Analysis of Postoperative Complications Following Laparoscopic Gastrectomy in 1332 Gastric Cancer Patients

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Purpose: To analyze postoperative complications for gastric cancer patients undergoing laparoscopic gastrectomy in single institution over long period of time.

Methods: The data of 1332 consecutive patients undergoing laparoscopic gastrectomy for gastric cancer at a single institution from January 2007 to December 2015 were reviewed. The patients were classified into the early or late surgery group; the initial 100 cases were classified as the initial group. We compared between the two groups and analyzed risk factors for postoperative complications.

Results: A total of 265 postoperative complications occurred in 223 patients (16.7%). Major complications occurred in 38 patients (2.9%) including 1 death (0.1%). Operative time and hospital stay were significantly shorter in the late group. Blood loss was greater in the initial group. Sex, comorbidity, tumor location, D2 LND, operative method, non B-I anastomosis, co-resection, long operative time, and blood loss were significant risk factors for overall postoperative complication. In the multivariate analysis, male sex, comorbidity, D2 lymph node dissection, total or proximal gastrectomy, non B-I anastomosis, co-resection, operative time and blood loss were associated with postoperative overall complications.

Conclusion: Sex, co-morbidity, D2 LND, operative method, co-resection, operative time and blood loss revealed as the risk factor of overall postoperative complication. And there was no significant differences of risk factor related to postoperative complication between initial and maturation surgical period. This suggests that beginners also can safely perform laparoscopic gastrectomy through the appropriate patient selection.

Keywords: Postoperative complication, Gastrectomy, Laparoscopy, Minimal invasive surgery, Gastric cancer

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INTRODUCTION

Since Kitano et al. first described laparoscopic distal gastrectomy,¹ several randomized controlled trials have validated

procedure as the accepted standard treatment for patients with early gastric cancer.²⁻⁵ The laparoscopic approach has been further refined over the past decade with improvements in surgical instrumentation and techniques. Numerous studies

are currently assessing the use of laparoscopic gastrectomy in patients with advanced gastric cancer and favorable outcomes have been reported in small-scale prospective and in several retrospective studies.⁵⁻⁷

Through accumulated surgical experience and extensive study, the laparoscopic gastrectomy procedure has become standardized and more familiar. However, this procedure may be technically challenging for inexperienced surgeons. A surgeon trained in a center with a large surgical volume and senior surgical instructors has a lower barrier to competency in laparoscopic surgery. In contrast, surgeons trained in centers with a low surgical volume with fewer and less experienced instructors may face some difficulties in learning proper laparoscopic techniques and accumulating the experiences.⁸ In particular, anastomotic complications may be a significant obstacle to safely performing laparoscopic gastrectomy or newer procedures because anastomotic complications are potentially fatal.

The incidence of postoperative complications can be used as a tool to evaluate “surgical quality”, but many previous studies have used different definitions for complications, making it difficult to compare the results because of a lack of objectivity.⁹⁻¹¹ The Clavien-Dindo classification of complications was established in 2004 as a more objective method to evaluate complications, and a significant number of studies have been conducted based on this classification. However, significant deviations in the frequency of complications are still observed in studies because of various factors. In this study, we aimed to analyze the risk factors for postoperative complications after laparoscopic gastrectomy using the Clavien-Dindo classification and to compare the incidence of postoperative complications in those undergoing surgery early in the study period with those undergoing surgery later in the study period.

MATERIALS AND METHODS

We enrolled 1332 patients who underwent laparoscopic gastrectomy for gastric cancer from January 2007 to December 2015 at Pusan National University Hospital. In all patients, preoperative endoscopic biopsy was performed to diagnose the cancer histologically and the stage and location of the tumor were evaluated by abdominal computed tomography and endoscopic ultrasonography. The indication for laparoscopic gastrectomy was limited to mucosal or submucosal invasion without lymph node metastasis (cT1a/T1bN0). Surgery was performed by three gastric surgeons who had experience in >100 open gastrectomies. The patients' medical records were prospectively collected. The 1332 enrolled patients were classified into early or late surgical groups; the initial 100 cases were classified as the initial group. (reached at August 2008)

We compared patient demographics, pathological data, and perioperative data between the two groups and analyzed the risk factors for postoperative complications. The Clavien-Dindo classification was used to analyze postoperative complications, and grade III or higher complications were defined as major complications¹² (Table 1). Delayed complication, which defines as occurrence after postoperative 30 days or readmission was also included in this study.

