

Original Article

The impact of laparoscopic radical gastrectomy on the inflammatory response and immune function of patients with gastric cancer

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Abstract



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The current study aimed to measure the effects of laparoscopic radical gastrectomy on inflammatory response along with immune function in gastric cancer (GC) patients. Seventy patients with GC in our hospital were retrospectively chosen to be the study objects and separated into control group (CG, 35 cases) and observation group (OG, 35 cases). Patients in the OG received radical laparotomy. Patients in the OG received laparoscopic radical gastrectomy. The surgical indicators, postoperative recovery indicators, inflammatory factors, immune function, incidence of adverse reactions along with quality of life of patients in both groups were compared. In contrast to the CG, the operation time of the OG presented as shorter ($P < 0.05$), and the amount of intraoperative blood loss together with postoperative VAS score in the OG presented lower ($P < 0.05$), but the number of lymph nodes dissection presented not statistically significant between 2 groups ($P > 0.05$). The postoperative exhaust time, feeding time as well as hospital stay in the OG presented shorter relative to the CG ($P < 0.05$). The serum levels of CRP, and IL-6 together with TNF- α presented elevated in both groups after surgery, and those in the OG presented lower when compared with the CG ($P < 0.05$). The serum levels of IgA, and IgG together with IgM presented declined in both groups after surgery, and those in the OG presented higher when compared with the CG ($P < 0.05$). The incidence of postoperative complications in the OG presented reduction relative to the CG ($P < 0.05$). The GLQI scores of the OG presented significantly higher relative to the CG at discharge ($P < 0.05$). Compared with radical gastrectomy, laparoscopic radical gastrectomy is more suitable for the treatment of GC, which can reduce the inflammatory response and promote the immune function of GC patients.

Keywords: Gastric cancer, Laparoscopic radical gastrectomy, Radical gastrectomy, Inflammatory response, Immune function.

1. Introduction

Gastric cancer (GC) belongs to a type of the most common malignant tumors in China, which is often accompanied by symptoms such as epigastric pain, lack of appetite and emaciation, and has a high incidence and mortality, which seriously threatens the physical and mental health and quality of life of patients [1]. The pathogenic factors of GC are complicated, and the early symptoms are not specific, which makes most patients with hematemesis, hematochezia and other obvious symptoms when they seek treatment, the tumor has already developed to the advanced stage (that is, the middle and late stage), resulting in patients missing the early conservative treatment, and radical surgery is needed for treatment [2].

In the past, laparotomy was the main surgical plan, and the purpose of tumor resection was achieved through the implementation of traditional radical gastrectomy [3]. However, the trauma caused by such surgery was usually large, which was not conducive to the rehabilitation and prognosis of patients [4]. Recently, with the widespread popularization of laparoscopic technology, laparoscopic surgery has been extensively applied in diagnosing and

treating GC as well as other diseases and has the advantages of less trauma, fewer complications, and faster postoperative recovery [5, 6]. For example, Wang et al. have discovered that laparoscopic pancreatoduodenectomy is a safe and feasible procedure for pancreatic or periampullary tumors, which is associated with a shorter length of stay compared to open pancreatoduodenectomy [7]. Marco Braga et al. have pointed that laparoscopic colorectal surgery reduces 30-day postoperative morbidity, and promote lymphocyte proliferation and gut oxygen tension [8]. Andreas Obermair et al. have indicated that laparoscopic hysterectomy is preferred superior to laparotomy in endometrial cancer patients [9], with a significantly decreased risk of major surgical adverse events.

In our study, we compared the effects of laparoscopic radical gastrectomy on inflammatory response along with immune function in GC patients.

2. Materials and methods

2.1. General data

Seventy patients with GC in our hospital were retrospectively chosen to be the study objects and separated into

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control group (CG, 35 cases) and observation group (OG, 35 cases) according to different treatment plans. The CG contained 18 males and 17 females. The average age was (59.56±5.62) years, ranging 36-75 years. There were 19 cases of stage II and 16 cases of stage IIIA. The mean tumor diameter was (2.87±0.26) cm. The OG contained 19 males and 16 females. The average age was (59.62±5.73) years, ranging 37-76 years. There were 20 cases of stage II and 15 cases of stage IIIA. The mean tumor diameter was (2.92±0.28) cm. No statistical significance was seen in the clinical data of GC patients between 2 groups ($P>0.05$), indicating comparability.

Inclusion criteria: (1) GC was confirmed by imaging and histopathology; (2) Had surgical indications; (3) Patients and their families were fully informed and participated voluntarily.

