International Journal of Technology Assessment in Health Care, 15:2 (1999), 380–391.

WOUND INFECTION IN OPEN VERSUS LAPAROSCOPIC APPENDECTOMY

A Meta-Analysis

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Abstract

The authors performed a meta-analysis to determine whether open or laparoscopic appendectomy would reduce wound infection incidence in adult patients with acute appendicitis. The meta-analysis included nine of seven patients from eight randomized controlled trials. Data were analyzed using the fixed effect-model method of Mantel-Haenszel. Wound infection incidence was lower in the laparoscopic group.

Keywords: Meta-Analysis, Randomized Trials, Appendectomy, Laparoscopic Surgery

Although appendectomy is the most common abdominal intervention in industrialized countries, with 300,000 to 500,000 cases per year in France (10;15;44), uncertainties remain about this operation. Since the first reports in the 1980s of laparoscopic appendectomy as a new treatment for acute appendicitis, some surgeons have recommended it because it reduces recovery time and the onset of immediate and late complications (34;43;48), while other prefer the conventional surgery because it is less expensive and involves a shorter operating time (12;38;44). Studies comparing open and laparoscopic appendectomy have reported conflicting results. In 1994 Gawenda and Said (13) published a review that presented 14 comparative studies (five retrospective studies, two comparing a retrospective group of open appendectomy with a perspective group of laparoscopic appendectomy, five nonrandomized prospective studies, and two randomized prospective studies), but found no conclusive evidence in favor of either of the procedures.

The authors thank Dr. F. Giraud for her help in our literature search, and Mrs. P. Johnson for her advice on English editing.

We performed a meta-analysis in order to determine whether open or laparoscopic appendectomy would reduce the incidence of wound infection in adult patients with acute appendicitis, because this parameter appeared to be the main relevant criterion after a critical appraisal of the literature on the subject.

METHODS

A literature search and a critical appraisal of studies comparing laparoscopic and open appendectomy were conducted, based on Medline data base and completed by references quoted in selected articles. Studies were independently selected by two observers for inclusion in the meta-analysis, according to the following selection criteria: randomized controlled trials, comparing appendectomy in male and female adult patients with clinical suspected acute appendicitis, published in either English, French or German. Data were analyzed using the fixed-effect-model method of Mantel-Haenszel. Sensitivity analysis was performed using the random-effect-model method of DerSimonian and Laird, and the cumulative fixed-effect-model method of Mantel-Haenszel according to study quality and number of patients. One unpublished study that we knew to have been performed in 1993 was also included, since it is a randomized trial that fulfills all the selection criteria (P. X. Barth, unpublished study, Department of General Surgery of Edouard Herriot Hospital, Hospices Civils de Lyon, France).

Quality Assessment and Classification of the Selected Studies

A critical reading guide was designed according to the McMaster University method (37), which allowed the quality assessment of the selected studies. These studies were classified according to methodological criteria, with the studies presenting more criteria being considered as better ones. The criteria, in descending order of importance, were: randomization, calculation of the required sample size, intention-to-treat analysis, and definition of the study objective. If studies were classified the same, we considered as better those that included more patients or that had attained their required sample size. The classification of the unpublished study was based on protocol design and whether this design was respected for data collection and analysis.

Analysis

Meta-analysis is a systematic, structured, and retrospective statistical integration of numerical information on a given subject, based on results of several independent studies. Its main features are the homogeneity of findings or the assessment of effect size (quantitative aspect), with a scoring of the studies according to a systematic and uniform application of predetermined criteria of quality (qualitative aspect) (19).

The endpoint was the incidence of wound infection, because it is the most common complication in both operations. In addition, it may lead to longer hospital stay and be responsible for later rupture, even though it is rarely serious (25;34).

The method used was the fixed-effect model method of Mantel-Haenszel, which assumes that treatment effect is the same in all studies (the heterogeneity test is not significant).

Sensitivity analysis aims at testing the robustness of the results by using other statistical models, or by taking into account factors such as quality score and sample size of the studies, or by removing unpublished studies (5;19). It was performed using the random-effect model method of DerSimonian and Laird (which assumes

https://doi.org/10.1017/S0266462399152000 Published online by Cambridge University Press

that treatment effect varies randomly from one study to another, and the heterogeneity test is significant), the Mantel-Haenszel method without the unpublished study and after classifying the studies according to number of patients included and recruitment, and the cumulative Mantel-Haenszel method according to quality score and sample size.

