

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Association for Academic Surgery

Clinical and socioeconomic factors associated with negative pediatric appendicitis



Genia Dubrovsky, MD,^a Josh Rouch, MD,^a Nhan Huynh, MD,^a
 Scott Friedlander, MS,^b Yang Lu, PhD,^b and Steven L. Lee, MD^{a,b,c,*}

^a Division of Pediatric Surgery, Department of Surgery, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California

^b Department of Pediatrics, Harbor-UCLA, Torrance, California

^c Division of Pediatric Surgery, Department of Surgery, Harbor-UCLA, Torrance, California

ARTICLE INFO

Article history:

Received 9 February 2017

Received in revised form

27 April 2017

Accepted 19 June 2017

Available online xxx

Keywords:

Pediatric appendicitis

Negative appendicitis

Perforated appendicitis

Length of stay

Cost

Morbidity

ABSTRACT

Background: Misdiagnosing appendicitis may lead to unnecessary surgery. The study evaluates the risk factors for negative appendectomies, as well as the clinical and socioeconomic consequences of negative appendectomy across three states.

Materials and methods: Data were obtained from the California, New York, and Florida State Inpatient Databases 2005–2011. Patients (<18 years) who underwent nonincidental appendectomies ($n = 156,660$) were evaluated with hierarchical and multivariate negative binomial regression analyses on outcomes including hospital cost, length of stay (LOS), and associated morbidity.

Results: From 2005 to 2011, there was a decrease in the rate of negative appendicitis and perforated appendicitis, whereas the rate of true acute nonperforated appendicitis increased. Whites, females, and privately insured patients were associated with higher negative appendicitis rates, whereas those at an increased risk for perforated appendicitis were African-Americans, males, and those with public or no insurance. Compared to patients with acute nonperforated appendicitis, those with negative appendicitis have significantly higher morbidity (2.5% versus 1.3%), longer LOS (3.4 versus 1.8 d), and greater hospital costs averaged over time (\$6926 versus \$6492 per patient).

Conclusions: Despite a low incidence, negative appendicitis is associated with greater morbidity, longer LOS, and higher cost than acute nonperforated appendicitis. Certain subpopulations are at higher risk for undergoing surgery for negative appendicitis, whereas others are at greater risk for presenting with perforated appendicitis. Further research is needed to understand what drives such disparities and to inform efforts to improve quality of hospital care across all groups of patients.

© 2017 Elsevier Inc. All rights reserved.

* Corresponding author. Division of Pediatric Surgery, Department of Surgery, Harbor-UCLA, 1000 W Carson Street, Box 461, Torrance, CA 90509 USA. Tel.: +1 310 222 2700; fax: +1 310 782 1562.

E-mail address: silleemd@yahoo.com (S.L. Lee).

0022-4804/\$ – see front matter © 2017 Elsevier Inc. All rights reserved.

<http://dx.doi.org/10.1016/j.jss.2017.06.063>

Introduction

Appendicitis is a common surgical disease with a lifetime incidence of 7%-9%.¹⁻³ It presents most often in the second decade of life and is also the most common surgical cause for nontraumatic abdominal pain in children.¹⁻⁵ Despite its ubiquity, acute appendicitis can be much more difficult to diagnose in a child than in an adult because children may not have typical findings on history and physical examination and because it may be difficult to elicit these findings from an uncooperative infant.^{1,6-8} Abdominal ultrasound, the imaging modality of choice in children, can also be less informative than a computed tomography (CT) scan as the sensitivity varies widely across sites from 35%-78%.⁹

A missed diagnosis of pediatric appendicitis carries significant consequences as these children are at higher risk for perforation and abscess formation leading to longer hospitalization and higher cost.^{1,6,10} Negative appendectomies are unnecessary operations and thus also pose a significant burden both to patients and to the health care system. Although historically they were accepted as a necessary means to reduce the rate of missed appendicitis, they are now recognized as being not inconsequential.¹¹⁻¹³ To better understand the relationship between true, negative, and perforated pediatric appendicitis, we look at their trends over time. We evaluate the clinical and socioeconomic consequences of negative appendectomies and determine the risk factors for undergoing a negative pediatric appendectomy.