Exclusion criteria: (1) Patients with other gastrointestinal diseases; (2) Surgical intolerance; (3) Severe organ dysfunction.

2.2. Methods

Patients in the OG received radical laparotomy. The patient was put in a supine position, and followed by general anesthesia, an incision was made from the sternal xiphoid process to 3 cm below the umbilical cord. The GC lesion was carefully investigated, and the relationship between the lesion and marginal tissue was observed. The primary tumor was removed along with the infiltrated tissue, followed by peritoneal irrigation, followed by peritoneal closure.

Patients in the OG received laparoscopic radical gastrectomy. The patient was put in a supine position and under general anesthesia, the umbilical hole was punctured and pneumoperitoneum was established, followed by laparoscopic implantation, and the main operating hole was placed at 5 cm below the costal margin of the patient's left anterior axillary line. After laparoscopic implantation through the observation hole, the intraperitoneal tumor and its surrounding conditions were explored. The primary tumor and the infiltrated tissue were excised through the operation hole, and the distance between the incisional edge and the tumor body should be controlled within 2 cm. Then abdominal cavity was irrigated, and the abdominal cavity was closed successively after completion.

2.3. Observation indicators

(1) Surgical indicators: The operative time, intraoperative blood loss, number of lymph node dissection as well as postoperative pain was observed in 2 groups. Visual analog scale (VAS) was implemented for evaluating postoperative pain [10].

(2) Postoperative recovery indicators: The postoperative exhaust time, feeding time as well as hospital stay of 2 groups were observed.

(3) Inflammatory factors: 3 mL of fasting venous blood was gathered from patients before and 3 days after operation, and serum was centrifugally separated. C-reactive protein (CRP) level was detected by scattering turbidimetry and tumor necrosis factor- α (TNF- α) along with interleukin-6 (IL-6) levels were examined with ELISA.

(4) Immune function: Before and 3 days after surgery, 5 mL of fasting venous blood was collected, serum was centrifuged, and immunoglobulin (IgA, IgG, IgM) levels were detected by immunoturbidimetry.

(5) Incidence of postoperative complications including anastomotic fistula, intestinal obstruction, gastric retention and infection, were analyzed in the two groups.

(6) The gastrointestinal quality of life index (GLQI) was adopted for assessing the patients' quality of life at discharge, with a total of 144 points, including physiological function, subjective symptoms, social activities and psychological emotions [11].

2.4. Statistical analysis

SPSS 22.0 statistical software was implemented for statistical analysis. Measurement data were exhibited as mean \pm standard deviation ($\bar{x}\pm s$), and T-test was adopted for comparison. The statistical data were exhibited as rate (%) and χ^2 test was adopted for comparison. $P<0.05$ meant statistical significance.

3. Results

3.1. Surgical indicators in both groups

Figure 1 revealed that the operation time of the OG presented shorter relative to the CG ($P<0.05$), and the amount of intraoperative blood loss along with postoperative VAS score in the OG presented lower relative to the CG ($P<0.05$), but the number of lymph nodes dissection was not statistically significant between 2 groups ($P>0.05$).

3.2. Postoperative recovery indicators in both groups

Figure 2 revealed that the postoperative exhaust time, feeding time as well as hospital stay in the OG presented shorter in contrast to the CG ($P<0.05$).

3.3. Levels of inflammatory factors in both groups

Figure 3 displayed no difference in CRP, and IL-6 together with TNF- α levels between 2 groups before surgery ($P>0.05$). The serum levels of CRP, and IL-6 together with TNF- α were elevated in both groups after surgery, and those in the OG presented lower when compared with the CG ($P<0.05$).

3.3. Immune function in both groups

Figure 4 revealed no difference in IgA, IgG and IgM levels between 2 groups before surgery ($P>0.05$). The serum levels of IgA, IgG and IgM declined in both groups

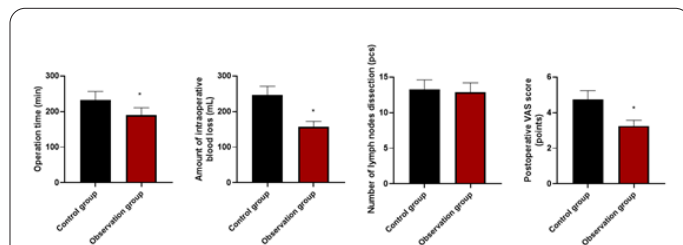


Fig. 1. Surgical indicators in both groups. * $P<0.05$.

