Laparoscopic versus Open Repair of Perforated Peptic Ulcer

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ABSTRACT
Background: H. pylori infection and nonsteroidal anti-inflammatory drug (NSAID) usage contribute to a great majority of cases. Thus, non-operative management of the disease is indicated in nearly all cases, with the exceptions of hemorrhage, perforation, obstruction, and refractory disease.
Objective: Comparison between laparoscopic and open repair of perforated peptic ulcer as regards postoperative advantage and complication. **Patients and methods:** 279 identified published observational studies (randomized control trials and clinical control trials) after search strategy. Participants were patients that had done repairing of perforated peptic ulcer. Laparoscopic versus open repair of perforated peptic ulcer.
Results: There was no significant difference in the operating time between the two groups (p Z 0.618). Overall, the laparoscopic group had fewer complications compared to the open group (14.3% vs. 36.8%, p Z 0.005). When reviewing specific complications, only the incidence of surgical site infection was statistically significant (laparoscopic 0.0% vs. open 13.2%, p Z 0.003). The other parameters were not statistically significant. Although total hospital costs were similar (P = .465), the median intraoperative costs were greater for LR than for OR patients, at U6772 and U5626, respectively (P < .001). The median cost of ward stay tended to be U865 less in the LR group but was not statistically relevant.
Conclusion: Laparoscopic surgery had upper hand over open procedure because of less intraoperative blood loss and postoperative pain, less postoperative complications, shorter hospital stay, surgical site infection rate, shorter nasogastric tube duration.
Keywords: Laparoscopic, Open repair, Perforated peptic ulcer, H. pylori.

INTRODUCTION

Direct Helicobacter treatment and eradication is paramount because complete mucosal healing occurs less than 0.5% of the time with persistent infection. Other notable sources implicated in benign disease include smoking, steroid usage, and Zollinger-Ellison syndrome [(1)].

Decades ago the practice of elective surgeries to correct this type of ulcer was common. However, with the advancement of conservative clinical treatment from the eradication of H. pylori and acid control, mainly through the use of H2 blockers and proton pump inhibitors (Ppis), the rate of performing these surgeries decreased considerably in the last three decades and the clinical management became enough to treat [(2)]. So, the surgical approaches current therapies are directed to cases of refractory peptic ulcer, perforated and bleeding (PUP) [(3)]. The fundamental goals treat or prevent complications of ulcer, reduce the secretion of acid to allow healing of the ulcer and tempering their recurrence and minimize postoperative sequelae related to operation [(1)]. Although good results in clinical management of peptic ulcer disease, emergency surgeries have increased drilling [(1, 4)]. It is estimated that 2% to 10% of patients with gastric or duodenal peptic ulcer perforation in the course of their lives have greater mortality risk in the elderly [(1)].

Currently the standard surgical treatment for the PUP is the laparotomy [(5)]. However, there are number of deficiencies in this procedure with regard to a larger incision, considerable pain during the post-operative period and slow recovery. By these implications, laparoscopy is a surgical approach to therapeutic option [(6)].

In this context, **Mouret *et al.*** [(7)] published in 1990 the first results on the performance of laparoscopy for correction of perforated peptic ulcer. The conclusion of the study showed that laparoscopy is a good choice of surgical approach and it has the advantages of reduction of problems with respect to the surgical wound and adhesions [(5, 7)]. Besides, improved and expanded view of the lesion, minor surgical incision, less pain during the post-operative and faster return of patient activities compared to post laparotomy findings [(1, 8)].

Despite, the development of laparoscopic surgery for peptic ulcer disease, no consensus conclusion favoring its application has been reached. Some research showed that laparoscopic surgery has substantial advantages over open abdominal surgery for peptic ulcer disease, including less postoperative pain and postoperative complications and shorter hospital stay. However, the other research showed that laparoscopic repair is not superior to open abdominal surgery for peptic ulcer disease, and may even have worse outcomes including longer operative time. These inconsistent results make surgeons confounding whether laparoscopic surgery have better advantages than open abdominal surgery for perforated peptic ulcer [(9)].

AIM OF THE WORK

To compare between laparoscopic and open repair of perforated peptic ulcer as regards postoperative advantages and complications.