Statistical analysis was performed using the meta-analysis application program (Meta-Analyst, J. Lau, 1995) from the Harvard School of Public Health.

RESULTS

Literature Search

Eight studies were included in the meta-analysis, seven selected out of 33 from the literature and one unpublished. Wound infection incidence was significantly lower in the laparoscopy group than in the open group: [OR = 0.33, 95% CI = 0.18; 0.61] with the Mantel-Haenszel method, [OR = 0.38, 95% CI = 0.21; 0.70] with the DerSimonian and Laird method. Sensitivity analysis confirmed the robustness of the results.

Characteristics of Selected Studies

The eight studies included in the meta-analysis (seven published and one unpublished) were all conducted between 1992 and 1995 (Table 1). According to the number of included patients, they could be classified into two groups: those with approximately 100 patients (1;11;17;22; Barth, unpublished study), and those with more than 140 patients (27;32;42). The numbers of patients in the open and laparoscopy groups matched with a randomized assignment, except for one study in which patients were initially randomized into three groups: one open group and two laparoscopy groups using two different ligature methods (32). The calculation of the required sample size was present in two studies. In one sample size was based on pain as the main measurement criterion and evaluated at 22 subjects per group (17); in the other it was based on quality-of-life criteria (visual analog scale, including pain, physical function, and cosmetic injury) and evaluated at 80 subjects per group (Barth, unpublished study). The incidence of patients lost to follow-up was reported in four studies: 0% (11;17), 13% (1), and 37% (42); loss to follow-up reached 29% in the unpublished study. Exclusion criteria were defined in only two studies; they included pregnancy, age under 18, incarceration, refusal or inability to obtain informed consent, and inability to respect the protocol (32; unpublished study). An upper age limit was defined in some studies. The ambivalence clause was not always specified.

Open appendectomy was always performed using a right lower quadrant muscle-splitting incision, and the laparoscopic procedure was similar in the eight studies. Routine preoperative antibiotic prophylaxis was mentioned in four studies, and postoperative antibiotic treatment, depending on the macroscopic aspect of the appendix, in two studies. Patient follow-up consisted of the immediate postoperative period, i.e., hospitalization, a visit on the day of discharge between the third and the 15th postoperative day, and a visit or a questionnaire between the first and the third postoperative month.

The surgeon's experience was specified in all of the studies and included qualifications, minimum number of prior laparoscopic appendectomies performed (between 10 and 15), or recognized skill in this type of surgery. There was no difference among the studies. We tried to evaluate the practice of the different teams by

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Table 1. List of the Studies Collected by Literature Search

Study	Country	Year of publication	Journal	Exclusion criteria
Attwood et al. (1)[a]	Ireland	1992	*Surgery*	—
Balique et al. (2)	France	1993	*Chirurgie*	Retrospective study
Bonanni et al. (4)	USA	1994	*J Am Coll Surg*	Retrospective study
Champault et al. (6)	France	1993	*J Chir Paris*	Prospect. nonrand.
Clarkson et al. (7)	Germany	1993	*Zentral Chir*	Descriptive study
Desgroseilliers et al. (9)	Canada	1995	*Can J Surg*	Retrospective stidy
Frazee et al. (11)[a]	USA	1994	*Ann Surg*	—
Fritts and Orlando (12)	USA	1993	*Arch Surg*	Prospect. nonrand.
Gawenda and Said (13)	Germany	1994	*Langenbecks Arch Surg*	Literature review
Heberbrand et al. (17)[a]	Germany	1994	*Chirurg*	—
Heinzelmann et al. (18)	Switzerland	1995	*Arch Surg*	Hist. comparison
Karaorman et al. (20)	Germany	1994	*Chirurg*	Prospect. nonrand.
Kollias et al. (21)	Australia	1994	*Aust. N Z J Surg*	Prospect. nonrand.
Kum et al. (22)[a]	Singapore	1993	*Br J Surg*	—
Lansdown et al. (24)	UK	1993	*Br J Surg*	Hist. comparison
Lujan-Mompean et al. (25)	Spain	1994	*Br J Surg*	Prospect. nonrand.
Martin et al. (27)[a]	USA	1995	*Ann Surg*	—
McAnena et al. (28)	Ireland	1991	*Lancet*	Prospect. nonrand.
McAnena et al. (29)	Ireland	1992	*Br J Surg*	Prospect. nonrand.
Meinke and Kossuth (30)	USA	1994	*Surg Endosc*	Prospect. nonrand.
Neal et al. (31)	USA	1994	*Surg Laparosc Endosc*	Retrospective study
Ortega et al. (32)[a]	USA	1995	*Am J Surg*	—
Reierstein et al. (33)	Norway	1994	*World J Surg*	Prospect. nonrand.
Richards et al. (34)	USA	1993	*Surg Gynaecol Obstet*	Prospect. nonrand.
Rosso et al. (35)	Germany	1993	*Helv Chir Acta*	Hist. comparison
Schirmer et al. (38)	USA	1993	*Am J Surg*	Retrospective study
Sosa et al. (40)	USA	1993	*J Laparoendosc Surg*	Prospect. nonrand.
Tate et al. (42)[a]	China	1993	*Lancet*	—
Tate et al. (41	China	1993	*Br J Surg*	Prospect. nonrand.
Vallina et al. (44)	USA	1993	*Ann Surg*	Hist. comparison
Varlet et al. (45)	France	1994	*Eur J Pediatr Surg*	Retrospective study, children
Williams et al. (46)	USA	1994	*South Med J*	Prospect. nonrand.
Zaninotto et al. (48)	Italy	1995	*Surg Endosc*	Prospect. nonrand., women

