International Journal of Chemical and Biochemical Sciences
(ISSN 2226-9614)

Journal Home page: www.iscientific.org/Journal.html

Role of Laparoscopic versus Open Approach in Acute Peptic Ulcer Perforation in Egyptian Population; A Randomized Controlled Trial

*George Abdel-Fady Nashed Aiad[1], Salma Fouad Dowara[2], Mohamed Abdalla Salman[1], Osama Ahmed Radwan[3], Ramy Abdelgawad Kamel Massoud[4]**

[1]*Department of General Surgery, Faculty of Medicine, Cairo University, Egypt.*

[2]*Former Head of General Surgery Department AFCM, Professor of General Surgery, Faculty of Medicine, Egypt. Cairo University, Dean Faculty of Medicine - Galala University, Egypt.*

[3]*Department of General Surgery Department, Al Maadi Military Hospital, Egypt.*

[4]*Department of general surgery M.B.B.Ch., Menoufia University, M.Sc., Ain Shams University, Egypt.*

Abstract

Peptic ulcer perforation is a life-threatening complication of peptic ulcer disease occurring in about 2-14% of cases of peptic ulcer disease to compare between laparoscopic and open approach in acute peptic ulcer perforation, in terms of: primary outcome: Technical feasibility, surgical outcome and secondary outcome: complications. This prospective, randomized controlled trial was conducted on 80 patients with peptic ulcer disease who presented with acute peptic ulcer perforation. They classified according to surgical technique of peptic ulcer repair into 2 groups: Laparoscopy group (40 patients) and open surgery group (40 patients) at Kasr El Ainy teaching hospital and El-Maadi military compound. The study lasted for 2 years. Comparative statistics between the 2 groups revealed: non-significant difference as regards age, sex of the patients, all co-morbidities, size and site of perforation, highly significant increase in operative time and highly significant decrease in blood transfusion need, complication's rate, and wound infection in Laparoscopy group; compared to open surgery group. Laparoscopic repair of perforated peptic ulcer proven to be safer and more efficient than open surgery repair, in terms of decreased post-operative pain, early return of bowel habit and short hospital stay days, along with decreased complications rates, but it was not superior to open surgery technique in terms of overall mortality rate.

Keywords: Perforated peptic ulcer, Laparoscopy, Open surgery, Peritonitis.

Full length article **Corresponding Author*, e-mail: ramymassoud888@gmail.com

1. Introduction

Peptic ulcer perforation is a life-threatening complication of peptic ulcer disease occurring in about 2-14% of cases of peptic ulcer disease [1]. NSAIDs, Helicobacter pylori (H. pylori), physiological stress, smoking, corticosteroids and previous history of PUD are risk factors for PPU [2]. Management of perforated peptic ulcer is primarily surgical and different suture techniques for closure of the perforation are described [3]. Laparotomy for all patients in the era of minimally invasive surgery is unjust due to both short-term and long-term morbidities. Laparotomies have been shown to induce a significant physiological stress response which can lead to significant morbidities [4]. Laparoscopic omental patch repair (LOPR) of perforated peptic ulcer (PPU) was introduced two decades ago. The earliest prospective studies successfully demonstrated the safety and feasibility of laparoscopic repair [5]. There is no evidence to suggest that laparoscopic repair is a more superior approach compared to open repair. In a recent meta-analysis. Zhou et al., found that laparoscopic repair is slightly advantageous in terms of less postoperative pain and shorter length of stay [6]. The major benefits of laparoscopic surgery stem from the requirement of only a few small incisions which would result in improved recovery, better cosmesis, and lesser pain in patients compared to open surgery [7]. Laparoscopic approach is a feasible, safe option and associated with shorter length of hospital stay for PPU patients with small perforation size presented to hospital in less than 48 hours from the onset of symptoms [8].

The aim of this work was to compare between laparoscopic and open approach in acute peptic ulcer perforation, in terms of: primary outcome: Technical feasibility, surgical outcome and secondary outcome: complications.

2. Patients and methods

This prospective, randomized controlled trial was conducted on 80 patients with peptic ulcer disease who presented with acute peptic ulcer perforation. They classified according to surgical technique of peptic ulcer repair into 2 groups: Laparoscopy group (40 patients) and open surgery group (40 patients) at Kasr El Ainy teaching hospital and El-Maadi military compound. The study lasted for 2 Years.

