Laparoscopic vs Open Appendectomy in Older Patients

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Hypothesis: The results of a meta-analysis of individual studies comparing laparoscopic vs open appendectomy in older patients may guide the choice of surgical approach.

Design: Meta-analysis.

Setting: Academic research.

Patients: MEDLINE, EMBASE, Web of Science, and Cochrane databases were searched for comparative studies of older patients with a diagnosis of acute appendicitis.

Main Outcome Measures: Primary outcomes were postoperative mortality and overall morbidity. Secondary outcomes were operative time, length of hospital stay, postoperative wound infection, and intra-abdominal collection. Using the lowest threshold from the articles included, older patients were defined as those older than 60 years.

Results: Analyzed were 6 studies comprising 15,852 appendectomies (4,398 laparoscopic and 11,454 open procedures). Laparoscopic appendectomy was associated with significant reductions in postoperative mortality (pooled odds ratio, 0.24; 95% CI, 0.15-0.37), postoperative complications (pooled odds ratio, 0.61; 95% CI, 0.50-0.73), and length of hospital stay (weighted mean difference, −0.51 days; 95% CI, −0.64 to −0.37 days) (P < .05 for all). No significant group differences were observed in operative time, postoperative wound infection, or intra-abdominal collection.

Conclusions: In older patients, laparoscopic appendectomy is associated with reduced postoperative mortality and morbidity, although randomized data are required to infer causality. A health economic analysis with quality-of-life metrics is needed to investigate potential benefits of the reduced length of hospital stay observed following laparoscopic appendectomy in this cohort.

Appendicitis is one of the most common causes of abdominal pain in the Western world, with a reported lifetime risk of approximately 8%. In 1983, Semm described a laparoscopic approach to appendectomy, sparking ongoing debate about the merits of this approach compared with the traditional open method by McBurney and Spenge. A meta-analysis among the general population demonstrated several benefits of the laparoscopic approach, including decreased postoperative wound infection, postoperative pain, and length of hospital stay. However, an increased incidence of intrabdominal abscess formation and a longer operative time have prevented the universal adoption of laparoscopic appendectomy as the gold standard technique among the general population.

The incidence of acute appendicitis is highest in the second and third decades of life, but the condition occurs at all ages. Older patients are increasing in number in the United Kingdom and by 2035 will represent almost one-quarter of the total population. Investigators have highlighted the difficulties of diagnosing appendicitis in older patients, of whom one-quarter have typical symptoms, one-third are seen after significant delay in seeking medical attention, and only half are diagnosed correctly on admission. Compared with younger patients, older patients with acute appendicitis have significantly increased rates of postoperative morbidity and mortality.

Therefore, appendicitis in older patients is a distinct diagnostic and therapeutic challenge and merits a focused analysis because the relative benefits of different operative techniques in this cohort remain poorly understood. The objective of this study is to provide a quantitative summary of the benefits of laparoscopic vs open appendectomy in older patients.

Methods

Study Design

A systematic literature search was performed of MEDLINE (January 1, 1950, through September 1, 2011), EMBASE (January 1, 1974, through
September 1, 2011), Web of Science (January 1, 1990, through September 1, 2011), and Cochrane (2011 issue 9) databases. Used in combination with the Boolean operators AND or OR were the search terms laparoscopy, appendectomy, appendectomy, open, elder, and over 60 and the Medical Subject Headings aged, laparoscopy, appendectomy and appendicitis, evidence-based medicine, and evidence-based practice. The electronic search was supplemented by a hand-search of published abstracts since January 1, 2003, onward from the European Association for Endoscopic Surgery, the Society for Academic and Research Surgery, the Association of Surgeons of Great Britain and Ireland, the American College of Surgeons, the Society for Surgery of the Alimentary Tract, the Association of Laparoscopic Surgeons of Great Britain and Ireland, and the Society of American Gastrointestinal and Endoscopic Surgeons. Reference lists for all relevant studies were reviewed, and the search included the Current Controlled Trials register (http://www.controlled-trials.com).