Surgical procedure

The operative method followed that used for conventional laparoscopic gastrectomy with lymph node dissection. A camera port for a 30-degree rigid scope was inserted through infra-umbilical incision. Two acting ports for the operator were inserted on the right side of each patient and 2 assistant ports were placed on the patient's left side. A 5 mm port for liver retraction was inserted in the epigastrium. The anastomosis for maintaining intestinal continuity was performed with a Billroth I, Billroth II, Roux-en-Y, or double-tract reconstruction. Roux-en-Y esophagojejunostomy was performed intracorporeally with a double-stapling method. Others anastomoses were performed extracorporeally through the 5 cm mini-laparotomy port in the epigastrium.

Table 1. Clavien-Dindo classification for the postoperative complication¹²

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IIIa	Intervention not under general anesthesia
Grade IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management
Grade IVa	Single organ dysfunction (including dialysis)
Grade IVb	Multiorgan dysfunction
Grade V	Death of a patient

*Brain hemorrhage, ischemic stroke, subarachnoidal bleeding, but excluding transient ischemic attacks. CNS = central nervous system; IC = intermediate care; ICU = intensive care unit.

Statistical analysis

All data were expressed as the mean $\pm$ the standard deviation. The chi-square test and student's *t*-test were used to compare categorical variables and continuous variables between groups, respectively. Multivariate analysis was performed using a logistic regression model to identify risk factors for postoperative complications. Two-tailed *p* values < 0.05 were considered statistically significant. Statistical analyses were performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Patient demographics

The mean age was 59.0 ± 11.1 years and body mass index was 23.5 ± 2.9 kg/m². A total of 831 (62.4%) patients were male and 501 (37.6%) patients were female. A total of 678 patients (50.9%) had a comorbidity. There were significant differences in age, body mass index, comorbidities, and American Society of Anesthesiologists (ASA) score. The patient demographics of the each study group are summarized in Table 2.

Pathologic data

The mean tumor size of all patients was 3.0 ± 1.9 cm and there was no significant difference in tumor size between the two groups (2.7 ± 2.0 cm vs. 3.0 ± 1.9 cm, *p* = 0.113). Tumors were most commonly located in the lower gastric region; however,

there was a tendency towards a higher incidence of upper gastric cancers in the late group. A total of 699 patients (52.5%) underwent a D2 lymph node dissection (LND), and a D2 LND was performed significantly less frequently in the late group. However, the number of harvested lymph nodes was greater in the late group compared with that seen in the initial group (35.9 ± 14.2 vs. 43.1 ± 17.8 , *p* < 0.001). Permanent pathological results confirmed early gastric cancer in most patients, and there were no differences in TNM stage between the two groups. The mean proximal and distal margin of all study patients were not shown the significant differences. All pathologic data are presented in Table 3.

Postoperative data

All patients in the early group underwent laparoscopic assisted distal gastrectomy. In the late group, laparoscopic distal gastrectomy, total gastrectomy, and proximal gastrectomy was performed in 1,136 patients (92.2%), 90 patients (7.3%), and 6 patients (0.5%), respectively. Operative time and hospital stay were significantly shorter in the late group. Blood loss was greater in the initial group compared to that seen in the late group (369.3 ± 226.7 mL vs. 214.6 ± 66.5 mL, respectively, *p* < 0.001). Postoperative complications occurred in 224 patients (16.8%), and major complications ($\geq$ grade IIIa Clavien-Dindo classification) occurred in 37 patients (2.8%). There was no significant difference in the incidence of postoperative complications, including major complications, between the two groups (Table 4). One death (0.1%) occurred in the initial group; a patient with coronary artery occlusive disease died

Table 2. Patient demographics

Variables	Initial group (n = 100)	Late group (n = 1,232)	Total (n = 1,332)	<i>p</i> value
Age (years)	56.2 ± 9.9	59.2 ± 11.2	59.0 ± 11.1	0.009
Sex				0.189
Male	67 (67.0%)	764 (62.0%)	831 (62.4%)	
Female	33 (33.0%)	468 (38.0%)	501 (37.6%)	
BMI (kg/m ²)	19.1 ± 8.8	23.5 ± 2.9	23.5 ± 2.9	0.023
Co-morbidity				0.008
Yes	37 (37.0%)	615 (49.9%)	678 (50.9%)	
No	63 (63.0%)	617 (50.1%)	654 (49.1%)	
ASA class				0.020
1	53 (53.0%)	445 (36.1%)	498 (37.4%)	
2	47 (47.0%)	768 (62.3%)	815 (61.2%)	
3	0 (0%)	19 (1.5%)	19 (1.4%)	

BMI = body mass index; ASA = American Society of Anesthesiologist.

