Annals of Pediatric Surgery

ORIGINAL RESEARCH Open Access

Aiming for minimally invasive treatment of pediatric acute appendicitis in a district hospital

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Abstract

Background: Appendicitis is the most common cause of acute abdomen. Although emergency surgery used to be the standard treatment for both simple and complex appendicitis, there are now options for interval surgery, laparoscopic surgery, and even non-surgical treatment. In this study, we aimed to establish better treatment strategies for pediatric acute appendicitis and to find out whether minimally invasive treatment is superior to the traditional open approach. We retrospectively reviewed the cases of acute appendicitis treated in our hospital during the period from 2013 to 2018. The patients who underwent appendectomy were divided into four groups. Group 1 underwent early appendectomy with open approach, group2 underwent interval appendectomy with open approach, group 3 underwent early appendectomy with laparoscopic approach, and group 4 underwent interval appendectomy with laparoscopic approach. In addition to the above groups, the non-surgical treatment group was also studied. Clinical presentation, laboratory findings, imaging results, operative time, morbidity, and length of hospital stay were reviewed.

Results: One hundred six children's records were reviewed. Thirty-five of them were selected for non-surgery as they were cases with no fecal stone and first onset appendicitis, and 15 of these 35 patients (42.9%) relapsed after antibiotic treatment. As for the appendix diameter, the relapse group was significantly larger than the non-relapse group (p=0.007). In cases of surgery, group 4 had significantly less intraoperative blood loss than group 1 (p<0.001). Group 4 had significantly fewer postoperative complications than groups 1 and 2 [group 4 vs. group 1 (p=0.009), group 4 vs. group 2 (p=0.034)]. The postoperative hospital stay in groups 2 and 4 were significantly shorter than group 1 [group 1 vs. group 2 (p=0.015), group 1 vs. group 4 (p<0.001)]. On the contrary, group 1 had significantly shorter total hospital stay than groups 2 and 4 [group 1 vs. group 2 (p=0.029), group 1 vs. group 4 (p<0.001)].

Conclusion: Interval laparoscopic appendectomy and non-surgical treatment were safe and effective in children. From the viewpoint of avoiding unnecessary emergency surgery and prolonged hospitalization, we believe that interval laparoscopic appendectomy or non-surgical treatment should be performed after identifying patients who do not require surgery, paying attention to the risk factors for relapse.

Keywords: Acute appendicitis, Children, District hospital, Interval laparoscopic appendectomy, Gasless transumbilical laparoscopic-assisted appendectomy

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Background

Acute appendicitis is one of the most common surgical emergencies seen in children [1]. The lifetime risk of developing appendicitis is 7.7% [1, 2]. Appendicitis is an inflammation of appendix. If untreated, the appendix may rupture, leading to complications such as abscess formation, paralytic ileus, and sepsis [3].

Appendectomy has been considered as an effective and safe treatment for acute appendicitis. Although urgent surgery has been considered as the standard treatment, the timing of an appendectomy varies from hospital to hospital and surgeon to surgeon [4–8]. Some perform an early appendectomy (EA), while others treat with initial antibiotics, followed by an interval appendectomy (IA) 4 to 8 weeks later. Although the latter approach is thought to reduce the complication rate and reduce the incidence of extensive resection (ileocecal resection or right hemicolectomy), a review of the literature comparing EA versus IA has shown mixed results [4, 5]. However, in recent year, the dogma that surgery is required has changed, and there are growing literatures suggesting that antibiotics without surgery may be an effective treatment for acute appendicitis in children [9–11].

Appendectomy can also be performed by open or laparoscopic techniques. Since its introduction into clinical practice in 1983, laparoscopic appendectomy (LA) has proven to be a feasible and safe procedure and has gained worldwide acceptance [12, 13]. The advantages of LA are considered to be less postoperative pain, early discharge, less wound infection, better cosmetic results, and faster return to normal school and daily life [14–20]. However, several retrospective studies, randomized studies, and meta-analyses comparing open appendectomy (OA) and LA have shown mixed results [21–25].

