Effectiveness of Patient Choice in Nonoperative vs Surgical Management of Pediatric Uncomplicated Acute Appendicitis

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**IMPORTANCE** Current evidence suggests that nonoperative management of uncomplicated appendicitis is safe, but overall effectiveness is determined by combining medical outcomes with the patient’s and family’s perspective, goals, and expectations.

**OBJECTIVE** To determine the effectiveness of patient choice in nonoperative vs surgical management of uncomplicated acute appendicitis in children.

**DESIGN, SETTING, AND PARTICIPANTS** Prospective patient choice cohort study in patients aged 7 to 17 years with acute uncomplicated appendicitis presenting at a single pediatric tertiary acute care hospital from October 1, 2012, through March 6, 2013. Participating patients and families gave informed consent and chose between nonoperative management and urgent appendectomy.

**INTERVENTIONS** Urgent appendectomy or nonoperative management entailing at least 24 hours of inpatient observation while receiving intravenous antibiotics and, on demonstrating improvement of symptoms, completion of 10 days of treatment with oral antibiotics.

**MAIN OUTCOMES AND MEASURES** The primary outcome was the 1-year success rate of nonoperative management. Successful nonoperative management was defined as not undergoing an appendectomy. Secondary outcomes included comparisons of the rates of complicated appendicitis, disability days, and health care costs between nonoperative management and surgery.

**RESULTS** A total of 102 patients were enrolled; 65 patients/families chose appendectomy (median age, 12 years; interquartile range [IQR], 9-13 years; 45 male [69.2%]) and 37 patients/families chose nonoperative management (median age, 11 years; IQR, 10-14 years; 24 male [64.9%]). Baseline characteristics were similar between the groups. The success rate of nonoperative management was 89.2% (95% CI, 74.6%-97.0%) at 30 days (33 of 37 children) and 75.7% (95% CI, 58.9%-88.2%) at 1 year (28 of 37 children). The incidence of complicated appendicitis was 2.7% in the nonoperative group (1 of 37 children) and 12.3% in the surgery group (8 of 65 children) (P = .15). After 1 year, children managed nonoperatively compared with the surgery group had fewer disability days (median [IQR], 8 [5-18] vs 21 [15-25] days, respectively; P < .001) and lower appendicitis-related health care costs (median [IQR], $4219 [$2514-$7795] vs $5029 [$4596-$5482], respectively; P = .01).

**CONCLUSIONS AND RELEVANCE** When chosen by the family, nonoperative management is an effective treatment strategy for children with uncomplicated acute appendicitis, incurring less morbidity and lower costs than surgery.

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Acute appendicitis accounts for 11.4% of pediatric emergency department admissions, with more than 70,000 children hospitalized for it annually in the United States.1,2 Although curative, appendectomy is an invasive procedure requiring general anesthesia with associated perioperative risks and postoperative pain and disability. Children may miss up to 2 weeks of activities and their caregivers may experience a similar disruption to their normal schedule.3–5 Reported rates of perioperative complications in patients undergoing an appendectomy for uncomplicated appendicitis range from 5% to 10%, with serious complications (such as reoperation or readmission) occurring in 1% to 7% of patients.3,4,6–17 Several recent European randomized clinical trials (RCTs) have demonstrated that nonoperative management of appendicitis is medically safe and effective in adults, with a success rate ranging from 63% to 85%.18–23 In addition, a recent European RCT in children demonstrated a 1-year success rate of nonoperative management of 66% and no difference in the rates of complicated appendicitis.24

Although promising, these results may not reflect the family’s assessment of the effectiveness of offering nonoperative management because patient preferences may affect outcomes.25–32 In making a treatment decision involving surgery, patients and families may have strong and varying treatment preferences based on the risks and outcomes that are most important to them such as pain, quality of life, disability, and the avoidance of general anesthesia. In addition, with nonoperative management of appendicitis, success may depend on the patient’s and family’s willingness to accept an ongoing risk for recurrent appendicitis.

