A meta-analysis comparing conservative treatment versus acute appendectomy for complicated appendicitis (abscess or phlegmon)

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Background. No standardized approach is available for the management of complicated appendicitis defined as appendiceal abscess and phlegmon. This study used meta-analytic techniques to compare conservative treatment versus acute appendectomy.

Methods. Comparative studies were identified by a literature search. The end points evaluated were overall complications, need for reoperation, duration of hospital stay, and duration of intravenous antibiotics. Heterogeneity was assessed and a sensitivity analysis was performed to account for bias in patient selection.

Results. Seventeen studies (16 nonrandomized retrospective and 1 nonrandomized prospective) reported on 1,572 patients: 847 patients received conservative treatment and 725 had acute appendectomy. Conservative treatment was associated with significantly less overall complications, wound infections, abdominal/pelvic abscesses, ileus/bowel obstructions, and reoperations. No significant difference was found in the duration of first hospitalization, the overall duration of hospital stay, and the duration of intravenous antibiotics. Overall complications remained significantly less in the conservative treatment group during sensitivity analysis of studies including only pediatric patients, high-quality studies, more recent studies, and studies with a larger group of patients.

Conclusion. The conservative management of complicated appendicitis is associated with a decrease in complication and reoperation rate compared with acute appendectomy, and it has a similar duration of hospital stay. Because of significant heterogeneity between studies, additional studies should be undertaken to confirm these findings. (Surgery 2010;147:818-29.)

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Although appendicitis is a common pathology, it can still become a challenging clinical problem. Most patients with acute appendicitis present early, and prior to developing complications, these patients are treated with acute appendectomy (AA). A group of patients presents with diffuse peritonitis caused by free perforation of the inflamed appendix into the peritoneal cavity, and they should be managed with an urgent operation. But another group of patients presents later, with appendicitis complicated by a local or contained perforation and with an appendiceal abscess or inflammatory mass. These patients will often have a palpable mass or at least a mass observed on computed tomography or ultrasonography, whether a contained phlegmon (inflammatory mass) or an actual abscess.

When managing a patient with complicated appendicitis who belongs to the latter group, the clinical dilemma exists whether to treat the patient conservatively with antibiotics or proceed with immediate operation. Conservative treatment (CT) may include radiologic drainage of a periappendiceal abscess. Moreover, after successful conservative management, some surgeons proceed with elective interval appendectomy (IA), whereas others do not. Currently, no consensus exists among surgeons regarding the optimal treatment for patients with complicated appendicitis.

The purpose of this study was to compare the outcomes of patients presenting with complicated appendicitis who underwent CT with or without IA.
versus patients who underwent AA. Meta-analytic techniques were used to assess each technique and to explain differences between the study methodologies and selection criteria. The limitations of this meta-analysis are also discussed.

METHODS

Study selection. A database search using Medline, EMBASE, Ovid, and Cochrane was performed on all studies to compare CT and AA for patients who presented with complicated appendicitis. The following MeSH search headings were used: “complicated appendicitis,” “perforated appendicitis,” “appendiceal abscess,” “appendiceal mass,” “conservative treatment,” “acute appendectomy,” “interval appendectomy,” “comparative study,” and “treatment outcome.” The above terms and their combinations were also searched as text words. The “related articles” function was used to broaden the search, and all abstracts, studies, and citations scanned were reviewed. The references of the articles acquired were also searched by hand. No language restrictions were made. The latest date for this search was June 2, 2008.

Data extraction. Two reviewers (C.S. and P.S.) extracted the following from each study independently: first author, year of publication, study population characteristics, study design, inclusion and exclusion criteria, matching criteria, number of subjects treated with each technique, mean duration of intravenous antibiotics and hospital stay, conversion rates, outcomes, and complications with each treatment. The 2 reviewers reached 100% agreement.

