

Clinicopathological Outcomes and Predictors of Postoperative Complications after Gastrectomy in Very elderly Patients with Gastric Cancer

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Abstract

Objective: Although the total number of deaths from gastric cancer (GC) has been decreasing in Japan, the number of deaths among the elderly has increased. Therefore, the present study examined the feasibility and safety of gastrectomy and the predictors of postoperative complications in elderly patients with GC.

Patients and methods: Patients were classified into a very elderly group (age ≥ 85 years old; Group A; $n=69$) and an elderly group (age 75-84 years old; Group B; $n=370$). Clinicopathological data, surgical outcomes, and postoperative complications were obtained from a prospectively maintained database. To analyze the risk factors for complications, patients in Groups A and B were separated into 2 groups: those who developed complications and those who did not.

Results: Group A included a significantly larger proportion of female patients, had a poor Eastern Cooperative Oncology Group Performance Status (ECOG-PS), and had a lower albumin level than Group B. The extent of resection was significantly smaller in Group A than in Group B ($p=0.047$). Therefore, the degree of lymphadenectomy was significantly lower, and the operation time was significantly shorter in Group A than in Group B. However, the overall postoperative complication rate was significantly higher in Group A than in Group B ($p<0.001$). The disease-specific survival rate was also significantly lower in Group A than in Group B ($p<0.001$). A history of dementia and a lower preoperative ECOG-PS score were significant risk factors for postoperative complications in Group A.

Conclusions: In order to increase disease-specific survival rates in very elderly patients, it is important to select patients with some degree of nutritional status and performance status and to determine the optimal treatment.

Keywords: elderly, gastric cancer, gastrectomy, prognostic factors, survival, postoperative complications

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I. INTRODUCTION

As the world population ages, the mean age and the number of patients with various malignancies have increased (1, 2). In Japan, the average lifetime of women is 87.57 years old, while that of men is 81.56 years old, and the life expectancies of 85-year-old women and men are 8.60 and 6.48 years, respectively (3). Gastric cancer (GC) is one of the most common malignancies in East Asia, resulting in 44,000 deaths annually in Japan. Although the total number of GC deaths has been decreasing in Japan, those among the elderly have increased (4).

Radical gastrectomy with lymphadenectomy is the most effective treatment for GC. However, GC surgery can lead to body weight loss, appetite loss, malnutrition, anemia, and osteoporosis after surgery,

despite the curative effect of such a resection (5, 6). Therefore, most elderly patients have a reduced physiological function, which can sometimes be an obstacle to safe surgical treatment. In such elderly patients, postoperative complications occur particularly frequently and may be occasionally fatal (7, 8). The indications for surgical treatment in elderly patients should be comprehensively evaluated based on a balance of radicality, safety, and appropriateness. To prevent postoperative complications in the elderly, it is important to evaluate the risk factors for postoperative complications according to the overall postoperative status and to vary postoperative care depending on the type of surgery and the specifics of the case.

The present study examined the feasibility and safety of gastrectomy and the predictors of postoperative complications in very elderly GC patients (≥ 85 years old; Group A; $n=69$) in comparison with elderly GC patients (75-84 years old; Group B; $n=370$).

Patients and methods

Patients

This study included 439 patients ≥ 75 years old who underwent gastrectomy for primary GC at Mitoyo General Hospital between January 2000 and December 2020. The patients were classified into Groups A and B based on their age, as described above.

Methods

Clinicopathological and surgical outcomes were collected from a prospectively maintained database as well as from individual patient records when necessary. Complications were graded according to the Clavien-Dindo (CD) system. Postoperative complications in this study were defined as any adverse event corresponding to a CD classification grade of $\geq II$ and occurring within 30 days of gastrectomy. To analyze the predictors of complications, patients in Groups A and B were separated into those who did and did not develop complications. We compared the overall survival and the disease-specific survival of Group A with those of Group B.

Evaluations

The degree of lymphadenectomy, the extent of gastrectomy, and the stage of disease were based on the Japanese Classification of GC, 15th edition, and the Japanese Gastric Cancer Treatment Guidelines 2021. All procedures were performed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and the 1964 Declaration of Helsinki and later versions. This study was approved by the ethics committee of Mitoyo General Hospital (approval number: 23-CR01-288; approval date: January 5, 2024).

