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Long-term outcomes of operative versus nonoperative treatment for uncomplicated appendicitis

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ABSTRACT

Purpose: Although nonoperative treatment for uncomplicated appendicitis is now an accepted approach, there are few reports in children. The aim of this study was to compare long-term outcomes between operative and nonoperative treatment in children.
Methods: Between April 2007 and December 2013, all uncomplicated appendicitis patients were asked to select either operative (laparoscopic surgery) or nonoperative treatment on admission. For nonoperative treatment, intravenous injection of antibiotics was continued until serum C-reactive protein concentration decreased to below 0.5 mg/dL. A questionnaire survey on satisfaction with treatment was added afterwards and performed more than 1 year after treatment.
Results: Eighty-six patients chose operative treatment, and 78 chose nonoperative treatment. The success rate of nonoperative treatment was 98.7%. There was no difference in the length of hospital stay between the two groups. Ileus occurred in two operatively-treated patients, while recurrence of appendicitis occurred in 22 nonoperatively-treated patients (28.6 %) after an average of 4.3 years of follow-up. The overall nonoperative treatment failure including both early failure and recurrence occurred more frequently among those with appendicoliths than without appendicoliths. Satisfaction levels were higher for operative treatment.
Conclusions: Although the success rate of nonoperative treatment was very high, a considerable number of patients experienced recurrence.

Nonoperative treatment for uncomplicated appendicitis is now an accepted approach, and there are meta-analyses of randomized, controlled trials in adults [1–6]. However, there are few reports concerning nonoperative treatment for uncomplicated appendicitis in children [7–9]. Moreover, there are no reports comparing outcomes between operative and nonoperative treatment for uncomplicated appendicitis more than a year after the treatment.

In April 2007, we started our prospective nonrandomized study of operative and nonoperative treatment for appendicitis. The operative and nonoperative treatment options were evenly explained to all patients on admission, and they were asked to select one. The aim of this study was to compare outcomes between operative and nonoperative treatments for uncomplicated appendicitis.

1. Materials and methods

This study was approved by the ethics committee of our hospital. Between April 2007 and December 2013, the operative and nonoperative treatment options were evenly explained using our informed consent form to all uncomplicated appendicitis patients on admission, and they were asked to select one. Although we also started a randomized trial for appendicitis treatment, few chose to participate and the number of patients was not enough to allow valid statistical analysis.

1.1. Diagnosis of uncomplicated appendicitis

Diagnosis of appendicitis was made by an abdominal ultrasound, a blood test, and physical examination. The criterion for appendicitis by abdominal ultrasound was a maximum diameter of ≥6 mm for the appendix [10,11]. When diagnosis could not be made by abdominal ultrasound, computed tomography was also performed. All ultrasound examinations and image readings were performed by pediatric radiologists, and the appendix was detected in all cases. Those with pan-peritonitis, an abscess or phlegmon, and other complications were excluded.

1.2. Operative treatment

Those who selected operative treatment underwent laparoscopic appendectomy on the day of or the day after admission. Twelve

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surgeons with more than two years of experiences in surgery preformed the operations with one of three instructors with more than 15 years of experience. The appendix was dissected and excised via transumbilical single-incision or three ports at the umbilicus, right upper flank, and left lower abdomen using a 10–12 mm Hg artificial pneumoperitoneum [12]. The operative time was similar in transumbilical single-incision surgery and three ports surgery [12]. Prophylactic antibiotics were administered intravenously until 48 hours after surgery. The patients were discharged when oral intake was satisfactory, with no fever and no unbearable abdominal pain.

1.3. Nonoperative treatment

Intravenous injection of antibiotics was administered according to our protocol without restricting oral intake. First, cefmetazole (100 mg/kg/d; maximum, 4 g/d) was administered. When white blood cell count did not decrease by 25% in 2 days, the antibiotic was changed to sulbactam/ampicillin (200 mg/kg/d; maximum, 6 g/d) and ceftazidime (150 mg/kg/d; maximum, 4 g/d). When this second prescription did not work or could not be used, meropenem or imipenem/cilastatin (60 mg/kg/d; maximum, 2 g/d) and gentamicin (5 mg/kg/d; maximum, 120 mg/d) were used. The patients were hospitalized with continuous intravenous injection of antibiotics until serum C-reactive protein (CRP) concentrations decreased to below 0.5 mg/dL, and they were discharged with no fever and no abdominal pain. All patients underwent checks to ensure that their appendices were no longer swollen 1–3 months after treatment to avoid overlooking carcinoid tumors.

When appendicitis recurred after nonoperative treatment, operative treatment was performed at our hospital, although some patients went to other hospitals and underwent further nonoperative treatment at the time of recurrence.

