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Laparoscopic Total Gastrectomy in Elderly Patients (≥70 Years) with Gastric Carcinoma: A Retrospective Study

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Purpose: To compare the surgical outcomes of laparoscopic total gastrectomy between elderly and non-elderly patients.
Materials and Methods: Between 2008 and 2015, a total of 273 patients undergoing laparoscopic total gastrectomy for gastric carcinoma were divided into two age groups: elderly (≥70 years, n=71) vs. non-elderly (<70 years, n=172). Postoperative outcomes, including length of hospital stay, morbidity, and mortality were compared between the groups.
Results: The elderly group showed a significantly higher rate of comorbidities and American Society of Anesthesiologists scores than those in the non-elderly group. No significant differences were found with respect to lymphadenectomy or combined organ resection between the groups. After surgery, the elderly group showed a significantly higher incidence of grade III and above complications than the non-elderly group (15.5% vs. 4.1%, P=0.003). Among the complications, anastomosis leakage was significantly more common in the elderly group (9.9% vs. 2.9%, P=0.044). Univariate and multivariate analyses showed that old age (≥70 years) was an independent risk factor (odds ratio=4.42, 95% confidence interval=1.50~13.01) for postoperative complications of grade III and above.
Conclusions: Elderly patients are more vulnerable to grade III and above complications after laparoscopic total gastrectomy than non-elderly patients. Great care should be taken to prevent and monitor the development of anastomosis leakage in elderly patients after laparoscopic total gastrectomy.

Key Words: Stomach neoplasms; Laparoscopy; Gastrectomy; Aged

Introduction

Despite its decreasing global incidence, gastric carcinoma is the second most common malignancy after thyroid cancer and the third leading cause of cancer-related death in Korea.[1] As life expectancy increases, surgeons now have more opportunities to treat elderly patients with gastric cancer. Making an appropriate surgical decision for elderly patients is not always easy because of concerns related to the increased operative risks due to common underlying comorbidities and low functional physiological reserves.[2] An optimal treatment decision in the elderly in terms of the operative approach or extent of surgery should be cautiously made to balance safety and curative impact.

With several clinical advantages over open surgery, laparoscopic surgery is becoming a standard treatment for early gastric carcinoma in Asian countries.[3,4] Some studies have suggested that laparoscopic gastrectomy is a suitable choice for elderly gastric cancer patients as it has shown acceptable surgical outcomes, comparable to those in non-elderly patients.[5-7] Unlike laparoscopic distal gastrectomy, laparoscopic total gastrectomy (LTG) is a technically demanding surgical procedure with a substantial risk of postoperative complications in the elderly. However, only a few studies have evaluated the outcomes of LTG in elderly patients with gastric carcinoma.[8-10] A better understanding of

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these operative risks may help in determining a proper treatment plan for elderly patients with gastric carcinoma. In the present study, we investigated the impact of old age on the surgical outcomes of LTG and determined which complications occur in the elderly after LTG.

Materials and Methods

1. Patients

Between 2008 and 2015, a total of 243 patients who underwent LTG for gastric carcinoma were enrolled in this study. Patients who underwent LTG for other malignant diseases or major organ resection with combined malignancies were not included. Patients were divided into two age groups: elderly (≥70 years) vs. non-elderly (<70 years), and short-term surgical outcomes were compared between the groups.

All patients underwent gastric resection and regional lymph node dissection (LND) as described by the 2010 Japanese gastric cancer treatment guidelines.[11] After surgery, patients were managed with standardized clinical protocols. Briefly, no preoperative fasting or bowel preparation was performed. Nasogastric tube and abdominal drain placement were not routinely performed. Intravenous or epidural anesthesia was used for postoperative pain control. Patients started an oral diet on postoperative day (POD) 1 or 2. Patients were discharged on POD 6 to 8 based on predefined discharge criteria: no laboratory or clinical evidence of complications, ability to fully ambulate without assistance, tolerable pain with no or only oral analgesics, and ability to tolerate an oral diet without significant gastrointestinal discomfort.