Table 3. Pathological data

Variables	Initial group (n = 100)	Late group (n = 1,232)	Total (n = 1,332)	p value
Tumor size (cm)	2.7 ± 2.0	3.0 ± 1.9	3.0 ± 1.9	0.113
Tumor location				0.018
Upper	7 (7.0)	137 (11.1)	144 (10.8%)	
Middle	27 (27.0)	463 (37.6)	490 (36.8%)	
Lower	66 (66.0)	632 (51.3)	698 (52.4%)	
Lymphadenectomy				0.002
D1 +	33 (33.0)	600 (48.7)	633 (47.5)	
D2	67 (67.0)	632 (51.3)	699 (52.5)	
Retrieved lymph nodes	35.9 ± 14.2	43.1 ± 17.8	42.1 ± 17.3	<0.001
Metastatic lymph nodes	0.2 ± 1.0	0.3 ± 2.1	0.3 ± 2.2	0.510
TNM stage				0.716
I	96 (96.0)	1161 (94.2)	1257 (94.4)	
II	3 (3.0)	59 (4.8)	62 (4.6)	
III	1 (1.0)	12 (1.0)	13 (1.0)	
Proximal margin	4.3 ± 2.6	4.0 ± 3.0	4.0 ± 3.0	0.365
Distal margin	6.8 ± 4.6	7.7 ± 4.8	7.6 ± 4.8	0.083

TNM stage was followed by AJCC 7th edition.

Table 4. Postoperative data

Variables	Initial group (n = 100)	Late group (n = 1,232)	Total (n = 1,332)	p value
Operation method				0.015
LADG	100 (100.0)	1136 (92.2)	1236 (92.8)	
LATG	0 (0)	90 (7.3)	90 (6.8)	
LAPG	0 (0)	6 (0.5)	6 (0.5)	
Reconstruction method				0.065
B-I	76 (76.0)	661 (53.7)	723 (54.3)	
Others	24 (24.0)	571 (46.3)	609 (45.7)	
Co-resection				0.089
Yes	18 (18.0)	156 (12.7)	174 (13.1)	
No	82 (82.0)	1076 (87.3)	1158 (86.9)	
Operative time (min)	271.1 ± 75.0	214.6 ± 66.5	218.4 ± 68.5	<0.001
Blood loss (ml)	369.3 ± 226.7	183.3 ± 164.3	195.8 ± 175.5	<0.001
Hospital stay (days)	9.4 ± 3.3	8.6 ± 3.3	9.3 ± 3.9	0.015
Postoperative complication	21 (21.0)	203 (16.5)	224 (16.8)	0.153
Major complication (Grade ≥ IIIa)*	2 (2.0)	35 (2.8)	37 (2.8)	0.465

LADG = laparoscopic assisted distal gastrectomy; LATG = laparoscopic assisted total gastrectomy; LAPG = laparoscopic assisted proximal gastrectomy; B-I = Billroth I, Other = Billroth II, Roux-en-Y, esophagogastrectomy and double tract reconstruction. *Grade of Clavien-Dindo classification.