1.4. Survey of patient satisfaction

We also performed a questionnaire with the parents of patients. This survey was added on the initial study design and approved by the ethics committee of our hospital with another informed consent. Letters querying satisfaction with their treatment were sent to all patients treated during the study period more than a year after treatment. The questionnaire was filled by the parents of the patients. Satisfaction levels were estimated on a scale of 1–5, with grade 1 being very disappointed and grade 5 being very satisfied.

1.5. Statistical analysis

Student's *t*-test, Fisher's exact test in 2×2 contingency table with minimum value ≤5, chi-square test in 2×2 contingency table with minimum value >5, and the Mann–Whitney U test were used to compare data. *P*-values < 0.05 were considered statistically significant.

2. Results

2.1. Operative treatment vs nonoperative treatment

There were 164 patients who met the criteria among 317 appendicitis (including complicated appendicitis) patients who were hospitalized during the study period. Among them, 86 patients selected operative treatment and 78 patients selected nonoperative treatment. The demographic data, white blood cell counts at admission, maximum CRP concentrations during treatment, diameter of the appendix at the time of diagnosis, and length of hospital stay of both patients groups are shown in Table 1. There was no significant difference between the two groups with respect to age, gender distribution, height, body weight, and duration of symptoms at arrival. All resected appendices were pathologically diagnosed as appendicitis [11]. No patients needed abscess or ascites removed by needle aspiration. Nonoperative treatment failed in one patient, leading to perforation of the appendix. Surgery was performed on the third day of hospitalization for this patient. Therefore, the success rate of nonoperative treatment was 98.7%. The failure rate of nonoperative treatment was 5.3% (1/19) for those with appendicoliths vs. 0% (0/59) for those without appendicoliths, and there was no statistical difference owing to the presence of appendicoliths ($P = 0.24$). Among the patients with successful nonoperative treatment, 85.7% (66/77) were treated only with first line antibiotics (cefmetazole). None of the patients in this study had carcinoid tumor causing appendicitis. For the patients who selected nonoperative treatment, it was checked with abdominal ultrasound by pediatric radiologists one to three months after complete cure of appendicitis.

Table 1
Patient characteristics.

	Operative treatment ($n = 86$)	Nonoperative treatment ($n = 78$)	*P*-value
Age (years)	10.4 ± 2.3 (range, 5.67–15.9)	10.1 ± 2.0 (range, 6.17–15.4)	0.44
Male/Female	61/25	52/26	0.61
Height (cm)	137 ± 17	137 ± 13	0.95
Weight (kg)	34.0 ± 10.4	31.7 ± 10.0	0.15
Duration of symptoms (hours)	21.0 ± 12.3	22.0 ± 15.5	0.63
WBC ($\times 10^9$/L)	15.3 ± 3.8	14.7 ± 3.7	0.27
Maximum CRP (mg/dL)	6.1 ± 5.7	4.7 ± 4.8	0.086
Maximum diameter of appendix (mm)	9.5 ± 2.3	8.9 ± 2.2	0.063
Hospital stay (d)	6.5 ± 2.4	6.6 ± 2.6	0.81
Complications	2/86 (ileus)	1/78 (conversion to surgery)	
Recurrence of appendicitis	0/86 (0%)	22/77 (28.6%)	
Follow-up period (year)	3.4 ± 2.0 (median, 3.3)	4.3 ± 2.1 (median, 4.5)	

WBC, white blood cells; CRP, C-reactive protein.

There was no difference in the length of hospital stay between the operative and nonoperative treatment groups (6.5 ± 2.4 d vs. 6.6 ± 2.6 d, $P = 0.81$). With respect to complications after treatment, ileus occurred during the hospital stay for appendectomy in two operatively treated patients, which were both cured conservatively, while recurrence of appendicitis occurred in 22 patients (28.6 %) among 77 nonoperatively-treated patients during an average of 4.3 years of follow-up. The median time to recurrence after nonoperative treatment was 6 months (range, 17 days–39 months) and the recurrence rate within 1 year was 20.8% (16 patients among 77 nonoperatively-treated patients) (Fig. 1).

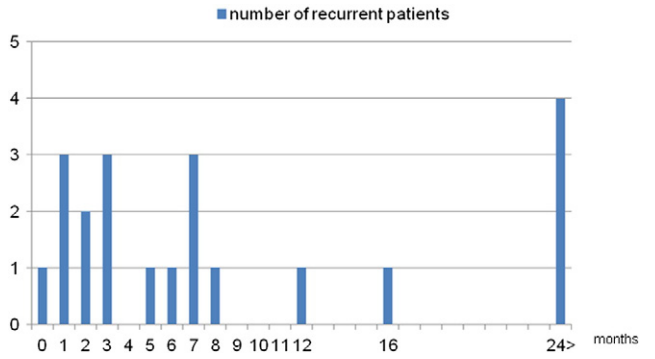

Fig. 1. The timing of recurrence after successful nonoperative treatment is shown. One patient was treated at another hospital at the time of recurrence more than 1 year after the initial treatment, but could not be tracked for the precise date of recurrence.