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## Laparoscopic repair for perforated peptic ulcer disease [Reviews]

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### Abstract

**Background:** Perforated peptic ulcer is a common abdominal disease that is treated by surgery. The development of laparoscopic surgery has changed the way to treat such abdominal surgical emergencies. The results of some clinical trials suggest that laparoscopic surgery could be a better strategy than open surgery in the correction of perforated peptic ulcer but the evidence is not strongly in favour or against this intervention.

**Objectives:** To measure the effect of laparoscopic surgical treatment versus open surgical treatment in patients with a diagnosis of perforated peptic ulcer in relation to abdominal septic complications, surgical wound infection, extra-abdominal complications, hospital length of stay and direct costs.

**Search strategy:** We searched the Cochrane Central Register of Controlled Trials (CENTRAL) on The Cochrane Library (Issue 2, 2004), PubMed/MEDLINE (1966 to July 2004), EMBASE (1985 to November 2004) and LILACS (1988 to November 2004) as well as reference lists of relevant articles.

**Selection criteria:** Randomised clinical trials comparing laparoscopic surgery versus open surgery for the repair of perforated peptic ulcer using any mechanical method of closure (suture, omental patch or fibrin sealant).

**Data collection and analysis:** Primary outcome measures included proportion of septic and other abdominal complications (surgical site infection, suture leakage, intra-abdominal abscess, postoperative ileus) and extra-abdominal complications (pulmonary). Secondary outcomes included mortality, time to return to normal diet, time of nasogastric aspiration, hospital length of stay and costs. Outcomes were summarized by reporting odds ratios and 95% confidence intervals, using the fixed-effect model.

**Main results:** We included two randomised clinical trials, which were of acceptable quality. We found no statistically significant differences between laparoscopic and open surgery in the proportion of abdominal septic complications (OR 0.66, 95% CI 0.30 to 1.47), pulmonary complications (OR 0.37, 95% CI 0.11 to 1.31) or actual number of septic abdominal complications (OR 0.72, 95% CI 0.33 to 1.58). Heterogeneity was significant only for pulmonary complications.

**Authors' conclusions:** This systematic review suggests that a decrease in septic abdominal complications may exist when laparoscopic surgery is used to correct perforated peptic ulcer. However, it is necessary to develop more randomised controlled trials that include a greater number of patients to confirm such an assumption, guaranteeing a long learning curve for

participating surgeons. With the information provided by the available clinical trials it could be said that laparoscopic surgery results are not clinically different from those of open surgery.

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## **Issue protocol first published**

2004 Issue 2

## **Date of last minor update**

29 September, 2004

## **Date new studies sought but none found**

04 April, 2005

## **Date new studies found and included or excluded**

04 April, 2004

## **Issue first published**

2005, Issue 4

## **Plain language summary**

The effectiveness of laparoscopic surgery for repair of a perforated peptic ulcer in comparison with open surgery was evaluated.

A perforated peptic ulcer can be repaired using either open surgery or laparoscopy. Two randomised controlled trials from Hong Kong were identified that compared the two methods. These trials included patients with clinical suspicion of perforated peptic ulcer, confirmed at surgery. Both laparoscopic and open repairs were made with an omentum patch or fibrin sealant. The primary outcomes assessed were septic abdominal and extra-abdominal complications. Secondary outcomes assessed were mortality, operation time and hospital length of stay. The quality of the trials was acceptable. There were no statistically significant differences in septic abdominal complications between laparoscopic and open repair of perforated peptic ulcer. More randomised controlled trials with a greater number of patients are needed to confirm such an assumption, guaranteeing a long learning curve for participating surgeons.

## **Background**

The appearance of laparoscopy in the late 1980s marked a milestone in surgery. Its advantages of diminished pain, surgical wound complications, hospital stay and global costs in uncomplicated cases of gallbladder disease ([Gadacz 2000](#)) led to the expansion of its use to other intra-abdominal organs such as the distal esophagus, the proximal stomach ([Chekan 1999](#); [Consensus 1997](#); [Horgan 1997](#); [Klingler 1999](#)) and the colon ([Rickard 2001](#); [Tisminezky 2000](#)).

Most of the early laparoscopic approaches were confined to elective surgery. However, with the improvement of technology and the gaining of experience, the laparoscopic approach for acute intra

abdominal pathologies can be applied more widely (Bergamaschi 2000; Pamoukian 2001; Sauerland 2002).

Peptic ulcer perforation is the second most frequent abdominal perforation that requires surgery, following perforated appendicitis. Peptic ulcer is a common disease in the general population. It is estimated that almost 10% of American men will suffer from duodenal ulcer in their lifetime although its incidence varies within a country (Paimela 1991) as it is more frequent in men and the incidence increases with age. Peptic ulcer disease has been associated with many etiological factors such as *Helicobacter pylori* infection, non-steroidal anti-inflammatory drug (NSAID) use, stress, cigarette smoking, diet and genetics but multifactorial hypotheses are widely accepted. Complications of peptic ulcer include bleeding, obstruction and perforation and are still treated by general surgeons.

Elective surgery for peptic ulcer disease has decreased significantly over the years due to the introduction of effective medical therapies, first with histamine type 2 (H<sub>2</sub>)-receptor antagonists and lately with proton pump inhibitors. The principal complications of perforation and hemorrhage remain indications for surgery, however (Paimela 1991; Svanes 1995).

Since the first description of surgery for acute perforated peptic ulcer many techniques have been recommended. Ulcers can be repaired by hand suturing the edges of the wound or using surgical stapling devices, covering the defect using an omental patch or closing it with a fibrin sealant or a gelatin plug product (Darzi 1993; Matsuda 1995; Tate 1993; Walsh 1993).

Since the early 1990s, some authors have suggested that in cases of perforated peptic ulcer the laparoscopic approach may offer theoretical advantages over the open approach. Such advantages include reduced size of the surgical wound and diminished postoperative pain; fewer postoperative complications; less intestinal manipulation, which should diminish post-operative ileus and the long-term risk of future adhesive obstructive complications; and the global costs derived from a shorter hospital stay and an earlier return to daily activities (Benoit 1993; Naesgaard 1999; Michelet 2000; Mouret 1990; Sunderland 1992). Furthermore, it has been suggested that laparoscopic repair could be the best choice for patients with adverse prognostic factors such as advanced age and coexisting cardiopulmonary diseases, or a clinical evaluation delayed beyond 12 hours from the onset of symptoms (Chou 2000; Hermansson 1999). However, some authors have also found that laparoscopic repair presents somewhat higher incidence of leaks and is a more time-consuming procedure (Lau 1995; Lee 2001).