The purpose of this study was to evaluate the overall effectiveness of nonoperative management for acute uncomplicated pediatric appendicitis, in the context of engaging the family in the treatment decision. This study used a patient choice design and assessed patient-centered outcomes and health care costs in addition to medical outcomes. We hypothesized that a successful nonoperative management strategy for uncomplicated appendicitis may improve the quality of care related to the treatment of pediatric appendicitis with potentially less morbidity, less disability, and lower costs than surgery.

Methods

Trial Design

This was a prospective patient choice cohort study comparing nonoperative management vs urgent laparoscopic appendectomy in pediatric patients with acute appendicitis. There were 2 planned analyses of this trial. The first analysis to assess feasibility and initial safety was performed after the initial 77 enrolled patients reached 30-day follow-up and has been previously reported.6 The first analysis demonstrated that the success rate of nonoperative management was within the acceptable range; therefore, the trial continued to full enrollment to allow assessment of our primary outcome, the success rate of nonoperative management at 1 year. This article reports the results after completion of trial enrollment and all participants reaching 1-year follow-up. This study was approved by the Nationwide Children’s Hospital Institutional Review Board. Written informed consent and assent (for children aged ≥9 years) were obtained. No stipends were provided for participation; $20 stipends were provided as an incentive to complete each survey after 30 days.

Patients presenting to our hospital from October 1, 2012, through March 6, 2013, who met the following inclusion criteria were approached for enrollment: aged 7 to 17 years; 48 hours or less of abdominal pain; white blood cell count less than 18,000/μL (to convert to ×10⁹ per liter, multiply by 0.001); radiographic evidence of nonruptured acute appendicitis with an appendiceal diameter of 1.1 cm or less without fecalith, abscess, or phlegmon on either ultrasonography or computed tomography; and surgical consultation confirming a clinical diagnosis of suspected acute appendicitis. These inclusion criteria were chosen to minimize the potential for harm as symptoms for longer than 48 hours, a white blood cell count higher than 18,000/μL, and an appendicolith on imaging have all been associated with higher rates of failure of nonoperative management.21,23,33 All patients with a radiology reading of suspected perforation were excluded. Exclusion criteria included diffuse peritonitis on clinical examination, C-reactive protein level higher than 40 mg/L if collected (to convert to nanomoles per liter, multiply by 9.524), a positive pregnancy test, or a history of chronic abdominal pain.

After counseling on the treatment options, eligible patients and their families chose between nonoperative management (nonoperative group) and laparoscopic appendectomy (surgery group). As all patients were younger than 18 years, the parents or legal guardians made the final treatment choice. To minimize bias, all potential participants were evaluated by 1 of 4 surgeons trained in the study methods to confirm eligibility and perform enrollment. Study data were managed using the Research Electronic Data Capture (REDCap) tool.34

Treatment Groups

Patients choosing nonoperative management were admitted to the hospital for observation and to receive intravenous antibiotics (piperacillin sodium–tazobactam sodium or ciprofloxacin hydrochloride and metronidazole hydrochloride if allergic) for a minimum of 24 hours. After having oral food and fluids withheld for at least 12 hours, patients with clinical improvement (decreased reported pain or decreased tenderness on examination) had their diet advanced. When tolerating a regular diet, patients were switched to oral amoxicillin–clavulanate potassium (or ciprofloxacin and metronidazole if allergic) with the first dose given as an inpatient to ensure tolerance. Patients were subsequently discharged with oral antibiotics to complete a 10-day total course. Showing signs of clinical worsening (increased pain or systemic signs of sepsis) or failure to show clinical improvement within 24 hours (decreased pain or tenderness, resolution of nausea/emesis, or improvement in fever curve) was considered a failure and resulted in prompt laparoscopic appendectomy. After discharge, any patient who returned with abdominal pain and had clinical workup or evaluation findings consistent with recur-
rent appendicitis underwent urgent laparoscopic appendectomy. Follow-up was performed at 2 to 5 days, 10 to 14 days, 30 days, 6 months, and 1 year after discharge.