Patient data, including demographic features, pathologic findings, operative results, hospital courses, and postoperative outcomes were prospectively recorded in our electronic gastric cancer database. Demographic data included age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, comorbidities, history of abdominal surgery, and preoperative laboratory data. Pathologic findings included tumor size, tumor location, Tumor Node Metastasis (TNM) stage, and differentiation. Operative results included the extent of lymphadenectomy, combined resection, type of esophagojejunostomy, operation time, intraoperative blood loss, and number of harvested lymph nodes. Postoperative outcomes included length of hospital stay, first flatus time, diet start time, morbidity, mortality, reoperation, and readmission. Morbidity and mortality were defined as complications or death within 30 days after surgery or during hospitalization, and the severity of complications was graded based on the Clavien-Dindo Classification of Surgical Complications.[12] TNM stages were based on the seventh edition of the Union for International Center Control/American Joint Committee on Cancer Classification System.[13,14]

2. Operative techniques

All operations were performed by four surgeons. Details of the operative techniques have been fully described in our previous report.[9] Briefly, the patient was placed in the semi-upright position with the legs apart. The operator performed the operation standing at the right side of the patient. Usually, five abdominal trocars were used, which consisted of two right side operator ports, two left side assistant ports, and one umbilical laparoscopy port. The liver was retracted using a simple suture technique or an additional epigastric 5-mm port. Esophagojejunostomy reconstruction was performed via either extracorporeal or intracorporeal technique, as appropriate. For the extracorporeal technique, a 6 to 7-cm mini-laparotomy was made at the epigastrium, and a 25-mm circular stapler was usually used. For intracorporeal anastomosis, side-to-side esophagojejunostomy was performed using linear staplers.

3. Statistical methods

All statistical data were analyzed using IBM SPSS software, ver. 21.0 (IBM Co., Armonk, NY, USA). Student's t-test was used to compare continuous variables, and the chi-square test or Fisher's exact test was used for categorical variables as appropriate. A logistic regression model was used for univariate and multivariate analyses of the risk factors for complications. A P-value of <0.05 was considered statistically significant.

Results

1. Clinicopathological characteristics

Table 1 shows the clinicopathological characteristics of the two age groups. The mean age of the elderly group was 73.9±2.8 years, with 48 men and 23 women. Among them, 47 (66.2%) had underlying comorbidities, and 13 (18.3%) had a history of abdominal surgery. The mean BMI was 23.2±3.4 kg/m^2. Fifteen patients (21.1%) had preoperative anemia, and one (1.4%) had hypoalbuminemia. The elderly group showed a significantly higher rate of comorbidities (66.2% vs. 51.2%, P=0.031) and

Table 1. Clinicopathological characteristics

Characteristic	Elderly (n=71)	Non-elderly (n=172)	P-value
Age (yr)	73.9±2.8	56.8±8.8	<0.001
Sex (male)	48 (67.6)	112 (65.1)	0.710
BMI (kg/m^2)	23.2±3.4	23.8±3.1	0.239
ASA score			<0.001
1	4 (5.6)	73 (42.4)	
2	62 (87.3)	95 (55.2)	
3	5 (7.0)	4 (2.3)	
Comorbidity	47 (66.2)	88 (51.2)	0.031
Cardiovascular	39 (54.9)	58 (33.7)	0.002
Endocrine	13 (18.3)	29 (16.9)	0.786
Pulmonary	13 (18.3)	21 (12.2)	0.213
Hepatobiliary	3 (4.2)	11 (6.4)	0.763
Cerobrovascular	0	6 (3.5)	0.185
Renal	2 (2.8)	1 (0.6)	0.205
Others	1 (1.4)	1 (0.6)	0.500
Abdominal operation history	13 (18.3)	23 (13.4)	0.427
Anemia*	15 (21.1)	31 (18.0)	0.592
Hypoalbuminemia†	1 (1.4)	2 (1.2)	1.000
Tumor size (mm)	29±16	30±18	0.853
Tumor location			0.765
Upper third	59 (83.1)	133 (77.3)	
Middle third	9 (12.7)	32 (18.6)	
Lower third	2 (2.8)	4 (2.3)	
Whole stomach	1 (1.4)	3 (1.7)	
Differentiation			0.005
Differentiated	47 (66.2)	78 (45.3)	
Undifferentiated	24 (33.8)	94 (54.7)	
Tumor invasion‡			0.670
1	59 (83.1)	131 (76.2)	
2	7 (9.9)	23 (13.4)	
3	4 (5.6)	11 (6.4)	
4	1 (1.4)	7 (4.1)	
Nodal metastasis‡			0.745
0	65 (91.5)	153 (89.0)	
1	2 (2.8)	10 (5.8)	
2	2 (2.8)	6 (3.5)	
3	2 (2.8)	3 (1.7)	
TNM stage‡			0.690
I	63 (88.7)	145 (84.3)	
II	6 (8.5)	20 (11.6)	
III	2 (2.8)	7 (4.1)	