Statistical analyses

Statistical analyses were performed using the R software program, version 4.2.2. with the survival package. Chi-square and Fisher's exact tests were used to compare categorical variables, and Student's *t*-test or the Mann-Whitney test was used to compare continuous variables. The overall survival was calculated using the Kaplan-Meier method, and differences in survival were determined using the log-rank test. All tests were two-sided, and values <0.05 were considered statistically significant.

II. RESULTS

Clinical characteristics

Group A included a significantly larger population of patients who were female, had a poor Eastern Cooperative Oncology Group Performance Status (ECOG-PS), and had a low albumin level than Group B. The L-region in the tumor location was significantly more common in Group A than in Group B (Table 1).

Surgical outcomes

The extent of resection was significantly smaller in Group A than in Group B ($p=0.047$). Therefore, the degree of lymphadenectomy was significantly lower and the operation time significantly shorter in Group A than in Group B. Rates of reoperation and the postoperative hospital stay duration did not differ markedly between the two groups. None of the patients in Group A received adjuvant chemotherapy and 62 patients (16.8%) in Group B received adjuvant chemotherapy (Table 2).

Postoperative complications

The overall postoperative complication rate was significantly higher in Group A than in Group B ($p < 0.001$). Complications were classified into surgical and nonsurgical complications. Although the surgical complication rate was not significantly different between the two groups, it tended to be higher in Group A than in Group B ($p = 0.081$). However, the nonsurgical complication rate was significantly higher in Group A than in Group B ($p < 0.001$). Regarding the surgical complication rate, the postoperative pancreatic fistula rate was not significantly different between the groups, but it tended to be higher in Group A than in Group B ($p = 0.054$). Regarding the nonsurgical complication rate, delirium and pneumonia were significantly more common in Group A than in Group B ($p < 0.001$, $p = 0.028$, respectively). The mortality rate did not differ markedly between the two groups (Table 3).

Histopathological characteristics

The tumor size was significantly larger in Group A than in Group B ($p = 0.034$). Differential histopathology was significantly more common in Group A than in Group B ($p = 0.034$). The pathological stage did not differ markedly between the two groups (Table 4).

The survival

The overall survival rates after surgery were significantly lower in Group A than in Group B ($p < 0.001$) (Fig. 1). The death rate from primary disease due to GC was significantly higher in Group A than in Group B ($p = 0.039$) (Table 5). Therefore, the disease-specific survival rate was significantly lower in Group A than in Group B ($p < 0.001$) (Fig. 2).

A comparison of patient characteristics subdivided according to the presence or absence of complications

A high frequency of a history of dementia and a poor ECOG-PS were significantly associated with operative morbidity in Group A ($p = 0.049$, $p = 0.018$, respectively). Although the frequency of cerebrovascular disease and low serum albumin levels were not significantly different between the groups, those tended to be higher associated with operative morbidity in Group A than in Group B ($p = 0.070$, $p = 0.064$, respectively). A high frequency of dementia, poor ECOG-PS, large amount of bleeding and advanced pathological stage were significantly associated with operative morbidity in Group B (Table 6).

III. DISCUSSION

Recently, the number of surgical interventions for the elderly has increased rapidly in Japan. Surgical resection in elderly patients is associated with significant perioperative mortality and frequent postoperative complications (7, 8). In addition, the life expectancy of this population is limited in comparison to younger patients. In general, elderly patients often have age-associated physiological problems, such as a decreased organ reserves, concomitant comorbidities, and mental imbalance. Therefore, surgeons are sometimes hesitant to perform surgery in elderly patients because of the high frequency of surgical complications and mortality associated with aging (9, 10). However, several recent studies have demonstrated that advances in surgical and anesthetic techniques have reduced the risk of surgical complications and consequently improved the short-term surgical outcomes in elderly patients (11-14). Therefore, the indications for surgical treatment should be comprehensively discussed based on various patient- and tumor-related factors.

