JOURNAL of MAINE MEDICAL CENTER

Journal of Maine Medical Center

Volume 3 | Issue 2 Article 7

2021

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Acknowledgements

Drs. Pandya and Jubulis for study design and initial approval. Drs. Pandya, Jubulis, Vernamonti and Cotter for data entry. Drs. Pandya, Jubulis, and Vernamonti for manuscript, data and statistical analysis. With special acknowledgement to Dr. Lee Lucas for statistical analysis and review of study design and to Dr. Wendy Craig for reviewing the manuscript from the Maine Medical Center Research Institute.

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ORIGINAL RESEARCH

Implementing a Clinical Practice Guideline for Pediatric Appendicitis Safely Reduced Health Care Use and Improved Antimicrobial Stewardship

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Introduction: Appendicitis is the most common emergency surgical disease in children. Those with perforated appendicitis have a more complicated and varied course. Through a clinical practice guideline (CPG), we sought to reduce computed tomography scans, laboratory draws, and exposure to broad-spectrum antibiotics without adversely affecting length of stay, hospital readmission, or repeat antibiotic administration.

Methods: Electronic records were retrospectively reviewed before and after CPG implementation, and data was collected in REDCap. Results were reported as mean or percent incidence, and statistical analysis was done using a Student's *t*-test, Mann-Whitney U test, or Pearson's $\chi 2$ with $P < .05$ considered significant.

Results: One hundred patients with a perforated appendix (50 before and 50 after CPG implementation) were included in our analysis. Length of stay (4.98 vs 4.46 days; $P = .25$), hospital readmission rate (10% vs 14%; $P = .54$), and additional antibiotic administration (2% vs 4%; $P = .56$) did not change. We observed no difference in the Pediatric Appendicitis Score (9 vs 9; $P = .48$) and a trending increase in evaluation at an outside hospital (56% vs 74%; $P = .06$). Rates of computed tomography scans did not differ overall (50% vs 40%; $P = .31$), but showed a decreasing trend at our institution (30% vs 12%; $P = .06$). We also found fewer post-operative laboratory studies (90% vs 38%; $P < .01$) and patients who received broad-spectrum intravenous antibiotics (92% vs 18%; $P < .01$).

Discussion: Through implementing the CPG we were able to understand our practice patterns and identify opportunities for improvement. Patients with perforated appendicitis were selected for study because they were affected by all components of the CPG and allowed for total adherence to be our primary outcome. Total adherence was set as the primary outcome knowing it would be difficult to achieve, but would also better identify opportunity for improvement and provide comprehensive assessment of the guideline.

Conclusions: Implementing a multidisciplinary CPG reduced health care use and improved antimicrobial stewardship without increasing complications in pediatric acute appendicitis.

Keywords: appendicitis, clinical practice guideline, antimicrobial stewardship, quality improvement

Appendicitis is the most common emergency surgical disease in children. Practice patterns have evolved in response to the pediatric appendicitis semi-annual report produced by the National Surgical Quality Improvement Program of the American College of Surgeons.[1] These quality metrics include components from the initial diagnosis, as well as management and post-operative complications associated with pediatric appendicitis. They are also designed to give institutions guidance on opportunities for standardization and improvement. At our institution, it was noticed that there was variability in how perforated appendicitis was managed in patients initially seen at our facility and those transferred from referring hospitals. Clinical practice guidelines

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(CPG) have been documented to change physician practice, standardize management, and improve outcomes.[2] The pediatric emergency medicine, radiology, infectious disease, and surgery divisions partnered to design and implement a multidisciplinary CPG for pediatric appendicitis (Figure 1). We measured adherence to the CPG and clinical outcomes.

