Pediatrics and Neonatology (2019) 60, 530–536

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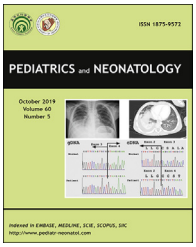

Original Article

Abscess and symptoms duration upon presentation should guide decision algorithms for early versus interval appendectomy in children

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Received Aug 20, 2018; received in revised form Nov 8, 2018; accepted Jan 15, 2019
Available online 19 January 2019

Key Words
abscess;
appendicitis;
early;
interval

Background: To compare outcomes for complicated appendicitis treated with early versus interval appendectomy and to identify which patients would likely benefit from early appendectomy.
Methods: A retrospective review of complicated appendicitis was performed from 2010 to 2015. Patients were divided into early (EA) versus interval appendectomy (IA) groups. We compared demographics, complications and outcomes. Pearson's Chi square analysis and Student's T test analysis were performed.
Results: We identified 316 patients (EA group 53% vs. IA group 47%). Interval appendectomy group had longer symptom duration [IA 3.8 vs. EA 2.3 days ($p = 0.0001$)], increased leukocytosis [IA 18.7 vs. EA 17.2 ($p = 0.008$)], more initial abscesses [IA 35% vs. EA 13% ($p = 0.0001$)], more complications [IA 30% vs. EA 19%, ($p = 0.013$) and prolonged total length of stay [(LOS), $p = 0.009$]. Subgroup analysis of all patients revealed 80% of patients presented with $\leq$3 cm abscess and duration of symptoms (DOS) $\leq$5 days. Interval appendectomy patients with DOS $\leq$5 days and or $\leq$3 cm abscess on admission had no differences in clinical presentation. However, these patients had prolonged total LOS (IA 7.7 vs. EA 6.3 days, $p = 0.01$) and increased complications (IA 29% vs. EA 19%, $p = 0.04$).
Conclusion: The majority of patients with complicated appendicitis in children present with small abscess ($\leq$3 cm) and short symptom duration ($\leq$5 days). This subset of patients might

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https://doi.org/10.1016/j.pedneo.2019.01.005

benefit from early appendectomy due to decreased LOS, resource utilization and reduced complications.

1. Introduction

Appendicitis is one of the most common surgical problems seen in children, having a lifetime risk of 7.7%.[1–3] Appendectomy is a relatively safe procedure with a mortality rate of 0.8/1000 for uncomplicated appendicitis.[2] Morbidity and mortality of an appendectomy including wound infections and intra-abdominal abscesses have dramatically decreased with the use of preoperative antibiotics.[4]

The classic definition of complicated appendicitis includes gangrenous and perforated appendicitis. More recently, St. Peter et al. demonstrated that purulent or gangrenous appendicitis does not possess the same abscess risk after surgery.[5] Instead, a hole in the appendix or a fecalith in the abdomen are clear factors for postoperative abscess formation in up to 20% of patients.[5] The importance of a standard definition for complicated appendicitis allows for significant therapy reduction in patients with uncomplicated appendicitis (acute, suppurative and gangrenous) where the complication rate is $<1\%$.[4] The treatment of complicated appendicitis varies from different institutions and from surgeon to surgeon. Some perform an early appendectomy, while others treat with initial antibiotics $\pm$ drain for abscess, followed by an interval appendectomy 4–8 weeks later. The latter approach was thought to decrease conversions to open surgery, morbidity and extensive resections (right hemicolectomy). Currently there are no standard criteria to identify which patients would most likely benefit the most from an interval appendectomy.[6] Some surgeons choose this method for patients presenting with drainable abscesses while others use signs of perforation, such as increased duration of symptoms upon admission, elevated white blood cell count (WBC), phlegmon or high fevers without evidence of abscess on admission.