Controlled trials have been carried out trying to evaluate this approach. However, the results are inconclusive because of methodological weaknesses in the trials and small numbers of participants (Druart 1997; Gomez-Ferrer 1996; Katkhouda 1999; Kum 1993; Lau 1995; Lau 1996; Lau 1998; Michelet 2000; Ozmen 1995; Robertson 2000; Siu 2002). A systematic review is, therefore, appropriate as meta-analysis may prove informative as to the comparative efficacy and complication rates for the two surgical approaches.

Thus, the present systematic review was developed to answer the following question: is laparoscopic treatment of perforated peptic ulcer associated with reduced wound complications, post-operative intra-abdominal sepsis, duration of hospitalization and overall cost compared to conventional (open approach)?

## Objectives

To assess laparoscopic surgical treatment versus open surgical treatment in patients with perforated peptic ulcer diagnosis in terms of abdominal septic complications, surgical wound infection, extra-abdominal complications, hospital stay and direct costs.

## Criteria for considering studies for this review

### Types of studies

The review included randomised controlled trials that were performed after 1988 (the date of the first surgical procedure using laparoscopy ([Mouret 1990](#))). Restrictions regarding language were not applied.

Studies including patients managed with an open abdomen from the beginning of surgery or that did not have information about relevant clinical outcomes (surgical wound infection, intra-abdominal infection and hospital length of stay) were excluded.

### Types of participants

Adult patients, older than 18 years, with a preoperative clinical diagnosis and intraoperative confirmation of a perforated ulcer (gastric or duodenal) that was corrected by any mechanical method (primary suture, omentum patch, synthetic material patch) by a surgeon.

### Types of intervention

Laparoscopic versus open surgery correction of the ulcer with any mechanical method (primary suture, omentum patch, synthetic material patch or resection), with or without insufflation.

### Types of outcome measures

#### Primary outcomes

Septic and other abdominal and extra-abdominal complications defined according to the Centers for Disease Control (CDC) classification ([Garner 1996](#)) and recorded as 'number of complications' and 'at least one abdominal complication'. We considered the following abdominal complications: intraabdominal abscess; anastomosis leakage; secondary peritonitis; surgical-site infection; prolonged ileus for more than 72 hours without recovery of bowel movement, clinically-determined and incisional hernia.

#### Secondary outcomes:

mortality;

number of interventions;

conversion rate for the laparoscopic group;

nasogastric tube duration;

total analgesic dose;

time to return to normal diet;

overall duration of hospitalisation;

operation time.

Outcome measures were measured within the period 30 days after surgery.

## Search methods for identification of studies

See: methods used in reviews.

A search was conducted to identify all published and unpublished randomised controlled trials.

Trials were identified by searching the following electronic databases: The Cochrane Library (Issue 2, 2004), MEDLINE (1966 to April 2004), EMBASE (1985 to April 2004) and LILACS (Latin American and Caribbean Health Sciences) (1988 to April 2004).

The following search strategy was constructed by using a combination of subject headings and textwords relating to the use of laparoscopic repair for the treatment of perforated peptic ulcers. The standard Cochrane search strategy filter for identifying randomised controlled trials was applied to all searches.

MEDLINE search strategy

exp peptic ulcer/

exp peptic ulcer hemorrhage/

exp peptic ulcer perforation/

exp duodenal ulcer/

exp stomach ulcer/

(duoden\$ adj5 ulcer\$).tw.

(stomach adj5 ulcer\$).tw.

(bleed\$ adj5 ulcer\$).tw.

(rebleed\$ adj5 ulcer\$).tw.

(recurrent adj5 bleed\$ adj5 ulcer\$).tw.

(acute adj5 bleed\$ adj5 ulcer\$).tw.

(gastrointestinal adj5 bleed\$).tw.

(gastrointestinal adj5 rebleed\$).tw.

(gastrointestinal adj5 hemorrhag\$).tw.

(gastrointestinal adj5 haemorrhag\$).tw.

(ulcer adj5 hemorrhag\$).tw.

(ulcer adj5 haemorrhag\$).tw.

(ulcer adj5 perforat\$).tw.

exp laparoscopy/

laparoscop\$.tw.

or/30-47

or/48-49

50 and 51

52 and 29

Reference lists from trials selected by electronic searching were screened to identify further relevant trials. Abstracts from the conference proceedings of the American Digestive Disease Week (DDW), published in *Gastroenterology* and the United European Gastroenterology Week (UEGW) and appearing in *Gut*, were handsearched.

In addition, members of the Cochrane Upper Gastric and Pancreatic Diseases Group, experts in the field and pharmaceutical companies were contacted and asked to provide details of any outstanding clinical trials or relevant unpublished studies. The international societies of minimally invasive surgery (European and American laparoscopic surgery societies) and the international gastrointestinal surgery societies (Gastrointestinal Surgery Society) were also contacted and asked to provide information on any unpublished studies. However, there was no response from these organizations to report unpublished studies.

## Methods of the review

CM and MV extracted the data using a previously designed format. They were trained at the beginning of the study on data extraction methods, especially on the non-imputation of results from the reports. The concordance between the extractors was evaluated using an intraclass correlation coefficient and kappa coefficient; the value was 0.99. For missing data, trial authors were contacted via e-mail. In cases where it was impossible to obtain the relevant data, the study (Lau 1998) was excluded. For cases in which the article data used measure units that differed from the review format, the extractor registered the original data and the review authors performed the necessary conversion. The studies were centrally blinded by the review authors for the title of the article, authors and publication source.

Quality assessment was performed by CM and MV. The assessment focused on which randomisation method was used; whether there was blinded assignment; whether blind evaluation was performed; whether there were follow-up losses, and the percentage; and whether the intention-to-treat method was used.

The evaluation of the studies was centrally blinded by the review authors regarding the article title, the authors, and the publications source.

A scale was not used and studies were part of a sensitivity analysis for quality if they did not meet more than three of the conditions specified as ideal (blinded assignment, less than 20 % losses to follow up, intention-to-treat analysis). Blind evaluation was considered as adequate when the authors reported some mechanism especially developed for diminishing the bias of result measurement (external evaluators for the detection of complications; secondary review of information on the appearance of complications, etc.)

