Laparoscopic versus open total radical gastrectomy for advanced gastric cancer: surgical outcomes

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AIM: *The aim of this study is to compare the oncologic efficacy of laparoscopic total gastrectomy (LTG) versus open total gastrectomy (OTG) for gastric cancer and to provide our experiences regarding this surgery.*
METHODS: *A total of 107 patients who underwent curative total gastrectomy for gastric adenocarcinoma between September 2015 and September 2018 were included in this study. Demographic characteristics, operative parameters, histopathological results, postoperative morbidity and mortality results of the patients were evaluated.*
RESULTS: *Of 107 patients, 70 were men and 37 women. OTG consisted of 89 patients and LTG consisted of 18 patients. The mean age in OTG was 59.4 years, the mean age in LTG was 57.3 years. The mean number of lymph nodes harvested was 30.5±14.6 in OTG and 33.0±10.1 in LTG. The number of metastatic lymph nodes harvested was 7.4±10.5 in OTG and 10.0±11.8 in LTG (p= 0.366), and there was no statistical difference between the two groups. The time of onset of oral intake, anastomotic leakage, and postoperative mortality was similar in both groups. Operative duration and length of hospital stay were significantly higher in LTG. Postoperative survival duration was similar in both procedures*
CONCLUSION: *Laparoscopic total gastrectomy for gastric cancer is an oncologically safe procedure but had a longer operation time and a longer hospital stay. There was no significant difference number of harvested lymph nodes, number of metastatic lymph nodes, and tumor localization between the two groups*

KEY WORDS: Gastric cancer, Laparoscopy, Gastrectomy

Introduction

Gastric cancer ranks fourth among the most common cancers with about one million new cases/year. It is responsible for 8% of cancer-related deaths [1]. In our country, the incidence of gastric cancer, according to cancer statistics data from Turkey, ranges from 6.3 to 14.2 per hundred thousand, and it ranks 2nd for cancer-related deaths in men and 4th in women [2].
Gastrectomy continues to be the most important step in the treatment of gastric cancer, and many centers are currently performing this surgery with the open technique. However, laparoscopic gastrectomy is rapidly gaining popularity in the last decades. The first application of laparoscopy in gastric cancer surgery dates back to the 1990s [3]. Early oncological outcomes for laparoscopic gastrectomy was similar to open surgery in patients diagnosed with early gastric cancer [4]. However, there is limited evidence regarding its oncologic safety, especially for total gastrectomy. In this study, we aimed to compare the results of laparoscopic total gastrectomy (LTG) vs. open total (OTG) techniques in gastric cancer.

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Material, method, and patients

In this study, patients who underwent total gastrectomy with the diagnosis of gastric adenocarcinoma between September 2015 and September 2018 in the general surgery clinic of Cukurova University Medical Faculty were analyzed retrospectively.

Patients who underwent palliative surgery or who had metastatic disease and who were not considered to have undergone D2 lymph dissection from the file information were excluded from the study. In addition, laparoscopic or open subtotal gastrectomies were excluded. A total of 107 patients who underwent total gastrectomy + D2 lymph dissection were included in the study.

Data were prospectively collected from patient medical charts, operation records, and pathology reports.

Tumor progression was evaluated by preoperative examinations, which included an endoscopy with biopsy, basic blood testing, chest radiography, abdominopelvic computed tomography, and liver ultrasonography. Preoperative or abdominal computed tomography was performed to diagnose invasion depth and lymph node staging. Endoscopic ultrasonography only was performed to patients who have early stomach cancer in imaging. PET-CT was planned in cases with suspected metastatic foci.

Demographic characteristics, body mass index (BMI), comorbid diseases, ASA scores, neoadjuvant treatment status, and tumor localization were recorded from the patient files and hospital information system records.

Fig. 1: Omentectomy performed from right to left.

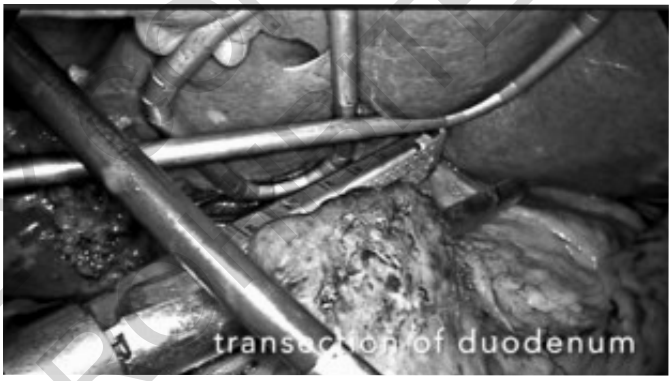


Fig. 2: Duodenal transection with endoscopic lineer stapler.

