A meta-analysis of laparoscopic versus open appendectomy in patients suspected of having acute appendicitis

Larissa K.F. Temple, MD;* Demetrius E. Litwin, MD;* Robin S. McLeod, MD*

OBJECTIVE: To determine if any significant differences exist between laparoscopic appendectomy (LA) and open appendectomy (OA).

DESIGN: A meta-analysis of randomized controlled trials (RCTs) comparing LA to OA.

DATA SOURCES: An extensive literature search was conducted for appropriate articles published between January 1990 and March 1997. Articles were initially retrieved through MEDLINE with MeSH terms "appendicitis" or "appendectomy" and "laparoscopy." Additional methods included cross-referencing bibliographies of retrieved articles, hand searching abstracts from relevant meetings and consultation with a content expert.

STUDY SELECTION: Only RCTs published in English in which patients had a preoperative diagnosis of acute appendicitis were included.

DATA EXTRACTION: The outcomes of interest included operating time, hospital stay, readmission rates, return to normal activity and complications. The Cochrane Collaboration Review Manager 3.0 was used to calculate odds ratios (OR), weighted mean differences (WMD) and 95% confidence intervals (CI). The random-effects model was used for statistical analysis.

DATA SYNTHESIS: Twelve trials met the inclusion criteria. Because there were insufficient data in some trials, operating time, hospitalization and return to work were assessed in only 8 trials. Mean operating time was significantly longer with LA (WMD 18.10 minutes, 95% CI 12.87 to 23.15 minutes). There were fewer wound infections in LA (OR 0.40, 95% CI 0.24 to 0.69), but no significant differences in intra-abdominal abscess rates (OR 1.94, 95% CI 0.68 to 5.58). There was no significant difference in the mean length of hospital stay (WMD –0.16 days, 95% CI –0.44 to 0.15 days) or readmission rates (OR 1.16, 95% CI 0.54 to 2.48). However, the return to normal activity was significantly earlier with LA (WMD –5.79 days, 95% CI –7.38 to –4.21 days). Sensitivity analyses did not affect the results.

CONCLUSION: This meta-analysis suggests that operating room time is significantly longer, hospital stay is unchanged but return to normal activities is significantly earlier with LA.

OBJECTIF : Déterminer s'il existe des différences importantes entre l'appendicectomie par laparoscopie (AL) et l'appendicectomie ouverte (AO).

CONCEPTION : Méta-analyse d'études contrôlées randomisées (ECR) comparant l'AL à l'AO.

SOURCES DE DONNÉES : On a procédé à une recherche poussée dans les écrits afin d'y trouver des articles appropriés publiés entre janvier 1990 et mars 1997. Les articles ont été extraits au début dans MEDLINE au moyen des termes MeSH «appendicitis» ou «appendectomy» et «laparoscopy». Les autres méthodes utilisées ont consisté notamment à établir des renvois à des bibliographies d'articles extraits, à effectuer des recherches manuelles dans des résumés de congrès pertinents et à consulter un expert en contenu.

SÉLECTION D'ÉTUDES : On n'a inclus que les ECR publiées en anglais et portant sur des patients chez lesquels on avait diagnostiqué avant l'intervention une appendicite aiguë.

From the Department of Surgery, Mount Sinai Hospital and University of Toronto, Toronto, Ont.

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**Mount Sinai Hospital Samuel Lunenfeld Research Unit, Toronto, Ont.*

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***Correspondence (no reprints available) to:** Dr. Robin S. McLeod, Ste. 449, Mount Sinai Hospital, 600 University Ave., Toronto ON M5G 1X5; fax 416 586-8644, rmcleod@mtsinai.on.ca*

EXTRACTION DES DONNÉES : Les résultats intéressants comprenaient la durée de l'intervention, le séjour à l'hôpital, les taux de réadmission, la reprise des activités normales et les complications. On a utilisé le logiciel Review Manager 3.0 de la Cochrane Collaboration pour calculer les risques relatifs (RR), les différences moyennes pondérées (DMP) et les intervalles de confiance (IC) à 95 %. On a utilisé le modèle des effets aléatoires pour effectuer l'analyse statistique.

