Хирургия. Журнал имени Н.И. Пирогова
2020, №3, с. 13-21
https://doi.org/10.17116/hirurgia202003113

Pirogov Journal of Surgery
2020, No. 3, pp. 13-21
https://doi.org/10.17116/hirurgia202003113

Comparison of laparoscopic and open suturing of perforated peptic ulcer complicated by advanced peritonitis

© A.V. SAZHIN, G.B. IVAKHOV, E.A. STRADYMOV, V.A. PETUKHOV, S.M. TITKOVA

Pirogov Russian National Research Medical University of the Ministry of Health of Russia, Moscow, Russia

ABSTRACT

Objective. To compare the results of open and laparoscopic interventions for PGDU complicated by advanced peritonitis.

Material and methods. A retrospective analysis enrolled 172 patients with PGDU who underwent surgery for the period 2014—2016. The research was performed at the bases of the Department of Faculty-Based Surgery No. 1 of the Medical Faculty of the Pirogov Russian National Research Medical University. Further analysis enrolled 138 patients in accordance with inclusion and exclusion criteria (laparoscopic intervention — 116 patients, open surgery — 22). Propensity score matching (pseudorandomization) was applied after comparative analysis of patients' characteristics and treatment outcomes in order to ensure maximum comparability of both groups.

Results. Length of hospital-stay (7.1 vs. 9.8 days), incidence of extra-abdominal complications (6.3%. vs. 41.2%) and adverse events Clavien—Dindo grade II (6.3% vs. 35.3%) were significantly lower after minimally invasive surgery ($p<0.05$).

Conclusion. Analysis of comparable groups of patients with PGDU complicated by peritonitis revealed that laparoscopic surgery is accompanied by significantly lower incidence of extra-abdominal postoperative complications and shorter hospital-stay compared with open surgery. Mortality and incidence of intra-abdominal postoperative complications were similar in both groups.

Keywords: perforated ulcer; diffuse peritonitis; postoperative complications; mortality; pseudo-randomization.

INFORMATION ABOUT THE AUTHORS:

Sazhin A.V. — e-mail: sazhin-av@ya.ru; https://orcid.org/0000-0001-6188-6093
Ivakhov G.B. — e-mail: ivakhovsurg@yandex.ru; https://orcid.org/0000-0002-9773-4953
Stradymov E.A. — e-mail: egr.stradymov@mail.ru; https://orcid.org/0000-0001-9414-7588
Petukhov V.A. — e-mail: pwa54@yandex.ru; https://orcid.org/0000-0003-1807-9864
Titkova S.M. — e-mail: stitkova63@yandex.ru; https://orcid.org/0000-0001-5477-0084
Corresponding author: Страдымов Е.А. — e-mail: egr.stradymov@mail.ru

TO CITE THIS ARTICLE:

Sazhin AV, Ivakhov GB, Stradymov EA, Petukhov VA, Titkova SM. Comparison of laparoscopic and open suturing of perforated peptic ulcer complicated by advanced peritonitis. *Pirogov Russian Journal of Surgery = Khirurgiya. Zhurnal im. N.I. Pirogova*. 2020;3:13-21. (In Russ.). https://doi.org/10.17116/hirurgia202003113

Introduction

Perforation is the most common complication of peptic ulcer of the stomach and duodenum requiring surgical intervention [1]. The obvious successes and progress in the diagnosis and treatment of perforated gastroduodenal ulcers (PGDU), as well as reduced number of patients with this complication in the world observed over the past two decades have little changed the values of postoperative morbidity and mortality. For example, postoperative morbidity varies from 17% to 63%, mortality — 10—40% [2—8].

Currently, the most common surgical approach in these patients is suturing of perforation using open and laparoscopic procedures [1, 9, 10].

Interest to laparoscopic interventions is growing steadily. The number of minimally invasive interventions is annually increased not only in scheduled surgery but also in urgent surgical practice. Moreover, meta-analysis enrolling 3 large randomized trials confirmed that laparoscopic and open management of PGDU is followed by equivalent outcomes [11]. However, almost all trials were based on small samples of patients while significant heterogeneity of these studies additionally complicates generalization of data [11]. In addition, most of researches devoted to the problem of PGDU were carried out before 2004 that undoubtedly requires new large-scale studies to reveal the true differences in the results of open and laparoscopic treatment.

Thus, more than 30-year experience of laparoscopic surgery for PGDU does not definitively answer the following question. What is the effectiveness and safety of laparoscopic suturing of PGDU complicated by advanced peritonitis compared with open surgery? [1, 10, 12].

As a result, the purpose of our study was to compare the results of open and laparoscopic interventions for PGDU complicated by advanced peritonitis.