Table 5. Details of postoperative complications (Initial group/Late group)

Clavien-Dindo classification	I	II	IIIa	IIIb	Iva	V	Total (n= 1,332, %)
Surgical complications							
Postoperative ileus	5/23	-	-	-	-	-	5/23 (2.1)
Subcutaneous emphysema	0/6	-	-	-	-	-	0/6 (0.5)
Delayed gastric emptying	0/3	0/2	-	-	-	-	0/5 (0.4)
Dumping syndrome	0/3	0/11	-	-	-	-	0/14 (1.1)
Wound infection	2/17	1/5	-	-	-	-	3/22 (1.9)
Small bowel obstruction	-	0/12	-	0/4	-	-	0/16 (1.2)
Chyle leakage	-	3/6	1/0	-	-	-	4/6 (0.8)
Greater omentum infarction	-	0/1	-	-	-	-	0/1 (0.1)
Intra-luminal bleeding	-	0/1	-	-	-	-	0/1 (0.1)
Intra-abdominal bleeding	-	0/1	0/1	-	-	-	0/2 (0.2)
Intra-abdominal abscess	-	0/3	0/6	-	-	-	0/9 (0.7)
Anastomotic stricture	-	-	1/7	-	-	-	1/7 (0.6)
Anastomotic leakage	-	1/4	0/4	0/2	-	-	1/10 (0.8)
Duodenal stump leakage	-	-	0/1	-	-	-	0/1 (0.1)
Pancreatic fistula	-	-	-	0/1	-	-	0/1 (0.1)
Jejunal perforation	-	-	-	0/1	-	-	0/1 (0.1)
Cecal perforation	-	-	-	0/1	-	-	0/1 (0.1)
Remnant gastric necrosis	-	-	-	0/1	-	-	0/1 (0.1)
Cholecysto-colonic fistula	-	-	-	0/1	-	-	0/1 (0.1)
Number of case in each grade (%)	7/52 (4.4)	5/46 (3.8)	2/19 (1.6)	0/11 (0.8)	-	-	14/128 (10.7)
Non-surgical complications							
Gastrointestinal							
Massive diarrhea	3/25	-	-	-	-	-	3/25 (2.1)
PMC	-	1/3	-	-	-	-	1/3 (0.3)
Pancreatitis	-	0/4	-	-	-	-	0/4 (0.3)
Respiratory							
Pleural effusion	3/8	-	0/3	-	-	-	3/11 (1.1)
Atelectasis	2/16	-	-	-	-	-	2/16 (1.4)
Pneumonia	-	3/19	-	-	-	-	3/19 (1.7)
Cardio-cerebral							
Myocardial infarction	-	0/1	-	-	0/3	1/0	1/4 (0.4)
Intracranial hypotension	0/1	-	-	-	-	-	0/1 (0.1)
Seizure	-	0/1	-	-	-	-	0/1 (0.1)
Occipital neuralgia	-	0/1	-	-	-	-	0/1 (0.1)

Table 5. Continued

Clavien-Dindo classification	I	II	IIIa	IIIb	Iva	V	Total (n= 1,332, %)
Renal	-	-	-	-	-	-	
Urinary difficulty	-	0/8	-	-	-	-	0/8 (0.6)
APN	-	0/1	-	-	-	-	0/1 (0.1)
AKI	0/3	-	-	-	-	-	0/3 (0.2)
CKD	-	-	-	-	0/1	-	0/1 (0.1)
Hepatobiliary	-	-	-	-	-	-	
Massive ascites	-	0/1	0/2	-	-	-	0/3 (0.2)
Hyperbilirubinemia	0/5	-	-	-	-	-	0/5 (0.4)
Hepatic encephalopathy	-	0/1	-	-	-	-	0/1 (0.1)
Others							
DVT	-	0/1	-	-	-	-	0/1 (0.1)
Delirium	-	0/4	-	-	-	-	0/4 (0.3)
Skin eruption	-	0/2	-	-	-	-	0/2 (0.2)
Thrombocytopenia	-	0/1	-	-	-	-	0/1 (0.1)
Number of case in each grade (%)	8/58 (5.0)	4/48 (3.9)	0/5 (0.4)	-	0/4 (0.3)	1/0 (0.1)	13/115 (2.9)
Total case number (%)	15/110 (9.4)	9/94 (7.7)	2/24 (2.0)	0/11 (0.8)	0/4 (0.3)	1/0 (0.1)	33/243

PMC = pseudomembranous colitis; APN = acute pyelonephritis; AKI = acute kidney injury; CKD = chronic kidney disease; DVT = deep vein thrombosis.

from an acute myocardial infarction on the day of surgery. Details of postoperative complication for the entire study group and the initial and late groups are presented in Table 5.