A review of the literature comparing early appendectomy versus interval appendectomy show mixed results. A meta-analysis of several retrospective studies concluded that interval appendectomy was associated with significantly fewer complications.[7] Another large database retrospective study identified 6190 children who had an appendiceal abscess upon presentation, of whom 1225 received non-operative treatment. Of these 1225 patients, 12% of patients were treated with percutaneous drainage and antibiotics, 6% had recurrent appendicitis, 15% underwent an interval appendectomy, and $<1\%$ had postoperative complications after the interval appendectomy.[8–11] Although the complication rate was small in all of these studies, they failed to compare results with patients that had an initial appendectomy.[8–11] More importantly, when reviewing the only 2 prospective trials for patients presenting with complicated appendicitis, one trial found a higher complication rate in patients undergoing interval appendectomy of 55% versus 30% for early appendectomy patients presenting with signs of perforation with or without abscess.[12] The second trial found that early appendectomy had longer operative times but no differences in total hospitalization, recurrent abscess rate, or total charges when compared to interval appendectomy in patients presenting with abscess, although 1 patient required a right hemicolectomy for uncertain diagnosis.[13] Another important aspect related to early appendectomy is cost and resource utilization reduction demonstrated by retrospective reviews and randomized trials.[14–16]

In an effort to establish an evidence-based protocol for the management of acute appendicitis, we set out to compare outcomes for complicated appendicitis treated with early versus interval appendectomy and to identify which patients would likely benefit from early appendectomy.

2. Methods

After institutional review board (IRB) approval was obtained, we performed a retrospective evaluation of all patients managed for complicated appendicitis in a large tertiary pediatric center from 2010 to 2015. International classification of disease nine (ICD-9) codes consistent with the diagnosis of acute appendicitis with abscess or peritonitis were obtained from the electronic health record (EHR) and included in this study. All patients were considered complicated based on the surgeon's designation upon admission or during appendectomy. A retrospective chart review of all patients who were managed for complicated appendicitis was performed. Patients were divided into two groups for study analysis. Group 1 patients underwent early appendectomy (EA) defined as appendectomy during the initial admission, while group 2 patients underwent interval appendectomy (IA), defined as patients initially treated with antibiotics $\pm$ drain and subsequent elective appendectomy 4–8 weeks later. Groups were compared based on demographic data, patient's clinical presentation, management and complications. The decision for surgical intervention versus interval appendectomy was based on the surgeon's preference, not on any guideline or protocol at our institution. Once the patient was deemed to be complicated appendicitis, the surgeon chose which treatment arm to pursue.

Demographic data obtained included age, gender, weight and race. Clinical presentation such as duration symptoms, tachycardia, fever, white blood cell count (WBC), radiographic use and imaging findings as well as the presence of intra-abdominal abscess on presentation were also recorded. Systemic inflammatory response syndrome

Table 1 Clinical presentation of patients with complicated appendicitis upon initial presentation.

	Group 1 (EA) n = 168	Group 2 (IA) n = 148	P-value
Symptom Duration, days (SD)	2.3 (1.4)	3.8 (3.9)	0.000
Abdominal symptoms $\leq$ 5 days	162 (96)	124 (81)	0.000
Tachycardia, n (%)	126 (75)	96 (64)	0.078
Tachypnea, n (%)	128 (76)	111 (75)	0.388
Tmax 24 h, F (SD)	100.6 (8)	101.1 (1.5)	0.033
Mean WBC on admission	17.2 (4.9)	18.7 (6.4)	0.008
Bands > 10%	31	20	0.077
SIRS, n (%)	148 (88)	128 (86)	0.397

IA, interval appendectomy; EA, early appendectomy; n, number of patients; SD, standard deviation; Tmax, maximal temperature on admission; F, Fahrenheit; WBC, white blood cell count; SIRS, systemic inflammatory response syndrome.
p values below 0.05 were statistically significant.