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PATIENTS AND METHODS

Criteria for considering studies for this review:

- **Types of studies:** Published observational studies (randomized control trials and clinical control trials).
- **Types of participants:** Participant were patients that had done repairing of perforated peptic ulcer.
- **Types of interventions:** Laparoscopic versus open repair of perforated peptic ulcer.
- **Types of outcome measures**

Primary outcomes were postoperative complications, mortality and reoperation. Postoperative complications included repair site leakage, intra-abdominal abscess, surgical site infection, postoperative ileus, pneumonia and urinary tract infection.

Secondary outcomes were operative time, postoperative pain, postoperative hospital stay, nasogastric tube duration and time to resume diet.

Search strategy for identification of studies:

The medline, embase and cochrane central register of controlled trials were systematically searched for randomized controlled trials (RCTs) comparing the outcomes of laparoscopic and open repair for perforated peptic ulcer between January 2000 and December 2017. Keywords used in the search were “laparoscopy/ laparoscopic”, “open/ conventional”, “peptic ulcer/duodenal ulcer/gastric ulcer”, “repair/surgery/closure”, and their combinations. To avoid overlooking other studies, the search was also maximized through manually screening the references of identified articles and relevant reviews. Our review included studies published in english.

Methods of the review:

Locating and selecting studies: Abstract of articles identified using the search strategy above were viewed to select the articles that fulfill the inclusion criteria. Each article identified will be reviewed and categorized into RCT (randomized controlled trials) or CCT (controlled clinical trial) that meets the described inclusion criteria and those where it is impossible to tell from the abstract, title or medical subject headings (MeSH).