Material and methods

A retrospective analysis enrolled 172 patients with PGDU who underwent surgery for the period 2014–2016. The research was performed at the bases of the Department

of Faculty-Based Surgery No. 1 of the Medical Faculty of the Pirogov Russian National Research Medical University.

Patients admitted to the hospital in an extremely severe condition (*n*=11) were excluded from further analysis. Severity of their state was determined by septic shock followed by hemodynamic instability.

Inclusion criteria were patients aged over 18 years who underwent suturing of PGDU complicated by advanced peritonitis.

Exclusion criteria were local peritonitis, perforation over 15 mm combined with pyloroduodenal stenosis and severe inflammatory periulcerous roller (> 15 mm), penetrating ulcer, septic shock.

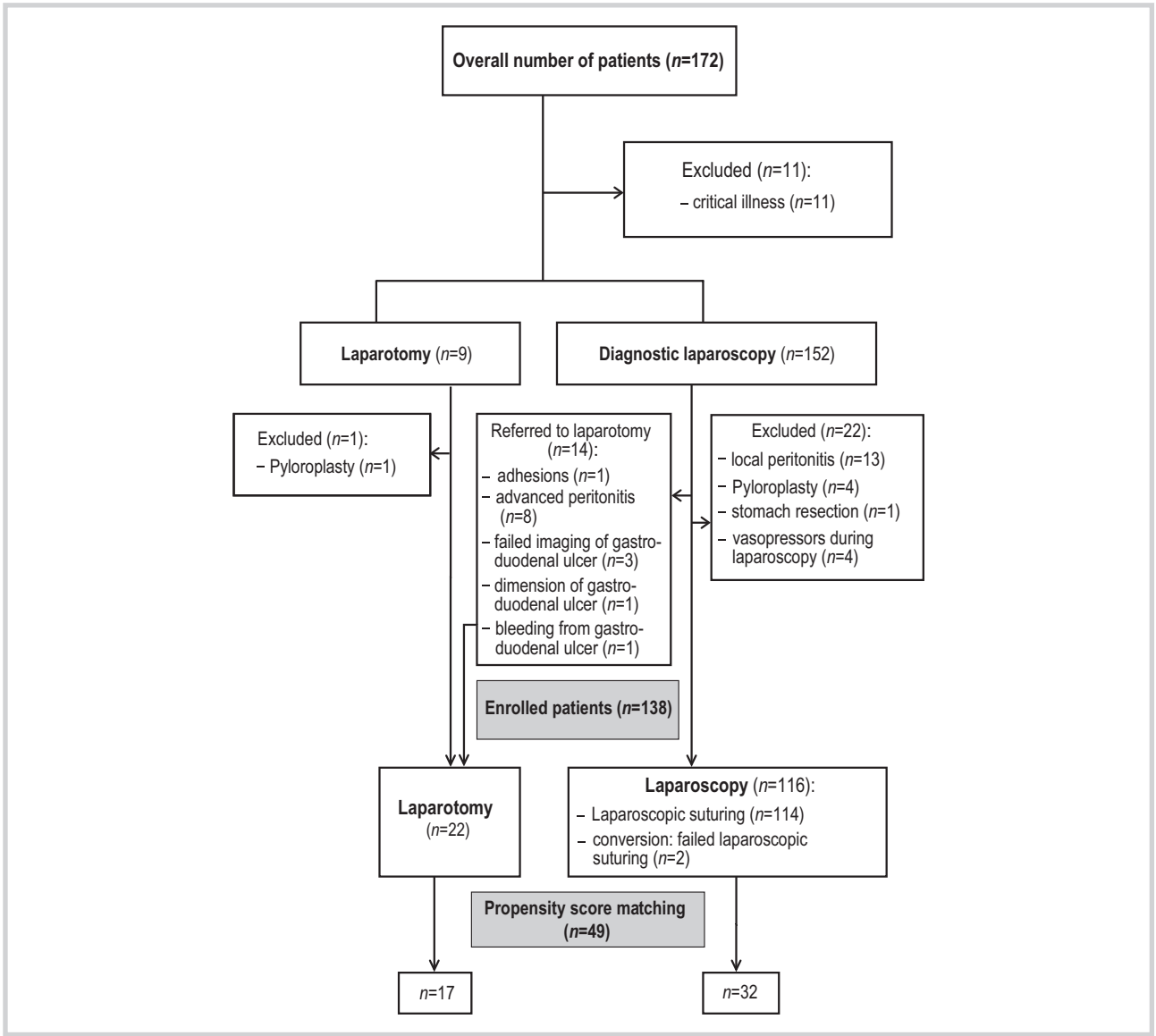
Nine patients underwent open surgery immediately after admission, 152 patients — diagnostic laparoscopy.

