

Serial Point of Care Ultrasounds in Monitoring the Progression of Non-operative Acute Appendicitis Pre- and Post- antibiotics Treatment Prior to Appendectomy

Exploration for Sonographic Features that Predict Medical Treatment Failure in Acute Appendicitis

Initiating PECARN Node: PEM-NEWS

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Proposal Investigators

David Kessler

Maria Kwok

Peter Dayan

Investigator Signatures

David Kessler

Maria Kwok

Peter Dayan

Corresponding Information: Address: 3959 Broadway, CHN 1-116, New York, NY 10032
Phone: 516-769-3777
E-mail: dk2592@cumc.columbia.edu

Background

Acute appendicitis is the most common surgical emergency in children. Early recognition, increasing diagnostic accuracy and surgical advances have dramatically lowered the morbidity of appendicitis, and virtually eliminated its mortality.¹⁻⁵ While urgent appendectomy cures appendicitis, preventing recurrence, and rarely is associated with major complications, surgery is associated with pain, discomfort, risk of complications, and decreased quality of life.⁶⁻⁹ Several randomized controlled trials (RCT) have found that early (also referred to as "uncomplicated") appendicitis in adults may be safely treated with antibiotics alone. In this select group of patients, more than 70% of patients with appendicitis treated with non-operative management resolved their symptoms of acute appendicitis and did not have a recurrence requiring appendectomy in a 1-year follow-up period).¹⁰⁻¹⁴ There were 2 small pediatric studies looking at the safety and resolution of symptoms with the use of antibiotics in children with simple acute appendicitis, raising concerns for safety and for efficacy of the use of antibiotics in pediatric patients with simple appendicitis. At the present time, it is unclear whether the non-operative management of acute pediatric appendicitis is safe and cost effective, and whether it improves health utility. Additionally, predictors of success of non-operative management of pediatric appendicitis have not yet been determined. The Pediatric Emergency Care Applied Research Network (PECARN) will be conducting a multi-center randomized controlled trial to further investigate the clinical safety of non-operative management of acute uncomplicated pediatric appendicitis, compared with urgent laparoscopic appendectomy. Secondary aims of this large multi-center study are: 1) to determine the long-term clinical safety of non-operative management of acute uncomplicated pediatric appendicitis, compared with urgent laparoscopic appendectomy, 2) to determine the cost and health utility of non-operative management of acute uncomplicated pediatric appendicitis, compared with urgent laparoscopic appendectomy, and 3) to determine the ability of clinical, laboratory, and imaging findings in predicting the outcomes of acute uncomplicated pediatric appendicitis and the success of non-operative management.

Ultrasound in the diagnosis of acute appendicitis is used as first diagnostic imaging test in pediatric emergency departments due to its low cost, lack of radiation, and availability.¹⁵ The use of point of care ultrasounds (POCUS) in the emergency department settings has been on a rise.^{16, 17} The ability to repeat imaging dynamically and in short timeframe without risk of ionizing radiation is a distinct advantage of ultrasound. Our overarching goal is to assess the usefulness of serial POCUS as a noninvasive, low-cost diagnostic tool to assess children receiving antibiotics for the treatment of simple acute appendicitis to predict disease outcome and severity.

Objectives:

This is a pilot study investigating the feasibility of doing point of care ultrasound in a pediatric ED and subsequently on the floor by trained medical providers.

Our aims are to 1) determine clinically important factors on point of care ultrasound that may 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 will collect the following ultrasound predictor:

- Largest diameter of appendix
- Anterior wall measurement

- Presence of fecalith
- Presence of surrounding free fluid
- Presence of surrounding inflammation (quantify?)
- Wall characterization (*look up other elements of obstructive vs inflammatory classification system- Spain lady)
- Length of appendix?
- Largest length of enlargement? (i.e. not just tip)
- Other features (e.g. hairpin turn)
- Puylart grade/stage?

