**Sonographic Puylart staging to differentiate complicated and uncomplicated appendicitis**

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**BACKGROUND**

Acute appendicitis is the most common surgical emergency in children with substantial health care burden associated with the 70,000 appendectomies performed annually in the United States (1). Early recognition, increasing diagnostic accuracy, and surgical advances have dramatically lowered the morbidity of appendicitis, and virtually eliminated its mortality (1-4). While the definitive treatment is appendectomy, surgery is associated with pain, anesthesia risks, post-operative complications, decreased quality of life, and non-negligible rates of negative appendectomy (5-9). Non-operative management options are increasingly accepted, with several recent randomized trials demonstrating that uncomplicated appendicitis in adults may be safely treated with antibiotics alone, with success rates between 60-85% at one year follow-up (10-15). In addition to avoiding surgery and its associated risks, non-operative treatment of appendicitis reduces exposures associated with hospital admission and surgical procedures for both patients and hospital staff during the ongoing COVID-19 pandemic.

Pediatric studies examining the safety and efficacy of antibiotics alone for the treatment of simple, acute appendicitis are more limited with a range of smaller studies that show more variable rates of failure than in adults (16-23). While some data suggest that initial non-operative treatment should be followed by interval appendectomy, conflicting studies show that non-operative management alone may be sufficient for most cases of uncomplicated appendicitis (24,25). The largest multicenter study to date of over 1,000 children who underwent non-operative treatment of uncomplicated appendicitis demonstrated a success rate of nearly 70% at one year follow-up but was not randomized (26). A single, small randomized study in Europe showed a one-year success rate of 66% among 24 children receiving non-operative management (27). Antibiotic-only treatment of simple appendicitis certainly shows promise for children and is preferred by parents (28), but little is known about potential clinical and radiographic predictors of successful non-operative treatment (16,18).

Ultrasound is the primary imaging modality for the diagnosis of acute appendicitis and is particularly attractive for use in children as it is low cost and avoids radiation exposure (1,29). In the emergency department (ED), point-of-care ultrasound (POCUS) is increasingly popular due to the advantages of dynamic, bedside imaging. POCUS for appendicitis has been show to decrease length of stay, healthcare costs, and computed tomography usage for children in the ED while having excellent test characteristics in the hands of experienced clinicians (30-33).

Various sonographic findings of appendicitis have been described that correlate to operative findings; isolated dilation and inflammation of an otherwise normal appearing appendix may be seen in simple appendicitis while loss of the submucosal layer, changes to pericecal fat, and free fluid are often seen in perforated appendicitis (34,35). Sonographic Puylaert staging assesses the submucosal layer of the appendix, which can easily be identified and characterized on POCUS to differentiate complicated from uncomplicated appendicitis (36-38). This distinction on POCUS may be useful to specifically identify children who are ideal candidates for non-operative management.

Our primary objective of this study was to determine whether Puylaert staging on POCUS accurately differentiates uncomplicated from complicated appendicitis in children when compared to surgical pathology findings. We also aimed to determine the ease-of-use for providers and acceptability to patients of POCUS used for this purpose in the ED.

**METHODS**

Design and population: We enrolled a convenient sample of healthy children 5 years to 17 years who were diagnosed with acute appendicitis by ultrasound, cat scans (CT), and/or magnetic resonance imaging (MRI) in any one of the eight participating emergency departments. We excluded patients with underlying medical conditions such as short gut syndrome, prior abdominal surgeries, presence of gastrostomy tubes, presence of jejunostomy tubes.

Study process: This was a prospective cohort study in a pediatric emergency department. Research coordinators and medical providers were trained on the study. When eligible patients were identified, and ED providers trained to perform bedside point-of-care ultrasound (POCUS) on acute appendicitis were available, then these patients were approached for consent and assent if children were over than 7 years old. Upon consent, a trained pediatric emergency medicine provider (fellow or attending physician) would perform a bedside point-of-care ultrasound (POCUS) when time permitted. A repeat POCUS would be performed prior to patients going to the operating room for the laparoscopic appendectomy.

Objectives: This was a pilot study investigating the feasibility of doing point of care ultrasound in a pediatric ED by trained medical providers. Our aims were to 1) determine clinically important factors on point of care ultrasound that might assist clinicians in determining progression of simple acute appendicitis diagnosed in children seen in an emergency department; 2) identify enabling and deterring factors for doing serial POCUS.