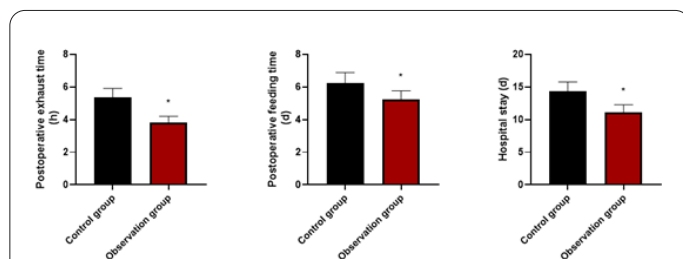
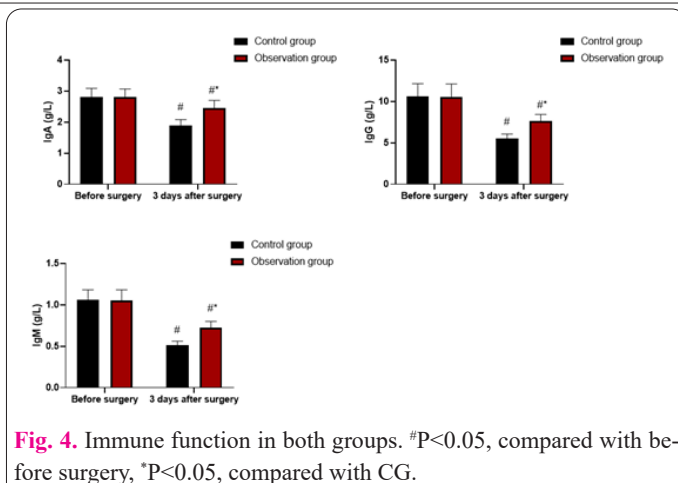
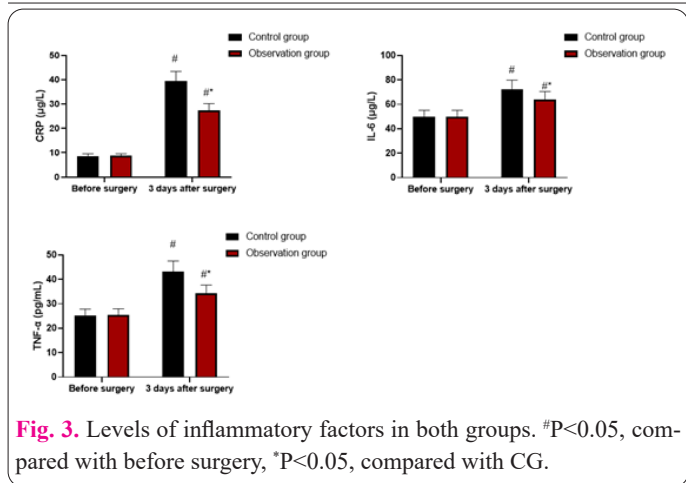


Fig. 2. Postoperative recovery indicators in both groups. * $P<0.05$.



after surgery, and those in the OG presented higher when compared with the CG ($P < 0.05$).

3.4. Incidence of postoperative complications in both groups

The incidence of postoperative complications in the OG presented reduction relative to the CG ($P < 0.05$, Table 1).

3.5. Quality of life of patients in both groups

The GLQI scores of the OG presented significantly higher relative to the CG at discharge ($P < 0.05$), as displayed in Figure 5.

4. Discussion

Clinical treatment of GC mainly adopts surgical operation, the principle of which is to resect the primary tumor, the metastatic lymph nodes along with infiltrated tissues, following the principle of no tumor, so as to improve the cure rate of GC [12]. However, intraoperative trauma can trigger an inflammatory response and immunosuppressive reaction of the body, and the greater the trauma, the more intense the reaction [13]. Recently, due to the development of laparoscopic technology along with its application in radical gastrectomy, the long-term effect of the operation is comparable to that of traditional laparotomy [14]. However, the study on the influence of different operation methods on the body is still incomplete. Hence, it is essential to explore the influence of laparoscopic surgery on inflammatory factors together with immune function in GC patients.

