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Lack of utility of measuring serum bilirubin concentration in distinguishing perforation status of pediatric appendicitis☆

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ABSTRACT

Background: Pediatric appendicitis is a common, potentially serious condition. Determining perforation status is crucial to planning effective management.
Purpose: Determine the efficacy of serum total bilirubin concentration [STBC] in distinguishing perforation status in children with appendicitis.
Methods: Retrospective review of 257 cases of appendicitis who received abdominal CT scan and measurement of STBC.
Results: There were 109 with perforation vs 148 without perforation. Although elevated STBC was significantly more common in those with [36%] vs without perforation [22%], the mean difference in elevated values between groups [0.1 mg/dL] was clinically insignificant. Higher degrees of hyperbilirubinemia [>2 mg/dL] were rarely encountered [5%]. Predictive values for elevated STBC in distinguishing perforation outcome were imprecise [sensitivity 38.5%, specificity 78.4%, PPV 56.8%, NPV 63.4%]. ROC curve analysis of multiple clinical and other laboratory factors for predicting perforation status was unenhanced by adding the STBC variable. Specific analysis of those with perforated appendicitis and percutaneously-drained intra-abdominal abscess which was culture-positive for *Escherichia coli* showed an identical rate of STBC elevation compared to all with perforation.
Conclusions: The routine measurement of STBC does not accurately distinguish perforation status in children with appendicitis, nor discern infecting organism in those with perforation and intra-abdominal abscess.

1. Introduction

An important factor in determining appendicitis management and predicting outcome is distinguishing perforation status. Children with perforated appendicitis often require prolonged hospitalization, performance of more radiographic imaging tests, and repeat hospitalization for evaluation and management of complications relative to those with uncomplicated appendicitis [1].

Assessment for appendicitis and risk-determination for perforation is multi-factorial. Particular physical findings can indicate peritoneal inflammation, yet lack specificity for perforation. Likewise, routinely assessed laboratory variables [like CBC WBC and differential counts] are often imprecise in distinguishing outcome [1,2]. Radiographic imaging, particularly abdominal CT scan, can accurately stratify risk; yet is not universally sensitive, nor routinely performed due to concern for exposing children to ionizing radiation.

Prior appendicitis studies of adults [3-12] and children [13] have reported utility of STBC in distinguishing perforation status. The purpose of this study is to determine the clinical efficacy of routine measurement of SBC in a large sample of children with appendicitis; and correlate results with appendicitis outcomes to determine the efficacy of this marker for distinguishing perforation status.

2. Methods

A retrospective analysis was conducted of consecutive cases of pediatric appendicitis presenting to the Pediatric Emergency Department at Maimonides Medical Center from 2009 to 2015. Studied were patients who presented with abdominal pain and received dual-contrast [oral and IV administered] abdominal CT scan. Diagnosis of appendicitis and distinction of perforation status were determined per radiologic criteria [14,15] given in Fig. 1. Those who also had measurement of serum bilirubin concentration [total and direct] on presentation per the discretion

Abbreviations: CT, computerized tomography scan; ED, emergency department; STBC, serum total bilirubin concentration; PPV, positive predictive value; NPV, negative predictive value.

☆ What's known: Prior studies of patients with appendicitis have reported variable results for serum total bilirubin concentration to distinguish perforation status.What this study adds: Assesses the efficacy of serum total bilirubin concentration in distinguishing perforation status of children with appendicitis.

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- **Appendicitis: visualization of an enlarged appendix measuring ≥7 mm in diameter in addition to inflammatory signs including hyperemia in the wall, peri-appendiceal fat stranding, or appendicolith**

- ***Perforated*** **appendicitis: criteria for appendicitis [above] with evidence of either intra-abdominal abscess, extra-luminal air, extra-luminal appendicolith, or focal defect in enhancing appendiceal wall**

Fig. 1 Abdominal CT criteria for perforated appendicitis [14,15].

of the managing ED physician were selected for study. Information analyzed included results of admission lab tests, abdominal CT scan imaging; abscess aspirate culture results for those who received percutaneous drainage; and for those who received appendectomy, dictated operative report by attending-level surgeon - specifically noting whether there was appendiceal tissue perforation visualized. Also analyzed were clinical variables of patient age, gender, presence of fever, duration of symptoms, and presence of appendicolith. An actionable change in clinical course for those with an abnormally elevated serum bilirubin level was defined as performing subsequent hepatic diagnostic blood tests, gastroenterology consultation, or specific imaging of the hepatobiliary system during the hospitalization.

