Meta-analysis of randomized trials on single-incision laparoscopic versus conventional laparoscopic appendectomy

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KEYWORDS: Single-incision; Single-access; Single-port; SILS; Laparoscopy; Appendectomy

Abstract

BACKGROUND: Single-incision laparoscopic appendectomy has emerged as a less invasive alternative to conventional laparoscopic surgery. High-quality relevant evidence is limited.

METHODS: A systematic review of electronic information sources was undertaken, with the objective of identifying randomized trials that compared single-incision with conventional laparoscopic appendectomy. Outcome measures included 30-day morbidity, abdominal abscess, wound infection, open conversion, reoperation, operative time, length of hospital stay, and postoperative pain. Fixed-effects and random-effects models were used to calculate combined overall effect sizes of pooled data. Data are presented as odds ratios or weighted mean differences with 95% confidence intervals (CIs).

RESULTS: Five randomized trials were identified, with a total of 746 patients. Thirty-day morbidity (9.6% vs 8.6%; odds ratio, 1.14; 95% CI, .69 to 1.89) and wound infection rates were similar between single-incision and conventional laparoscopy (4.0% vs 4.8%; odds ratio, .83; 95% CI, .41 to 1.68), whereas the duration of surgery was longer in the single-incision group (46.3 vs 40.7 minutes; weighted mean difference, 6.01; 95% CI, 2.26 to 9.76). Available data were not adequately robust to reach conclusions regarding the remaining outcome measures.

CONCLUSIONS: Similar postoperative morbidity and wound infection rates for single-incision and conventional laparoscopic appendectomy are supported by the current literature, but single-incision surgery requires longer operative time.

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Laparoscopic surgery through a single incision has evolved with the objectives of minimizing surgical trauma, reducing postoperative pain, shortening convalescence, and providing improved cosmesis. Recent meta-analyses of
single-incision laparoscopic cholecystectomy have demonstrated similar complication rates to conventional laparoscopy, but they have failed to provide uniform results regarding pain.¹² Emerging evidence suggests that the appealing idea of minimizing surgical trauma must be weighed against associated direct and indirect risks.³ A systematic review of single-incision laparoscopic cholecystectomy has demonstrated increased risk for common bile duct injuries compared with historic complication rates of conventional cholecystectomy.⁴

Evidence demonstrates clear superiority of laparoscopic appendectomy over open surgery in terms of wound-related complications, although conflicting data suggest longer operative time for the laparoscopic approach.⁵⁶ Similar operative morbidity for open and laparoscopic appendectomy has rendered the latter an acceptable alternative. Insufficient high-quality data on single-incision laparoscopic appendectomy exist; nevertheless, many institutions have used the single-incision method outside a frame of randomization.⁷ A meta-analysis by the Cochrane Collaboration in 2011 could not identify any randomized studies comparing single-incision with conventional laparoscopic appendectomy.⁸

The aim of the present meta-analysis was to compare outcomes of single-incision laparoscopic appendectomy with those of conventional laparoscopic appendectomy, as expressed by the incidence of postoperative complications, the need for conversion to open surgery, duration of surgery, reoperation rate, overall cost, postoperative pain, and time to resume to normal diet.

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**Figure 1** Flow diagram of search history. RCT = randomized controlled trial.
Methods

Eligibility criteria and study selection

A protocol was established before initiation of the study to determine the criteria for inclusion, the methods for analysis, and the investigated outcomes. Randomized studies in adult populations comparing single-incision with conventional laparoscopic appendectomy and reporting ≥1 of the predetermined outcome measures were considered for inclusion. Nonrandomized studies and studies including pediatric patient populations were excluded. The primary outcome measure of the present analysis was the incidence of 30-day morbidity. Secondary outcome measures included the incidence of intra-abdominal abscess, wound infection rate, reoperation rate, conversion to open surgery, duration of surgery, overall cost, time to resume to liquid diet, time to resume to solid diet, length of hospital stay, and postoperative pain (6 to 24 hours after surgery).