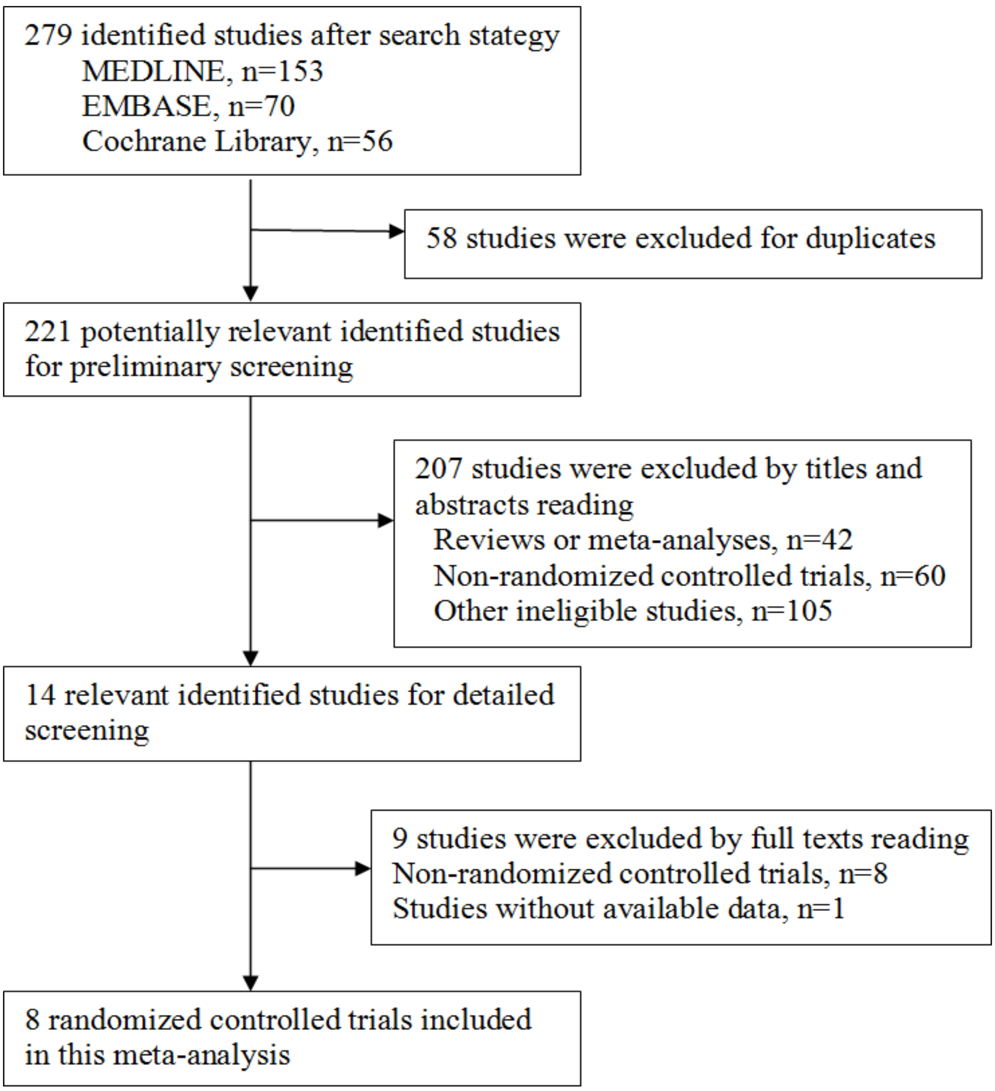

Figure (1): Flow chart of literature.

Inclusion criteria:

- Patients who agreed to participate in the study (by taking informed consent).

- Patients older than 16 years with a perforated peptic ulcer presenting within 24 hours of symptoms.
- When there was doubt, a second reviewer will assess the article and consensus will be reached.

Exclusion criteria:

- Patients with a surgical diagnosis other than perforated peptic ulcer
- Patients presenting with perforated peptic ulcer with symptoms persisting beyond 24 hours.
- Patients who absconded or left the study or died during the period of study.
- Patients with cardiac and chest condition (excluded from laparoscopic).

Data Extraction:

Two review authors independently extracted the data from the included studies using a previously designed data extraction form. Extracted data were then crosschecked between the two authors, and any discrepancy was resolved by consensus discussion. The following data were collected: the name of the first author, year of publication, country, study period, No. of patients, sex, age, and outcomes of interest.

Evidence of publication bias:

Risk of bias assessment of the included studies was independently performed by two review authors with the use of the Cochrane Collaborations risk of bias tool. The assessment contained seven elements: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, (6) selective reporting, and (7) other bias. Each element was graded as having a high risk of bias (seriously weakens confidence in the results), a low risk of bias (unlikely to seriously alter the results), or an unclear risk of bias (no sufficient information to judge). Any discrepancy was resolved by consensus discussion with the two authors.

Statistical considerations

Data management and statistical analysis were carried out by Review Manage software version 5.1.0 from the Cochrane Collaboration. For continuous outcome data, if the variable was presented in the same scale, weighted mean difference (WMD) was calculated otherwise, standard mean difference (SMD) was used. If continuous variables were reported as medians and ranges, we imputed the means and standard deviations (SDs), but interquartile ranges were reported, we assumed them to be 1.35 SDs according to the Cochrane Collaboration's handbook. For dichotomous outcome data, odds ratio (OR) was calculated. Pooled estimates were all presented with 95% confidence interval (CI). Chi^2 test was employed to assess heterogeneity. When there was evidence of significant heterogeneity (P < 0.001), a random-effects model was used and sensitive analysis was further performed to identified studies contributing to the heterogeneity; otherwise, the fixed- effects model was employed. Statistical significance was considered if the two-sided P value was < 0.05 for outcome data comparison.

RESULTS

Table (1): Meta-analysis for operation time (minutes)

Study	Effects		Difference		P
	Laparoscopic Mean ± SD	**Open Mean ± S D**	**Mean ± S E**	**95% C I**	
Siu 2002 [10]	42.0 ± 25.1	52.3 ± 24.8	-10.3 ± 4.5	- 19.2–-1.4	**0.025***
Bertleff 2009 [11]	75.0 ±35.0	50 ± 18.9	25.0 ± 5.6	13.9–36.1	**<0.001***
Ge 2015 [12]	70.0 ± 7.5	75.0 ± 7.5	-5.0 ± 1.4	-7.7–-2.3	**<0.001***
Sze 2016 [13]	108.0 ± 40.4	104.9 ± 37.2	3.1 ± 6.8	- 10.2–16.4	0.648
Ibrahim 2017 [14]	62.0 ± 10.6	45 ± 12.9	17.0 ± 2.8	11.5–22.5	**<0.001***
Vaibhav 2018 [15]	101.9 ± 6.4	60.3 ± 3.8	41.6 ± 1.2	39.1–44.0	**<0.001***
Schietroma 2013 [16]	54.3 ± 15.8	57.8 ± 17.8	-3.5 ± 3.1	-9.6–2.6	0.266
Overall effect	--	--	17.5±0.8	5.9–19.1	0.339 **(z=0.95 7)**
Heterogeneity	I^2	99.179	**P**	**<0.001***	