While there are various treatment options for pediatric acute appendicitis, it is very important to investigate safer and less burdensome treatment strategies. To establish a better treatment strategy for pediatric acute appendicitis, we compared and evaluated the outcomes of non-surgical treatment with antibiotics and surgical treatment with various methods as described above for pediatric acute appendicitis in a district hospital in terms of patient's data, operative time, morbidity, and length of hospital stay (LOS). Then, we aimed to find out whether minimally invasive treatment is superior to the traditional open approach in the treatment of children.

Methods

We included patients (age <15 years) who were diagnosed and treated for acute appendicitis in the Department of Surgery, at author's institute between January 2013 and December 2018. The study was performed in accordance to the ethical principles of the Declaration of Helsinki and has been approved by our hospital Ethics Committee (reference number: 2020 - 01). The study included 106 children with a diagnosis of acute appendicitis obtained by clinical assessment and confirmed by laboratory blood tests and ultrasonography (US) and/or computed tomography (CT). We analyzed each patient's data including age, gender, white blood cell (WBC) counts, C-reactive protein (CRP) level at admission, pediatric appendicitis score, and CT findings (appendix diameter, fecal stone, and abscess formation).

According to the surgical approach, the patients were divided into four groups. Group 1 underwent EA with open approach (EOA), group 2 underwent IA with open approach (IOA), group 3 underwent EA with laparoscopic approach (ELA), and group 4 underwent IA with laparoscopic approach (ILA). In our institution, we introduced IA for the treatment of acute appendicitis in 2015 and LA in 2016. We have now introduced ILA as the standard treatment for simple and complicated cases of acute appendicitis. These four groups were compared in terms of operative time, postoperative complications (surgical site infection, paralytic ileus, remnant abscess, and others), and postoperative and total LOS. Pediatric appendicitis score [26] was calculated in all patients. Although EOA was the standard treatment for acute appendicitis before 2014, with the introduction of IA and LA, the timing and methods of surgery have changed. Currently, conservative treatment with antibiotics is the first choice, except in cases of acute pan-peritonitis or in cases of severe inflammation with extensive abscess formation at the time of initial diagnosis. Patients who started conservative treatment were treated with single or double intravenous antibiotics (cefmetazole or tazobactum/piperacillin±metronidazole) until WBC counts and CRP level reached almost normal and the patient became afebrile. In all cases of intra-abdominal abscesses, repeated US was routinely performed for evaluation of the abscess. If intra-abdominal abscesses increased or abdominal symptoms worsened after initiation of treatment, we performed early appendectomy during hospitalization. Since there are many reports that fecal stones are a risk factor for perforation [27] and relapse [28–31], and that the risk of relapse increases with each relapse [32], IA was not performed in cases of no fecal stones and in cases of first-onset appendicitis. IA was performed after the antibiotic treatment described above in cases with fecal stones and/or cases of relapse. As there was no clear definition for the relapse of appendicitis, we defined relapse as the recurrence of inflammation within 1 year of the initial appendicitis.

Laparoscopic procedures were performed according to a standardized technique using three trocars, one 10 mm and two 5 mm, and 3-grade, 5-mm rigid scope. After achieving pneumoperitoneum, adhesion and mesoappendix were dissected and appendicular root was secured using two endoloops (Vicryl Endoloop-0, Ethicon Endo-Surgery, Cincinnati, Ohio, USA). Although Harmonic® scalpel (Ethicon Endo-Surgery, Cincinnati, Ohio, USA) was sometimes used in cases of severe adhesions, such cases were very rare. We adopted single incisional transumbilical laparoscopic-assisted appendectomy (TULAA) [33] in a mild appendicitis without abscess formation. We developed a modified TULAA technique, gasless-TULAA, which involves lifting the abdominal wall with a retractor, without pneumoperitoneum and another incision. A 1.5-cm vertical transumbilical incision was made within the umbilical dimpling, and wound protector was applied to the incision site. After intraperitoneal examination without pneumoperitoneum, the appendix was clamped with a 5-mm grasper and pulled through the transumbilical incision, and then appendectomy was performed.

Statistical analysis was performed by Mann-Whitney *U* test and Kruskal-Wallis test using the Microsoft Excel for Windows Version 1908 (Microsoft Corporation). A *p* value < 0.05 was considered statistically significant.