Abstracts of citations identified by the search were scrutinized independently by 2 of us (E.S. and N.V.) to determine eligibility for inclusion. Studies were included if they met each of the following criteria: the study was a comparative or randomized controlled trial, patients were divided into laparoscopic and open appendectomy groups, and it focused on older patients (>60 years). Trials without division of patients into laparoscopic and open groups and those reporting results in younger adults or children were excluded.

Primary outcomes were postoperative mortality (in-hospital or 30-day mortality) and postoperative complications (within the first month of surgery as a direct result of the initial operation). Secondary outcomes were operative time (in minutes), length of hospital stay (in days), postoperative wound infection (infective complication of the wound developing within 1 month of surgery as a direct result of the primary procedure), and intra-abdominal collection (within 1 month of surgery as a direct result of the primary procedure). The reported incidence of appendiceal perforation was compared as a confounding variable between the laparoscopic and open groups.

STATISTICAL ANALYSIS

The quality of each trial was assessed using the Oxford Centre for Evidence-Based Medicine levels of evidence (March 2009).7 Analysis was performed using commercially available software (StatsDirect 2.5.7; StatsDirect Ltd). Weighted mean differences were calculated to assess the size of the effect of laparoscopic appendectomy on continuous variables (operative time and length of hospital stay). Pooled odds ratios (95% CIs) were calculated to assess the size of the effect of laparoscopic appendectomy on discrete variables (postoperative mortality, postoperative complications, postoperative wound infection, and intra-abdominal collection). Pooled outcome measures were determined using random-effects models as described by DerSimonian and Laird.8 Heterogeneity among trials was assessed by the Cochran Q statistic,9 a null hypothesis in which P < .05 indicates the presence of significant heterogeneity. The Egger test was used to assess the funnel plot and significant asymmetry as indications of possible publication bias or other biases.

RESULTS

The initial search identified 435 publications, of which 68 were screened for inclusion eligibility (Figure 1). Seven studies met the inclusion criteria. Despite our contacting the authors, we were unable to obtain the data from a poster presentation,10 which was excluded from the meta-analysis. Six studies were analyzed, which reported 15 852 appendectomies (4398 laparoscopic and 11 454 open procedures). Characteristics of the studies included in the meta-analysis are listed in Table 1. Primary and secondary outcomes for each study are given in Table 2 and Table 3, respectively.

PRIMARY OUTCOMES

Postoperative Mortality

Five studies11-14,16 of 6 reported postoperative mortality rates in the laparoscopic group vs the open group. One study15 was excluded from this analysis because no deaths were observed in either group. Postoperative mortality was significantly lower in the laparoscopic group compared with the open group (pooled odds ratio, 0.24; 95% CI, 0.13-0.37; P < .05) (Figure 2). No statistically significant heterogeneity (Cochran Q = 0.92, P = .82, I2 = 0%) or bias (−0.38 by Egger test, P = .62) was observed.

Postoperative Complications

Postoperative complications were reported in all 6 studies11-16 and were less likely to occur in patients undergoing laparoscopic compared with open appendectomy (pooled odds ratio, 0.61; 95% CI, 0.50-0.73; P < .05) (Figure 3). No statistically significant heterogeneity (Cochran Q = 9.81, P = .08, I2 = 49%) or bias (−0.30 by Egger test, P = .78) was observed.

SECONDARY OUTCOMES

Operative Time

Three studies14-16 reported operative time. No statistically significant difference was observed between the study groups (weighted mean difference, 0.06; 95% CI, −0.16 to 0.29; P = .58) (eFigure 1; http://www.archsurg.com). No evidence of heterogeneity was observed (Cochran Q = 1.86, P = .40). Data were insufficient to allow calculation of the I2 value for heterogeneity or to assess statistical bias using the Egger test.

