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The Short- and Long-term Outcomes of Gastrectomy in Elderly Patients With Gastric Cancer

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Abstract. *Background: The short- and long-term outcomes of gastrectomy in elderly patients with gastric cancer have not been fully evaluated. Patients and Methods: Patients who underwent gastrectomy were classified into two groups: Non-elderly patients (<80 years old) and elderly patients (≥80 years old). The surgical morbidity, overall and cancer-specific survival in the two groups were compared. Results: A total of 411 patients were evaluated. The rate of overall complication was 29.4% in the non-elderly and 32.4% in the elderly (p=0.699). In the elderly, the overall and cancer-specific survival rates at 5 years after surgery were inferior to those of the younger group (59.8% vs. 66.7%, p=0.103 and 67.9% vs. 78.2%, p=0.028, respectively). Conclusion: The short-term outcomes after gastrectomy were almost equal for the two groups in the present study. The prognosis was poor in elderly patients, especially those with advanced gastric cancer.*

Gastric cancer is one of the main health problems (1). It is the fifth-most frequently diagnosed cancer and the third leading cause of cancer death worldwide. The 5-year survival rate ranges from 10.3% to 57.9% in all stages (1). Surgical resection is accepted as curative treatment for gastric cancer (2). However, complications after gastrectomy remain a clinically relevant problem. Indeed, the morbidity and mortality after gastric resection have been reported in the range of 22.0-42.9% and 0%-0.8%, respectively (3-6).

The number of elderly patients is increasing worldwide, with the proportion of elderly over 80 years old increasing at a rate of 4.0% annually (7). In elderly patients, conditions such as functional impairment and physiological problems are common, which can result in postoperative complications and poor survival (8-10). Surgical procedures, perioperative care, and surgical strategies should thus be carefully planned for elderly patients. However, there have been few previous studies reporting on the safety and feasibility of gastric cancer surgery for older patients. Furthermore, the long-term survival of elderly patients after gastric cancer surgery is largely still unknown.

It is therefore essential to clarify characteristics of elderly patients and assess the effect of age on their treatment outcomes. The present retrospective study compared the short- and long-term outcomes after gastric cancer surgery in elderly patients with those in non-elderly patients.

Patients and Methods

Patients. The study subjects were collected from among consecutive patients in the hospital registry indicated for gastric cancer surgery at the Yokohama City University Hospital between January 2000 and September 2012. Patients with the following were enrolled: Histologically proven gastric adenocarcinoma, no metachronous or concurrent malignancies, and gastrectomy for gastric cancer with curative D1+ or D2 dissection as a first-line treatment. The removed tumor specimens were examined histopathologically, and staging was performed based on tumor invasion and lymph node metastasis, in line with the criteria of the Third English Edition of the General Rules for Gastric Cancer, published by the Japanese Gastric Cancer Association (2).

Surgical procedure. All patients underwent total, distal, or proximal gastrectomy and lymphadenectomy for gastric cancer. As a general rule, D1+ dissection was performed for cT1N0 tumors, while D2

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Key Words: Gastric cancer, elderly patients, gastrectomy, short-term outcomes, long-term outcomes.

Table I. *A comparison of the baseline characteristics [n (%)] for the whole cohort and according to age.*