(SIRS) was defined as tachycardia (heart rate >90 beats/min), tachypnea (respiratory rate >20 breaths/min), fever or hypothermia (temperature >38 or <36 °C), and leukocytosis, leukopenia, or bandemia (white blood cells >1200/mm^3, <4000/mm^3 or bandemia $\geq$10%). All patients received intravenous (IV) piperacillin/tazobactam during hospital admission, or ciprofloxacin and metronidazole if they had penicillin allergy. Time of surgery, type of surgery, intraoperative findings and need for post discharge antibiotics were analyzed. Complications studied included abscess development after initiation of treatment, interval appendectomy (IA) < 28 days, conversion to open procedure, ileostomy creation, surgical site infection (SSI), fistula development, bowel obstruction, Clostridium Difficile infection, percutaneous inserted central catheter (PICC) line infection, hernia, wound dehiscence and minor complications (admission for nausea, vomiting, dehydration, unable to tolerate oral antibiotics or diet and admission for abdominal pain with no abscess or phlegmon). Discharge criteria were universal for all patients regardless of management. These criteria included ability to tolerate diet, being afebrile for 24 h, resolution of abdominal pain and hemodynamic stability.

In order to perform subgroup analysis, we further subdivided the patients based on presence/size of abscess and duration of symptoms on admission, since these were the most commonly used parameters to determine intervention in our practice. Chi-squared analysis was performed for categorical data, Student's T-test was used for parametric continuous data, and Mann–Whitney U was used for nonparametric continuous data.

3. Results

We identified 316 patients that were managed for complicated appendicitis at our institution during the study period. One hundred and sixty-eight patients received surgery during the index admission (Group 1) while 148 received an interval appendectomy (Group 2). Both groups were demographically similar with no difference in their gender, race, age or admission weight.

Clinical variables measures included mean duration of prehospital abdominal symptoms, age-specific tachycardia, maximal temperature (Tmax) within 24 h of admission, admission white blood cell count (WBC), bandemia on admission and abscess on presentation as shown in Table 1. Management group and definition of complicated appendicitis was based on surgeon's preference and not on a predetermined definition or protocol. Historically at our institution, fevers, WBC, tachycardia and duration of symptoms were the most commonly used factors to determine treatment arm. In this cohort symptom duration, tachycardia,

Table 2 Preoperative imaging by group.

	Group 1 (EA) n = 168	Group 2 (IA) n = 148	P-value
Ultrasound, n (%)	50 (29)	68 (46)	0.002
Abdomen CT, n (%)	40 (24)	88 (59)	0.000
Fecalith, n (%)	73 (43)	80 (54)	0.038
Phlegmon, n (%)	36 (21)	79 (53)	0.000
Abscess on presentation, n (%)	22 (13)	52 (35)	0.000
Abscess size, cm, mean, SD	3.2 (1.5)	5.4 (2.9)	0.028
Abscess $\leq$3 cm, n (%)	8 (36)	9 (17)	0.026

IA, interval appendectomy; EA, early appendectomy; n, number of patients; SD, standard deviation; CT, computed tomography.
p values below 0.05 were statistically significant.

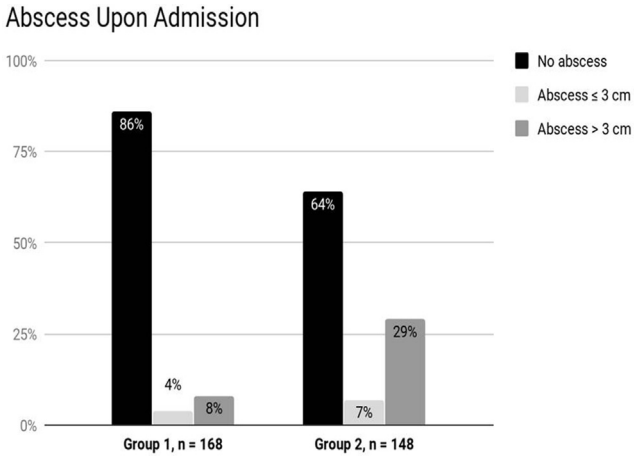

Figure 1 Patients abscess on admission.

fevers and WBC were significantly higher in patients treated with interval appendectomy, although there was no significant difference in SIRS on presentation between groups.

Preoperative imaging characteristics performed at our institution for both groups are compared in Table 2. Patients in group 2 had more preoperative CT scans (59% vs. 24%, $p < 0.000$). Most patients in both groups, presented with no abscess (77%) on admission. Only 5% of patients presented with abscess $\leq$3 cm and 18% presented with abscess >3 cm as shown in Fig. 1. However, there were significantly more fecaliths, phlegmons and abscesses on presentation on interval appendectomy patients.