For aim 1, we collected the following ultrasound predictors: 1) largest diameter of appendix, 2) anterior wall measurement, 3) presence of fecalith, 4) presence of surrounding free fluid, 5) presence of surrounding inflammation, 6) wall characterization, 7) Puylart grade/stage. There are 4 stages in the Pyulaert stages: stage 1 is a thin and smooth submucosal layer which suggests early appendicitis, stage 2 shows a thick and smooth submucosal layer that is suggestive of suppurative appendicitis, stage 3 indicates a submucosal layer that is thick and irregular, or thin and intermittent which reflects gangrenous appendix, and stage 4 defines as an unidentifiable submucosal layer with amorphous inner structures, suggestive of a perforated appendicitis. *Kaneko K, Tsuda M. Ultrasound-based decision making in the treatment of acute appendicitis in children. Journ Ped Surg. 2004;1316-1320*.  For the repeat POCUS, we collected these additional predictors: 1) time from antibiotics given, 2) change in the diameter of the appendix, 2) change in the amount of periappendiceal fluid, 3) change in wall thickness, 4) wall features. The characteristics of sequential POCUS may change over time. We collected time of symptoms onset, time of first US conducted, time of second US conducted, time of antibiotics given, and time of surgery. This allowed us to determine if changes between the two US could be the result of time difference. In addition, we collected surgical report through chart review so we could compare POCUS findings to the surgical report.

For aim 2, we collected the following data: 1) availability of trained PEM medical provider to perform POCUS, 2) time to perform POCUS, 3) reasons for not able to perform POCUS.

Additional Data collection: As in all ultrasounds, the images of POCUS depends on the performer and patients’ characteristics. As such, we collected data on the person and department that performed the POCUS. We also gathered patients’ characteristics including age, gender, weight, and height.

Participating sites transmitted to us de-identified information documented on the data collection form to us.

Sample size:  We anticipated to enroll 100 subjects across all sites. This would allow us a reasonable sample size to assess for potential associations.

Data analyses:

We performed descriptive analyses to describe the population. To compare the difference between Surgical Pathology Reports stage and Puylaert Stages, we built the 2x2 contigency table and used McNemar test to examine the marginal homogeneity. We analyzed characteristics in the ultrasound findings between different groups using t-test and ANOVA for continuous variables, and Fisher’s exact test for nominal variables. In addition, we used logistic regression to predict surgical stages by related characteristics we test above. In the end, we selected the best prediction model by comparing their performance. We conducted all of above data analyses by using R version 4.02.

**RESULTS**

Between February 2019 and February 2020, we enrolled 97 subjects across all eight sites. Table 1 described the demographics of the patients enrolled. Table 2 illustrated the association between the Puylaert stages seen on ultrasound and the surgical pathology report. It appeared that the Puylaert staging may overestimate the clinical finding on surgical report, When stages 1 and 2 of the Puylaert stages are combined together as do the surgical report where early and suppurative are combined as a group; gangrenous and perforated appendicitis were combined as another group (Table 3) using McNemar test, we found that when patients were found to have Puylaert stages 1 or 2, none of them had worrisome surgical pathology findings such as gangrenous or perforated appendicitis. The sensitivity of using Puylart staging to determine complicated appendicitis (gangrenous or perforated appendicitis) is 1 with specificity of 0.650; positive predictive value of 0.416 and negative predictive value of 1. When controlled for gender, age, height, and weight, we did not observe any statistical significance in the outcomes.

The first US were primarily performed by the radiology department (n=64; 58.7%) and by the ED physicians doing point-of-care ultrasound (POCUS) (n=28; 25.7%). The second ultrasounds were primarily done by ED physicians (n=80; 73.4%) and radiology department in 8 patients (7.3%). The average time to perform POCUS by ED trained providers was 7.22 minutes compared to the US performed by the radiology department with the mean of 11.5 minutes. When we examined the time of antibiotics given prior to the 2nd ultrasounds, the mean time was 4 hours and 40 minutes (SD 3hr 57 min). Mean time from 2nd ultrasound to surgery was 5 hours and 56 minutes (SD +/- 5 hr 3min). Mean time from first antibiotic administration to time of surgery was 10 hr 31 min (SD +/- 6 hr 52 min).

Individual characteristics on the ultrasound findings were further evaluated. The mean largest diameter of the appendix in the second POCUS was 1.03 cm (+/- 0.27 cm; min 0.33, max 1.74).  The mean maximal mural thickness was 0.22 cm (+/- 0.13 cm; min 0.06, max 1.00). Six subjects had complex fluids; 37 subjects had simple fluid, and 35 subjects did not have any fluids on US. Thirty-one patients had fecalith while no fecalith was seen on POCUS in 55 of the patients.  Table 4 illustrates the largest diameter of the appendix, maximal mural thickness, presence of fecalith, and presence of fluids in the 4 types of surgical report findings, namely simple, suppurative, gangrenous, and perforated. According to the group difference shown in Table 4, we did ANOVA test for largest diameter of the appendix and maximal mural thickness separately, but none of them have significant group difference at 0.05 significance level (largest diameter of the appendix p value = 0.882, maximal mural thickness p value = 0.323). In the Fisher’s exact test of presence of fecalith and presence of fluids, both of them show association with surgical result (presence of fecalith p value = 0.0095, presence of fluids p value 0.0136).