SYNTHÈSE DES DONNÉES : Douze études satisfaisaient aux critères d'inclusion. Comme certaines ne comportaient pas suffisamment de données, on a évalué la durée de l'intervention, l'hospitalisation et le retour au travail dans huit cas seulement. L'intervention a duré en moyenne beaucoup plus longtemps dans le cas de l'AL (DMP 18,10 minutes, IC à 95 %, 12,87 à 23,15 minutes). L'AL a causé moins d'infections de la plaie (RR 0,40, IC à 95 %, 0,24 à 0,69), mais il n'y a avait pas de différence significative quant au taux d'abcès intra-abdominaux (RR 1,94, IC à 95 %, 0,68 à 5,58). Il n'y avait pas de différence significative dans la durée moyenne du séjour à l'hôpital (DMP –0,16 jours, IC à 95 %, –0,44 à 0,15 jours) ou dans les taux de réadmission (RR 1,16, IC à 95 %, 0,54 à 2,48). Le retour à l'activité normale a toutefois été beaucoup plus rapide à la suite d'une AL (DMP –5,79 jours, IC à 95 %, –7,38 à –4,21 jours). Les analyses de sensibilité n'ont pas modifié les résultats.

CONCLUSION : Cette méta-analyse indique que le temps passé à la salle d'opération est beaucoup plus long, le séjour à l'hôpital ne change pas, mais le retour à l'activité normale est beaucoup plus rapide dans le cas de l'AL.

Appendicitis is a common condition generally affecting young, healthy people. Surgical removal of the appendix through a small right lower quadrant (McBurney) incision is the standard treatment. Typically, patients recover quickly, are discharged from hospital within days after surgery and return to work within weeks.

Given the acceptance of laparoscopic cholecystectomy, laparoscopy is being used by some surgeons to both diagnose and treat appendicitis. As with laparoscopic cholecystectomy, laparoscopic appendectomy (LA) is thought to cause less injury to the abdominal wall. Thus, patients may have fewer complications, less postoperative pain, and leave hospital and return to work earlier.

There are now a number of published randomized controlled trials (RCTs) comparing open appendectomy (OA) to LA.[1–17] However, the findings are inconsistent, and some studies have small sample sizes so the risk of a type 2 error is high. Meta-analysis is a quantitative, systematic summary of a collection of separate studies for the purpose of obtaining information that cannot be derived from any of the studies alone.[18] It allows data from several studies to be combined to increase the statistical power of the analysis. We, therefore, performed a meta-analysis to compare the outcome after LA and OA.

Methods

Studies were included in this meta-analysis if there was random allocation of patients into LA or OA, the preoperative diagnosis was acute appendicitis, the laparoscopic intervention was intended to be therapeutic rather than diagnostic, a minimum of 80% of randomized patients were followed up for at least one of the main outcomes (i.e., length of operation, length of hospitalization, return to normal activity) and the results were published in the English language. Articles were retrieved through MEDLINE between January 1990 and March 1997 with the MeSH terms "appendicitis" or "appendectomy" and "laparoscopy." The search was limited to English language publications and controlled clinical trials, multicentre trials or RCTs. Additional methods of retrieval included cross-referencing bibliographies of retrieved articles, hand searching the abstracts from the 1993 to 1997 meetings of the Society of American Gastrointestinal Endoscopic Surgeons and European Association for Endoscopic Surgery, and consultation with a content expert.

The outcomes of interest included operating time, hospital stay, return to normal activity and complications (rates of wound infection, abscesses, conversion, readmission and serious but rare complications). Other outcomes such as analgesia requirements and potential confounders such as surgical experience could not be systematically evaluated because they were not consistently reported.

