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Outcomes Of Setting Standards In The Management Of Children With Appendicitis

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ABSTRACT

***Objective**: Recent studies have focused on approaches based on clinical parameters rather than predetermined therapy. The clinical outcomes based on setting of protocols are limited. In 2020, our institutional protocol was revised to standardize management of appendicitis. We aim to present the clinical outcomes of setting standardization in the management of appendicitis.*

***Methods**: A retrospective study was conducted in patients who were diagnosed with appendicitis and underwent appendectomy according to the settled preoperative, operative and postoperative standards, between April 2020 and October 2020. The results of the same number of patients treated before standardization (Pre-S) and those treated after standardization (Post-S) were compared.*

***Results**: 17 patients (mean age - 7 years) underwent surgery. Early recurrence occurred in one patient. There was no prolonged constipation, bladder dysfunction or mesh related complications.*

***Results:** The data of 388 patients were analyzed, 13/188 (7%) patients in the Pre-S group and 5/188 (3%) in the Post-S group were found to have negative laparotomy and were excluded from the groups. There was no difference between the groups in terms of demographic, clinical and operative characteristics (p>.05). It was found that the length of hospital stay decreased in Posy-S patients, but the difference was not significant (p>0.05). In cases with perforated appendicitis, a significant decrease was found in the Post-S group in terms of total number of complications and re-admission to the hospital (p<0.05).*

***Conclusion**: It was concluded that setting standards in the approach to appendicitis in children improve clinical outcomes, especially in patients with perforated appendicitis. Children with appendicitis managed with standard protocols may benefit more from treatments. We recommend the development and implementation of standards in terms of fewer negative laparotomies, fewer complications, and fewer re-admissions.*

***Keywords**: Appendicitis, The standardization protocol for the management of appendicitis, perforated appendicitis*

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Introduction

Appendicitis is one of the most common conditions requiring emergency surgery in children with an incidence of approximately 1/1000, the lifetime risk of appendicitis is 7-8%, it peaks between the ages of 10-19 years and 15-20% of the cases present with perforation[1]. The pathophysiology, diagnosis, and management of the disease have not been clearly defined for many years and still investigated. Recent studies now support narrower-spectrum antibiotics and early transition to oral antibiotics, and focus on approaches based on clinical parameters rather than predetermined duration of therapy [2].

In our clinic, which is located in a general hospital that provides the tertiary medical service in the region of our country and the specialty training (residency); approximately 300 appendectomies were performed every year. Until about a year ago, there were no standard practices in the management of patients with appendicitis in our clinic, and pediatric surgeons approached their own knowledge and experience. We set standards by reviewing the recent literature on the management of appendicitis in children, as part of the quality improvement initiative, from April 2020. We hypothesized that standardized protocols for the management of patients with appendicitis would reduce variiation in practice, conserve health resources, and improve clinical outcomes. If our hypothesis is proven correct, patients can be operated with the most appropriate and standard method at the optimal time, proven the using appropriate and correct antibiotics, stay in the hospital for a shorter duration, and reduce complication and re-admission rates.

The clinical results of the established protocols in the management of appendicitis are insufficient, and it is reported that more data are required to determine standard protocols [3-9]. The aim of this study is to present our clinical outcomes of setting standardization in the management of appendicitis in children.

Materials and Methods

We conducted this retrospective study following the study's approval by the Ethics Committee for Clinical Research in the University of Health Sciences (*date: 26.01.2021, decision number: 2011 KAEK-25 2021/02-22*), the Pediatric Surgery Department in Bursa Faculty of Medicine, University of Health Sciences. To evaluate the results of the standard protocols, we created two groups: patients managed before setting the standard (Pre-S) and those managed after setting the standard protocols (Post-S). Between April 2020 and October 2020, data of patients with surgically treated appendicitis were retrospectively collected from medical records after the standards were established (Post-S). To form the comparison group (Pre-S), data from the same number of patients who underwent appendectomy between October 2019 and April 2020 were collected from medical charts. All patients were evaluated and operated by the same surgical team (three pediatric surgeons and four residents). Patients' age, gender, physical examination findings, body mass index (BMI), laboratory tests, imaging studies, time between admission and surgery, surgery methods, surgical findings, early complications, time of hospital stay, late complications, re-admission to the hospital and re-hospitalization were analyzed. The patients who received medical treatment, interval appendectomies, and operated in another center were excluded. The patients were divided into subgroups according to the surgical findings as acute, perforated appendicitis and the total number of patients. All patients were followed for at least 6 months to evaluate late complications.