2.1. Inclusion criteria

Patients who are haemo-dynamically stable, patient with acute abdomen with early onset within 48 hours, clinical signs and symptoms of PPU (sudden onset of abdominal pain, tachycardia and abdominal rigidity...etc.) and patient with suspected hollow viscus injury (signs of intraperitoneal free air on X-ray & CT, fluid collection at Pelvi-abdominal U/S).

2.2. Exclusion criteria

Patient with acute abdomen of more than 48 hours, patients with repeated upper abdominal operations, sever profound shock (septic shock), extremes of age, bleeding tendency and refusal to enrol with study.

2.3. Methods

2.3.1. Preoperative work up

All patients received intravenous antibiotics prior to operation in form of amoxicillin/clavulanate 1.2 – 2.2 g or ceftriaxone 2g and metronidazole 500mg [9].

2.4. Operative techniques

2.4.1. The open surgical procedure

The open surgical procedure was performed through an upper abdominal midline incision. Closure of PPU was to be achieved by sutures with an omental patch. After repair of the defect cultures were drawn from the peritoneal fluid, after which the peritoneal cavity was lavaged. During lavage it was permissible to insufflate the stomach with nasogastric tube to test for leakage of the closed defect. Mass closure is continuous fascial closure with a single suture of the abdomen.

2.4.2. Laparoscopic repair

Laparoscopic repair was performed with the patient and the team set up in the ‘‘French’’ position. Insufflation using carbon dioxide as the insufflation gas to minimize the amount of peritoneal irritation to a pressure of 12- 15 mmHg. Trocars were placed at the umbilicus (video scope) and on the left and right midclavicular line above the level of the umbilicus (instruments). (Working ports). Surgeons were free to use 30 degrees’ video scopes for the procedure. The rest of the procedure was identical to that described above for open repair.

2.4.3. Intraoperative parameters

Site of perforation**,** size of perforation, operative time and blood transfusion

2.5. Post-operative outcomes of the study

2.5.1. Primary efficacy outcomes (main outcomes)

Post-operative pain scale (NRS or VAS score)**,** return of bowel habit and hospital stay.

2.5.2. Secondary safety outcome

Complications rate (including: wound infection and dehiscence, burst abdomen, incisional hernia and leakage at repair site), mortality rate and rate of conversion to open laparotomy and number of cases completed laparoscopically.

2.6. Ethical considerations

The nature of the present study and laboratory or radiological procedures was explained to all participants. Consent was obtained from all participants. At the end of the study, all patients were informed about the results of the examinations performed and received appropriate recommendations, and treatment. The World Health Organization (WHO) and the Declaration of Helsinki recommendations were followed, in terms of protecting the rights and well-being of the studied people [10].

2.7. Statistical Methodology

Data entry, processing and statistical analysis was carried out using MedCalc ver. 20 (MedCalc, Ostend, Belgium). Tests of significance (Mann-Whitney’s, Chi square tests, logistic regression analysis, Spearman’s correlation, and ROC Curve analysis) were used. Data were presented and suitable analysis was done according to the type of data (parametric and non-parametric) obtained for each variable. P-values less than 0.05 (5%) was considered to be statistically significant: P- value: level of significance: $P > 0.05$: Non-significant (NS). $P < 0.05$: Significant (S). $P < 0.01$: Highly significant (HS). Descriptive statistics: Mean, Standard deviation (± SD) and range for parametric numerical data, while Median and Inter-quartile range (IQR) for non-parametric numerical data. Frequency and percentage of non-numerical data. Analytical statistics: Mann-Whitney's Test (U test) was used to assess the statistical significance of the difference of a non-parametric variable between two study groups. Chi-Square test was used to examine the relationship between two qualitative variables. Correlation analysis (using Spearman's method): To assess the strength of association between two quantitative variables. The correlation coefficient denoted symbolically "r" defines the strength and direction of the linear relationship between two variables. Logistic regression: useful in the prediction of the presence or absence of an outcome based on a set of independent variables. It is similar to a linear regression model but is suited when the dependent variable is qualitative (categorical). The ROC Curve (receiver operating characteristic) provides a useful way to evaluate the Sensitivity and specificity for quantitative Diagnostic measures that categorize cases into one of two groups.