Values are presented as mean±standard deviation or number (%). BMI = body mass index; ASA = American Society of Anesthesiologists; TNM = Tumor Node Metastasis. *A serum hemoglobin level of <12 g/dl for females and <13 g/dl for males. †A serum albumin level of <3.5 g/dl. ‡The TNM stages are based on the seventh edition of the Union for International Center Control/American Joint Committee on Cancer classification system.

ASA scores (ASA ≥2, 94.3% vs. 57.5%, P<0.001) than the non-elderly group, whereas sex, BMI, history of abdominal surgery, preoperative anemia, and hypoalbuminemia were similar in the two groups. Sixty-three (88.7%) patients had stage I, six (8.5%) had stage II, and two (2.8%) had stage III tumors in the elderly group, and there was no significant differences in TNM stages between the two groups.

2. Short-term surgical outcomes

In the elderly group, 12 patients (16.9%) underwent D2 LND, and eight patients (11.3%) underwent combined organ resection. The mean operation time was 287±89 minutes, and the mean intraoperative blood loss was 178±176 ml. Compared with the non-elderly group, there were no significant differences in the types of esophagojejunostomy, operation time, operative blood loss, and the number of harvested lymph nodes between the two groups (Table 2).

After surgery, there were no significant differences in overall morbidity between the elderly (23.9%) and non-elderly (16.3%) groups (P=0.203). However, complications of grade III and above severity were significantly more common in the elderly group (15.5% vs. 4.1%, P=0.003). Two patients (2.8%) died in the elderly, and none died in the non-elderly group (P=0.085). The causes of death were anastomosis leakage in one patient and aspiration pneumonia in the other. Among the postoperative complications, anastomosis leakage was significantly more common in the elderly group (9.9% vs. 2.9%, P=0.044), whereas the incidences of other complications were similar between the groups (Table 3, 4).

3. Analysis of the risk factors for complications

Table 5 shows the results of univariate and multivariate analyses of the risk factors for complications of grade III and

Table 2. Operative outcomes

Variable	Elderly (n=71)	Non-elderly (n=172)	P-value
Lymphadenectomy*			0.905
Less than D2	59 (83.1)	144 (83.7)	
D2	12 (16.9)	28 (16.3)	
Combined resection	8 (11.3)	7 (4.1)	0.074
Gall bladder	6	5	
Spleen	2	2	
Operating time (min)	287±89	267±79	0.088
Type of esophagojejunostomy			1.000
Extracorporeal	70 (98.6)	168 (97.7)	
Intracorporeal	1 (1.4)	4 (2.3)	
Operative blood loss (ml)	178±176	181±216	0.930
No. of harvested lymph nodes	46.1±17.9	51.5±19.7	0.047
Morbidity	17 (23.9)	28 (16.3)	0.203
Systemic	5 (7.0)	4 (2.3)	0.127
Local	15 (21.1)	26 (15.1)	0.255
Mortality	2 (2.8)	0	0.085
Complication severity†			0.020
Grade I	2 (2.8)	6 (3.5)	
Grade II	4 (5.6)	14 (8.1)	
≥Grade III	11 (15.5)	7 (4.1)	
Hospital stay (d)	11.9±13.0	8.8±5.1	0.835

Values are presented as number (%) or mean±standard deviation.
*According to Japanese gastric cancer treatment guidelines 2010 (ver. 3).
†According to the Clavien-Dindo Classification of Surgical Complications.