Results

One hundred six children (age <15 years) were included in the study. Fifty-four patients underwent EA while 52 received antibiotic treatment. Of these 52 patients, 17 underwent IA according to our treatment algorithm for acute appendicitis. The mean duration from discharge to IA was 70.5 days. The remaining 35 patients were treated with antibiotics followed by no surgery. There were not any no-show patients among them, and all of them could be followed up to see whether they had relapsed or not. Fifteen of these patients had relapse of appendicitis and underwent IA after another round of antibiotic treatment (Fig. 1).

Of note, for the 35 patients who did not undergo surgery after antibiotic treatment, there were significant differences in WBC counts (15.8 $\times 10^3$/μl vs. 11.1 $\times 10^3$/μl; p=0.006), appendix diameter (10.3 mm vs. 7.8 mm; p=0.007) and pediatric appendicitis score (6.3 vs. 4.4; p<0.001) between the two groups with and without relapse. There was also a significant difference in LOS between the two groups (7.4 days vs. 4.4 days; p=0.015). The mean appendix diameter of the 52 cases treated conservatively at our hospital was 9.6 ± 5.1 mm. Setting a cutoff value of 10 mm, the percentage of cases with an appendix diameter ≥10 mm was significantly higher in the relapse group than in the non-relapse group [9/15 (60%) vs. 1/20 (5%); p< 0.001] (Table 1). Furthermore, the relapse rate was significantly higher in cases with an appendix diameter ≥10 mm [9/10 (90%) vs. 6/25 (24%); p<0.001] (Fig. 2).

The patients who underwent appendectomy were divided into four groups. There were 49 patients in group 1, 6 patients in group 2, 5 patients in group 3, and 26 patients in group 4. There were no significant statistical differences in demographic data (age, gender), preoperative laboratory values (WBC counts, CRP level), pediatric appendicitis score, and CT findings (appendix diameter, fecal stone, and abscess formation) between the four groups (Table 2).

In the open approach, a single incision in the lower right section (alternate incision or pararectal incision) or

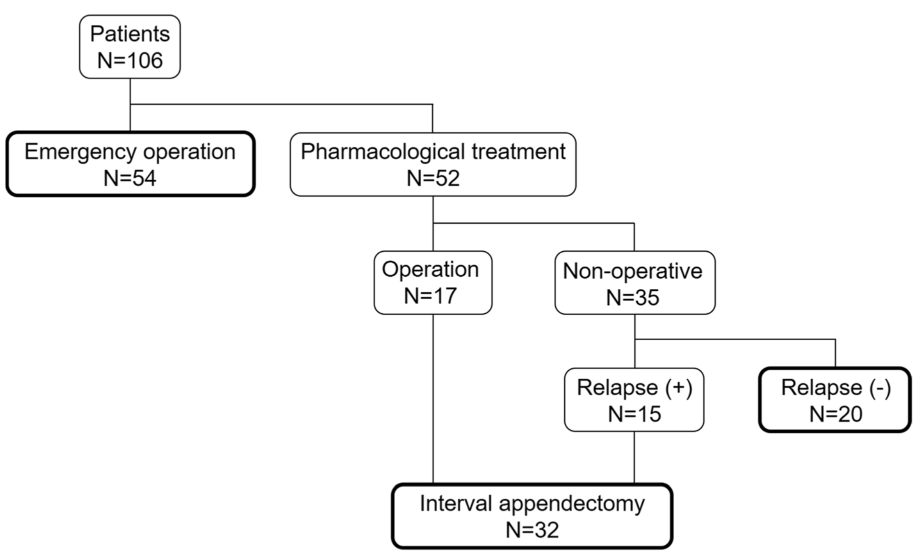

Fig. 1 Flowchart on treatment for pediatric acute appendicitis. Fifty-four (50.9%) patients received EA while 52 (49.1%) received antibiotic treatment. Of these 52 patients, 17 underwent IA in accordance with our treatment algorithm for acute appendicitis. The remaining 35 patients were treated with antibiotics followed by no surgery. Fifteen (42.9%) of these patients had a relapse of appendicitis and underwent IA after another round of antibiotic treatment