Comparison was made between the type of treatment and septic and other complications: abdominal including surgical site infection, intra-abdominal abscess, leakage from the suture site and prolonged ileus; and extra abdominal, specifically pulmonary complications; number of re-operations; mortality and hospital length of stay. Statistical analysis was performed using the Cochrane RevMan 4.1 software.

The results for each outcome were measured using the crude odds ratio (OR) for categorical variables not related by time; log hazard ratio for time-to-event variables; and means differences for continuous variables. The 95% confidence interval was also estimated.

Heterogeneity analysis was performed using the Q test, being considered significant when P value < 0.1.

The fixed-effect model and the Mantel-Haenszel method for the measurement of the global effects outcome were used. If there was significant heterogeneity, a re-analysis with the random-effects method was done as well as a sensitivity analysis to try to consider the potential source of heterogeneity. The origin of the heterogeneity was explained qualitatively. Although a stratified analysis by disease severity was planned in the protocol, as a way to explain any heterogeneity, it was impossible to do because of the poor information about the severity of the disease in the included reports.

The identification of publication bias with the funnel graphic, planned in the protocol, could not be performed because of the low number of articles included in the review.

## **Description of studies**

Seven studies were identified by the primary search. Four of these were excluded because they were comparative studies and did not use randomisation ([Bergamaschi 2000](#); [Katkhouda 1999](#); [Mehendale 2002](#); [Robertson 2000](#)); another was excluded because of missing data ([Lau 1998](#)). We tried to contact the authors, without any response.

All studies were identified in MEDLINE and all were in the English language. The one article that was in a language other than English stated clearly in the abstract that it was not a randomised controlled trial, so it wasn't translated.

Requests to authors and other sources of information did not provide further studies.

Inclusion criteria were similar for the two selected trials: adult patients with a clinical diagnosis

of perforated peptic ulcer (as shown by peritoneal irritation, pneumoperitoneum on chest x-ray) made by the attending surgeon.

Exclusion criteria also were similar for both included studies: a) previous abdominal surgery; b) concomitant bleeding of the ulcer, or gastric outlet obstruction; c) intra-operative diagnosis of hollow viscus perforation different from peptic ulcer; d) perforated peptic ulcer that required definitive surgery, criteria not reported; e) cardiopulmonary severe disease that impeded a long-duration procedure; and f) clinically sealed ulcer by the omentum at the time of surgery (Lau 1996; Siu 2002).

The studies did not report on baseline differences in participant age, sex, disease severity (measured with APACHE II score and ASA classification), shock, concomitant diseases, ulcer localization or perforation size. Nor did they mention the grade of peritonitis.

Interventions were as follows. Open surgery was by a midline laparotomy with closure of the ulcer with omentum using the technique of Cellan-Jones. In the Lau (Lau 1996) study, two more groups were created within the open and laparoscopic surgery groups: one with the Cellan-Jones technique and the other using sponge and fibrin sealant and peritoneal toilet. Laparoscopic surgery included the creation of a pneumoperitoneum with carbon dioxide at 15 mm Hg using a 10 mm trocar and the insertion of a further two or three 5 mm trocars, and closure of the perforation with omentum sutured by the same technique as with open surgery or using a sponge and fibrin sealant. All patients received antibiotics; one study for a day (Lau 1996) and the other for five days (Siu 2002). Postoperative analgesia was maintained with pethidine (1 mg/kg every 4 hours).

Both studies mentioned that the surgical procedures were performed by trained surgeons, or by residents accompanied by trained surgeons, with experience in open and laparoscopic surgery. However, none of the studies described the number of procedures that the surgeon had previously carried out.

## Methodological quality

Both studies made the randomisation using computer-generated random numbers and the concealment of assignment was made with sealed envelopes. Assessment of outcomes was not blinded in either of the studies but, in both, the pain evaluation was made by a person different from the attending team. In Siu 2002 an independent surgeon made the evaluation of return to normal activities and work.

Follow up was at day thirty but in one study there were losses of 27% for the laparoscopy group and 31% for the open surgery group (Lau 1996) (Table 2).

An intention-to-treat analysis for primary outcomes was made in all studies.

CM and MV differed in their assessment of outcomes related to suture dehiscence and morbidity in the Siu article (Siu 2002) and with blind outcome assessment, operative time and nasogastric aspiration time in the Lau article (Lau 1996). AS reviewed the articles and resolved the differences.

## Results

The two studies included ([Lau 1996](#); [Siu 2002](#)) recruited 214 patients: 111 in the laparoscopy group (48 in [Lau 1996](#); and 63 in [Siu 2002](#)) and 103 in the open-surgery group (45 in [Lau 1996](#); and 58 in [Siu 2002](#)).

Results for the primary outcomes were as follows.

Twelve of 111 (10.8%) patients in the laparoscopy group had an abdominal complication against 16 of 103 (15.5%) in the open-surgery group. The OR was 0.66 (95% CI 0.30 to 1.47). No statistically significant differences or heterogeneity were observed. The absolute number of septic abdominal complications was 13 (11.7%) in the laparoscopy group and 16 (15.5%) in the open-surgery group. The OR was 0.72 (95% CI 0.33 to 1.58) but the difference was not statistically significant. Only one patient in the laparoscopic group, from the [Siu 2002](#) study, had two concurrent complications (suture leakage and intra-abdominal abscess).

Three patients in the laparoscopic group (2.7%) and eight (7.7%) in the open-surgery group had a surgical site infection (OR 0.33, CI 95% 0.08 to 1.26). Suture dehiscence was similar in both groups (two patients in each group) with an OR of 0.93 (95% CI 0.13 to 6.71). Four patients had intra-abdominal abscesses in the laparoscopic group and none in the open-surgery group (OR 4.8, CI 95% 0.55 to 42.0) but this difference was not statistically different. Postoperative ileus occurred in four patients from the laparoscopy group and in six from the open-surgery group with an OR of 0.60 (CI 95% 0.16 to 2.22); incisional hernia incidence was similar between groups with two patients for laparoscopic repair and one for the open-surgery group (OR 1.40, CI 95% 0.23 to 8.51). None of these comparisons showed a statistically significant difference or heterogeneity.

Septic extra-abdominal complications, specifically pulmonary complications, occurred in four patients in [Lau 1996](#) (three in the laparoscopic group) and seven in [Siu 2002](#) (none in the laparoscopic group). The OR was 0.37 (CI 95% 0.11 to 1.31) which was not statistically significant. The heterogeneity test had a P value of 0.0028 and I<sup>2</sup> was 79.3%. As stated in the protocol, we performed an analysis using the random-effects method but without any change in the results.