Appendectomy was performed laparoscopically in 93% (n = 298), open in 5% (n = 16) and laparoscopic converted to open in 2% (n = 6). For patients undergoing early appendectomy, intraoperative findings of perforation were reported by the surgeon in 97% of patients (n = 163). In total of 37 drains were placed intraoperatively (22%) for early appendectomy patients and 2 intraoperative drains were placed at the time of interval appendectomy. There was no significant difference in the reported difficulty of the procedure as stated by the operative report (EA 28% vs. IA 31%, p = 0.315). Intraoperative definition of complicated appendicitis was based on the surgeon's description.

During initial admission there were no significant differences in duration of fevers, anorexia and time to full feeds by group. Patients treated with early appendectomy had 21 postoperative CT scans during admission and 3 after discharge. This was not significantly different from the interval appendectomy groups, which had 14 CT scans during admission and 15 after discharge. There were no differences in number of PICC lines placed, patients discharged with PICC lines or hospital day of placement per group. All patients received intravenous (IV) antibiotics during their

Table 3 Postoperative intervention by groups for complicated appendicitis.

	All Patients, n = 316	Group 1 (EA) n = 168	Group 2 (IA) n = 148	P-value
Discharged antibiotics on 1st admission, n (%)	291 (92%)	146 (86)	145 (98)	0.000
Discharged antibiotics on readmission, n (%)	24 (7.6%)	8 (5)	16 (10)	0.035
Type of DC antibiotics, n (%)				
Augmentin	38 (13%)	26	12	
Flagyl	71 (24%)	9	62	
Augmentin/Flagyl	142 (48.6%)	87	55	0.000
Discharge oral antibiotic duration (days), mean (SD)	20.4 (15)	10.7 (6.3)	30 (15)	0.000
Discharge on IV antibiotics, n (%)	11 (3.5%)	6	5	0.586
Discharge on IV antibiotic duration (days), mean (SD)	9.4 (4.5)	9 (3.5)	10 (6)	0.375
WBC DC value elevated on discharge for index admission, n (%)	23 (9.8%)	6	17	0.012

IA, interval appendectomy; EA, early appendectomy; n, number of patients; SD, standard deviation; WBC, white blood cell count; DC, discharge; IV, intravenous.
p values below 0.05 were statistically significant.

Table 4 Complications by group.

	All Patients, n = 316	Group 1 (EA) n = 168	Group 2 (IA) n = 148	P-value
Complications, n (%)	77 (24%)	32 (19%)	45 (30%)	0.013
Abscess after initial surgery for EA patients, n (%)	—	22 (13%)	—	—
Abscess development after initiation of treatment for IA patients, n (%)	—	—	26 (18%)	—
Interval appendectomy < 28 days, n (%)	—	—	5 (3.4%)	—
Conversion to open, n (%)	4 (1.3%)	1 (0.6%)	3 (2%)	0.265
Ileostomy, n (%)	1 (0.3%)	1 (0.6%)	0 (0)	0.532
Wound infection/SSI, n (%)	6 (1.9%)	4 (2.4%)	2 (1.4%)	0.404
Wound dehiscence, n (%)	2 (0.6%)	0 (0)	2 (1.4%)	0.219
Fistula, n (%)	5 (1.6%)	0 (0)	5 (3.4%)	0.022
Bowel obstruction, n (%)	10 (3.2%)	7 (4.2%)	3 (2%)	0.255
Port Hernias, n (%)	1 (0.3%)	0	1 (0.7%)	0.468
Minor complications[a], n (%)	18 (5.7%)	5 (3%)	13 (8.8%)	0.023

IA, interval appendectomy; EA, early appendectomy; n, number of patients; SD, standard deviation; SSI, surgical site infection.
p values below 0.05 were statistically significant.
[a] Minor complications: abdominal pain and/or vomiting and/or unable to tolerate oral intake and/or unable to tolerate oral antibiotics requiring admission.

entire admission. Group 2 had significantly more patients discharged on oral antibiotics and significantly more days on antibiotics after discharge (30 (15) days vs. 10.7 (6.3), p = 0.000). Table 3 summarizes differences in discharge antibiotics and WBC prior to discharge.