Risk factors for postoperative complications after laparoscopic gastrectomy

In the univariate analysis, male sex, the presence of a co-morbidity, tumor location, D2 lymph node dissection, laparoscopic total gastrectomy (LTG) or laparoscopic proximal gastrectomy (LPG), non B-I anastomosis, co-resection, operative time, and blood loss were significantly associated with the overall incidence of postoperative complications. Major complications were associated with male sex, ASA score, tumor location, operation method such as LTG/LPG and non B-I anastomosis (Table 6). In the multivariate analysis, overall postoperative complications were significantly associated with male sex (odds ratio [OR], 1.719; 95% confidence interval [CI], 1.242~2.442; $p=0.002$), presence of a co-morbidity (OR, 1.473; 95% CI, 1.084~2.001; $p=0.013$), D2 LND (OR 1.615; 95% CI, 1.152~2.264; $p=0.005$), operation method-LTG/LPG (OR, 4.622; 95% CI, 2.809~7.606; $p<0.001$), co-resection (OR, 1.806; 95% CI, 1.210~2.696; $p=0.004$), operation time (OR, 1.426; 95% CI, 1.001~2.032; $p=0.049$) and blood loss (OR 2.662; 95% CI, 1.816~3.904; $p<0.001$). Male sex (OR, 3.123;

95% CI, 1.273~7.660; $p=0.013$), ASA score (OR, 12.203; 95% CI, 3.582~41.568; $p<0.001$), operation method-LTG/LPG (OR, 2.819; 95% CI, 1.028~7.731; $p=0.044$) and non B-I anastomosis (OR, 2.609; 95% CI, 1.061~6.416; $p=0.037$) were significant risk factors for the major complication, which was similar to the results of the univariate analysis (Table 7).

DISCUSSION

Differences in the postoperative complication rates in previous studies

Laparoscopic gastrectomy has been accepted as the standard surgery for early gastric cancer patients, and advanced gastric cancer is become a more frequent indication for laparoscopic gastrectomy. Several studies from the 2000s reported a postoperative complication rate ranging from 4.7% to 23.3% after laparoscopic gastrectomy.^{10,13-16} Several reports since 2010 have shown no significant change in the rate of postoperative complications despite improvements in surgical instrument and technique.¹⁷⁻¹⁹ In 2004, Dindo et al. developed a classification system for postoperative complications in an effort to standardize the quality assessment of surgery; however, a large variation in the incidence of complications is still seen in recent studies. Dindo et al. defined a complication as “any

Table 6. Univariate analysis of risk factors of postoperative complication after laparoscopic gastrectomy

Variables	Overall complication		<i>p</i> value	Major complication		<i>p</i> value
	Yes (n = 224)	No (n = 1,108)		Yes (n = 37)	No (n = 1,295)	
Age (years)	58.5 ± 10.4	58.9 ± 11.2	0.475	61.0 ± 9.5	58.9 ± 11.1	0.261
Sex			0.001			0.006
Male	165 (19.9)	666 (77.7)		31 (3.7)	800 (96.3)	
Female	59 (11.8)	442 (88.2)		6 (1.2)	495 (98.8)	
BMI (kg/m ²)	23.3 ± 3.0	23.5 ± 2.9	0.448	23.9 ± 3.1	23.5 ± 2.9	0.429
Co-morbidity			0.003			0.133
Yes	129 (19.7)	525 (80.3)		23 (3.5)	631 (96.5)	
No	95 (14.0)	583 (86.0)		14 (2.1)	664 (97.9)	
ASA class			0.075			<0.001
1	73 (14.7)	425 (85.3)		13 (2.6)	485 (97.4)	
2	145 (17.8)	670 (82.2)		20 (2.5)	795 (97.5)	
3	6 (31.6)	13 (68.4)		4 (21.1)	15 (78.9)	
Tumor Location			<0.001			0.003
Upper	46 (31.9)	98 (68.1)		10 (6.9)	134 (93.1)	
Middle	72 (14.7)	418 (85.3)		8 (1.6)	482 (98.4)	
Lower	106 (15.2)	592 (84.8)		19 (2.7)	679 (97.3)	
Lymphadenectomy			0.003			0.869
D1 +	86 (13.7)	541 (86.3)		18 (2.9)	609 (97.1)	
D2	138 (19.6)	567 (80.4)		19 (2.7)	686 (97.3)	
Operation method			<0.001			<0.001
LADG	185 (15.0)	1051 (85.0)		25 (2.0)	1211 (98.0)	
LATG/LAPG	39 (40.6)	57 (59.4)		11 (11.5)	85 (88.5)	
Reconstruction method			<0.001			<0.001
B-I	154 (14.4)	912 (85.6)		19 (1.8)	1047 (98.2)	
Others [#]	70 (26.3)	196 (73.7)		18 (6.8)	248 (93.2)	
Co-resection			<0.001			0.352
Yes	50 (28.7)	124 (71.3)		6 (3.4)	168 (96.6)	
No	174 (15.0)	984 (85.0)		31 (2.7)	1127 (97.3)	
Operative time (min)	252.4 ± 89.0	211.5 ± 61.5	<0.001	230.1 ± 85.8	218.0 ± 68.0	0.291
≤240	121 (12.4)	852 (87.6)	<0.001	21 (2.2)	952 (97.8)	0.037
>240	103 (28.7)	256 (71.3)		16 (4.5)	343 (95.5)	
Blood loss (ml)	296.8 ± 276.5	175.7 ± 138.8	<0.001	200.8 ± 190.8	195.7 ± 175.1	0.861
≤200	132 (12.9)	890 (87.1)	<0.001	27 (2.6)	995 (97.4)	0.558
>200	92 (29.7)	218 (70.3)		10 (3.2)	300 (96.8)	
Hospital stay (days)	12.7 ± 7.7	8.7 ± 1.8	<0.001	18.8 ± 13.9	9.1 ± 2.7	<0.001