Search strategy

The electronic database of the National Library of Medicine (MEDLINE; provider Ovid, from 1966 to April 2013) was searched to identify relevant articles. No language restrictions were applied. The Medical Subject Headings “laparoscopy” and “appendectomy” and the terms “single incision,” “single port,” “single access,” and “SILS” (single-incision laparoscopic surgery) were used combined with the Boolean operators AND and OR (Appendix). A second-level manual search included the reference lists of the retrieved articles. The last search was run on April 11, 2013. Eligibility assessment was performed independently in an unblinded standardized manner by 2 reviewers. Disagreements between reviewers were resolved by consensus. The literature review conformed to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses standards.9

### Table 1: Study characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Year of publication</th>
<th>Country</th>
<th>Participating centers</th>
<th>Period of treatment</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frutos et al</td>
<td>2013</td>
<td>Spain</td>
<td>Single center</td>
<td>September 2009 to December 2010</td>
<td>Age &gt;11 y, migrating pain, abdominal defense</td>
<td>Cirrhosis, coagulation disorders, abscess or peritonitis, septic shock, contraindication to laparoscopic surgery, contraindication to general anesthesia, pregnancy</td>
</tr>
<tr>
<td>Lee et al</td>
<td>2013</td>
<td>Korea</td>
<td>Single center</td>
<td>March 2010 to September 2011</td>
<td>Age &gt;16 y, migrating pain, nausea, fever &gt;38°C or leukocyte count &gt;10^3/mL, guarding, tenderness</td>
<td>Refusal of laparoscopic surgery, abscess, cirrhosis, coagulation disorders, circulatory failure, contraindication to laparoscopic surgery, contraindication to general anesthesia, pregnancy, neoplasm</td>
</tr>
<tr>
<td>Sozutek et al</td>
<td>2013</td>
<td>Turkey</td>
<td>Single center</td>
<td>September 2010 to May 2011</td>
<td>NR</td>
<td>Age &lt;18 y, ASA score 4 or 5, anticoagulation treatment, absence of macroscopic findings of appendicitis</td>
</tr>
<tr>
<td>Teoh et al</td>
<td>2012</td>
<td>China</td>
<td>Single center</td>
<td>October 2009 to March 2011</td>
<td>Age 18–75 y, migrating pain, fever &gt;38°C or leukocyte count &gt;10^3/mL, guarding, tenderness</td>
<td>Duration of symptoms &gt;5 d, palpable mass in the right lower quadrant, cirrhosis, coagulation disorders, abscess or peritonitis, septic shock, contraindication to general anesthesia, pregnancy, previous abdominal surgery, ascites, malignancy</td>
</tr>
<tr>
<td>Vilallonga et al</td>
<td>2012</td>
<td>Spain, Egypt, Turkey</td>
<td>Multicenter</td>
<td>July 2009 to March 2010</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

NR = not reported.

### Table 2: Patient allocation

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients included</th>
<th>Patients completing follow-up</th>
<th>Patients allocated to SILA</th>
<th>Patients allocated to CLA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frutos et al</td>
<td>184</td>
<td>184</td>
<td>91</td>
<td>93</td>
</tr>
<tr>
<td>Lee et al</td>
<td>248</td>
<td>248</td>
<td>114</td>
<td>116</td>
</tr>
<tr>
<td>Sozutek et al</td>
<td>75*</td>
<td>75*</td>
<td>25</td>
<td>25</td>
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<tr>
<td>Teoh et al</td>
<td>200</td>
<td>195</td>
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<td>97</td>
</tr>
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<td>Vilallonga et al</td>
<td>87</td>
<td>87</td>
<td>46</td>
<td>41</td>
</tr>
</tbody>
</table>

CLA = conventional laparoscopic appendectomy; SILA = single-incision laparoscopic appendectomy.

*Includes a 3rd group of patients allocated to open appendectomy.
Data collection

An electronic data extraction sheet was developed and refined accordingly. One review author extracted the data from included studies, and a second author checked the extracted data. The latter included the name of the primary author, year of publication, country (or countries) of participating institution(s), number of participating centers, patient recruitment period, inclusion and exclusion criteria for patient enrollment in the studies, number of patients assigned to randomization, number of patients having completed follow-up, number of patients allocated to either group, method of closure of the appendiceal stump, method of specimen extraction, and results of the aforementioned outcome measures.