Inclusion criteria. For studies to be included in the analysis, the must fulfill the following criteria: (1) compare CT to AA for complicated appendicitis; (2) report on at least 1 outcome measure mentioned below; (3) document the treatment clearly as “conservative treatment” or “acute appendectomy,” and define the inclusion criteria for each group; (4) report clearly the indications for treatment for each of the “conservative treatment” and “acute appendectomy” groups; and (5) include either the study of greater quality or the most recent publication in the analysis when 2 studies were reported by the same institution and/or authors.

Exclusion criteria. Studies were excluded from the analysis if (1) the outcomes of interest were not reported clearly for the 2 different modalities of treatment; (2) it was impossible to extrapolate or calculate the necessary data from the published results; (3) patients were included with acute, uncomplicated appendicitis or with diffuse peritonitis caused by a freely perforated appendix; and (4) a considerable overlap was found among authors, centers, or patient cohorts evaluated in the published literature.

Outcomes of interest and definitions. Complicated appendicitis was defined as appendicitis complicated by a local or contained perforation with an appendiceal abscess or mass formation. Patients with acute, uncomplicated appendicitis and patients with diffuse peritonitis caused by a freely perforated appendix were excluded.

The CT group was composed of patients with complicated appendicitis who either failed CT or resolved their symptoms with antibiotic treatment and subsequently had IA or no later appendectomy. The AA group was composed of patients who had immediate operative exploration.

The following outcomes were used to compare patients in the CT group versus the AA group:

1. Duration of hospital stay comprised the mean duration of hospital stay during the first hospital admission and the overall duration of hospital stay. The overall duration of hospital stay included hospitalizations for IA and complications.

2. Duration of antibiotics was defined as the average number of days the patient had intravenous antibiotic therapy as an inpatient but excluded any oral courses completed after discharge.

3. Complications included overall complications and wound infection defined as superficial or deep after wound closure but excluded any abscess formation, abdominal/pelvic abscess defined as a collection of fluid in the pelvis or abdomen diagnosed on radiologic imaging or at reoperation or at IA, ileus or bowel obstruction diagnosed after CT or postoperatively, pneumonia, sepsis/diffuse peritonitis, deep venous thrombosis/pulmonary embolism, death, adhesions, and fistula formation. These particular complications were chosen because they were reported most commonly by the individual studies to compare the 2 groups.

4. Reoperations comprised reoperations needed as a result of postoperative complications after IA or AA, and this group included reoperations during the same hospitalization and/or during any readmissions.

Statistical analysis. The meta-analysis was performed in line with recommendations from the Cochrane Collaboration and the Quality of Reporting of Meta-analyses guidelines. A statistical analysis for dichotomous variables was conducted using the odds ratio (OR) as the summary statistic. The OR represents the odds of an adverse event occurring in the CT group compared with the AA group. An OR of less than 1 favored the CT, and the point
estimate of the OR was considered to be statistically significant at the $P < .05$ level if the 95% confidence interval (CI) did not include the value 1.

For continuous variables, such as duration of hospital stay or duration of antibiotics, a statistical analysis was conducted using the weighted mean difference (WMD) as the summary statistic. WMDs summarize the differences between the two groups with respect to continuous variables, accounting for sample size, and was reported with 95% CIs. For studies that presented continuous data as means and range values, the standard deviations (SDs) were calculated using statistical algorithms and checked using “bootstrap” resampling techniques. Thus, all continuous data were standardized for analysis. For WMDs, the negative values favored the CT group, whereas positive values favored the AA group.

In a random-effect model, it is assumed that a variation exists between studies, and therefore the calculated OR has a more conservative value. The random-effect model is preferable when meta-analytic techniques are used in surgical research for a given surgical technique; each center has its own patient selection criteria, and these patients have different risk profiles. Yate’s correction was used for those studies that contained a zero in 1 cell for the number of events of interest in 1 of the 2 groups. These “zero cells” created problems with the computation of ratio measure and its standard error of the treatment effect. This problem was resolved by adding the value 0.5 in each cell of the $2 \times 2$ table for the study in question. If no events were found for both CT and AA groups for an outcome of interest, the study was discarded from the meta-analysis of that outcome.