The quality of each study was evaluated using a 10-point scale designed to assess the overall quality of RCTs.[19] Two of the authors, one of whom was blinded (R.M.), extracted data and evaluated the quality of each article. In trials with randomized and nonrandomized patients, only data from the randomized patients were used.[8] Discrepancies in data extraction were resolved by consensus. The data were double-entered. Given the significant variation in methodologic quality of the trials, the random-effects model was used to combine the data. This model is more conservative than the fixed-effects model and incorporates within-study and between-study variance.[20]

Statistical analysis was done using the Cochrane Collaboration Review Manager 3.0. 95% confidence intervals (CIs) around the odds ratio (OR) for dichotomous data and weighted mean differences (WMDs) for continuous data were calculated. Tests for homogeneity were calculated for each outcome (Breslow–Day method). When the CIs of the OR or WMD included 1, the 2 groups were not statistically different. Odds ratios and WMDs with CIs that were less than 1 favoured LA and those greater than 1 favoured OA. Sensitivity analyses to test the "robustness" of the results were performed. For many of the studies, there were missing data, and authors were contacted by telephone, facsimile, mail or personally for further information.

Results

Twenty-two trials were identified through the initial search strategy. Ten articles were excluded because they did not fit the inclusion criteria: patients were not randomized,[21–25] there was less than 80% follow-up of randomized patients,[13,14] manuscripts from abstracts were not available from authors[15,16] or the trial was not reported in English.[17] Of the 12 RCTs that met the inclusion criteria, 11 have been published.

The overall quality of the 12 trials included in the meta-analysis was 6.4 out of 10 with an inter-rater reliability of 0.81 as measured by an unweighted κ statistic. Because some authors reported medians[2,10,12] and means without standard deviations,[2,9,11] the length of operation, hospitalization and return to work could only be assessed in 8 trials. The agreement between the 2 assessors on the data extraction of the main outcomes was 93%.

In total, 1383 patients were randomized to LA (730 patients) and OA (653 patients). The patient characteristics for the 2 groups are shown in Table I. Although 2 trials excluded women and 1 trial excluded men, the distribution of gender between LA and OA groups was equal (OR 0.90, 95% CI 0.64 to 1.26). There was no difference in the mean age between the LA and OA groups (WMD –0.65, 95% CI –2.92 to 1.65). There were no differences in the frequency of normal appendices at operation in the OA and LA groups (OR 1.23, 95% CI 0.89 to 1.71). In studies that differentiated between a perforated and inflamed appendix, there were no differences in the distribution between the LA or OA groups (OR 0.92, 95% CI 0.74 to 1.14) .

Eight trials[1–8] had sufficient data to be combined to assess the length of operation (Fig. 1). There was signifi-

Table I

Demographics of Patients in This Meta-analysis

Demographic	No. of trials with data	Laparoscopic appendectomy	Open appendectomy
Mean age, yr	5	30.2	31.6
Sex, %			
Male	11	62.1	63.4
Female	11	37.8	37.9
Condition of appendix, %			
Normal	10	18.5	15.4
Inflamed	7	65.7	69.2
Perforated	7	16.6	16.5

