

ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Short-term outcomes of laparoscopic radical gastrectomy for advanced gastric neoplasms – a single center experience

Miloš Bjelović^{1,2}, Milan Veselinović², Dragan Gunjić², Tamara Babić², Luka Nikolić³¹University of Belgrade, School of Medicine, Belgrade, Serbia;²Clinical Center of Serbia, University Hospital for Digestive Surgery, Department for Minimally Invasive Upper Digestive Surgery, Belgrade, Serbia;³University of Edinburgh, Edinburgh Medical School, College of Medicine and Veterinary Medicine, Biomedical Sciences, Edinburgh, United Kingdom**SUMMARY****Introduction/Objective** The objective was to assess the effectiveness of laparoscopic gastrectomy, analyzing short-term outcomes of laparoscopic radical gastrectomy in treatment of advanced gastric neoplasms.**Methods** We performed a prospective cohort observational study, which included 30 patients who underwent elective radical laparoscopic gastrectomy (total or subtotal) for stomach neoplasms, performed in the period between March 2013 and February 2017.**Results** Thirteen patients (43%) had been diagnosed with distal gastric tumors, seven (23%) with proximal gastric tumors, four (13%) with pangastric tumors, four (13%) with mediogastric tumors, and two (7%) with bicentric tumors. Mean operation duration was 286 minutes. The average blood loss was 183 mL. Conversion rate was 10% (three patients). Total of seven (23%) patients had postoperative complications, and mean intensive care unit stay was 1 day. Mean hospital stay after surgery was 13.08 days. The average number of harvested lymph nodes was 33.9, and R0 resection was performed in 87% patients. The overall 30-day mortality rate was 0%.**Conclusion** Although technically challenging, laparoscopic gastrectomy is a safe and oncologically adequate procedure in the radical surgical treatment of advanced gastric neoplasms.**Keywords:** gastric neoplasms; surgery; minimally invasive gastrectomy; laparoscopy**INTRODUCTION**

When laparoscopic surgery began in the mid-20th century, no one really believed that large and demanding procedures such as esophagectomy and gastrectomy would be performed laparoscopically. The official history of laparoscopic gastric resection began in Singapore in 1992, when Goh et al. [1] performed the first totally intra-abdominal laparoscopic distal gastrectomy with Billroth II reconstruction, in an elderly patient with a chronic gastric ulcer.

In 1993, Azagra et al. [2] performed the first minimally invasive total gastrectomy (TG) for gastric cancer. In 2007, Kitano et al. [3] published a multicenter study conducted in Japan for early-stage gastric cancer and confirmed that the laparoscopic treatment is not inferior to open surgery for stages I and II of gastric cancer. However, meta-analysis published by Kodera et al. [4] opened a whole new perspective for laparoscopic gastrectomy (LG) and its use not only for early but also for advanced gastric cancer.

Radical LG for gastric neoplasms has been performed at the Department for Minimally Invasive Surgery, Clinic for Digestive Surgery, Clinical Center of Serbia, since March 2013.

The study objective was to assess the effectiveness of LG, analyzing the short-term out-

comes of laparoscopic radical gastrectomy in the treatment of advanced gastric neoplasms.

METHODS

This prospective cohort observational study included 30 patients who underwent elective radical LG (total or subtotal), for stomach neoplasms, performed at the Department for Minimally Invasive Surgery, Clinic for Digestive Surgery, Clinical Centre of Serbia, in the period between March 2013 and February 2017.

Standard preoperative diagnostics included anamnesis and physical examination, barium swallow radiography, upper flexible endoscopy with biopsy, and computed tomography scanning of the chest and abdomen.

All of the patients received antibiotic and thromboembolic prophylaxis. Standard surgical technique is described further in the text. A nasogastric tube is routinely placed after subtotal gastrectomy (STG) and removed on the first or second postoperative day, depending on the quantity and dynamics of the discharge. All of the patients received early mobilization. Control barium radiography was performed routinely on the seventh postoperative day after TG, followed by the clear liquid diet. A control

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Koste Todorovića 6
Beograd
milos.bjelovic@gmail.com

barium meal was not routinely performed in the patients after STG, and these patients began with the clear liquid diet on the third postoperative day.