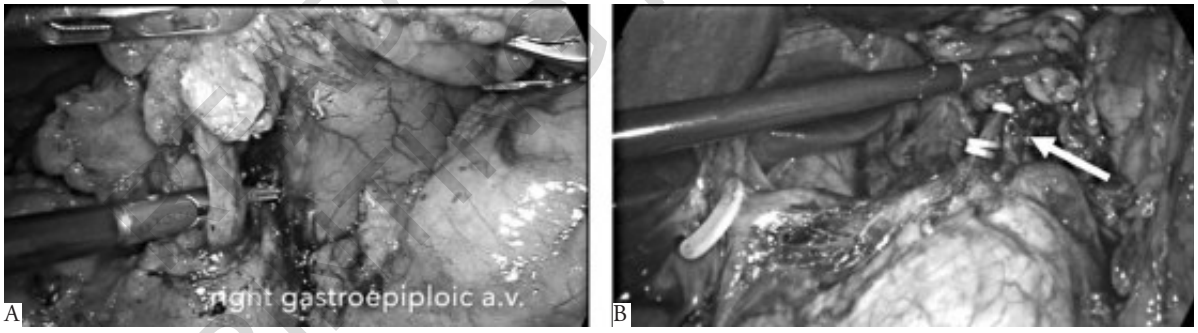


Fig. 3: A) Lymph node station 6; B) Lymph nodes with a number of 7, 8a, 9, 12a, harvested and left gastric artery clipped, white arrow.

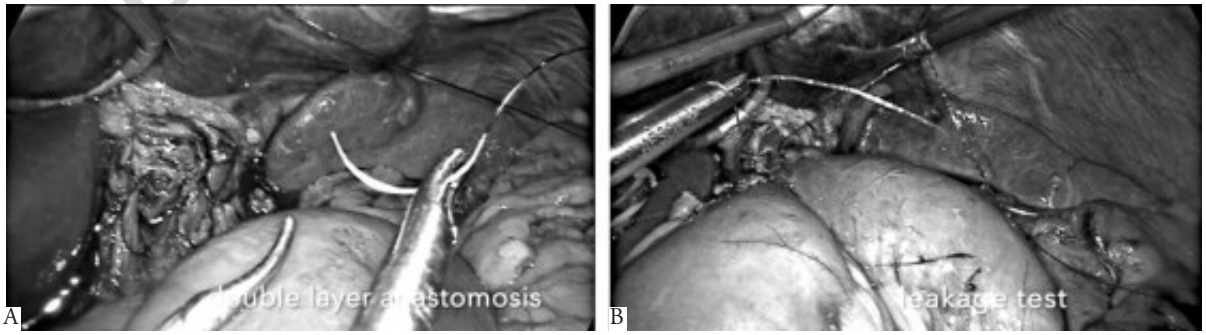


Fig. 4: A) Esophagojejunostomy anastomosis performed double layer; B) Leakage test performed with methylene blue.

Operation time, mean blood loss, mean time to onset of oral intake, major postoperative complication status according to Clavien Dindo classification [5], length of hospital stay (LoHS), total number of harvested lymph nodes, number of harvested metastatic lymph nodes, pathological stage, first 30-day mortality, and unplanned hospital admission within first 30 days were examined.
The patients were divided into two groups as open total gastrectomy (Group 1) and laparoscopic total gastrectomy (Group 2).
In Group 1, duodenum transection was performed with a linear incisor closure stapler, all esophagojejunostomy anastomoses were performed with a circular 26-29 mm diameter stapler, and jejenojejunal anastomoses were performed with linear incisor closure stapler or manually. Omentectomy was performed independently of the stage in both groups (Fig. 1).
In Group 2, duodenal transection (Fig. 2), gastric resection, jejunum resection, and jejenojejunal anastomoses were all performed intracorporeally using an endo-linear stapler. Lymphadenectomy was performed in both groups according to the Japanese gastric cancer guidelines (Figs. 3 A,B) [6]. Depending on the preference of the surgeon, esophagojejunal anastomosis was performed with an endoluminal stapler (OrVil) or laparoscopic double-suture hand-sewn anastomosis and leakage test was performed under direct vision (Figs. 4 A,B). All openings in the intestinal meso were closed with 3/0 non-absorbable sutures.
SPSS 24.0 IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA) was used for statistical analysis of the data. Mean, standard deviation, median, minimum and maximum values of group data were determined. Statistical analyses were performed using Chi Fisher, Student T-test and Mann Whitney U test. Kaplan-Meier analysis and Log Rank test were used for survival analysis. Statistical significance level was taken as 0.05 in all tests.