Materials and methods

Data collection

We used the California, New York, and Florida State Inpatient Databases (SIDs) from the Healthcare Cost and Utilization Project, which include all inpatient discharges from nongovernmental hospitals in each state. The SID provides discharge data such as patient demographics, insurance status, discharge diagnoses, procedures performed, length of stay (LOS), and total charges. Cost was derived and inflation adjusted to 2010 dollars using the cost-to-charge ratio files provided by Healthcare Cost and Utilization Project and published medical consumer price index.

The study sample consisted of pediatric (age <18 y) inpatient admissions for which a nonincidental appendectomy was the primary procedure. Cases were identified by searching SID for the years of 2005-2011 for all discharges with the ICD-9 codes of 47.0 (appendectomy), 47.01 (laparoscopic appendectomy), and 47.09 (other appendectomy) listed as the primary procedure. This is similar to the method used in previous studies. We included all patients with an ICD-9 code for nonincidental appendicitis as the primary procedure, although we excluded those with the codes listed as a secondary procedure.^{2,14,15} The code 47.09 for "other appendectomy" was used to capture patients that had undergone an open appendectomy.

We categorized appendectomy admissions into three broad types: negative appendicitis (NA), nonperforated

appendicitis, and perforated appendicitis. NA was defined as a nonincidental appendectomy without a diagnosis of appendicitis. Appendectomies where a diagnosis of appendicitis was not among the first three diagnoses were also considered negative, given the possibility that suspected appendicitis upon presentation is coded as a nonprimary appendicitis diagnosis even without eventual confirmation of the diagnosis of appendicitis.

Appendectomy with nonperforated appendicitis was identified with one or more of the following ICD-9 diagnosis codes: 540.9 (acute appendicitis without mention of peritonitis), 541 (appendicitis, unqualified), and 542 (other appendicitis). Appendectomy with perforated appendicitis was identified by either ICD-9 diagnosis code 540.0 (acute appendicitis with generalized peritonitis) or 540.1 (acute appendicitis with peritoneal abscess).

Complications commonly associated with appendectomy were also investigated, using appropriate ICD-9 codes. These included infection, bleeding, retained foreign body, obstruction, cardiovascular complications (e.g., deep vein thrombosis, pulmonary embolus, stroke, and cardiac arrest), respiratory complications (e.g., atelectasis, pneumothorax, pulmonary edema, and acute respiratory syndrome), and renal complications (e.g., renal insufficiency).

Covariates included in the study were age, gender, race/ethnicity, insurance type, type of appendectomy (open versus laparoscopic), hospital ownership (public or private), quartiles of hospital volume (number of appendectomies performed per year), and calendar year.

Statistical analysis

Analyses were performed at the patient level, in which we examined predictors of NA as well as its implications on cost, LOS, and comorbidity as compared to appendectomies with nonperforated and perforated appendicitis. Multivariate logistic regression was performed on the outcomes of NA and comorbidity. Multiple median regression was performed on the outcome of cost with clustered standard errors, and negative binomial regression was performed on the outcome of LOS. All patient-level analyses were clustered by the hospital's respective Federal Information Processing Standard county code. All analyses were performed using Stata 14.1.

Results

We were able to identify a total of 156,660 nonincidental inpatient appendectomies from 2005-2011. Patient demographics are presented in Table 1. Pooling results from the three states together, we see an overall decrease in the rate of both negative appendicitis (3.3% in 2005 to 1.8% in 2011, $P < 0.01$) and perforated appendicitis (27.1% in 2005 to 25.0% in 2011, $P < 0.01$; Fig. 1). This reflects an increase in true acute nonperforated appendicitis (69.6% in 2005 to 73.2% in 2011). Although LOS decreased by 13.7% for nonperforated appendicitis (2.0-1.7 d) and by 4.1% for perforated appendicitis (5.6-5.3 d), it increased by 5.6% for negative appendicitis (3.1-3.3 d; Fig. 1, $P < 0.01$). Averaged over time, hospital costs are

Table 1 – Demographic characteristics of the study population.