A

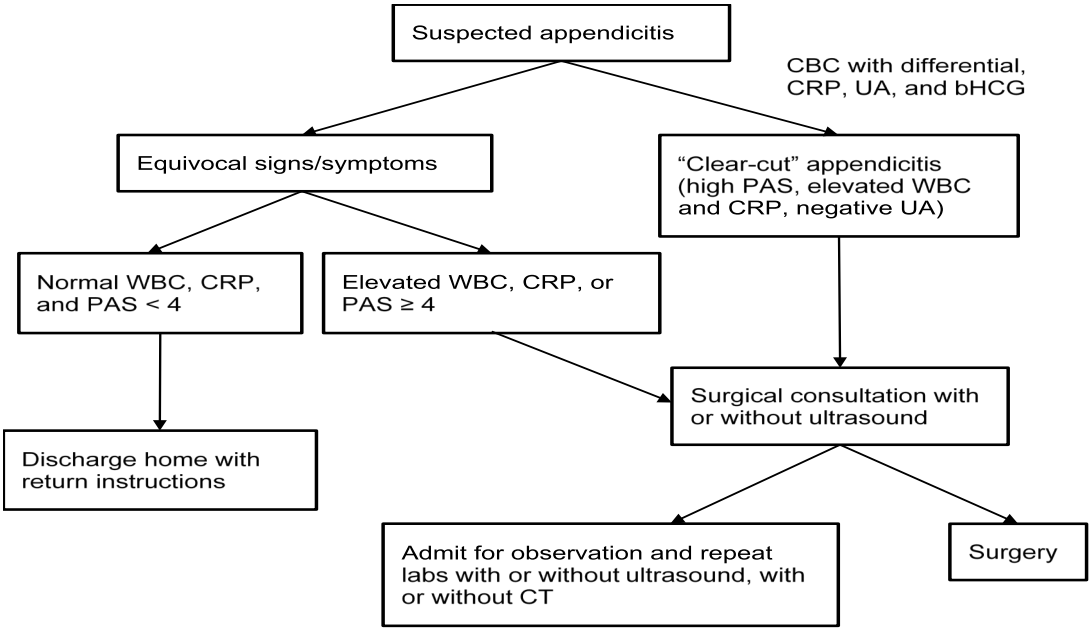

Figure 1. Clinical Practice Guideline. **A**, Pre-operative algorithm. **B,** Antibiotic selection. **C,** Post-operative management. bHCG, beta Human Chorionic Gonadotropin; CBC, complete blood cell count; CRP, C-reactive protein; CT, computed tomography; IV, intravenous; PAS, Pediatric Appendicitis Score; UA, urinalysis; WBC, white blood cell count.

B

Regimen	Antibiotics
Intravenous	Ceftriaxone (50 mg/kg/q24hrs, max 2 gm/day) or ciprofloxacin (10 mg/kg/q12hrs, max 750 mg/dose) -Plus- Metronidazole (10 mg/kg/q8hrs, max 1.5 gm/day)
Intra-operative (if IV regimens not initiated before arrival in operating room)	Cefotetan (40 mg/kg/dose, max 2 gm)
Oral (to complete a total course of 7-10 days of antibiotic therapy)	Cefdinir (7 mg/kg/dose q12h, up to 300 mg q12h) or ciprofloxacin (10 mg/kg/q12hrs, max 750 mg/dose) -Plus- Metronidazole (10 mg/kg/q8hrs, max 1.5 gm/day)

C

Post-operative management
• Avoid routine post-operative CRP/WBC • Transition to oral antibiotics based on tolerating enteral feeds, remaining afebrile, and clinical improvement in activity and pain • Post-operative labs, imaging, and interventions as directed by clinical course

METHODS

Setting

This study was conducted at Maine Medical Center, a 637-bed academic medical center located in Portland, Maine. Housed within this larger institution, the Barbara Bush Children's Hospital comprises 140 beds, including a 51-bed continuing care nursery and neonatal intensive care unit (level II/III), a 10-bed pediatric intensive care unit, and a 10-bed pediatric emergency department. The hospital serves as a training site for over 240 residents and fellows, most of whom rotate through and interact with the pediatric population. Surgical patients are cared for by 5 pediatric surgeons and 2 advanced practice providers. This study was approved by the Maine Medical Center Institutional Review Board.

Development of the CPG

After literature review, we developed a CPG focusing on evaluating patients with suspected appendicitis. The algorithm relied on the Pediatric Appendicitis Score (PAS) and C-reactive protein (CRP)[4,5] (added for initial triage). Pre-existing familiarity with CRP values as an inflammatory marker for appendicitis led to its inclusion in our institutional algorithm. The PAS is a tool that assigns weighted values to common symptoms and laboratory evaluation of appendicitis: fever, anorexia, emesis, peritonitis, right lower quadrant pain, leukocytosis, and neutrophilia. Patients are given a score 0 through 10, with 10 being most likely to have appendicitis. The score is most predictive at either end of the spectrum, and our cutoffs and interpretation are incorporated into the decision algorithm in Figure 1.