Excellent accuracy = 0.90 to 1 (%). Good accuracy = 0.80 to 0.90 (%). Fair accuracy = 0.70 to 0.80 (%). Poor accuracy = 0.60 to 0.70 (%). Failed accuracy = 0.50 to 0.60 (%)

3. Results and Discussion

Comparative statistics between the 2 groups revealed non-significant difference as regards age, sex of the patients ($p > 0.05$) and all co-morbidities ($p > 0.05$). Which came in agreement with Lee et al., who reported that, majority of the patients were male (87.5% were male patients in LOPR group but 89.8% were male patients in OR group; $p = 0.92$). Both groups were comparable in terms of demographic and preoperative physiologic status [11]. Swartz et al., also reported that, there was no difference between the age (p=0.56), gender (p=0.82), race (p=0.7), comorbidities (p=0.48), the mechanism of injury (p=0.63) and severity of injuries (p=0.41) between the two groups [12]. Comparative statistics between the 2 groups revealed; highly significant increase in Operative time, in Laparoscopy group; compared to open surgery group ($p < 0.01$), highly significant decrease in blood transfusion need, in Laparoscopy group; compared to open surgery group ($p < 0.05$) and non-significant difference as regards size and site of perforation ($p > 0.05$) Which came in agreement with Zhou et al., and Vakayil et al., [6,13]. Zhou et al., reported that, longer operative times were found in the LR group compared with the OR group (WMD, 11.77; 95% CI, 1.75, 21.79; P = 0.021) [6]. Vakayil et al., also reported that, OS was associated with a significantly shorter operative time (OR < 0.1; 95% CI 0.001–0.006, P < 0.001) but a longer hospital stays (OR 2.3; 95% CI 1.4–3.7, P < 0.001) [13]. Comparative statistics between the 2 groups revealed non-significant difference as regards size and site of perforation ($p > 0.05$). Which came in agreement with Siow et al., and Quah et al., [14-15]. Siow et al., concluded that, in the overall study population, the most common location for perforation was juxtapyloric (87 patients, 66.4%), followed by duodenum (30 patients, 22.9%), and stomach (14 patients, 10.7%). No significant difference was observed between the two groups in terms of perforation size (16.2 mm vs. 15.8 mm, p= 0.714), site of perforation (juxtapyloric, 66.7% vs. 66.2%, p= 0.323), and operating time (108.3 minutes vs. 104.9 minutes, p= 0.618) [14]. Quah et al., also concluded that, the most frequent site of perforation was duodenal (312 patients, 49.4%), followed by gastric (97 patients, 15.4%) and juxtapylorus (79 patients, 12.5%). The site of the perforation was not defined in 143 (22.7%) patients. There was no significant difference in perforation site between the two groups. There was no difference in the mean size of the perforation between the LR (6.6 mm) and OR (5.2 mm) ($p = 0.23$) [15]. Comparative statistics between the 2 groups revealed; highly significant decrease in post-operative pain, return of bowel habit and hospital stay days, in Laparoscopy group; compared to Open surgery group ($p < 0.05$ respectively). Which came in agreement with Zhou et al., Lee et al., and Tan et al., [6,11,16]. Zhou et al., reported that, postoperative pain was evaluated by counting the days of analgesic use or the dosage. The patients who underwent the laparoscopic procedure used fewer analgesics (days: WMD, − 3.60; 95% CI, − 5.50, − 1.70; P < 0.001; dosage: WMD, − 106.59; 95% CI, − 124.01, − 89.17; P < 0.001) [6]. Lee et al., also reported that, in terms of short-term outcome measure, the LOPR group was associated with significantly shorter length of hospital stay (4 days in LOPR group versus 5 days in OR group; $p < 0.01$). Other outcome measures did not differ significantly between the two groups although results tended to favor the LOPR group [11]. Tan et al., also reported that, the postoperative pain was reported in four included studies. There was significant heterogeneity among these studies (Chi2 = 12.18, P < 0.1, I2 = 67 %). Thus, we performed the statistics using a random-effects model, and the results showed that laparoscopic repair had less postoperative pain than open repair for perforated peptic ulcer (OR: -0.54, 95% CI: -0.88--0.19, P < 0.05).