In the present study, the nutritional status and performance status were significantly lower in very elderly patients than in elderly patients. However, Takama et al (15) reported that the nutritional status of very elderly and elderly patients did not differ to a statistically significant extent. In addition, Hikage et al (16) reported that the albumin levels of very elderly patients were significantly lower than those of elderly patients, and parameters that reflected the physical condition, such as the serum albumin level, more strongly affected the survival. Accordingly, the indications for gastrectomy in very elderly patients with a poor nutritional and performance statuses should thus be carefully considered.

The CD classification of postoperative complications is an important method for comparing and evaluating the safety of different types of gastrectomy (17). The incidence of postoperative overall and nonsurgical complications was significantly higher in very elderly patients than in elderly patients. Specifically, the incidence rates of non-surgical complications of delirium and pneumonia were significantly higher in very elderly patients than in elderly patients.

Postoperative delirium can cause unexpected medical accidents and may lead to prolonged hospitalization. It has been reported that 10-50% of elderly patients who undergo surgical treatment develop

postoperative delirium (17, 18). Although the mechanisms underlying the development of delirium remain unclear, multiple factors are known to be involved (19). Besides an advanced age, a recent study showed that systemic stress and inflammatory responses may play important roles in its development (20). To minimize the occurrence of delirium in patients in very elderly patients, it is important to reduce perioperative stress and inflammatory responses. Accordingly, investigating potential preoperative risk factors is critical to prevent postoperative delirium. The albumin/fibrinogen ratio, neutrophil/lymphocyte ratio, sleeping pill use, and duration of intensive care unit stay were independent risk factors for postoperative delirium (21). Postoperative pneumonia had an adverse impact on overall survival in elderly patients undergoing gastrectomy with curative intent. The analysis showed that postoperative pneumonia was also an independent predictor of worse survival. These findings indicate that postoperative pneumonia affects the prognosis separately from preoperative health status, operative procedure, and disease stage in very elderly patients (22). Perioperative interventions, including respiratory rehabilitation, oral care, and early mobilization programs, are effective in preventing postoperative pneumonia (23, 24).

The pathological stage did not differ markedly between the two groups. The extent of resection and degree of lymphadenectomy were significantly lower in very elderly patients than in elderly patients. None of very elderly patients received adjuvant chemotherapy and 62 elderly patients (16.8%) received adjuvant chemotherapy. The overall survival rates after surgery were significantly lower in very elderly patients than in elderly patients. However, Takama et al (15) reported that the postoperative prognosis did not differ significantly between groups very elderly and elderly patients. The rate of death from primary disease (specifically GC) was significantly higher in very elderly patients than in elderly patients. Therefore, the disease-specific survival rates were significantly lower in very elderly patients. Hikage et al (16) reported that the overall survival of very elderly patients was significantly lower than in elderly patients; however, the disease-specific survival was not markedly different between the two groups. In both groups, approximately 10% of the patients died of GC. In our hospital, the selection of patients with a relatively good nutritional and performance status and the determination of the optimal treatment are considered important for increasing the disease-specific survival rates in very elderly patients.

In the present study, we found that a history of dementia and a lower level of preoperative ECOG-PS score were the predictors of postoperative complications following gastrectomy in very elderly patients. Previous studies have demonstrated a strong relationship between lower level of preoperative ECOG-PS scores and postoperative complications (25, 26). Elderly patients tend to have additional risk factors relative to younger patients, such as poor ECOG-PS, malnutrition, and an impaired respiratory function. Advanced age can be considered a risk factor for postoperative pneumonia (27). In addition, a history of dementia is strongly correlated with postoperative delirium, which has previously been reported to cause postoperative complications (28-32). Therefore, we should consider the indications for gastrectomy more seriously in very elderly patients with poor nutrition, poor performance status, and a history of dementia than in those without these conditions.

Several limitations associated with the present study warrant mention. This study was conducted at a single center, and the study population was relatively small. Therefore, there may have been potential selection bias. Further large-scale, multicenter studies should be performed to confirm our findings.

IV. CONCLUSIONS

The incidence of postoperative all complications was significantly higher in very elderly patients than in elderly patients. The presence of a history dementia and a low preoperative ECOG-PS score were predictors of postoperative complications following gastrectomy in very elderly patients. Disease-specific survival rates were significantly lower in very elderly patients than in elderly patients. In order to increase disease-specific survival rates in very elderly patients, it is important to select patients with some degree of nutritional status and performance status and to determine the optimal treatment.