For the secondary outcomes, three patients died in the laparoscopic group (2.7%) and four patients in the open-surgery group (3.8%) with an OR of 0.69 (CI 95% 0.15 to 3.14). The deaths were secondary to abdominal sepsis in two patients for each study. Six patients were re-operated on the laparoscopic group (5.4%), almost twice as many as in the open-surgery group (three patients (2.9%)) but this difference was not statistically significant (OR 1.89, CI 95% 0.46 to 7.71).

The operation time was different between studies. [Siu 2002](#) reported a lower time for laparoscopic repair (42 +/- 25.1 min) than in the open-surgery group (52.3 +/- 24.8 min); the difference was statistically significant (P value 0.02). To the contrary, [Lau 1996](#) reported a longer operation time for the laparoscopic group (94.3 +/- 40.3 min) than the open-surgery group (53.7 +/- 42.6 min); this difference was statistically significant (P value 0.001). The weighted mean difference was 0.77 min (95% CI -7.10 to 8.64), not statistically significant, but with a highly statistically significant heterogeneity test (P value < 0.00001, I<sup>2</sup> 96.3%). The analysis with random-effects model did not change the heterogeneity test P value. The conversion rate for the laparoscopy group was nine patients in each study and the global frequency was 16.2%.

Table 1 contains the medians and ranges for the outcomes time of nasogastric aspiration, time to return to oral diet, analgesic doses and hospital length of stay.

## Discussion

The results of this systematic review must be interpreted carefully because of the small sample size of the included trials.

Clinical heterogeneity was not identified in the relevant clinical variables of the studies included so it is probably that patients were similar, but readers must realize that both studies were from Hong Kong. However, we do not believe this compromises the generalizability of results.

Although there was a tendency to a decrease in septic intra-abdominal complications, surgical site infection, postoperative ileus, pulmonary complications and mortality with laparoscopic repair compared with open surgery none of these were statistically significant. However, there was a tendency to an increase in the number of intra-abdominal abscesses and re-operations, but without statistical significance. This finding could be related to surgeon experience in laparoscopic surgery. It is not possible to draw any conclusions about suture dehiscence and incisional hernia with the two procedures.

Other important variables, time of nasogastric aspiration and time to return to oral diet, were reported in a non-parametric format and were not statistically different between groups. In [Siu 2002](#), hospital length of stay was statistically in favour of laparoscopic repair, but not in [Lau 1996](#). Both included trials reported lower analgesic dose requirements for the patients in the laparoscopic group. With these findings it is impossible to suggest any beneficial effects in terms of direct costs, and this subject should be assessed in other studies specifically designed to assess cost-effectiveness.

Statistical heterogeneity was found in the frequency of pulmonary complications and in operation times. It is hard to explain heterogeneity for pulmonary complications with the available data. In the case of operation time, the most recent study ([Siu 2002](#)) showed a lower operation time for the laparoscopic procedure than did the older study ([Lau 1996](#)). This could be explained by greater experience with minimally-invasive surgery.

In general terms the quality of the trials was acceptable. There are concerns about blind assessment of outcomes. This quality criterion is difficult to obtain in surgical trials, where it is impossible to blind evaluators to the surgical group. To improve the outcome evaluation and to be closer to ideal blind assessment, it has been proposed that evaluators who are independent from the treating team, or non-physician evaluators, are equipped with a pre-designed data form and used ([Solomon 1998](#); [Thomas 2004](#)). Such strategies were applied in the included clinical trials so we consider that outcomes evaluation, although bias susceptible, was strong enough to support the results. Those lost to follow up in the study of [Lau 1996](#) were greater than 20% in both groups. However, it is probable that these losses only affected the measures of time to return to work and to normal activities as surgical complications usually occur during the first week when patients are still in hospital.

Another important point to discuss is the learning curve for surgeons. It is accepted that

surgical procedures are highly dependent on ability and the familiarity that surgeons have with different techniques. Introduction of a new surgical technique has a better prognosis when experience with it is greater (Solomon 1998). For the included trials, there was no objective information that helped to define the point on the learning curve of the surgeons, which affects the generalizability of the results. However, conversion rate of 16% shows that experience with the technique is enough to consider the laparoscopic approach in these cases. The high number of patients operated on per month and the low conversion rates suggest high experience. It is probable that new trials will provide better outcomes because of greater experience with laparoscopic techniques. In relation to the generalizability of the results, it is important to highlight that both included studies were from Hong Kong, which could be important, especially in relation to age, obesity and comorbid conditions of presenting patients.

This systematic review suggests that a decrease in septic abdominal complications may result when laparoscopic surgery is used to correct a perforated peptic ulcer as compared with open surgery. However, more trials are needed to confirm such an assumption and to assess the effect of the learning curve on outcomes, thus guaranteeing a long learning curve for participating surgeons. From the information provided by the clinical trials included in this review, outcomes from laparoscopic surgery for perforated peptic ulcers are not clinically different from those of open surgery, which is the actual gold standard. With conversion rates found in this systematic review, laparoscopic surgery could be the first therapeutic option in patients with perforated peptic ulcer after considering other variables such as experience, costs and availability.

## **Authors' conclusions**

### Implications for practice

With present data, it is not clear whether laparoscopic surgery offers advantages in terms of a decrease in septic abdominal complications when compared with open surgery. There is a trend towards reduction in these outcomes but the limited number of clinical trials prevents any strong conclusion. Surgeons that decide to apply this technology must make a judicious cost-benefit assessment, about which there is little related evidence.

### Implications for research

It is necessary to have randomised controlled trials with large sample sizes, better outcomes assessments and in different populations. Besides, variables that measure the experience of surgeons with laparoscopic repair must be introduced and assessed. Data about cost and resources consumption variables are also needed.

## **Potential conflict of interest**

None known.

## **Acknowledgements**

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and Marta Roque for language amendments.

## Characteristics of included studies

### Study Lau 1996

**Methods** 28 months, RCT parallel design, randomized using computer generated random numbers by the block method, concealment of allocation using sealed envelopes, outcome assessment was made by two assessors (not stated if independent from the treating team and blind) for pain evaluation and by the treating team for activity, work return evaluation and complications, lost to follow-up at 4 weeks: 73% for laparoscopic group vs 69% for open surgery group, intention-to-treat analysis

**Participants** 93 patients (48 for laparoscopic group and 45 for open surgery group).

Sex: 79 men/14 women

Mean age 47.8 to 52.3

Site of perforation: duodenum (76), juxtapyloric (11), gastric (6)

Size of perforation 1-25 mm

Age of inclusion not reported, but probably adults.

