Initial laparoscopic appendectomy versus initial nonoperative management and interval appendectomy for perforated appendicitis with abscess: a prospective, randomized trial


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Treatment;
Perforated appendicitis;
Abscess;
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Abstract

Introduction: Perforated appendicitis is a common condition in children, which, in a small number of patients, may be complicated by a well-formed abscess. Initial nonoperative management with percutaneous drainage/aspiration of the abscess followed by intravenous antibiotics usually allows for an uneventful interval appendectomy. Although this strategy has become well accepted, there are no published data comparing initial nonoperative management (drainage/interval appendectomy) to appendectomy upon presentation with an abscess. Therefore, we conducted a randomized trial comparing these 2 management strategies.

Methods: After internal review board approval (#06 11-164), children who presented with a well-defined abdominal abscess by computed tomographic imaging were randomized on admission to laparoscopic appendectomy or intravenous antibiotics with percutaneous drainage of the abscess (when possible), followed by interval laparoscopic appendectomy approximately 10 weeks later. This was a pilot study with a sample size of 40, which was based on our recent volume of patients presenting with appendicitis and abscess.

Results: On presentation, there were no differences between the 2 groups regarding age, weight, body mass index, sex distribution, temperature, leukocyte count, number of abscesses, or greatest 2-dimensional area of abscess in the axial view. Regarding outcomes, there were no differences in length of total hospitalization, recurrent abscess rates, or overall charges. There was a trend toward a longer operating time in patients undergoing initial appendectomy (61 minutes versus 42 minutes mean, \( P = .06 \)).

Conclusions: Although initial laparoscopic appendectomy trends toward a requiring longer operative time, there seems to be no advantages between these strategies in terms of total hospitalization, recurrent abscess rate, or total charges.

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Appendectomy for perforated appendicitis with abscess

Historically, an initial operation for perforated appendicitis with a well-formed abscess has been a technically arduous procedure, which has been fraught with postoperative complications. Over 2 decades ago, interventional radiologists (IRs) developed the ability to drain the abscess that allows for a subsequent appendectomy when the localized infection had been cleared. This strategy rapidly became the preferred management of children presenting with appendicitis and an abscess [1-5]. Despite the widespread application of drainage followed by interval appendectomy, there have been little data published describing the expected course for these patients. We recently performed a retrospective review of our experience with attempted drainage, antibiotics, and laparoscopic interval appendectomy and found that drainage complications, persistent symptoms, recurrent abscesses, multiple computed tomographic (CT) scans, numerous home health care visits, and a heavy financial burden may be detriments to this management strategy [6]. However, in this retrospective review, we found that there was not a standardized management strategy among the various surgeons. Therefore, before there are no published data comparing drainage/interval appendectomy to appendectomy at initial presentation, we conducted this prospective, randomized trial comparing these 2 approaches.

1. Methods

Approval was obtained from the Children’s Mercy Hospital Internal Review Board (IRB) (IRB# 06 11-164) before enrolling patients in this study. Patients were subsequently enrolled only after obtaining consent from the patient’s legal guardian. Patients who were 7 years or older were approached for assent. When they were not coherent enough to allow for cognitive recognition of assent (because of narcotic administration), it was attained at a later date. Data were collected only on patients where both consent and assent were adequately attained. The consent forms and consent process were carefully evaluated by the IRB on a continual basis. The study was registered with clinicaltrials.gov at the inception of enrollment (NCT# 00414375).

1.1. Participants

The study population consisted of children younger that 18 years found to have a well-defined abdominal abscess by CT imaging at the time of initial presentation. Patients with a postoperative abscess were not candidates for this study. Exclusion criteria included patients with a comorbid condition that would limit their recovery.

1.2. Interventions

Patients were randomized to undergo either laparoscopic appendectomy on presentation (initial operation group) or attempted percutaneous drainage of the abscess followed by antibiotic therapy with the intent of performing a laparoscopic interval appendectomy approximately 10 weeks after presentation (initial nonoperative management group).

1.3. Sample size

The study was designed as a pilot study without a primary outcome variable for sample size calculation. Based on our recent volume of experience with this condition, a sample size of 40 was determined to allow the study to be completed in approximately 2 years.