RR: Relative rate, CI: confidence interval, *Significant

The **operation time** was reported in the seven included studies. There was significant heterogeneity among these studies. Thus, we performed the statistics using a random-effects model, and the results showed that laparoscopic repair non-significantly had higher operation time.

Table (2): Meta-analysis for postoperative pain

	Effects	Difference	

Study	Laparoscopi c Mean ± SD	Open Mean ± S D	Mean ± S E	95% C I	P
Siu 2002	1.4 ± 3.5	1.3 ± 6.4	0.1 ± 0.9	-1.7–1.9	0.914
Bertleff 2009	1.0 ± 0.9	1.6 ± 0.9	-0.6 ± 0.2	-1.0–-0.2	**<0.001***
Ge 2015	0.7 ± 0.3	1.0 ± 0.4	-0.3 ± 0.1	-0.4–-0.2	**<0.001***
Overall effect	--	--	-0.3 ± 0.1	-0.5–-0.2	**<0.001* (z=5.457)**
Heterogeneity	I^2	25.759	**P**	0.260	

RR: Relative rate, CI: confidence interval, *Significant

The **postoperative pain** was reported in the three included studies. There was non-significant heterogeneity among these studies. Thus, we performed the statistics using a fixed-effects model, and the results showed that laparoscopic repair significantly had lower **postoperative pain**. **Postoperative pain** was evaluated using Visual analogue scale (VAS-10).

Table (3): Meta-analysis for postoperative hospital stay (days)

Study	Effects		Difference		P
	Laparoscop ic Mean ± SD	**Open Mean ± S D**	**Mean ± S E**	**95% C I**	
Siu 2002	6.0 ± 7.8	7.0 ± 8.8	-1.0 ± 1.5	-4.0–2.0	0.508
Bertleff 2009	6.5 ± 6.9	8.0 ± 5.4	-1.5 ± 1.2	-3.9–0.9	0.226
Schietroma 2013	8.1 ± 3.8	13.8 ± 2.5	-5.7 ± 0.6	-6.9–-4.5	**<0.001 ***
Sze 2016	4.4 ± 3.3	7.3 ± 7.8	-2.9 ± 1.1	-5.0–-0.8	**0.006***
Ibrahim 2017	3.6 ± 0.9	4.2 ± 1.2	-0.6 ± 0.3	-1.1–-0.7	**0.018***
				0.1	
Vaibhav 2018	8.4 ± 0.7	12.1 ± 2.8	-3.7 ± 0.5	-4.7–-2.6	**<0.001***
Overall effect	--	--	-1.8 ± 0.2	-2.2–-1.4	**0.011*** (z=2.52 8)
Heterogeneity	I^2	93.652	**P**	**<0.001***	

RR: Relative rate, CI: confidence interval, *Significant

The **postoperative hospital stay** was reported in the six included studies. There was significant heterogeneity among these studies. Thus, we performed the statistics using a random-effects model and the results showed that laparoscopic repair significantly had lower **postoperative hospital stay**.

Table (4): Meta-analysis for urinary tract infection

Study	Laparoscopic (event/total)	Open (event/total)	RR (95% CI)	P
Bertleff 2009	0 (52)	2 (49)	0.19 (0.01–3.83)	0.278
Schietroma 2013	2 (58)	3 (57)	0.66 (0.11–3.78)	0.636
Overall effect	2 (110)	5 (106)	0.48 (0.11–2.17)	0.490 (z=955)
Heterogeneity	I^2	0.000	**P**	0.309

RR: Relative rate, CI: confidence interval, *Significant

The **urinary tract infection** was reported in the two included studies. There was non-significant heterogeneity among these studies. Thus, we performed the statistics using a fixed-effects model and the results showed that laparoscopic repair non-significantly had lower **urinary tract infection**.