Appendectomy type	California (n = 93,447)			New York (n = 33,683)			Florida (n = 29,530)		
	Nonperforated (70.1%)	Perforated (27.5%)	Negative (2.5%)	Nonperforated (74.6%)	Perforated (22.8%)	Negative (2.6%)	Nonperforated (75.6%)	Perforated (22.6%)	Negative (1.9%)
Age									
1-5 (ref)	3.7	14.3	10.8	4.3	14.5	15.0	4.8	13.7	18.2
6-10	33.4	39.7	32.5	29.0	34.7	23.7	29.7	32.2	22.0
11-15	32.7	29.8	26.8	44.8	37.4	40.9	43.9	39.9	37.9
16-17	30.3	16.3	29.8	21.9	13.4	20.5	21.6	14.2	22.0
Sex									
Male	71.3	70.2	41.0	61.7	60.4	45.5	62.4	62.3	46.6
Female	28.8	29.8	59.0	38.3	39.6	54.5	37.6	37.7	53.4
Race									
White	31.8	20.6	43.1	55.8	50.3	69.3	52.7	52.4	66.1
Hispanic	63.0	73.6	49.3	7.6	8.7	9.3	8.7	11.4	10.9
African-American	1.6	1.8	3.3	23.1	26.3	13.1	33.1	30.6	18.5
Other	3.5	4.1	4.4	13.5	14.8	8.3	5.6	5.6	4.5
Type of operation									
Open	35.8	45.1	37.4	38.0	48.0	40.1	28.0	60.0	31.4
Laparoscopic	64.2	54.9	62.6	62.0	52.0	59.9	72.0	40.0	68.6
Insurance									
Private	52.8	40.5	58.5	59.1	51.8	66.2	49.1	42.3	47.3
Public	39.7	51.8	35.9	32.5	38.7	25.9	36.5	42.8	38.9
Unknown	3.4	3.7	2.9	2.0	2.0	3.1	8.0	7.5	8.8
No insurance	4.1	4.0	2.7	6.5	7.5	4.8	6.5	7.4	5.0
Hospital volume									
1-41	22.3	16.1	23.0	37.2	34.9	46.5	27.2	24.2	28.6
41-86	29.8	26.8	32.1	24.1	22.2	18.1	13.4	15.1	15.7
87-170	28.9	28.7	30.4	23.0	25.0	21.0	12.6	18.1	17.7
171+	19.1	28.4	14.5	15.7	17.9	14.4	46.8	42.7	38.0
Total cost (mil)	\$445.2	\$313.9	\$20.2	\$129	\$75	\$6.2	\$136	\$73	\$5.6
Median cost	\$7191	\$11,602	\$7542	\$5266	\$8863	\$5236	\$5884	\$9251	\$6530
LOS (d)	1.8	5.3	2.9	1.9	5.7	3.6	1.8	5.9	4.6
Complications	1.3%	9.4%	2.4%	1.5%	10.7%	3.1%	1.0%	8.9%	2.7%

All values are given as percentages, unless otherwise specified. Total n = 156,660.