3.1. Outcomes and complications

Initial hospital length of stay (LOS) was not statistically significant between groups (EA 6 days vs. IA 5.9 days, p = 0.266). However, interval appendectomy patients had a significantly longer total hospital LOS [7.8 (4.8) days vs. 6.2 (3.7) days, p = 0.009], a significantly higher number of imaging tests performed during index admission [2.49 (2) vs. 1.8 (1.6), p = 0.022], and significantly increased ER visits after initial admission (26% vs. 13%, p = 0.002). However, there was no difference in the total number of CT scans or the unexpected readmission rates between groups. The total complication rate was 24% (n = 77) in this cohort as shown in Table 4. More importantly, group 2 patients had a significantly higher number of complications (IA 30% vs. EA 19%, p = 0.01). For early appendectomy patients the postoperative abscess rate was 13% (n = 22), whereas the abscess rate after initiation of treatment for interval patients was 18% (n = 26). Interval appendectomy patients failed initial medical management in 28% of the patients (abscess formation, appendectomy in <28 days and bowel obstruction). One patient in the EA group had an intraoperative iatrogenic bowel injury and an ileostomy was created. This patient had to return to the operating room for ileostomy takedown at a later date. Five patients in group 2 developed a fistula. Two of these were due to an iatrogenic drain placement into the bowel, and the other 3 were discovered at the time of the IA. One patient was initially admitted with a phlegmon/abscess and a drain was placed. The patient was noted to have significant output and a drain study confirmed placement in the cecum. The drain was removed at the time of the IA and the fistula tract was treated with a partial cecectomy. The second patient had an iatrogenic placement of the interventional radiology (IR)-guided drain into the distal ileum (bilious drainage). This patient presented with a small bowel obstruction a month after presentation and 2 days after drain removal. The patient underwent an exploratory laparotomy, appendectomy, lysis of adhesions and primary repair of small bowel fistula without resection. The third patient presented with a phlegmon/abscess on CT scan and was treated with 6 weeks of antibiotics without drain. At the time of IA, the patient was noted to have an ileo-appendicular fistula, which was divided laparoscopically without resection. The fourth patient presented with no abscess on admission and received 6 weeks of antibiotics. During IA the appendix was seen to have fistulized into the cecum. The operation was converted to a laparotomy and the patient received a partial cecectomy. The fifth patient was also a fistula from the appendix to the cecum discovered during interval appendectomy and treated with a partial cecectomy laparoscopically. Minor complications (admission for nausea, vomiting, dehydration, inability to tolerate oral antibiotics or diet and admission for abdominal pain with no abscess or phlegmon) were significantly higher for IA patients (IA 8% vs. EA 3%, p = 0.23).

3.2. Subgroup analysis of complicated appendicitis patients

Our cohort of patients demonstrated that 82% of complicated appendicitis patients presented with no abscess (n = 242) or ≤3 cm abscess (n = 17). Furthermore, 90% of all patients presented with ≤5 days of abdominal symptoms on admission. Based on these results, we decided to further subdivide our patients on abscess and duration of symptoms (DOS). Once we controlled both groups for abscess ≤3 cm and DOS ≤5 days upon presentation, we found no significant differences in admission demographics or clinical variables (age, weight, Tmax, tachypnea, tachycardia or SIRS) between groups. Nonetheless, IA patients presenting with abscess ≤3 cm and DOS ≤5 days had a significantly longer LOS (IA 7.7 days vs. EA 6.3 days, p = 0.01) and a significantly higher rate of complications [IA 29% vs. EA 19% (p = 0.04)].