Table (5): Meta-analysis for surgical site infection

Study	Laparoscopic	Open	RR (95%	P

	(event/total)	(event/total)	CI)	
Siu 2002	2 (63)	7 (58)	0.26 (0.06–1.22)	0.087
Bertleff 2009	0 (52)	3 (49)	0.13 (0.01–2.54)	0.181
Schietroma 2013	10 (58)	23 (57)	0.43 (0.22–0.82)	**0.010***
Ge 2015	1 (58)	2 (61)	0.53 (0.05–5.64)	0.596
Sze 2016	0 (63)	9 (68)	0.06 (0.00–0.96)	**0.046**
Vabihav 2018	0 (31)	0 (38)	--	--
Overall effect	--	--	0.36 (0.21–0.63)	**<0.001*** (z=3.607)
Heterogeneity	I^2	0.000	**P**	0.626

RR: Relative rate, CI: confidence interval, *Significant

The **surgical site infection** was reported in the six included studies. There was non-significant heterogeneity among these studies. Thus, we performed the statistics using a fixed-effects model, and the results showed that laparoscopic repair non-significantly had lower **surgical site infection**.

Table (6): Meta-analysis for mortality

Study	Laparoscopic (event/total)	Open (event/total)	RR (95% CI)	P
Siu 2002	1 (63)	3 (58)	0.31 (0.03–2.87)	0.297
Bertleff 2009	2 (52)	4 (49)	0.47 (0.09–2.46)	0.370
Ge 2015	1 (58)	1 (61)	1.05 (0.07–16.43)	0.971
Nicolas 2015	0 (50)	3 (50)	0.14 (0.01–2.70)	0.194
Sze 2016	1 (63)	2 (68)	0.54 (0.05–5.81)	0.610
Ibrahim 2017	0 (34)	0 (37)	--	--
Overall effect	--	--	0.43 (0.16–1.17)	0.098 (z=1.654)
Heterogeneity	I^2	0.000	**P**	0.897

RR: Relative rate, CI: confidence interval, *Significant

The **mortality** was reported in the six included studies. There was non-significant heterogeneity among these studies. Thus, we performed the statistics using a fixed-effects model, and the results showed that laparoscopic repair non-significantly had lower **mortality**.

Table (7): Meta-analysis for reoperation

Study	Laparoscopic (event/total)	Open (event/total)	RR (95% CI)	P
Siu 2002	5 (63)	1 (58)	4.60 (0.55–38.24)	0.152
Ge 2015	1 (58)	0 (61)	3.15 (0.13–75.86)	0.478
Nicolas 2015	2 (50)	4 (50)	0.50 (0.10–2.61)	0.411
Ibrahim 2017	1 (34)	1 (37)	1.09 (0.07–16.73)	0.952
Overall effect	--	--	1.29 (0.43–3.89)	0.648 (z=0.457)
Heterogeneity	I^2	0.000	**P**	0.396

RR: Relative rate, CI: confidence interval, *Significant

The **reoperation** was reported in the 7 included studies. There was significant heterogeneity among these studies. Thus, we performed the statistics using a random-effects model, and the results showed that laparoscopic repair significantly had lower **reoperation**.

DISCUSSION

In **Ibrahim *et al.*** **(14)** the data demonstrated homogeneous results for the outcome variables of morbidity and complications, while operation time and hospital length of stay differed significantly. Statistical significance could not be reached for any of these variables, although odd ratios were consistently in favour of the laparoscopic repair. Similarly, the laparoscopic approach resulted in a lower rate of minor complications (10% vs. 23%). Total lengths of stay post-open repair was 4.2 ± 1.2 days and after laparoscopic repair was 3.6 ± 0.9 days. At the same time there were observed longer operating times for laparoscopic repair of PPU, which constituted 62 ± 10.6 minutes whereas open repair took only 45 ± 12.9 minutes. Peritoneal lavage has been a factor of prolonged duration of laparoscopic surgery.

In **Byrge *et al.*** **(4)** after matching, the 2 groups had similar characteristics. The rates of wound complications, organ space infections, prolonged ventilation, postoperative sepsis, return to the operating room and mortality tended to be lower for the LA, although not significantly. Length of hospital stay was significantly shorter for the LA by an average of 5-4 days.

