ORIGINAL ARTICLE

Risk Factors for the Development of Abdominal Abscess Following Operation for Perforated Appendicitis in Children

A Multicenter Case-Control Study

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Hypothesis: The morbidity following treatment for perforated appendicitis in children is significant, with intra-abdominal abscess being one of the more serious complications. This can lead to prolonged hospitalizations and antibiotic administration, multiple computed tomographic scans, and invasive procedures. The purpose of our study was to determine risk factors for developing an intra-abdominal abscess following treatment for perforated appendicitis.

Design: Case-control study.

Setting: Four tertiary care children's hospitals.

Patients: Children aged 1 to 18 years with appendicitis.

Intervention: Multivariable logistic regression.

Main Outcome Measures: Development of postoperative abscess, length of hospital stay, presence or absence of fever, and tolerance of diet on postoperative day 3.

Results: Thirty-five (13.2%) of 265 children developed an abscess. Ten factors with a bivariate *P* value <.20 were included in the regression model. The final multivariable model revealed only 2 factors influencing abscess development: an intraoperative fecalith (odds ratio, 8.77 [95% confidence interval, 1.50-51.40]) and diarrhea at presentation. Many factors proposed to be associated with abscess were not, including pain history, type and timing of preoperative antibiotics, abscess at operation, laparoscopic procedure, and length of antibiotics postoperatively. Thiry-seven children were discharged on or before postoperative day 3. Another 21 children were afebrile and tolerating a diet at that time but remained in the hospital. There were no significant differences between the 2 groups. None of the early-discharge group developed an abscess, and 2 of those remaining in the hospital developed an abscess (*P*=.06).

Conclusions: Clinical factors commonly thought to be predictive of abscess formation following perforated appendicitis were not reliable predictors of this outcome. Our results suggest that if children are afebrile and eating on postoperative day 3 they can be discharged with a low rate of abscess development.

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ACUTE APPENDICITIS IS THE most common reason for emergency abdominal surgery in children, with approximately 80 000 cases per year in the United States.[1-5] Recent studies have shown that between one third and three quarters of children presenting with appendicitis, depending on age, have a perforation at the time of diagnosis.[4,6] If an appendix has ruptured, the morbidity and mortality increase significantly for the patient, with complication rates as high as 58%.[7] Complications following perforated appendicitis lead to the need for more radiographic studies, more invasive procedures, longer administration of antibiotics, and prolonged hospital stays. Prior studies have shown that the high rates of perforation are mainly determined by delays in seeking care at a hospital rather than errors in diagnosis or hospital delays.[8] However, efforts to decrease the complication rates following perforation have led to many studies and reports, most of which are single-institution case series. Despite these studies, the treatment of children with perforated appendicitis

See Invited Critique at end of article

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Demographic	Hospital Admission Data	Radiographic Findings	Perioperative Care	Postoperative Care
Age, y	Pain Duration (Days Prior to Admission)	CT Scan	Antibiotics Within 2 h of OR (Y/N)	Days of Antibiotics
Sex	Pain Location • RLQ • Diffuse	Free Fluid (Y/N)	Gram-positive Coverage (Y/N)	Fever Postoperatively Y/N for Each Day
Race • White • Black • Other	Nausea (Y/N)	Abscess (Y/N)	Gram-negative Coverage (Y/N)	
Insurance • Private • Medicaid • Self-pay	Vomiting (Y/N)		Anaerobe Coverage (Y/N)	
Hospital Site of Care	Decreased Appetite (Y/N)		Type of Surgery • Open • Laparoscopic	
	Diarrhea (Y/N)		Drain Placement (Y/N)	
	Fever (Y/N) (Temperature >38.5°C)		Intraoperative Findings • Abscess • Fecalith • Gross Perforation (Could Have More Than One)	
	Peritoneal Signs on Examination (Y/N)			
	White Blood Cell Count in 1000 per Microliter			

Figure 1. Variables of interest. CT indicates computed tomographic; OR, operating room; RLQ, right lower quadrant; Y, yes; and N, no.

remains widely disparate between centers and surgeons, without consensus on how to decrease complications. A survey of members of the American Pediatric Surgical Association in 2000 revealed that the majority of pediatric surgeons based their care of patients on individual surgeon's preferences, which has led to significant variations in clinical practice regarding the major aspects of preoperative, intraoperative, and postoperative care.[5]