BMI = body mass index; ASA = American Society of Anesthesiologist; LADG = laparoscopic assisted distal gastrectomy; LATG = laparoscopic assisted total gastrectomy; LAPG = laparoscopic assisted proximal gastrectomy; B-I = Billroth I; Other = Billroth II, Roux-en-Y, esophagogastrostomy and double tract reconstruction.

Table 7. Multivariate analysis of risk factors of postoperative complication after laparoscopic gastrectomy

Variables	Overall complication		Major complication	
	OR (95% CI)	p value	OR (95% CI)	p value
Sex (Male vs. Female)	1.719 (1.242 ~ 2.442)	0.002	3.123 (1.273 ~ 7.660)	0.013
Co-morbidity	1.473 (1.084 ~ 2.001)	0.013		
ASA (3 vs. 1/2)			12.203 (3.582 ~ 41.568)	<0.001
Tumor Location (upper vs. mid/lower)	1.475 (0.808 ~ 2.694)	0.206		
Lymphadenectomy (D2 vs. D1)	1.615 (1.152 ~ 2.264)	0.005		
Operation method (Others vs. LDG)	4.622 (2.809 ~ 7.606)	<0.001	2.819 (1.028 ~ 7.731)	0.044
Reconstruction (B-I vs. others)	1.173 (0.727 ~ 1.894)	0.514	2.609 (1.061 ~ 6.416)	0.037
Co-resection	1.806 (1.210 ~ 2.696)	0.004		
Operative time (>240 vs. ≤240 min)	1.426 (1.001 ~ 2.032)	0.049		
Blood loss (>200 vs. ≤200 ml)	2.143 (1.523 ~ 3.017)	<0.001		

ASA = American Society of Anesthesiologists; Others = laparoscopic total gastrectomy/proximal gastrectomy; LDG = laparoscopic distal gastrectomy.

deviation from the ideal postoperative course". Because this definition is vague with terms such as "any" or "ideal", there is a significant possibility that the researcher's subjective judgment will influence study results. Variations in the complication rates between studies are due to differences in operative procedures, operator and patient characteristics, as well as the definition of postoperative complications.¹⁶ Jung et al. has validated the Accordion Severity Grading System, described by Strasberg et al., to overcome shortcomings of the Clavien-Dindo classification.¹⁸

Risk factors for postoperative complications after laparoscopic gastrectomy

Two hundred twenty-four of 826 patients (16.8%) experienced at least one postoperative complication in the present study. The incidence of major complications (≥grade III Clavien-Dindo classification) was 37 (2.8%) and there were a total of 276 postoperative complications in the present study. The incidence of postoperative complications we report is not significantly different from that of previous reports, but the risk factors associated with postoperative complications are.