For the repeat POCUS, we will collect these additional predictors:

- Time from antibiotics given
- Delta Size
- Delta periappendiceal fluid
- Delta wall thickness
- Delta wall features?

For aim 2, we will the following data:

- Availability of trained PEM medical provider to perform POCUS
- Time to perform POCUS
- Proportion of patients approached who consent to POCUS
- Reasons for not able to perform POCUS

Methods:

Patient population: We will enroll children up to and including 17 years who have been diagnosed with acute simple appendicitis. Acute simple appendicitis is defined as have a combination of the following (not all clinical, history or laboratory parameters must be present):

- History and physical examination
- Fever (or low-grade fever)
- Right lower quadrant pain, migratory pain (umbilical-to-right-lower-quadrant)
- Nausea, vomiting – typically following onset of pain
- Point-tenderness in McBurney's point (right lower quadrant), rebound tenderness
- Rovsing sign (referred right lower quadrant pain on palpating or release in left quadrant)
- Obturator sign (internal rotation of right leg) or psoas sign (active flexion of right thigh)
- Duration of symptoms less than 48 hours
- Onset of pain must be less than 48 hours from time of admission the emergency department
- Laboratory evaluation (complete blood count and urinalysis) consistent with this diagnosis
- Leukocytosis: elevated ($>11,000/\text{mm}^3$) or high-normal ($8,000\text{--}11,000/\text{mm}^3$)
- Bandemia ($>5\%$ immature neutrophils)
- Urinalysis: fewer than 20 WBC per high-powered field; mild ketonuria ($<3+$)
- Positive imaging study (ultrasound, computed tomography, or magnetic resonance imaging)

A positive ultrasound finding includes:

- Outer diameter of appendix >6 mm during adequate compression
- Mural thickness >3 mm and/or loss of laminar architecture
- Increased transmural blood flow by color doppler
- Periappendeal fatty edema or free fluid (not a stand-alone criterion) appendicolith
- Intraluminal appendiceal fluid.

A positive computed tomography includes

- Outer diameter >8 mm
- Mural thickening
- Mural hyperemia
- Mucosal hyperemia
- Periappendiceal fat stranding
- Periappendiceal free fluid (not a stand-alone criterion) appendicolith

Study Process:

This is a prospective cohort study in a pediatric emergency department. Research coordinators and medical providers will be trained on the study. Once eligible patients are identified, consent and/or assent will be obtained. Upon informed consent, a trained pediatric emergency medicine provider (fellow or attending physician) will perform a bedside ultrasound (POCUS). A repeat POCUS will be performed prior to going to the operating room for the laparoscopic appendectomy. We will record the time of antibiotics administered if applicable. We will document the time the repeat POCUS is performed. This will allow to see if changes can be seen via ultrasound pre- and post- antibiotics used. This will help us determine if POCUS will be useful in the larger study.

We will also review patient's medical record for demographic information, radiology reports and operative reports to confirm the diagnosis of acute uncomplicated appendicitis. We will record these finding onto the data collection form. Participating sites will only transmit to us de-identified information documented on the data collection form to us.

Sample size:

This will be a multi-center study. We anticipate to enroll a total of 100 patients. At the Columbia University Medical Center, we plan on enrolling 50 patients. Our pediatric ED has an annual volume of 54,000 patients. We have approximated 150 cases of acute appendicitis annually. We have 7 certified pediatric emergency medicine providers in our pediatric ED.

Analysis:

We will perform descriptive analysis to describe the population. We will analyze changes in the ultrasound findings for each patient over time using t-test for continuous variables; and chi-square for dichotomous variables.

Confidentiality:

All ultrasounds done at our site will be kept in an encrypted p-drive that is currently used for all of our POCUS done in the emergency department. All data sheets will be kept in locked cabinets in locked offices. Data will be stored electronically in encrypted, password protected p-drive.