Table 1 Clinical presentation of patients without surgery after antibiotic treatment: relapse (+) vs. relapse (–)

	Relapse (+)	Relapse (–)	*p*
n (boy/girl)	15 (12/3)	20 (8/12)	0.018
Age (years) (range)	12.6±1.2 (9-15)	11.4±1.3 (6-15)	0.95
WBC (×10^3/μl) (range)	15.8±4.6 (7.5-25.0)	11.1±4.8 (4.1-26.4)	0.006
CRP (mg/dL) (range)	5.1±5.8 (0.1-20.8)	3.0±1.8 (0.9-6.5)	0.197
Appendix diameter (mm) (range)	10.3±3.2 (7-20)	7.8±2.0 (6-14)	0.007
Appendix diameter (≥10 mm)	9 (60%)	1 (5%)	<0.001
Pediatric appendicitis score (range)	6.3±1.1 (4-8)	4.4±1.8 (2-7)	<0.001
Length of hospital stay (day) (range)	7.4±3.0 (4-16)	4.4±3.5 (0-9)	0.015
Interval to relapse (day) (range)	99±51.1 (21-204)		

WBC White blood cell, *CRP* C-reactive protein

Of the 35 patients who did not have surgery after antibiotic treatment, there were significant differences in WBC counts [relapse (+): 15.8 ×10^3/μl vs. relapse (–): 11.1 ×10^3/μl (p=0.006)], appendix diameter [relapse (+): 10.3 mm vs. relapse (–): 7.8 mm (p=0.007)] and pediatric appendicitis score [relapse (+): 6.3 vs. relapse (–): 4.4 (p<0.001)] between the two groups of patients with and without relapse. There was also a significant difference in LOS between the two groups [relapse (+): 7.4 days vs. relapse (–): 4.4 days (p=0.015)]. Setting a cutoff value of 10 mm, the relapse group had a significantly higher percentage of cases with appendix diameters ≥10 mm than the non-relapse group [9/15 (60%) vs. 1/20 (5%); p<0.001]

lower midline (median incision) was made. Each surgeon decided the incision procedure. In the laparoscopic approach, we performed gasless-TULAA in many cases safely. No open conversion was observed in groups 3 and 4.

The mean operative time were 66.2 min in group 1, 51.8 min in group 2, 92.8 min in group 3, and 54.8 min in group 4, with no statistically significant difference (p= 0.061) as shown in Fig. 3a. There was a significant difference in intraoperative blood loss between groups 1 and 4 [group 1: 32.6 g vs. group 4: 3.85 g (p<0.001)] (Fig. 3b). The total postoperative complication rate was 13.9% (11/86) in this cohort. Group 4 had significantly fewer complications than groups1 and 2 [group 4: 0 vs. group 1: 11 (p=0.009), group 4: 0 vs. group 2: 1 (p=0.034)] (Fig. 3c).

Group 1 had significantly longer postoperative LOS than groups 2 and 4 [group 1: 7.7 days vs. group 2: 4.5 days (p=0.015), group 1: 7.7 days vs. group 4: 2.7 days (p<0.001)] (Fig. 4a). On the contrary, group 1 had significantly shorter total LOS than groups 2 and 4 [group 1: 10.2 days vs. group 2: 19.5 days (p=0.029), group 1: 10.2 days vs. group 4: 15.5 days (p<0.001)] (Fig. 4b).

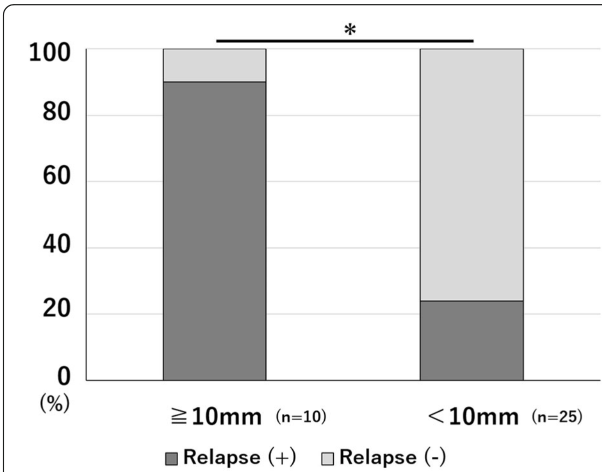

Fig. 2 Rate of relapse according to the appendix diameter. Nine of the 10 patients (90%) with appendix diameter ≥10 mm relapsed, and 6 of the 25 patients (24%) with appendix diameter <10 mm relapsed, with a statistically significant difference between the two groups (*p<0.001)