Results

Nineteen of 107 patients, included in the study were started laparoscopically. One patient in the laparoscopy group was converted to open surgery because of adhesions due to previous operations and this patient was included in the open surgery group. Eighty-nine patients underwent OTG (Group 1) and 18 patients underwent LTG (Group 2).
Both groups were similar in terms of age and sex distribution. ASA scores were lower (p=0.033), concomitant diseases were lower (p=0.032), and body mass index (BMI) was higher (p=0.005) in Group 2 (Table I).
The mean number of harvested lymph nodes were 30.5 (min: 13-max: 63) in Group 1 and 33.0 (min: 12-max: 53) in Group 2 (p: 0.496). The number of metastatic lymph nodes were 7.4 (min: 0-max: 47) in Group 1 and 10.0 (min: 0-max: 40) in Group 2 (p:0.366). There was no significant difference number of harvested lymph nodes, number of metastatic lymph nodes, and tumor localization between the two groups. Pathological stages were similar in two groups (Table II).
In Group 1, the operation time was significantly shorter, but blood loss was higher. The time to onset of oral intake was similar in both groups. When the complications were examined, Clavien Dindo 3a and 5 complications were statistically significantly higher in Group 1. The length of hospital stay was longer in Group 2 than Group 1 (p:0.009). When the number and reasons of patients who had unplanned hospital admissions within 30 days were evaluated, both groups had similar rates (Table III).
The survival durations were 26.7 and 25.5 months, respectively (Table IV) (Graph 1). Mortality occurred only in Group 1 (10 patients) during follow-up.

TABLE I - *Patient characteristics*

		Group 1 n. 89	Group 2 n. 18	p*
Age (min-max)		59,46±15,3 (14-89)	57,28±12,4 (34-81)	0,571
Sex	Male	58 (65,2)	12 (66,7)	0,903
	Female	31 (34,8)	6 (33,3)	
ASA score	1	53 (59,6)	6 (33,3)	0,033
	2	22 (24,7)	10 (55,6)	
	3	14 (15,7)	2 (11,1)	
BMI (min-max)		23,8±3,7 (16-36)	26,7±4,4 (21-40)	0,005
Concurrent illnesses	DM	3 (3,4)	3 (16,7)	0,032
	HT	9 (10,1)	4 (22,2)	
	CAD	8 (9,0)	0 (0,0)	
	More than one accompanying illness	12 (13,5)	0 (0,0)	
	None	57 (64,0)	11 (61,1)	
Neoadjuvant Chemotherapy	No	66 (74,2)	11 (61,1)	0,261
	Yes	23 (25,8)	7 (38,9)	

*p<0.05
DM: Diabetes Mellitus; HT: Hypertension; CAD: Coronary Artery Disease

Discussion

Surgery is still the cornerstone of the treatment of gastric cancer. Total or subtotal gastrectomy with D2 lymph node dissection with conventional open surgery is still the most common procedure in many centers. On the other hand, the rapid developments in laparoscopy technology and the acceptance of laparoscopic procedures by many centers raised the question "Is there a place for