Intra-abdominal Collection

Three studies13,15,16 reported rates of intra-abdominal collection. No significant difference was observed between the study groups (pooled odds ratio, 1.19; 95% CI, 0.61-2.31; P = .62) (eFigure 2). No evidence of heterogeneity was observed (Cochran Q = 1.43, P = .23), but the data were insufficient to allow calculation of the I2 value for heterogeneity or to assess statistical bias using the Egger test.

Postoperative Wound Infection

Three studies13,15,16 reported the incidence of postoperative wound infection. No significant difference was observed between the study groups (pooled odds ratio, 0.53; 95% CI, 0.11-2.63; P = .44) (eFigure 3). No evidence of statistically significant heterogeneity was observed (Cochr-
ran Q = 4.65, P = .10, I^2 = 57%). Data were insufficient to calculate statistical bias.

Length of Hospital Stay

Four studies\textsuperscript{12,14-16} reported the length of hospital stay. Laparoscopic appendectomy was associated with a significantly reduced length of hospital stay compared with open appendectomy (weighted mean difference, −0.51 days; 95% CI, −0.64 to −0.37 days; P < .05) (eFigure 4). No evidence of statistically significant heterogeneity (Cochran Q = 3.64, P = .30, I^2 = 18%) or bias (0.94 by Egger test, P = .40) was observed.

CONFOUNDING VARIABLE ANALYSIS

Five studies\textsuperscript{11,13-16} reported the incidence of appendiceal perforation. No significant difference was observed between the study groups (pooled odds ratio, 0.72; 95% CI, 0.48-1.10; P = .13) (eFigure 5). No evidence of statistically significant heterogeneity (Cochran Q = 27.75, P < .001, I^2 = 86%) or bias (0.51 by Egger test, P = .82) was observed.

The main finding of this study is that laparoscopic appendectomy in older patients is associated with significantly reduced postoperative mortality and complications compared with open appendectomy. In an analysis of secondary outcomes, laparoscopic appendectomy was associated with a reduced length of hospital stay.

The literature on appendicitis in younger adults offers limited discussion of postoperative mortality given that appendectomy represents low-risk surgery in this age group.\textsuperscript{3,11} However, the risk of death from this condition in older patients is up to 14 times that of the general adult population.\textsuperscript{5,6} This is generally attributed to its later atypical presentation, greater medical comorbidity, and reduced physiological reserve and impaired inflammatory response in older age.\textsuperscript{3,17}

Analysis of secondary outcomes showed no significant difference in operative time, postoperative wound

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Table 1. Characteristics of Studies Included in the Meta-analysis\textsuperscript{a}

<table>
<thead>
<tr>
<th>Source</th>
<th>Trial Design</th>
<th>No. of Patients</th>
<th>Age, Mean (SD), y</th>
<th>Male-Female Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guller et al\textsuperscript{11} 2004</td>
<td>Retrospective</td>
<td>1475 (Laparoscopic) 8001 (Open)</td>
<td>72.5 (6.3) (Laparoscopic) 73.9 (6.7) (Open)</td>
<td>695:780 (Laparoscopic) 4105:3896 (Open)</td>
</tr>
<tr>
<td>Harrell et al\textsuperscript{12} 2006</td>
<td>Retrospective</td>
<td>534 (Laparoscopic) 2188 (Open)</td>
<td>72.3 (7.2) (Laparoscopic) 73.2 (7.2) (Open)</td>
<td>249:289 (Laparoscopic) 1179:1009 (Open)</td>
</tr>
<tr>
<td>Kim et al\textsuperscript{13} 2011</td>
<td>Retrospective</td>
<td>2235 (Laparoscopic) 1100 (Open)</td>
<td>73.0 (6.6) (Laparoscopic) 74.2 (6.9) (Open)</td>
<td>1055:1180 (Laparoscopic) 548:552 (Open)</td>
</tr>
<tr>
<td>Paranjape et al\textsuperscript{14} 2007</td>
<td>Retrospective</td>
<td>68 (Laparoscopic) 48 (Open)</td>
<td>68.7 (6.2) (Laparoscopic) 71.9 (7.2) (Open)</td>
<td>245:240 (Laparoscopic) 1179:1009 (Open)</td>
</tr>
<tr>
<td>Wang et al\textsuperscript{15} 2006</td>
<td>Prospective</td>
<td>24 (Laparoscopic) 29 (Open)</td>
<td>69 (Laparoscopic) 70 (Open)</td>
<td>14:10 (Laparoscopic) 17:12 (Open)</td>
</tr>
<tr>
<td>Wu et al\textsuperscript{16} 2011</td>
<td>Retrospective</td>
<td>62 (Laparoscopic) 88 (Open)</td>
<td>75.3 (7.8) (Laparoscopic) 75.5 (8.1) (Open)</td>
<td>33:29 (Laparoscopic) 46:42 (Open)</td>
</tr>
</tbody>
</table>