This study was devoted to suturing of perforated ulcers complicated by advanced peritonitis. Therefore, patients with local peritonitis (*n*=13), those who underwent stomach resection (*n*=1), pyloroplasty (*n*=5), and patients who needed inotropic support during diagnostic laparoscopy and subsequent conversion (*n*=4) were excluded from the study.

In accordance with the intention-to-treat concept, 2 patients with failed minimally invasive intervention were assigned to the laparoscopic group.

As a result, there were 116 patients in the group of laparoscopic intervention and 22 patients in the group of open surgery **(Fig.)**.

Propensity score matching (pseudorandomization) was applied after comparative analysis of patients' characteristics and treatment outcomes in order to ensure maximum comparability of both groups [13]. The following variables were considered in pseudorandomization: Boey score [14], Boey score modified in our clinic (mBoey), PULP [15], Mannheim peritonitis index (MPI) [16] and perforation size.



Flow-diagram of research.

***Table 1*. Pre- and intraoperative characteristics of patients in both groups (prior to PSM).**

Variables	Overall sample (*n*=138)	Laparoscopic repair (*n*=116)	Open suturing (*n*=22)	*p*-value
Age, years	46,1±19,7 41 [30,61]	43,9±19,4 38,5 [29,56]	57,5±17,9 65 [40,68]	0,0013
Female, *n* (%)	35 (25,4)	26 (22,4)	9 (40,9)	0,0434
Duration of disease, hours	9±7,9 7 [5,10]	8±4,6 7 [5;9,5]	14,1±16,1 9 [7,12]	0,0217
Duodenal ulcer, *n* (%)	86 (62,3)	74 (63,8)	12 (54,5)	0,1706
Gastric ulcer, *n* (%)	52 (37,7)	42 (36,2)	10 (45,5)	0,1706
Duration of perforation ⩾ 24 hours, *n* (%)	8 (5,8)	4 (3,4)	4 (18,2)	0,0309
Septic shock at admission, *n* (%)	2 (1,4)	2 (1,7)	–	–
Boey score	0,3±0,6 0 [0,1]	0,2±0,5 0 [0,0]	0,8±0,8 1 [0,1]	0,0018
Boey ⩾ 1, *n* (%)	36 (26,1)	23 (19,8)	13 (59,1)	0,0001
mBoey score	0,7±0,9 0[0,1]	0,6±0,9 0[0,1]	1,4±1,1 2[0,2]	0,0015
PULP score	2,1±2,8 1 [0,3]	1,6±2,5 1 [0,1]	4,2±3,4 4,5 [1,7]	0,0003
PULP > 7, *n* (%)	12 (8,7)	7 (6)	5 (22,7)	0,0544
ASA class	1,9±0,9 2 [1,3]	1,8±0,8 2 [1,2]	2,6±1 3 [2,3]	0,0007
ASA class ⩾ III, **n** (%)	35 (25,4)	23 (19,8)	12 (54,5)	0,0004
WSES sepsis severity score	3,8±1,5 3 [3,5]	3,6±1,3 3 [3,3]	4,6±2 3 [3,6]	0,0364
WSES SSS > 5, *n* (%)	21 (15,2)	12 (10,3)	9 (40,9)	0,0024
Mannheim peritonitis index	18,9±6,2 16 [16,25]	18,1±5,8 16 [16,21]	23,5±6,7 25 [16,26]	0,0007
MPI ⩾ 22, *n* (%)	35 (25,4)	23 (19,8)	13 (54,2)	0,0004
Serous-fibrinous peritonitis, *n* (%)	97 (70,3)	85 (73,3)	12 (54,5)	0,0572
Fibrinous-purulent peritonitis, *n* (%)	41 (29,7)	31 (26,7)	10 (45,5)	0,0572
Size of perforation, mm	5,7±4,6 5 [3,6]	4,8±2,1 4 [3,5]	10,3±9,5 7,5 [5,10]	0,00002
Surgery time, min	91,8±30,1 90 [70,105]	88,4±27,6 85 [70,100]	109,8±36,4 105 [90,140]	0,0049
Hospital-stay, days	7,3±4,7 6 [5,9]	6,7±4,2 6 [4,8]	10,5±6,1 9 [7,16]	0,0004

Note: percentages are calculated in relation to the total number of patients in each group.

PSM in 1:2 fashion was performed (2 patients from the laparoscopic group were matched with one patient from the open group). Therefore, laparoscopic group comprised 32 patients, open group — 17 patients **(Fig.)**.