In the absence of high-quality clinical evidence, surgeons must base their practice on their training, anecdotal experience, or institutional norms. The resulting variability in care may be wasteful if there is not evidence of demonstrated benefit. In a study by Newman and colleagues,[9] there was no outcome difference between the patients who received antibiotics at a cost of $400 and those receiving $4000 worth of antibiotics. Clearly, the potential for saving resources is significant. Furthermore, some have suggested that variability in care may also represent variability in quality, with implications for complication rates and lengths of hospitalizations.[10]

Risk stratification of children presenting with perforated appendicitis may be one way to reduce excesses of care and identify subsets of patients in whom some interventions are more necessary or useful. In pediatric surgery, there are very few studies that attempt to characterize high-risk patients. Identifying those patients who are at higher risk for developing a complication would enable care to be directed appropriately and cost-effectively. The purpose of our study was to determine risk factors for the development of an intra-abdominal abscess after surgical treatment for perforated appendicitis.

METHODS

STUDY DESIGN

A multicenter case-control study was designed and conducted at 4 geographically diverse, academic tertiary care children's hospitals. Institutional review board approval was received from all institutions prior to study initiation.

All children aged 1 to 18 years who presented to these 4 hospitals between May 1998 and June 2003 with a diagnosis of perforated appendicitis were enrolled. For the purposes of this study, perforated appendicitis was defined as evidence on preoperative abdominal ultrasonography or computed tomographic scan of perforated appendicitis or appendiceal mass suggesting perforation; evidence of gangrenous or perforated appendicitis in the operating room; or perforation confirmed on pathology report. Cases of gangrenous appendicitis were not included in the analysis. Primary variables of interest were divided into categories of demographic information, hospital admission clinical variables, radiographic findings, perioperative care, and postoperative care (**Figure 1**).

For the purposes of the study, an intra-abdominal abscess was defined as a single or multiple fluid collection[s] on abdominal ultrasonography or computed tomographic scan with an enhancing rim. Any collection, no matter what size, that was drained was considered an abscess. If a fluid collection was smaller than 3 cm and not drained, it was considered a phlegmon. These 2 categories, however, were ultimately analyzed together because there were only 2 cases of phlegmon and the computed tomography features were close enough to some of those drained that they were considered indistinguishable from the other cases. Postoperative days of antibiotics only included those days of antibiotics prior to the development of a complication in order to avoid the confounding effect of antibiotics being used as a treatment modality once a complica-

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Table 1. Characteristics of the 265 Study Patients

Variable	No.* (%)
Sociodemographic factor	
Age, y, mean ± SD	10.1 ± 4.0
Male	155 (58.5)
Female	110 (41.5)
Race	
White	112 (42.2)
Black	26 (9.8)
Other	32 (12.1)
Missing	95 (35.8)
Insurance	
Private	130 (49.2)
Medicaid	77 (29.2)
Self-pay	27 (10.2)
Site distribution (hospital)	
A	18 (6.8)
B	65 (24.5)
C	68 (25.7)
D	114 (43.0)
Type of operation	
Open appendectomy	146 (55.1)
Laparoscopic appendectomy	109 (41.1)
Conversion from laparoscopic to open	10 (3.8)
Outcome: abscess	35 (13.2)

*May not sum to 265 because of missing variables.

tion occurred. Patients who were treated by laparoscopic appendectomy that required conversion to open appendectomy were categorized as having undergone laparoscopic appendectomy based on intention-to-treat principles.

SELECTION OF CASES AND CONTROLS

The case group for the primary study consisted of all patients who developed an intra-abdominal abscess postoperatively. Those patients who did not develop a postoperative intra-abdominal abscess made up the control group. All patients treated nonoperatively were excluded from the analysis for this study.

STATISTICAL ANALYSIS

All statistical analysis was completed using SAS 8.01 for Windows (SAS Institute, Cary, NC). Descriptive characteristics were obtained by univariate analysis and presented as means with standard deviations, or percentages.

Bivariate analysis was performed to test the association of each variable with the outcome of interest, intra-abdominal infectious complication, from here on referred to as postoperative abscess. The unpaired *t* test, χ^2 statistic, and Fisher exact test were used. The unadjusted odds ratio with a 95% confidence interval was obtained for each of the categorical variables. A significance level of $\alpha = .05$ was chosen for all statistical tests and all *P* values are 2-tailed. Multicollinearity was examined on all of the variables.

Multivariate analyses using logistic regression was then used to obtain adjusted odds ratios and 95% confidence intervals for factors that were associated with postoperative abscess development. A sample population using three quarters of the data was used for the bivariate analysis and the logistic regression model. The final model was then tested on the remaining quarter of the data using receiver operating characteristic curve comparison.