In **Sze *et al.*** **(13)** a total of 131 patients underwent emergency repair for PPU (laparoscopic repair, n Z 63, 48.1% vs. open repair, n Z 68, 51.9%). There were no significant differences in baseline characteristics between both groups in terms of age (p Z 0.434), gender (p Z 0.305), body mass index (p Z 0.180) and presence of comorbidities (p Z 0.214). Both groups were also comparable in their American Society of Anesthesiologists (ASA) scores (p Z 0.769), Boey scores 0/1 (p Z 0.311), Mannheim Peritonitis Index > 27 (p Z 0.528), shock on admission (p < 0.99) and the duration of symptoms > 24 hours (p Z 0.857). There was no significant difference in the operation time between the two groups (p Z 0.618). Overall, the laparoscopic group had fewer complications compared to the open group (14.3% vs. 36.8%, p Z 0.005). When reviewing specific complications, only the incidence of surgical site infection was statistically significant (laparoscopic 0.0% vs. open 13.2%, p Z 0.003). The other parameters were not statistically significant. The laparoscopic group had a significantly shorter mean postoperative stay (p Z 0.008) and lower pain scores in the immediate postoperative period (p < 0.05). Mortality was similar in both groups (open, 1.6% vs. laparoscopic, 2.9%, p < 0.99).

In **Vaibhav *et al.*** **(15)** a total of 69 patients were included in this study. Number of doses of analgesics required in laparoscopic group was 9.48 ± 1.82, while those required in conventional open group was 18.16 ± 2.24. In laparoscopic duodenal perforation repair group, duration of hospital stay (in days) was 8.42 ± 1.44 as compared to 12.08 ± 4.82 in open repair group. Laparoscopic group had significantly fewer post-operative complications but had longer mean operative time (101.90 minutes compared to 60.32 minutes in open repair group).

In **Ge *et al.*** **(12)** the operative times for LR versus OR did not differ greatly (70 [interquartile range 60–90] vs 75 [60– 90] minutes, respectively, P = .692), nor did postoperative complications. The LR group required substantially less fentanyl than the OR group (0.74 ± 0.33 mg vs 1.04 ± 0.39 mg, P < .001). Moreover, the duration of hospital stay for the LR group was much shorter than those of the OR group (7 [5– 9] vs 8 [7–10] days, respectively, P < .001). Although total hospital costs were similar (P = .465), the median intraoperative costs were greater for LR than for OR patients, at U6772 and U5626, respectively (P < .001). The median cost of ward stay tended to be U865 less in the LR group but was not statistically relevant.

However, the present meta-analysis has some limitations. **First**, the overall methodological quality of the included studies was moderate due to several sources of bias, especially the selection bias. For example, previous studies revealed that hemodynamically unstable patients are not ideal candidates for laparoscopic surgery and open surgery remains reliable postoperative outcomes in those with unstable hemodynamics [8, 17]. However, some hemodynamically unstable patients were included for laparoscopic or open repair for perforated peptic ulcer in this meta-analysis and it may weaken the advantages of the laparoscopic surgery, although there were no significant differences for the unstable hemodynamics between the laparoscopic and open group in this study. **Second**, the outcomes of laparoscopic surgery may be influenced by the learning curve for the surgeons in different medical center and many emergency operations for perforated peptic ulcer are often performed by the young surgeons, and they are not always laparoscopically trained. **Third**, significant heterogeneity was detected for the outcomes including overall postoperative complication rate, operative time, postoperative pain and postoperative hospital stay, which may affect the quality and legitimacy of the results we obtained.

In our study laparoscopic surgery had upper hand over open procedure as regards less intraoperative blood loss and postoperative pain, less postoperative complications, shorter hospital stay, les surgical site infection rate and shorter nasogastric tube duration.

CONCLUSION

Perforated peptic ulcer is common in surgical emergency. Patients who suffer from perforated peptic ulcer disease usually require emergent surgery to close the defect and flush peritoneal cavity. Laparoscopic surgery had upper hand over open procedure as regards less intraoperative blood loss and postoperative pain, less postoperative complications, shorter hospital stay, less surgical site infection rate and shorter nasogastric tube duration.

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