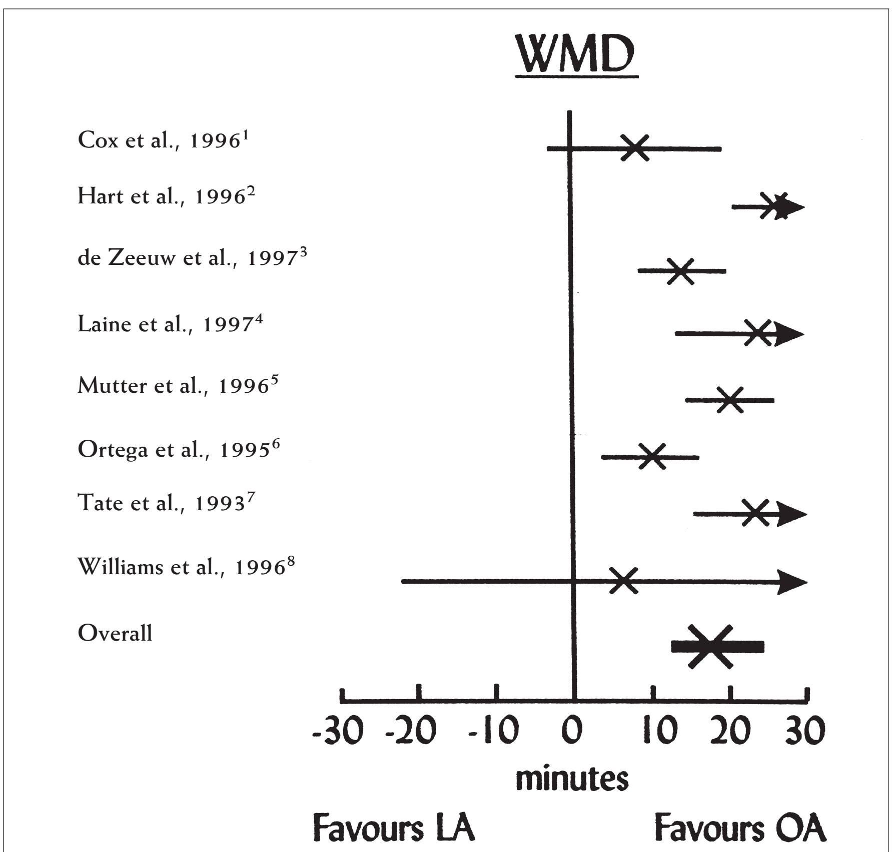

FIG. 1. Operating time in 8 studies. WMD = weighted mean difference. A WMD less than 0 favours laparoscopic appendectomy (LA) and a WMD greater than 0 favours open appendectomy (OA). The X marks the mean operative time for each trial. The horizontal line represents the 95% confidence interval.

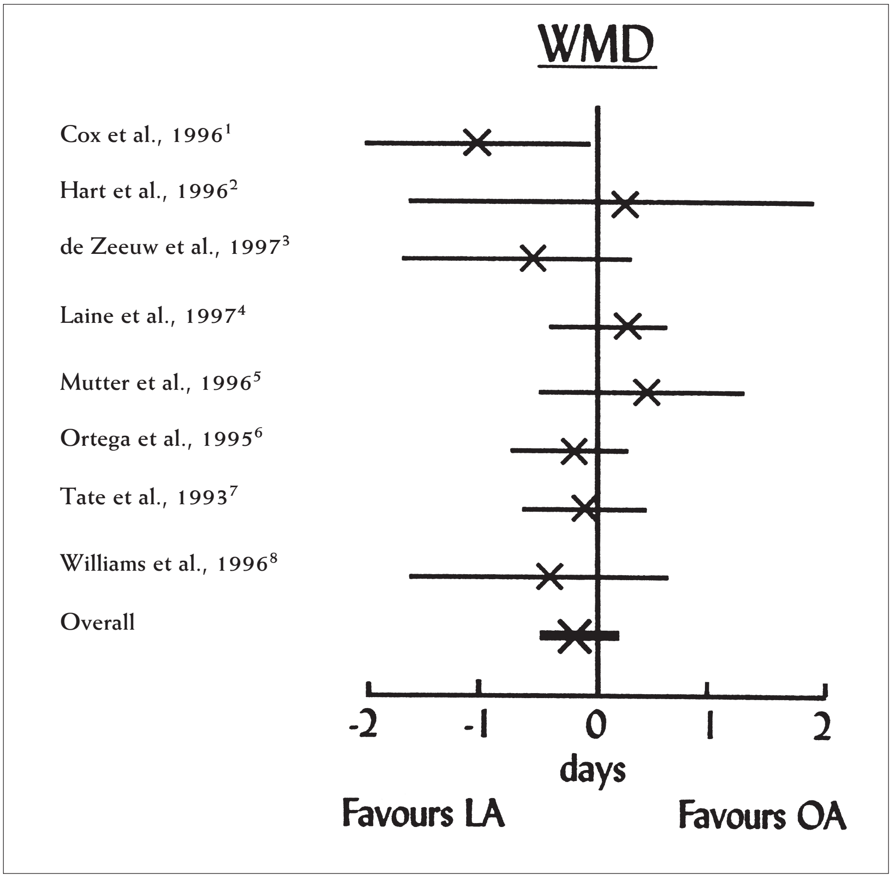

FIG. 2. Length of hospitalization in 8 studies.