Inclusion criteria:

clinical diagnosis of perforated peptic ulcer made by the surgeon and confirmed at the operation room.

Exclusions criteria:

Complicated ulcers that required definitive surgery (criteria not stated)

Bleeding ulcer

Previous abdominal operations

Serious associated cardiopulmonary diseases

Clinically sealed perforation

Severity assessed by APACHE II score. Median 6.

**Interventions** Intravenous cefuroxime 750 mg and metronidazole 500 mg was given at the time of induction and for the first postoperative day.

For postoperative analgesia, patients were prescribed pethidine 1 mg/kg every 4 hours as required.

Upper midline incisions were made in patients assigned to open repair. Perforations were repaired with the Cellan-Jones method or using a rolled piece of gelatin sponge placed in the

perforation and secured with fibrin sealant.

For laparoscopic repair, pneumoperitoneum was established at 15 mm Hg, and three trocars were introduced and the ulcer was sutured with a piece of omentum and non-absorbable suture or using a gelatin and fibrin sealant.

The number of participating surgeons, the number of cases previously operated by the surgeon and the number of patients operated by each surgeon was not reported.

The study divided laparoscopic and open surgery groups in two branches: one repaired with suture and the other repaired with fibrin sealant. Re-compilation of data did not consider this division.

### **Outcomes** Complications

Time of nasogastric aspiration

Time of intravenous fluid maintenance

Pain assessed with Visual Analogue Scale

Conversion rate for laparoscopic group

Operation time

Analgesic use

Time to resume oral diet

Length of hospital stay

**Notes** Sample size was calculated using the analgesic doses using a previous study made by the same authors.

**Allocation concealment** A - Adequate

### **Study Siu 2002**

**Methods** 41 months, RCT parallel design, randomized using computer generated random numbers by the block method, concealment of allocation using sealed envelopes, outcome assessment was made by assessors independent from the treating team for pain evaluation; by independent surgeons not blinded, for discharge and by the treating surgeon not blinded for activity, work return evaluation and complications, intention-to-treat analysis, without losses to follow up

**Participants** 121 patients (63 for the laparoscopic group and 58 for the open surgery group)

Sex: 98 men/ 23 women

Mean age: 53.8 to 56.1

Site of perforation: duodenum (93), pyloric-prepyloric (27), gastric (1)

Size of perforation: 4.7 to 5.2 mm

Age: Patients older than 16 years old

Inclusion criteria:

Clinical diagnosis of perforated peptic ulcer made by the surgeon and confirmed at the operating room.

Exclusion criteria:

Gastric outlet obstruction

Bleeding ulcer

Previous abdominal operations

Clinically sealed perforation

Severity assessed by ASA classification and Boey risk factors scale. 81% of patients classified as ASA I and II and 95% as Boey risk scale 0 and 1 (good prognosis)

**Interventions** Intravenous cefuroxime 750 mg was given at the time of induction and continued for 5 days.

For postoperative analgesia, patients were prescribed pethidine 1 mg/kg every 4 hours as required.

Upper midline incisions were made in patients assigned to open repair. Perforations were repaired with the Cellan-Jones method.

For laparoscopic repair, pneumoperitoneum was established at 15 mm Hg, and three trocars were introduced and the ulcer was sutured with a piece of omentum and non-absorbable suture.

The number of participating surgeons, the number of cases previously operated by the surgeon and the number of patients operated by each surgeon was not reported.

**Outcomes** Complications

Analgesic use

Time of nasogastric aspiration

Time of intravenous fluid maintenance

Pain assessed with Visual Analog Scale

Conversion rate for laparoscopic group

Operation time

Time to resume oral diet

Length of hospital stay

**Notes** Sample size was calculated using the analgesic doses using a previous study made by other authors.

**Allocation concealment** A - Adequate

## Characteristics of excluded studies

**Study** Reason for exclusion

**Bergamaschi 2000** Prospective non-randomised clinical trial

**Katkhouda 1999** Prospective non-randomised clinical trial

**Lau 1998** Missing data about septic complications

**Mehendale 2002** Prospective non-randomised clinical trial

**Robertson 2000** Prospective non-randomised clinical trial

## Additional tables

Table 01

Table 02

## Analyses

Comparison 01

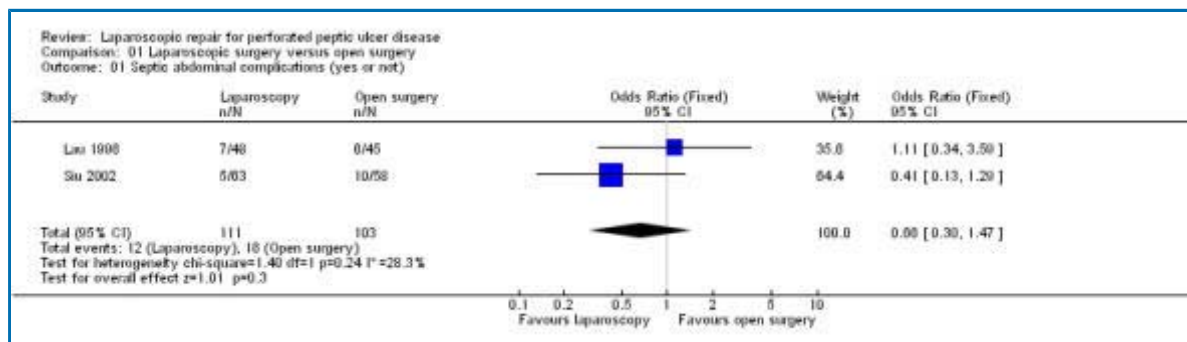
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External sources of support