Risks:

Patients may experience pain for which analgesics may be provided at the discretion of treating physicians. While we will do execute measures to ensure confidentiality of all data, there is a small risk of breach of information.

Benefits:

The study can potentially allow us to determine the usefulness of POCUS in predicting success of non-operative treatment of acute appendicitis in the larger study.

Data Safety and Monitoring:

We will form a data safety and monitoring committee consisting of a radiologist, a pediatric emergency medicine physician to meet annually to ensure compliance to the study protocol.

REFERERNCES:

1. Fowler GR. II. Observations upon Appendicitis. *Ann Surg* 1894;19:146-71.
2. Guerry le G. A Study of the Mortality in Appendicitis. *Ann Surg* 1926;84:283-7.
3. Soreide O. Appendicitis--a study of incidence, death rates and consumption of hospital resources. *Postgrad Med J* 1984;60:341-5.
4. Malatani TS, Latif AA, Al-Saigh A, Cheema MA, Abu-Eshy S. Surgical audit: A prospective study of the morbidity and mortality of acute appendicitis. *Ann Saudi Med* 1991;11:209-12.
5. Wysocki AP, Allen J, Rey-Conde T, North JB. Mortality from acute appendicitis is associated with complex disease and co-morbidity. *ANZ J Surg* 2015;85:521-4.
6. Muehlstedt SG, Pham TQ, Schmeling DJ. The management of pediatric appendicitis: a survey of North American Pediatric Surgeons. *J Pediatr Surg* 2004;39:875-9; discussion -9.
7. Sauerland S, Jaschinski T, Neugebauer EA. Laparoscopic versus open surgery for suspected appendicitis. *Cochrane Database Syst Rev* 2010:CD001546.
8. Oka T, Kurkchubasche AG, Bussey JG, Wesselhoeft CW, Jr., Tracy TF, Jr., Luks FI. Open and laparoscopic appendectomy are equally safe and acceptable in children. *Surg Endosc* 2004;18:242-5.
9. Uhr JH, Fields AC, Divino CM. Lack of a clinically significant impact of race on morbidity and mortality in abdominal surgery: an analysis of 186,466 patients from the American College of Surgeons National Surgical Quality Improvement Program database. *Am J Surg* 2015;210:236-42.
10. Salminen P, Paajanen H, Rautio T, et al. Antibiotic Therapy vs Appendectomy for Treatment of Uncomplicated Acute Appendicitis: The APPAC Randomized Clinical Trial. *JAMA* 2015;313:2340-8.
11. Eriksson S, Granstrom L. Randomized controlled trial of appendicectomy versus antibiotic therapy for acute appendicitis. *Br J Surg* 1995;82:166-9.
12. Hansson J, Korner U, Khorram-Manesh A, Solberg A, Lundholm K. Randomized clinical trial of antibiotic therapy versus appendicectomy as primary treatment of acute appendicitis in unselected patients. *Br J Surg* 2009;96:473-81.
13. Styrd J, Eriksson S, Nilsson I, et al. Appendectomy versus antibiotic treatment in acute appendicitis. a prospective multicenter randomized controlled trial. *World J Surg* 2006;30:1033-7.
14. Vons C, Barry C, Maitre S, et al. Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. *Lancet* 2011;377:1573-9.
15. Garcia Pena BM, Taylor GA, Fishman SJ, Mandl KD. Cost and effectiveness of ultrasounography and limited computed tomography for diagnosing appendicitis in children. *Pediatrics* 2000; 106(4):672-676.
16. Elikashvili I, Tay ET, Tsung JW. The effect of point-of-care ultrasonography on Emergency department length of stay and computed tomography utilization in children with suspected appendicitis. *Acad Emerg Med* 2014;21:163-70.
17. Cundy TP, Gent R, Frauenfelder C, Lukic L, Linke RJ, Goh DW. Benchmarking the value of ultrasound for acute appendicitis in children. *J Pediatr Surg*. 2016;51(12):1939-1943