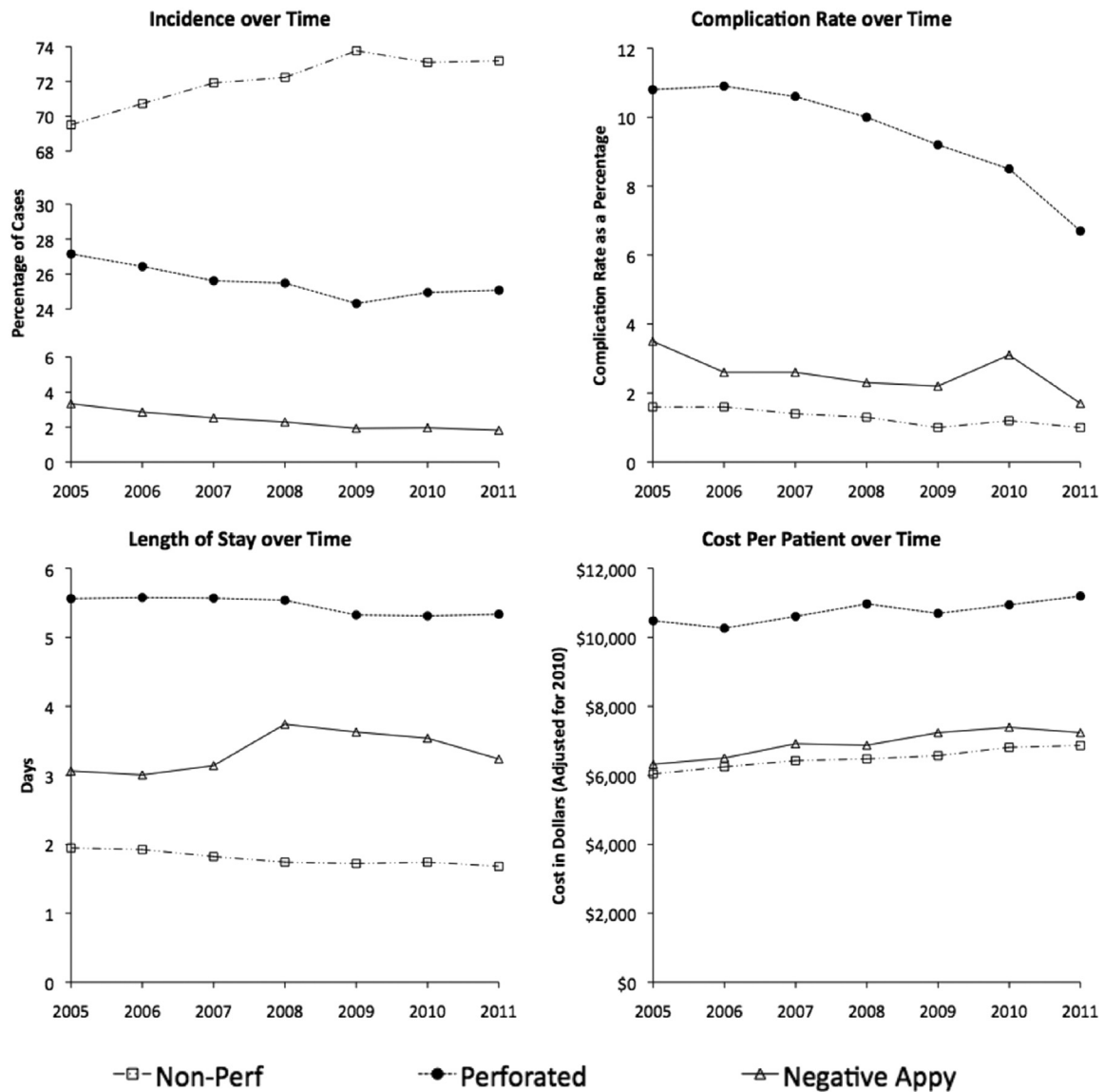


Fig. 1 – Incidence, complication rate, LOS, and median cost per patient of true nonperforated appendicitis (Non-Perf), perforated appendicitis (Perforated), and negative appendicitis (Negative Appy) over time.

higher for negative appendicitis than for acute nonperforated appendicitis (\$6926 versus \$6492 per patient, $P < 0.01$), and morbidity is higher (2.5% versus 1.3%, $P < 0.01$).

Multivariate analysis results are shown in Table 2. The risk factors for negative appendicitis include youngest age group (<5 y), whites, females, use of laparoscopy, having private insurance, and care at a low-volume hospital. In contrast, significant risk factors for perforated appendicitis include youngest age group (<5 years), African-Americans, males, having open surgery, and having public or no insurance. Both higher cost and longer LOS were associated with youngest age group (<5 years), African-Americans, females, and complications. Higher cost was also associated with use of laparoscopy and low-volume hospitals, whereas longer LOS was associated with open surgery, high-volume hospitals, and public or unknown insurance. A higher rate of complications was

associated with youngest age group (<5 y), African-Americans, males, and low-volume and nonprofit hospitals.