In our study, we found that the operation time of the OG presented significantly shorter relative to the CG, the amount of intraoperative blood loss and postoperative VAS score in the OG was also significantly lower relative to the CG, and the postoperative exhaust time, feeding time as well as hospital stay in the OG presented significantly shorter than those in the CG. The results indicated that laparoscopic radical gastrectomy was beneficial

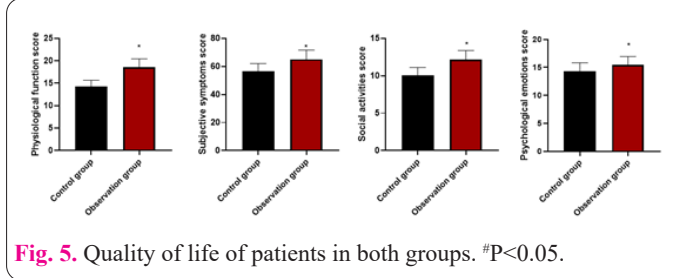


Fig. 5. Quality of life of patients in both groups. # $P < 0.05$.

to shorten postoperative recovery time. The reason is that the incision of traditional open surgery is large, which is easy to causes greater injury to the body, resulting in more intraoperative blood loss, increasing the pain of patients, and reducing their willingness and ability to get out of bed early after surgery, thus affecting their physical recovery speed and prolonging the hospital stay. Laparoscopic radical gastrectomy for GC is performed with laparoscopically guided ultrasound knife to complete gastric dissociation, and the incision is small, which can decrease the amount of intraoperative blood loss, relieve the pain of patients, promote the recovery of gastrointestinal function, and thus reduce the length of hospital stay [15].

TNF- α is an inflammatory factor that can participate in systemic inflammatory response, and it is also one of the cytokines that stimulate the acute phase response [16]. IL-6 is one of the sensitive indicators of inflammation and can be expressed in the early stage of surgery. It can increase the proliferation of T cells and enhance phagocytosis. The higher the serum IL-6 concentration, the more serious the trauma to the body [17]. CRP is an acute-phase reaction protein stimulated and synthesized by IL-6 [18]. The postoperative infection rate of GC patients is higher, and the more severe the surgical trauma, the higher the infection rate. The surgical trauma can activate mononuclear macrophages, lead to the increase of neutrophils and white blood cells, and thus increase the release of inflammatory factors containing TNF- α , IL-6 along with CRP, and activate the complement system [19]. Besides, IgA, IgM and IgG are

Table 1. Incidence of postoperative complications in both groups.

Groups	N	Anastomotic fistula	Intestinal obstruction	Gastric retention	Infection	Total incidence rate
Control group	35	2	2	2	2	8 (22.86)
Observation group	35	1	0	1	0	2 (5.71%)
χ^2						4.20
P						<0.05

common immunoglobulins, and the higher the concentration, the stronger the immune capacity of the body [20]. In our study, the outcomes revealed that after surgery, the serum levels of CRP, IL-6 along with TNF- α in the OG presented lower when compared with the CG, while the serum levels of IgA, IgG along with IgM in the OG presented higher when comparing with the CG. The results indicated that laparoscopic radical gastrectomy was beneficial to reduce inflammation and improve immune function. The reason is that laparoscopic surgery is carried out in the operating hole, the surgical exposure is much lower than that of traditional open surgery, and the surgical wound is small. Therefore, the inflammatory response generated by the body is relatively weak, thus reducing the immune suppression response of the body and reducing the occurrence of complications [21, 22].

In addition, our study indicated that the incidence of postoperative complications in the OG presented reduction relative to the CG, while the GLQI scores of the OG presented significantly higher than that of the CG at discharge, implying that laparoscopic radical gastrectomy could decrease the incidence of postoperative complications along with promote the quality of life of GC patients, which was in line with previous studies [23-27].

In conclusion, compared with radical gastrectomy, laparoscopic radical gastrectomy is more suitable for the treatment of GC, which can reduce the inflammatory response and promote the immune function of GC patients.

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Conflict of interests

The author has no conflicts with any step of the article preparation.

Consent for publications

The author read and approved the final manuscript for publication.

Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors' contributions

LJ and WX conducted the experiments and wrote the paper; LJ and WX analyzed and organized the data; YJ conceived, designed the study and revised the manuscript.

