Critical Review Form
Therapy

Feasibility of a nonoperative management strategy for uncomplicated acute appendicitis in children. J Am Coll Surg. 2014 Aug.

Objectives: **"to determine the feasibility of a nonoperative management strategy for uncomplicated acute appendicitis in children." (p. 273)**

Methods: **This was a prospective, nonrandomized trial comparing appendectomy with nonoperative management of acute appendicitis in children, conducted at Nationwide Children's Hospital in Columbus, Ohio. Patients age 7 to 17 years with ≤ 48 hours of symptoms, a WBC < 18K cells/μL, and evidence of non-ruptured acute appendicitis with an appendiceal diameter ≤ 1.1 cm on either CT scan or ultrasound were eligible for enrollment. Exclusion criteria included pregnancy, peritonitis on exam, or chronic intermittent abdominal pain. The decision to proceed with surgery or non-operative management was made by the families of eligible patients after counseling using a standardized, scripted presenting process by 1 of 3 trained physicians in order to minimize selection bias.**

Nonoperative management consisted of 24 hours of IV antibiotics and observation. Patients who improved were transitioned to oral antibiotics once tolerating a regular diet, to complete a total 10-day course of antibiotics. Patients with clinical worsening of symptoms (increased pain, signs of sepsis) or without improvement within 24 hours of antibiotics were deemed to have failed non-operative management and underwent laparoscopic appendectomy. Any patient managed non-operative who returned after discharge with abdominal pain and an evaluation consistent with appendicitis also underwent laparoscopic appendectomy. Follow-up was conducted at 2 to 5 days, 10 to 14 days, and 30 days after discharge by phone or in person.

The primary end-point was the success rate of non-operative management, i.e. those not requiring an appendectomy. Secondary outcomes included hospital length of stay (LOS), disability days (days to return to normal activity for the child and days to return to work for the parent), number of school days missed, and quality of life at 30 days as measured using the PedsQL Quality of Life Inventory. Out of 398 patients with appendicitis, 77 were enrolled in the study: 30 chose non-operative management while 47 chose surgery. Of the patients undergoing surgery, 2 were found to have gangrenous appendixes while 4 were found to be perforated.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?**	
1.	Were patients randomized?	No. This was a prospective, nonrandomized study in which the decision to perform surgery or attempt non-operative management was at the discretion of the patients' families after counseling on treatment options.
2.	Was randomization concealed (blinded)?	N/A
3.	Were patients analyzed in the groups to which they were randomized?	Yes. Patients who underwent urgent appendectomy were analyzed in the surgical group whether pathology confirmed appendicitis or not; 2 patients were found not to have appendicitis on pathology (1 normal, 1 with granulomas). Patients in the non-operative group were analyzed in this group even if they later required a laparoscopic appendectomy. Therefore an intention to treat analysis was used.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	No. The two groups were similar with respect to age, gender, insurance status, duration of pain, WBC, and the presence of fever, vomiting, and diarrhea. However, patients in the surgical group had a much higher incidence of perforation (n = 4) and gangrenous appendix (n = 2) indicating that they may have been a sicker group at the outset.
B.	**Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?**	
1.	Were patients aware of group allocation?	Yes. This was a nonrandomized study and the decision to perform urgent surgery or attempt non-operative management was at the family's discretion. Given the nature of the study and involvement of children, it seems unlikely that performance bias on the part of the patients or families would affect the outcomes.
2.	Were clinicians aware of group allocation?	Yes. It is possible as a result that some form of performance bias on the part of the clinicians could influence the outcomes (i.e. earlier discharge).
3.	Were outcome assessors aware of	Yes. The outcomes were fairly objective (need for appendectomy), and hence it seems unlikely that **observer bias**

<table>
<tr><td></td><td>group allocation?</td><td>would affect the results.</td></tr>
<tr><td>4.</td><td>Was follow-up complete?</td><td>No. For the primary outcome, data was available for all 30 patients in the non-operative management group. Two of these patients were lost to follow-up after discharge, and hence no secondary outcome data were available. Of the 47 subjects in the surgical management group, 2 subjects withdrew from the study and 7 could not be reached for follow-up, leaving 38 subjects with secondary outcome data in this group. There is the potential for attrition bias a result of this loss to follow-up.</td></tr>
<tr><td>II.</td><td>What are the results (answer the questions posed below)?</td><td></td></tr>
<tr><td>1.</td><td>How large was the treatment effect?</td><td>

Two of the 30 patients in the non-operative group underwent appendectomy during the initial hospitalization due to failure to improve, for an initial success rate of 93% (95% CI 78-99). One additional patient required an appendectomy for recurrent pain one day after discharge, for a 30-day success rate of 90% (95% CI 79-100); this patient had a normal appendix on pathology with reactive lymph nodes. No patient in this group developed appendiceal rupture or gangrene.
Patients choosing non-operative management had longer LOS, but a shorter time to return to normal activities and fewer days of school missed. Quality of life scores at 30 days were higher in the non-operative management group, but parental satisfaction with care was similar in both groups (Table 1).