1.4. Assignment

An individual unit of randomization was used in a nonstratified sequence in blocks of 4. With confirmation of a well-defined abscess by the surgeon, the family was approached for consent. The randomization sequence was accessed to identify the next allotment after the consent was signed.

1.5. Protocol

The laparoscopic appendectomies were performed by 1 of the 7 staff surgeons as dictated by the call schedule. Nasogastric tubes were not used after the operation [7].

The postoperative orders for the group that randomized to early operation were controlled via a standard electronic order set for all operations. These patients received a 5-day course of once-a-day dosing of ceftriaxone (50 mg/kg) and metronidazole (30 mg/kg) according to the protocol that was validated in a previous prospective trial [8]. A leukocyte count was drawn on postoperative day 5 in all patients. If this was normal, the patient was afebrile, and was tolerating a regular diet, he/she was discharged home without oral antibiotics. If leukocytosis was found at 5 days, the patient received 2 additional days of antibiotics with a repeat white blood cell evaluation on postoperative day 7. If the leukocyte count remained elevated, the patient received another 3 days of antibiotics and a CT scan was obtained to evaluate for the presence of an abscess. In addition, a CT scan was obtained if the patient’s clinical condition suggested an abdominal abscess at any time after 7 days.

The patients randomized to the initial nonoperative management group were evaluated by IR for drain placement (when possible) and a peripherally inserted central catheter. These patients received a 2-week course of the same antibiotic regimen as the other group (ceftriaxone [50 mg/kg] and metronidazole [30 mg/kg]). They were discharged when tolerating their diet, and the drain was removed when the output was minimal. Repeat CT scan at the time of drain removal was at the discretion of the IR and generally reserved for those with symptoms worrisome for undrained areas. All these patients followed-up with 1 provider (SSP).
at the completion of their antibiotic course to standardize the management of these patients. At that time, the determination for discontinuing (or continuing) the antibiotics was made on clinical grounds alone. Ongoing pain, tenderness, or a palpable mass was a reason to continue antibiotics for another week. Clinical worsening or suspicion for recurrent abscess precipitated repeat CT scan at this point. When the decision to discontinue antibiotics was made, the peripherally inserted central catheter line was removed and the patient was scheduled for laparoscopic appendectomy with the surgeon who was on call at the time of the original diagnosis at approximately 10 weeks from initial presentation.

1.6. Data collection

All data were collected prospectively. At the time of presentation, the patient’s age, sex, weight, body mass index, maximum temperature, white blood cell count, and greatest 2-dimensional area of the abscess from axial images were collected. Operative variables collected included the operative approach, operative time, and intraoperative complications.

The outcome variables included maximum daily temperatures for each of the first 5 posttreatment days, time to regular diet, total length of hospitalization, abscess rate, wound infection rate, doses of narcotics, number of health care visits, number of CT scans, and total hospital charges incurred including interventional radiology charges.

1.7. Statistical analysis

Continuous variables were compared using an independent sample, 2-tailed Student’s $t$ test. Discrete variables were analyzed with $\chi^2$ test with Yates correction where appropriate. Significance was defined as a $P$ value $\leq .05$. Descriptive statistics are expressed as mean ± SD.

2. Results

From December 2006 through November 2008, data were collected on 40 consecutive patients who were enrolled in the study.

2.1. Demographics

There was an equal sex distribution with 11 males in the initial operation group and 10 males in the initial nonoperative group. At presentation, there were no differences in age, weight, body mass index, leukocyte count, maximum temperature, or maximum axial area of the abscess between the 2 groups (Table 1). It should be emphasized that these abscesses were not small. The mean maximum area calculated in the axial plane on the CT scan was 29.2 and 26.2 cm² in the 2 groups.