In a large-scale Korean multicenter study reported by Kim et al., the incidence of systemic complications was significantly increased in patients over 60 years old.¹⁶ Nagasako et al. reported that the incidence of complications was significantly increased in patients >70 years old.²⁰ Lee et al. reported that the incidence of complications was increased in patients older than 70 years, but not the incidence of major complications (grade III Clavien-Dindo or higher).²¹ In contrast, Ryu et al. reported that age was not associated with complications after

laparoscopic distal gastrectomy.¹¹ Jung et al. also reported that there was no significant correlation between age and complications in a multivariate analysis of their study data.¹⁸ Age is the patient's factor that reflects the physical condition along with ASA score and co-morbidity. In the present study, there was no association between age and the incidence of postoperative complications. The age of patients experiencing a major complication was slightly higher than that of the study group, but this difference was not statistically significant. This may be due to relatively young patients – the mean age was <60 years (58.5 years). However, careful attention should be paid to the preoperative evaluation and postoperative management of older patients, because numerous reports suggest that advanced age affects the incidence of postoperative complications.¹⁹

Overall complications were more common in men, and there was also correlation between major complications and sex. This may be associated that men more frequently smoke and drink alcohol than do women, but this has not been proven to be the cause of increased complications in previous studies. The presence of co-morbidity was a risk factor for postoperative complications, but was not a risk factor for major complications. However, severe cardiovascular or pulmonary disease is known to increase the occurrence of postoperative complications.¹⁸ The only mortality in this study was caused by an acute myocardial infarction in a patient with coronary artery occlusive disease.

LTG, which is performed in patients with upper gastric cancer, is known to be more difficult and challenging than partial gastric resection. The incidence of overall complications was 31.9% in patients with upper gastric cancer, and there was

significant difference in the incidence of major complications between the tumor locations. In addition, the LTG/LPG group showed a significantly higher overall and major complication incidence than that seen in the LDG group. The multivariate analysis showed results similar to the univariate analysis. This may be due to the result of postoperative strictures in the LTG/LPG group. Kubota et al. has reported that the complication rate in upper gastric cancer patients was higher than that seen in patients with lower gastric cancer, and Jeong et al. also has reported a higher incidence of complications in patients undergoing LTG compared to that seen in patients undergoing LDG.^{22,23}

In order to evaluate the efficacy of extended LND, two western randomized trials were conducted by the Medical Research Council in the United Kingdom and the Dutch Gastric Cancer Group in the Netherlands.^{24,25} In both trials, the morbidity and mortality rates were substantially higher in patients who underwent D2 LND. Although these large scale randomized controlled trials had some limitations, it is generally accepted that the greater the extent of the LND, the higher the complication rate.^{26,27} Recently, various efforts to reduce complications related to radical LND have been made with the function preserving surgery such as sentinel node navigation

surgery. Improvements in techniques and instruments now allow D2 LND to be performed more safely. In the present study, the overall complication was higher in patients undergoing D2 LND; however, there was no difference in the rate of major complications between D1+ and D2 LND patients. Some prior studies have reported that the extent of LND does not affect postoperative complications, but this remains an issue of ongoing debate.^{18,19,21} Moreover, patients undergoing adjacent organ resection, such as the pancreas, spleen, or colon, were not rarely included in this study. Because most patients enrolled in this study preoperatively diagnosed as the early stage cancer, adjacent organ invasion was very rare. Actually, 169 (97.1%) of 174 patients performed the co-resection (concurrent resection of another organ during the gastrectomy) underwent a simple cholecystectomy due to cholelithiasis. This may lead the result that co-resection was not risk factor for major complications in the present study, unlike the findings of previous European studies conducted in the 1990s.