Table 1. Secondary outcomes
<table>
<tr><th>Outcome</th><th>Nonoperative (n = 28)</th><th>Surgery (n = 38)</th><th>p-value</th></tr>
<tr><td>LOS, h</td><td>38.0 (31.0-42.0)</td><td>20.0 (16.0-34.0)</td><td>< 0.0001</td></tr>
<tr><td>Days to return to normal activity</td><td>3.0 (2.5-6.5)</td><td>16.5 (9.0-21.0)</td><td>< 0.0001</td></tr>
<tr><td>Days of school missed</td><td>3.0 (2.0-5.0)</td><td>5.0 (3.0-6.0)</td><td>0.008</td></tr>
<tr><td>Child QOL questionnaire score</td><td>93.0 (87.0-96.7)</td><td>87.5 (81.5-93.5)</td><td>0.011</td></tr>
<tr><td>Parent proxy for child QOL questionnaire score</td><td>95.7 (90.8-98.9)</td><td>89.7 (82.6-95.7)</td><td>0.026</td></tr>
<tr><td>Parental satisfaction score</td><td>99.0 (95.8-100.0)</td><td>99.0 (95.9-100.0)</td><td>0.721</td></tr>
<tr><td colspan="4">All data reported as medians (IQR)</td></tr>
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2.	How precise was the estimate of the treatment effect?	See above. This was a small study, and as a result the 95% confidence intervals for the primary outcome were wide, with a low end of 79% for the 30-day success rate.
III.	**How can I apply the results to patient care (answer the questions posed below)?**	
1.	Were the study patients similar to my patient?	Yes. These were pediatric patients with uncomplicated acute appendicitis seen in a large teaching hospital in the US. The results should be applicable to patients seen in our Children's Hospital ED.
2.	Were all clinically important outcomes considered?	Mostly yes. The authors considered 30-day failure rates, LOS, time until return to normal activities, days of school missed, and quality of life at 30 days. They could additionally have assessed healthcare costs and more long-term risks of treatment failure.
3.	Are the likely treatment benefits worth the potential harm and costs?	Uncertain. This was a small, open-label, nonrandomized study and could potentially have been subject to selection bias, performance bias, and observer bias. The results do suggest that selective non-operative management of acute, uncomplicated, pediatric appendicitis is safe and may prevent a significant number of children from requiring surgical intervention. The results also suggest that such a management strategy results in faster return to normal activities and return to school, with similar satisfaction scores. Larger randomized trials will need to be performed to confirm the potential benefits of non-operative management, and potentially longer follow-up should be performed to assess for the potential need for appendectomy beyond 30 days after treatment.

Limitations:

1. **This was a very small study enrolling only 77 patients. The resulting confidence intervals for the outcomes are wide.**

2. **The study was nonrandomized, and the decision to proceed with surgical or non-operative management was at the discretion of the parents. It is possible that children felt to be sicker by the parents were more likely to undergo urgent appendectomy (selection bias). Possible evidence of this is the relatively high rate of perforated (n = 4) and gangrenous (n = 2) appendixes in this group.**

3. **There was significant loss to follow-up for such a small study. Importantly, loss to follow-up was greater in the surgical group (n = 9) than in the non-operative group (n = 2) (attrition bias).**

Bottom Line:

This small, open-label, nonrandomized study suggests that selective non-operative management of acute, uncomplicated, pediatric appendicitis is safe and may prevent a significant number of children from requiring surgical intervention, with a 30-day failure rate of only 10%. The results also suggest that such a management strategy results in faster return to normal activities and return to school, with similar satisfaction scores. Larger randomized trials will need to be performed to confirm the potential benefits of non-operative management, and potentially longer follow-up should be performed to assess for the potential need for appendectomy beyond 30 days after treatment.