Abbreviations: prospect. nonrand. = prospective nonrandomized study; hist. comparison = historical comparison (comparison of a series of patients who received laparoscopic appendectomy with a retrospective group of patients who received open appendectomy, matched for sex, age, severitry of disease, etc.
[a] Studies selected to be included in meta-analysis.

Table 2. Characteristics of Patients

Study	Number (OA/LA)	Mean age (extremes)	Sex (M/F)	Normal appendix (%)	Perforated appendix (%)
Heberbrand et al. (17)	23/25	23.5 (11–84)	23/25	10.4	10.4
Barth (unpublished study)	27/24	24.5 (10–49)	26/25	15.7	—
Attwood et al. (1)	32/30	23.9 (12–67)	—	11.3	—
Frazee et al. (11)	37/38	28.9 (10–70)	36/39	—	17.3
Kum et al. (22)	57/52	31.8 (—)	33/76	15.3	6.4
Tate et al. (42)	70/70	32.2 (28–37)	86/54	2.9	34.3
Martin et al. (27)	88/81	28 (—)	100/69	—	17.8
Ortega et al. (32)	86/167	24.9 (—)	180/73	16.9	17.4

Abbreviations: OA = open appendectomy; LA = laparoscopic appendectomy; M/F = male/female.

taking into account the duration of the period of patients' inclusion. Thus, we could distinguish between studies in which four to eight patients were included in a month (1;11;17; Barth, unpublished study) and studies in which 19 to 24 patients were included in a month (22;27;42).

The characteristics of the patients are presented in Table 2. Age was within the normal range for patients with acute appendicitis, with mean ages between 23 and 32 years and extremes at 10 and 84 years (14;26;39;47). The sex ratio matched literature data, except for two studies reporting a male-to-female ratio of 2:1 (22;32). The incidences of perforated and normal appendix were also within the normal range, except for one study reporting a high incidence of perforated appendix with a low incidence of normal appendix (42).

Quality assessment and classification of the selected studies are presented in Table 3. A quality scale was defined that attributed a ranking of 1 to the study considered as the best. Two studies were classified *ex aequo,* one in which the required sample size has not been calculated (1) and one in which it had been calculated but not attained (Barth, unpublished study).

Analysis

The data used to perform the analysis were the results of the selected studies (Table 4). The incidence of wound infection ranged from 0% to 10% in the laparoscopy groups and from 2.7% to 14.3% in the open groups. One study had the highest wound infection incidences in both groups (42). The incidence of wound infection was lower in laparoscopic appendectomy than in open appendectomy in all the studies (odds ratio or between 0.09 and 0.97), but this result was significant only in the study with the biggest sample size: OR = 0.17, 95% CI = 0.05; 0.54 (32).

