The impact of modifying the laparoscopic lymphadenectomy technique on the extent of lymphadenectomy in laparoscopically operated gastric cancer patients. A single-center study.

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Abstract

Background. When we introduced laparoscopic surgery for gastric cancer at our center, we felt that the lymphadenectomy was insufficient for implementation of laparoscopic surgery in locally advanced gastric cancer patients. In order to refine our method, we modified our technique. We analyzed the results of the modified technique to determine whether laparoscopic gastrectomies could potentially be applied in locally advanced gastric cancer.

Methods. From 2015 onward, 23 patients were laparoscopically operated on for gastric cancer. Patients were divided into two groups depending on the method of laparoscopic lymphadenectomy. Seven patients were included in the first period (P1). In the second period (P2), the lymphadenectomy technique was modified. Sixteen patients were included in P2.

Results. The number of lymph nodes extracted was significantly higher in P2 (11.8 ± 8.3 lymph nodes in P1 vs. 22.9 ± 10.6 lymph nodes in P2; $p = 0.036$). The duration of the operation and the duration of the hospitalization were similar in both periods. The complication rate rose significantly in P2 ($p = 0.027$). The TNM distribution also changed significantly in P2 ($p = 0.049$). Whereas most of the operated patients in P1 had either GIST (28.6%) or pT1a adenocarcinoma (28.6%), most patients in P2 had pT3 adenocarcinoma (43.8%).

Conclusion. Although the observation time is too short for evaluation of long-term results, we believe that in the case of early and locally advanced gastric cancer laparoscopic gastrectomy is a viable alternative in selected patients and in the hands of experienced surgeons.

Introduction

The introduction of laparoscopy in recent years has shown many potential benefits such as faster postoperative recovery, shorter hospital stay, better cosmesis, and better quality of life [1–3]. Many centers would like to translate these benefits to gastric cancer patients. Despite growing experience, laparoscopy has only slowly been implemented for gastric cancer treatment [1–11]. The introduction of laparoscopy in treating gastric cancer patients has encountered some obstacles. The reconstruction of an esophago-jejunostomy is very demanding and can be performed safely only by surgeons skilled in laparoscopy [12]. Even more so, a D2 lymphadenectomy is extremely challenging. Therefore, laparoscopic gastrectomies were first introduced for distal early gastric cancer, in which less challenging gastro-jejunostomy and less extensive lymphadenectomy removing only perigastric lymph nodes are performed [1]. It rapidly gained popularity, especially in Asian centers, where randomized controlled studies clearly confirmed benefits for laparoscopic distal subtotal gastrectomies compared to open surgery. Consequently, laparoscopic distal subtotal gastrectomy is now acknowledged as standard care in Japanese guidelines [3, 13]. The cornerstone of therapy for locally advanced gastric cancer, however, is extensive lymphadenectomy that eradicates all potential metastatic lymph nodes. Therefore, a D2 lymphadenectomy for all stages of gastric cancer except for early gastric cancer is recommended in gastric cancer guidelines [13]. Extensive laparoscopic D2 lymphadenectomy presents a considerable challenge to date even for experienced laparoscopists [6, 9].

Laparoscopic gastrectomies were introduced at our center in 2015. Similar to other centers, this technique was at first reserved for patients with early distal gastric cancer. The lymphadenectomy of stations 4sb, 5, and 2a in particular has been insufficiently performed. Dissatisfied with the extent of the lymph node (LN) clearance, we were reluctant to implement laparoscopic surgery for locally advanced gastric cancer patients. In order to refine our method, we modified our technique as proposed by Huang et al. [14]. This article reports our results using the modified technique to determine whether laparoscopic gastrectomies could potentially be applied in locally advanced gastric cancer.

Methods

Patients

Since 2015, 23 patients have been laparoscopically operated on for gastric cancer. These patients were included in our study. All patients had histologically verified adenocarcinoma of the stomach or a gastrointestinal stromal tumor of the stomach. The preoperative workup included upper gastrointestinal endoscopy, abdominal ultrasound, chest X-ray, endoscopic ultrasound for early lesions (T1a = tumor involving the lamina mucosa, T1b = tumor involving the lamina submucosa), abdominal CT for locally advanced gastric cancer (T2 or higher = tumor infiltrating beyond lamina muscularis propriae), chest CT for tumors infiltrating the upper third of the stomach, or suspicion of mediastinal or pulmonary metastases.