\textsuperscript{a}The level of evidence according to the Oxford Centre for Evidence-Based Medicine\textsuperscript{7} was level 2b for all studies.

Table 2. Primary Outcomes

<table>
<thead>
<tr>
<th>Source</th>
<th>Postoperative Mortality, No. (%)</th>
<th>Postoperative Morbidity, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Laparoscopic Group</td>
<td>Open Group</td>
</tr>
<tr>
<td>Guller et al\textsuperscript{11} 2004</td>
<td>7 (0.4)</td>
<td>192 (2.4)</td>
</tr>
<tr>
<td>Harrell et al\textsuperscript{12} 2006</td>
<td>2 (0.4)</td>
<td>46 (2.1)</td>
</tr>
<tr>
<td>Kim et al\textsuperscript{13} 2011</td>
<td>15 (0.7)</td>
<td>25 (2.3)</td>
</tr>
<tr>
<td>Paranjape et al\textsuperscript{14} 2007</td>
<td>0</td>
<td>1 (2.1)</td>
</tr>
<tr>
<td>Wang et al\textsuperscript{15} 2006</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Wu et al\textsuperscript{16} 2011</td>
<td>. . .</td>
<td>. . .</td>
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</table>
Table 3. Secondary Outcomes

<table>
<thead>
<tr>
<th>Source</th>
<th>Laparoscopic Group</th>
<th>Open Group</th>
<th>Laparoscopic Group</th>
<th>Open Group</th>
<th>Laparoscopic Group</th>
<th>Open Group</th>
<th>Laparoscopic Group</th>
<th>Open Group</th>
<th>Laparoscopic Group</th>
<th>Open Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guller et al.11, 2004</td>
<td>438 (29.7)</td>
<td>2880 (36.0)</td>
<td>438 (29.7)</td>
<td>2880 (36.0)</td>
<td>438 (29.7)</td>
<td>2880 (36.0)</td>
<td>438 (29.7)</td>
<td>2880 (36.0)</td>
<td>438 (29.7)</td>
<td>2880 (36.0)</td>
</tr>
<tr>
<td>Harrell et al.12, 2006</td>
<td>203 (38.0)</td>
<td>1229 (58.9)</td>
<td>203 (38.0)</td>
<td>1229 (58.9)</td>
<td>203 (38.0)</td>
<td>1229 (58.9)</td>
<td>203 (38.0)</td>
<td>1229 (58.9)</td>
<td>203 (38.0)</td>
<td>1229 (58.9)</td>
</tr>
<tr>
<td>Kim et al.13, 2011</td>
<td>56 (2.5)</td>
<td>19 (1.7)</td>
<td>56 (2.5)</td>
<td>19 (1.7)</td>
<td>56 (2.5)</td>
<td>19 (1.7)</td>
<td>56 (2.5)</td>
<td>19 (1.7)</td>
<td>56 (2.5)</td>
<td>19 (1.7)</td>
</tr>
<tr>
<td>Paranjape et al.14, 2007</td>
<td>82.5 (39.4)</td>
<td>80.4 (48.1)</td>
<td>18 (26.5)</td>
<td>9 (18.8)</td>
<td>18 (26.5)</td>
<td>9 (18.8)</td>
<td>18 (26.5)</td>
<td>9 (18.8)</td>
<td>18 (26.5)</td>
<td>9 (18.8)</td>
</tr>
<tr>
<td>Wang et al.15, 2006</td>
<td>70 (28)</td>
<td>60 (22)</td>
<td>9 (37.5)</td>
<td>11 (37.9)</td>
<td>3</td>
<td>1</td>
<td>4.8 (3)</td>
<td>5 (3.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wu et al.16, 2011</td>
<td>57.7 (30.3)</td>
<td>59.1 (31.8)</td>
<td>15 (24.2)</td>
<td>25 (28.4)</td>
<td>0</td>
<td>5</td>
<td>5.4 (3.6)</td>
<td>8.5 (8.5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 2. Forest plot showing pooled odds ratios (95% CIs) for postoperative mortality after laparoscopic vs open appendectomy. Diamond indicates overall summary estimate for the analysis (width of the diamond represents the 95% CI); square, the effect estimate; the size of the square, the weight that the corresponding study exerts in the meta-analysis (Mantel-Haenszel weight); horizontal line through the square, pooled estimate; and horizontal line within diamond, narrow 95% CI.