After the procedure, the operating surgeon dissected all of the extracted lymph nodes, separating them from the specimen. Histopathological examination and staging were based on the revised TNM tumor classification including tumor stage grouping.

Demographic data, preoperative diagnostics, intraoperative details (such as the length of the procedure, blood loss, etc.) and details regarding postoperative course were all analyzed, as well as the pathohistological data. Postoperative complications were analyzed separately and graded according to the Dindo–Clavien classification [5].

After discharge from the hospital, the first check-up was one month post-surgery and then periodically, according to the criteria of the European Society for Medical Oncology [6].

The study objective was to assess the effectiveness of LG in the treatment of advanced gastric neoplasms (carcinoma, primary gastric lymphoma, and mesenchymal tumors). Primary endpoints were significant early postoperative complications (defined as grade II and over according to the Dindo–Clavien classification). Secondary endpoints were analyses of the short-term outcomes other than postoperative complications, i.e. perioperative characteristics (duration of the operation, blood loss, ICU and overall hospital stay) and 30-day mortality and oncological outcomes (based on the number of harvested lymph nodes and R status).

Surgical technique

The position of the patient and trocars were adopted from Pennathur et al. [7]. Standard surgical technique in patients with gastric cancer includes omentectomy, D2 lymph node dissection, and TG or STG, according to criteria of the Japanese Gastric Cancer Association [8]. In patients with primary gastric lymphoma, total omentectomy is not mandatory in radical surgical treatment, while in patients with mesenchymal neoplasm of the stomach, there is no need for lymph node dissection. Reconstruction after TG was performed using retrocolically placed Roux-en-Y limb, followed by mechanical esophagojejunal anastomoses. The continuity of the digestive tube, in patients with STG, was provided by forming retrocolic, inframesocolic hand-sewn gastro-jejunal anastomoses. After restoring the continuity of the gastrointestinal tract, it is mandatory to close all of the defects created in the mesentery, to prevent internal herniation, both in the early and late postoperative periods. At the end of the procedure, the surgical specimen is placed in an extraction bag, and removed from the abdomen through a 5 cm long Pfannenstiel incision.

Statistical analysis

The descriptive statistics, including the numbers and percentages of categorical data or mean, median, and range of numerical data were used to summarize the sample

data. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22 (IBM Corp., Armonk, NY, USA).

RESULTS

The two sexes are almost equally distributed (43% female, 57% male) in the patient population, with a mean age of 61.37 years. Average Karnofsky and ASA scores were 87.27 and 1.83, respectively, while the mean BMI of the patients being 25.51 kg/m² (Table 1). In the majority of cases, the tumor was localized to the distal parts of stomach (13 patients, 43%), followed by the proximal stomach (seven patients, 23%), while four patients had a pangastric tumor (13%), and a further four of them (13%) had a tumor of the mediogastric segment, and only two patients (7%) had a bicentric tumor of the stomach. Histologically, adenocarcinoma was slightly more prevalent (60%) to primary gastric lymphomas (37%), and one patient was presented with a large mesenchymal tumor of the distal stomach (3%). Seventeen patients (57%) were submitted to TG, while the rest (13 patients, 43%), underwent STG. The average operative time was 297 minutes for TG and 272 minutes for STG (Table 2). The overall conversion rate was 10% (three patients) – in two patients submitted to TG (12%) and in one submitted to STG (8%). In two out of three patients (67%) the reason for conversion was a locally advanced tumor, while the reason for the third conversion was a technical problem with esophagojejunostomy. Time spent in the intensive care unit postoperatively was practically the same for both groups – one day. The average blood loss after TG was 215 mL, as opposed to 141 mL in the STG group. Mean hospital stay was 13 days after TG and 12 days after STG. The average number of harvested lymph nodes was 33.9 (34.7 in patients after TG and 32.4 after STG). The majority of our patients had an advanced stage stomach neoplasm. Average tumor size was 73.68 mm in diameter (range 30 to 160 mm). We had no patients with Tis and T1 tumor, 26% of our patients had T2 tumor, while