The first evaluation of the patients who admitted with the suspicion of appendicitis was made by the residents and the final decision was made by the physicians. In the history of the patients, in addition to general information, such as pain intensity, pain migration, localization and amount, presence or absence of other symptoms, presence of nausea or vomiting, presence of anorexia, were obtained. On physical examination, body temperature, abdominal distention, painful tenderness on palpation, rebound tenderness and mass were assessed. Routine white blood cell count (WBC), C-reactive protein (CRP), and biochemical analysis, as well as plain abdominal radiography and abdominal ultrasonography (US), were performed to confirm the diagnosis of appendicitis and exclude other diseases such as hepatobiliary, urinary or gynecological diseases. Data from physical examination and laboratory tests were also used to calculate the Alvarado score [10]. Details of Alvarado scoring are shown in Table1.

Table 1. Alvarado score system for appendicitis

	Feature	Score
1	Migration of pain	1
2	Anorexia	1
3	Nausea/vomiting	1
4	Right lower quadrant tenderness	2
5	Rebound pain	1
6	Elevated temperature	1
7	Leukocytosis (>10000/mm^3)	2
8	Left shift WBC differential	1

Points	Scoring system	Recommend action
5-6	Compatible with appendicitis	Observe
7-8	Probable appendicitis	Surgery
9-10	Very probable appendicitis	Surgery

Preoperative standards

Positive US findings were determined as uncompressible appendix with swelling of its lumen (appendiceal diameter> 6 mm), present of appendicolith, target sign, high echogenicity around the appendix, pericecal and perivesical free

Table 2. Demographic and clinical features of the patients

	Pre S (n=175)			**Post S (n=183)**			
Patients' characteristics	Acute	Perforated	Total	Acute	Perforated	Total	p
Age(year, mean±SD)	12.6±3.3	10.9±4.8	12.2±3.7	12.3±3.1	10.4±3.9	11.7±3.5	p>0.05
Gender (F/M)	46/89	11/29	57/118	35/88	23/37	58/125	p>0.05
WBC (/dL, mean±SD)	13938±508	16135±646	14325±545	13613±525	16135±541	14440±542	p>0.0
CRP (mg/L, mean±SD)	19±31	94±86	36±59	21±30	68±69	37±51	p>0.05
Positive US findings(n)	65	17	82	60	25	85	p>0.05
Alvarado score(mean±SD)	-	-	-	7.6±1.3	9.3±0.9	8.2±1.5	-
BMI (mean±SD)	23.3±3.7	22.1±2.5	23.0±3.5	23.0±2.4	22.5±2.5	22.9±2.4	p>0.05

SD: Standard deviation, **F:** Female; **M:** Male; **WBC:** White blood cell count; **CRP:** C-Reactive Protein; **US:** Ultrasonography; **BMI:** Body mass index

Table 3. Comparison of surgical preferences.

	Pre S (n=175)			**Post S (n=183)**			
	Acute	Perforated	Total	Acute	Perforated	Total	p-value
Time interval from admission to surgery (hours, mean±SD)	9.8±13.2	8.9±9.4	9.58±12.4	8.4±8.6	8.4±8.5	8.43±8.5	p>0.05
Operative Procedure (laparoscopic/open)	48/87	4/4	52/123	34/89	36/56	38/145	p>0.05
Drain usage (n)	-	38 (21%)	38 (21%)	-	41 (23%)	41 (23%)	p>0.05

SD: Standard deviation.

Table 4. Comparison of postoperative results

	Pre S (n=175)			Post S (n=183)			
	Acute	Perforated	Total	Acute	Perforated	Total	p-value
Change of antibiotics after surgery (n)	5/135	9/40	14/175	6/123	11/60	17/183	p>0.05
Complications (n, SSI/A/I)	-/-/-	6/3/-	6/3/-	-/-/1	2/1/-	2/1/1	p<0.05[a,b]
Length of hospital stay (d, mean±SD)	3.5±0.9	7.2±2.8	4.4±2.2	3.6±1.3	6.5±2.3	4.6±2.2	p>0.05
Re-admission (n)	8 (4.5%)	8 (4.5%)	16 (9%)	2 (1%)	5 (3%)	7 (4%)	p<0.05[a]
Re-hospitalization (n)	2	4	6	2	5	7	p>0.05

