Original Contribution

Effect of delay in presentation on rate of perforation in children with appendicitis

Chaitan K. Narsule MD[a], Eden J. Kahle MD[a], Daniel S. Kim MD[a], Angela C. Anderson MD[b], Francois I. Luks MD, PhD[a],*

[a]Division of Pediatric Surgery, Hasbro Children's Hospital and Warren Alpert Medical School of Brown University, Providence, RI 02905, USA
[b]Division of Pediatric Emergency Medicine, Hasbro Children's Hospital and Warren Alpert Medical School of Brown University, Providence, RI 02905, USA

Abstract

Introduction: Appendicitis is the most common emergency operation in children. The rate of perforation may be related to duration from symptom onset to treatment. A recent adult study suggests that the perforation risk is minimal in the first 36 hours and remains at 5% thereafter. We studied a pediatric population to assess symptom duration as a risk factor for perforation.

Methods: We prospectively studied all children older than 3 years who underwent an appendectomy over a 22-month period.

Results: Of 202 patients undergoing appendectomies, 197 had appendicitis. Median age was significantly lower in the perforated group, but temperature and leukocytosis were not. As expected, length of hospital stay was longer in the perforated group (4-13 vs 2-6 days). The incidence of perforation was 10% if symptoms were present for less than 18 hours. This incidence rose in a linear fashion to 44% by 36 hours. Prehospital delays were greater in patients with perforated appendicitis. However, in-hospital delay (from presentation to surgery) was less than 5 hours in the perforated group and 9 hours in the nonperforated group.

Discussion: Appendiceal perforation in children is more common than in adults and correlates directly with duration of symptoms before surgery. Perforation is more common in younger children. Unlike in adults, the risk of perforation within 24 hours of onset is substantial (7.7%), and it increases in a linear fashion with duration of symptoms. In our experience, however, perforation correlates more with prehospital delay than with in-hospital delay.

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1. Introduction

Appendicitis is the most common emergency that requires surgical intervention in children. In the United States, more than 341 000 open or laparoscopic appendectomies are performed each year [1]. Children tend to have higher rates of appendiceal perforation than do adults [2-4]. Several factors may contribute to this observation. First, children may present with a variety of atypical symptoms, in contrast with the classic periumbilical pain that later migrates to the right lower quadrant. In addition, very young children may have little omentum and intraabdominal fat, allowing peritoneal

spread to occur more readily [5,6]. Finally, children tend to present later than adults, thereby causing a delay in diagnosis that contributes to a higher perforation rate [6].

In 2006, Bickell et al [7] studied the effect of the duration of symptoms on the risk of rupture in 219 adult patients. The study suggested that the risk of rupture rises to 5% after the first 36 hours and remains unchanged thereafter. Although the rate of appendiceal perforation tends to be higher in children, no pediatric-specific study has looked at the risk of rupture over time. We undertook this study to determine the relationship between the rate of perforation and the duration of symptoms in children with appendicitis.

2. Methods

We prospectively studied all children between the ages of 3 and 18 years who underwent open or laparoscopic appendectomy for suspected appendicitis from October 2006 through August 2008. All patients presented to a tertiary care children's hospital and level I trauma center. Data collected included age, sex, symptoms (abdominal pain, nausea, vomiting, diarrhea, or anorexia), heart rate, temperature, white blood cell count, and, if applicable, findings on imaging studies (ultrasound or computed tomography). Time data points included the specific date and time of onset of symptoms, time of contact with a health care provider, time of arrival in the emergency department (ED), time of imaging (if performed), time of decision to proceed with appendectomy, and start time of the operation.

We excluded patients in whom the appendectomy was negative. Children younger than 3 years typically are not able to express and localize pain reliably; consequently, these patients were excluded as well. Preschoolers (3-7 years) were included but were analyzed separately to identify potential differences in presentation and perforation rates.

This study was approved by the institutional review board of Hasbro Children's/Rhode Island Hospital. It was conducted and is being reported in accordance with the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology statement [8].

Statistical analysis of perforated vs nonperforated appendicitis was performed using Student t test and χ^2 analysis, with $P < .05$ considered significant.

3. Results

A total of 202 consecutive patients aged 3 to 18 years who underwent an appendectomy from October 2006 through August 2008 were studied. Six patients were found at surgery or on pathology to have a normal appendix. These patients were excluded, leaving 197 patients for analysis. Table 1 summarizes patient demographic characteristics, symptoms, and clinical findings. There was no statistical difference in male-female ratio; however, children with perforated appendicitis were significantly younger (median age, 8 years) than those with non-perforated appendicitis (median age, 13 years). Interestingly, there was no statistical difference in either median white blood cell count or median temperature between the perforated and nonperforated groups. Whereas children younger than 3 years were excluded because of their very high rate of perforation, we analyzed the cohort of 3- to-7-year-olds to detect possible differences with older children. Twenty-one children were younger than 7 years. Of these, 6 had perforated appendicitis (29%), not statistically different from the perforation rate in older children (χ^2 analysis).

