
African American	2.357	1.109–5.007	0.0258
Hispanic	1.8	0.580–5.58	0.3088
Symptoms			
Anorexia	3.810	1.243–11.676	0.0192
Diarrhea	1.583	0.754–3.323	0.2244
Emesis	3.268	1.176–9.082	0.0231
Duration $>$ 48 h	11.511	4.991–26.547	$<$ 0.0001
Signs			
Temperature $>$ 38°C	4.514	2.205–9.241	$<$ 0.0001
Localized RLQ ttp	0.078	0.034–0.176	$<$ 0.0001
Rebound RLQ ttp	0.725	0.335–1.567	0.4131
Diffuse ttp	12.912	5.647–29.526	$<$ 0.0001
Generalized peritonitis	18.364	5.086–66.303	$<$ 0.0001
WBC $>$ 19,400 cells/μL	4.049	1.926–8.509	0.0002
CT findings			
Extraluminal air	8.654	1.782–42.025	0.0074
Fecalith	4.070	1.893–8.752	0.0003
Free fluid	1.703	0.822–3.528	0.1520
Abscess	14.194	4.464–45.131	$<$ 0.0001
Dilated appendix	0.767	0.372–1.579	0.4710

RLQ, right lower quadrant; ttp, tenderness to palpation.

Table 5. Multivariate Analysis for Ruptured Appendicitis

Variable	Odds ratio	95% CI	p Value	Beta coefficient
Generalized tenderness	7.4	2.2–24.5	$<$ 0.01	2.00
Abscess on CT	6.7	1.6–27.1	$<$ 0.01	1.90
Duration $>$ 48 h	6.4	1.9–21.7	$<$ 0.01	1.86
WBC $>$ 19,400 cells/μL	5.6	1.6–19.6	$<$ 0.01	1.75
Fecalith on CT	4.5	1.4–14.7	0.01	1.51

Table 6. Ruptured Appendicitis Scoring System

Variable	Points
Generalized tenderness	4
Abscess on CT	3
Duration > 48 h	3
WBC > 19,400 cells/μL	2
Fecalith on CT	1

Development of a novel scoring system

The beta coefficients of these 5 variables were then used to develop a scoring system to potentially improve the accuracy of delineating RA preoperatively (Table 6). Pain not localized to the right lower quadrant had a beta coefficient of 2.00 and was assigned 4 points. Abscess on CT scan and duration of symptoms greater than 48 hours had similar coefficients (1.90 and 1.86, respectively) and were assigned 3 points each. WBC count greater than 19,400 cells/μL had a beta coefficient of 1.75 and was assigned 2 points, and fecalith on CT scan had the lowest significant correlation with ruptured appendicitis, with a beta coefficient of 1.51 (1 point). When applying the scoring system back to the dataset, the specificity, sensitivity, and likelihood ratio for each score is listed in Table 7. Although the scoring system was not sensitive for diagnosing RA, it improved the specificity of the diagnosis compared with the pediatric surgeon's preoperative diagnosis.