Using multivariate analysis to compare California, New York, and Florida to each other shows that California had the highest cost, highest complication rate, and highest rates of both negative and perforated appendicitis (Table 1).

Discussion

Historically, adult negative appendicitis rates have been decreasing.^{12,16} Although rates as high as 15%-30% were considered acceptable in the past, more recently, the rate of negative appendicitis has dropped to 8.5% in 2007.¹² One reason for this is improved diagnostics with the use of CT imaging.¹⁶ However, CT scans are used much less frequently

Table 2 – Multivariate analysis.

Factor	Perforated (OR)	Negative (OR)	Complications (OR)	LOS (relative risk)	Cost (median)
Appendectomy type					
Nonperforated (ref)	—	—	—	—	—
Perforated	—	—	7.66 [†]	2.63 [†]	3793 [†]
Negative	—	—	1.87 [†]	1.77 [†]	300 [†]
Age					
1-5 (ref)	—	—	—	—	—
6-10	0.42 [†]	0.41 [†]	0.71 [†]	0.85 [†]	–418 [†]
11-15	0.33 [†]	0.37 [†]	0.70 [†]	0.83 [†]	–308 [†]
16-17	0.23 [†]	0.41 [†]	0.75 [†]	0.78 [†]	–267 [*]
Sex					
Male (ref)	—	—	—	—	—
Female	0.89 [*]	1.77 [†]	0.84 [†]	1.02 [†]	167 [†]
Race					
White (ref)	—	—	—	—	—
African-American	1.18 [†]	1.09	1.69 [†]	1.27 [†]	620 [†]
Hispanic	1.07	0.50 [†]	1.04	1.04	116
Other	1.06	0.63 [†]	1.13	1.09 [†]	504 [†]
Type of operation					
Open (ref)	—	—	—	—	—
Laparoscopic	0.69 [†]	1.18 [†]	0.94	0.83 [†]	1170 [†]
Insurance					
Private (ref)	—	—	—	—	—
Public	1.36 [†]	0.85 [†]	0.98	1.10 [†]	141 [*]
Unknown	1.23 [†]	0.97	0.83 [*]	1.08 [†]	121
No insurance	1.33 [†]	0.66 [†]	0.91	1.05 [*]	87
Hospital volume					
1-41	—	—	—	—	—
41-86	1.03	0.88	0.84 [*]	1.04	–294
87-170	1.11 [*]	0.90	0.76 [*]	1.10 [†]	–620 [†]
171+	1.38 [†]	0.61 [†]	0.50 [†]	1.18 [†]	–321
Complications					
No complications	—	—	—	—	—
Infection	6.91 [†]	0.56 [†]	—	2.38 [†]	8003 [†]
Gastrointestinal	9.63 [†]	0.54 [†]	—	1.83 [†]	3791 [†]
Other	3.27 [†]	1.52 [†]	—	1.83 [†]	3825 [†]
State					
CA (ref)	—	—	—	—	—
FL	0.68 [†]	0.64 [†]	0.68 [†]	1.02	–1699 [†]
NY	0.73 [†]	0.78	0.72 [*]	1.05	–2269 [†]

OR = odds ratio.

Perforated appendicitis, negative appendicitis, and complications are in terms of OR. The LOS is in terms of relative risk, with >1 meaning longer LOS and <1 meaning shorter LOS. The cost is in terms of the median cost, with positive values meaning higher cost and negative values meaning lower cost.

*Indicates P value <0.05.

†Indicates P value <0.01.

in the workup of pediatric appendicitis. Interestingly, we still saw a significant decrease in the rates of both negative and perforated pediatric appendicitis from 2005-2011, suggesting an improved ability to diagnose true nonperforated acute appendicitis. Unfortunately, our data set does not provide any specifics about what exactly was the cause for this decrease.