Table II - *Tumor Characteristics*

		Group 1 n. 89	Group 2 n. 18	p*
Tumor localization	Lower	29 (32,6%)	9 (50%)	0,209
	Middle	51 (57,3%)	9 (50%)	
	Upper	2 (2,2%)	0 (0,0%)	
	Linitis Plastica	7 (7,9%)	0 (0,0%)	
Total number of harvestedlymph nodes (mean) (min-max)		30,5+14,6 (13-63)	33,0+10,1 (12-53)	0,496
Number of positive lymphnodes (mean) (min-max)		7,4±10,5 (0-47)	10,0±11,8 (0-40)	0,366
pSTAGE	1A	10 (11,2%)	4 (22,2%)	0,686
	1B	6 (6,7%)	1 (5,6%)	
	2A	5 (5,6%)	1 (5,6%)	
	2B	21 (23,6%)	4 (22,2%)	
	3A	9 (10,1%)	3 (16,7%)	
	3B	9 (10,1%)	0 (0,0%)	
	3C	29 (32,6%)	5 (27,8%)	

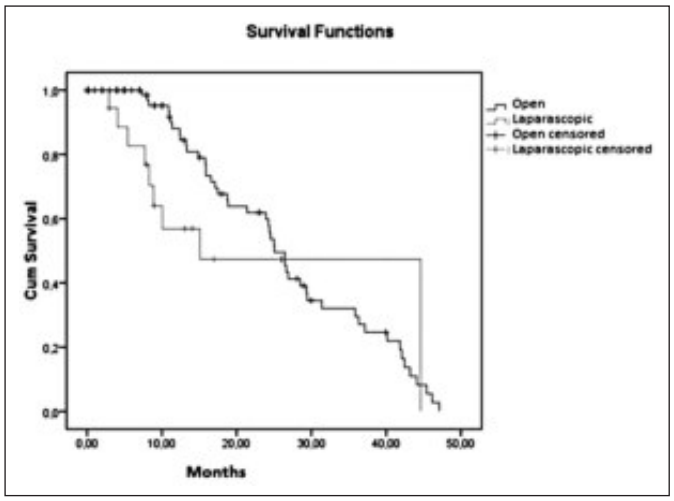
* p<0.05 EGJ Esophagogastric junction

Table III - *Intraoperative and Postoperative Outcomes*

		Group 1 n. 89	Group 2 n. 18	p*
Operation duration (min)	210,0±21,0 (160-250)	321,9±92,6 (150-500)	0,000	
Mean blood loss (ml)	363,1±51,0 (200-500)	143,0±97,6 (50-400)	0,000	
Mean onset to oral intake (day)	5,19±4,0 (2-40)	5,56±5,7 (1-28)	0,749	
Complication (Clavien Dindo)	3A	10 (11,2)	6 (33,3)	0,000
	3B	2 (2,2)	1 (5,6)	
	5	6 (6,7)	0 (0,0)	
Anastomotic leak	No leak	82 (92,1)	14 (77,8)	0,180
	Stump leak	3 (3,4)	2 (11,1)	
	Esophagojejunostomy	4 (4,5)	2 (11,1)	
Length of hospital stay (day)	10,26±7,0 (6-46)	15,72±11,4 (8-40)	0,009	
30-day hospital readmission	None	71 (85,5)	15 (83,3)	0,793
	Ileus	2 (2,4)	0 (0,0)	
	Oral intake disorder	1 (1,2)	0 (0,0)	
	Pneumonia	1 (1,2)	0 (0,0)	
	Wound site infection	8 (9,7)	3 (16,7)	
Mortality	Yes	10 (11,2)	0 (0,0)	0,145
	No	79 (88,8)	18 (100,0)	

Table IV - *Survival duration in terms of the type of operation*

		Average (Mean±sd)(Min-Max)	Median (Mean±sd)(Min-Max)	p
Type of operation	Open	26,7±1,6 (23,4-30,0)	25,0±1,2 (22,5-27,5)	0,287
	Laparoscopic	25,5±5,1 (15,5-35,5)	15,0±8,2 (0-31,2)	



Graph 1: Overall survival in terms of the type of operation.

laparoscopy in gastrectomy with D2 lymph node dissection?" Many studies seeking answers to this question have been published in the literature. The most important of these studies were published in Asia. Korean Laparoscopic Gastrointestinal Surgery Study Group (KLASS), Japanese Laparoscopic Surgery Group (JLSSG) and China Laparoscopic Surgery Group performed prospective randomized controlled multicenter studies [7-9]. Each of these studies focused on early-stage gastric cancer patients who underwent open distal gastrectomy (ODG) and laparoscopic distal gastrectomy (LDG). In these studies, no statistically significant difference was found in both arms (open vs laparoscopic distal gastrectomy) in terms of dissected lymph nodes, general complications, and oncological outcomes. In the last decades, Japanese guideline defined laparoscopic gastrectomy is a safe and feasible method for distal early-stage gastric cancer patients [10].