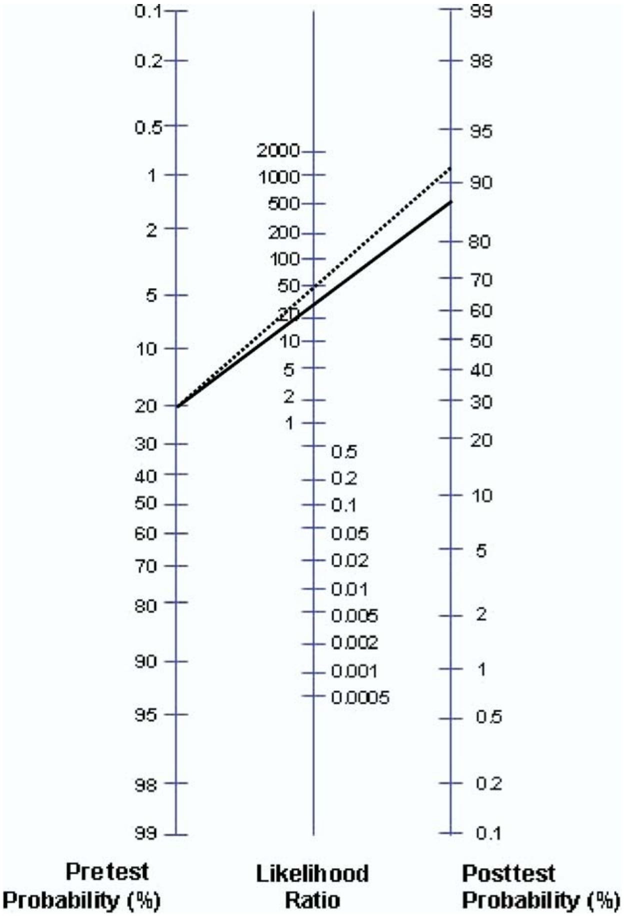

Figure 1. Posttest probability for ruptured appendicitis. Solid line, surgeon's diagnosis; dashed line, score of 9 from scoring system.

Table 7. Accuracy of Ruptured Appendicitis Scoring System

Score	Sensitivity	Specificity	PDLR	NDLR
1	98	46	1.8	0.04
2	96	56	2.1	0.07
3	92	65	2.6	0.12
4	92	81	4.9	0.1
5	82	90	7.9	0.19
6	78	92	9.1	0.24
7	68	94	11.3	0.33
8	62	97	24.26	0.38
9	47	98	27	0.53
10	35	99	41	0.65
11	18	1	—	0.82
12	7	1	—	0.92
13	6	1	—	0.94

NDLR, negative diagnostic likelihood ratio; PDLR, positive diagnostic likelihood ratio.

Likelihood ratios

The positive LR of the surgeon's preoperative diagnosis is 23, and the positive LR for a score of 9 is 27. Both of these LRs are high and greatly increase the likelihood of a given patient having RA (posttest probability) compared with the pretest probability. Applying these LRs to the pretest probability in our study cohort (21% of the total cohort had final diagnosis of RA) indicates that the posttest probability of having RA with the surgeon's diagnosis is 86% and with a score of 9 is 92% (Fig. 1).

DISCUSSION

Minimizing appendectomy in patients whose abdominal pain is from some condition other than appendicitis has been the goal of surgeons for decades. So much of the published literature in appendicitis diagnosis focuses on the distinction between appendicitis and nonappendicitis conditions causing abdominal pain. This study focused on eliminating confusion in diagnosing acute versus ruptured appendicitis preoperatively, because this diagnostic error can also lead to suboptimal treatment. Determination of the diagnostic error rate in our institution was especially important, because of a concurrent prospective randomized trial comparing early with delayed appendectomy as treatment for perforated appendicitis in children.

The prospective design of this study allows use of standardized data forms, more complete data collection, and increased validity of the measurement of the preoperative surgeon's diagnostic accuracy. We have also completed a contemporary analysis of this diagnostic question using a variety of different assessments, including likelihood ratios. There are very few appendicitis diagnostic studies performed by pediatric surgeons; most are by pediatric emergency medicine physicians or radiologists. And, last, this study focuses on an area with relatively few earlier studies, ie, distinction of AA from RA preoperatively.

The overall accuracy of the pediatric surgeon's preoperative diagnosis was 92%, which was close to that hypothesized before starting the study. Also supporting a high accuracy was the negative appendectomy rate of 4%. It should be noted that during this study period, attending surgeons were acutely aware that the accuracy of distinguishing AA from RA was being measured, and this likely increased attention and effort in this activity. This study was done concurrently with a randomized trial evaluating early versus interval appendectomy for children with RA, which is still ongoing. The preoperative diagnosis was a team effort and more time may have been spent with the family, patient, radiologist consultation, and review of data in this study setting compared with usual clinical practice. It is possible that the accuracy might be lower outside of the study setting. Also, the accuracy did vary between pediatric surgery attending physicians from 97% to 83%. In an earlier retrospective study focusing on differentiating AA from nonappendicitis, Kosloske and associates[23] also reported very high accuracy of the surgeon's diagnosis (99% sensitivity, 92% specificity, 97% accuracy). This is one of the few diagnostic studies in the literature related to appendicitis from the pediatric surgeon's perspective.