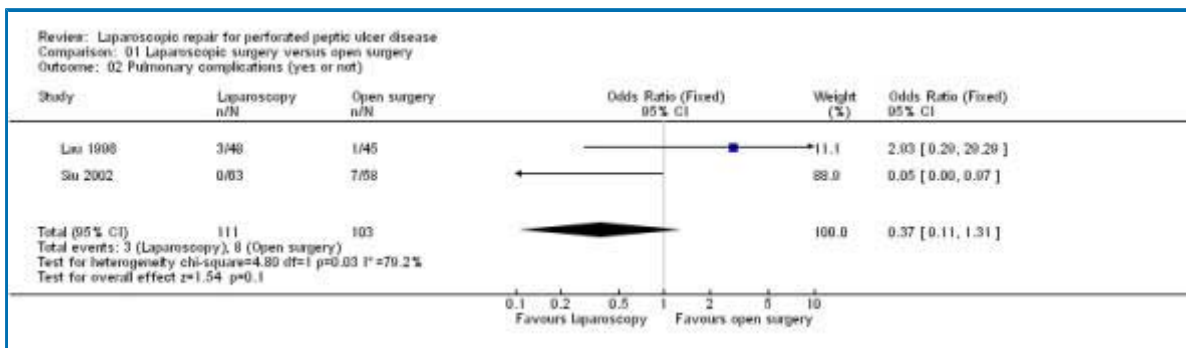
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- \* Centre Cochrane Iberoamerica SPAIN

Internal sources of support

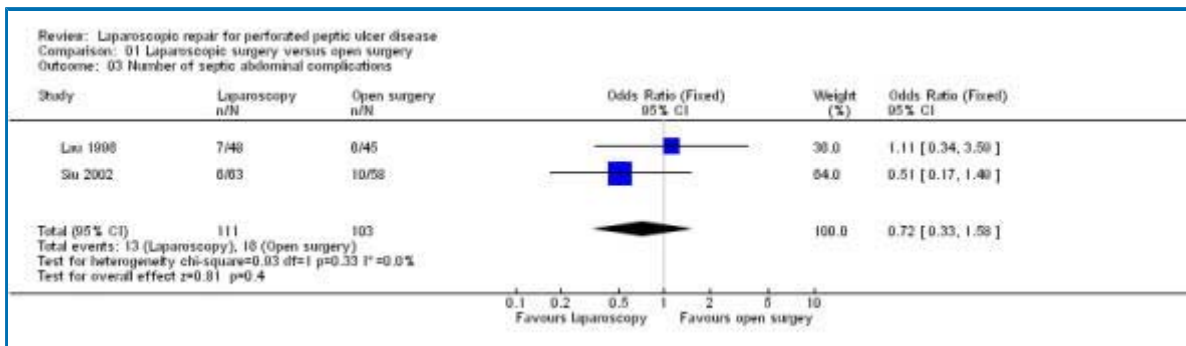
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- \* Grupo de Epidemiologia Clinica. Facultad de Medicina. Universidad de Antioquia COLOMBIA



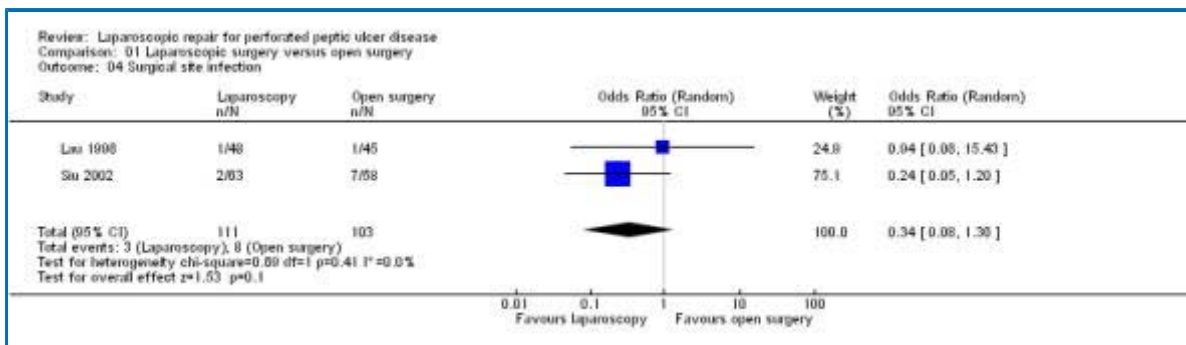
Comparison 01 Laparoscopic surgery versus open surgery, Outcome 01 Septic abdominal complications (yes or not)



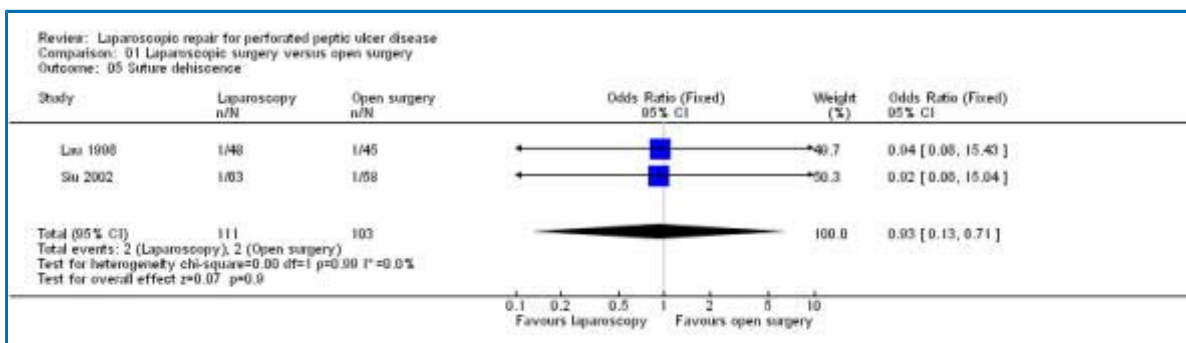
Comparison 01 Laparoscopic surgery versus open surgery, Outcome 02 Pulmonary complications (yes or not)



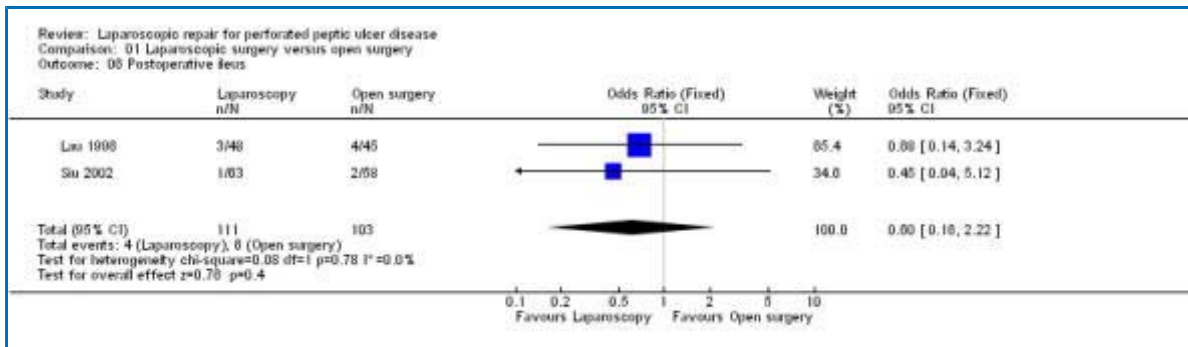
Comparison 01 Laparoscopic surgery versus open surgery, Outcome 03 Number of septic abdominal complications