When calculating the OR and WMD, heterogeneity (HG) between individual studies was considered to be statistically significant at the $P < .10$. 

**Fig 1.** Study selection flowchart.
level. Three strategies were used to assess heterogeneity quantitatively. First, graphic exploration with funnel plots was used to evaluate publication bias.4,7 Second, data were reanalyzed using both random-effect and fixed-effect models. Third, a sensitivity analysis was conducted using the following subgroups: studies including only pediatric patients, studies of greater quality, those published during or after 2001, and studies with a total number of patients more than 90.

The quality of the studies was assessed by use of the Newcastle-Ottawa Scale8 with some modifications to match the needs of this study.9,10 The quality of the studies was evaluated by 2 assessors (C.S. and P.S.) by examining the following 3 factors: patient selection, comparability of the 2 study groups, and assessment of outcome. Studies that achieved more than 6 points (from a maximum of 12) were considered to be of greater quality.

An analysis was conducted by using the statistical software Review Manager Version 4.2 (The Cochrane Collaboration, Software Update, Oxford, UK).

RESULTS

Eligible studies. Using the search key words listed above, 74 publications were identified. In all, 48 studies were excluded after reviewing the title and abstract. These results included 21 studies reporting on only 1 modality of treatment, 11 studies reporting on appendiceal mass/abscess formation, and 5 studies reporting on histologic or radiologic evaluation of appendiceal specimens. Furthermore, the excluded studies consisted of 5 case-based discussions on appendiceal masses/abscesses and 6 studies that did not define the groups of interest clearly, and the data were not extractable. This left 26 studies that were investigated in detail in full (Fig 1).11-36 An examination of the references of these studies did not provide any more studies for evaluation. Of these 26 studies, 3 studies27,35,36 were excluded because their AA group included patients who presented with diffuse peritonitis caused by a freely perforated appendix. Two studies15,33 were excluded because they compared appendectomy versus antibiotic therapy for acute, noncomplicated appendicitis. Two studies11,26 were excluded because the 2 groups of interest were not defined clearly. One study30 was excluded because the data were not extractable suitably to meet the inclusion criteria of this meta-analysis. Finally, 1 study19 was excluded because it was a review of the studies already used in this meta-analysis.

A total of 17 studies12-14,16-18,20-25,28,29,31,32,34 published between 1969 and 2007 fulfilled the selection criteria for this meta-analysis. A summary of the included studies is presented in Table I.
criteria and were included in this meta-analysis. In all, the meta-analysis included 16 nonrandomized, retrospective studies and 1 nonrandomized prospective study. An analysis was performed on 1,572 patients, of which 847 (53.9%) patients received CT and 725 (46.1%) patients underwent AA for complicated appendicitis. Of the 847 patients who received CT, 483 proceeded to have interval appendectomy. The study characteristics are shown in Table I.

## Results from overall meta-analysis

The results from the meta-analysis of the studies with regard to complications, duration of hospital stay, duration of antibiotics, and reoperations for CT versus AA are summarized in Table II.

### Meta-analysis of duration of antibiotics and hospital stay

Four studies reported on the duration of intravenous antibiotics given to patients, which was found to be similar between CT and AA (WMD, 1.02; 95% CI, −1.30–3.34; P = .39), but significant heterogeneity between studies was observed (P < .001; Fig 2).

No difference was found in the duration of first hospitalization (WMD, 0.49; 95% CI, −2.70–3.69; P = .76), which was reported by 8 studies. In addition, no difference was found in the overall duration of hospitalization (WMD, 0.04; 95% CI, −3.87–3.95; P = .98), which was reported by 7 studies. Heterogeneity was observed between studies for these 2 outcomes (P < .001; Fig 2).

### Meta-analysis of complications

Sixteen studies reported on complications comparing the 2 treatment approaches, and they were found to be more common in the AA appendectomy group compared with the CT group (OR, 0.24; 95% CI, 0.13–0.44; P < .001), and heterogeneity between studies was observed (P < .001; Fig 3).