SECONDARY ANALYSIS

Records of cases and controls were reviewed to select those patients who would meet certain hospital discharge criteria on or before postoperative day 3: being afebrile and tolerating a regular diet. Of those patients meeting those criteria, a comparison was performed between those who were actually discharged on or before postoperative day 3 and those who remained in the hospital. The rate of complications between these 2 groups was compared.

RESULTS

CHARACTERISTICS OF STUDY POPULATION

Data were collected on 371 patients from the 4 hospitals. The 48 patients treated nonoperatively were excluded from analysis, as were 58 patients with purely gangrenous appendicitis. Two hundred sixty-five patients were included in the study: 35 developed an intra-abdominal abscess postoperatively and became the cases; 230 did not and became the controls. As shown in **Table 1**, the mean±SD age of the population was 10.1±4.0 years. The overall postoperative abscess rate was 13.2%.

STATISTICAL ANALYSIS

Preoperative and perioperative variables reaching a significance of $P < .20$ in the bivariate analysis were initially entered into the multivariable regression model. These variables included sex, insurance, pain lasting more than 3 days, diffuse pain, right lower quadrant pain, diarrhea, vomiting, abscess found in the operating room, fecalith found in the operating room, and days of postoperative antibiotics (**Table 2** and **Table 3**). Age and site were also included in the analysis. The adjusted odds ratios for the 2 factors predictive of abscess development on multivariable analysis, diarrhea on presentation and fecalith in the operating room, were 3.63 (95% confidence interval, 1.29-10.21) and 8.77 (95% confidence interval, 1.50-51.40), respectively.

The final model was tested for an interaction between these variables, and there was no significant interaction. There were no individual observations identified on the examination of the diagnostics that needed to be removed from the data set because of unusual influence or unusual variable values.

APPLICATION OF THE DERIVED MODEL TO THE TEST DATA

The multivariable regression model developed from the sample population was applied to a test population. At a probability level of 0.1, the sensitivity was 62.5% and the specificity was 58.8%. However, at a probability of 0.5, the sensitivity was 0% while the specificity was 98%. The receiver operating characteristic curve for the model applied to the test data set is shown in the **Figure 2**. The area under the curve was calculated at 0.636, which would indicate that the model is poor at discriminating between those who will get an abscess and those who will not.

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Table 2. Demographic Comparison of Cases and Controls of Sample Population

Demographic	No. (%) Cases (n = 26)	No. (%) Controls (n = 173)	OR (95% CI)	χ^2 Value, *df*	*P* Value
Male	11 (42.3)	106 (61.3)	NA	3.36, 1	.07
Age, y, mean ± SD	10.44 ± 4.24	10.12 ± 3.91	NA	−0.38, 197	.70
Race				7.95, 2	.02
White	12 (52.2)	74 (69.8)	1 [Reference]		
Black	8 (34.8)	12 (11.3)	4.18 (1.47-11.91)		
Other	3 (13.0)	20 (18.9)	0.65 (0.17-2.38)		
Insurance				10.02, 3	.02
Private	8 (30.8)	90 (52.3)	1 [Reference]		
Medicaid	7 (26.9)	49 (28.5)	0.92 (0.37-2.34)		
Self-pay	7 (26.9)	14 (8.1)	4.16 (1.49-11.58)		
Other	4 (15.4)	19 (11.1)	1.46 (0.46-4.70)		

Abbreviations: CI, confidence interval; NA, not applicable; OR, odds ratio.