4. Discussion

Appendicitis is a common surgical emergency seen in pediatric patients with a prevalence of 7–8%.[1,3] Laparoscopic appendectomy continues to be the treatment of choice for uncomplicated appendicitis, although more recently medical management has shown some promise.[7] On the other hand, the management of complicated appendicitis with or without abscess remains controversial.[5,8–14] Some patients are treated with early appendectomy while others are treated with antibiotics ± drainage, followed by an interval appendectomy. We believe that the main reasons behind this controversy revolve around the lack of preoperative definitions for complicated appendicitis and the lack evidence-based decision algorithms. Current pediatric criteria [5,12] and the American College of Surgeons National Surgery Quality Improvement Program (NSQIP) database have provided some standard definitions that can be used to guide protocols and research. A meta-analysis of several retrospective studies has shown that interval appendectomy is associated with fewer complications.[10] However, a recent prospective trial reported fewer adverse events for patients treated with early appendectomy (30% vs. 50%), when compared to interval appendectomy patients.[12] Similarly, for patients presenting with complicated appendicitis with an abscess, there is still controversy. Some argued that early appendectomy increases morbidity, conversion to open, extensive resections and more complications. Although several retrospective studies seemed to have corroborated these theoretical disadvantages,[7,8,11] a more recent prospective study showed that early appendectomy leads to less radiation exposure and fewer health care visits with no difference in complication rates.[12,13]

Our results showed that patients treated with interval appendectomy had increased antibiotic use and duration, increased time away from normal activities, increased number of imaging tests performed, more ER visits, increased total length of stay and more complications. However, this patient group on presentation had a longer