Surgical management consisted of admission to the hospital with prompt initiation of intravenous antibiotics and laparoscopic appendectomy within 12 hours. All appendectomies were performed by pediatric surgeons with anesthesia administered by pediatric anesthesiologists. Patients were instructed to resume activities as tolerated, with resumption of heavy activity or sports (eg, weight lifting, football) 2 weeks postoperatively. Follow-up was performed at 30 days and 1 year after discharge.

Outcomes
The primary outcome was the 1-year success rate of nonoperative management with success defined as not having undergone an appendectomy at 1 year. Secondary outcomes included rates of complicated appendicitis at 1 year; disability days for the child at 1 year, defined as days on which the child did not participate in all of his or her normal activities including gym, recess, sports, and after-school activities; disability days for the parent at 1 year, defined as days until he or she resumed his or her normal schedule; health-related quality-of-life (HRQOL) measures at 1 year using Pediatric Quality of Life Inventory instruments; and appendicitis-related total health care costs at 1 year. A patient was defined as having complicated appendicitis if pathological analysis revealed ruptured, perforated, or gangrenous appendix.

Hospital charges were calculated as a sum of charges from the initial encounter and all clinical encounters within 1 year related to appendicitis or treatment for appendicitis. Charges were converted to costs using ratios of cost-to-charge estimators. Products and services provided prior to enrollment were not included in the calculations. For encounters outside our institution, billable items were itemized and valued using costs from our institution. Costs for visits after the initial visit were adjusted using the US Consumer Price Index medical sector inflation rate (2.2% annual) over the study period. Patient direct and indirect charges were self-reported.

Statistical Analysis
Based on an expected 1-year success rate of nonoperative management of 80%, 37 patients treated nonoperatively were needed to have a 95% confidence interval with a lower limit of 65%, based on the exact binomial distribution. The 65% lower limit was considered the lowest acceptable 1-year success rate to offer nonoperative management to patients in clinical practice.

Variables were described with medians and interquartile ranges (IQRs) or frequencies and percentages and compared using Mann-Whitney U tests, Fisher exact tests, or \( \chi^2 \) tests. Confidence intervals for estimated proportions were calculated using the adjusted Wald method. Kaplan-Meier survival analysis was used to examine time to appendectomy (in months) for the nonoperative group. A sensitivity analysis to evaluate potential health care costs in patients lost to follow-up was performed. For the surgery group, we assumed no additional costs beyond those incurred prior to loss to follow-up. For nonoperative management, assumed costs were equal to the maximum costs in similar patients depending on whether nonoperative management failed or succeeded.

All tests were 2-sided with \( P < .05 \) used to determine statistical significance. All analyses were performed using SAS version 9.3 statistical software (SAS Institute, Inc).

Results
Demographic and Clinical Characteristics
During the study period, 629 patients presented with acute appendicitis, of whom 136 (21.6%) met inclusion criteria (Figure 1). Of 102 patients who were enrolled, 37 chose nonoperative management (median age, 11 years; IQR, 10-14 years; 24 male [64.9%]) and 65 chose surgery (median age, 12 years; IQR, 9-13 years; 45 male [69.2%]). Compared with individuals who chose surgery, individuals who chose nonoperative management were less likely to have been transferred from another institution (28 [43.1%] vs 5 [13.5%]; \( P = .002 \)) and more likely to speak a primary language other than English at home (2 [3.1%] vs 8 [21.6%]; \( P = .004 \) Table 1). There were no other significant differences in baseline characteristics between the groups. In patients choosing surgery, the negative appendectomy rate was 6.2% (4 patients) based on pathology.

Success Rates of Nonoperative Management
The success rate of nonoperative management was 94.6% (95% CI, 81.8%-99.3%) at hospital discharge (35 of 37 children), 89.2% (95% CI, 74.6%-97.0%) at 30 days (33 of 37 children), and 75.7% (95% CI, 58.9%-88.2%) at 1 year (28 of 37 children). At a median follow-up of 21 months, the overall success rate of nonoperative management was 75.7% (28 of 37 patients). A Kaplan-Meier analysis of the success rate of nonoperative management is shown in Figure 2.