Later, the Chinese and Korean groups published new studies about laparoscopically treated advanced gastric cancers. In 2016, CLASS-01 multicenter randomized study published in China, 1056 gastric cancer patients with T2-4aN0-3M0 were examined. In this study, D2 lymphadenectomy was performed as standard in LDG and ODG for advanced gastric cancer and it was emphasized that there was no statistical difference between the two groups in terms of postoperative morbidity and mortality [11]. Similarly, in another study conducted in Korea, a statistically significant difference was not detected between LDG and ODG in terms of complications and lymph node dissection rates, for patients with $T_{2\text{-}4a}N_{0\text{-}2}M_0$ gastric cancer [12].

After these publications on laparoscopic distal gastrectomy in early and advanced gastric cancer, studies on laparoscopic total gastrectomy (LTG) started to be discussed. But the LTG technique is more difficult than the LDG technique and it is not as widely used as the LDG technique. Therefore, there are fewer studies on LTG. There is limited data to support LTG, especially in advanced gastric cancer.

In 2015, 675 patients participated in a study comparing laparoscopic and open total gastrectomy (OTG) cases. The operation time was shorter in the OTG group. Intraoperative blood loss and hospital stay were less in the LTG group. The total number of lymph nodes removed, morbidity and mortality rates were similar in two groups [13]. In our study, 89 of 107 gastric cancer patients underwent OTG and 18 underwent LTG.

Increased BMI is a predictor of increased postoperative complications, including anastomotic leak, but it is not a predictor of survival in gastric cancer [14]. In our study, we found that patients who underwent laparoscopy had higher BMI. Likewise the literature, in our series there was no difference in postoperative complications, morbidity, and mortality between the two groups. Our study showed that laparoscopic total gastrectomy can be performed safely in patients with a high BMI.

In the literature, it is recommended that patients undergoing laparoscopic surgery have a low ASA score [13]. However, in our study, higher ASA scores were found in the laparoscopy group.

In recent years, neoadjuvant therapy protocols have been developed in the treatment of gastric cancer in Europe and America. Neoadjuvant therapy for stages 2 and 3 gastric cancer can reduce staging, which does not increase perioperative complications [15]. Several studies have been performed to improve survival for locally advanced gastric cancer with neoadjuvant chemotherapy and/or radiotherapy. Two randomized studies, the Intergroup 0116 trial, and the MAGIC trial changed current clinical practice for resectable gastric cancer in the Western world [16]. However, the rate of neoadjuvant chemotherapy in the gastric cancer series in the literature still varies. In our clinic, neoadjuvant therapy has started to use as a primary treatment for advanced gastric cancer, since 2017. Therefore, there is no homogeneity in terms of neoadjuvant therapy in the present study. The number of patients receiving neoadjuvant therapy is 23 patients in Group 1 and 7 patients in Group 2.

It is reported in the literature that the operation time for open technique gastrectomy is between 120-594 minutes and it's 140-516 minutes for laparoscopic gastrectomy [17]. In our study, the operative times were consistent with the literature in Group 1 but were longer than those reported in the literature in Group 2. There was a statistically shorter operation time in Group 1 than Group 2.

In the literature, postoperative complication rates were lower in laparoscopy in both early and advanced gastric cancers [17]. In our study, postoperative complications were evaluated according to the Clavien Dindo scoring system, and in the open surgery group, grades 3a and 5 were seen more commonly. Also, there was no difference between the two groups in the unplanned admission rates in the first 30 days.

There are different opinions about anastomotic leakage

in the literature. Although there are some texts reporting higher leakage rates in laparoscopic surgery, similar leakage rates have been found in both open and laparoscopic surgery in many meta-analyses [18,19]. In our series, the incidence of anastomotic leakage and stump leakage was similar in both groups.

One of the advantages of laparoscopic approaches is that intraoperative tissue trauma is less in laparoscopy and the amount of bleeding due to this is less than open surgery. In the literature, there are publications stating blood loss is 208.1 ± 164.4 ml in open total gastrectomy and 85.8 ± 117.9 ml in laparoscopic total gastrectomy [20]. In our study, blood loss has found statistically higher in Group 1.