SD: Standard deviation **SSI/A/I:** Surgical site infection/Abscess/Ileus [a] Compared with the total number of groups, [b] Compared with patients with perforation in groups

fluid and intestinal loops thickened with decreased peristalsis. Suspected cases were re-evaluated by serial examinations, and if necessary, by laboratory and imaging methods. Those with an Alvarado score above 6 were operated, but if there is a suspicion of appendicitis in clinical evaluation and/or advanced imaging methods, surgery was recommended even if the score was low. In suspected cases, the decision to perform surgical exploration was made considering the age and comorbidity of the patient. Patients who were diagnosed with appendicitis and decided to be operated on were fasted with intravenous antibiotic and fluid therapy. Ampicillin/sulbactam and aminoglycoside were initiated empirically at appropriate doses in patients with acute appendicitis, or metronidazole additionally if perforation is suspected and third generation cephalosporin, aminoglycoside and metronidazole were administered in patients with palpable abdominal mass or abscess on US.

Operative standards

Interval appendectomy was not performed during the study period. None of the patients were operated at night and appendectomy was performed as soon as possible after fasting for at least 6 hours. If open appendectomy was to be performed, laparotomy was performed by Rocky Davis incision in acute cases, and a right paramedian incision and transrectal laparotomy in those who suspected perforation. In the laparoscopic method, the three-port technique was used. In both open and laparoscopic surgery, the mesentery of the appendix was divided with an electrothermal bipolar vessel sealing device (Liga-Sure™), and the stump was tied with 2/0 silk suture and not buried. For perforated cases, the abdomen was irrigated with normal saline, and those that penrose drains into the Douglas and Morison pouch were routinely placed.

Postoperative standards

The same antibiotics were used following appendectomy for acute appendicitis. If perforation was found at laparotomy, narrow spectrum antibiotics administered on admission were replaced with broad-spectrum antibiotics. WBC and CRP control was performed on the postoperative 2nd day in acute cases and on the 4th day in perforated cases. Drains were removed once the drainage has stopped.

We determined discharge criteria as the patients' consecutive body temperature is less than 38.0°C in 24-hour, able to tolerate light diet and move independently, in need of analgesia minimally, decreased leukocytosis (WBC <11.000/dL) with the reducing CRP level. Patients with acute diagnosis who met our criteria were discharged on the 2nd day without antibiotic, and those with perforation were discharged on the 4th day with oral amoxicillin/clavulanic acid for 7 days. Otherwise, blood, urine, wound or drain cultures were obtained, ileus and intra-abdominal abscess were investigated by imaging studies, re-evaluated after three days, and those who met the criteria were discharged.

Statistics

The data of all patients in Pre-S and Post-S groups, and subgroups of patients diagnosed with acute and perforated appendicitis were compared. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS 21.0; IBM, Armonk, NY). Comparisons between pre- and post-standards subgroups for categorical variables were compared using chi-square test, and using t-tests for continuous variables. Data were expressed as means, standard deviation, frequency and percentages. Statistical significance was defined as a p value of less than 0.05.

Results

Data were obtained from 376 patient's records that underwent appendectomy over a period of 12 months. Negative laparotomy was performed in 13 (7%) patients in the Pre-S group and five (3%) in the Post-S group, and the difference was significant ($p<0.05$), but the clinical outcomes of these patients were not compared in the study. On the other hand, there was no difference in the number of perforated appendicitis ($p>0.05$). A detailed retrospective chart review was performed of 175 patients who diagnosed appendicitis in the Pre-S group and 183 patients in the Post-S group. The mean follow-up of patients was 14 months (range, 6 to 18 months). The two groups were similar in terms of demographic and clinical characteristics, laboratory results, and US positivity ($p>0.05$, Table 2).

As shown in Table 3, although the time between admission and surgery was shorter in the post-S group, the difference was not significant ($p>0.05$). Laparoscopy in Post-S patients was preferred less when compared with Pre-S ones, but there was no statistical difference ($p>0.05$). There was no significant difference in terms of drain placement frequency ($p>0.05$).

When the postoperative data were examined, no significant difference was found between the groups in terms of postoperative antibiotic changing frequency. Patients diagnosed with perforated appendicitis were hospitalized for almost one day less in the Post-S group, but no significant difference was found by

. **Table 5: Characteristics of seven studies by setting a clinical pathway in appendicitis management and our study**