Comparison of Outcomes Between Nonoperative Management and Surgery
Compared with the surgery group, the nonoperative group had a longer length of stay (median [IQR], 20 [15-30] vs 37 [29-41] hours, respectively; \( P < .001 \)). Rates of appendicitis-related medical care within 30 days were similar between the groups (Table 2). Two patients in the nonoperative group were readmitted within 30 days and underwent laparoscopic appendectomy for recurrent appendicitis (Table 2).

The rates of complicated appendicitis at 1 year were similar between the nonoperative management and surgery groups (2.7% [1 of 37 children] vs 12.3% [8 of 65 children], respectively; \( P = .15 \) Table 2). The postoperative complication rate at 1 year in patients choosing surgery was 7.7% (5 of 65 patients), with 2 major complications (1 readmission, 1 reoperation). There were no postoperative complications among the nonoperative patients who eventually underwent appendectomy. The HRQOL scores for the nonoperative and surgery groups were similar at 1 year (median [IQR] child-reported scores: 95.7 [89.1-98.9] vs 91.3 [87.0-98.9], respectively; \( P = .31 \); median [IQR] parent-reported scores: 91.9 [87.0-98.9] vs 93.0...
Nonoperative management, compared with surgery, was associated with significantly fewer disability days at 1 year (median [IQR], 8 [5-18] vs 21 [15-25] days, respectively; \( P < .001 \)) and with lower total appendicitis-related health care costs at 1 year (median [IQR], \$4219 [\$2514-\$7795] \) vs \$5029 [\$4596-\$5482], respectively;
In the cost sensitivity analysis, total appendicitis-related health care costs at 1 year remained significantly lower in the group treated nonoperatively than in the surgery group (median [IQR], $4219 [$2691-$6536] vs $4992 [$4688-$5636], respectively; \( P = .01 \)).

**Discussion**

When chosen by the family, nonoperative management with antibiotics alone is an effective treatment strategy for children with uncomplicated appendicitis. It incurs less morbidity and lower costs than surgery. By 1-year follow-up, 75.7% of patients who chose nonoperative management did not undergo an appendectomy. There was no difference in the rate of complicated appendicitis between those who had undergone appendectomy secondary to failure of nonoperative management and those who chose surgery initially. Compared with surgery, nonoperative management was associated with fewer disability days, lower total health care costs, and no difference in HRQOL at 1 year.

Several RCTs investigating nonoperative management of acute appendicitis in adult patients have been reported from non-US countries. The 1-year success rates of nonoperative management in these trials range from 63% to 85%. A meta-analysis of these trials concluded that antibiotic use is a safe initial treatment for appendicitis and that nonoperative management of appendicitis is associated with a significantly lower risk of complications with no difference in the risk of developing complicated appendicitis. These studies confirm that nonoperative management is a viable alternative from the surgeon's perspective, but they did not assess its overall effectiveness from the patient's and family's perspective. Our study demonstrates that an initial nonoperative management strategy is associated with fewer disability days and lower costs at 1 year than urgent appendectomy. These additional results can help to further inform the decision-making process of patients and families choosing between surgery and antibiotics alone.

A recently published RCT of nonoperative management of uncomplicated appendicitis in children by Svensson et al reported a 1-year success rate of 66%. In addition to using a randomized design, there are several notable differences between these studies. First, the study by Svensson and colleagues did not limit eligibility based on duration of symptoms, white blood cell count, or an appendicolith on imaging, which have all been associated with higher rates of failure of nonoperative management. Second, nonoperative patients in the study by Svensson and colleagues received a minimum of 48 hours of intravenous antibiotics and had oral

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**Figure 2. Kaplan-Meier Curve for the Success Rate of Nonoperative Management of Acute Appendicitis**