Methods of analysis

A fixed-effects model was initially applied to synthesize the data; however, if significant heterogeneity among the included studies was identified, random-effects analysis according to DerSimonian and Laird was used. Weighted mean differences (WMDs) with 95% confidence intervals (CIs) were calculated to assess the size of the effect of each type of procedure on continuous variables. Pooled odds ratios (ORs) with 95% CIs were calculated to measure the effect of each type of procedure on categorical variables. Heterogeneity was assessed using the $I^2$ statistic, a method expressing the percentage of variation across studies. $I^2$ values between 0% and 25% suggest low heterogeneity, values >25% suggest moderate heterogeneity, and values >75% suggest high heterogeneity. Publication bias was assessed visually evaluating the symmetry of funnel plots. Statistical analysis was performed using Review Manager version 5.2 (The Nordic Cochrane Centre, Copenhagen, Denmark). Statistical expertise was provided by one of the study authors (G.A.A.).

Methodologic assessment

To assess the methodologic quality of eligible randomized controlled trials, respective data from each study protocol were extracted, and the Jadad score was calculated. This scoring system takes into account the randomization process, the blind assessment of the outcome, and reporting of withdrawals or dropouts. The minimum score of 1 indicates poor methodologic quality, whereas the maximum score of 5 suggests excellent methodologic quality.

Results

Search results and study selection

The electronic search identified a total of 192 records. Some 185 articles were discarded on the basis of their titles or abstracts as not relevant studies (n = 102), studies with pediatric patient populations (n = 25), review articles (n = 22), nonrandomized

Table 3 Quality assessment of included randomized trials

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Frutos et al</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>Yes</td>
<td>3</td>
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<tr>
<td>Lee et al</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>Yes</td>
<td>3</td>
</tr>
<tr>
<td>Sozutek et al</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>Yes</td>
<td>3</td>
</tr>
<tr>
<td>Teoh et al</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>Vilallonga et al</td>
<td>Yes</td>
<td>No</td>
<td>NA</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>Yes</td>
<td>2</td>
</tr>
</tbody>
</table>

NA = not applicable.

Table 4 Outcome data

<table>
<thead>
<tr>
<th>Study</th>
<th>30-d morbidity</th>
<th>Abdominal abscess</th>
<th>Wound infection</th>
<th>Reoperation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SILA CLA</td>
<td>SILA CLA</td>
<td>SILA CLA</td>
<td>SILA CLA</td>
</tr>
<tr>
<td>Frutos et al</td>
<td>4/91 4/93</td>
<td>0/91 0/93</td>
<td>0/91 0/93</td>
<td>0/91 1/93</td>
</tr>
<tr>
<td>Lee et al</td>
<td>15/114 18/116</td>
<td>6/114 2/116</td>
<td>6/114 12/116</td>
<td>0/114 1/116</td>
</tr>
<tr>
<td>Sozutek et al</td>
<td>1/25 1/25</td>
<td>0/25 0/25</td>
<td>1/25 1/25</td>
<td>0/25 0/25</td>
</tr>
<tr>
<td>Teoh et al</td>
<td>14/98 9/97</td>
<td>4/98 9/97</td>
<td>8/98 5/97</td>
<td>NR NR</td>
</tr>
<tr>
<td>Vilallonga et al</td>
<td>2/46 0/41</td>
<td>0/46 0/41</td>
<td>0/46 0/41</td>
<td>0/46 0/41</td>
</tr>
</tbody>
</table>

CLA = conventional laparoscopic appendectomy; SILA = single-incision laparoscopic appendectomy.

*Standard deviation not reported.
studies (n = 17), technical notes (n = 9), comments (n = 5), letters (n = 3), and an article not reporting any of the investigated outcome parameters (n = 1). A potentially eligible recent randomized trial could not be retrieved from national and international libraries, and the corresponding author did not respond to our request for the full text. The reports of 7 randomized trials were retrieved. Two studies had focused on pediatric patient populations and were therefore excluded. No additional eligible studies were identified in the reference lists of the included articles. Finally, a total of 5 randomized trials entered the meta-analytic models (Fig. 1).15–19

**Study characteristics and methodologic quality**

All studies were published in the English language in 2012 and 2013. The number of participating institutions ranged between 1 and 3. Inclusion and exclusion criteria were similar among studies (Table 1). The study population consisted of 794 patients, whereas 765 patients had completed follow-up. The single-incision and conventional laparoscopic groups included 374 and 372 patients, respectively (Table 2). The appendiceal stump was commonly secured using the ENDOLOOP (Ethicon Endo-Surgery, Cincinnati, OH) in both treatment arms, whereas in 4 studies, retrieval bags were used to extract the specimens. Four studies reported on methods of randomization, but only 1 study was double blinded (Table 3). Jadad scores ranged between 2 and 5, with an overall mean value of 3.2.