Variables		All patients (n=411)	<80 years (n=377)	≥80 years (n=34)	*p*-Value
Age, years	Median (range)	69 (29-89)	68 (29-79)	82 (80-89)	
Gender, n (%)	Male	311 (75.6%)	288 (76.4%)	23 (67.6%)	0.296
	Female	100 (24.4%)	89 (23.6%)	11 (32.4%)	
Body mass index, kg/m	Median (range)	22.6 (13.8-35.5)	22.4 (18.7-35.5)	23.0 (13.8-31.0)	0.873
ASA-PS, n (%)	1, 2	224 (54.5%)	212 (56.2%)	12 (35.3%)	**0.030**
	3, 4	187 (45.5%)	165 (43.8%)	22 (64.7%)	
Co-morbidity, n (%)	Cardiovascular disease	152 (36.5%)	132 (35.0%)	20 (58.2%)	**0.009**
	Respiratory disease	27 (6.6%)	24 (6.4%)	3 (8.8%)	0.480
	Diabetes mellitus	50 (12.2%)	44 (11.7%)	6 (17.6%)	0.281
Site of tumor, n (%)	Upper	109 (26.5%)	104 (27.6%)	5 (14.7%)	0.241
	Middle	150 (36.5%)	138 (36.6%)	12 (35.3%)	
	Lower	152 (37.0%)	135 (35.8%)	17 (50.0%)	
Histology, n (%)	Differentiated	225 (54.7%)	201 (53.3%)	24 (70.6%)	0.071
	Undifferentiated	186 (45.3%)	176 (46.7%)	10 (29.4%)	
Tumor diameter, mm	Median (range)	40 (2-250)	40 (2-250)	42 (5-123)	0.527
No. of harvested lymph nodes	Median (range)	36 (3-98)	34 (3-98)	25 (7-59)	**0.005**
Peritoneal lavage cytology, n (%)	Positive	25 (6.1%)	23 (6.1%)	2 (5.9%)	0.702
	Negative	226 (55.0%)	205 (54.4%)	21 (61.8%)	
	Unknown	160 (38.9%)	149 (39.5%)	11 (32.3%)	
Pathological T factor, n (%)	T1	213 (51.8%)	201 (53.3%)	12 (35.3%)	**0.049**
	T2, T3, T4	198 (48.2%)	176 (46.7%)	22 (64.7%)	
Pathological N factor, n (%)	N0	241 (58.6%)	226 (59.9%)	15 (44.1%)	0.101
	N1, N2, N3	170 (41.4%)	151 (40.1%)	19 (55.9%)	
Pathological stage, n (%)	I	233 (56.7%)	220 (58.4%)	13 (38.2%)	0.072
	II, III, IV	178 (43.3%)	157 (41.6%)	21 (61.8%)	
Lymphatic invasion, n (%)	Negative	237 (57.7%)	223 (59.2%)	14 (41.2%)	**0.047**
	Positive	174 (42.3%)	154 (40.8%)	20 (58.8%)	
Vascular invasion, n (%)	Negative	233 (56.7%)	220 (58.4%)	13 (38.2%)	**0.030**
	Positive	178 (43.3%)	157 (41.6%)	21 (61.8%)	

ASA-PS: American Society of Anesthesiologists Physical Status. Bold values indicate statistical significance.

was indicated for cN+ or cT2-T4 tumors, and the spleen was removed during total gastrectomy with lymphadenectomy.

Adjuvant treatment. Patients who were diagnosed with pStage II or III disease generally received adjuvant chemotherapy such as S-1, capecitabine plus oxaliplatin, and S-1 plus docetaxel based on clinical trials or common practice after July 2006. Within 6 weeks after surgery, the patients received 60, 50, or 40 mg of S-1, depending on their body surface area, twice daily for 4 weeks followed by a 2-week rest as a course (6-week schedule) or 2 weeks followed by a 1-week rest as a course (3-week schedule) (11).

Follow-up. In principle, we followed-up patients at outpatient clinics. The blood test results, including tumor markers carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9), and clinical findings were evaluated at least once every 2 weeks in the S-1 treatment group. In the surgery-only group, patients visited the hospital for a re-examination at least once every 3 months for the first year after surgery. After the second year, all patients were followed-up in the same way. Recurrence was confirmed by imaging tests, such as computed tomography, ultrasonography, and endoscopy. Patients had at least one imaging examination every 6 months for the first 3 years after surgery and every year thereafter up to 5 years after surgery.

Definition of postoperative complications. Postoperative complications of grade 2-5 [in accordance with the Clavien-Dindo classification (12)] during the course of hospitalization or within 30 days after surgery were retrospectively determined from the patient's chart. We did not evaluate grade 1 complications in order to eliminate the chance of description bias from the patient's chart.

Evaluations and statistical analyses. The overall survival (OS) was defined as the time from surgery to death. The cancer-specific survival (CSS) was defined as the time from surgery to death from gastric cancer. The information on the patients who did not experience an event was collected on the last observation day. OS and CSS curves were calculated the using the Kaplan-Meier method and compared by log-rank test. Patients were divided into two groups: Non-elderly patients, <80 years old; and elderly patients, ≥80 years old. Comparisons between the two groups were conducted using Student's *t*-test or the unpaired chi-squared method. A value of $p<0.05$ was considered statistically significant. The median with range, or frequency was used to describe the data. All data were analyzed using EZR (Jichi Medical University, Saitama, Japan) and R software (version 3.4.3) (13). The study was approved by the Institutional Review Board of Yokohama City University Hospital (B160707003).