The rate of conversion from laparoscopic gastrectomy is between 3-10% in the literature. The most common causes are advanced disease, hemorrhage, and technical difficulties in the formation of esophagojejunostomy anastomosis [18,21]. In our study, only one patient had a conversion to open surgery due to severe adhesions and this patient was included in the open surgery group.

Many meta-analyses show a faster return to full oral diet after laparoscopic surgery. In the literature, this period varies between 3.4-6 days in the laparoscopic gastrectomy cases and 4.7-8 days in open gastrectomy cases [19,22,23]. In our study, the mean duration of onset of oral intake was similar in both groups.

The literature indicates that laparoscopic gastrectomy provides shorter hospital stay (9-14 days) than open gastrectomy [13,24,25]. In our study, in contrast to the literature, the length of hospital stay was found significantly higher in the laparoscopy group due to esophagojejunal anastomotic leakage occurred one patient (LoHS: 40 days) which needed to treat with an esophageal stent.

Many studies pointed out that the number of laparoscopic harvested lymph nodes in early-stage cancer is similar to open surgery [18,26,27]. In our study, the mean number of lymph nodes harvested in both groups was over 30. The fact that these numbers are above the number of lymph nodes required for adequate staging shows that laparoscopic D2 dissection can be performed safely. In addition, in our study there is no statistical difference was found between the two groups in terms of pathological stage, tumor grade and mean survival time.

In the literature, mortality rates in gastric cancer surgery are 3-11% in the open technique and 2-4.6% in laparoscopy [28-30]. In our series, despite high ASA scores and high BMI rates in the laparoscopic group, mortality did not develop in Group 2. However, during the follow-up, mortality occurred in 10 patients in Group 1. Six of the patients died due to operative complications. The other 4 patients died during the follow-up period due to disease.

Conclusion

In our study, laparoscopic radical total gastrectomy group was associated with a long operation time but less blood loss. Fewer of the general advantages of laparoscopy of shorter hospitalizations and early onset of oral feeding was not observed in our series. On the other hand, similar number of harvested lymph nodes and similar surveillance rates in both groups showed that laparoscopic total gastrectomy can be performed safely with similar oncological outcomes. In our study, the small number of patients in the laparoscopy group is the most important limiting factor. Therefore, the results of our study should be evaluated with prospective randomized controlled studies in larger patient groups.

Riassunto

Lo scopo di questo studio è di confrontare l'efficacia oncologica della gastrectomia totale laparoscopica (LTG) rispetto alla gastrectomia totale ad addome aperto (OTG) per il cancro gastrico e di fornire le nostre esperienze in merito a questo intervento chirurgico.

Sono stati inclusi in questo studio un totale di 107 pazienti sottoposti a gastrectomia curativa totale per adenocarcinoma gastrico tra settembre 2015 e settembre 2018, e ne sono state valutate le caratteristiche demografiche, i tempi operatori, i risultati istopatologici, la morbilità postoperatoria e i risultati di mortalità dei pazienti.

Risultati: Di 107 pazienti, 70 erano uomini e 37 donne. La chirurgia ad addome aperto ha riguardato 89 pazienti e quella laparoscopica 18 pazienti. Età media in OTG 59,4 anni; età media in LTG 57,3 anni. Il numero medio di linfonodi raccolti è stato di 30,5 ± 14,6 in OTG e 33,0 ± 10,1 in LTG. Il numero di linfonodi metastatici raccolti è stato 7,4 ± 10,5 in OTG e 10,0 ± 11,8 in LTG (p = 0,366) senza alcuna differenza statistica tra i due gruppi. Il tempo di ripresa dell'alimentazione orale, e l'incidenza di deiscenza anastomotica e di mortalità postoperatoria è risultata simile in entrambi i gruppi. La durata dell'intervento e la durata della degenza ospedaliera sono risultate significativamente più elevate nella LTG. La durata della sopravvivenza postoperatoria è stata simile in entrambe le procedure.

Conclusione: la gastrectomia totale laparoscopica per carcinoma gastrico è una procedura oncologicamente sicura ma ha avuto un tempo di intervento più lungo e una degenza ospedaliera più lunga. Non è risultata alcuna differenza significativa nel numero di linfonodi raccolti, numero di linfonodi metastatici e localizzazione del tumore tra i due gruppi

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