**Synthesis of results and outcome**

Summary outcome data are presented in Table 4. No comparative data on hospitalization costs were provided. Furthermore, resumption of oral diet was either not reported or not specifically documented for liquid or solid diet. Therefore, the above outcome data could not enter the meta-analysis models.

**Table 4 (continued)**

<table>
<thead>
<tr>
<th>Conversion</th>
<th>Duration of surgery (min), mean ± SD</th>
<th>Hospital stay (h), mean ± SD</th>
<th>Postoperative pain* (VAS score)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SILA</td>
<td>CLA</td>
<td>SILA</td>
</tr>
<tr>
<td>0/91</td>
<td>38.13 ± 13.49</td>
<td>32.12 ± 12.44</td>
<td>18.86 ± 9.77</td>
</tr>
<tr>
<td>0/114</td>
<td>43.8 ± 21.3</td>
<td>35.8 ± 18.9</td>
<td>72*</td>
</tr>
<tr>
<td>0/25</td>
<td>32.6 ± 9.9</td>
<td>29.5 ± 6.8</td>
<td>1.1 ± 0.3</td>
</tr>
<tr>
<td>8/98</td>
<td>63.0 ± 27.2</td>
<td>60.2 ± 31.7</td>
<td>84.72 ± 70.08</td>
</tr>
<tr>
<td>1/46</td>
<td>40.4*</td>
<td>35.0*</td>
<td>44.4*</td>
</tr>
</tbody>
</table>
Thirty-day morbidity. The incidence of 30-day morbidity was 9.6% and 8.6% in the single-incision and conventional laparoscopic groups, respectively (OR, 1.14; 95% CI, 0.69 to 1.89; \( P = .60 \); Fig. 2). No significant heterogeneity among the studies was identified (\( I^2 = 0 \% \)), and the likelihood of publication bias was low (Fig. 3).

Abdominal abscess. Abdominal abscess developed in 2.7% of the single-incision and 1.3% of the conventional laparoscopy patients (OR, 2.06; 95% CI, 0.69 to 6.11; \( P = .20 \); Fig. 4). No heterogeneity existed among the studies (\( I^2 = 0 \% \)).

Wound infection. Surgical-site infections occurred in 4.0% and 4.8% in the single-incision and conventional laparoscopic groups, respectively (OR, 0.83; 95% CI, 0.41 to 1.68; \( P = .60 \); Fig. 5). No heterogeneity among the studies was found (\( I^2 = 0 \% \)).

Reoperation rate. Two patients in the conventional laparoscopy group underwent reoperation, whereas none of the
patients in the single-incision group required reoperation (OR, .34; 95% CI, .03 to 3.26; $P = .35$; Fig. 6). No heterogeneity among the studies was identified ($I^2 = 0\%$).

**Conversion to open surgery.** The conversion rates for the single-incision and conventional laparoscopy groups were 2.4% and .8%, respectively (OR, 2.78; 95% CI, .79 to 9.71; $P = .11$; Fig. 7). There was no evidence of heterogeneity ($I^2 = 0\%$).

**Duration of surgery.** The duration of single-incision surgery was an average of 5.6 minutes longer than that of conventional surgery (46.29 vs 40.73 minutes; WMD, 6.01; 95% CI, 2.26 to 9.76; $P < .0001$; Fig. 8). No significant heterogeneity among the studies was found ($I^2 = 0\%$), and the possibility of publication bias was low (Fig. 9).

**Hospital stay.** The length of hospital stay was similar in the single-incision and conventional laparoscopy groups (48.9 vs 45.1 hours, respectively; WMD, −2.19; 95% CI, −5.05 to −.68; $P = .14$; Fig. 10). There was no evidence of heterogeneity.

**Postoperative pain.** No significant differences in visual analogue scale score between the 2 groups were identified (3.04 vs 3.41, respectively; WMD, −.26; 95% CI, −1.76 to 1.24; $P = .74$; Fig. 11). Significant heterogeneity among the studies existed ($I^2 = 94\%$).