Discussion

In this retrospective comparative analysis, ILA in children was found to be a safe and effective surgical procedure, with a low frequency of postoperative complications and a short postoperative LOS. However, the total LOS was significantly longer in groups 2 and 4, i.e., those who underwent IA. Although there was no statistically significant difference, patients who underwent ELA had no postoperative complications and tend to have shorter postoperative and total LOS.

Several earlier studies have reported the superiority of LA over OA in terms of faster postoperative recovery [25, 34], lower complication rates [21, 35], and shorter LOS [36, 37]. In addition, meta-analyses of several retrospective studies showed that IA was associated with fewer complications [38]. However, a recent prospective study reported that patients treated with EA had fewer adverse events than those treated with IA [5]. Another prospective study showed that EA did not significantly increase the complication rate and contributed to a decrease in radiation exposure and fewer health care visits [5, 39]. These reports suggest that ELA may be a safer and less burdensome option for children. Several reports have recommended ELA as the standard treatment for acute appendicitis [5], and Badru et al. reported that

Table 2 Baseline characteristics of patients undergoing appendectomy

Group	1	2	3	4	Total
n (boy/girl)	49 (40/9)	6 (3/3)	5 (3/2)	26 (14/12)	86 (60/26)
Age (years) (range)	11.1±2.9 (5-15)	11.0±2.2 (8-15)	13.3±1.2 (12-15)	11.7±2.8 (5-15)	11.3±2.8
WBC (×10^3/μl) (range)	16.5±5.4 (6.8-31.9)	15.8±2.3 (13.5-19.3)	13.3±2.1 (9.7-14.9)	15.0±4.3 (5.6-23.5)	15.8±4.8
CRP (mg/dl) (range)	6.8±7.4 (0.01-30.8)	5.8±3.8 (1.8-10.8)	4.1±5.9 (0.1-13.9)	7.3±7.8 (0.1-25.3)	6.7±7.2
Appendix diameter (mm) (range)	11.9±4.4 (5-26)	9.2±3.2 (4-13)	11.2±3.3 (8-16)	11.1±6.5 (5-40)	11.5±5.0
Fecal stone (%)	36	4	2	15	57 (66.3)
Abscess formation (%)	9	2	2	3	16 (18.6)
Pediatric appendicitis score (range)	5.9±1.6 (3-8)	6.1±0.8 (5-7)	6.2±0.8 (5-7)	5.8±1.6 (3-8)	5.9±1.5

WBC White blood cell, *CRP* C-reactive protein
There were no significant statistical differences in demographic data (age, gender), preoperative laboratory values (WBC counts, CRP level), pediatric appendicitis score, and CT findings (appendix diameter, fecal stone, and abscess formation) between the four groups

complicated appendicitis with small abscesses and short duration of disease can be discharged early without complications with early surgery [40].

Although we did not perform appendectomy in cases without fecal stones or first-onset appendicitis, only 20 cases (57.1%) were spared from surgery. We defined a relapse of appendicitis as a recurrence of inflammation within 1 year of initial appendicitis, and the above 20 cases did not relapse after more than 1 year of follow up. The mean duration from the initial onset to relapse in the 15 patients who with relapse was 99 days (range, 21-204 days), indicating the validity of a 1-year follow-up period. Although there were no postoperative complications in patients who underwent ILA, relapse is one of the perioperative complications of ILA since it is caused by prior drug treatment. Therefore, a more