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Figure Legends

Fig. 1. Overall survival curves of patients in both groups using Kaplan-Meier methods. A significant difference was observed in the 5-year overall survival rates between Groups A and B ($p<0.001$).

Fig. 2. Disease-specific survival curves of patients in both groups using Kaplan-Meier methods. A significant difference was observed in the 5-year disease-specific survival rates between Groups A and B ($p<0.001$).

Table 1. Clinical characteristics

Table 2. Surgical outcomes

Table 3. Postoperative complications

Table 4. Histopathological characteristics

Table 5. Cause of death within five years after surgery

Table 6. A comparison of patient characteristics subdivided according to the presence or absence of complications

Fig. 1

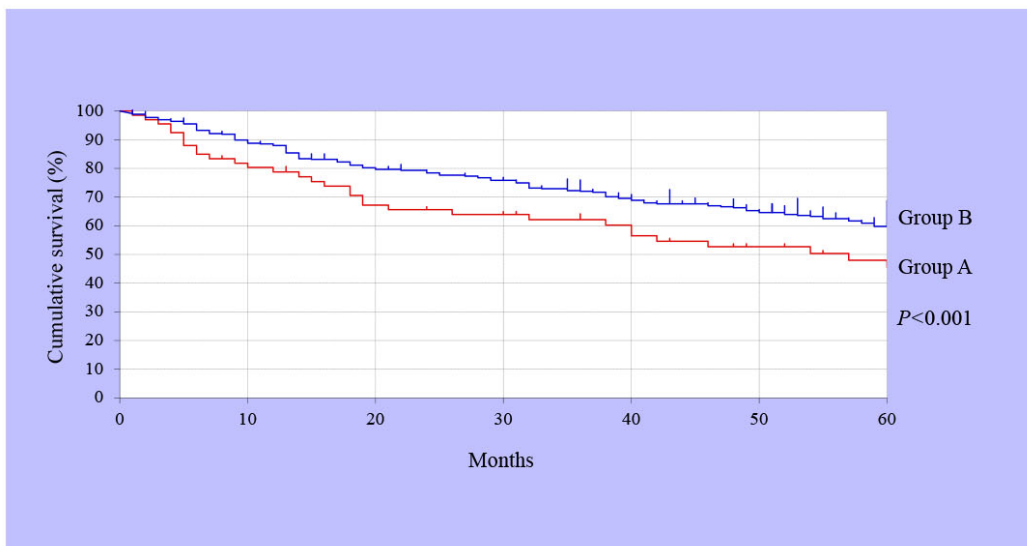


Fig. 2

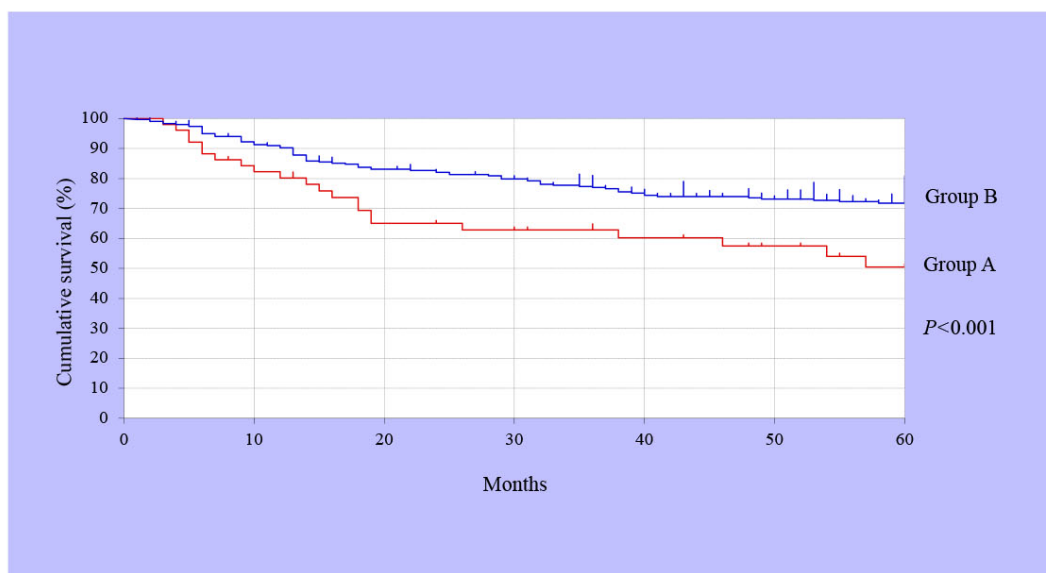


Table 1

	Group A (n=69)	Group B (n=370)	p value
Age (years)	87 ± 2.1	78.8 ± 2.6	< 0.001
Sex			0.029
Male	36 (52.2 %)	246 (66.5 %)	
Female	33 (47.8 %)	124 (33.5 %)	
BMI (kg/m ²)	22.4 ± 3.6	22.5 ± 2.5	0.674
ECOG-PS score			0.018
0	14 (20.3 %)	141 (38.1 %)	
1	31 (44.9 %)	131 (35.4 %)	
≥ 2	24 (34.8 %)	98 (26.5 %)	
Respiratory function			
%VC	75.5 ± 7.1	74.89 ± 7.7	0.561
Nutrition			
Serum albumin level (g/dl)	3.4 ± 0.6	3.7 ± 0.6	< 0.001
Renal function			
Serum creatinine level (mg/dl)	1.0 ± 0.5	0.89 ± 0.55	0.168
Comorbidity			0.438
Yes	50 (72.5 %)	287 (77.6 %)	