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References

- Smyth EC, Nilsson M, Grabsch HI, van Grieken NC, Lordick F (2020) Gastric cancer. *Lancet* 396 (10251): 635-648. doi: 10.1016/s0140-6736(20)31288-5
- Tan Z (2019) Recent Advances in the Surgical Treatment of Advanced Gastric Cancer: A Review. *Med Sci Monit* 25: 3537-3541. doi: 10.12659/msm.916475
- Wu X, Wang X, Wang Y, Cui W, Liu P (2020) Comparison of clinical efficacy between laparotomy and laparoscopic radical surgery for gastric cancer and their effects on CRP, CEA and insulin resistance. *J buon* 25 (1): 324-331. doi: 10.1016/j.jbu.2020.07.053
- Wu X, Wang X, Wang Y, Cui W, Liu P (2020) Comparison of clinical efficacy between laparotomy and laparoscopic radical surgery for gastric cancer and their effects on CRP, CEA and insulin resistance. *J buon* 25 (1): 255-261. doi: 10.1016/j.jbu.2020.07.053
- Mari G, Scanziani R, Auricchio S, Crippa J, Maggioni D (2017) Laparoscopic Surgery in Patients on Peritoneal Dialysis: A Review of the Literature. *Surg Innov* 24 (4): 397-401. doi: 10.1177/1553350617708723
- Guerrini GP, Esposito G, Magistri P, Serra V, Guidetti C, Olivieri T, Catellani B, Assirati G, Ballarin R, Di Sandro S, Di Benedetto F (2020) Robotic versus laparoscopic gastrectomy for gastric cancer: The largest meta-analysis. *Int J Surg* 82: 210-228. doi: 10.1016/j.ijso.2020.07.053
- Wang M, Li D, Chen R, Huang X, Li J, Liu Y, Liu J, Cheng W, Chen X, Zhao W, Li J, Tan Z, Huang H, Li D, Zhu F, Qin T, Ma J, Yu G, Zhou B, Zheng S, Tang Y, Han W, Meng L, Ke J, Feng F, Chen B, Yin X, Chen W, Ma H, Xu J, Liu Y, Lin R, Dong Y, Yu Y, Liu J, Zhang H, Qin R (2021) Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours: a multi-centre, open-label, randomised controlled trial. *Lancet Gastroenterol Hepatol* 6 (6): 438-447. doi: 10.1016/s2468-1253(21)00054-6
- Braga M, Vignali A, Gianotti L, Zuliani W, Radaelli G, Gruarin P, Dellabona P, Di Carlo V (2002) Laparoscopic versus open colorectal surgery: a randomized trial on short-term outcome. *Ann Surg* 236 (6): 759-766; discussion 767. doi: 10.1097/01.Sla.0000036269.60340.Ae
- Obermair A, Janda M, Baker J, Kondalsamy-Chennakesavan S, Brand A, Hogg R, Jobling TW, Land R, Manolitsas T, Nascimento M, Neesham D, Nicklin JL, Oehler MK, Otton G, Perrin L, Salfinger S, Hammond I, Leung Y, Sykes P, Ngan H, Garrett A, Laney M, Ng TY, Tam K, Chan K, Wrede DH, Pather S, Simcock B, Farrell R, Robertson G, Walker G, McCartney A, Gebiski V (2012) Improved surgical safety after laparoscopic compared to open surgery for apparent early stage endometrial cancer: results from a randomised controlled trial. *Eur J Cancer* 48 (8): 1147-1153. doi: 10.1016/j.ejca.2012.02.055
- Sung YT, Wu JS (2018) The Visual Analogue Scale for Rating, Ranking and Paired-Comparison (VAS-RRP): A new technique for psychological measurement. *Behav Res Methods* 50 (4): 1694-1715. doi: 10.3758/s13428-018-1041-8
- Chen L, Tao SF, Xu Y, Fang F, Peng SY (2005) Patients' quality of life after laparoscopic or open cholecystectomy. *J Zhejiang Univ Sci B* 6 (7): 678-681. doi: 10.1631/jzus.2005.B0678
- Li GZ, Doherty GM, Wang J (2022) Surgical Management of Gastric Cancer: A Review. *JAMA Surg* 157 (5): 446-454. doi: 10.1001/jamasurg.2022.0182
- Li X, Pan K, Vieth M, Gerhard M, Li W, Mejías-Luque R (2022) JAK-STAT1 Signaling Pathway Is an Early Response to Helicobacter pylori Infection and Contributes to Immune Escape and Gastric Carcinogenesis. *Int J Mol Sci* 23 (8). doi: 10.3390/ijms23084147
- Chen QY, Xie JW, Zhong Q, Wang JB, Lin JX, Lu J, Cao LL, Lin M, Tu RH, Huang ZN, Lin JL, Zheng HL, Li P, Zheng CH, Huang CM (2020) Safety and Efficacy of Indocyanine Green Tracer-Guided Lymph Node Dissection During Laparoscopic Radical Gastrectomy in Patients With Gastric Cancer: A Randomized Clinical Trial. *JAMA Surg* 155 (4): 300-311. doi: 10.1001/jamasurg.2019.6033
- Li HZ, Chen JX, Zheng Y, Zhu XN (2016) Laparoscopic-assisted versus open radical gastrectomy for resectable gastric cancer: Systematic review, meta-analysis, and trial sequential analysis of randomized controlled trials. *J Surg Oncol* 113 (7): 756-767. doi: 10.1002/jso.24243