Fig. 1 shows the relation between duration of symptoms (from onset to surgery) and the incidence of perforation. As expected, a longer delay between onset of symptoms and surgical intervention was associated with increased of rates of perforation. No child with symptoms for less than 12 hours had perforated appendicitis. The perforation rate rose in a linear fashion from 10% by 18 hours to 44% by 36 hours. If symptoms were present for more than 2 days, the risk of perforation was greater than 40%.

Fig. 2 further qualifies the delays between onset of symptoms and time of surgery. In the group of patients with perforated appendicitis, the average time from onset of symptoms to presentation to the hospital was 24 hours. As a group, these patients went from admission to diagnosis within 2.1 hours and from admission to operation in less than

Table 1 Patient characteristics: comparison between perforated and nonperforated groups

	Total (n = 197)	Perforated (n = 62)	Nonperforated (n = 135)	P value
Age, median (range), y	11 (3-17)	8 (3-17)	13 (3-17)	<0.001 [a]
Female-male ratio	1:1.38	1:1.92	1:1.16	NS [b]
Temperature, median (range), °F	100 (97.2-104.6)	101 (98.2-104.6)	99.9 (97.2-104.0)	NS [a]
WBC, median, /μL	15 800	15 800	15 760	NS [a]
Nausea/vomiting, %	54.2	84.2	37.7	<.001 [b]
Anorexia, %	15.9	31.6	7.2	<.001 [b]
Diarrhea, %	10.3	18.4	5.8	<.05 [b]

NS indicates not significant; WBC, white blood cells.
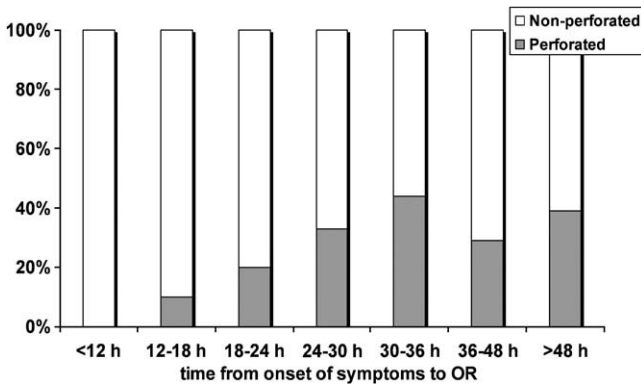 [a] Student t test.
  [b] χ^2 test.

Fig. 1 Relationship between duration of symptoms (onset of symptoms to operation) and risk of perforation. OR indicates Operating room.

5 hours. In the nonperforated group, patients presented earlier (15.5 hours). In-house delays were longer (9 hours), as many patients required time to repeat examinations or confirm the diagnosis by ultrasonography or computed tomography. Once a diagnosis was established, time to surgery was relatively short (3.5 hours), but not as short as in the perforated group. Overall, 2 patients waited more than 24 hours for appendectomy. One child had nonperforated appendicitis, and the other had perforated appendicitis. The analysis of children 7 years or older showed similar median delay between onset of symptoms and presentation to the hospital (20.0 vs 17.0 hours for the entire group) and the same delays between onset and presentation for perforated (24.0 hours in both groups) and nonperforated (16.0 vs 15.5 hours) appendicitis.

4. Discussion

Appendectomy is the most common emergency operation performed in children in the United States. Some
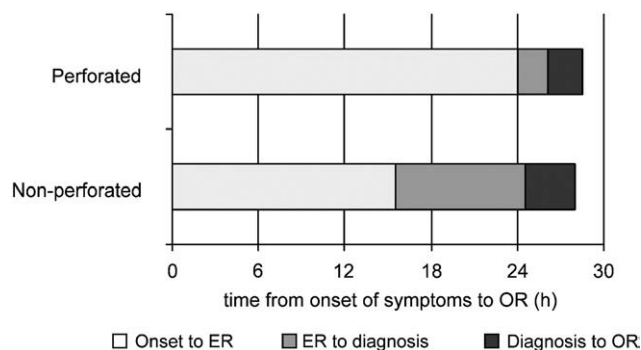

Fig. 2 Time line from onset of symptoms to operation, perforated vs nonperforated appendicitis. Note longer delay before presentation to the emergency department in perforated appendicitis. In this group, time from presentation to operation was short, making it less likely that perforation occurred in-hospital. ER indicates Emergency Room, OR indicates Operating Room.