Patients were discussed at a multidisciplinary board meeting, where the decision was made whether patients should receive preoperative chemotherapy or not. Patients without contraindications for laparoscopy were considered for laparoscopic resection. Patients with tumors infiltrating other organs, extensive retroperitoneal lymphadenopathy, or morbidly obese patients were considered unfit for laparoscopic resection. All laparoscopic operations were carried out by the same surgeon (TJ), who is experienced in laparoscopy for gastric cancer. All patients gave their informed consent before the operation. Patients were divided into two groups depending on the method of the laparoscopic lymphadenectomy. In the first period (P1), lymphadenectomy was performed similarly as in open surgery. Seven patients were included in P1. In the second period (P2), the lymphadenectomy technique was modified. Sixteen patients were included in P2.

The tumor stages, locations, duration of the procedure, number of LNs extracted, BMI, time to first stool passage, and duration of intravenous analgesic treatment were noted. All data were stored prospectively in a hospital database. The patients gave their written consent. The study was approved by the local ethics committee.

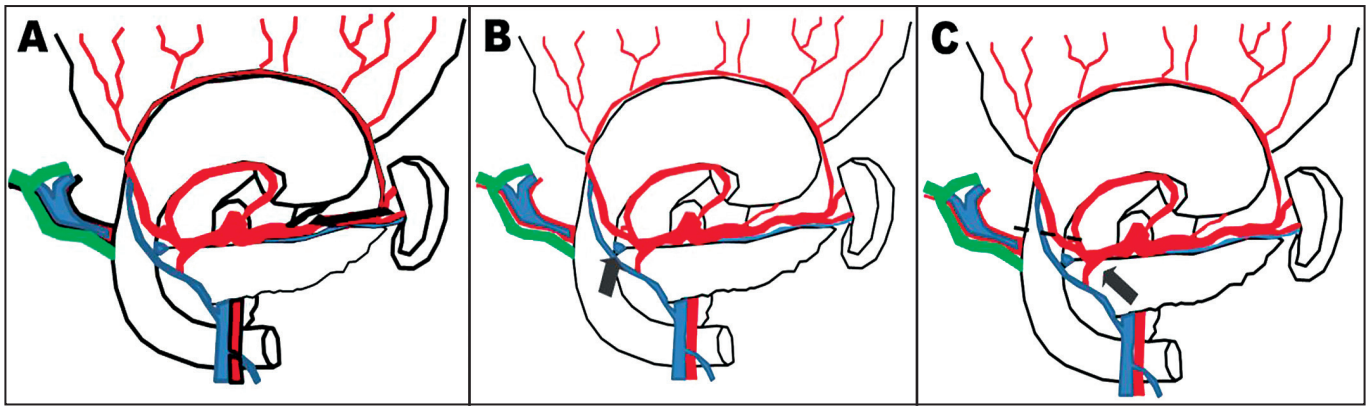

Figure 1. Surgical steps of the modified laparoscopic lymphadenectomy. A) The lymphadenectomy starts on the left with dissection of the left gastroepiploic artery. The surgeon follows the splenic vein toward the splenic hilum and dissects the left gastroepiploic vein and artery at their origin. This is the starting point for the lymphadenectomy of the distal part of the splenic artery. B) The dissection moves toward the right. Over the head of the pancreas, the distal part of the gastroduodenal artery, right gastroepiploic artery, and vein are dissected. C) After duodenal transection, traction is exerted on the hepatogastric ligament over the right gastric artery.

Surgical technique for laparoscopic lymphadenectomy

Since 2015, 23 patients have been laparoscopically operated on for gastric cancer. Patients with tumors in the distal third of the stomach or well-differentiated tumor histology underwent a distal subtotal gastrectomy providing that sufficient macroscopic margins could be obtained (6–8 cm). Patients with tumors located in the middle third received a total gastrectomy. A side-to-side anastomosis using an Endo GIA 60 mm linear stapler was performed for reconstruction after distal subtotal gastrectomy. The opening was closed with a continuous 3-0 vicryl suture. Reconstruction after total gastrectomy was a side-to-side anastomosis, using Endo GIA linear stapler anastomosis. The opening was closed with a continuous 3.0 vicryl suture. In two patients, the surgeon was not satisfied with the esophago-jejunal anastomosis, and therefore laparoscopically assisted circular 25 mm stapled anastomosis was performed through a small midline incision. In one patient a proximal subtotal gastrectomy was performed. The reconstruction was performed using a transorally inserted anvil with an OrVil circular stapler. In this case, an esophago-gastrostomy was fashioned.