Length of in-hospital stay, postoperative morbidity and mortality were compared in both groups. All postoperative complications were divided into 3 groups: extra-abdominal, intra-abdominal and local (wound) complications [12,17]. Moreover, adverse events were ranged in accordance with the Clavien-Dindo classification [18].

Statistical analysis was performed using Statistica 10, (StatSoft, Inc.) and XLSTAT 2019 software packages for Microsoft Excel. Data were shown as mean values and standard deviations for continuous variables with normal distribution, median and interquartile range for continuous data with abnormal distribution and absolute values with percentages for categorical variables. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to estimate quality of distribution. Student's t-test was used to compare continuous variables with normal distribution in independent samples, Mann-Whitney U-test – for variables without normal distribution. Categorical data and percentages were compared using the Pearson χ^2 test, Pearson χ^2 test with Yates correction or two-sided Fisher's exact test. Differences were significant at p-value <0.05. Odds ratios (OR) with 95% confidence interval (95% CI) were determined to assess correlation between the type of surgery and risk of complications.

Results

Laparoscopic closure of PGDU complicated by peritonitis was made in 71.7% of cases. Females significantly prevailed in the group of open suturing (22.4 vs. 40.9%, p<0.05).

A comparative analysis of pre- and intraoperative factors revealed significant predominance of more severe patients in the group of open suturing of PGDU. This was due to older age, longer period of disease, higher scores of prognostic scales Boey, mBoey, PULP, ASA, MIP and larger diameter of the perforated ulcer compared with patients from the laparoscopic group (p <0.05) **(Table 1)**.

Table 2. **Postoperative complications in patients undergoing emergent laparoscopic and open repair of perforated peptic ulcers complicated by diffuse peritonitis *(before PSM)*.**

Postoperative complication	Overall sample (*n*=138)	Laparoscopic repair (*n*=116)	Open suturing (*n*=22)	*p*-value
Intraabdominal complications, *n* (%)	10 (7,2)	7 (6)	3 (13,6)	0,1989
Leakage after suturing of perforation, *n* (%)	6 (4,3)	4 (3,4)	2 (9,1)	0,244
Extraabdominal complications, *n* (%)	20 (14,5)	8 (6,9)	12 (54,5)	<0,0001
Pneumonia, *n* (%)	14 (10,1)	5 (4,3)	9 (40,9)	<0,0001
Wound infection, *n* (%)	1 (0,7)	-	1 (4,5)	–
Overall number of complications, *n* (%)	31	15 (48,4*)	16 (51,6*)	–
Overall number of patients with complications, *n* (%)	27 (19,6)	15 (12,9)	12 (54,5)	<0,0001

Note: percentages are calculated in relation to the total number of patients in each group; * - percentages of the total number of postoperative complications.

Table 3. **Clavien-Dindo grading of postoperative complications in patients undergoing emergent laparoscopic and open repair of perforated peptic ulcers complicated by diffuse peritonitis *(before PSM)*.**

Clavien-Dindo grade of postoperative complications	Overall sample (*n*=138)	Laparoscopic repair (*n*=116)	Open suturing (*n*=22)	*p*-value
I, *n* (%)	1 (0,7)	1 (0,9)	–	–
II, *n* (%)	16 (11,6)	6 (5,2)	10 (45,5)	<0,0001
IIIA, *n* (%)	4 (2,9)	2 (1,7)	2 (9,1)	0,1194
IIIB, *n* (%)	7 (5,1)	6 (5,2)	1 (4,5)	1,000
IVA, *n* (%)	4 (2,9)	2 (1,7)	2 (9,1)	0,1194
V, *n* (%)	10 (7,2)	4 (3,4)	6 (27,3)	0,0012

Note: percentages are calculated in relation to the total number of patients in each group.

A comparative assessment of the results of surgical treatment of PGDU complicated by peritonitis is shown in **Tables 1—3**. Length of hospital-stay (6.7 vs. 10.5 days), incidence of extra-abdominal complications (6.9 vs. 54.5%), adverse events Clavien-Dindo grade II (5.2 vs. 45.5%) and mortality CDC grade V (3.4 vs. 27.3%) were significantly higher in the group of open suturing of the perforated ulcer ($p<0.05$). Incidence of intra-abdominal postoperative complications was similar in both groups ($p> 0.05$).

The risk of extra-abdominal complications after open repair was 13.3 times higher than after laparoscopic surgery (OR 13.3, 95% CI 4.5–38.8), risk of pneumonia was 13 times higher (OR 13.1, 95% CI 3.9-44.3).

There were no significant differences in pre- and intraoperative characteristics between both groups of patients after PSM **(Table 4)**.