Clinical pathways	**Outcomes**			
	Postoperative	**Postoperative complications**	**Length of hospital stay**	**Readmission**
No	Antibiotics usage, discharge criteria	No difference in both AAs and PAs	Reduced in both AAs and PAs	Not tudied
Incision selection, stump inversion, drain usage	Antibiotics usage, abscess investigation, discharge criteria	Not studied	no difference in PAsReduced in AAs	Not studied
No culture, no drain	Antibiotics usage, ileus investigation, discharge criteria	No difference in both AAs and PAsReduced in both AAs, prolonged in PAsNo difference in AAs, decreased in PAs		
Interval appendectomy if abscess present on CT	Discharge criteria	Decreased	No difference	Decreased
Operative findings, drain usage	Antibiotics and TPN usage, abscess investigation, discharge criteria	Decreased	No difference	No difference
No	Antibiotics usage, abscess investigation	No difference in PAs	Reduced in PAs	No difference in PAs
Operative findings	Abscess investigation, discharge criteria	No difference	AAs and PAsReduced in both	No difference in both AAs and PAs
sion selection, drain usagecriteriaAntibiotics usage, abscess investigation, discharge		No difference in AAs, decreased in PAs	No difference in both AAs and PAs	Decreased in both AAs and PAs

comparing the groups and subgroups (p>0,05, Table 4).

The total number of complications was found to be significantly lower in the Post-S group when the perforated subgroups were compared (p<0.05). There was no difference in the development of surgical site infection (SSI), abscess and adhesive ileus in the patients with acute appendicitis (p>0.05). Although there was no significant difference between the subgroups, the number of re-admission applications was found to be significantly reduced in the Post-S group (p<0.05), but there was no difference in terms of the number of re-hospitalization (p>0.05).

Discussion

There are many studies in the literature about the benefits of setting a standard protocol in the management of the patients with appendicitis [3-9]. These protocols have been shown to reduce variation in the management of appendicitis, reduce resource utilization, and improve outcomes. On the other hand, standardization in the management of children with suspected appendicitis is difficult due to many factors such as the different clinical patterns depending on the degree of inflammation, the progression of the disease and the lack of classical clinical appearance[4]. All or some of the standard protocols for the management of the children with appendicitis presented here are already routinely applied in many centers. In this study, two groups with similar demographic and clinical characteristics were compared. The standardized protocols we created by reviewing the literature provided an opportunity to evaluate both our routine practices and the results of the standards.

Although clinical laboratory and imaging are helpful, diagnosis of appendicitis and detection of perforation may be difficult. Classical signs and symptoms such as abdominal pain migrating to the right lower quadrant, rebound tenderness and fever are present in less than half of the patients, and if the patient is younger this ratio decreased even more[1]. Many markers for the detection of acute appendicitis have been most extensively studied, but there is no specific laboratory test that is an independent predictor of appendicitis. The most commonly studied laboratory values are WBC, absolute neutrophil count, and CRP. It has been suggested that especially high WBC and CRP together are valuable in the diagnosis of appendicitis [11]. In this study, WBC and CRP levels, which are already routine laboratory tests, were used for diagnosis and discharge criteria.

Imaging methods have significant benefits in diagnosing appendicitis, but US is operator dependent and computed tomography (CT) has ionizing radiation concerns. Thus, it encouraged researchers to create clinical scores and algorithms to aid in the diagnosis of appendicitis [12]. Although appendicitis scoring systems set optimal limits for pediatric and adult patients, but the data are of low quality, not widely accepted, and unlikely to change clinical practice [13]. Nevertheless, it has been suggested that if these systems are incorporated into the comprehensive clinical practice, it is a safe and practical option to standardize risk stratification and care [14]. Many scoring systems have been reported in the diagnosis of appendicitis. Because of the Alvarado scoring system is known a good adjuvant method to help in the early diagnosis of appendicitis, we used in our clinic practice. In addition to the history and physical examination, routine laboratory analyzes and US were used for diagnosis before the study. In present study, we did not set a defined cut-off for WBC, but used WBC >10,000/mm^3 for the Alvarado score. WBC and CRP levels were analyzed both at diagnosis and at discharge criteria, and high and low levels of both at the same time were considered significant.

Non-surgical treatment of acute appendicitis by using antibiotics alone is still controversial in children. Non-operative treatment is not used in our clinical basic practices; however, this approach can be tried in the future if the definitive diagnosis of acute appendicitis is made with advanced diagnostic methods. The benefits of starting antibiotics during the diagnosis of appendicitis with suspected intra-abdominal sepsis or complicated appendicitis have been proven, but it has been reported that a single dose administration is sufficient for simple appendicitis [12,15]. Despite the lack of evidence, our institutional protocol has included preoperative antibiotics for several reasons. Most important reason is that identifying simple and perforated appendicitis prior to surgery can be clinically difficult. Other is to prevent the progression of the disease if surgical treatment is delayed. Moreover, as a legal issue, parents may become aware of the risk of perforation and subsequent complications to be significantly higher than the actual risks [15]. In our study, the duration of intravenous antibiotic use was reduced to 2 days in acute cases and 4 days in perforated. There was no difference between the groups in terms of the need for changing antibiotics started preoperatively. However, the results of our study encouraged us to review many unnecessary routine practices and to make more

radical decisions, we think that a single dose of antibiotics would be useful.