have suggested that the perforation rate and morbidity in children with appendicitis are similar to those in adults [4], whereas others have reported far higher perforation rates in the pediatric age group [9,10]. Two main factors can influence the rate of perforation in appendicitis. Very young age is typically associated with a higher rate of rupture [11], reaching 75% in children younger than 5 years [5]. In a series of 27 children younger than 3 years, Alloo et al [12] found perforation in all patients at the time of surgical intervention. In older children, duration of symptoms is the most important determinant of perforation [3,11,13,14]. Duration of symptoms may also be a factor in the high perforation rate seen in very young children, as signs and symptoms may be less specific [5,6]. However, other factors, such as the lack of a well-developed omentum, may also contribute to the rapid progression of the disease in toddlers. Although it is generally understood that appendicitis in very young children behaves differently, the exact age cutoff is less clear. In our study, we excluded children younger than 3 years, and we analyzed the cohort of patients aged 3 to 7 years separately. We did not find significant differences in perforation rates or delays in presentation between preschoolers and older children.

The risk of perforation has recently been studied in adults [7]. The results of that study suggested that the risk of rupture is virtually nil within the first 36 hours after onset of symptoms and remains at 5% thereafter. In our prospective study, 62 (32%) of 197 patients over a 20-month period had perforated appendicitis. Unlike the retrospective study in adults, the present study shows a more linear relationship between duration of symptoms and the risk of perforation, which rises from 10% at 18 hours to more than 40% at 48 hours. Overall, the rate of perforation doubles every 6 hours for the first 1 to 2 days after the onset of symptoms.

At first glance, this would emphasize the importance of rapid intervention and the possibility that a substantial number of perforations occur in the hospital, while the patient awaits further testing and surgery. If confirmed, this would contradict findings by others [15,16] who suggested that few, if any, patients with ruptured appendicitis were not yet perforated on admission to the hospital. However, further analysis shows a very different course between perforated and nonperforated appendicitis patients. In nonperforated appendicitis, the median duration of symptoms (from onset to presentation to the ED) was less than 24 hours. In this setting of early appendicitis, symptoms and signs are often either mild or equivocal, and further workup may be necessary. The need for repeat examinations or confirmatory imaging studies results in a relatively long in-hospital delay (10-12 hours). Because these patients were found to have simple appendicitis at operation, it appears that the delay did not increase the risk of in-hospital rupture and, in fact, may have allowed a better accuracy of diagnosis and, therefore, a better

specificity (in an earlier study [17], we reported a 4% false-positive rate of appendicitis, well below most historic and even some contemporary reports).

The course of perforated appendicitis was very different. Diagnosis of appendicitis was established within 2 hours of arrival to the hospital, and the time from decision to operation was only 2.5 hours. Taking into consideration the need for intravenous hydration and resuscitation, as well as the practical constraints of a busy hospital, it is unlikely that this time interval could be reduced substantially. Moreover, 24 to 30 hours after the onset of symptoms, the progression curve of perforation has flattened (Fig. 1), reducing the effect of a 4- to 5-hour delay on the risk of perforation. This confirms the common belief that few, if any, perforations occur during the patient's hospital stay [16]. Of course, outliers and atypical presentations are unavoidable. In our series, 2 patients had a delay of more than 12 hours, and 1 waited more than 24 hours after admission. Only 1 of these patients with prolonged delay (the 1 who waited more than 12 hours) was perforated at the time of the operation —1 of 197 who could have perforated in-hospital while awaiting treatment. However, review of the history reveals that this patient's symptoms lasted for a week before presentation to the hospital, suggesting that perforation occurred well before admission.

When comparing the time courses of acute and perforated appendicitis (Fig. 2), it is remarkable that the average time from onset of symptoms to operation is virtually identical in both groups. It is possible that there exist 2 distinct populations of patients with appendicitis and that some progress more rapidly to perforation. Still, Fig. 2 implies that perforation correlates more with prehospital delay than with in-hospital stay, further reducing the impact of delay from ED to operating department as a risk for perforation. It is unclear whether supportive care, including intravenous hydration, helps slow down the progression from acute appendicitis to perforation or whether other factors are at play (we do not administer antibiotics preoperatively in acute appendicitis). This finding does reinforce prehospital delay as a significant risk for perforation. Prehospital delay depends on many factors, some of which are difficult to control. Local and regional differences in referral patterns, cultural considerations, and others are highly variable and probably account for some of the differences in perforation rates reported in the literature [10,11,18-22]. We did not specifically examine the prehospital referral patterns within our community in the present study. We do not know, therefore, how many patients were seen by their primary care physician and/or "walk-in" clinics before arriving at Hasbro Children's Hospital and which patients waited before seeking any medical help. The results of the present study could be used to educate the public and first-line health care providers about the risks of delay in appendicitis in children.

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