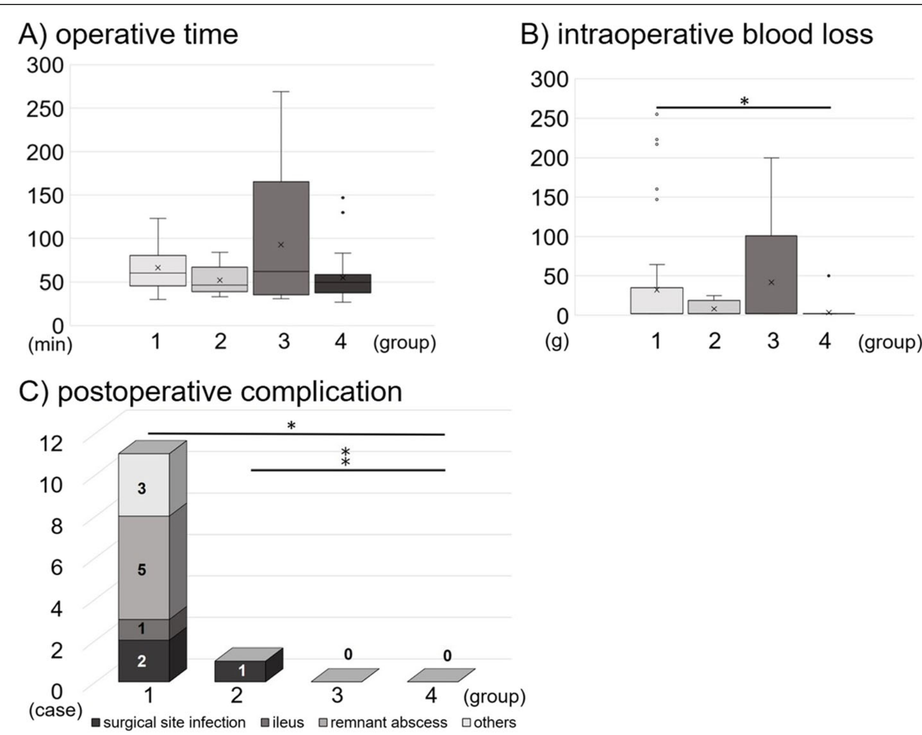

Fig. 3 Comparison of the postoperative characteristics. **a** Comparison of the mean operative time. The mean operative time were 66.2±25.9 min (range 30-123 min) for group 1, 51.8±18.3 min (range 33-84 min) for group 2, 92.8±99.4 min (range 31-269 min) for group 3 and 54.8±27.9 min (range 27-147 min) for group 4, with a no statistically significant difference (p=0.061). **b** Comparison of the amount of intraoperative blood loss. The average value of group 1 was 32.6±66.1 g (range 2-255 g), group 2 was 8.33±10.1 g (range 2-25 g), group 3 was 41.6±88.5 g (range 2-200 g) and group 4 was 3.85±9.41 g (range 2-50 g). A significant difference was observed between groups 1 and 4 (*p<0.001). **c** Comparison of the postoperative complications. Group 4 had a significantly lower number of complications than groups 1 and 2 [group 4: 0% vs. group 1: 22.4% (*p=0.009), group 4: 0% vs. group 2: 16.7% (p=0.034)]