Table 1. Demographic characteristics and preoperative data

Feature	Value
Gender	Male 17 (57%)
	Female 13 (43%)
Mean age (years)	61.37 (22–85)
Karnofsky score (%)	87.27 (80–90)
ASA score	1.83 (1–3)
BMI	25.51 (19.3–34.47)
Localization of the tumor	Proximal stomach 7 (23%)
	Medial stomach 4 (13%)
	Distal stomach 13 (43%)
	Pangastric 4 (13%)
	Bicentric 2 (7%)
Pathohistology	Adenocarcinoma 18 (60%)
	Lymphoma 11 (37%)
	Mesenchymal tumor 1 (3%)

ASA score – American Society of Anesthesiologists physical status classification system; BMI – body mass index

Table 2. Intraoperative and postoperative course details

Feature		Subtotal gastrectomy	Total gastrectomy	Σ
Intraoperative details	Number of patients	13 (43%)	17 (57%)	30
	Duration of operation (min.)	272 (180–330)	297 (190–420)	286 (180–420)
	Conversion	1 (8%)	2 (12%)	3 (10%)
Postoperative course details	ICU stay (days)	0.77 (0–1)	1.12 (1–3)	0.97 (0–3)
	Transfusion (mL)	141 (0–735)	215 (0–1,325)	183 (0–1325)
	Hospital stay (days)	12.08 (7–27)	13.47 (9–20)	13.08 (7–27)
	30-day mortality	0	0	0
	Harvested lymph nodes	32.4 (21–45)	34.7 (19–73)	33.9 (19–73)
	Tumor size (mm)	60 (30–115)	82.53 (35–160)	73.68 (30–160)

ICU – intensive care unit

Table 3. Postoperative complications

Feature	Number	
Total number of postoperative complications	7	
Diarrhoea syndrome	3 (10%)	
Wound/trocar site infection	3 (10%)	
Acalculous cholecystitis	1 (3%)	
Number of patients with complications	7 (23%)	
Dindo–Clavien classification	I	1 (3%)
	II	4 (13%)
	III	1 (3%)
	IV	1 (3%)
	V	0

74% had more advanced tumor. According to the involved lymph nodes, 73% of our patients had N+ stadium of the disease, with more than half of them (56%) with a N2 status or higher. Nevertheless, a clear resection margin (R0) was achieved in 87% of the patients. The overall 30-day mortality rate was 0%.

In total, seven patients had a postoperative complication (23%), four in the TG group of patients and three in the STG group. Three of these patients (10%) had diarrheal syndrome. Surgical site infection was also found in three patients (10%), while only one patient (3%) developed biliary peritonitis on the 11th postoperative day, due to post-vagotomic acalculous cholecystitis. The overall re-intervention rate was 3%. All of the postoperative complications were graded according to the Dindo–Clavien classification (Table 3).

DISCUSSION

Gastric neoplasms have the fourth highest incidence globally, and the second highest in relation to mortality [9, 10]. In spite of all the advantages of chemotherapy, surgery remains the best treatment modality for gastric cancer and gastrointestinal stromal tumor, as well as the second most often used treatment for primary gastric lymphoma [11]. For a long time, open gastric surgery has been presented as the gold standard, with substantial scepticism towards laparoscopic surgery.

Laparoscopy has undergone intense development over the past twenty years, for use in gastric cancer and other gastrointestinal diseases [12]. Indications for laparoscopic surgery have changed year after year [13]. In comparison

with former laparoscopic interventions, which were almost exclusively associated with benign gastric pathology, laparoscopic gastric surgery is steadily becoming the standard procedure for treatment of malignant gastric disease [14, 15].