**Table 2. Comparison of Outcomes Between Nonoperative Management and Surgery**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Nonoperative Management</th>
<th>Surgery</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendicitis-related medical care within 30 d, No. (%)</td>
<td>(n = 37)</td>
<td>(n = 58)</td>
<td></td>
</tr>
<tr>
<td>Outpatient visit or urgent car^a^</td>
<td>4 (10.8)</td>
<td>12 (20.7)</td>
<td>.21</td>
</tr>
<tr>
<td>Emergency department</td>
<td>3 (8.1)</td>
<td>2 (3.4)</td>
<td>.37</td>
</tr>
<tr>
<td>Hospital admission</td>
<td>2 (5.4)</td>
<td>0</td>
<td>.15</td>
</tr>
<tr>
<td>Surgery or other invasive procedure</td>
<td>2 (5.4)</td>
<td>0</td>
<td>.15</td>
</tr>
<tr>
<td>1 y after enrollment (n = 35)</td>
<td>(n = 50)</td>
<td></td>
<td>.001</td>
</tr>
<tr>
<td>Disability days, median (IQR)^b^</td>
<td>8 (5-18)</td>
<td>21 (15-25)</td>
<td>.15</td>
</tr>
<tr>
<td>Complicated appendicitis, No. (%)^c^</td>
<td>1 (2.7)</td>
<td>8 (12.3)</td>
<td>.31</td>
</tr>
<tr>
<td>Health care costs, median (IQR), $</td>
<td></td>
<td></td>
<td>.76</td>
</tr>
<tr>
<td>Initial hospital stay</td>
<td>3641 (2474-4227)</td>
<td>4960 (4588-5373)</td>
<td>.001</td>
</tr>
<tr>
<td>All appendicitis-related care</td>
<td>4219 (2514-7795)</td>
<td>5029 (4596-5482)</td>
<td>.01</td>
</tr>
<tr>
<td>HRQOL questionnaire score, median (IQR)</td>
<td></td>
<td></td>
<td>.67</td>
</tr>
<tr>
<td>Child^d^</td>
<td>95.7 (89.1-98.9)</td>
<td>91.3 (87.0-98.9)</td>
<td>.31</td>
</tr>
<tr>
<td>Parent proxy^e^</td>
<td>91.9 (87.0-98.9)</td>
<td>93.0 (87.0-97.8)</td>
<td>.76</td>
</tr>
</tbody>
</table>

Abbreviations: HRQOL, health-related quality of life; IQR, interquartile range.

^a^ Outpatient visit excludes scheduled follow-up visits with the primary surgical team from the initial inpatient stay.

^b^ Sum of the following: length of stay (in days); number of days of normal activity missed for the child; number of days of normal activity missed for the parent or guardian; and office, emergency department, and inpatient visits.

^c^ Sample sizes are 37 for the nonoperative group and 65 for the surgery group.

^d^ Sample sizes are 17 for the nonoperative group and 32 for the surgery group.

^e^ Sample sizes are 18 for the nonoperative group and 34 for the surgery group.
food and fluids withheld for 24 hours compared with a minimum of 24 hours of intravenous antibiotics and 12 hours of withholding oral food and fluids in our study. Our nonoperative treatment protocol was developed to minimize length of stay as patients undergoing a laparoscopic appendectomy for uncomplicated appendicitis in the United States usually spend 1 day in the hospital.

Engaging families in shared decision making in pediatric clinical care has been shown to improve medical outcomes. We believe that the results of our study reflect the effectiveness of offering nonoperative management to patients and their families in clinical practice for 2 reasons. First, the patient choice design allows the patient’s and family’s preferences to be aligned with their choice of therapy, thereby minimizing the potential effects of treatment preferences on outcomes. For families who do not want to accept the risk of recurrent appendicitis, nonoperative management may potentially harm the child. For example, if a family is so afraid of a recurrence that they visit the emergency department every time their child has abdominal pain, then their child will likely undergo increased imaging and will eventually undergo an appendectomy. In this case, letting them choose an appendectomy up front may be the better choice for that child. Second, in contrast to an RCT in which preferences may deter families from enrolling in the trial, the patient choice design can lead to broader enrollment among eligible patients. In our trial, 82.9% of approached eligible patients enrolled and no appendectomies were performed without a clinical presentation suggesting that a patient’s appendicitis had recurred. In contrast, the study by Svensson et al.,24 only 40% of approached eligible participants agreed to enroll and 25% of patients in the nonoperative management group underwent appendectomy at surgeon and parental discretion within 1 year without developing recurrent appendicitis. The high enrollment rate and alignment of treatment choice with preferences in our study allow our results to be generalizable to clinical practice.