Table 3. Bivariate Comparison of Cases and Controls in Sample Population

	No. (%) Cases (n = 26)	No. (%) Controls (n = 173)	OR (95% CI)	χ^2_1 Value	*P* Value
Clinical presentation					
WBC count, × 10^3/μL, mean ± SD	17.65 ± 7.73	17.18 ± 5.81	NA	NA	.77
Temperature, °C, mean ± SD	38.1 ± 1.0	38.0 ± 1.0	NA	NA	.51
Pain duration, d, mean ± SD	5.22 ± 4.35	3.56 ± 2.57	NA	NA	.08
Pain >3 d	17 (65.4)	64 (37.0)	3.22 (1.35-7.64)	7.55	.006
Diffuse pain	10 (41.7)	37 (22.8)	2.41 (1.00-5.88)	3.92	.048
RLQ pain	9 (37.5)	93 (56.7)	0.46 (0.19-1.11)	3.11	.08
Nausea	21 (91.3)	127 (88.2)	1.41 (0.30-6.53)	0.19	.66
Vomiting	23 (95.8)	139 (86.3)	3.64 (0.47-28.33)	*	.32
Peritoneal signs	15 (57.7)	116 (67.1)	0.67 (0.29-1.55)	0.88	.35
Diarrhea	15 (71.4)	61 (41.5)	3.52 (1.29-9.60)	6.65	.01
CT findings					
Free fluid	6 (28.6)	30 (20.1)	1.59 (0.57-4.44)	0.79	.38
Abscess	3 (14.3)	23 (15.4)	0.91 (0.25-3.35)	*	>.99
Preoperative management					
No preoperative antibiotics	4 (16.0)	27 (15.8)	1.02 (0.32-3.19)	*	>.99
No gram-positive coverage	14 (53.9)	91 (52.9)	1.04 (0.45-2.37)	0.01	.93
No gram-negative coverage	5 (19.2)	44 (25.6)	0.96 (0.25-1.95)	0.49	.48
No anaerobe coverage	9 (34.6)	53 (30.8)	1.19 (0.50-2.84)	0.15	.70
Type of operation					
Open	15 (60)	97 (56.1)	1 [Reference]	0.14	.71
Laparoscopic	10 (40)	76 (43.9)	0.85 (0.36-2.00)		
Drain placed	5 (19.2)	24 (14.3)	1.43 (0.49-4.15)	0.43	.51
Operative findings					
Abscess	10 (38.5)	42 (24.3)	1.95 (0.82-4.62)	2.36	.12
Fecalith	3 (11.5)	5 (2.9)	4.38 (0.98-19.57)	*	.07
Outcomes					
Length of postoperative antibiotics, d, mean ± SD	7.1 ± 2.9	5.8 ± 2.8	NA	NA	.03
Length of postoperative fever, d, mean ± SD	2.04 ± 1.25	1.22 ± 1.14	NA	NA	.001
Fever POD 1	14 (53.9)	87 (50.6)	1.14 (0.50-2.61)	0.10	.76
Fever POD 2	15 (57.5)	55 (32.0)	2.90 (1.25-6.73)	6.54	.01
Fever POD 3	12 (46.2)	37 (21.5)	3.13 (1.33-7.33)	7.36	.007
Fever POD 4	3 (11.5)	18 (10.5)	1.12 (0.30-4.09)	*	.74
Length of hospital stay, d, mean ± SD	14.77 ± 7.45	5.94 ± 3.55	NA	NA	<.001

Abbreviations: CI, confidence interval; CT, computed tomographic; NA, not applicable; OR, odds ratio; POD, postoperative day; RLQ, right lower quadrant; WBC, white blood cell.

*By Fisher exact test, not χ^2.

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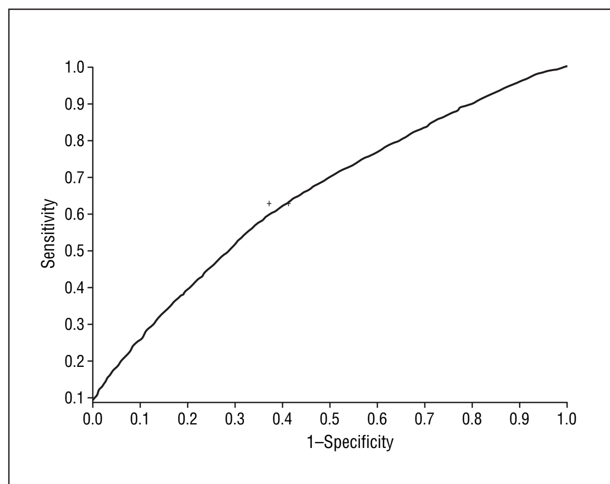

Figure 2. Receiver operating characteristic curve for model applied to test data set. Crosses indicate points (the sensitivity at given specificities) estimated by SAS version 8.01 for Windows (SAS Institute, Cary, NC) to calculate the best-fit curve.

SECONDARY ANALYSIS

Thirty-seven children were discharged on or before postoperative day 3. Another 21 children were afebrile and tolerating a diet at that time but remained in the hospital. Of the group discharged early, 76% had undergone laparoscopic appendectomy vs 38% of the others ($P = .008$). There were no other significant differences between the 2 groups. None of the early-discharge group developed an abscess, and 2 of those remaining in the hospital developed an abscess ($P = .06$).

COMMENT

The model created from three quarters of the study population found that diarrhea at the time of presentation to the hospital substantially increased the odds of developing an intra-abdominal infectious complication postoperatively. Diarrhea may occur from irritation of the bowel due to diffuse peritoneal inflammation or infection. Diarrhea, however, is a relatively subjective complaint, with health care professionals using different definitions as to what classifies as true diarrhea. Furthermore, it may not have been reported in medical records by all health care professionals, and for this retrospective study, we are limited to data that was reported. Additionally, the finding of a fecalith at the time of operation substantially increased the odds of developing a postoperative abscess. The confidence interval for this variable was extremely wide, which can be explained by the fact that there were only 9 cases where a fecalith actually was documented. The low incidence of this finding impedes its usefulness as a good prognostic factor.