### Table 1 Patient characteristics at the time of admission

<table>
<thead>
<tr>
<th></th>
<th>Initial operation (n = 20)</th>
<th>Initial nonoperative management (n = 20)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>10.1 ± 4.2</td>
<td>8.8 ± 4.2</td>
<td>.31</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>37.0 ± 16.2</td>
<td>37.1 ± 20.8</td>
<td>.98</td>
</tr>
<tr>
<td>Body mass index (kg/cm²)</td>
<td>18.0 ± 4.5</td>
<td>19.5 ± 5.5</td>
<td>.39</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>17.4 ± 6.6</td>
<td>16.9 ± 6.8</td>
<td>.84</td>
</tr>
<tr>
<td>Maximum temperature</td>
<td>37.8 ± 1.0</td>
<td>37.7 ± 0.9</td>
<td>.95</td>
</tr>
<tr>
<td>Maximum axial area of abscess (cm²)</td>
<td>29.2 ± 29.7</td>
<td>26.2 ± 21.1</td>
<td>.75</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD.

2.2. Initial operation group

On average, the operating time was almost 20 minutes longer in the initial operation group ($P = .06$; Table 2). There were no conversions to an open procedure in the initial nonoperative group who subsequently underwent interval laparoscopic appendectomy compared with one conversion in the initial operation group. The one conversion in the initial operation group was because of a fragmented appendix where the appendiceal base could not be identified well, so a right lower quadrant incision was used for better visualization. In addition, 1 patient in the initial operation group underwent a laparoscopic-assisted ileocecectomy for a dense inflammatory mass, which seemed to be creating a pseudotumor around the cecum.

2.3. Initial nonoperative management group

Drains were inserted in 11 of the 20 patients who randomized to initial nonoperative management. In 3 patients, the abscess was aspirated, but no drain was placed. In 6 patients, a drain was not inserted because IR felt the abscess was not accessible. There were no major injuries caused by the drains.

There were 4 patients (20%) who failed initial nonoperative management and underwent laparoscopic appendectomy before the planned 10-week time frame. One of these patients underwent appendectomy 1 day after drain placement owing to progression of peritonitis. Another patient underwent operation 5 days after drainage because of an unrelenting bowel obstruction. A third patient underwent laparoscopic appendectomy after 3 weeks of treatment because of persistent fever and pain with a persistent abscess on imaging. The final patient had persistent nausea with intermittent emesis for 6 weeks, and her mother requested an early operation that was performed 48 days after diagnosis.
The mean (SD) time from diagnosis to operation for the remaining 16 patients was 69 (8) days. The mean (SD) length of hospitalization after the interval laparoscopic appendectomy was 2.4 (3.5) days. However, for the 16 patients who made it to the scheduled interval appendectomy date, the mean (SD) hospitalization after interval appendectomy was 1.1 (0.6) days.

2.4. Outcomes between groups

Outcomes are outlined in Table 2. There was no difference in the total length of hospitalization or the total charges between groups. Patients initially treated nonoperatively tolerated a regular diet much sooner than those who underwent initial laparoscopic appendectomy. However, those initially treated nonoperatively had more health care visits. There was no significant difference detected in mean maximum daily temperatures after diagnosis between the 2 groups.

3. Discussion

This study represents the first data set comparing initial operation at presentation to initial nonoperative management followed by laparoscopic appendectomy in children presenting with appendicitis and a well-formed abdominal abscess. Our previous retrospective report on our experience with initial nonoperative management and interval appendectomy showed some concerning data [6]. In that report, the patients had a 17% rate of recurrent abscess formation, which was about the same as our known rate of abscess development after laparoscopic appendectomy for perforated appendicitis (18%) [8]. In addition, there was almost a 10% incidence of major drain complications. In our mind, these data were compelling justification for performing this prospective randomized trial, accepting there are risks of operative complications and postoperative abscess formation. However, in this prospective study, we still found a high percentage of patients developing a posttreatment abscess (20% and 25% in the 2 groups). Moreover, when laparoscopic appendectomy is performed on admission for abscess, the rate of development of another abscess (20%) is almost identical to the rate we have prospectively demonstrated in patients with perforated appendicitis and no abscess (18%) [8]. There were no major operative or drainage complications in this study. However, with a relatively small sample size, we make no conclusions from this finding and assume that there continues to be a risk of iatrogenic complications in dealing with this difficult clinical problem regardless of approach or strategy. Our data suggest that the risk of major complications is probably less than 10%.