The last decade has brought substantial improvement in laparoscopic surgery, which has led to greater appreciation of the many advantages of minimally invasive surgery, which has been validated by various meta-analyses. In recent years, comprehensive meta-analyses have been published, showing both the short- and long-term effects of minimally invasive approaches, and demonstrating encouraging results in comparison to open surgery [16–19].

In their meta-analysis comparing patients with advanced-stage gastric cancer, Chen et al. [20] noted a significantly lower rate of bleeding during LG in comparison to open gastrectomy (OG), as well as a shorter hospital stay, faster postoperative recovery, and reduced intensity of postoperative pain, all in favor of LG. The individual parameters that are covered by our study fully correlate with the results of this extensive meta-analysis. Intraoperative blood loss that the analysis by Chen et al. [20] reported ranged 10–250 ml, while the length of hospital stay ranged 5–16.3 days. In our study, patients had lost an average of 183 ml of blood, while the average length of hospital stay was 13.08 days. The most likely explanation for the decreased intraoperative blood loss is certainly reduced tissue trauma, as well as better visualization using the laparoscopic camera, which has a zoom feature and therefore the possibility to facilitate the perception of small blood vessels.

Some centers, depending on the treatment practice and the experience of the operating team, demonstrated that patient's postoperative hospital stay was shortened by more than three days when operated on with a minimally invasive approach compared to open surgery, with an average length of hospital stay of 10 days and a range of 6–21 and 7–24 days [21, 22]. Our research shows similar results, with an average length of postoperative recovery of 13 days and a range of 7–27 days. It is certain that, with the expansion of the operative experience in this pathology, length of hospitalization can be significantly reduced, particularly in conjunction with full utilization of Enhanced Recovery after Surgery (ERAS) concept. Lower intensity of pain after laparoscopic surgery has been demonstrated by earlier exclusion of analgesic therapy [20].

One parameter in favor of open surgery is certainly the duration of the operation [23]. It is assumed that this is a

consequence of the extensive surgical dissection which must be carried out in advanced stages of gastric cancer, although many authors suggest that the time difference can be equated with open surgery by overcoming the learning curve, that is, by acquiring the skills in laparoscopic surgery. Data suggest that a plateau, which determines the time spent in the operating room even with open surgery, is achieved after performing 40 operations [24, 25, 26]. In the previously mentioned meta-analysis conducted by Chen et al. [20], the average length of surgery ranged 144–369.7 minutes, while the average duration of surgery in our study amounted to 286 minutes. The effect of the learning curve was more than obvious, with the average duration of more than 300 minutes at the very beginning, and less than 200 minutes in the last couple of cases.

Particularly important when comparing these two methods is the oncological principle itself. It was noted that LG is equal, and in some segments superior to OG, as far as oncological validity [20]. In advanced gastric cancer, D2 dissection is considered standard, and is essential for the quality of the operation [27]. In a meta-analysis by Zou et al. [28], it is demonstrated that OG with D2 dissection and LG with D2 dissection, at similar stages of the disease, have identical prognosis. The only problem is the learning curve and it is recommended that LG should not be performed in centers with limited experience in the treatment of this pathology. It was also observed that there was no significant difference in the number of harvested lymph nodes between OG and LG [20]. The average number of removed lymph nodes after LG in this meta-analysis ranges 20.5–63.7, while in our series, an average of 33.9 lymph nodes has been removed.

The resection margins are an important prognostic factor for the appearance of local recurrence [29]. In a meta-analysis by Chen et al [20], it is demonstrated that there is no statistically significant difference in the percentage of positive resection margins after OG and after LG.