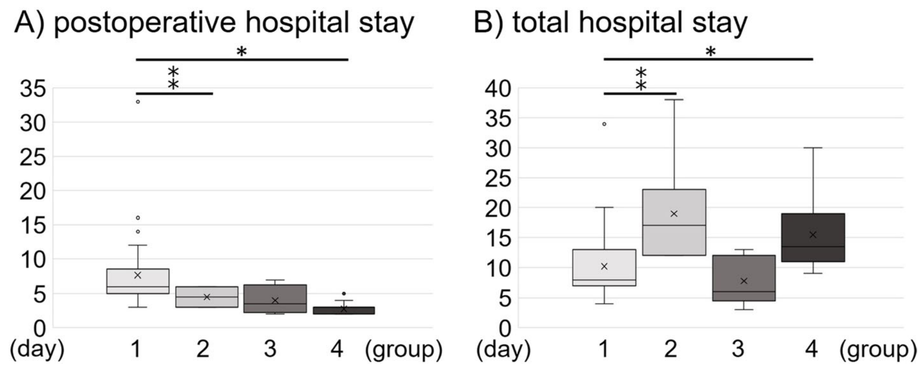

Fig. 4 Comparison of the length of hospital stay. **a** Comparison of the postoperative hospital stay. Mean postoperative hospital stay were 7.7±4.7 days (range 3-33) in group 1, 4.5±1.4 days (range 3-6) in group 2, 4.0±1.9 days (range 2-7) in group 3, and 2.7±0.8 days (range 2-5) in group 4, with statistically significant difference between groups 1 and 2 (p=0.015), and groups 1 and 4 (*p<0.001). **b** Comparison of the total hospital stay. Mean total hospital stay were 10.2±5.6 days (range 4-34 days) in group 1, 19.5±10.9 days (range 12-38 days) in group 2, 7.8±4.1 days (range 3-13 days) in group 3, and 15.5±5.5 days (range 9-30 days) in group 4, with statistically significant difference between groups 1 and 2 (p=0.029), and groups 1 and 4 (*p<0.001)

accurate assessment of the risk of relapse of appendicitis is important to make ILA and non-surgical treatment the standard treatment strategy for appendicitis.

There have been several reports on the association between appendix diameter and relapse [41–43], and in our study, the appendix diameter was significantly larger in the relapse group. Furthermore, the relapse rate was significantly higher in patients with an appendix diameter ≥10 mm, suggesting that appendix diameter may be a risk factor for relapse of appendicitis. Based on these results, we decided to add an appendix diameter ≥10 mm to the criteria for surgical indications (Fig. 5).

We had a major limitation of being a retrospective and non-randomized comparison, as it was clear that the surgical trend in the treatment of acute appendicitis at our hospital had shifted from early to interval surgery and from open to laparoscopic approach. In the IA group, cases of acute pan-peritonitis or severe inflammation were excluded,

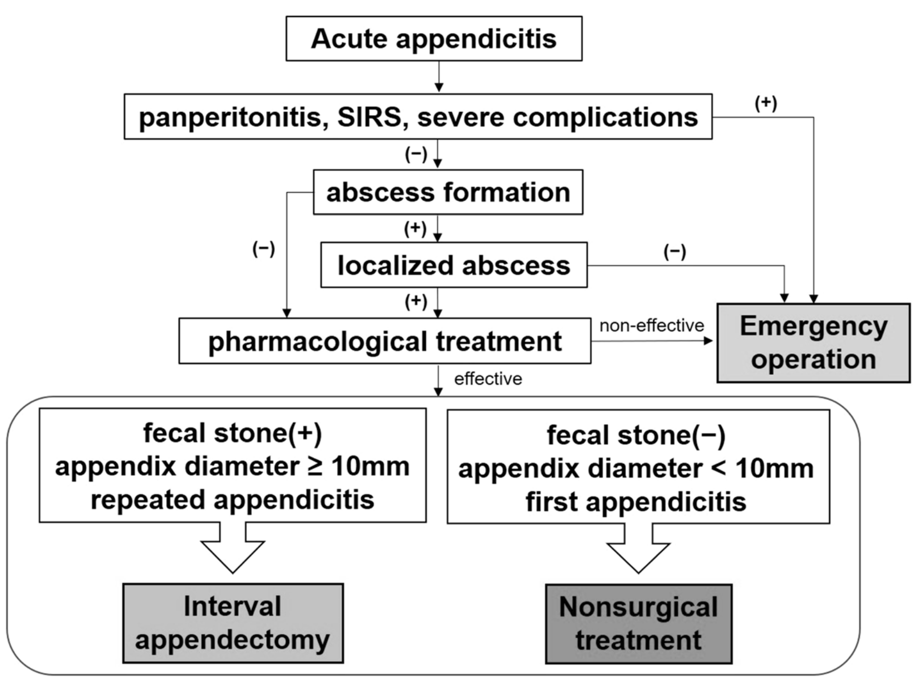

Fig. 5 Therapeutic algorithm for treatment of acute appendicitis. Conservative treatment with antibiotics is the first choice, except in cases of acute pan-peritonitis or severe inflammation with extensive abscess formation at the time of initial diagnosis. Early surgery may also be performed if it is determined that antibiotic treatment is not curative. IA is performed after antibiotic treatment in cases with fecal stones, appendix diameter ≥10 mm, and recurrent cases

while not in the EA group. Although this criterion could lead to significant bias in comparison with other groups, the effect was considered relatively small as the basic patient background was not statistically significant among the four groups, as shown in Table 2.