In the first seven cases, lymphadenectomy was performed in a similar fashion as in open surgery. Usually a monopolar hook was used for the LN dissection. The dissection started with the dissection of the hepatoduodenal ligament. After the clearance of the LN on the anterior side of the proper hepatic artery, the origin of the right gastric artery was dissected. Once the origin of the right gastroepiploic artery was dissected, the duodenum was transected and the lymphadenectomy was carried out toward the coeliac axis. The left gastric vein and artery were clipped and transected. The final stages were the dissection of the left gastroepiploic artery and short gastric arteries.

The modified technique was carried out as suggested by Huang et al. [14] in 16 patients. The dissection began in reverse order starting with the opening of the gastrocolic ligament and the mobilization of the splenic flexure of the colon. The left gastroepiploic artery was dissected at the origin of the distal splenic artery. The dissection continued toward the greater curvature with the clipping of the short gastric arteries. The next step was the dissection of the distal part of the splenic artery continuing toward the tripus coeliacus. Moving toward the right, the distal part of the gastroduodenal artery was dissected and followed toward the origin of the right gastroepiploic artery and vein. The dissection was continued above the gastroduodenal artery, exposing the distal part of the common hepatic artery, the proper hepatic artery, and the right gastric artery retroduodenally. Afterward, the duodenum was transected. Pulling

the preserved right gastric artery, traction was exerted on the hepatoduodenal ligament, allowing safer and more precise dissection of the hepatoduodenal ligament. Before the dissection of the posterior LN around the portal vein, the right gastric artery was clipped. Finally, the common hepatic artery was dissected and clipping of the left gastric artery and vein was performed. The sequence of the steps is depicted in Figure 1.

Statistical analysis

Continuous data are expressed as means ± SD and median ± IQR, and categorical variables are given as percentages. The Shapiro–Wilk test was used to determine whether the continuous data were normally distributed. Comparisons of continuous variables were carried out with Student's t-test for parametric data and the Mann–Whitney U test for nonparametric data. A chi-square test was used for comparisons of discrete variables. SPSS version 20 for Windows 10 and Microsoft Excel 2010 for Windows were used for the statistical analysis.

Results

Clinicopathological characteristics

The clinicopathological characteristics are presented in Table 1. The patients operated on laparoscopically had a mean age of 67.9 ± 10.6 years, 47.8% were male, and 52.2% were female. Most of the patients had minor comorbidity, and 21.7% of them had more than one accompanying disease. The BMI was above normal in most of the operated patients, and the average BMI was 24.8 ± 3.8 kg/m^2. Most of the patients had a pT3 tumor (30.4%), followed by pT1b (21.7%). The average number of LNs extracted per operation was 19.7 ± 11.1. The majority of the patients had a pN0 disease (65.2%). The average hospital stay was 15.8 ± 18.1 days.

Comparison of two periods of laparoscopic lymphadenectomy

Of the 23 laparoscopic patients, seven were operated on in P1 and 16 in P2. The characteristics of the patients from both periods are presented in Table 2. Patients were comparable with regard to

Table 1. Clinicopathological characteristics of laparoscopic patients for gastric cancer. LN = lymph node.

Variable	Value
Age	67.9 ± 10.6 years
Sex	
Male	47.8%
Female	52.2%
BMI (kg/m^2)	24.8 ± 3.8
Days to passage of stool	3.6 ± 1
Days of intravenous analgesics	4.5 ± 1
ASA (n, %)	
I	6 (26.6%)
II	10 (47.6%)
III	5 (23.8%)
T stage (n, %)	
Benign	3 (13%)
T1a	5 (21.7%)
T1b	3 (13%)
T2	3 (13%)
T3	7 (30.4%)
T4a	2 (8.7%)
N stage (n, %)	
N0	15 (65.2%)
N1	2 (8.7%)
N2	4 (17.4%)
N3	2 (8.6%)
Number of harvested LNs	19.7 ± 11.1
Number of positive LNs	2 ± 4
Hospital stay (days)	15.8 ± 18

Table 2. Comparison of patients operated on before and after modification of laparoscopic lymphadenectomy. P1 = first period, P2 = second period, NS = non-significant, LN = lymph node.