There are several opinions as to how the rate of postoperative complications is influenced by operative time and intraoperative bleeding. New anesthesia techniques and improvements in perioperative management have reduced the complication rates in patients with unfavorable intraoperative

Fig. 1. Anastomotic leakage management. (A) Tubography revealed the anastomotic fistula to the remnant stomach. (B) It shows the anastomotic fistula near a staple line (blue arrow). (C) Endoscopic hemoclips were applied around the fistula and tightened with detachable snare (at postoperative day 17). (D) No remarkable leakage finding was observed in upper gastrointestinal contrast test after procedure (at postoperative day 20).

circumstances. In the present study, the overall complication rate was associated with operative time and blood loss; however, major complications were not associated with these factors. In the multivariate analysis, blood loss was the potent risk factor that increased the occurrence of overall postoperative complications. Generally, transfusion and volume over-load occurring during the treatment of excessive blood loss could cause complications such as atelectasis or ileus. However, Wu et al. has reported that blood transfusions decreased mortality in patients with lower hemoglobin levels and in elderly patients.²⁸ And prolonged operative time has also been reported to be associated with wound complications or sepsis, but this has not been found to be a risk factor in recent reports.^{19,29}

Anastomosis-related complications and their management

Anastomosis-related problems are a great concern to surgeons except for systemic complications. Strictures are often easily treated endoscopically with interventional balloon dilatation and localized abdominal abscess can be controlled with external drainage and antibiotics. However, because of the risk of sepsis from a fistula or leakage, more careful management of anastomosis-related problems is required. Although the learning curve for procedural competence in laparoscopic gastrectomy is known to be around 50 cases,³⁰ we could not find any statistical significance between the frequency of postoperative complications and the learning curve in the present study. This may be because the surgeons in this study had extensive experience in gastrectomy and because there was variation in the operative team. Anastomotic leakage occurred in eleven patients and ten patients in the late surgery group. Nine patients underwent LDG with a Billroth-I anastomosis, and five of them were treated with conservative management including antibiotics. The other two patients were managed with percutaneous catheter drainage, and two patients were recovered with endoscopic intervention to close an anastomotic fistula. Endoscopic intervention was performed, placing hemoclips around the fistula and tightening them with a detachable snare (Fig. 1) This method may be effective if the fistula is not large and fibrosis has well formed at the periphery of the fistula. Actually two patients underwent the endoscopic intervention for closing the fistula at postoperative 14 day and 17 day, respectively. All anastomotic leakages were well controlled without any mortality. Anastomotic stricture occurred in eight patients and mostly in LTG or LPG (six patients). All patients was performed several endoscopic ballooning and its result was satisfied. Anastomotic intraluminal bleeding was occurred in 1 patients, who recovered with blood transfusion. Authors check the bleeding into anastomotic site

through the gastrotomy after all reconstruction and control the bleeding with suturing if it is necessary. This may be the reason why incidence of intraluminal bleeding was very low in this study.

Comparison of postoperative complications according to the time of surgery

Patients in the initial surgery group were younger, thinner, had fewer comorbidities, and were in better physical condition than those in the late surgery group. This may be because the patient selection was more stringent at the early period of laparoscopic gastrectomy. The prolonged operative time and increased blood loss in initial group suggest that the operative technique had not yet fully evolved, even though all patients in the initial group underwent LADG. Also, the longer hospital stay in the initial group may have been due to concerns regarding perioperative management. Consequently, the overall complication and major complication rates were not significantly different between the initial and late surgery groups. This suggests that an experienced surgeon can perform laparoscopic gastrectomy without great difficulty through appropriate initial patient selection.

Study limitations

This study has some limitations. The Clavien-Dindo classification is a simple assessment tool, but leaves room for the researcher's subjective judgment by using terms like "any deviation". This classification was designed for use in retrospective analyses, and many retrospective studies can miss grade I or II low-grade complications. The authors of the present study tried to minimize this bias by collecting the data prospectively. Although we enrolled a significant number of patients in our study, a larger study volume would allow a more effective analysis because the incidence of major complications was less than 5% in the present study. However, we believe that our study's data and findings are reliable because 1) the cases were collected over a long period of time, 2) the complication patterns were confirmed during the development of improved surgical techniques and instruments, and 3) the participating surgeons were from a single institution and shared a similar surgical technique.

In conclusion, there were no significant differences in the incidence of postoperative complications in those patients undergoing laparoscopic gastrectomy during the initial operative period compared with those undergoing surgery after maturation of the surgical procedure. These results suggest that beginners also can safely perform laparoscopic gastrectomy with LND through appropriate patient selection, even if they are

familiar with the open surgical anatomy. The only risk factor for major postoperative complications in our study's multivariate analysis was the operative method used (total gastrectomy or proximal gastrectomy). However, because studies of complication rates are often affected by various biases, further research is needed to provide additional clarification.

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