If the diagnosis remained in question after compiling the history, physical exam, and laboratory data, our CPG directed providers to first use an ultrasound for further workup. In discussion with the radiology division, standardized reporting for pediatric appendiceal ultrasounds were adopted[6] and followed the American College of Radiology guidelines for obtaining ultrasound before considering a contrast enhanced, abdominal-pelvic computed tomography (CT) scan.[7] The CPG allowed for CT scan use at surgeon discretion in the Emergency Department versus admission and observation with no CT scan; however, admission and observation were encouraged.

The next phase of the CPG sought to reduce exposure to broad-spectrum antibiotics defined as piperacillin-tazobactam or ampicillin-sulbactam for intravenous (IV) therapy and amoxicillin-clavulanate for oral therapy. The Barbara Bush Children's Hospital has a pediatric-specific antibiogram, which we used to select the initial regimen for the CPG. The IV antibiotics began when the decision was made to offer appendectomy. If the patient was at low risk for appendicitis and being admitted for observation, they were discouraged from being given antibiotics that could mask their serial abdominal exams.

Intraoperative culture data from 40 patients with perforated appendicitis was collected to validate regimens previously published (Table 1). Our antibiogram revealed strong susceptibility to both ceftriaxone and ciprofloxacin, with decreased susceptibility of *Escherichia coli* to ampicillin-sulbactam. After considering local resistance patterns, and in discussion with our division of pediatric infection disease, IV antibiotic regimen was narrowed from either ampicillin-sulbactam or piperacillin-tazobactam to metronidazole and either ceftriaxone or ciprofloxacin (if there was a documented penicillin allergy).[8,9] We also incorporated early transition to oral metronidazole and cefdinir or ciprofloxacin in perforated appendicitis based on clinical improvement (eg, resolved fevers, diminished abdominal pain, resolution of ileus). Total antibiotic therapy was given for 7 to 10 days based on recommendations from the American Pediatric Surgical Association.[10] The specific duration within this window was determined by the attending surgeon.

Finally, before the CPG, our practice routinely assessed for normalized CRP and leukocytosis before discharge on oral antibiotics. A protocol was adopted to determine suitability for oral antibiotics, discharge based on clinical criteria, and avoid routine labs unless clinically indicated.

The CPG was developed through a multidisciplinary approach with input from corresponding departments. There was then a period of education in which the CPG lead met with representatives from each department and discussed implementation. Patient capture for adherence was done after a 6-month roll-out period to allow provider education. The education and distribution began in January 2017 with the goal to fully adopt the CPG for the academic year starting July 2017. Patients for this study were selected before education began for the control group and after the roll-out period for the intervention group to avoid bias during the transition. This study was an analysis of interval adherence, and feedback from the CPG lead was done ad hoc with respective department contributors.

Study design

Patients with perforated appendicitis present later, and have a longer, more severe clinical course than those with simple appendicitis. They were also at the highest risk for adverse events with our new management protocol, and the population that would be most affected by all aspects of the CPG. Therefore, we selected this group of patients to study. Our inclusion criteria were pediatric patients under age 18 years who had perforated appendicitis and underwent surgical intervention. We identified the first 50 patients immediately before and after implementation of the CPG in a

Table 1. Cultured Organisms*

Cultured organisms (n = 40)	Positive cultures, No. (%)	Antibiotic	Sensitive, No. (%)	Indeterminate, No. (%)	Resistant, No. (%)	Not tested, No. (%)
Escherichia coli	27 (68)	Ampicillin	19 (70)	0	8 (30)	0
		Ampicillin/ Sulbactam	20 (74)	3 (11)	4 (15)	0
		Cefazolin; trimethoprim/ sulfamethoxazole	24 (89)	0	3 (11)	0
		Quinolone	26 (96)	0	1 (4)	0
		Piperacillin/ tazobactam; cefoxitin; ceftriaxone; cefepime; imipenem; meropenem	27 (100)	0	0	0
Streptococcus species	16 (40)	Penicillin; ceftriaxone; vancomycin	6 (38)	0	0	10 (62)
Pseudomonas	8 (20)	Imipenem; meropenem	6 (75)	0	1 (12)	1 (12)
		Piperacillin/ tazobactam; cefepime; quinolone; gentamicin; amikacin	7 (88)	0	0	1 (12)
Non-speciated, gram-negative rods	5 (12.5)	NA	0	0	0	5 (100)
Non-speciated, gram-positive cocci	5 (12.5)	NA	0	0	0	5 (100)