No	19 (27.5 %)	83 (22.4 %)	
Main tumor location			0.034
U	10 (14.5 %)	85 (23.0 %)	
M	23 (33.3 %)	152 (41.1 %)	
L	36 (52.2 %)	133 (35.9 %)	

BMI: body mass index

ECOG-PS: Eastern Cooperative Oncology Group Performance

Status

%VC:

percent vital capacity

Table 2

	Group A (n=69)	Group B (n=370)	<i>p</i> value
Approach			0.136
Open	65 (94.2 %)	322 (87.0 %)	
Laparoscopy-assisted	4 (5.8 %)	48 (13.0 %)	
Extent of resection			0.047
Total	9 (13.0 %)	95 (25.7 %)	
Distal	52 (75.4 %)	226 (61.1 %)	
Proximal	1 (1.4 %)	16 (4.3 %)	
Pylorus preserving	3 (4.3 %)	28 (7.7 %)	
Segmental	3 (4.3 %)	4 (1.1 %)	
Local resection	1 (1.4 %)	1 (0.3 %)	
Lymphadenectomy			0.027
D0	5 (7.2 %)	5 (1.4 %)	
D1	26 (37.7 %)	128 (34.5 %)	
D1+	13 (18.8 %)	53 (15.1 %)	
D2	25 (36.2 %)	184 (49.5 %)	
Operation time (minutes)	184.7 ± 58.8	208.5 ± 57.8	0.002
Blood loss (ml)	254 ± 212.6	302.3 ± 265.3	0.185
Reoperation	1 (1.4 %)	4 (1.1 %)	0.537
Postoperative hospital stay (days)	25.9 ± 17.7	26.2 ± 18.9	0.900
Adjuvant chemotherapy			< 0.001
Yes	0 (0.0 %)	62 (16.8 %)	
No	69 (100.0 %)	308 (83.2 %)	

Table 3

	Group A (n=69)	Group B (n=370)	<i>p</i> value
All complications (Grade II or higher, patients)			< 0.001
Yes	23 (33.3 %)	55 (14.9 %)	
No	46 (66.7 %)	315 (85.1 %)	
Surgical complications (Grade II or higher, patients)			0.081
Yes	11 (7.2 %)	33 (8.9 %)	
No	58 (92.8 %)	337 (91.1 %)	
Non-surgical complications (Grade II or higher, patients)			< 0.001
Yes	14 (20.3 %)	24 (6.5 %)	

