Use of White Blood Cell Count and Polymorphonuclear Leukocyte Differential to Improve the Predictive Value of Ultrasound for Suspected Appendicitis in Children

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BACKGROUND: The objective of this study was to examine the use of WBC count and polymorphonuclear leukocyte differential (PMN%) for improving the predictive value of ultrasound (US) in children with suspected appendicitis.

STUDY DESIGN: We conducted a retrospective cohort study of children undergoing US for suspected appendicitis between January 1, 2010 and December 31, 2012 at a single children's hospital (n = 845). Negative (NPV) and positive predictive values (PPV) for appendicitis were calculated for common constellations of US findings and compared with and without the use of laboratory thresholds (WBC $>9 \times 10^3/\mu L$ and PMN% >65% for PPV; WBC $\leq 9 \times 10^3/\mu L$ and PMN% $\leq$65% for NPV).

RESULTS: Fifty-one percent of US were considered "equivocal" (ie, appendix incompletely visualized, no primary or secondary signs, or presence of fluid only) and NPV increased significantly for this cohort using laboratory thresholds (41.9% vs 95.8%; $p < 0.001$). Primary signs of appendicitis, without secondary signs, were documented in 18% of examinations, and the PPV associated with this cohort increased from 79.1% to 91.3% ($p < 0.001$) using laboratory thresholds. Secondary signs with or without primary signs were documented in 24% of examinations, and laboratory thresholds improved the PPV in this cohort from 89.1% to 96.8% ($p < 0.001$). Guidelines recommending against the use of CT for very high-risk and low-risk categories (NPV >95% and PPV >95%) on the basis of combined US and laboratory data could have reduced the number of CTs by 27.1% (101 of 373) during the study period.

CONCLUSIONS: The incorporation of WBC count and PMN% can substantially improve the predictive value of US in the diagnosis of suspected appendicitis in children. (J Am Coll Surg 2015;220: 1010−1017. © 2015 by the American College of Surgeons)

Appendicitis is the most common abdominal surgical emergency in the pediatric population, yet the diagnosis remains challenging in many cases. Clinical scoring systems, such as the pediatric appendicitis score and Alvarado score, have been developed to streamline the diagnostic pathway, although prospective studies have found that neither can be used reliably for this purpose.[1-3] The use of clinical judgment has been found to be more reliable than the Alvarado score in some studies, although the use of the clinician's impression for diagnostic purposes is often heavily dependent on their experience, which can vary greatly between and within hospitals.[4,5] Use of laboratory data as a diagnostic adjunct has similarly been associated with relatively low sensitivity, and children with pathology-proven appendicitis can often present with a normal leukocyte count.[6,7]

The poor diagnostic yield of clinical and laboratory data has led to an ongoing reliance on diagnostic imaging, including ultrasound (US), CT, and MRI. With

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Abbreviations and Acronyms
NPV = negative predictive value
PMN% = polymorphonuclear leukocyte differential
PPV = positive predictive value
RLQ = right lower quadrant
US = ultrasound

increasing public health concern surrounding radiation exposure, and mounting pressure from national specialty organizations to limit the use of CT, US is the preferred initial imaging modality in the evaluation of children with suspected appendicitis.[8-13] Despite its benefits over CT, however, diagnostic accuracy of US has been reported to be quite variable and heavily dependent on operator experience.[9,14] Rates of nondiagnostic US have exceeded 50% in some series, and many children might still undergo CT scanning or admission to the hospital for additional observation in equivocal cases.[14,15]

To our knowledge, no study has examined the predictive value of combining laboratory and US data together in children with suspected appendicitis. It is conceivable that laboratory data could improve the negative (NPV) and positive predictive value (PPV) of different constellations of US findings, and provide a widely generalizable strategy for improving diagnostic accuracy, given the common practice of routinely obtaining both CBC and US during the diagnostic evaluation.[16] The main objective of this study was to examine the predictive value of US findings in children with suspected appendicitis and with stratification by laboratory data.

METHODS

We conducted a retrospective cohort study of patients 3 to 18 years of age evaluated in the emergency department at a single freestanding children's hospital with a chief symptom of abdominal pain between January 1, 2010 and December 31, 2012. Patients were considered for inclusion if they received a consultation by the surgical service for suspected appendicitis and received an abdominal or pelvic US as part of their diagnostic evaluation. Patients were excluded if there was a history of abdominal surgery, cognitive delay or neurologic impairment, immunodeficiency disorder, antibiotic use for another condition at presentation, missing laboratory data, or if they received any advanced diagnostic imaging test of the abdomen or pelvis during the week before presentation.

Demographic and laboratory data were obtained from the medical record, including age, sex, weight, and race, WBC count, and polymorphonuclear leukocyte differential (PMN%). Ultrasound reports were reviewed using standardized definitions and case report forms, and findings were documented on the basis of appendiceal visualization (partially, fully, or not at all), primary signs of appendicitis (hyperemia of the appendiceal wall or wall thickness >7 mm), secondary signs of appendicitis (fecalith or echogenic fat), and the presence of free fluid in the right lower quadrant (RLQ) and pelvis. Ultrasound findings from each patient were also grouped to identify the most common constellations of US findings in the study cohort.

To identify clinically relevant laboratory threshold cutoff values on the basis of both PPV and NPV, scatterplots were generated by plotting WBC count against PMN% for patients with and without pathology-proven appendicitis for each constellation of US findings. It was our intent to define one clinically relevant set of threshold values for WBC and PMN% that could be used for each constellation of US findings. Medical records were also reviewed for disposition after initial emergency department evaluation (eg, operation, discharge, or inpatient admission for serial abdominal examinations), total hospital cost, CT use, and finalized pathology results.

Positive and negative predictive values for pathology-proven appendicitis were calculated along with their 95% CIs (based on binomial proportions) on the basis of laboratory threshold values, constellations of different US findings, and for combinations of US findings and laboratory values together. Positive and negative predictive values were then compared between those derived from the combined data and those derived from laboratory thresholds and US findings constellations alone using chi-square statistics.

To explore using combined laboratory and US data to reduce radiation exposure and resource use through guidelines targeting high and low-risk cases (NPV >95% and PPV >95%), rates of CT use and inpatient admission were calculated for each constellation of US findings with and without stratification by laboratory threshold values. The marginal cost of an inpatient admission for serial abdominal examinations vs that associated with discharge from the emergency department directly was estimated by comparing the difference in median hospital costs between these cohorts.

RESULTS

We identified 1,056 patients that met inclusion criteria and 845 were included in the analysis after applying exclusion criteria (Fig. 1). Forty-eight percent were male, 48.3% were white, and median age at presentation was 11 years (interquartile range 7 to 14 years).