Abbreviations: NA, not applicable.
*Summarizes bacterial species cultures from routine intraoperative culture swabs from patients with a perforated appendectomy treated between October 2015 and October 2018. Sensitivities to antibiotics are grouped from most to least resistant for each organism.

quality improvement study. This selection was done to focus on the effect of the CPG and separate its effect from general practice trends. Patients were excluded if they had perforated appendicitis with abscess managed by percutaneous drain, non-perforated appendicitis, or unspecified abdominal pain managed with observation.

The primary endpoint was defined as full adherence to the CPG. The secondary endpoints were post-operative complications defined as additional surgical or interventional radiology procedures, including peripherally inserted central catheters or central venous catheters, length of stay, hospital readmission or emergency department presentation, and repeat antibiotic administration (after completing an initial course).

Records were identified using appendectomy billing codes, and then manually verified through operative reports. Patient data was captured from October 2015 through October 2018. Due to variability in definitions of perforated appendicitis[11], we defined perforation as an appendix with either

a free fecalith or visible hole during surgery.[12] All data was managed in a REDCap database[13,14], and records reviewed were analyzed within REDCap for data completeness and accuracy. Records with ambiguous terminology or data were flagged and manually reviewed for consistency and accuracy by the entire working group.

Results were summarized as mean (standard deviation) or frequency. Statistical comparisons were performed using a Student's *t*-test, Mann-Whitney U test, or Pearson's χ2 with $P < .05$ considered as significant (*https://www.socscistatistics.com/* and *Microsoft Excel 2016*).

RESULTS

One hundred patients were included in the study. Patient characteristics for pre-CPG and post-CPG implementation groups are shown in Table 2. There was a significant difference in age between pre-CPG and post-CPG groups (mean age 8.9 ± 3.7 vs 10.9 ± 3.5 years, $P < .01$). Between the 2 groups, there was no significant difference in sex, race, body mass index, evaluation at referring facility, or transfer times. There was also no difference in initial severity markers, such as PAS, CRP, or white blood cell count.

Table 2. Demographics of Pre-CPG and Post-CPG Groups

	Pre-CPG (n = 50)	Post-CPG n = 50)	P value
Age, mean (SD), y	8.9 (3.7)	10.9 (3.5)	<.01
Sex			
Female, No. (%)	22 (44)	15 (30)	.15
Male, No. (%)	28 (56)	35 (70)	.15
Caucasian race, No. (%)	43 (86)	48 (96)	.08
Black or African American	1 (2)	2 (4)	.55
Hispanic/Latinx	2 (4)	0	.15
Asian American Pacific Islander	1 (2)	0	.31
Not reported	3 (6)	0	.08
Seen at outside hospital, No. (%)	28 (56)	37 (74)	.06
Transfer times from outside hospital, mean (SD), h	8.2 (12.3)	5.1 (2.0)	.17
Antibiotics initiated at outside hospital, No. (%)	18 (64)	24 (65)	.96
Pediatric Appendicitis Score	9	9	.48
C-reactive protein, mean (SD), mg/L	123.0 (86.2)	118.4 (84.8)	.83
White blood cell count, mean (SD), $x10^2/\mu L$	18.2 (6.1)	18.4 (6.0)	.87
Body mass index, mean (SD), kg/m^2	19.0 (4.4)	19.9 (4.3)	.30

The practice metrics collected for CPG evaluation are shown in Table 3 and included post-operative laboratory tests, overall rates of CT scans (at the referring facility and at our institution), rates of IV and oral broad-spectrum antibiotic use, and total antibiotic duration. We also assessed adherence to the CPG by comparing performance rates for the various elements included in the CPG before and after its implementation. Adherence to the CPG was defined as a patient with perforated appendicitis who was managed without deviation from the protocol. After implementing the CPG, there was a significant reduction in patients receiving post-operative laboratory tests (90% to 38%; $P < .01$), either ampicillin-sulbactam or piperacillin-tazobactam during admission (92% to 18%; $P < .01$), and oral amoxicillin-clavulanate (68% to 6%; $P < .01$) at discharge. We did not see a significant decrease in overall or total antibiotic duration. There was a notable trend toward lower CT scan use at our institution. We observed a significant increase in practice patterns with total adherence to the CPG (4% to 64%; $P < .01$).