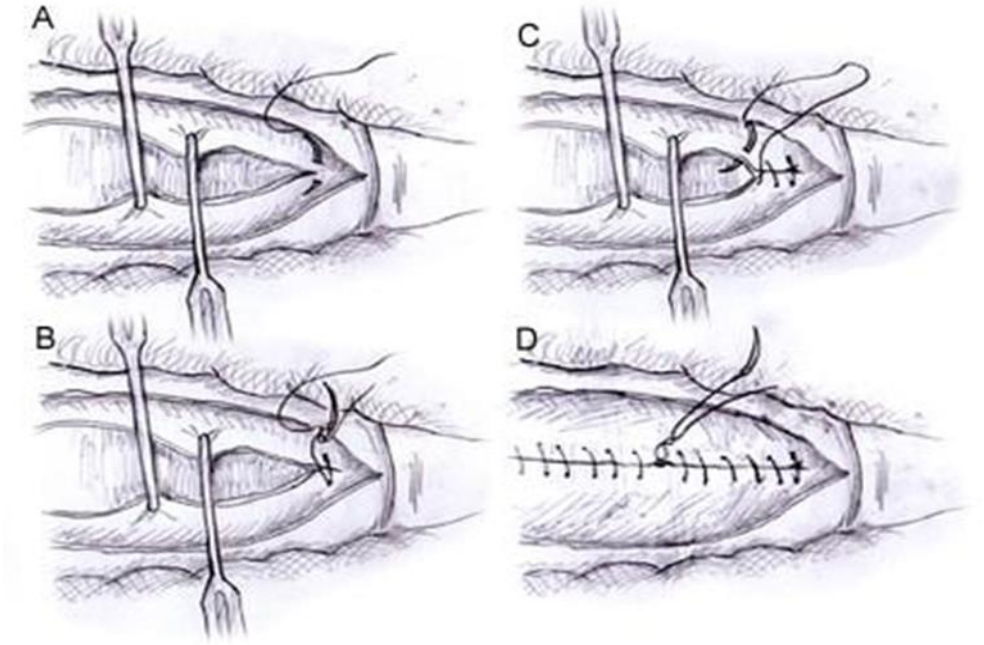

Figure 1: (A) Fascial closure. (B) Looping of 0 polydioxanone (PDS) at vertex. (C) Continuous suture. (D) Two PDS ends meeting in middle of incision, tied together, and cut.

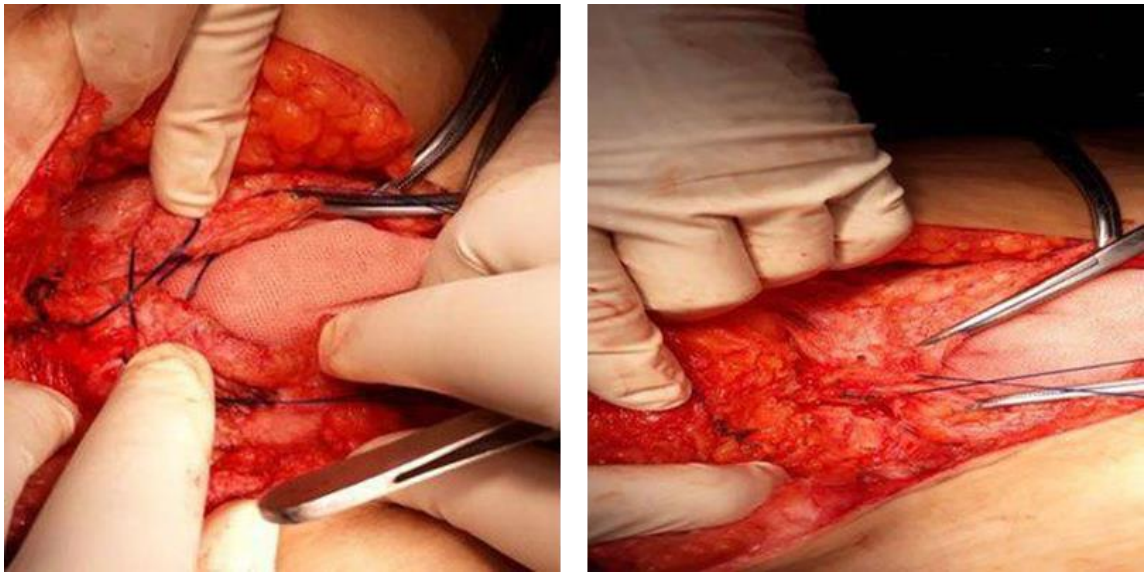

Figure 2: Fascial closure using two PDS ends meeting in middle of incision, tied together, and cut.

Table 1: Comparison between the 2 groups as regards socio-demographic data using Mann-Whitney's U and Chi square tests.