Table 3. Postoperative complications

Variable	Overall (n=243)	Elderly (n=71)	Non-elderly (n=172)	P-value
Local complications				
Anastomosis site leakage	12 (2.7)	7 (9.9)	5 (2.9)	0.044
Intraluminal bleeding	13 (2.9)	5 (7.0)	8 (4.7)	0.532
Intra-abdominal abscess	7 (1.6)	2 (2.8)	5 (2.9)	1.000
Intraperitoneal bleeding	3 (0.7)	0	3 (1.7)	0.558
Ileus	3 (0.7)	0	3 (1.7)	0.558
Ascites	2 (0.4)	0	2 (1.2)	1.000
Pancreatitis	1 (0.2)	1 (1.4)	0	0.292
Systemic complications				
Pulmonary	7 (1.6)	4 (5.6)	3 (1.7)	0.119
Urinary	2 (0.4)	1 (1.4)	1 (0.6)	0.500

Values are presented as number (%).

Table 4. Postoperative complications of grade III* and above

Variable	Elderly (n=71)	Non-elderly (n=172)	P-value
Total	11 (15.5)	7 (4.1)	0.003
Anastomosis site leakage	7 (9.9)	3 (1.7)	0.008
Intraluminal bleeding	1 (1.4)	3 (1.7)	1.000
Intra-abdominal abscess	3 (4.2)	1 (0.6)	0.076

Values are presented as number (%). *According to the Clavien-Dindo Classification of Surgical Complications.

above severity. In univariate analysis, old age (≥70 years), male sex, the number of comorbidities, and operative blood loss were significantly associated with complications of grade III and above severity. Multivariate analysis showed that old age is an independent risk factor for grade III and higher complications (odds ratio [OR]=4.42, 95% confidence interval [CI]=1.50~13.01), along with male sex (OR=5.61, 95% CI=1.14~27.67) and operative blood loss.

Discussion

Elderly surgical patients are more likely to develop postoperative complications after major abdominal surgery due to common underlying comorbidities and low functional reserves.[2,15] However, the impact of old age on the outcomes of laparoscopic gastrectomy remains unclear. Some argue that laparoscopic gastrectomy does not increase operative risk in the elderly, and studies have shown comparable surgical outcomes between elderly and non-elderly patients.[5-7] However, most previous studies have evaluated the feasibility in elderly patients after laparoscopic distal gastrectomy. To the best of our knowledge, this is the first study to investigate surgical outcomes after LTG in elderly patients with gastric carcinoma. We found that old age (≥70 years) is an independent predictor of grade III and above complications after LTG. More specifically, anastomosis leakage was significantly more common in elderly patients after LTG.

Elderly patients often have a decreased functional reserve with common underlying comorbidities.[2] Thus, some surgeons have suggested performing less invasive surgery such as limited LND in elderly patients with gastric carcinoma for safety reasons.[16,17] However, some also argue that elderly patients can safely undergo standard surgery without increased operative risks, and that age alone should not be a determining factor in

Table 5. Univariate and multivariate analyses of the risk factors for grade III* and above complications

Variable	Univariate		Multivariate	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age (≥70 yr)	4.32 (1.60~11.67)	0.004	4.42 (1.50~13.01)	0.007
Sex (male)	4.50 (1.01~20.07)	0.049	5.61 (1.14~27.67)	0.034
BMI (≥25 kg/m^2)	1.21 (0.43~3.34)	0.721		
ASA score		0.190		
1	1			
2	3.96 (0.89~17.78)			
3	4.69 (0.38~57.61)			
No. of comorbidities		0.042		0.114
0	1		1	
1	0.66 (0.16~2.73)		0.47 (0.11~2.09)	0.322
2	2.98 (0.94~9.40)		2.33 (0.66~8.21)	0.187
3	5.67 (0.94~34.27)		3.34 (0.50~22.14)	0.212
Preoperative anemia	2.31 (0.82~6.53)	0.113		
TNM stage (I vs. II~III)†	0.33 (0.04~2.57)	0.290		
Abdominal operation history	1.72 (0.53~5.57)	0.363		
Lymphadenectomy (≥D2)	2.09 (0.70~6.23)	0.187		
Combined resection	0.89 (0.11~7.15)	0.910		
Operating time (h)		0.402		
<3	1			
3~4	2.20 (0.22~22.15)	0.505		
4~5	1.29 (0.13~12.87)	0.831		
5~6	3.96 (0.47~33.77)	0.208		
≥6	3.87 (0.41~36.66)	0.238		
Operative blood loss (ml)		0.052		0.055
<150	1		1	
150~250	4.19 (1.33~13.18)	0.014	4.22 (1.22~14.61)	0.023
250~350	4.67 (1.06~20.60)	0.042	5.95 (1.15~30.64)	0.033
≥350	1.51 (0.30~7.81)	0.626	1.26 (0.22~7.27)	0.799