In addition, insufficient number of ELA cases was also considered to be one of the limitations of this study. If the number of ELA cases increases sufficiently, results showing the usefulness of ELA could be obtained. Prolonged LOS can be a heavy burden not only on the children but also on their families. In hospitals where urgent surgery is available, ELA can be the first choice of treatment, but it can be difficult in rural city hospitals. Although we had 6 surgeons who were always available for emergency surgery, we had only 2 full-time anesthesiologists, and we were not always ready for emergency surgery. In an under-staffed hospital described above, conservative treatment followed by surgery 4 to 8 weeks later is a practical strategy. Although we were unable to perform emergency surgery due to the various restrictions described above, in the future, we should consider the option of performing LA 2 to 3 days after admission.

Persistent presence of fecal stone has been reported to be associated with a significantly higher relapse rate (66.7%) [44]. Although this indicates that the risk of relapse may vary widely depending on patient factors, meta-analyses have reported recurrence rates of 5-29% [45] and 0-28.6% [46] for acute uncomplicated appendicitis treated non-surgically. Considering the fact that relapse is relatively rare in patients with appendicitis treated non-surgically at first occurrence, our strategy of treating acute appendicitis with antibiotics as a first choice and performing surgery in case of relapse seems to be appropriate.

Furthermore, non-surgical treatment has been reported to be successful in 97% of children [46], indicating the safety of antibiotic treatment for acute uncomplicated appendicitis. Most importantly, we should recognize that urgent surgery is an excessive invasion for children who may not require appendectomy.

Conclusions

We proved that ILA is safe with few postoperative complications. In addition, many children were spared from surgery, suggesting that non-surgical treatment is also a worthwhile option for the treatment of acute appendicitis. It is also very important to accurately assess the risk of relapse for further improvement of the efficacy of our current ILA and non-surgical treatment. For children, it is very important to avoid unnecessary surgery. Our treatment strategy is to treat acute uncomplicated appendicitis with antibiotics, then identify patients who do not require surgery with attention to risk factors for relapse, and then continue to perform ILA for those who are indicated for surgery.

Abbreviations

EA: Early appendectomy; IA: Interval appendectomy; LA: Laparoscopic appendectomy; OA: Open appendectomy; LOS: Length of hospital stay; CT: Computed tomography; WBC: White blood cell; CRP: C-reactive protein; EOA: Early open appendectomy; IOA: Interval open appendectomy; ELA: Early laparoscopic appendectomy; ILA: Interval laparoscopic appendectomy; TULAA: Transumbilical laparoscopic-assisted appendectomy

Acknowledgements

We would like to thank Dr. Takeshi Hirabayashi, PhD, from Hirosaki University and Dr. Yasushi Fuchimoto, PhD, from International University Health and Welfare Narita Hospital for their assistance in editing this manuscript. We are grateful to all patients who contributed to this study and their families, as well as clinicians who helped collect patient information.

Authors' contributions

TK and YT designed the study; TK conceptualized the manuscript and wrote the original draft; TK, AI, TY, YW, HJ, MN, KA, HK, and ME performed the data collection and analyzed the follow-up data; KA assisted in writing and editing the manuscript; HJ assisted in performing the statistical analysis; YT critically reviewed the manuscript and supervised the entire study process. All authors read and approved the final manuscript.

Funding

No funding was obtained for this study.

Availability of data and materials

The datasets supporting the conclusions of this article are available from the hospital database and the hospital record registry.

Declarations

Ethics approval and consent to participate

This study was performed in accordance to the ethical principles of the Declaration of Helsinki and has been approved by our hospital Ethics Committee (Reference number: 2020 - 01). Under the Personal Information Protection Law, which was revised and enforced in 2017, we do not need to obtain consent from research participants if the research is processed to prevent the identification of specific personal information.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Received: 3 December 2020 Accepted: 5 March 2021
Published online: 07 June 2021

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