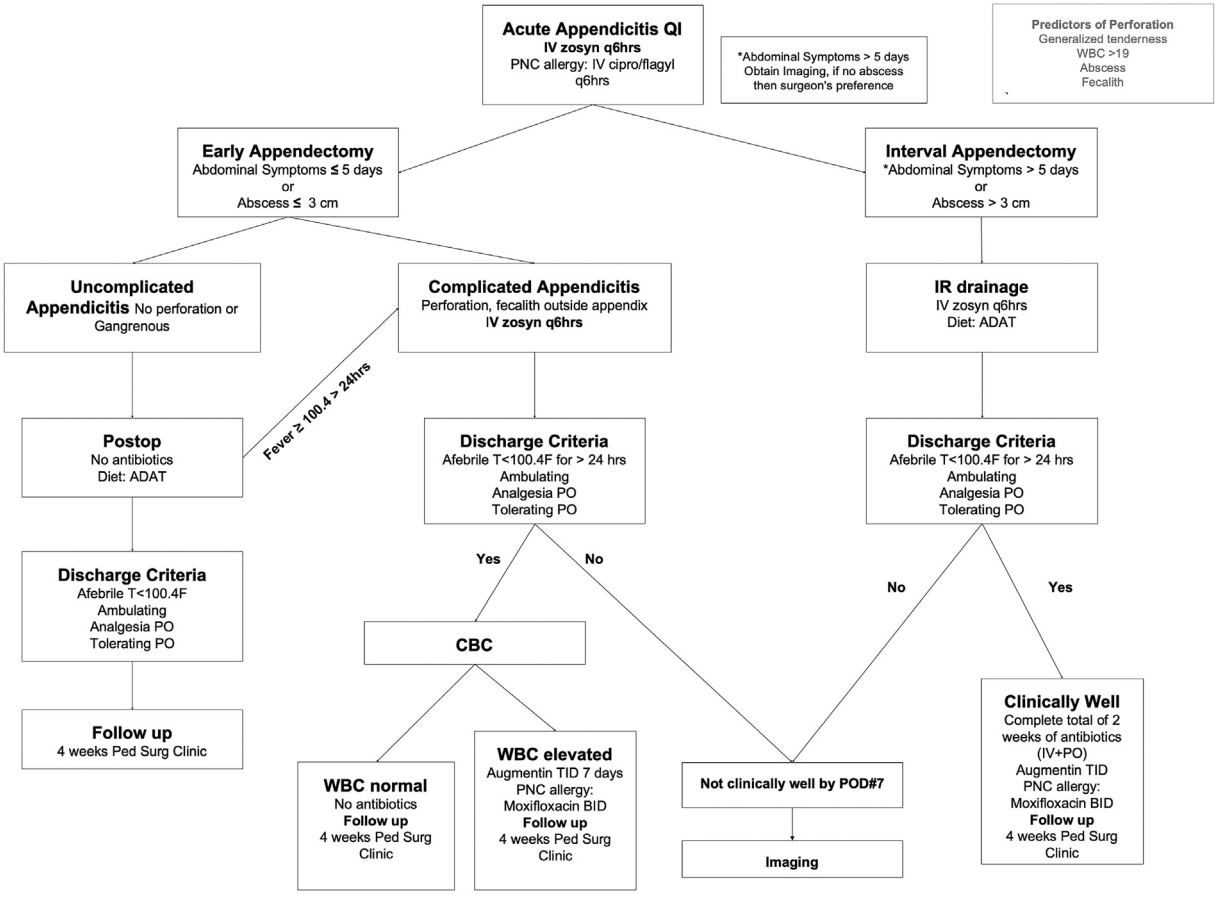

Figure 2 Cardinal Glennon Children's Hospital inpatient appendicitis management protocol.

duration of symptoms, increased leukocytosis and more initial abscesses (35%), which could easily lead to the conclusion that sicker patients were shunted to the interval group explaining the higher complications. Since the majority of children with complicated appendicitis in our study cohort had no abscess (77%) or abscess $\leq$3 cm (5%) on admission and duration of abdominal symptoms of $\leq$5 days (90%), we decided to analyze these patients further. Once we controlled both groups (early versus interval) for abscess $\leq$3 cm and DOS $\leq$5 days upon presentation, we found no significant differences in admission demographics or clinical variables (age, weight, Tmax, tachypnea, tachycardia or SIRS) between groups. Nonetheless, IA patients presenting with abscess $\leq$3 cm and DOS $\leq$5 days had a significantly longer LOS and a significantly more complications. Based on these findings, we created a quality improvement protocol to standardize management of patients presenting with acute appendicitis at our institution as shown in Fig. 2. For patients presenting with complicated appendicitis with a duration of symptoms $\leq$5 days and abscess $\leq$3 cm (90% of patients), we recommend an early appendectomy as the first line therapy. For patients presenting with an abscess $>$3 cm and DOS $>$5 days, we recommend an interval appendectomy. The caveat for this recommendation is that clinical status of the patient may affect the type of intervention needed. Finally, for patients presenting with DOS $>$5 days, we now require advanced imaging to evaluate the presence of an abscess (70% of these patients have an abscess on presentation). Interestingly, we found that patients with DOS $>$5 days and no abscess on admission had no complications on either group, so we leave these patients to the discretion of the operating surgeon.

We acknowledge that in this retrospective review there were no standard preoperative or intraoperative definitions for complicated appendicitis, and more importantly the decision to undergo early versus interval management was based on the surgeon's preference. Patients with longer duration of symptoms were shunted to the interval group, even though $>$60% of these patients had no abscess on admission. We believe this to be the biggest limitation of our study. Despite these limitations, we believe early appendectomy should be the treatment of choice for all types of appendicitis given our results and current evidence. Nevertheless, the role of interval appendectomy should not be eliminated from the armamentarium of pediatric surgeons, since there is likely a small subset of patients that will likely benefit from this option. We advocate that patients with complicated appendicitis presenting with an abscess $>$3 cm and symptoms $>$5 days should be the subset of patients considered for interval appendectomy. This group has no difference in complications whether treated by early or interval appendectomy and most surgeons would be uncomfortable operating in this group.

The management of complicated appendicitis continues to challenge pediatric surgeons around the world. To our knowledge this is the first article to describe preoperative factors (presence of abscess and duration of symptoms) that might help identify patients who would be least likely to benefit from interval appendectomy. We believe abscess and symptoms duration upon presentation should guide decision algorithms in children with complicated appendicitis. In the future, we plan to compare outcomes and complications before and after protocol implementation and to evaluate the effectiveness of our protocol.

5. Conclusion

The majority of patients with complicated appendicitis in children present with small abscess ($\leq$3 cm) and short symptom duration ($\leq$5 days). This subset of patients might benefit from early appendectomy due to decreased LOS, resource utilization and reduced complications.

Conflict of interest

No conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pedneo.2019.01.005.