Post-operative complications examined are listed in Table 4. After CPG implementation, there was no significant change in the following post-operative parameters: placement of peripherally inserted

Table 3. Adherence to Clinical Practice Guideline

	Pre-CPG (n = 50)	Post-CPG (n = 50)	P value
Post-operative labs, No. (%)	45 (90)	19 (38)	<.01
Computed tomography rates			
Overall, No. (%)	25 (50)	20 (40)	.31
Outside hospital, No. (%)*	14 (50)	16 (43)	.59
Maine Medical Center, No. (%)†	11 (31)	4 (12)	.06
Broad-spectrum antibiotics			
Intravenous, No. (%)	46 (92)	9 (18)	<.01
Oral, No. (%)	34 (68)	3 (6)	<.01
Total duration, mean (SD), d	11.02(3.3)	10.48 (3.5)	.43
CPG adherence, No. (%)	2 (4)	32 (64)	<.01

Abbreviations: CPG, clinical practice guideline.
*See Table 2 for patient numbers.
†Rate defined as percentage of patients without a prior CT scan who underwent CT scan at MMC emergency department. Includes patients who initially present to MMC and those transferred from referring facilities.

Table 4. Post-operative Complications

	Pre-CPG (n = 50)	Post-CPG (n = 50)	P value
PICC/CVC, No. (%)	5 (10)	3 (6)	.44
IR procedure/reoperation, No. (%)	3 (6)	4 (8)	.70
Length of stay, mean (SD), d	4.98 (2.5)	4.46 (2.0)	.25
Completed prescribed oral antibiotics, No. (%)	48 (96)	45 (90)	.24
Readmit/ED visit, No. (%)	5 (10)	7 (14)	.54
Antibiotics restarted, No. (%)	1 (2)	2 (4)	.56
Follow-up, mean (SD), d	10.62 (7.5)	12.4 (8.0)	.27

Abbreviations: CPG, clinical practice guideline; CVC, central venous catheters; ED, emergency department; IR, interventional radiology; PICC, peripherally inserted central catheter.

central catheters or central venous catheters, rates of interventional radiology intervention, need for reoperation, length of stay, percentage who completed prescribed antibiotic course, hospital admission/emergency department visit, resumption of antibiotics after completing a prescribed course, and mean follow-up duration.

DISCUSSION

By using the benchmarks outlined by the National Surgical Quality Improvement Program Pediatric and a current literature review, we successfully created a multidisciplinary CPG suited to our practice and population. Our new CPG resulted in significant changes in practice without increasing the rates of complications and while improving antibiotic stewardship and resource use. We will use these data to continue studying our patient population and further improve our clinical practice. We studied patients with perforated appendicitis because they encompass all phases of the CPG. This approach also allowed us to do a more complete assessment of adherence in the most clinically

severe patients. If patients with simple appendicitis were included, there would have been bias toward CPG adherence due to lack of post-operative antibiotic and laboratory use, as well as selection bias toward a healthy population and reduced complications. While our study design may bias against the CPG, we believe this approach is the most objective interval assessment of adherence.

We observed a significant increase in the age of patients presenting with a perforated appendix after CPG implementation. Reports correlated younger age at presentation with more advanced disease.[15] However, the observed difference was not associated with differing clinical outcomes, suggesting that the age group difference was not clinically significant nor a confounding variable.