To predict the surgical outcome, we included covariates related to appendix (indicator of diameter of appendix with cutoff point at 1mm), fecalith (presence of fecalith), fluids (presence of fluids), and Puylart staging (cut between stage 2 and 3). After comparing the logistic regressions based on various combination of these covariates, we selected the model include appendix, fecalith, and Puylart staging because of its highest accuracy (0.865) and kappa (0.560) which indicates moderate classification performance. The sensitivity of this model is 0.600 with specificity of 0.932.

Physicians who performed the POCUS in the emergency department were surveyed at the end of each case. Ninety percent (74/82) of the physicians agreed or strongly agreed that it was “easy to perform POCUS”. Ninety-two percent (77/84) of the physicians felt that POCUS was well tolerated by the patients. Ninety-nine percent (85/86) of the physicians reported that POCUS was well accepted by the families.

Of the 87 submitted surveys, 76% (66/87) reported no issues with performing and obtaining data elements requested.  24% (21/87) encountered one of more barriers. The most cited barriers to successfully complete POCUS in the ED was the abdominal pain experienced by the patients (13/21 or 62%). This was followed by change in location of the patients (e.g. being admitted or left for the operating room; 8/21 or 38%), too busy in the emergency department (7/21 or 33%%), location of the appendix (6/21 or 29%), and patients’ habitus (2/21 or 10%).

**DISCUSSION:**

Our results suggest that the Puylaert Stages on the ultrasounds for the evaluation of acute appendicitis has good specificity while it has a fair sensitivity. POCUS can over estimate the severity of the patients with acute appendicitis. However, for patients who may benefit from non-operative treatment, POCUS will less likely miss anyone with gangrenous or perforated appendicitis. This finding is consistent with prior literature which found the integrity of the submucosal wall to be more predictive of the severity of acute appendicitis.[ *Kaneko K, Tsuda M. Ultrasound-based decision making in the treatment of acute appendicitis in children. Journ Ped Surg. 2004;1316-1320*.   *Vignault F, Filiatrault D, Brandt ML, et al: Acute appendicitis in children: Evaluation with US. Radiology. 176:501-504, 1990, Quillin SP, Siegel MJ, Coffin CM: Acute appendicitis in children: Value of sonography in detecting perforation. AJR Am J Roentgenol 159:1265-1268, 1992. Wong ML, Casey SO, Leonidas JC, et al: Sonographic diagnosis of acute appendicitis in children. J Pediatr Surg 29:1356-1360, 1994]*

Our results were also similar to prior literature in that the presence of complicated fluids was suggestive of having complicated appendicitis.*[Carpenter JL, Orth RC, Zhang W, Lopez ME, Mangona KL, Guillerman RP. Diagnostic performance of US for differentiating perforated from Nonperforated pediatric appendicitis: a prospective cohort study. Radiology 2017; 282: 835–41. doi: https://doi. org/10.1148/radiol.2016160175 22. Tulin-Silver S, Babb J, Pinkney L, Strubel N, Lala S, Milla SS, et al. The challenging ultrasound diagnosis of perforated appendicitis in children: constellations of sonographic findings improve specificity. Pediatr Radiol 2015; 45: 820–30. doi: https:// doi.org/10.1007/s00247-014-3232-5 23. Callahan MJ, Rodriguez DP, Taylor GA.]*

Our study differed from this prior study. The fisher’s exact test show the association between fecalith and surgical stages. Having appendiceal fecalith did not increase the risk of having complicated appendicitis *[Fitz R. Perforating inflammation of the vermiform appendix: with special reference to its early diagnosis and treatment. Philadelphia, PA; 1886.]*

However, our study differed from prior in that the increase in appendiceal diameter did not correlate with having complicated appendicitis. This could be due to the small number of patients in surgical stages 3 and 4 combined.

During the model building, we have tried model selection by AIC, but it removed all other covariates except Puylart staging. So, we test the association between Puylart staging and other covariates by Fisher’s exact test. The result shows that Puylart staging is correlated with other covariates.

One of the limitations of this study was that the Puylaert stage was standardized. Other features were left to the performer’s experience. So the complex fluid was not well defined for the performers.  A second limitation was that the feedback was from the physicians who performed the POCUS. They were not feedback from the patients directly. Another limitation was that this was a convenient small sample. It’s not a sample powered to measure small differences in the ultrasound features among the varying surgical pathologies seen in acute appendicitis. Finally, the operators and the ultrasound machines were not standardized for this study.