A comparative analysis of laparoscopic and open repair of perforated gastroduodenal ulcers complicated by diffuse peritonitis showed that minimally invasive interventions are followed by less incidence of extra-abdominal postoperative complications (6.3 vs. 41.2%) including pneumonia (6.3 vs. 29.4%), complications CDC class II (6.3 vs. 35.3%) and length of hospital-stay (7.1 ± 3.2 vs. 9.8 ± 4.9 days) ($p <0.05$).

Incidence of postoperative intra-abdominal complications and mortality rate were similar in both groups **(Tables 5, 6)**.

Open repair was associated with 5.3-fold higher risk of extra-abdominal postoperative complications (OR 5.3, 95% CI 1.5-18.8) and 6.2-fold higher risk of pneumonia (OR 6.2, 95% CI 1.4-27.2) compared with laparoscopic procedure.

Discussion

There are 5 available randomized clinical trials (RCTs) with overall sample size of 406 patients (n=208 for laparoscopy and n=198 for laparotomy). These researches confirmed controversial results of surgical treatment of PGDU [19—23]. The first meta-analysis revealed significantly lower incidence of wound suppuration, reduced postoperative pain syndrome and need for analgesics after laparoscopic surgery. However, longer duration of intervention and higher incidence of redo procedures were observed [24]. Higher incidence of leakage after laparoscopic repair of PGDU was observed in the following review [25]. However, later meta-analyses did not reveal significant differences in the incidence of postoperative complications and mortality after both interventions [12, 26]. Zhou C. et al. reported less incidence of postoperative complications and redo interventions after minimally invasive operations [27]. Controversial data may be explained by heterogeneity of the groups [27]. Baseline predominance of more severe patients in the group of open interventions prevented correct comparative assessment of surgical outcomes in patients with PGDU complicated by diffuse peritonitis. We applied PSM to correct uneven distribution of confounders between the laparoscopic and open groups and reduce systematic

Table 4. **Perioperative characteristics of patients undergoing emergent laparoscopic and open repair of perforated peptic ulcers (*after PSM*).**

Variable	Overall sample (*n*=49)	Laparoscopic repair (*n*=32)	Open suturing (*n*=17)	*p*-value
Age, years	53,1±18,4 52 [37,66]	53±19,2 51,5 [35,63]	53,2±17,3 62 [39,67]	0,7315
Female, *n* (%)	16 (32,7)	11 (34,4)	5 (29,4)	0,974
Duration of disease, hours	10,4±7,7 8 [7,11]	9,6±5,4 8 [6,5;11,5]	11,8±10,9 9 [7,11]	0,9586
Duodenal ulcer, *n* (%)	30 (61,2)	21 (65,6)	9 (52,9)	0,5759
Gastric ulcer, *n* (%)	19 (38,8)	11 (34,4)	8 (47,1)	0,5759
Duration of perforation ⩾ 24 h, *n* (%)	6 (12,2)	3 (9,4)	3 (17,6)	0,4055
Septic shock at admission, *n* (%)	2 (4,1)	2 (6,3)	-	-
Boey score	0,6±0,7 0 [0,1]	0,5±0,7 0 [0,1]	0,6±0,8 0 [0,1]	0,716
Boey ⩾ 1, *n* (%)	22 (44,9)	14 (43,8)	8 (47,1)	0,9362
mBoey score	1,1±1,1 1 [0,2]	1,1±1,1 1 [0,2]	1,2±1,2 1 [0,2]	0,779
PULP score	3±2,9 1 [1,5]	2,9±2,9 1 [1,5]	3,2±3,2 1 [1,7]	0,7316
PULP > 7, *n* (%)	6 (12,2)	4 (12,5)	2 (11,8)	1,000
ASA class	2,3±0,9 2 [2,3]	2,3±1 2 [2,3]	2,3±0,8 2 [2,3]	0,9917
ASA class ⩾ III, *n* (%)	20 (40,8)	13 (40,6)	7 (41,2)	0,7888
WSES sepsis severity score	4,1±1,8 3 [3,5]	3,9±1,8 3 [3,5]	4,5±1,8 3 [3,6]	0,2216
WSES SSS > 5, *n* (%)	12 (24,5)	5 (15,6)	7 (41,2)	0,1029
Mannheim peritonitis index	21,7±6,1 21 [16,26]	21,4±5,9 21 [16,26]	22,1±6,7 21 [16,25]	0,9255
MPI ⩾ 22, *n* (%)	20 (40,8)	13 (40,6)	7 (41,2)	0,7888
Serous-fibrinous peritonitis, *n* (%)	27 (55,1)	17 (53,1)	10 (58,8)	0,9362
Diffuse peritonitis, *n* (%)	26 (53,1)	16 (50)	10 (58,8)	0,773
Size of perforation, mm	6,6±2,8 6 [5,8]	6,5±2,5 6 [5,8]	6,8±3,2 5 [5,10]	0,9751
Surgery time, min	99,9±36,9 90 [75,120]	97±36,2 90 [75;107,5]	105,3±38,9 100 [80,130]	0,3872
Hospital-stay, days	8±4 8 [6,9]	7,1±3,2 6,5 [5,9]	9,8±4,9 9 [8,10]	0,0192