Figure 3. Forest plot showing pooled odds ratios (95% CIs) for overall postoperative complications after laparoscopic vs open appendectomy. Diamond indicates overall summary estimate for the analysis (width of the diamond represents the 95% CI); square, the effect estimate; the size of the square, the weight that the corresponding study exerts in the meta-analysis (Mantel-Haenszel weight); horizontal line through the square, pooled estimate; and horizontal line within diamond, narrow 95% CI.

infection, or intra-abdominal collection between older patients undergoing laparoscopic vs open appendectomy. Furthermore, analysis of appendiceal perforation as a confounding variable that may have influenced these outcomes revealed no significant difference between the laparoscopic and open groups. Most studies11,13,15,16 included in this meta-analysis adjusted for (or observed little difference in) patient age and comorbidities in each study group. Our analysis demonstrated that postoperative mortality was significantly reduced among the older patients undergoing laparoscopic appendectomy. However, these findings must be interpreted with caution because of the nonrandomized nature of the studies included, introducing the possibility that selection bias may have influenced our results. Reported benefits of laparoscopic surgery, including decreased overall inflammatory response13,16 and postoperative morbidity,3 are presumed to contribute to the observed reduced postoperative mortality. Results of some studies12,13 have suggested that laparoscopy carries particular risk via carbon dioxide insufflation in a patient with reduced cardiopulmonary reserve, causing diaphragmatic splinting, reducing venous return and cardiac output, and predisposing the patient to myocardial infarction and basal atelectasis. However, the present analysis showed that older patients seem to benefit from a less invasive approach compared with open appendectomy.

The laparoscopic approach was associated with significantly reduced rates of overall postoperative complications compared with open appendectomy, despite no significant difference in rates of postoperative wound infection or intra-abdominal collection. Investigators comparing these 2 approaches in the general adult and pediatric populations reported that laparoscopic appendectomy is associated with lower rates of postoperative wound infection but with higher rates of intra-abdominal collection.3 These observations did not hold in our meta-analysis of studies among older patients. Only 2 studies11,13 included herein performed analyses that showed statistically significant differences in specific postoperative complications between the study groups. Kim et al13 reported that pneumonia, venous thromboembolism, and sepsis were significantly reduced in patients undergoing laparoscopic appendectomy compared with the open approach. Guller et al11 found that laparoscopic appendectomy was associated with significantly reduced rates of pulmonary and cardiovascular complications com-
pared with the open procedure. The decreased rates of these nonsurgical complications are likely responsible for the reduced overall morbidity seen with laparoscopic appendectomy in our meta-analysis. However, the influence of selection bias cannot be excluded because no randomized data were available for analysis.