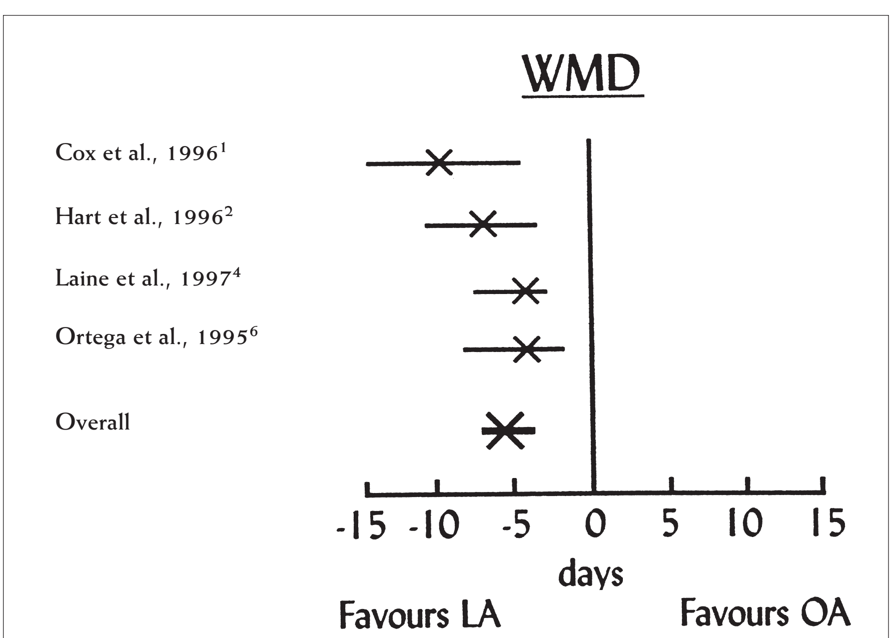

FIG. 3. Return to normal activity in 4 studies.

cant statistical heterogeneity (χ^2 [7 df] 20.17, $p < 0.001$). The mean length of operation was significantly longer with LA than OA (WMD 18.10 minutes, 95% CI 12.87 to 23.15 minutes $p < 0.05$). The overall conversion rate from LA to OA was 11% (range from 5% to 20%).

Complications were reported in 10 trials. There was no statistical heterogeneity in the 10 trials that reported wound infection rates (χ^2 [9 df] 9.02, $p > 0.5$), the 6 trials that reported intra-abdominal abscess rates (χ^2 [5 df] 3.25, $p > 0.05$) or the 5 trials that reported rare but serious complications (χ^2 [4 df] 0.50, $p > 0.8$). There were fewer wound infections after LA (OR 0.40, 95% CI 0.24 to 0.69, $p > 0.05$) but no difference in intra-abdominal abscesses (OR 1.94, 95% CI 0.68 to 5.58, $p > 0.05$) or rare but serious complications (OR 1.00, 95% CI 0.27 to 3.65, $p > 0.05$).

The 8 trials with sufficient data on the length of hospitalization were statistically homogeneous (Fig. 2) (χ^2 [7 df] 7.22, $p > 0.25$). Although the mean length of hospital stay was slightly less with LA, the difference was not clinically or statistically significant (WMD –0.16 days, 95% CI –0.44 to 0.15 days, $p > 0.05$). In addition, there was no significant difference in the readmission rates of patients who underwent LA (6.4%) and OA (6.3%) (OR 1.16, 95% CI 0.54 to 2.48, $p > 0.05$).

There were 4 trials with sufficient data to examine return to normal activity (Fig. 3). The 4 trials were statistically homogeneous (χ^2 [3 df] 3.09, $p > 0.50$). Return to normal activity was significantly earlier after LA (WMD –5.79 days, 95% CI –7.38 to –4.21 days, $p < 0.05$).