Protocol deviations in the study were reviewed to identify ways to improve adherence. For antimicrobial stewardship, the primary cause for non-adherence was the decision to continue the antibiotic regimen initiated at referring hospitals. Piperacillin-tazobactam monotherapy is easier to initiate and ensure adequate coverage than dual therapy in patients that may be transferring quickly to avoid antibiotic delay. We achieved statistical reduction in post-operative laboratory tests; however, this decrease was a significant contributor to all protocol deviations occurring within our institution. Before this CPG, our group obtained bloodwork before discharge, and this standard was difficult to alter. After the CPG was developed, we had multiple education sessions with residents who primarily wrote orders because as new learners, they joined the service after the initial educational roll-out. We will evaluate whether these additional educational sessions have reduced deviations.

The number of patients initially evaluated at a referring facility increased by 32% in the post-CPG group. This evaluation likely affected the rates of overall CT scans, as there was a larger trend toward reduced CT scans at our institution (30% to 12%) than at referring facilities (50% to 43%) during the same time; although, neither result is statistically significant. We believe that with further study and an increased sample size, we would see significantly reduced CT rates to diagnose perforated appendicitis at our institution. Additionally, all CT scans were reported toward our count, even if appendicitis was not the suspected initial diagnosis or indication for imaging. Because an unexpected diagnosis of appendicitis will continue to be made based on CT, we anticipate that CT rates can be decreased, but not eliminated, although elimination will remain our target.

As the tertiary care center for a rural state, there are times when application of the CPG may not be feasible or in the patient's best interest. Transporting patients also carries potential adverse outcomes that were outside the scope of this study. Cost, burden on family, and traffic incidents weigh into the decision to transfer before or after CT scan, particularly on the outer perimeter of our referral base. We want to empower regional centers to make the best decisions for patients, and this effort is part of our outreach.

Implementation of the CPG most successfully reduced broad-spectrum antibiotic exposure and frequency of routine post-operative laboratory draws. There was concern with a high *Pseudomonas* frequency (20% of cultures) that choosing regimens without pseudomonal coverage in initial IV antibiotics would increase post-operative complications; however, we did not see this outcome. We hypothesize that adequate source control was enough to counteract the lack of pseudomonal coverage. The reduced post-operative laboratory draws and reliance on clinical decision for when to discharge on oral antibiotics also did not adversely affect outcomes.

We reported that there was no significant difference in patients who completed the original course of prescribed antibiotics, but there may be some clinical difference between the groups. In the pre-CPG cohort, 2 patients were reported as not taking the prescribed course of antibiotics because they were lost to follow-up and no documentation of completion was available. In the post-CPG cohort, 3 of the 5 patients reported as not completing the course of antibiotics were lost to follow-up; however, 2 of the 5 had documented intolerance and reported gastrointestinal symptoms requiring a change in oral regimen with the successful completion of antibiotics. The post-CPG regimen was metronidazole-based, which has known gastrointestinal side effects and may be the contributing agent to these 2 cases.

There are some limitations to this study, most notably the rarity of adverse secondary outcomes. While we did not find a significant increase in the

measured complications, we are mindful that given the frequency of adverse events, our study might not have been large enough to detect them. Therefore, we are continuing to collect and monitor these important metrics. Additionally, we have a relatively short mean follow-up time, which may not account for complications that present to referral centers. As we are the primary children's hospital for the state, most post-operative complications would be transferred and identified in our chart review; however, this belief is an assumption for which we have not done surveillance phone calls. Lastly, although we have documented a statistically significant change in practice associated with implementing the CPG, adherence after implementation was 64%. We defined successful implementation as adherence to the entire CPG, from presentation through discharge, knowing that this approach would provide more opportunities for non-adherence. This approach allowed us to better understand our own system and areas for further intervention. We are mindful that increasing adherence further may have a corresponding increase in adverse outcomes and will monitor this possibility as we continue to pursue complete adherence.

CONCLUSIONS

We successfully implemented an evidence-based, multidisciplinary CPG to decrease resource use, improve antimicrobial stewardship, and reduce radiation exposure for pediatric patients with suspected appendicitis. To further collaborate with referral centers, these data and CPG were presented at a statewide surgical chapter. We have also extended this CPG to referring emergency departments and have encouraged transfer initiation to lower barriers for interhospital discussion with centers without pediatric surgeons. We will continue to educate providers in multiple disciplines at our institution and conduct outreach to referring hospitals to further standardize management of pediatric appendicitis in our region.

Conflict of Interest: None

Disclosures: Data was presented as a podium presentation at the Canadian Association of Pediatric Surgeons annual meeting 2019.