Treatment of several inflammatory intra-abdominal diseases has changed from primarily surgical management to initial medical management, with patients who fail medical management subsequently undergoing surgery. These include intra-abdominal abscesses from Crohn disease, tubo-ovarian abscesses, and acute diverticulitis. These changes in practice have evolved because most of these patients can be effectively treated with medical management, with minimal adverse effects occurring in patients who fail medical management and require surgery. Based on our study and those reported in the literature, treatment of uncomplicated appendicitis appears to be similar. Initial treatment with antibiotics alone allows 3 in 4 patients to avoid surgery, with 1 in 4 patients requiring appendectomy for failure of antibiotic therapy. An initial trial of nonoperative management does not increase the rate of complicated appendicitis and is associated with fewer surgical complications, fewer disability days, and lower costs.

Compared with an RCT, the patient choice design may lead to unbalanced patient characteristics that may partially account for treatment differences. In our trial, more patients choosing surgery were transferred from other institutions, and patients with parents or guardians who spoke a primary language other than English were more likely to select nonoperative management. These differences between the groups are likely due to differences in preferences of the families. Patients who were transferred from other institutions came farther distances and many expressed concerns about the distance and time necessary to come back if the appendicitis were to recur. The higher proportion of parents who spoke a primary language other than English choosing nonoperative management is likely due to cultural values to avoid surgery if possible. Accounting for these real-life concerns is important in establishing the true effectiveness of a treatment in clinical practice. The patient choice design allows a therapy to be aligned with preferences of the patient and his or her family, thereby minimizing the potential negative effects of preferences.

The patient choice design creates the possibility of selection bias on the part of the medical team. We attempted to minimize the bias introduced by using well-defined inclusion and exclusion criteria and a standardized scripted consenting process. Another limitation of the patient choice design is that the treatment choice may be affected by a specific patient characteristic. There were no significant pretreatment differences between the groups with the exception of transfer status and primary language as discussed earlier. In addition, our reported cost analysis excluded all costs incurred prior to enrollment (including outside hospital emergency department charges) to minimize any effect of a higher proportion of surgery patients having been transferred. Finally, differences in disability days may vary based on the recommendations for activity resumption used in clinical practice by different surgeons.

Conclusions

When an initial nonoperative management strategy was chosen by patients and families, 3 in 4 children with uncomplicated appendicitis avoided surgery at 1 year. Compared with urgent appendectomy, nonoperative management was associated with fewer disability days and lower health care costs at 1 year and no difference in rates of complicated appendicitis or reported HRQOL.
Patient Choice in Management of Pediatric Appendicitis

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Previous Presentation: The interim analysis was presented at Clinical Congress 2014 of the American College of Surgeons; October 29, 2014; San Francisco, California.

REFERENCES


The question of safety has been addressed in adult and pediatric trials, and there has been emerging consensus that in a subset and have outcomes superior to those previously reported using the selection criteria set out in this study.

The authors cite decreases in morbidity and cost in nonoperative treatment of appendicitis in comparison with operative therapy. Morbidity was determined by days of disability. This included length of stay, days of normal activity missed by the patient and caretaker, and office, emergency department, and inpatient visits. The length of hospital stay was actually shorter in the operative group. However, return to normal activity was significantly longer in the operative group. This was in large part due to activity restrictions imposed after surgery by the surgeon. Normal activity was missed for 2 weeks postoperatively. This significantly increased the total number of days of disability in the operative group.

There was a clear cost benefit with nonoperative treatment. The mean cost difference was $710 between the 2 groups, which constitutes significant health care savings when applied to the more than 70,000 children hospitalized annually for appendicitis.

Interestingly, this study showed a preference for non-English speakers to choose nonoperative management over operative management, which should be further explored. Cultural bias plays an important role in medical decision making, and an awareness of this bias by the physician is necessary.