Negative appendicitis should not be treated as a benign condition, as we show that it results in longer LOS, higher complication rate, and higher cost than true nonperforated appendicitis. In fact, LOS and cost for negative appendicitis have increased since 2005. On average, negative appendicitis cost California, New York, and Florida a combined \$4.6 million

annually from 2005-2011. Patients with negative appendicitis pose a diagnostic dilemma, and therefore, it is understandable that they experience a longer LOS and higher associated costs. It is less clear why they have more complications. The types of complications they experience are similar to the ones that develop in patients with nonperforated appendicitis. Nearly 50% of the complications in both groups are gastrointestinal related (such as obstruction or *C. diff* infection). However, a higher proportion of the complications are respiratory (such as atelectasis or pneumonia) in negative appendicitis patients than in nonperforated patients (22% compared to 13%). One explanation for the overall higher rate of complications in negative appendicitis patients may be that the “complications” are in fact the primary reason that prompted the patient to present, and these were instead misdiagnosed as appendicitis. When the correct diagnosis was established after surgery, it may have been coded as a complication.

It is unsurprising that the youngest children (age <5 y) and women are at increased risk for negative appendicitis as these represent populations where it is more difficult to arrive at a correct diagnosis. Young children have lower rates of appendicitis, and it is more difficult to obtain an accurate history and examination from them. Women pose a diagnostic challenge because of many gynecologic diseases that can mimic appendicitis. Our findings that whites had higher rates of negative appendicitis than Hispanics support previous work.^{13,14} Oyetunji et al. had also noted a higher rate of negative appendicitis among African-Americans, which was not seen in an earlier study by Smink et al. and was not seen in our study either.^{13,14} We do however show that African-Americans are at increased risk for perforated appendicitis, higher rate of complications, longer LOS, and thus higher cost. This ethnic disparity is striking, and further studies are needed to determine the exact reasons for it. Some possibilities include decreased access to health care, treatment differences, or a difference in the presentation of African-American patients. We did see the effect of disparity in access to health care when looking at types of insurance. Patients with private insurance had increased rates of negative appendicitis, whereas those with public or no insurance were more likely to have perforated appendicitis.

Comparing different types of hospitals, it was not surprising to see that low-volume hospitals had higher rates of negative appendicitis, higher cost, and more complications. However, we found that high-volume hospitals had significantly longer lengths of stay. This can be explained by the fact that they also have higher rates of perforated appendicitis, which is likely a reflection of the more complex cases being referred to high-volume centers.

Finally, we were interested to see that out of the three states, California had the highest rate of both negative and perforated appendicitis, resulting in more complications and higher costs. Although our data cannot determine the cause for this, it is certainly an area for future study as there is great potential to improve outcomes and to lower costs.

The rate of negative appendicitis in our study, 1.8%-3.3%, is quite lower than the previously reported rates of 5.2%-8.1% in 2000-2006 and 8.4% in 1997.^{13,14} This is surprising since we followed similar methods of classification

as these two previous studies. In fact, we had slightly more rigorous criteria for true appendicitis and therefore expected to see more patients classified as having negative appendicitis. Patients not only needed an appendicitis-related diagnosis but also needed to be one of the first three diagnoses listed on discharge to fall into the category of true appendicitis. It is possible that this low rate could represent an error in coding, as we did not have access to pathologic data. It could also represent a true decrease in the rate of negative appendicitis over time, possibly as a result of improved imaging.

One limitation of our study is that our inclusion criteria omit patients who were treated nonsurgically for their appendicitis. Children who presented with advanced perforated appendicitis and underwent drain placement with a delayed appendectomy on future admission and children with nonperforated appendicitis that elected to have treatment with antibiotics were not included in our study. The incidence of both acute nonperforated appendicitis and perforated appendicitis may therefore be higher. We did not include these groups of patients since they represent separate treatment arms and therefore a different set of associated complications, lengths of stay, and costs.

Other limitations of our study include reliance on a data set for analysis, which depends on accurate coding. Any errors in entering billing codes would effect our study results. We also did not have access to ancillary data such as laboratory or imaging studies to confirm diagnoses. Finally, our study compares three large states from different parts of the United States, but our findings may not be generalizable to broader populations.