Acknowledgements:

Drs. Pandya and Jubulis for study design and initial approval. Drs. Pandya, Jubulis, Vernamonti and Cotter for data entry. Drs. Pandya, Jubulis, and Vernamonti for manuscript, data and statistical analysis. With special acknowledgement to Dr. Lee Lucas for statistical analysis and review of study design and to Dr. Wendy Craig for reviewing the manuscript from the Maine Medical Center Research Institute.

REFERENCES

1. Smink DS, Finkelstein JA, Kleinman K, Fishman SJ. The effect of hospital volume of pediatric appendectomies on the misdiagnosis of appendicitis in children. Pediatrics. 2004;113(1 pt 1):18-23. doi:10.1542/peds.113.1.18
2. Willis ZI, Duggan EM, Bucher BT, et al. Effect of a clinical practice guideline for pediatric complicated appendicitis. JAMA Surg. 2016;151(5):e160194. doi:10.1001/jamasurg.2016.0194
3. Bhatt M, Joseph L, Ducharme FM, Dougherty G, McGillivray D. Prospective validation of the pediatric appendicitis score in a Canadian pediatric emergency department. Acad Emerg Med. 2009;16(7):591-596. doi:10.1111/j.1553-2712.2009.00445.x
4. Kwan KY, Nager AL. Diagnosing pediatric appendicitis: usefulness of laboratory markers. Am J Emerg Med. 2010;28(9):1009-1015. doi:10.1016/j.ajem.2009.06.004
5. Buyukbese Sarsu S, Sarac F. Diagnostic value of white blood cell and C-reactive protein in pediatric appendicitis. BioMed Res Int. 2016;2016: 6508619. doi:10.1155/2016/6508619
6. Nielsen JW, Boomer L, Kurtovic K, et al. Reducing computed tomography scans for appendicitis by introduction of a standardized and validated ultrasonography report template. J Pediatr Surg. 2015;50(1):144-148. doi:10.1016/j.jpedsurg.2014.10.033
7. Expert Panel on Pediatric Imaging:, Koberlein GC, Trout AT, et al. ACR Appropriateness Criteria® suspected appendicitis-child. J Am Coll Radiol. 2019;16(5S):S252-263. doi:10.1016/j.jacr.2019.02.022
8. Cameron DB, Melvin P, Graham DA, et al. Extended versus narrow-spectrum antibiotics in the management of uncomplicated appendicitis in children: a propensity-matched comparative effectiveness study. Ann Surg. 2018;268(1):186-192. doi:10.1097/SLA.0000000000002349
9. Desai AA, Alemayehu H, Holcomb GW 3rd, St Peter SD. Safety of a new protocol decreasing antibiotic utilization after laparoscopic appendectomy for perforated appendicitis in children: a prospective observational study. J Pediatr Surg. 2015;50(6):912-914. doi:10.1016/j.jpedsurg.2015.03.006
10. Lee SL, Islam S, Cassidy LD, Abdullah F, Arca MJ, 2010 American Pediatric Surgical Association Outcomes and Clinical Trials Committee. Antibiotics and appendicitis in the pediatric population: an American Pediatric Surgical Association Outcomes and Clinical Trials Committee systematic review. J Pediatr Surg. 2010;45(11):2181-2185. doi:10.1016/j.jpedsurg.2010.06.038
11. Rogers AP, Zens TJ, Leys CM, Nichol PF, Ostlie DJ. A call for a standardized definition of perforated appendicitis. J Pediatr Surg. 2017;52(1):89-92. doi:10.1016/j.jpedsurg.2016.10.026
12. St Peter SD, Sharp SW, Holcomb GW 3rd, Ostlie DJ. An evidence-based definition for perforated appendicitis derived from a prospective randomized trial. J Pediatr Surg. 2008;43(12):2242-2245. doi:10.1016/j.jpedsurg.2008.08.051

13. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010
14. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform. 2019;95:103208. doi:10.1016/j.jbi.2019.103208
15. Bansal S, Banever GT, Karrer FM, Partrick DA. Appendicitis in children less than 5 years old: influence of age on presentation and outcome. Am J Surg. 2012;204(6):1031-1035; discussion 1035. doi:10.1016/j.amjsurg.2012.10.003