Variable		Laparoscopy group (40)	Open surgery group (40)	Mann-Whitney's U test
		Median (IQR)	Median (IQR)	P value
Age (years)		46.5 (32.5 – 61.5)	50 (40 – 65)	= 0.2762
Variable		Laparoscopy group (40)	Open surgery group (40)	Chi square test
				P value
Gender	Female	8 (20%)	5 (12.5%)	= 0.3663
	Male	32 (80%)	35 (87.5%)	

IQR: inter-quartile range. * Percentage of Column Total.
Comparative statistics between the 2 groups revealed non-significant difference as regards age and sex of the patients (p > 0.05).

Table 2: Comparison between the 2 groups as regards co-morbidities using Chi square test.

Variable		Laparoscopy group (40)	Open surgery group (40)	Chi square test
				P value
HTN	+ve	8 (20%)	5 (12.5%)	= 0.3663
DM	+ve	4 (10%)	6 (15%)	= 0.5017
IHD	+ve	4 (10%)	8 (20%)	= 0.2133
Overall comorbid patients	+ve	11 (27.5%)	11 (27.5%)	= 1.0000

* Percentage of Column Total.
Comparative statistics between the 2 groups revealed non-significant difference as regards all co-morbidities (p > 0.05).

Table 3: Comparison between the 2 groups as regards operative data using Mann-Whitney's U and Chi square tests.

Variable		Laparoscopy group (40)	Open surgery group (40)	Mann-Whitney's U test
		Median (IQR)	Median (IQR)	P value
Size of perforation (mm)		20 (15 – 20)	20 (15 – 25)	= 0.2451
Operative time (min)		45 (40 – 50)	30 (25 – 37.5)	< 0.0001**
Variable		**Laparoscopy group (40)**	**Open surgery group (40)**	**Chi square test**
				P value
Blood transfusion	+ve	1 (2.5%)	6 (15%)	= 0.049**
Site of perforation	Post-pyloric	27 (67.5%)	30 (75%)	= 0.5118
	Pre-pyloric	12 (30%)	10 (25%)	
	Pyloric	1 (2.5%)	0 (0%)	

* Percentage of Column Total.
Comparative statistics between the 2 groups revealed; highly significant increase in Operative time, in Laparoscopy group; compared to open surgery group ($p < 0.01$), highly significant decrease in Blood transfusion need, in Laparoscopy group; compared to open surgery group ($p < 0.05$) and non-significant difference as regards size and site of perforation ($p > 0.05$).

Table 4: Comparison between the 2 groups as regards Primary outcome data using Mann-Whitney's U test.

Variable	Laparoscopy group (40)	Open surgery group (40)	Mann-Whitney's U test
	Median (IQR)	Median (IQR)	P value
Post-operative pain (NRS)	5 (4 – 5.5)	8 (6.5 – 9)	< 0.0001**
Return of bowel habit (days)	2 (2 – 3)	4 (3 – 4)	< 0.0001**
Hospital stays (days)	5 (4 – 5)	9 (7 – 9)	< 0.0001**

Median was done as the data were not-normally distributes, median equal mean (the same meaning).
Comparative statistics between the 2 groups revealed; highly significant decrease in post-operative pain, return of bowel habit and hospital stay days, in Laparoscopy group; compared to Open surgery group ($p < 0.05$ respectively).

Table 5: Comparison between the 2 groups as regards Complication's outcome data using Mann-Whitney's U and Chi square tests.

Variable		Laparoscopy group (40)	Open surgery group (40)	Chi square test
				P value
Complication's rate	+ve	3 (7.5%)	18 (45%)	= 0.0002**
- Wound infection	+ve	2 (5%)	16 (40%)	= 0.0002**
- Leakage at repair site	+ve	1 (2.5%)	2 (5%)	= 0.5587
Mortality rate	+ve	0 (0%)	2 (5%)	= 0.1547

* Percentage of Column Total.
Comparative statistics between the 2 groups revealed; highly significant decrease in complication's rate, and wound infection, in Laparoscopy group; compared to Open surgery group ($p < 0.05$ respectively) and non-significant difference as regards Leakage at repair site and mortality ($p > 0.05$).

Table (6): Roc-curve of laparoscopic surgery to predict Primary.

Variable	AUC	SE	Sensitivity (%)	Specificity (%)	P value
Post-operative pain	0.932	0.0259	75	95	<0.0001**
Return of bowel habit	0.896	0.0345	65	95	<0.0001**
Hospital stays	0.933	0.0319	77.5	100	<0.0001**

ROC (Receiver operating characteristic), AUC= Area under curve, SE= Standard Error.
By using ROC-curve analysis, laparoscopic surgery technique predicted: decreased post-operative pain, with excellent (93%) accuracy, sensitivity= 75% and specificity= 95% ($p < 0.01$), decreased post-operative return of bowel habit, with good (89%) accuracy, sensitivity= 65% and specificity= 95% ($p < 0.01$) and decreased post-operative hospital stay, with excellent (93%) accuracy, sensitivity= 77.5% and specificity= 100% ($p < 0.01$).