No	55 (79.7 %)	346 (93.5 %)	
Mortality	2 (2.9 %)	6 (1.6%)	0.624
Details			
Surgical complications (Grade II or higher, patients)			
Anastomotic leakage	1 (1.4 %)	9 (0.3 %)	0.950
Stump leakage	1 (1.4 %)	1 (0.3 %)	0.718
Anastomotic stricture	1 (1.4 %)	4 (1.1 %)	0.537
Intra-abdominal abscess	2 (2.9 %)	5 (1.4 %)	0.601
Ileus	2 (2.9 %)	5 (1.4 %)	0.601
Pancreatic fistula	4 (5.8 %)	5 (1.4 %)	0.054
Bleeding	0 (0.0 %)	2 (0.5 %)	0.330
Wound infection	1 (1.4 %)	3 (0.8 %)	0.490
Peritonitis	0 (0.0 %)	3 (0.8 %)	0.426
Wound deficiency	0 (0.0 %)	1 (0.3 %)	0.169
Bile leakage	1 (1.4 %)	1 (0.3 %)	0.718
Stasis	0 (0.0 %)	1 (0.3 %)	0.169
Non-surgical complications (Grade II or higher, patients)			
Delirium	8 (11.6 %)	6 (1.6 %)	< 0.001
Pneumonia	4 (5.8 %)	4 (1.1 %)	0.028
Heart disease	3 (4.3 %)	4 (1.1 %)	0.143
DIC	1 (1.4 %)	2 (0.5 %)	0.964
Hepatic disease	0 (0.0 %)	2 (0.5 %)	0.330
Enterocolitis	0 (0.0 %)	2 (0.5 %)	0.330
Cerebrovascular disease	0 (0.0 %)	1 (0.3 %)	0.169
Urinary tract infection	0 (0.0 %)	1 (0.3 %)	0.169
Thrombosis	0 (0.0 %)	1 (0.3 %)	0.169
Renal disease	0 (0.0 %)	1 (0.3 %)	0.169

Grade: complication grading using the Clavien-Dindo classification

DIC: disseminated intravascular coagulation

Table 4

	Group A (n=69)	Group B (n=370)	<i>p</i> value
T classification			0.736
1	30 (43.5 %)	164 (44.3 %)	
2	5 (7.2 %)	37 (10.0 %)	
3	8 (11.6 %)	51 (13.8 %)	
4	26 (33.3 %)	118 (31.9 %)	
N classification			0.120

0	35 (50.7 %)	204 (55.1 %)	
1	5 (7.2 %)	55 (14.9 %)	
2	15 (21.8 %)	50 (13.5 %)	
3	14 (20.3 %)	61 (16.5 %)	
Tumor size (mm)	52 ± 21.93	48.1 ± 31.2	0.034
Tumor type			0.975
0	30 (43.5 %)	161 (43.5 %)	
1	3 (4.3 %)	16 (4.3 %)	
2	15 (21.8 %)	96 (25.9 %)	
3	12 (17.4 %)	56 (15.1 %)	
4	8 (11.6 %)	35 (9.5 %)	
5	1 (1.4 %)	6 (1.6 %)	
Histological type			0.043
Differentiated	50 (72.5 %)	220 (59.5 %)	
Undifferentiated	19 (27.5 %)	150 (40.5 %)	
Pathological stage			0.691
I	30 (43.5 %)	174 (47.0 %)	
II	12 (1.4 %)	64 (17.3 %)	
III	15 (21.8 %)	87 (23.5 %)	
IV	12 (17.4 %)	45 (12.2 %)	

Table 5

	Group A (n=69)	Group B (n=370)	p value
Total	30 (43.5 %)	136 (36.8 %)	0.344
Surgery-related death	2 (2.9 %)	5 (1.4 %)	0.601
Gastric Cancer	22 (31.9 %)	74 (20.0 %)	0.039
Others	6 (11.6 %)	57 (15.4 %)	0.190
Other malignancies	0 (0.0 %)	11 (3.0 %)	
Pneumonia	1 (1.4 %)	16 (4.3 %)	
Cardiac failure	2 (2.9 %)	2 (0.5 %)	
Cerebrovascular disease	3 (4.3 %)	2 (0.5 %)	
Renal failure	0 (0.0 %)	1 (0.3 %)	
Trauma	0 (0.0 %)	3 (0.8 %)	
Natural	0 (0.0 %)	4 (1.1 %)	
Unknown	0 (0.0 %)	18 (4.9 %)	