Specifically, a greater incidence of ileus/bowel obstruction was found in the AA group compared with the CT group (OR, 0.35; 95% CI, 0.17–0.71; P = .004), with no heterogeneity between studies (Fig 3). In addition, the AA group was found to have a greater rate of abdominal/pelvic abscess formation (OR, 0.19; 95% CI, 0.07–0.58; P = .003), with heterogeneity between studies (P = .003; Fig 4). Finally, wound infection was found to be more common in the AA group compared with the CT group (OR, 0.28; 95% CI, 0.13–0.60; P = .001). This finding was associated with heterogeneity between studies (P = .04; Fig 4).

No difference was shown between the 2 groups when comparing pneumonia (OR, 1.11; P = .89), sepsis/diffuse peritonitis (OR, 0.54; P = .36), deep venous thrombosis/pulmonary embolism (OR,
0.37; $P = .20$), mortality (OR, 0.70; $P = .67$), adhesions (OR, 3.35; $P = .39$), and fistula formation (OR, 0.22; $P = .07$).

Meta-analysis of reoperations. Four studies$^{13,18,20,25}$ compared the reoperation rate between the AA group and IA; reoperation was found to be greater in the AA group (OR, 0.17; 95% CI, 0.04--0.75; $P = .02$). This finding was not associated with significant heterogeneity between studies (Fig 5).

Sensitivity analysis. The sensitivity analysis (Table III) included 8 studies$^{13,17,18,21-23,31}$ that considered only pediatric patients and 11 studies$^{12,13,16,20-23,29,31,32,34}$ that scored more than 6 points on the modified Newcastle-Ottawa scale. Furthermore, we included 8 studies$^{12,14,22,23,29,31,32,34,37}$ published during or after 2001 and 8 studies$^{12,20,22,25,28,29,31,34}$ with a total number of patients more than 90.

Studies reporting on pediatric patients. An analysis of the studies that included only pediatric patients$^{13,17,18,21-23,31}$ revealed that, compared with the CT group, the AA group had a greater rate of overall complications (OR, 0.21; 95% CI, 0.11--0.38; $P < .001$), wound infections (OR, 0.22; 95% CI, 0.07--0.66; $P = .007$), and abdominal/pelvic abscess formation (OR, 0.11; 95% CI, 0.04--0.35; $P < .001$). None of these findings was related with significant heterogeneity between studies. No differences were found between the 2 groups in the duration of first hospitalization (WMD, 2.68; $P = .36$), ileus/bowel obstruction (OR, 0.58; $P = .47$), and reoperations (OR, 0.17; $P = .10$).

High-quality studies ($>6$ stars). An analysis of the high-quality studies$^{12,13,16,20-23,29,31,32,34}$ showed that the AA group had a greater rate of the following findings: overall complications (OR, 0.15; 95% CI, 0.06--0.33; $P < .001$) with heterogeneity between studies ($P < .001$), wound infections (OR, 0.27; 95% CI, 0.12--0.64; $P = .003$) without heterogeneity between studies, and abdominal/pelvic abscess formation (OR, 0.16; 95% CI, 0.05--0.51; $P = .002$) with heterogeneity between studies ($P = .03$). No differences were found between the 2 groups in the duration of first hospitalization (WMD, 0.71; $P = .68$), ileus/bowel obstruction (OR, 0.45; $P = .07$), and reoperations (OR, 0.24; $P = .17$).

Studies published in or after 2001. More recent reports$^{12,14,22,23,29,31,32,34}$ revealed that the AA group had more overall complications (OR, 0.13; 95% CI, 0.05--0.33; $P < .001$), wound infections (OR, 0.43; 95% CI, 0.18--1.01; $P = .05$), and abdominal/pelvic abscesses (OR, 0.10; 95% CI, 0.03--0.32; $P < .001$) compared with the CT group.
Heterogeneity was observed between studies for the first finding ($P < .001$) but not for the latter 2 findings. No significant differences were found in the duration of first hospitalization (WMD, 0.24; $P = .90$) and ileus/bowel obstruction (OR, 0.45; $P = .08$).