A sensitivity analysis was performed using the fixed-effects model. Although CIs were narrower, the fixed-effects model did not change the results of the main outcomes (length of operation, length of hospitalization, return to work) with the exception of there being significantly more intra-abdominal abscesses with LA (OR 2.64, 95% CI 1.02 to 6.82, $p < 0.05$). A further sensitivity analysis was done by including 4 of the excluded trials:[13–16] 2 trials with less than 80% follow-up[13,14] and the 2 trials reported in abstract form with no manuscript.[15,16] By including these RCTs, there was significant heterogeneity in length of operation (χ^2 [10 df] 49.39, $p < 0.05$), length of hospitalization (χ^2 [9 df] 24.86, $p < 0.05$) and return to normal activity (χ^2 [6 df] 25.3, $p < 0.001$). However, the results did not change.

Because the quality was similar in all the trials, sensitivity analyses were not done including or excluding trials of different methodologic quality. Given the reporting of the trials, sensitivity analyses could not be done to examine the effects of appendiceal disease or gender.

Discussion

Meta-analysis is a powerful method for synthesizing data on a particular problem from multiple RCTs. By combining the data, the sample size is increased and the risk of a type 2 error decreased. Thus, a meta-analysis is useful in reconciling results when individual trials produce inconclusive or reach contradictory conclusions. Finally, it may lead to increased generalizability of results.

There have been multiple published randomized controlled trials comparing LA to OA. Although most have concluded that there are no significant differences in outcomes, it was felt that the risk of a type 2 error was high and clinically important differences might exist. It was for this reason that we undertook this meta-analysis.

When the data were combined in this systematic review, there were no significant differences in the mean length of hospitalization or in the overall complication rate. Wound infection rates were significantly lower, and the time to return to normal activity favoured LA. However, the mean operative time was significantly longer with LA.

The validity of the results of any meta-analysis depends on the rigour of the methodology of the meta-analysis and of the individual trials included in the review. We believe that the methodology used in this meta-analysis was rigorous. First, a broad search strategy was used to ensure that all RCTs were identified. An attempt to ascertain all RCTs, especially small or negative trials, was made by consulting several content experts and hand searching the abstracts from recent laparoscopic meetings. However, given that LA is a new technology, it is quite possible that there may be other ongoing or unpublished RCTs. Our inclusion criteria were broad to include most trials and patients. The inclusion criteria were created a priori, and the eligibility of trials was determined by 2 independent assessors. We only excluded 2 trials because in each, more than 20% of randomized patients were excluded. These studies excluded randomized patients with normal[13,14] or perforated appendices[13] so the results may be biased as well as less generalizable.

Despite the overall mean quality score being 6.4, a large number of reporting and methodologic flaws were identified in 10 of the 12 trials. Tables and text had discrepant data,[6,12] means without any mention of the variance were reported[9–12] and differences between LA and OA reported to be significantly different were not statistically different on repeat analysis.[2] No study calculated a sample size a priori. Outcomes such as wound infections[1,4–8,10] were not defined objectively. Follow-up was either not described[2,4–6,8] or was incomplete.[7] In addition, statistical heterogeneity was found in length of surgery, suggesting that there were significant differences between the trials. It is likely that the combination of different definitions and surgical experience between the trials accounted for some of the statistical heterogeneity. For instance, in some trials OA and LA were done by experienced staff surgeons,[1–3,5,6,10,11] whereas in others the OAs were done by residents and LAs by staff surgeons.[4,12]

In addition to general concerns about the methodologic quality of the individual trials, certain aspects may have introduced significant bias. There are 3 specific concerns that may bias the results of this meta-analysis.