Table 6

Complication	Group A (n=69) (≥ 85 years)		p value	Group B (n=370) (75-84 years)		p value
	No (n=46)	Yes (n=23)		No (n=315)	Yes (n=55)	
Sex			0.307			0.353
Male	22 (47.8 %)	14 (60.9 %)		206 (65.4 %)	40 (72.7 %)	
Female	24 (52.2 %)	9 (39.1 %)		109 (34.6 %)	15 (27.3 %)	
Past history						
Dementia	1 (2.2 %)	4 (17.4 %)	0.049	1 (0.3 %)	5 (9.1 %)	< 0.001
Lung disease	3 (6.5 %)	3 (13.0 %)	0.365	32 (10.2 %)	5 (9.1 %)	0.801
Diabetes mellitus	4 (9.0 %)	4 (17.4 %)	0.425	46 (14.6 %)	7 (12.7 %)	0.834
Cerebrovascular disease	2 (4.3 %)	4 (17.4 %)	0.070	13 (4.1 %)	2 (3.6 %)	0.711
ECOG-PS score			0.018			0.009
0	13 (28.3 %)	1 (4.3 %)		128 (40.6 %)	13 (9.1 %)	
1	21 (47.7 %)	10 (43.5 %)		112 (35.6 %)	18 (32.7 %)	
≥ 2	12 (26.1 %)	12 (52.2 %)		75 (23.8 %)	23 (41.8 %)	
Respiratory function			0.220			0.088
%VC	74.72 \pm 7.5	76.97 \pm 6.3		75.2 \pm 7.7	73.3 \pm 7.7	
Nutrition						0.175
Serum albumin level (g/dl)	3.5 \pm 0.6	3.2 \pm 0.6	0.064	3.8 \pm 0.6	3.6 \pm 0.6	
Renal function						
Serum creatinine level (mg/dl)	1.0 \pm 0.6	0.9 \pm 0.4	0.823	0.9 \pm 0.4	1.1 \pm 1.1	0.098
Operation factor						
Extent of resection			0.902			0.092
Total	5 (10.9 %)	4 (17.4 %)		79 (25.1 %)	16 (29.1 %)	
Distal	35 (79.1 %)	17 (31.2 %)		191 (60.6 %)	35 (63.6 %)	
Proxymal	1 (2.2 %)	0 (0.0 %)		12 (3.8 %)	4 (7.3 %)	
Pylorus preserving	2 (4.3 %)	1 (4.3 %)		14 (4.4 %)	0 (0.0 %)	
Segmental	2 (4.3 %)	1 (4.3 %)		18 (5.7 %)	0 (0.0 %)	
Local resection	1 (2.2 %)	0 (0.0 %)		1 (0.3 %)	0 (0.0 %)	
Lymphadenectomy			0.513			0.063
D0	4 (9.0 %)	2 (8.7 %)		20 (6.3 %)	0 (0.0 %)	

D1	19 (41.3 %)	6 (26.1 %)		98 (31.1 %)	15 (27.3 %)	
D1+	9 (19.6 %)	4 (17.4 %)		44 (14.0 %)	10 (18.2 %)	
D2	14 (30.4 %)	11 (47.8 %)		153 (48.6 %)	30 (54.5 %)	
Operation time (minutes)	180.5 ± 59.4	200.6 ± 52.3	0.411	208.6 ± 60.5	207.7 ± 39.6	0.911
Blood loss (ml)	233.3 ± 220.0	270 ± 194.7	0.244	290.0 ± 260.2	364.6 ± 287.2	0.049
Pathological stage			0.930			0.035
I	21 (45.7 %)	9 (39.1 %)		158 (50.2 %)	16 (29.1 %)	
II	8 (17.4 %)	4 (17.4 %)		51 (16.2 %)	13 (23.6 %)	
III	9 (19.6 %)	6 (26.1 %)		69 (21.9 %)	18 (32.7 %)	
IV	8 (17.4 %)	4 (17.4 %)		37 (11.7 %)	8 (14.5 %)	