**CONCLUSIONS**

In conclusion, Puylaert stage is a good predictor for more advanced acute appendicitis compared to other ultrasound features.

**ACKNOWLEDGEMENT**

We want to thank the research coordinators at the Columbia University Irving Medical Center, Megan Nye and Marc Vindas for their assistance in collecting data from the various sites, and statisticians Yiling Yang, and Shing M Lee from the Department of Biostatistics at the Columbia University Mailman School of Public Health for their assistance in data analysis.

Table 1: Demographic of subjects enrolled

|  |  |
| --- | --- |
|  | N = 97\* |
| **Age** (years), n = 95   Mean (+/- SD)   Range | 10.99 (+/- 4.04)  1.6 -18 |
| **Gender**, n = 96    Female    Male | 31 (32.29%)  65 (67.71%) |
| **Height** (in), n = 72    Mean (+/- SD)    Range | 63.02 (+/- 23.28)  32.00 – 175.00 |
| **Weight** (kg), n = 95    Mean (+/- SD)    Range | 48.69 (+/- 24.95)  12.00 – 152.30 |
| **Department 1st US**, n = 92    ED US (POCUS)    Radiology US (RADUS) | 28 (30.11%)  64 (68.82%) |
| **Department 2nd US**, n = 88    ED US (POCUS)    Radiology US (RADUS) | 80 (89.89%)  8 (8.99%) |

\*One subject’s information was not collected, leaving total to 96.

SD = standard deviation

Table 2: Puylaert stages on US compared to surgical report

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Surgical Pathology Report** | | | |  |
| **Puylaert Stage on US#2** | **Simple** | **Suppurative** | **Gangrenous** | **Perforated** | **Total** |
| **1** | 11 | 0 | 0 | 0 | 11 |
| **2** | 21 | 7 | 0 | 0 | 28 |
| **3** | 12 | 6 | 4 | 9 | 31 |
| **4** | 2 | 1 | 0 | 2 | 5 |
| **Total** | 46 | 14 | 4 | 11 | 75 |

Table 3: Combined Puylaert stages compared to surgical report of gangrenous/perforated appendicitis by surgical report

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Surgical Pathology Reports** | |  |
| **Puylaert Stages** | **Early/Suppurative** | **Gangrenous/perforated** | **Total** |
| Combined 1 & 2 | 39 | 0 | 39 |
| Combined 3 & 4 | 21 | 15 | 36 |
| **Total** | 60 | 15 | 75 |

Sensitivity = 0.65; Specificity =  1.00; Positive Predictive Value (PPV) = 1.00; Negative Predictive Value (NPV) = 0.42.

Table 4: US Characteristics compared to surgical report

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **US Characteristics** | **Surgical Pathology Report Findings** | | | | **Statistical Significance** |
| **Simple**  **(n = 48)** | **Suppurative**  **(n = 14)** | **Gangrenous**  **(n = 4)** | **Perforated**  **(n = 11)** |
| **Largest diameter of the appendix (cm)** | 0.96 +/- 0.25  (0.33 – 1.65) | 1.12 +/- 0.20  (0.77 – 1.40) | 1.42 +/- 0.22  (1.27 – 1.74) | 1.14 +/- 0.32  (0.7 – 1.6) | p = 0.884\* |
| **Maximal mural diameter (cm)** | 0.21 +/- 0.09  (0.06-0.46) | 0.23 +/- 0.09  (0.1-0,4) | 0.20 +/- 0.05  (0.17 – 0.25) | 0.30 +/- 0.26  (0.1 -1.0) | p = 0.323\* |
| **Fecalith** | Yes = 13 (27%)  No = 35 (73%) | Yes = 6  No = 8 | Yes = 4  No = 0 | Yes = 8  No = 3 | p = 0.013\*\* |
| **Fluid** | Complicated = 2  Simple = 21  No fluid = 25 | Complicated = 0  Simple = 7   No fluid = 7 | Complicated = 0  Simple = 4   No fluid = 0 | Complicated = 4  Simple = 5  No lfuid = 2 | p = 0.001\*\* |

\*ANOVA was performed; \*\*Pearson Chi Square was used.

Table 5: Feedback from Physicians who Performed POCUS

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Strongly Agree** | **Agree** | **Neutral** | **Disagree** | **Strongly Disagree** | **Total** |
| Easy to do POCUS | 46 (56%) | 28 (34%) | 8 (10%) | 0 | 0 | 82 |
| POCUS was well tolerated by patients | 55 (66%) | 22 (26%) | 7 (8%) | 0 | 0 | 84 |
| POCUS was well accepted by families | 63 (73%) | 22 (26%) | 1 (1%) | 0 | 0 | 86 |

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