Studies reporting on more than 90 patients. An analysis of the studies with more patients revealed that the AA group had increased overall complications (OR, 0.16; 95% CI, 0.07–0.34; $P < .001$) with significant heterogeneity between studies ($P < .001$), more wound infections (OR, 0.30; 95% CI, 0.11–0.80; $P = .02$) with significant heterogeneity between studies ($P = .02$), more abdominal/pelvic abscesses formation (OR, 0.24; 95% CI, 0.07–0.83; $P = .02$) with significant heterogeneity between studies ($P = .002$), and more ileus/bowel obstructions (OR, 0.33; 95% CI, 0.15–0.71; $P = .005$) without significant heterogeneity between studies. No significant differences were found between the 2 groups regarding the duration of first hospitalization (WMD, −1.39; $P = .06$) and reoperations (OR, 0.18; $P = .10$).

Publication bias. A funnel plot of all the studies used in the meta-analysis reporting on wound infections is shown in Fig 6, A. This figure is a scatter plot of the treatment effects estimated from individual studies plotted on the horizontal axis (OR) against the standard error of the estimate shown on the vertical axis (SE[logOR]). All studies except 2 lie inside the 95% CIs and are distributed evenly about the vertical, showing no evidence of publication bias. Heterogeneity was observed among the studies ($P = .04$). When only high-quality studies were considered (Fig 6, B), all studies lie within the 95% CIs and are distributed evenly about the vertical, showing no evidence of publication bias. No significant heterogeneity was found between the studies of this subgroup.

**DISCUSSION**

No standardized approach is available to the management of patients who present with appendicitis complicated by a local or contained perforation and with an appendiceal abscess or mass
formation. Traditionally, appendectomy was considered the treatment of choice for complicated appendicitis, based on the surgical principle of removing the offending organ to resolve infection. However, the current meta-analysis showed that CT of complicated appendicitis results in a decreased overall complication rate compared with AA. Specifically, the CT group had fewer wound infections, abdominal/pelvic abscesses, and ileus/bowel obstructions. Furthermore, the CT group was found to have less reoperations compared with the AA group.

No significant differences were found between the CT group and the AA group regarding the duration of intravenous antibiotics and the duration of first hospitalization. If subsequent admissions (including those for IA and complications) were included, still there were no significant differences between the 2 groups. Even though conservative management seems more complex and
requires multiple procedures and hospitalizations, it is associated with less morbidity and a lesser duration of overall hospital stay.

CT seems to be a safer option for complicated appendicitis. This observation may be because an operation at the peak of the inflammatory process may result in the subsequent stimulation of an already primed inflammatory system with excessive activation of the cytokine cascade. Overstimulation of the inflammatory response may result in complications and morbidity for the patient. An appendectomy can be delayed for a later stage, when the inflammation has subsided and the patient is appropriately prepared. The conservative approach aims at localizing the inflammatory process and decreasing the risk of abscess formation, which allows time for the edematous inflamed bowel to recover.

The arguments for acute exploration are that the illness is dealt with in a single admission, at a time when the benefit is most apparent to the patient, and the risk of recurrent appendicitis is resolved. Furthermore, if conservative management of complicated appendicitis is not successful, then it may result in substantial morbidity for patients. The predictive factors of CT failure should be examined to direct treatment to the appropriate patients. Nadler et al suggested that patients with a phlegmon on imaging tests as opposed to an abscess are more likely to respond to conservative management. These authors also suggested that the need for abscess drainage increases the failure rate, perhaps because of inadequate source control. Kogut et al suggested that an increased initial band count of ≥15% is associated with an