Consistent with these reduced rates of overall morbidity, patients undergoing laparoscopic appendectomy had a significantly shorter length of hospital stay. A shorter length of hospital stay may be attributed to a lower incidence of postoperative complications and to decreased postoperative pain observed with laparoscopic appendectomy. Early discharge from the hospital offers health benefits to older patients and economic advantages to service providers. Cost is an important consideration for any common surgical procedure, especially in the context of the economic implications of health care delivery to an aging population. Prolonged inpatient stay has been associated with falls, delirium, malnutrition, functional decline, and increased rates of nosocomial infection in older patients. These complications have potential economic implications for health care providers.

Only 1 study herein provided comparative cost data for the 2 surgical techniques and subsequent care. Harrell et al reported higher surgical charges for laparoscopic appendectomy but found no significant difference in the total treatment charges between the 2 approaches. The higher cost of the laparoscopic procedure may be negated by the shorter length of hospital stay and decreased postoperative care requirements. Similar observations have been made by investigators comparing laparoscopic and open appendectomy in the general population, with the laparoscopic approach resulting in higher operative costs but in lower costs for postoperative care and extrahospital expenses. Although it is clear from the meta-analysis herein that laparoscopic appendectomy is associated with reduced length of hospital stay, formal health economic analysis is needed and should incorporate analysis of quality-of-life metrics and patient preferences.

The findings of this meta-analysis echo the consensus in the literature that laparoscopic appendectomy may be of particular benefit in certain subgroups of patients, particularly pediatric populations and patients with obesity, because of the benefits provided, including reduced length of hospital stay and complication rates compared with open appendectomy. The lower incidence of postoperative complications in more recent investigations of laparoscopic appendectomy among older patients is likely consistent with improvements in techniques and training in laparoscopy owing to its increasingly widespread use. The diagnostic value of laparoscopy is of particular relevance among this patient group, in whom presentation is neutulous and diagnosis is challenging even with improved access to imaging. The authors of a recent Cochrane review that compared appendectomy with antibiotic treatment for acute appendicitis concluded that appendectomy remains the gold standard but that antibiotic treatment may be useful in conditions or patients in which surgery is contraindicated. The benefits of a less invasive approach in older patients demonstrated herein may be enhanced by nonoperative management in a specific cohort of older patients having multiple medical comorbidities and representing high surgical risk. However, further high-powered randomized controlled trials of appendectomy vs antibiotic treatment in older patients are required before this conclusion may be reached.

Inference of causality in the present analysis was limited by the quality of the evidence that was available, in this case 6 observational studies (5 retrospective and 1 prospective). Secondary outcomes that were notably absent from this meta-analysis are postoperative pain, cosmesis, patient satisfaction, and cost. Where present, assessment of these factors in the included studies was insufficient for meta-analysis. Therefore, the results of this study should be interpreted with a degree of caution. Adequately powered randomized controlled trials focused on older patients are needed to provide robust assessment of the differences in outcomes suggested by the findings of our meta-analysis.

In conclusion, this meta-analysis of comparative studies demonstrated clear potential benefits of laparoscopic appendectomy over open appendectomy in older patients, with significantly reduced postoperative mortality and morbidity and shorter length of hospital stay associated with laparoscopic surgery. Randomized controlled trials are required to eliminate the influence of selection bias and to elucidate differences in additional outcomes, including postoperative pain, cosmesis, and patient satisfaction, to improve our understanding of reduced morbidity and to provide an accurate cost-effectiveness comparison.

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Author Contributions: Dr Zaidi had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Karthikesalingam and Markar. Acquisition of data: Southgate and Vousden. Analysis and interpretation of data: Karthikesalingam, Black, and Zaidi. Drafting of the manuscript: Southgate, Vousden, Karthikesalingam, and Markar. Critical revision of the manuscript for important intellectual content: Southgate, Vousden, Karthikesalingam, Markar, Black, and Zaidi. Supervision: Black and Zaidi.

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REFERENCES