**Comments**

Data derived from randomized trials of single-incision laparoscopic appendectomy are deemed sufficiently robust to support similar 30-day morbidity compared with conventional laparoscopic surgery. An attempt was made to comparatively evaluate the incidence of postoperative abdominal abscess, but only 2 studies reporting on this
complication could enter the meta-analytic model.\textsuperscript{16,18} Although there was a trend toward a higher incidence of abdominal abscess for the single-incision group (2.7% vs 1.3%), this difference did not reach statistical significance.

An adequate number of studies reported on the duration of surgery; in these terms, individual differences in means were constantly in favor of conventional laparoscopic surgery. This trend has also been confirmed for single-incision laparoscopic cholecystectomy compared with standard laparoscopy\textsuperscript{3} and may be associated to technical difficulties due to inadequate triangulation, difficulties manipulating laparoscopic instruments, and difficulty managing intraoperative complications. Furthermore, only 2 studies provided adequate data on postoperative pain, rendering comparative evidence of limited importance. Nevertheless, 4 of the 5 studies providing some data on this outcome measure reported no difference between the study groups.

The lower incidence of surgical-site infection is one of the primary advantages of laparoscopic appendectomy over conventional surgery. Strong evidence provided by the present meta-analysis does not support lower wound infection rates for single-incision laparoscopic appendectomy. Relevant data were documented by all trials, but 2 studies with zero incidence of wound infection in both arms could not enter the meta-analytic model. It may thus be suggested that reducing the number of access sites in laparoscopic appendectomy does not result in a reduction of wound infection rates. The incidence of incisional hernia was reported by 3 studies only,\textsuperscript{15,17,19} thus providing limited comparative evidence. A recent meta-analysis that compared this complication after single-incision or conventional laparoscopic appendectomy found no significant difference between the 2 approaches.\textsuperscript{3} Furthermore, because of the low frequency of the need for conversion and reoperation, synthesis of the results was inconclusive regarding these outcome measures. Two patients from the conventional laparoscopy group required reoperation (.5%) compared with none in the single-incision group, whereas the respective rates for conversion to open surgery were .8% and 2.4%. A potential significance of the latter result cannot be estimated by the present meta-analytic approach.

Randomized studies of single-incision laparoscopic appendectomy were published exclusively within the past 2 years. The overall methodologic quality was fair, but only 1 trial was blinded to patients and assessors. The increasing interest and the limited evidence on single-incision surgery are expected to be expressed by the publication of further data on this field. It is of specific importance for novel trials to be of adequate quality and to report on a wide range of outcome measures, including postoperative pain, cost, time to resume to oral diet, and time of convalescence. Moreover, because the learning curve may have a significant effect on operative time and surgical outcomes, future randomized trials that adequately report on previous surgeons’ experience with single-incision laparoscopy surgery are essential. Furthermore, to detect potential

\begin{longtable}{|l|c|c|c|c|c|c|c|c|}
\hline
Study or Subgroup & \text{Mean} & \text{SD} & \text{Total} & \text{Mean} & \text{SD} & \text{Total} & \text{Weight} & \text{Mean Difference} \\
\hline
Vialalonga et al 2012 & 44.4 & 0 & 46 & 34 & 0 & 41 & & \\
Tech et al 2012 & 84.72 & 70.08 & 98 & 76.8 & 56.64 & 97 & 2.6% & 7.92 [-9.96, 25.80] 2012 \\
Fruotos et al 2013 & 18.86 & 9.77 & 91 & 21.32 & 11.72 & 93 & 84.7% & -2.46 [-5.57, 0.65] 2013 \\
Lee et al 2013 & 0 & 0 & 114 & 0 & 0 & 116 & & Not estimable 2013 \\
\hline
Total (95% CI) & 374 & & & & & & & 100.0% & -2.19 [-5.05, 0.68] \\
\hline
\end{longtable}
differences in ORs for abdominal abscess and conversion to open surgery, larger patient populations are required. The best evidence suggests similar overall postoperative morbidity and similar wound infection rates for single-incision laparoscopic appendectomy compared with conventional laparoscopy; however, single-incision surgery requires longer operative time. Meta-analytic synthesis of data on other outcome measures was inconclusive. Further randomized trials in this field are warranted.

References

Appendix

Combination of search terms

Search terms:


A.
1. single incision
2. single access
3. single port
4. one access
5. SILS

B.
laparoscopic

C.
1. appendectomy
2. appendicectomy