There have been several retrospective studies addressing which patient characteristics are associated with an increased risk for RA rather than AA. The most common variables reported to increase the risk of RA from these studies include longer duration of symptoms (> 2 to 3 days), signs of diffuse peritoneal irritation on abdominal examination, age < 8 to 9 years, higher temperature elevation, and multiple CT findings.[15-20] Laboratory data reported to be associated with ruptured appendicitis include elevated C-reactive protein, erythrocyte sedimentation rate > 25 mm/hour, increased band neutrophils, and increased total white blood cell count.[15,17,18,20] Our data provide a ranking of variables that are routinely available preoperatively in patients referred for surgical consultation to "rule out appendicitis" in order of strength of association with a final diagnosis of RA. The most important preoperative risk factors identified in our study cohort, in rank order, were duration of symptoms > 48 hours, diffuse abdominal pain, WBC > 19,400 cells/μL, abscess identified on CT, and fecalith identified on CT. Age was not an independent significant risk factor for RA. The multivariable regression model developed in this study was highly predictive of RA, with an area under the receiver operating characteristic (ROC) curve of 0.92.

Scoring systems focusing on differentiating AA from nonappendicitis conditions in adults and children are plentiful in the literature.[24,25] The Alvarado[26] and Samuel[27] scoring systems have received the most attention. The goal of these systems, as opposed to the one developed in our study, is to determine which patients are at high risk for having appendicitis and might benefit from advanced imaging or surgical evaluation. The reported accuracy of these scoring systems has varied, depending on the study cohort involved.[28]

The derivation of a novel scoring system, based on the variables found to be significant in the multivariable regression analyses, is an attempt to improve the diagnostic accuracy of RA in the future. As mentioned earlier, the pediatric surgeon's preoperative diagnosis was somewhat variable between the five attending surgeons participating in this study. Because the distinction between AA and RA was a major part of this prospective study, it is possible that this distinction in routine clinical practice could be somewhat lower. Also, the accuracy of other pediatric surgeon groups and other medical centers is largely unknown. An objective scoring system, if validated, could decrease the variability of this diagnostic process and potentially improve overall distinction between AA and RA. Depending on the cut point chosen, the sensitivity and specificity of the scoring system vary considerably. We propose that a cut point that achieves a high specificity (at the expense of sensitivity) would potentially be most valuable. Our data indicate that the pediatric surgeons accurately distinguish appendicitis from nonappendicitis abdominal pain with high sensitivity, specificity, and accuracy. Distinguishing AA from RA is more difficult. Once a diagnosis of appendicitis has been made, the scoring system might be used to assist in distinguishing the acute from the ruptured form. Deciding where the cut point should be in this scoring system significantly influences its performance. As the cut point value increases, specificity and the positive likelihood ratio increase, and the sensitivity decreases markedly. Using a cut point of 9, the scoring system outperforms the surgeon's preoperative diagnosis in terms of positive LR and specificity by a degree that, if reproducible, would likely help practicing pediatric surgeons make clinically relevant decisions. Confirmation of this scoring system in a different patient cohort will be necessary to validate its clinical utility. To this end, plans are underway to test this scoring system in a multicenter, prospective cohort study. It should be noted that many scoring systems appear very accurate when applied to the study populations from which they are derived, but then are less accurate when one attempts to validate them in other studies.[28]

Limitations of this study include its single center design, relatively low numbers of patients, and frequent use of advanced imaging (especially abdominal CT). It remains unknown how accurate pediatric surgeons' preoperative diagnoses are across multiple centers or how the scoring system might perform in larger and more diverse study populations. As more data are published about potential harmful effects of ionizing radiation from abdominal and pelvic CT scans, heavy reliance on these studies is problematic. It is unknown if we can maintain a high level of accuracy in distinguishing AA from RA with significantly reduced use of advanced imaging techniques.

Author Contributions

Study conception and design: Williams, Blakely, Fischer
Acquisition of data: Williams, Streck, Dassinger, Gupta, Renaud
Analysis and interpretation of data: Williams, Blakely, Fischer
Drafting of manuscript: Williams, Blakely, Fischer
Critical revision: Williams, Blakely, Fischer, Streck, Dassinger, Gupta, Eubanks, Huang, Hixson, Langham

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