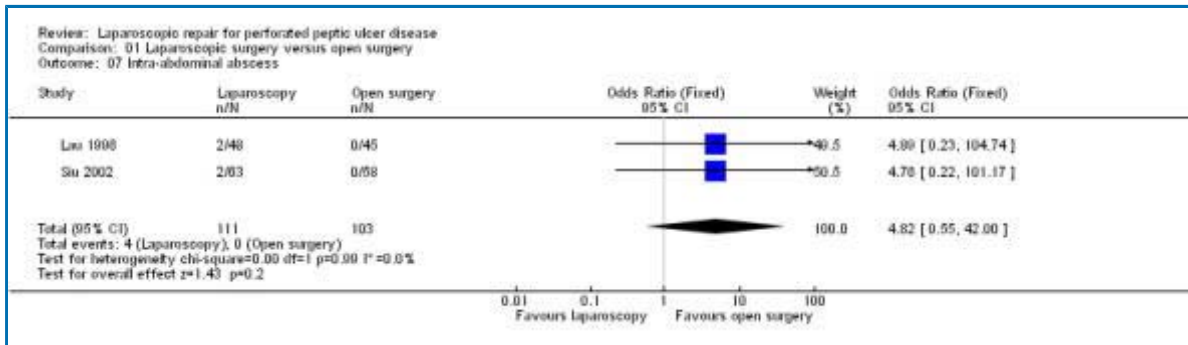
Comparison 01 Laparoscopic surgery versus open surgery, Outcome 04 Surgical site infection



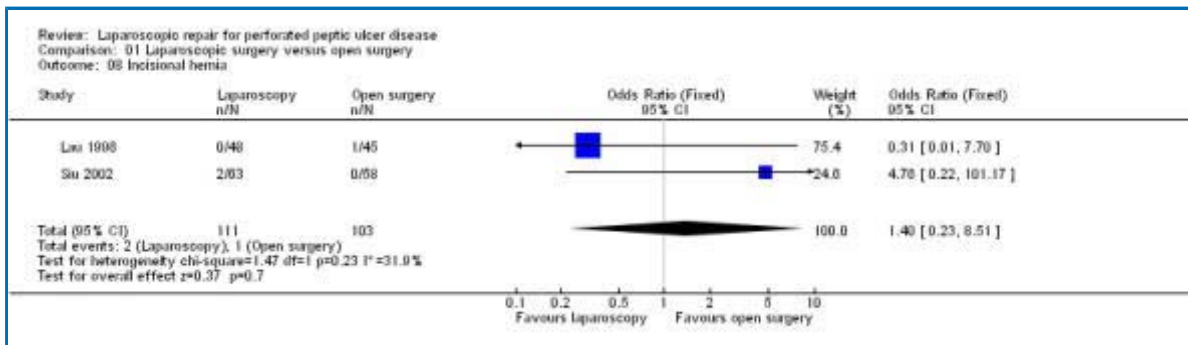
Comparison 01 Laparoscopic surgery versus open surgery, Outcome 05 Suture dehiscence



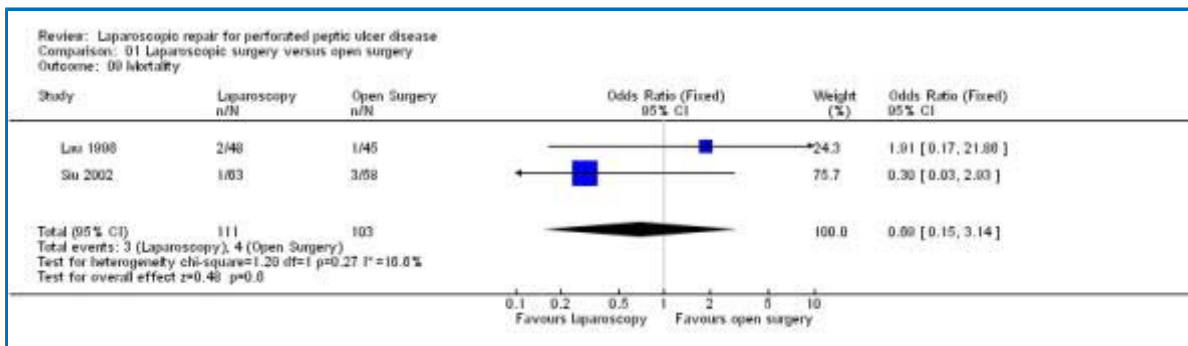
Comparison 01 Laparoscopic surgery versus open surgery, Outcome 06 Postoperative ileus



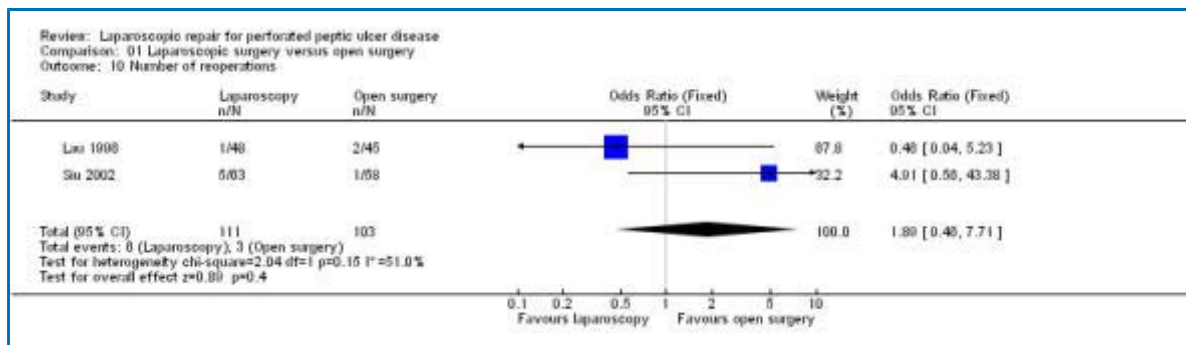
Comparison 01 Laparoscopic surgery versus open surgery, Outcome 07 Intra-abdominal abscess