Table 5. **Postoperative complications in patients undergoing emergent laparoscopic and open repair of perforated peptic ulcers complicated by diffuse peritonitis *(after PSM)*.**

Postoperative complication	Overall sample (*n*=49)	Laparoscopic repair (*n*=32)	Open suturing (*n*=17)	*p*-value
Intraabdominal complications, *n* (%)	6 (12,2)	4 (12,5)	2 (11,8)	1,000
Leakage after suturing of perforation, *n* (%)	5 (10,2)	3 (9,4)	2 (11,8)	1,000
Extraabdominal complications, *n* (%)	9 (18,4)	2 (6,3)	7 (41,2)	0,005
Pneumonia, *n* (%)	7 (14,3)	2 (6,3)	5 (29,4)	0,0406
Overall number of complications, *n* (%)	15	6 (40*)	9 (60*)	–
Overall number of patients with complications, *n* (%)	13 (26,5)	6 (18,8)	7 (41,2)	0,1762

Note: percentages are calculated in relation to the total number of patients in each group; * - percentages of the total number of postoperative complications.

bias. Perforation diameter, severity of peritonitis, concomitant diseases, duration of disease and patient's age, Boey and mBoey scores, PULP, Mannheim Peritonitis Index (MIP) were enrolled as confounders considering the importance of these factors. Significant increase of the risk of extra-abdominal postoperative complications (OR 5.3, 95% CI 1.5—18.8) was revealed for open surgery after PSM. However, incidence of leakage after suturing of perforation and other intra-abdominal postoperative complications, mortality rate were similar in both groups ($p > 0.05$). Some authors argue that laparoscopic procedures contribute to the development of pneumonia in patients with peritonitis [28]. These data are confirmed by experimental studies. Laparoscopy-associated pneumoperitoneum increases the risk of bacteremia and sepsis in patients with duration of peritonitis over 12 hours [29, 30]. However, the data of our study refute this fact. Incidence of pneumonia was significantly lower in the

Table 6. **Clavien-Dindo grading of postoperative complications in patients undergoing emergent laparoscopic and open repair of perforated peptic ulcers complicated by diffuse peritonitis *(after PSM)*.**

Clavien-Dindo grading of postoperative complications	Overall sample (*n*=49)	Laparoscopic repair (*n*=32)	Open suturing (*n*=17)	*p*-value
II, *n* (%)	8 (16,3)	2 (6,3)	6 (35,3)	0,015
IIIA, *n* (%)	2 (4,1)	1(3,1)	1 (5,9)	1,000
IIIB, *n* (%)	3 (6,1)	3 (9,4)	–	0,5423
IVA, *n* (%)	1 (2)	–	1 (5,9)	0,3469
V, *n* (%)	6 (12,2)	2 (6,3)	4 (23,5)	0,1643

Note: percentages are calculated in relation to the total number of patients in each group.

laparoscopic group (6.3 vs. 29.4%) although mean duration of diffuse peritonitis was 10.4±7.7 hours. Laparoscopic repair of PGDU was performed in 71.7% of cases. This value is many times higher than mean incidence (6—11.5%) of laparoscopic suturing reported in observational European and world studies (CIAO, CIAOW) [31, 32]. Thus, laparoscopic repair is safe and effective in patients with PGDU complicated by diffuse peritonitis. It should be emphasized that improvement of manual skills in laparoscopy, further clinical researches, the progress of anesthesiology and intensive care are likely to further increase the incidence of laparoscopic interventions for PGDU. Conclusion Analysis of comparable groups of patients with PGDU complicated by peritonitis revealed that laparoscopic surgery is accompanied by significantly lower incidence of extra-abdominal postoperative complications and shorter hospital-stay compared with open surgery.

No conflict of interests to declare.