First, 5 RCTs excluded randomized patients from the analyses.[2,6,8,11,12] As a result of not analysing the results on an intention-to-treat basis, the analysis may be biased. In 4 trials, between 6%[12] and 16%[11] of patients who were randomized to LA but required conversion to OA were excluded in the length of hospital stay analysis. Another trial excluded 5 patients who had hospital stays longer than 9 days.[6] All 5 patients had had LA. In all of these instances, exclusion of these patients may bias the results in favour of LA and the difference in mean hospital stay may be even less than that found in this meta-analysis. One other trial excluded patients in both groups who were found to have normal appendices, possibly reducing the potential for bias.[12]

The second concern relates to the reporting of return to normal activity data. Only 7 of the 12 trials reported these data and, of these, only 4 reported sufficient data (i.e., means and standard deviations) so they could be combined. There are 2 possible reasons why return to normal activity data were not reported: this factor was not measured or the difference was not significant. The latter might represent a "publication bias" in that subgroup analyses that are positive are more likely to be reported than those that are negative. In this meta-analysis we found that the mean time to return to work was significantly shorter in the LA group, but if the data from the other 8 trials were not reported because the results were not significant, then the results of the meta-analysis might be biased in favour of LA. In either event, results from this meta-analysis must be interpreted cautiously since they are based on results from only 4 trials.

The third methodologic concern relates to the lack of blinding. Although blinding is important for the rigour of an RCT, especially if the outcome measures are subjective, it is accepted that blinding may be difficult in surgical trials. Nevertheless, a recent report by Majeed and colleagues[26] emphasized the potential bias due to lack of blinding. In this RCT comparing laparoscopic to mini-cholecystectomy, a large dressing was applied to the abdomen to blind the patient and hospital staff to the type of procedure performed. The day of discharge was determined by the patient. There were no significant differences in the mean length of hospitalization or time to return to work between the 2 groups. Since previous unblinded trials and case series have reported significantly shorter hospital stays in patients having laparoscopic cholecystectomy,[27] the findings from this trial suggest that the patients' and clinicians' expectations may be altered by knowing the type of procedure performed. Patients and hospital staff were not blinded in any of the trials included in this meta-analysis. Potentially, results may have changed if they had been blinded especially with regard to length of hospital stay and time to return to normal activities. The lack of blinding is of less concern with assessment of complications (i.e., wound and intra-abdominal infections) since these are more objective measures.

The trials included in this meta-analysis were published between 1993 and 1997. Since laparoscopic appendectomy was first described in 1982, the results of these trials may represent the early experience with this procedure. In 7 trials, minimum requirements for the laparoscopic surgeon were set,[1–3,6,7,11,12] but none described their experience with laparoscopic appendectomy. Although Chalmers[28] has advocated randomization of the first patient, most surgeons believe that there is a learning curve with surgical procedures, and results may improve as experience with the procedure is gained.Thus, the results from these RCTs may represent early experience with LA and may not be as good as current results.

Two other meta-analyses on this topic have been reported.[29,30] Kazemir and colleagues combined the data from 9 studies.[29] Their conclusions were similar to ours in that they reported that operative time favoured OA whereas the return to normal activity favoured LA.[29] However, they included 1 large non-RCT[22] and 1 RCT with less than 80% follow-up,[13] and they did not include 5 RCTs that were included in our meta-analysis. In addition, there was significant statistical heterogeneity in all 3 main outcomes, suggesting that the pooling of the data from the 9 studies was inappropriate. More recently, McCall and colleagues[30] published a review of 8 trials that were included in our meta-analysis. They also came to the same conclusions regarding length of operation and return to normal activity but found that the length of hospitalization was shorter after LA.[30] However, although they reported the data from each study in table form, there was no attempt to combine the data quantitatively, and their conclusions are based on a subjective impression of the data. This may account for the discrepancy in results.

In conclusion, the results from this meta-analysis suggest that LA can be performed safely although operative time is lengthened. Hospital stay is similar with either procedure but return to normal activity may be shorter after LA. At present, therefore, the decision whether to perform appendectomy open or laparoscopically may depend on local expertise and the availability of operative and hospital resources. There is a real need for further RCTs before adopting or disregarding LA because of the methodologic concerns of the published trials. As well, the laparoscopic expertise of most surgeons has increased. Future trials should be performed by experienced laparoscopists. Besides the usual methodologic necessities, blinding is essential before any firm conclusions can be made about the real benefit of LA to patients. Future trials should probably also incorporate patient preferences, quality of life assessments and an economic analysis.

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