OR = odds ratio; CI = confidence interval; BMI = body mass index; ASA = American Society of Anesthesiologists; TNM = Tumor Node Metastasis.
*According to the Clavien-Dindo Classification of Surgical Complications. †TNM stages are based on the seventh edition of the Union for International Center Control/American Joint Committee on Cancer classification system.

deciding the extent of surgery.[18] Although our study identified an increased operative risk in the elderly after LTG, this may not preclude elderly patients from undergoing laparoscopic surgery. Determining the correct choice between open and laparoscopic approaches in elderly patients may require further evaluation of surgical outcomes in elderly patients with upper gastric carcinoma. Considering the benefits of laparoscopic surgery, such as less postoperative pain, superior cosmetic results, rapid bowel recovery, and a better quality of life, elderly patients may benefit from laparoscopic gastrectomy over open surgery.[4,19-22]

Several studies have investigated the feasibility of laparoscopic gastrectomy in elderly patients. Kunisaki et al.[5] showed no significant difference in postoperative morbidity and mortality between the elderly and non-elderly groups after laparoscopy-assisted distal gastrectomy. However, Kim et al.[23] demonstrated significantly more major complications, such as anastomotic leakage or intraluminal bleeding, in the elderly group after laparoscopic distal gastrectomy. Two recent studies that included

LTG patients suggested that postoperative complications in elderly patients were similar to those of young patients.[24,25] Yet, since the numbers of patients with LTG were small in these studies, the outcomes of elderly patients after LTG were not fully investigated.

Anastomosis leakage is one of the most serious complications after LTG. In the present study, we found that old age is an important predictor for anastomosis leakage after LTG. Although there is no clear explanation for this, several factors may contribute to the increased rate of anastomosis leakage in the elderly, such as frequent malnutrition, delayed wound healing, or impaired intestinal blood supply. To minimize anastomosis-related complications, the proper choice of anastomosis technique is important, but currently there is no standard esophagojejunal anastomosis technique for LTG with proven optimal safety and technical feasibility. At the start of this study, extracorporeal anastomosis was performed in most patients. Intracorporeal anastomosis was performed in selected cases as surgeons accumulated experience during the later stage of the study. Intracorporeal anastomosis was usually performed for the patients for whom extracorporeal anastomosis was deemed to be difficult, such as the obese. Besides making a proper choice of anastomosis technique, identifying the risk factors for the development of anastomosis leakage is also important.[26] Great care should be taken to monitor the development of anastomosis leakage in the subset of patients at higher risk of anastomosis complications after LTG.

The present study has some limitations. First, as with other retrospective studies, the possibility of patient selection introducing bias was inherent. There is a possibility that the treatment decision could be biased according to patients' age and underlying conditions, which can affect surgical outcomes in elderly patients. Second, the number of elderly patients was relatively small. Because of the low incidence of upper gastric carcinoma in our region, a multicenter study with a larger patient database will be required to further determine the impact of old age on the surgical outcomes of LTG.

In conclusion, the present study showed that elderly patients (≥70 years) are more prone to developing grade III and above complications after LTG than non-elderly patients. Proper treatment decisions based on understanding the possible operative risks in the elderly should be discussed between the surgeon and the patient. Finally, great care should be taken to prevent and monitor the development of anastomosis leakage in elderly patients after LTG.

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Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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