4. Conclusions

Laparoscopic repair of perforated peptic ulcer proven to be safer and more efficient than open surgery repair, in terms of decreased post-operative pain, early return of bowel habit and short hospital stay days, along with decreased complications rates, but it was not superior to open surgery technique in terms of overall mortality rate.

References

[1] M. J. Bertleff, J. F. Lange. (2010). Perforated peptic ulcer disease: a review of history and treatment. Digestive surgery. 27 (3): 161-169.

[2] M. Mustafa, J. Menon, R. K. Muiandy, R. Fredie, M. M. Sein, A. Fariz. (2015). Risk factors, diagnosis, and management of peptic ulcer disease. Journal of Medical and Dental Sciences. 14 (7): 40-46.

[3] K. T. Chung, V. G. Shelat. (2017). Perforated peptic ulcer-an update. World journal of gastrointestinal surgery. 9 (1): 1.

[4] B. Jaffray. (2005). Minimally invasive surgery. Archives of disease in childhood. 90 (5): 537.

[5] D. J. K. Lee, M. Ye, K. H. Sun, V. G. Shelat, A. Koura. (2016). Laparoscopic versus open omental patch repair for early presentation of perforated peptic ulcer: matched retrospective cohort study. Surgery Research and Practice, 2016.

[6] C. Zhou, W. Wang, J. Wang, X. Zhang, Q. Zhang, B. Li, Z. Xu. (2015). An updated meta-analysis of laparoscopic versus open repair for perforated peptic ulcer. Scientific reports. 5 (1): 13976.

[7] N. Greaves, J. Nicholson. (2011). Single incision laparoscopic surgery in general surgery: a review. The Annals of The Royal College of Surgeons of England. 93 (6): 437-440.

[8] A. Pansa, H. Kurihara, M. A. Memon. (2020). Updates in laparoscopic surgery for perforated peptic ulcer disease: state of the art and future perspectives. Annals of Laparoscopic and Endoscopic Surgery. 5.

[9] S. Nakajima, D. Y. Graham, T. Hattori, T. Bamba. (2000). Strategy for treatment of Helicobacter pylori infection in adults II. Practical Policy in 2000. Current pharmaceutical design. 6 (15): 1515-1529.

[10] M. D. Goodyear, L. A. Eckenwiler, C. Ells. (2008). Fresh thinking about the Declaration of Helsinki. British medical journal. 337.

[11] D. J. K. Lee, M. Ye, K. H. Sun, V. G. Shelat, A. Koura. (2016). Laparoscopic versus open omental patch repair for early presentation of perforated peptic ulcer: matched retrospective cohort study. Surgery Research and Practice, 2016.

[12] T. Swartz, F. Jehan, A. Tang, L. Gries, M. Zeeshan, N. Kulvatunyou, B. Joseph. (2018). Prospective evaluation of low health literacy and its impact on outcomes in trauma patients. Journal of Trauma and Acute Care Surgery. 85 (1): 187-192.

[13] V. Vakayil, B. Bauman, K. Joppru, R. Mallick, C. Tignanelli, J. Connett, J. V. Harmon. (2019). Surgical repair of perforated peptic ulcers: laparoscopic versus open approach. Surgical endoscopy. 33: 281-292.

[14] S. L. Siow, H. A. Mahendran, C. M. Wong, M. Hardin, T. L. Luk. (2018). Laparoscopic versus open repair of perforated peptic ulcer: Improving outcomes utilizing a standardized technique. Asian journal of surgery. 41 (2): 136-142.

[15] G. S. Quah, G. D. Eslick, M. R. Cox. (2019). Laparoscopic repair for perforated peptic ulcer disease has better outcomes than open repair. Journal of Gastrointestinal Surgery. 23: 618-625.

[16] S. Tan, G. Wu, Q. Zhuang, Q. Xi, Q. Meng, Y. Jiang, N. Li. (2016). Laparoscopic versus open repair for perforated peptic ulcer: a meta-analysis of randomized controlled trials. International Journal of Surgery. 33: 124-132.