Comparison 01 Laparoscopic surgery versus open surgery, Outcome 08 Incisional hernia



Comparison 01 Laparoscopic surgery versus open surgery, Outcome 09 Mortality



Comparison 01 Laparoscopic surgery versus open surgery, Outcome 10 Number of reoperations

## Measures reported in non-parametric form

**Variable:** Nasogastric aspiration time (median and range)

**Study:** Siu 2002

**Laparoscopic group:** 3 (2-33)

**Open surgery group:** 3(1-8)

**P value:** 0.28

**Variable:**

**Study:** Lau 1996

**Laparoscopic group:** 2 (1-4)/ 3 (2-1)

**Open surgery group:** 2 (1-13)/ 3(1-17)

**P value:** No significant (P value not reported)

**Variable:** Time to return to oral diet

**Study:** Siu 2002

**Laparoscopic group:** 4 (3-35)

**Open surgery group:** 5 (3-24)

**P value:** 0.06

**Variable:**

**Study:** Lau 1996

**Laparoscopic group:** 4 (3-7)/ 4 (2-11)

**Open surgery group:** 4 (3-16)/ 4 (3-19)

**P value:** No significant (P value not reported)

**Variable:** Length of stay

**Study:** Siu 2002

**Laparoscopic group:** 6 (4-35)

**Open surgery group:** 7 (4-39)

**P value:** 0.004

**Variable:**

**Study:** Lau 1996

**Laparoscopic group:** 5 (3-20)/ 6 (3-11)

**Open surgery group:** 5 (3-19)/ 5 (2-21)

**P value:** No significant (P value not reported)

**Variable:** Analgesic doses

**Study:** Siu 2002

**Laparoscopic group:** 0 (0-11)

**Open surgery group:** 6 (1-30)

**P value:** <0.001

**Variable:**

**Study:** Lau 1996

**Laparoscopic group:** 1 (0-12)/ 2 (0-17)

**Open surgery group:** 3 (0-10)/ 4 (1-9)

**P value:** 0.03

## Quality criteria for included studies

**Study:** Lau 1996

**Design:** RCT parallel design, randomized using computer generated random numbers by the block method, concealment of allocation using sealed envelopes, outcome assessment was made by two assessors (not stated if independent from the treating team and blind) for pain evaluation and by the treating team for activity, work return evaluation and complications, lost of follow-up at 4 weeks: 73% for laparoscopic group vs 69% for open surgery group, intention-to-treat analysis

**Duration:** 28 months

**Setting:** Prince of Wales Hospital, Shatin, New Territories, Hong Kong

**Study:** Siu 2002

**Design:** RCT parallel design, randomized using computer generated random numbers by the block method, concealment of allocation using sealed envelopes, outcome assessment was made by assessors independent from the treating team for pain evaluation; by independent surgeons not blinded, for discharge and by the treating surgeon not blinded for activity, work return evaluation and complications, intention-to-treat analysis, without losses to follow up

**Duration:** 41 months

**Setting:** Pamela Youde Nethersole Eastern Hospital, Chai Wan, Hong Kong, SAR, China

## Laparoscopic surgery versus open surgery

**Outcome title:** 01 Septic abdominal complications (yes or not)

**No. of studies:** 2

**No. of participants:** 214

**Statistical method:** Odds Ratio (Fixed) 95% CI

**Effect size:** 0.66 [0.30, 1.47]

**Outcome title:** 02 Pulmonary complications (yes or not)

**No. of studies:** 2

**No. of participants:** 214

**Statistical method:** Odds Ratio (Fixed) 95% CI

**Effect size:** 0.37 [0.11, 1.31]

**Outcome title:** 03 Number of septic abdominal complications

**No. of studies:** 2

**No. of participants:** 214

**Statistical method:** Odds Ratio (Fixed) 95% CI

**Effect size:** 0.72 [0.33, 1.58]

**Outcome title:** 04 Surgical site infection

**No. of studies:** 2

**No. of participants:** 214

**Statistical method:** Odds Ratio (Random) 95% CI

**Effect size:** 0.34 [0.08, 1.36]

**Outcome title:** 05 Suture dehiscence

**No. of studies:** 2

**No. of participants:** 214

**Statistical method:** Odds Ratio (Fixed) 95% CI

**Effect size:** 0.93 [0.13, 6.71]

**Outcome title:** 06 Postoperative ileus

**No. of studies:** 2

**No. of participants:** 214

**Statistical method:** Odds Ratio (Fixed) 95% CI

**Effect size:** 0.60 [0.16, 2.22]

**Outcome title:** 07 Intra-abdominal abscess

**No. of studies:** 2

**No. of participants:** 214

**Statistical method:** Odds Ratio (Fixed) 95% CI

**Effect size:** 4.82 [0.55, 42.00]

**Outcome title:** 08 Incisional hernia

**No. of studies:** 2

**No. of participants:** 214

**Statistical method:** Odds Ratio (Fixed) 95% CI

**Effect size:** 1.40 [0.23, 8.51]

**Outcome title:** 09 Mortality

**No. of studies:** 2

**No. of participants:** 214

**Statistical method:** Odds Ratio (Fixed) 95% CI

**Effect size:** 0.69 [0.15, 3.14]

**Outcome title:** 10 Number of reoperations

**No. of studies:** 2

**No. of participants:** 214

**Statistical method:** Odds Ratio (Fixed) 95% CI

**Effect size:** 1.89 [0.46, 7.71]

## **Contribution of Reviewer(s)**

Sanabria AE.

Conceived, designed and coordinated the review

Developed search strategy

Undertook searches

Screened search results

Managed papers retrieval

Screened retrieved papers against inclusion criteria

Wrote to authors of papers for additional information

Provided additional data about papers

Managed data for the review

Entered data into RevMan

Analysed data

Interpreted data

Provided a methodological perspective

Provided a clinical perspective

Wrote the review

Morales CH and Villegas MI

Collected data for the review

Developed search strategy

Undertook searches

Screened search results

Organised retrieval of papers

Screened retrieved papers against inclusion criteria

Appraised quality of papers

Abstracted data from papers

Managed data for the review

Interpreted data

Provided a methodological perspective

Provided a clinical perspective

Wrote the review

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GASTRODUODENAL DISORDERS; Complicated gastroduodenal disease (perforation); acute treatment; surgical interventions; Humans; \*Laparoscopy; \*Peptic Ulcer Perforation/sg (surgery); Randomized Controlled Trials

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