Variable	P1	P2	p
Age (years)	69.3 ± 10.5	67.3 ± 11	NS
Sex (n, %)			
Male	2 (28.6%)	9 (56.2%)	NS
Female	5 (71.4%)	7 (43.8%)	
BMI (kg/m^2)	25.3 ± 5.6	24.4 ± 2.8	NS
Days to passage of stool	4 ± 1.2	3.4 ± 0.9	NS
Days of intravenous analgesics	4.6 ± 0.9	4.4 ± 1.5	NS
ASA (n, %)			
I	1 (14.3%)	5 (35.7%)	NS
II	4 (57.1%)	6 (42.9%)	
III	2 (28.6%)	3 (21.4%)	
T stage (n, %)			
Benign	2 (28.6%)	1 (6.2%)	
T1a	2 (28.6%)	3 (18.8%)	
T1b	0 (0%)	3 (18.8%)	p = 0.049
T2	2 (28.6%)	1 (6.2%)	
T3	0 (0%)	7 (43.8%)	
T4a	1 (14.3%)	1 (6.2%)	
N stage (n, %)			
N0	6 (85.7%)	9 (56.2%)	
N1	0 (0%)	2 (12.5%)	NS
N2	1 (14.3%)	3 (18.8%)	
N3	0 (0%)	2 (12.5%)	
Number of harvested LNs	11.8 ± 8.4	22.9 ± 10.6	p = 0.027
Number of positive LNs	0.6 ± 1.5	2.7 ± 4.7	NS
Hospital stay (days)	10.7 ± 6.2	18.2 ± 21.4	NS
30-day mortality (n, %)	0 (0%)	0 (0%)	NS
Complications (n, %)			
No	5 (71.4%)	10 (62.5%)	NS
Yes	2 (28.6%)	6 (37.5%)	

age, comorbidities, sex, and BMI in both periods. The number of LNs extracted, however, was significantly higher in P2 (p = 0.036). The number of LNs extracted was 11.8 ± 8.3 in P1, compared to 22.9 ± 10.6 in P2. Even though the lymphadenectomy was more extensive, the duration of the operation and the duration of the hospitalization were similar in both periods. However, there were more complications in P2 (p = 0.027). The TNM distribution also changed significantly in P2 (p = 0.049). Whereas most of the operated patients in P1 had either a gastrointestinal stromal tumor (28.6%) or pT1a adenocarcinoma (28.6%), most patients in P2 had pT3 adenocarcinoma (43.8%).

Discussion

Laparoscopic gastrectomy was introduced in 1991 by Kitano et al. [11], but the technically demanding nature of esophago-jejunal reconstruction and especially laparoscopic lymphadenectomy have stood in the way of wider use of laparoscopy for gastric cancer patients. Laparoscopic gastrectomy is mainly performed at high-volume centers by experienced surgeons, where the first results have shown that this operation confers many functional advantages compared to open surgery [1–11]. Many surgeons are still struggling with laparoscopic D2 lymphadenectomies. They therefore settle for a less extensive lymphadenectomy and for patients with early gastric cancer in whom a more conservative surgical approach can be taken. However, the undoubtedly better functional results should not outweigh the importance of precise lymphadenectomy. Although a modified lymphadenectomy suffices for early gastric cancer, patients with advanced gastric cancer can only be cured with a D2 lymphadenectomy.

When we introduced laparoscopy for gastric cancer at our center in 2015, we had doubts about the adequacy of the laparoscopic lymphadenectomy. Hence, we only used this approach for early gastric cancer patients. In our opinion, especially the dissection of the hepatoduodenal ligament, the common hepatic artery, and the left gastroepiploic artery were insufficient to safely use laparoscopy for locally advanced gastric cancer patients. To improve the lymphadenectomy, we adopted a technique for laparoscopic lymphadenectomy that was advocated by Huang et al. [14] and has been used in many centers across Asia [6, 9, 14]. In this article we evaluated whether this modification of laparoscopic lymphadenectomy has yielded the desired improvement in lymphadenectomy quality.

The patients selected for laparoscopy were not subjected to any selection; therefore they had the same clinical and pathological characteristics as patients operated on with open surgery. We consider this an advantage of our study because, with this selection bias eliminated, the results have a greater weight. The patients in our study are therefore characteristically similar to patients operated on with open surgery. Even so, the duration of hospitalization and the duration of the operation were found to be comparable to other centers performing laparoscopic and open surgery [1–11]. Our experience was that patients recovered extremely well after laparoscopic gastrectomies and were satisfied with the functional results.