Conclusions

This study further corroborates the continued decrease in rates of pediatric negative appendicitis. However, this condition should not be dismissed as it has significantly higher morbidity, LOS, and cost than acute nonperforated appendicitis. Certain subgroups are at increased risk for undergoing surgery for negative appendicitis. There is also variability in rates of negative and perforated appendicitis in different states. Further research is needed to understand what drives such disparities and to inform efforts to improve quality of hospital care.

Acknowledgment

The authors like to acknowledge the Health Services Outcomes Network of the Department of Pediatrics at Harbor-UCLA for their assistance. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions: G.D., J.R., and N.H. contributed to the writing of this manuscript. S.F. and Y.L. contributed to the data extraction and analysis portion. S.L. oversaw the project and provided guidance and direction from conception to completion.

Disclosure

The authors declare no conflicts of interest to disclose.

REFERENCES

1. Rothrock SG, Pagane J. Acute appendicitis in children: emergency department diagnosis and management. *Ann Emerg Med.* 2000;36:39–51. Review.
2. Addiss DG, Shaffer N, Fowler BS, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol.* 1990;132:910–925.
3. Anderson JE, Bickler SW, Chang DC, Talamini MA. Examining a common disease with unknown etiology: trends in epidemiology and surgical management of appendicitis in California, 1995–2009. *World J Surg.* 2012;36:2787–2794.
4. Reynolds SL, Jaffe DM. Diagnosing abdominal pain in a pediatric emergency department. *Pediatr Emerg Care.* 1992;8:126–128.
5. Scholer SJ, Pituch K, Orr DP, Dittus RS. Clinical outcomes of children with acute abdominal pain. *Pediatrics.* 1996;98:680–685.
6. Choi JY, Ryoo E, Jo JH, Hann T, Kim SM. Risk factors of delayed diagnosis of acute appendicitis in children: for early detection of acute appendicitis. *Korean J Pediatr.* 2016;59:368–373.
7. Podevin G, De Vries P, Lardy H, et al. An easy-to-follow algorithm to improve pre-operative diagnosis for appendicitis in children. *J Visc Surg.* 2016. <http://dx.doi.org/10.1016/j.jviscsurg.2016.08.011> [Epub ahead of print].
8. Ross MJ, Liu H, Netherton SJ, et al. Outcomes of children with suspected appendicitis and incompletely visualized appendix on ultrasound. *Acad Emerg Med.* 2014;21:538–542.
9. Mittal MK, Dayan PS, Macias CG, et al. Pediatric emergency medicine Collaborative research Committee of the American Academy of pediatrics. Performance of ultrasound in the diagnosis of appendicitis in children in a multicenter cohort. *Acad Emerg Med.* 2013;20:697–702.
10. Graff L, Russell J, Seashore J, et al. False-negative and false-positive errors in abdominal pain evaluation: failure to diagnose acute appendicitis and unnecessary surgery. *Acad Emerg Med.* 2000;7:1244–1255.
11. Christian F, Christian GP. A simple scoring system to reduce the negative appendectomy rate. *Ann R Coll Surg Engl.* 1992;74:281–285.
12. Seetahal SA, Bolorunduro OB, Sookdeo TC, et al. Negative appendectomy: a 10-year review of a nationally representative sample. *Am J Surg.* 2011;201:433–437.
13. Oyetunji TA, Ong'uti SK, Bolorunduro OB, Cornwell 3rd EE, Nwomeh BC. Pediatric negative appendectomy rate: trend, predictors, and differentials. *J Surg Res.* 2012;173:16–20.
14. 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;113:18–23.
15. Flum DR, Morris A, Koepsell T, Dellinger EP. Has misdiagnosis of appendicitis decreased over time? A population-based analysis. *JAMA.* 2001;286:1748–1753.
16. Boonstra PA, van Veen RN, Stockmann HB. Less negative appendectomies due to imaging in patients with suspected appendicitis. *Surg Endosc.* 2015;29:2365–2370.