The meta-analysis showed that incidence of wound infection is approximately three times lower in laparoscopic appendectomy than in open appendectomy. Results provided a significant overall odds ratio that favored laparoscopic appendectomy: OR = 0.33, 95% CI = 0.18; 0.61 (Figure 1). The DerSimonian and Laird method provided similar results: OR = 0.38, 95% CI = 0.21; 0.70. Bias did not appear when the number of patients or the recruitment rate were taken into account, neither in cumulative analysis of study quality and number of patients nor when the analysis was performed without the data from the unpublished study: OR = 0.34, CI 95% = 0.18; 0.63.

Table 3. Critical Reading Guide Applied to Selected Studies and Quality Classification Obtained

Criteria[a]	Importance of criteria[b]	Heberbrand et al. (17)	Barth (unpublished study)	Attwood et al. (1)	Frazee et al. (11)	Kum et al. (22)	Tate et al. (42)	Martin et al. (27)	Ortega et al. (32)
General									
Title	+++	Yes	—	Yes	Yes	Yes	Yes	Yes	Yes
Summary	++	Yes	—	Yes	Yes	±	Yes	Yes	Yes
Language[c]	±±±	G	—	E	E	E	E	E	E
Methodology									
Objective	++	Yes	Yes	Yes	No	Yes	±	No	No
Randomization	±±±	Yes	Yes	Yes	Yes?	Yes	Yes	Yes?	Yes
Sample size	+++	Yes	Yes	No	No	No	No	No	No
Initial comparison	++	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Analysis	+++	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Quality ranking		1	2	2	8	6	4	7	5

[a] Title: Presents a randomized controlled trial comparing open and laparoscopic appendectomy.
Summary: Are the objective, the type of the study, and the patients in accordance with our study?
Objective: Is the objective of the study clearly defined?
Randomization: Have the patients been randomly assigned to open/laparoscopic group? Yes? = Method used to randomize patients not given.
Sample size: Has required sample size been calculated?
Initial comparison of the groups: Has it been made?
Analysis? Have the patients been analyzed in their random assignment?
[b] Importance of the criteria: ±±± = essential; +++ = major; ++ = important; + = minor.
[c] Publication language: E = English; G = German.

Table 4. Meta-analysis Data

Study	INF. LA	TOTAL LA	INF. OA	TOTAL OA
Heberbrand et al. (17)	0	25	1	23
Barth (unpublished study)	0	24	1	27
Attwood et al. (1)	0	30	1	32
Frazee et al. (11)	1	38	1	37
Kum et al. (22)	0	52	5	57
Tate et al. (42)	7	70	10	70
Martin et al. (27)	3	81	6	88
Ortega et al. (32)	4	167	11	86

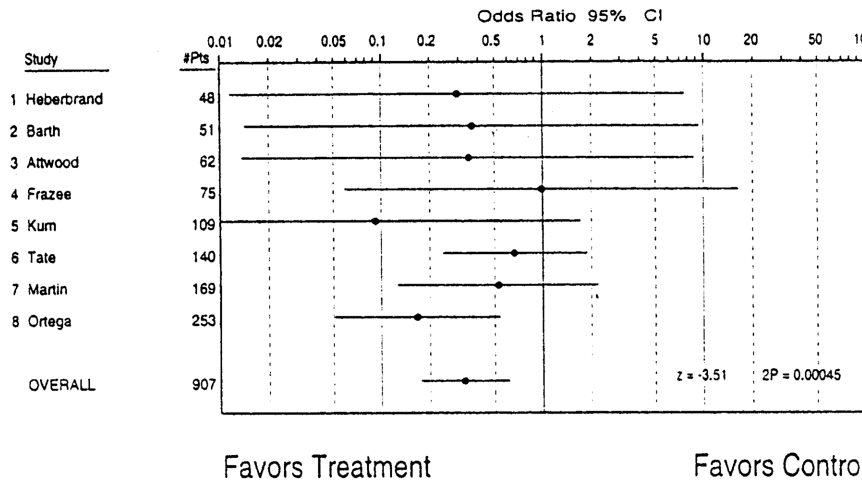
Abbreviations: INF. LA = number of wound infection cases in the laparoscopic appendectomy group; TOTAL LA = number of patients in the laparoscopic appendectomy group; INF. OA = number of wound infection cases in the open appendectomy group; TOTAL OA = number of patients in the open appendectomy group.