ЛИТЕРАТУРА/REFERENCES

1. Di Saverio S, Bassi M, Smerieri N, Masetti M, Ferrara F, Fabbri C. Diagnosis and treatment of perforated or bleeding peptic ulcers: 2013 WSES position paper. *World J Emerg Surg*. 2014;9:45. https://doi.org/10.1186/1749-7922-9-45
2. Ермолов А.С., Смоляр А.Н., Шляховский И.А., Храменков М.Г. 20 лет неотложной хирургии органов брюшной полости в Москве. *Хирургия*. 2014;5;7-16.
   Ermolov AS, Smolyar AN, Shlyakhovsky IA, Khramenkov MG. 20 years of emergency abdominal surgery in Moscow. *Khirurgiya*. 2014;5;7-16. (In Russ.)
3. Тимербулатов В.М., Кунафин М.С., Тимербулатов М.В. Экстренная абдоминальная хирургия в регионе Российской Федерации: анализ за 40 лет. *Вестник хирургии им. И.И. Грекова*. 2014;6:89-92.
   Timerbulatov VM, Kunafin MS, Timerbulatov MV. Emergency abdominal surgery in the region of the Russian Federation: analysis for 40 years. *Vestnik khirurgii im. I.I. Grekova*. 2014;6:89-92. (In Russ.)
4. Циммерман Я.С. *Нерешенные и спорные вопросы современной гастроэнтерологии*. М.: МЕДпресс; 2013.
   Tsimmerman YaS. *Unresolved and controversial issues of modern gastroenterology*. M.: MEDpress; 2013. (In Russ.)
5. Bertleff MJ, Lange JF. Perforated peptic ulcer disease: a review of history and treatment. *Dig Surg*. 2010;27:161-169. https://doi.org/10.1159/000264653
6. Møller MH, Adamsen S, Wøjdemann M, Møller AM. Perforated peptic ulcer: how to improve outcome? *Scand J Gastroenterol*. 2009;44:15-22. https://doi.org/10.1080/00365520802307997
7. Svanes C. Trends in perforated peptic ulcer: incidence, etiology, treatment and prognosis. *World J Surg*. 2000;24:277-283. https://doi.org/10.1007/s002689910045
8. Thorsen K, Glomsaker TB, von Meer A, Søreide K, Søreide JA. Trends in diagnosis and surgical management of patients with perforated peptic ulcer. *J Gastrointest Surg*. 2011;15:1329-1335. https://doi.org/10.1007/s11605-011-1482-1
9. Chung KT, Shelat VG. Perforated peptic ulcer — an update. *World WJGS*. 2017;9(1):1-12. https://doi.org/10.4240/wjgs.v9.i1.1
10. Sartelli M, Chichom-Mefire A, Labricciosa FM. The management of intra-abdominal infections from a global perspective: 2017 WSES guidelines for management of intraabdominal infections. *World J Emerg Surg*. 2017;12:36. https://doi.org/10.1186/s13017-017-0141-6
11. Søreide K, Thorsen K, Søreide JA. Strategies to improve the outcome of emergency surgery for perforated peptic ulcer. *BJS*. 2014;101:51-64. https://doi.org/10.1002/bjs.9368
12. Sanabria A, Villegas MI, Morales Uribe CH. Laparoscopic repair for perforated peptic ulcer disease. *Cochrane Database Syst Rev*. 2013;2:Cd004778. https://doi.org/10.1002/14651858.cd004778.pub3
13. Гржибовский АМ, Иванов СВ, Горбатова МА, Дюсупов АА. Использование псевдорандомизации (propensity score matching) для устранения систематических различий сравниваемых групп в обсервационных исследованиях с дихотомическим исходом. *Экология человека*. 2016;5:50-64.
   Grzhibovsky AM, Ivanov SV, Gorbatova MA, Dyusupov AA. Propensity Score Matching as a Modern Statistical Method for Bias reduction in Observational Studies with Binary Outcome. *Ekologiya cheloveka*. 2016;5:50-64. (In Russ.)
14. Boey J, Choi SK, Poon A, Alagaratnam TT. Risk stratification in perforated duodenal ulcers. A prospective validation of predictive factors. *Ann Surg*. 1987;205:22-26. https://doi.org/10.1097/00000658-198701000-00005
15. Moller MH, Engebjerg MC, Adamsen S, Bendix J, Thomsen RW. The peptic ulcer perforation (PULP) score: a predictor of mortality following peptic ulcer perforation. A cohort study. *Acta Anaesthesiol Scand*. 2012;56(5):655-662. https://doi.org/10.1111/j.1399-6576.2011.02609.x
16. Linder MM, Wacha H, Feldmann U, Wesch G, Streifensand RA, Gundlach E. The Mannheim Peritonitis Index. An instrument for the intraoperative prognosis of peritonitis. *Chirurg*. 1987;58:84-92. https://doi.org/10.1007/978-3-642-73008-5_6
17. Савельев ВС. *Руководство по неотложной хирургии органов брюшной полости*. Руководство для врачей. М.: МИА; 2014.
   Savelyev VS. *Abdominal Emergency Surgery Guide*. Rukovodstvo dlya vrachej. M.: MIA; 2014. (In Russ.)
18. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R,