When applied to the remaining one quarter of the data, the model did not fit well. One problem with the one quarter of the data was that there were only 9 cases of abscess postoperatively, which are very few cases for testing the model. The lack of sensitivity and specificity of the model demonstrates that finding a predictive model using the clinical variables we collected is very difficult, if not impossible.

Perhaps more remarkable than the factors that were important in the multivariable model were the factors that were not significant predictors of abscess development. In fact, many previously established critical aspects of care did not seem to affect the development of an abscess.

A history of pain longer than 3 days also was not associated with an increased risk of postoperative abscess development once incorporated into a multivariable model. This finding is contrary to the previous study by Kokoska et al,[11] who found increased abscess development in patients presenting with pain lasting more than 72 hours.

The use of laparoscopic appendectomy for cases of perforated appendicitis has been hotly debated, with some investigators citing higher rates of complications while others have found no increase in complications.[12-18] Our results did not support an association between method of operation and the development of a postoperative abscess.

Antibiotic coverage also was not associated with postoperative development of an intra-abdominal infectious complication. Surprisingly, we found that 15% of patients did not receive antibiotics within 2 hours of the time of operation, 22% did not receive adequate gram-negative coverage, and 30% did not receive anaerobic coverage. However, none of these variables was correlated with abscess development. Furthermore, length of postoperative administration of antibiotics was also not correlated with abscess development.

Many institutions have practice patterns of a uniform time of hospitalization and intravenous antibiotic administration following operation for perforated appendicitis. In our secondary analysis, we examined all of those patients who were afebrile and tolerating a diet on postoperative day 3. There was no difference between those patients who were discharged home (and, thus, stopped receiving intravenous antibiotics) and those who remained in the hospital receiving antibiotics. This suggests that there may be little benefit to prolonged hospitalization and antibiotic administration if patients otherwise appear clinically well. These results need to be verified prospectively.

This study used historical data from multiple centers in an attempt to determine if certain risk factors could be identified that might predispose a pediatric patient to develop an intra-abdominal infection postoperatively. In our model, only 2 factors were significant. One of these factors had a very low incidence, the finding of a fecalith at the time of the operation, and is not a clinically useful marker. Diarrhea on hospital admission may reflect a state of intraperitoneal contamination that could lead to higher rates of abscess development. However, as mentioned earlier, diarrhea is a highly subjective variable.

This study examined a relatively large data set and found that those factors typically thought to be associated with abscess development were not. The absence of reliable predictive factors suggests that it is extremely difficult to predict which children with perforated appendicitis will develop this complication. Future studies will need to examine the predictive value of measures that are more sophisticated than the common clinical and laboratory variables examined in this study. Perhaps proteomic profiles will reveal early signs of abscess development or genetic profiles will identify patients at high

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risk. This study suggests that common clinical impressions may not prove correct when subjected to rigorous analysis. Clinical care guidelines, therefore, should be designed and tested prospectively.

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Invited Critique

At first glance, the conclusions of this report would imply that there are few "definites" when it comes to the management of perforated appendicitis in children. Henry et al have bravely chosen to wade into waters that have long been muddied by clinical perceptions. Most surgeons view their own treatment algorithm of appendicitis as a core competency, one resistant to challenge or change. Noble, perhaps, but potentially outdated. In this looming "pay for performance" era, payers can and will look past history and dogma to determine how health care resources are allocated for treating common ailments such as appendicitis. This report brings to light misconceptions regarding the treatment of this disease. Many may be surprised to find that their own beliefs were not confirmed, most notably that neither type nor timing of antibiotics, choice of surgery (open vs laparoscopic), nor duration of antibiotic therapy were associated with a change in abscess incidence. Heresy, indeed. But, instead of using a "Joan of Arc" response and burning the conclusions, the 21st century surgeon has in his or her armamentarium an even greater matchstick: the electronic medical record. With its inherent database capabilities, the electronic medical record can be used to make true "apples-to-apples" comparisons of like risk groups and analyze the impact of treatment changes on outcome. The result of such an analysis gives today's surgeons the weapons to compete in the pay for performance arena. Studies, like this one, that identify and define the appropriate "benchmarks" for care will play an increasingly prominent role in the future of surgery. The battle for improved clinical care is one that can and should be fought from every stage, from the tertiary academic medical center to the local specialty surgery practice. Better clinical outcomes should be the goal for all.

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