A heterogeneity test was performed to check the assumption that differences in the results of the studies were due to chance alone; it was not significant (Q = 6.26 with 7 ddl, $p > .05$) and confirmed that the selected trials were homogeneous. The association test was significant (U = 11.84 with 1 ddl, $p < .001$) and thus showed that there was a significant difference between open and laparoscopic appendectomy in terms of wound infection.

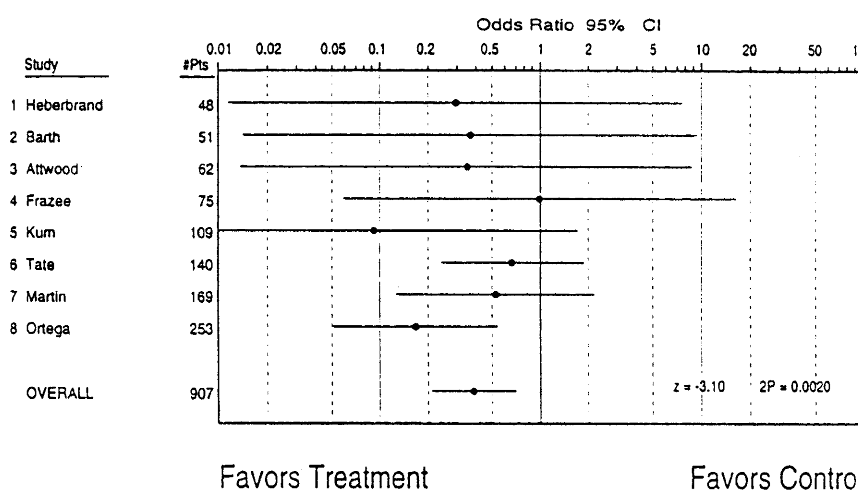
DISCUSSION

This meta-analysis of randomized controlled trials comparing open and laparoscopic appendectomy indicated that the incidence of wound infection is threefold less in laparoscopic appendectomy than in open appendectomy. Sensitivity analysis showed the robustness of these results. Nevertheless, they are not sufficient to make a choice between laparoscopic and open appendectomy. According to literature reports, morbidity seems to be an important factor when deciding between two surgical treatments that are equally effective and whose mortality rate approaches zero. Wound infection is the most frequent postappendectomy complication (from 4 to 7% after open appendectomy (2;20;42) and from 0 to 3.6% after laparoscopic appendectomy (15;25;43), and it is a clinical criterion that is easy to measure. Late complications such as rupture and adhesions may also be relevant because they may influence morbidity, hospitalization for treatment, and temporary inability to work (10). But their incidence is difficult to evaluate as they occur long after surgery, and a clear link cannot always be established. Despite the use of other endpoints in many studies, we did not choose them for the following reasons: operating time and the incidence of perioperative complications depend on the surgical team's experience in laparoscopic appendectomy; postoperative or total length of hospital stay depends on departmental customs and cannot be compared from one country to another; other immediate postoperative complications and mortality rates are very low and would require a too large number of subjects to reveal a difference. In addition, other relevant factors, such as time before return to activity, postoperative pain, aesthetics, and costs, also need to be considered using standardized methods of measurement.

Even though much care was taken to perform the literature search, there is always a risk that it is not comprehensive. The language of publication introduces a selection bias. In order to avoid publication bias, we asked the international



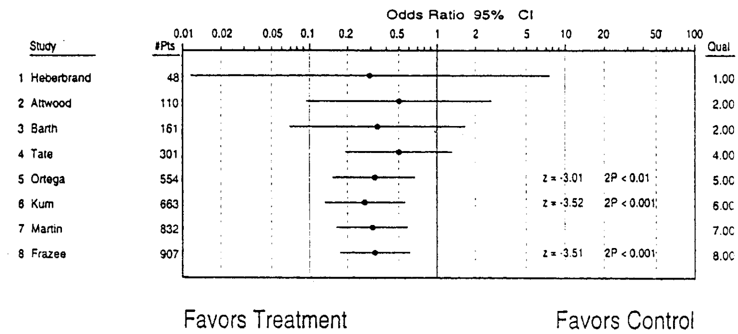
(Fixed-effect model method of Mantel-Haenszel)