Table III. Results of sensitivity analysis comparing CT versus AA*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies</th>
<th>Number of patients</th>
<th>OR/ WMD</th>
<th>95% CI</th>
<th>P value</th>
<th>HG</th>
<th>Chi-squared</th>
<th>HG P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studies reporting on pediatric patients</td>
<td>Duration of first hospitalization (days)</td>
<td>3</td>
<td>237</td>
<td>2.68</td>
<td>-3.09–8.44</td>
<td>.36</td>
<td>40.58</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Overall complications</td>
<td>7</td>
<td>473</td>
<td>0.21</td>
<td>0.11–0.38</td>
<td>&lt;.001</td>
<td>5.98</td>
<td>.42</td>
<td></td>
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<tr>
<td>Wound infection</td>
<td>5</td>
<td>315</td>
<td>0.22</td>
<td>0.07–0.66</td>
<td>.007</td>
<td>4.24</td>
<td>.38</td>
<td></td>
</tr>
<tr>
<td>Abdominal/pelvic abscess</td>
<td>4</td>
<td>334</td>
<td>0.11</td>
<td>0.04–0.35</td>
<td>&lt;.001</td>
<td>0.65</td>
<td>.88</td>
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</tr>
<tr>
<td>Ileus/bowel obstruction</td>
<td>4</td>
<td>256</td>
<td>0.58</td>
<td>0.14–2.48</td>
<td>.47</td>
<td>3.98</td>
<td>.26</td>
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<tr>
<td>Reoperation</td>
<td>2</td>
<td>139</td>
<td>0.17</td>
<td>0.02–1.37</td>
<td>.10</td>
<td>0.01</td>
<td>.94</td>
<td></td>
</tr>
<tr>
<td>Studies published in or after 2001</td>
<td>Duration of first hospitalization (days)</td>
<td>6</td>
<td>589</td>
<td>0.24</td>
<td>-3.63–4.10</td>
<td>.90</td>
<td>144.12</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Overall complications</td>
<td>7</td>
<td>639</td>
<td>0.15</td>
<td>0.06–0.33</td>
<td>&lt;.001</td>
<td>34.81</td>
<td>&lt;.001</td>
<td></td>
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<tr>
<td>Wound infection</td>
<td>6</td>
<td>600</td>
<td>0.27</td>
<td>0.12–0.64</td>
<td>.003</td>
<td>9.62</td>
<td>.14</td>
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<td>Abdominal/pelvic abscess</td>
<td>5</td>
<td>729</td>
<td>0.16</td>
<td>0.05–0.51</td>
<td>.002</td>
<td>12.05</td>
<td>.03</td>
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<tr>
<td>Ileus/bowel obstruction</td>
<td>5</td>
<td>547</td>
<td>0.45</td>
<td>0.19–1.07</td>
<td>.07</td>
<td>4.48</td>
<td>.35</td>
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<tr>
<td>Reoperation</td>
<td>2</td>
<td>181</td>
<td>0.24</td>
<td>0.03–1.89</td>
<td>.17</td>
<td>0.06</td>
<td>.81</td>
<td></td>
</tr>
<tr>
<td>Studies reporting on more than 90 patients</td>
<td>Duration of first hospitalization (days)</td>
<td>5</td>
<td>641</td>
<td>-1.39</td>
<td>-2.86–0.08</td>
<td>.06</td>
<td>6.92</td>
<td>.14</td>
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<tr>
<td>Overall complications</td>
<td>8</td>
<td>1,075</td>
<td>0.16</td>
<td>0.07–0.34</td>
<td>&lt;.001</td>
<td>36.61</td>
<td>&lt;.001</td>
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<tr>
<td>Wound infection</td>
<td>6</td>
<td>805</td>
<td>0.30</td>
<td>0.11–0.80</td>
<td>.02</td>
<td>13.39</td>
<td>.02</td>
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<tr>
<td>Abdominal/pelvic abscess</td>
<td>6</td>
<td>835</td>
<td>0.24</td>
<td>0.07–0.83</td>
<td>.02</td>
<td>19.17</td>
<td>.002</td>
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<tr>
<td>Ileus/bowel obstruction</td>
<td>5</td>
<td>786</td>
<td>0.53</td>
<td>0.15–0.71</td>
<td>.005</td>
<td>3.11</td>
<td>.54</td>
<td></td>
</tr>
<tr>
<td>Reoperation</td>
<td>2</td>
<td>224</td>
<td>0.18</td>
<td>0.02–1.37</td>
<td>.10</td>
<td>0.26</td>
<td>.61</td>
<td></td>
</tr>
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</table>