The reference range of normal STBC level is <1.3 mg/dL; and for serum direct bilirubin <0.5 mg/dL [16]. A separate analysis was performed of the subset of patients with perforated appendicitis/intra-abdominal abscess who received percutaneous drainage with abscess culture positive for *E. coli* and had TBC measured.

2.1. Statistical analysis

Assuming a clinically significant difference of 0.5 mg/dL in STBC between groups [with a ±0.6 SD] [13], we calculated that a sample of 25 patients in each group would yield a power of 81%. Utilizing a total sample size of 250 patients was expected to yield a power of 100%. Statistical comparisons between patients with and without perforation were performed using independent group Student *t*-tests for continuous predictor variables; and x [2] tests were used to compare categorical predictors. All tests were carried out using $p < 0.05$ as the significance level and were done using IBM SPSS Statistics for Windows, version 20 (IBM Corp, Armonk, NY). Separate ROC curves were generated for STBC alone; and in combination with other variables [patient age, gender, presence of fever, duration of symptoms, CBC WBC count, presence of appendicolith] to determine predictive value in distinguishing perforated vs non-perforated appendicitis.

The study was approved by our IRB.

3. Results

There were 257 patients with CT confirmed appendicitis (during the study period who received SBC measurement [Fig. 2]). There were 161 males. Rates of gender distribution, mean patient age, ED-measured fever, and mean CBC WBC count were not significantly different between those with and without perforation [Table 1; p = NS].

Laparoscopic appendectomy was performed in 57/109 with perforation vs all 148 without perforation. All 52 patients managed non-operatively met CT criteria for perforated appendicitis; all who received appendectomy had surgeon report of visualized appendix tissue morphology [perforated vs non-perforated].

Fig. 2 shows a majority in each group had a normal SBC. Of those with elevated STBC, the mean difference between groups was 0.1 mg/dL. The rate of abnormally elevated SBTC was significantly greater [$p = 0.02$] in those with vs without perforation. Predictive values for elevated STBC and perforation outcome are: sensitivity 38.5%, specificity 78.4%, PPV 56.8%, NPV 63.4%. ROC curves displaying predictive values of total and direct bilirubin level for perforation outcome [Fig. 3] indicate poor discriminatory value [AUC 0.58]. When STBC is added to other laboratory and clinical variables [patient age, gender, presence of fever, duration of symptoms, CBC WBC count, presence of appendicolith], the ROC curve AUC was unchanged [0.82]. In no case did performance of a STBC test result in an actionable change in clinical course.

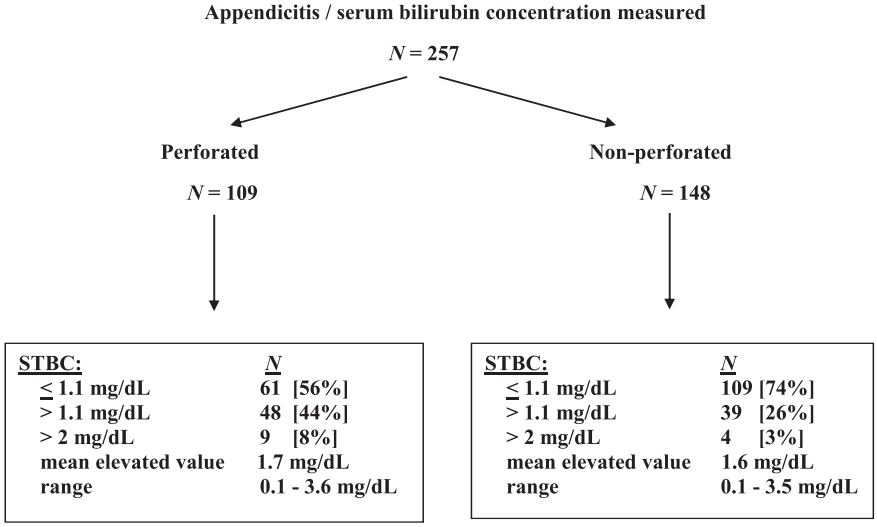

Fig. 2. Demographic and outcome profile.

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