Another concerning finding from our retrospective review was the number of CT scans that were performed with initial nonoperative management [6]. The reason is that these patients were not managed by a standardized protocol, and decisions were made on an individual basis by a large number of caregivers resulting in a mean number of 3.5 CT scans per patient. This was one of the more alarming findings from our retrospective study, especially with the current concern about the known radiation exposure of CT scans. An abdominal CT is estimated to produce the equivalent of 25.7 months of natural background radiation exposure [9]. The fact that the risk of radiation induced malignancy from a CT scan decreases with age is important to those who treat the pediatric population when the lifetime risk of a fatal radiation induced malignancy is estimated at 0.18% for a 1-year-old child [10]. Stated another way, one malignancy would result from a CT scan performed on 555 one-year-old patients, whereas about twice as many 15-year-olds would need to be scanned to equal that same risk. In this prospective study, a single caregiver followed the patients treated in the initial nonoperative arm with repeat CT scans performed only in patients who had signs of persistent or recurrent abscess. Using this approach, the mean number of CT scans was reduced to 2.1, which is a significant decrease ($P = .001$).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Outcomes comparing initial operation and initial abscess drainage followed by interval appendectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial operation (n = 20)</td>
</tr>
<tr>
<td>Operation time (min)</td>
<td>62.1 ± 38.7</td>
</tr>
<tr>
<td>Total length of hospitalization (d)</td>
<td>6.5 ± 3.8</td>
</tr>
<tr>
<td>Recurrent abscess after initial treatment (%)</td>
<td>20%</td>
</tr>
<tr>
<td>Doses of narcotics</td>
<td>9.7 ± 4.0</td>
</tr>
<tr>
<td>Total health care visits</td>
<td>2.8 ± 1.1</td>
</tr>
<tr>
<td>No. of CT scans</td>
<td>1.5 ± 0.7</td>
</tr>
<tr>
<td>Time to goal intake (h)$^a$</td>
<td>74.8 ± 53.9</td>
</tr>
<tr>
<td>Total charges</td>
<td>$44,195 ± 19,384$</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD, unless otherwise indicated.

$^a$ Time to regular diet after drain placement or evaluation by interventional radiology in the initial nonoperative group.
This finding strongly suggests that surgeons using the management strategy of initial nonoperative therapy should have strict criteria for follow-up imaging.

The heavy financial burden (mean, $40,414) identified in our retrospective audit of patients treated with initial nonoperative management led us to hypothesize that early operation may be able to decrease the total financial resources required in the care of these patients initially presenting with an abscess. However, this study demonstrates that the costs required to treat these patients is exceedingly high, regardless of whether the patient undergoes an initial operation or is initially management nonoperatively. Because both groups underwent an operation at some point, this enormous cost (mean charges, $44,195 and $41,687 in the 2 groups) was large because of the fact that there was no difference in the total number of hospital days.

The utility of this information for the practicing surgeon needs to be framed in the context of the experience of the surgeon and the resources of the institution. These results may not be generalizable to all pediatric surgical groups. Our group has a large experience with patients with complicated appendicitis. We have used the laparoscopic approach for all patients with appendicitis for the past 8 years, regardless of whether the patient had acute or perforated appendicitis, because of our markedly reduced incidence of wound infections in patients undergoing laparoscopic appendectomy for perforated appendicitis when compared with the open approach. Some groups have reported treating all patients suspected of perforated appendicitis with antibiotics initially with or without interval appendectomy [11-14]. In addition to the need to have laparoscopic experience with complex operations, the good results attained in the nonoperative group depend on an experienced group of IRs within one’s institution. It is important that one can complete the majority of these operations laparoscopically in spite of the abscess because this approach obviates the wound issues often incurred from the open operation in the presence of such contamination [15,16]. The associated morbidity of the open approach would likely push the data toward favoring the interval strategy. In addition to the technical capacity of the laparoscopic approach for the operation group, the results attained in the interval group depend on an experienced department of interventional radiology within the institution. For those surgeons for whom these results are applicable, these data leave the surgeon with the treatment choice to be made on an individual basis. Also, this information empowers surgeons with well-captured prognostic data for discussion with families and identifies the advantages of each strategy. Drainage allows for a more rapid return to regular diet and, on average, a 20-minute shorter laparoscopic appendectomy. On the other hand, an operation at presentation results in fewer CT scans and health care visits. The financial charges to the family are not significantly different [15,16].

References