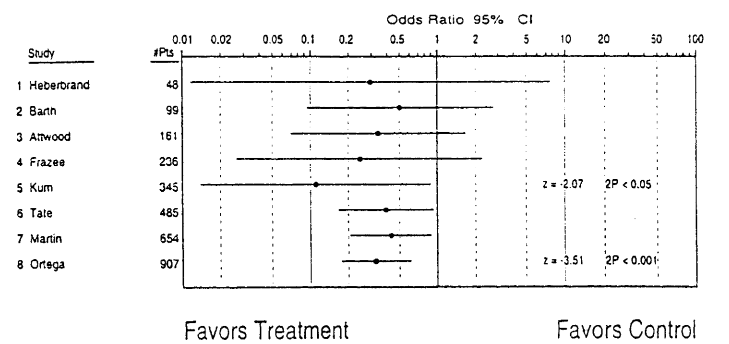
(Random-effect model method of DerSimonian and Laird)

Figure 1. Comparison of wound infection incidence in laparoscopic and open appendectomy: meta-analysis of 8 randomized trials. Odds ratios are represented by the plots, with their 95% confidence interval limits. The laparoscopic appendectomy (treatment) is on the left, and the open appendectomy (control) on the right; the vertical line represents the odds ratio of 1. Wound infection incidence is lower in laparoscopic appendectomy when the plot is on the left of the odds ratio of 1. Results are considered significant if the 95% CI does not override the ratio of 1.

Cochrane Collaboration in Boston about trials concerning our theme that might not have been published. Moreover, as we used the study results and not the individual data, we were unable to check details about elements that may have had an effect on the incidence of wound infection: antibiotic treatment, definition of wound infection, which was not specified in the selected studies, and method of extraction of the appendix used in the laparoscopic intervention. Nevertheless, all the selected studies were similar in terms of characteristics of included patients,



(Cumulative Mantel-Haenszel method according to descending order of quality classification)



(Cumulative Mantel-Haenszel method according to ascending number of patients)

Figure 1. (cont.).

surgeons' experience, patient follow-up, and use of the incidence of wound infection as a measurement criterion.

Concerning meta-analysis, the choice of the method and the model should respond to the effect-model and the separative power of the method (the separative power of the method makes it possible to discern the actual treatment effect from its variations according to the characteristics of the studies, such as sample size) (5;23;36). These elements being most often unknown, the method and the model are chosen according to the type of endpoint and data (3;8). We chose the Mantel-Haenszel method because we used the results of the selected studies and not individual data, our endpoint was qualitative, and the heterogeneity test was not significant. This method is particularly convenient with small numbers of patients and events. Although there is no consensus concerning determination of significance level, the value taken for the risk α is usually 0.05.

The heterogeneity test has limited statistical power. Similarity of results obtained with the Mantel-Haenszel method and with the DerSimonian and Laird method confirmed the assumption of homogeneity of the data and justified the choice of a fixed-effect model method. The number of patients and the recruitment were two factors in the selected studies that might have influenced the incidence of wound infection and results. Analysis performed when classifying the studies according to these criteria confirmed that they did not introduce bias in the observed results. The overall odds ratio and the odds ratio of Ortega's study were the only significant ones. This study might modify the overall result because it was performed on the biggest sample. In the cumulative analysis performed by including the studies in order of increasing number of patients, the odds ratio became significant when the fifth study was included and the total number of patients reached 345. As Ortega's study was the eighth to be included, the assumption of a bias was invalidated.

Although the literature on methodology recommends including study quality in meta-analysis, there is no evidence of a correlation between the quality scores and the outcomes of randomized controlled trials. Of the various methods proposed to assess the quality of clinical trials (16;19), we used the McMaster University method, which is commonly used in critical reading of clinical studies. We included study quality in the cumulative analysis by introducing the studies in descending order of quality according to the classification we had defined, in order to assess the lack of effect when studies of lesser quality were introduced (16). However, this critical appraisal was conducted on published reports of the studies and may be limited by the quality of reporting.

CONCLUSION

According to the published data available in mid-1996, the results of this meta-analysis showed that the incidence of wound infection is three times lower after laparoscopic appendectomy than after open appendectomy. However, other relevant endpoints should be taken into account to determine which approach is the treatment of choice for acute appendicitis, particularly because this disease mostly affects young people. Considering length of hospital stay, quality of life, duration of inability to work, and costs would help to decide which types of patients with acute appendicitis would benefit from laparoscopic surgery.

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