The main question of our analysis was whether the lymphadenectomy could be made more efficient by modification of the laparoscopic technique. Therefore, we compared the number of LNs extracted before and after the modification of lymphadenectomy. The results confirmed that the average number of lymph nodes extracted was significantly higher after the modification of the technique. Moreover, the average number of LNs extracted was similar to the number defined by the seventh TNM classification as D2 lymphadenectomy [15]. Regardless of the number of the LNs extracted per operation, an even more important factor of lymphadenectomy quality is the anatomical completeness of the LN station removal defined as D2 lymphadenectomy in the revised Japanese classification [13]. During the operation, the clearance of each LN station was video documented, which was clearly mirrored by the more efficient LN yield. We successfully extracted all LN stations defined as the D2 lymphadenectomy.

The better lymphadenectomy quality in P2 did not prolong the operation times compared to P1. This is a testimony to the proficiency of the modified technique, which uses the ability of laparoscopy to work in confined spaces and magnification to its advantage. The more aggressive LN dissection, however, resulted in a moderate rise in the morbidity rates in P2. Although the mortality was similar in both periods, the rise in morbidity is surely attributed to the learning curve phenomenon. With more operations we will become more skilled

and the rate of complications will eventually be similar to open surgery.

The main drawback of this study is the small number of patients included and the non-randomized nature of the study. Although we agree that the small number of patients is insufficient to allow a definite evaluation of the modified laparoscopic lymphadenectomy technique, it clearly shows an improvement of the laparoscopic gastrectomy technique that can be achieved even at a less experienced center. Although the observation time is too short to evaluate the long-term results, we believe that for early and locally advanced gastric cancer laparoscopic gastrectomy could be a viable alternative in selected patients and in the hands of experienced surgeons.

References

1. Haverkamp L, Weijs TJ, van der Sluis PC, et al. Laparoscopic total gastrectomy versus open total gastrectomy for cancer: a systemic review and meta-analysis. Surg Endosc. 2013; 27: 2661–1.
2. Shim JH, Oh SI, Yoo HM, et al. Short-term outcomes of laparoscopic versus open total gastrectomy: a case matched-cohort study. Am J Surg. 2013; 206: 346–51.
3. Kodera Y, Yoshida K, Kumamaru H, et al. Introducing laparoscopic total gastrectomy for gastric cancer in general practice: a retrospective cohort study based on a nationwide registry database in Japan. Gastric Cancer. 2018; doi: 10.1007/s10120-018-0795-0. [Epub ahead of print]
4. Best LMJ, Mughal M, Gurusamy KS. Laparoscopic versus open gastrectomy for gastric cancer. Cochrane Database Syst Rev. 2016; 3:CD011389.
5. Haverkamp L, Ruurda JP, Offerhaus GJ, et al. Laparoscopic gastrectomy in western European patients with advanced gastric cancer. Eur J Surg Oncol. 2016; 42: 110–5.
6. Park YK, Yoon HM, Kim YW, et al. Laparoscopy-assisted versus open D2 distal gastrectomy for advanced gastric cancer. Ann Surg. 2017; 20: 1–8.
7. Kelly KJ, Selby L, Chou JF, et al. Laparoscopic versus open gastrectomy for gastric adenocarcinoma in the west: a case-control study. Ann Surg Oncol. 2015; 22: 3590–6.
8. Son T, Hyung WJ. Laparoscopic gastric cancer surgery: current evidence and future perspectives. World J Gastroenterol. 2016; 22: 727–35.
9. Wang W, Li Z, Tang J, et al. Laparoscopic versus open total gastrectomy with D2 dissection for gastric cancer: a meta-analysis. J Cancer Res Clin Oncol. 2013; 139: 1721–34.
10. Son T, Kwon IG, Hyung WJ. Minimally invasive surgery for gastric cancer treatment: current status and future perspectives. Gut Liver. 2014; 8: 229–36.
11. Straatman J, van der Wielen N, Cuesta MA, et al. Minimally invasive versus open total gastrectomy for gastric cancer: a systematic review and meta-analysis of short-term outcomes and completeness of resection. World J Surg. 2015: 1–10.
12. Inokuchi M, Otsuki S, Fujimori Y, et al. Systematic review of anastomotic complications of esophagojejunostomy after laparoscopic total gastrectomy. World J Gastroenterol. 2015; 21: 9656–65.
13. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2010 (ver. 3). Gastric Cancer; 2011; 14: 113–23.
14. Huang CM, Chen QY, Lin JX, et al. Huang's three-step maneuver for laparoscopic spleen-preserving no. 10 lymph node dissection for advanced proximal gastric cancer. Chin J Cancer Res; 2014; 26: 208–10.
15. Wittekind C, Oberschmid B: [TNM classification of malignant tumors 2010: general aspects and amendments in the general section]. Pathologe. 2010; 31: 333–4, 336–8.