In the literature, when comparing appendectomies performed within 5 hours and 17 hours after admission, it was found that there was no difference in terms of perforation, operation time, postoperative complications, SSI, hospital stay, and re-admission [16,17]. The patients in both groups did not undergo night appendectomy, and they were taken into surgery as soon as possible if whose fasting period is sufficient. Although the interval between admission and operation time was less in the Post-S group compared to the Pre-S period, the difference was not significant. The desire to cleave to the protocol may have encouraged us to perform surgery earlier.

It is suggested that laparoscopic appendectomy may be more preferred in children due to its advantages such as lower postoperative pain, lower incidence of surgical site infection, and higher quality of life [12]. On the other hand, discussions on drain usage in perforated appendicitis still continue. Prophylactic use of abdominal drainage after appendectomy for perforated appendicitis in children has been reported to prevent postoperative complications, however, abdominal drains may have a lot of complications such as SSI, impair immune system of peritoneal cavity, evisceration or enteric fistula [18-20]. Indeed, the combination of these factors seems to shift the risk-benefit balance in favor of abandoning prophylactic abdominal drains. In our study, we preferred both open and laparoscopic appendectomy before and after setting protocol, it was found that drains were placed at similar rates (21-23%) in both groups.

The results of different studies on clinical protocols applications in children with appendicitis are shown in Table 5 [3-9]. When the results of the different standardized protocols determined for the preoperative, operative and postoperative periods are reviewed, it is seen that the postoperative complication rates in perforated appendicitis are mostly reduced. In our study, when evaluated results of our established standards in terms of the total number of complications, it was found that it did not change in patients with acute appendicitis, but decreased in the perforated. We think that complications are reduced due to the surgeon's adherence to the standard protocol.

As shown in Table 4, the length of hospital stay was shortened in many studies, especially in the patients with acute appendicitis. In our study, while there was no significant difference when compared groups in term of the length of hospital, it was found that patients with perforated appendicitis in the post-S group were hospitalized for one less day. This result may be related to the low incidence of complications in the subgroup and early control of discharge criteria in the Post-S group may have resulted in fewer hospitalizations.

Dening et al. found that the rate of re-admission after simple appendectomy was 2.8%, and this rate was 5.3% in perforated patients in their 9-month retrospective analyze of all patients who underwent surgery in pediatric surgery practice [21]. Lansdale et al., however, found that with the new clinical pathway they created in patients with complicated appendicitis, the rate of re-admission increased from 13% to 16%, depending on intra-abdominal collection[8]. In this study, it was determined that the total hospital readmissions decreased from 9% to 4% after standardization. It is seen that the studies presented in Table 4 did not change the rate of re-admission except for two series. This decrease in the number of re-admissions to the hospital seems to be associated with postoperative complications. Ferguson et al. found that oral administration of antibiotics for 7 days after discharge reduced the likelihood of re-admission [22]. (Ferguson Standardized Discharge Antibiotics May Reduce Readmissions in Pediatric Perforated Appendicitis).

The most important limitation of our study is that it is retrospective. There is no enough data on which criteria should be considered when determining the standard protocols in the diagnosis, treatment and postoperative management of appendicitis. Each of the determined protocols may have an impact on the results individually, on the other hand, it is not possible to know which one is effective and how much. Moreover, it is possible that the use of standard protocols together may weaken or increase the effect on the results. In addition, the fact that this study was conducted without considering many impact factors such as the seasonal occurrence of appendicitis may have an effect on the correlation of the results. More and multicenter studies are needed.

In conclusion, our study showed that establishing a standard protocol reduces the frequency of negative laparotomy in patients with suspected appendicitis, shortens the hospital stay, reduces postoperative complications, and reduces re-admissions to the hospital, especially in patients with perforated appendicitis. However, many factors such as the presence of complicated appendicitis, the patient's nutritional status, concomitant chronic disease, long-term drainage, and delayed nutritional tolerance may affect these outcomes, and we think that establishing a standard protocol alone may have a limited effect.

Ethics approval: Health Sciences University Local Ethics Committee granted approval for this study (Date: 26.01.2021, number of decision: 2011-KAEK-25 2021/02-22).

Conflicts of interest:

The authors declare that they have no conflict of interest.

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