Vonlanthen R, Padbury R, Cameron JL, Makuuchi M. The Clavien—Dindo classification of surgical complications: five-year experience. *Ann Surg.* 2009;250(2):187-196. https://doi.org/10.1097/sla.0b013e3181b13ca2

19. Lau WY, Leung KL, Kwong KH, Davey IC, Robertson C, Dawson JJ, Chung SC, Li AK. A randomized study comparing laparoscopic versus open repair of perforated peptic ulcer using suture or sutureless technique. *Ann Surg.* 1996;224:131-138. https://doi.org/10.1097/00000658-199608000-00004
20. Lau JY, Lo SY, Ng EK, Lee DW, Lam YH, Chung SC. A randomized comparison of acute phase response and endotoxemia in patients with perforated peptic ulcers receiving laparoscopic or open patch repair. *Am J Surg.* 1998;175(4):325-327. https://doi.org/10.1016/s0002-9610(98)00006-3
21. Siu W, Leong H, Law B, Chau CH, Li AC, Fung KH, Tai YP, Li MK. Laparoscopic repair for perforated peptic ulcer: a randomized controlled trial. *Ann Surg.* 2002;235:313-319. https://doi.org/10.1097/00000658-200203000-00001
22. Bertleff MJ, Halm JA, Bemelman WA, van der Ham AC, van der Harst E, Oei HI, Smulders JF, Steyerberg EW, Lange JF. Randomized Clinical Trial of Laparoscopic Versus Open Repair of the Perforated Peptic Ulcer: The LAMA Trial. *World J Surg.* 2009;33(7):1368-1373. https://doi.org/10.1007/s00268-009-0054-y
23. Schietroma M, Piccione F, Carlei F, Sista F, Cecilia EM, Amicucci G. Peritonitis from perforated peptic ulcer and immune response. *J Invest Surg.* 2013;26(5):294-304. https://doi.org/10.3109/08941939.2012.762073
24. Lau H. Laparoscopic repair of perforated peptic ulcer: a meta-analysis. *Surg Endosc.* 2004;18:1013-1021. https://doi.org/10.1007/s00464-003-8266-y
25. Lunevicius R, Morkevicius M. Systematic review comparing laparoscopic and open repair for perforated peptic ulcer. *Br J Surg.* 2005;92:1195-1207. https://doi.org/10.1002/bjs.5155
26. Antoniou SA, Antoniou GA, Koch OO. Meta-analysis of laparoscopic versus open repair of perforated peptic ulcer. *JSLS.* 2013;17(11):15-22. https://doi.org/10.4293/108680812x13517013317752
27. Zhou C, Wang W, Wang J, Zhang X, Zhang Q, Li B, Xu Z. An Updated Meta-Analysis of Laparoscopic Versus Open Repair for Perforated Peptic Ulcer. *Sci Rep.* 2015;5:13976. https://doi.org/10.1038/srep13976
28. Jm N, Edwin B, Reiertsen O, Trondsen E, Faerden AE, Rosseland AR. Laparoscopic and open operation in patients with perforated peptic ulcer. *Eur J Surg.* 1999;165:209-214. https://doi.org/10.1080/110241599750007063
29. Evasovich MR, Clark TC, Horattas MC, Holda S, Treen L. Does pneumoperitoneum during laparoscopy increase bacterial translocation? *Surg. Endosc.* 1996;10:1176-1179. https://doi.org/10.1007/s004649900273
30. Gurtner GC, Robertson CS, Chung SC, Ling TK, Ip SM, Li AK. Effect of carbon dioxide pneumoperitoneum on bacteraemia and endotoxaemia in an animal model of peritonitis. *Br J Surg.* 1995;82:844-848. https://doi.org/10.1002/bjs.1800820639
31. Sartelli M, Catena F, Ansaloni L, Leppaniemi A, Taviloglu K. Complicated intra-abdominal infections in Europe: a comprehensive review of the CIAO study. *World J Emerg Surg.* 2012;7(1):36. https://doi.org/10.1186/1749-7922-7-36
32. Sartelli M, Catena F, Ansaloni L, Moore E, Malangoni M, Velmahos G. Complicated intra-abdominal infections in a worldwide context: an observational prospective study (CIAOW Study). *World J Emerg Surg.* 2013;8(1):1. https://doi.org/10.1186/1749-7922-8-1

Поступила 10.09.19
Received 10.09.19
Принята в печать 21.10.19
Accepted 21.10.19