16. Balkwill F (2006) TNF-alpha in promotion and progression of cancer. *Cancer Metastasis Rev* 25 (3): 409-416. doi: 10.1007/s10555-006-9005-3
17. Tanaka T, Narazaki M, Kishimoto T (2018) Interleukin (IL-6) Immunotherapy. *Cold Spring Harb Perspect Biol* 10 (8). doi: 10.1101/cshperspect.a028456
18. Del Giudice M, Gangestad SW (2018) Rethinking IL-6 and CRP: Why they are more than inflammatory biomarkers, and why it matters. *Brain Behav Immun* 70: 61-75. doi: 10.1016/j.bbi.2018.02.013
19. Navaei-Alipour N, Mastali M, Ferns GA, Saberi-Karimian M, Ghayour-Mobarhan M (2021) The effects of honey on pro- and anti-inflammatory cytokines: A narrative review. *Phytother Res* 35 (7): 3690-3701. doi: 10.1002/ptr.7066
20. Chen K, Magri G, Grasset EK, Cerutti A (2020) Rethinking mucosal antibody responses: IgM, IgG and IgD join IgA. *Nat Rev Immunol* 20 (7): 427-441. doi: 10.1038/s41577-019-0261-1
21. Albers KI, Polat F, Helder L, Panhuizen IF, Snoeck MMJ, Polle SBW, de Vries H, Dias EM, Slooter GD, de Boer HD, Diaz-Cambronero O, Mazzinari G, Scheffer GJ, Keijzer C, Warlé MC (2022) Quality of Recovery and Innate Immune Homeostasis in Patients Undergoing Low-pressure Versus Standard-pressure Pneumoperitoneum During Laparoscopic Colorectal Surgery (RECOVER): A Randomized Controlled Trial. *Ann Surg* 276 (6): e664-e673. doi: 10.1097/sla.0000000000005491
22. Bulut O, Aslak KK, Levic K, Nielsen CB, Rømer E, Sørensen S, Christensen IJ, Nielsen HJ (2015) A randomized pilot study on single-port versus conventional laparoscopic rectal surgery: effects on postoperative pain and the stress response to surgery. *Tech Coloproctol* 19 (1): 11-22. doi: 10.1007/s10151-014-1237-6
23. Santos A, Mentula P, Pinta T, Ismail S, Rautio T, Juusela R, Lähdesmäki A, Scheinin T, Sallinen V (2021) Comparing Laparoscopic Elective Sigmoid Resection With Conservative Treatment in Improving Quality of Life of Patients With Diverticulitis: The Laparoscopic Elective Sigmoid Resection Following Diverticulitis (LASER) Randomized Clinical Trial. *JAMA Surg* 156 (2): 129-136. doi: 10.1001/jamasurg.2020.5151
24. Ismaili A, Yari K, Moradi MT, Sohrabi M, Kahrizi D, Kazemi E, Souri Z. (2015). IL-1B (C+3954T) gene polymorphism and susceptibility to gastric cancer in the Iranian population. *Asian Pac J Cancer Prev* 16(2):841-4. doi: 10.7314/apjcp.2015.16.2.841. PMID: 25684535.
25. Kazemi E, Kahrizi D, Moradi MT, Sohrabi M, Yari K. (2016). Gastric Cancer and Helicobacter pylori: Impact of hopQII Gene. *Cell Mol Biol (Noisy-le-grand)*. 62(2):107-10. PMID: 26950460.
26. Kazemi E, Kahrizi D, Moradi MT, Sohrabi M, Amini S, Mousavi SA, Yari K. (2016). Association between Helicobacter pylori hopQI genotypes and human gastric cancer risk. *Cell Mol Biol (Noisy-le-grand)*. 62(1):6-9. PMID: 26828979.
27. Zhao S, Zheng H, Zhan L, Zhu M (2017). Clinical observation of wrist-ankle needle therapy combined with patient controlled intravenous analgesia for pain after laparoscopic surgery for eccyosis]. *Zhongguo Zhen Jiu* 37 (11): 1173-1175. doi: 10.13703/j.0255-2930.2017.11.009