*Statistically significant results are shown in bold. An OR < 1 or a WMD < 0 favored the CT group.

<table>
<thead>
<tr>
<th>OR</th>
<th>WMD</th>
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<td>DVT, Deep venous thrombosis; PE, pulmonary embolism.</td>
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</table>
increased likelihood of failure and complications. Subsequent studies are required to examine the possible predictive factors for failed conservative management.

The need for an IA after successful conservative management of complicated appendicitis also remains controversial. Without interval appendectomy, there is a risk of recurrent appendicitis and missed pathologic findings (eg, Meckel’s diverticulitis, Crohn’s disease, and malignancy). In contrast, some authors have challenged the necessity of an IA because of the low risk of recurrent appendicitis and the potential complications of an elective operation.

Studies have suggested that patients with complicated appendicitis should be treated expectantly with antibiotics for a period of time and that those patients whose symptoms fail to resolve should
have elective appendectomy is not undertaken, patients should be counseled about the possibility of a recurrence of appendicitis and encouraged to seek medical attention early should symptoms occur.\textsuperscript{26,28,43} Patients older than 40 years of age who have not undergone appendectomy should be followed-up with colonoscopy or computed tomography to exclude malignancy.\textsuperscript{28}

A careful interpretation of the results of this study is required because of the retrospective nature of the included studies and the heterogeneity found between individual studies that persisted during sensitivity analysis. The heterogeneity may have resulted because the included studies have not specifically considered or analyzed the effects of some potentially confounding variables, such as demographic characteristics, interim treatments, or laboratory features. Also, there may have been differences in methodology between studies (eg, what defines failure of CT and the differences in antibiotic regimens).

Furthermore, in some centers, the patients in the AA group may be more likely to be operated urgently because they may be sicker compared with the patients treated conservatively, and the increased complications of the AA group may have resulted from their initial disease process. Each study used a different set of criteria to determine which patients are treated by which approach. Some studies may have not controlled for inherent differences in the clinical status of the patients treated conservatively versus those treated with AA (eg, duration of symptoms, inflammatory markers, heart rate, and temperature).

Critics argue that meta-analyses “reinforce the inherent systematic biases of the studies, produce spurious statistical stability and discourage further research.”\textsuperscript{48,49} In contrast, it can be argued that pooling the results from many studies and statistical quantification may provide an “excellent tool for identifying reasons for variability and inconsistency” and that the finding of heterogeneity “sets the stage for further research on a given topic.”\textsuperscript{50} A meta-analysis of nonrandomized studies is useful in the absence of randomized, controlled trials as well as to guide researchers toward properly informed randomization in future studies.

Additional randomized, controlled trials or prospective analyses are needed to compare CT and AA for complicated appendicitis before definitive conclusions can be made. These studies should have predefined entry and outcome criteria to be less prone to biases. We hope that our study will promote subsequent research on this important subject.

In conclusion, this meta-analysis showed that conservative management of complicated appendicitis, with or without IA, is associated with a decreased complication and reoperation rate compared with AA. Specifically, CT is associated with less wound infections, abdominal/pelvic abscesses, and ileus/bowel obstructions. Furthermore, CT has similar duration of hospital stay and duration of intravenous antibiotics compared with AA, but because of the heterogeneity between studies and the potential for significant bias arising from the included studies, subsequent studies should be conducted to confirm these findings.

REFERENCES