Chen et al. [20] also recorded significantly fewer postoperative complications in patients after LG in comparison to OG. In our study, the overall rate of postoperative complications was 23%, which matches the average values of the meta-analysis (5–39%). This is most likely a consequence of the minimally invasive approach itself [11]. There was no statistically significant difference between

LG and OG in regard to the probability of anastomotic leakage, while the probability of pulmonary complications was lower after LG [23]. In our series, a significant number of postoperative complications had been caused by diarrheal syndrome, which occurred despite the fact that the patients were given antibiotics in the protocol of antibiotic prophylaxis.

Given the small percentage of postoperative complications and consequential shorter postoperative hospitalization, it is assumed that patients can begin with postoperative chemotherapy sooner, and are more likely to benefit from chemotherapy, but in practice these assumptions have not yet been proven. This applies both to patients with invasive adenocarcinomas and to patients with primary gastric lymphomas, who are candidates for postoperative adjuvant chemotherapy.

Based on the foregoing, it can be said that the use of LG in advanced gastric cancer is equally effective to OG concerning their oncological standing, with a lot of favorable factors. The only benefit of OG compared to LG is the shorter duration of surgery, which, most authors believe, could be equated through greater surgical operative experience.

Last but not least, when LG is performed in concordance with the ERAS concept, there is a positive relationship between the costs and the effects of LG compared to OG, with no significant difference in short-term postoperative morbidity and mortality.

In addition to LG, robotically performed gastrectomy is also slowly advancing into surgery, but time and scientific research have yet to show the advantages and disadvantages of this type of surgery.

CONCLUSION

There is no doubt that there is an intuitive attraction towards LG among both surgeons and patients. Although technically challenging, LG is a safe and oncologically adequate procedure in the radical surgical treatment of advanced gastric neoplasms. At the moment, this advanced laparoscopic procedure should be reserved for surgeons with sufficient experience in both advanced laparoscopic surgery and gastric tumor surgery

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Лапароскопска радикална гастректомија у лечењу узнапредовалог неопластичног обољења желуца – искуство једног центра

Милош Бјеловић^{1,2}, Милан Веселиновић², Драган Гуњић², Тамара Бабич², Лука Николић³

¹Универзитет у Београду, Медицински факултет, Београд, Србија;

²Клинички центар Србије, Универзитетска клиника за дигестивну хирургију, Одељење за минимално инвазивну хирургију горњег дигестивног тракта (Х одељење), Београд, Србија;

³Универзитет у Единбургу, Медицински и ветеринарски факултет, Биомедицинске науке, Единбург, Уједињено Краљевство

САЖЕТАК

Увод/Циљ Циљ студије је процена ефикасности лапароскопске гастректомије, анализирањем краткорочних резултата лапароскопске радикалне гастректомије у лечењу узнапредовалог неопластичног процеса желуца.

Метод Спроведена је ретроспективна кохортна опсервациона студија са 30 болесника подвргнутих елективној радикалној лапароскопској гастректомији (тоталној или субтоталној) због неопластичног процеса желуца у периоду од марта 2013. до фебруара 2017.

Резултати Тумор је углавном био локализован у дисталном желуцу (13 болесника, 43%), потом на проксималном желуцу (седам болесника, 23%), четири болесника су имала пангастрични тумор (13%), четири тумор медиогастричног сегмента (13%), док је код два болесника дијагностикован

бицентрични тумор желуца (7%). Просечно време трајања операције је било 286 минута, просечан губитак крви 183 mL, док је стопа конверзије износила 10% (три болесника). Укупно седам болесника (23%) имало је постоперативне компликације. Непосредно постоперативно боравили су један дан у јединици интензивног лечења, а са болничког лечења су отпуштани 13. постоперативног дана. Просечно је уклоњено 33,9 лимфних нодуса, док је R0 ресекција постигнута код 87% болесника. Смртних исхода није било. **Закључак** Иако технички захтевна, лапароскопска гастректомија је сигурна и онколошки исправна процедура у лечењу узнапредовалог неопластичног процеса желуца.

Кључне речи: неоплазме желуца; минимално инвазивна гастректомија; лапароскопија