Results

Patient characteristics. Four-hundred and eleven patients were included in this present study: 377 were non-elderly patients, while 34 were elderly. The demographic characteristics and clinicopathological findings of the

Table II. *A comparison of the surgical findings for the whole cohort and according to age.*

Variables		All patients (n=411)	<80 years (n=377)	≥80 years (n=34)	*p*-Value
Approach, n (%)	Open	278 (67.6%)	250 (66.3%)	28 (82.4%)	0.058
	Laparoscopy	133 (32.4%)	127 (33.7%)	6 (17.6%)	
Type of surgery, n (%)	Distal gastrectomy	225 (54.8%)	203 (53.8%)	22 (64.7%)	0.610
	Total gastrectomy	158 (38.4%)	147 (39.1%)	11 (32.3%)	
	Proximal gastrectomy	14 (3.4%)	13 (3.4%)	1 (3.0%)	
	Other	14 (3.4%)	14 (3.7%)	0 (0.0%)	
Lymph node dissection, n (%)	D1+	209 (50.9%)	191 (50.7%)	18 (52.9%)	0.859
	D2	202 (49.1%)	186 (49.3%)	16 (47.1%)	
Reconstruction, n (%)	Billroth-I	189 (46.0%)	169 (44.8%)	20 (58.8%)	0.309
	Roux-Y	205 (49.9%)	192 (50.9%)	13 (38.2%)	
	Other	17 (4.1%)	16 (4.3%)	1 (3.0%)	
Operative time (min)	Median (range)	317 (107-800)	320 (107-800)	248 (112-502)	**0.004**
Intraoperative blood loss (ml)	Median (range)	350 (0-4885)	330 (0-4000)	356 (35-4885)	0.257

Bold values indicate statistical significance.

Table III. *Postoperative complications [n (%)] for the whole cohort and according to age.*

Variables		All patients (n=411)	<80 years (n=377)	≥80 years (n=34)	*p*-Value
Surgical complication	Overall	122 (29.7%)	111 (29.4%)	11 (32.4%)	0.699
	Anastomotic leakage	24 (5.8%)	18 (4.8%)	6 (17.6%)	**0.009**
	Pancreatic fistula	19 (4.6%)	17 (4.5%)	2 (5.9%)	0.664
	Abdominal abscess	14 (3.4%)	13 (3.4%)	1 (2.9%)	0.325
	Respiratory disease	12 (2.9%)	12 (3.1%)	0 (0.0%)	0.610
	Anastomotic stenosis	11 (2.7%)	11 (2.9%)	0 (0.0%)	0.611
	Ileus	13 (3.2%)	10 (2.7%)	3 (8.8%)	0.261
	Surgical site infection	7 (1.7%)	6 (1.6%)	1 (2.9%)	0.456
	Delirium	6 (1.5%)	5 (1.3%)	1 (2.9%)	0.406
	Postoperative bleeding	5 (1.2%)	5 (1.3%)	0 (0.0%)	>0.99
	Chylous ascites	5 (1.2%)	5 (1.3%)	0 (0.0%)	>0.99
	Cardiovascular disease	4 (1.0%)	4 (1.1%)	0 (0.0%)	>0.99
	Other	48 (11.7%)	46 (12.2%)	2 (5.9%)	0.404
Mortality	Yes	2 (0.5%)	2 (0.5%)	0 (0.0%)	>0.99
	No	409 (99.5%)	375 (99.5%)	34 (100.0%)	

Bold values indicate statistical significance.

patients are shown in Table I. The patients with an American Society of Anesthesiology (ASA) score ≥3 were more frequent in the elderly group than in the non-elderly (64.7% *vs*. 43.8%, respectively, *p*=0.030). The rate of cardiovascular disease was significantly higher in the elderly group than in the younger one (35.0% *vs*. 58.2%, *p*=0.009).

Surgical and pathological findings. The intra-operative details are indicated in Table II. The median operative time was significantly longer in the elderly group (320 *vs*. 248 min, respectively, *p*=0.004). The proportion of patients with pathological stage I was higher in the non-elderly group than in the elderly one (58.4% *vs*. 38.2%, *p*=0.072). The median number of harvested lymph nodes was significantly fewer in the elderly group (25 *vs*. 34, *p*=0.005). The proportions of patients with pathological T2 or more tumors and lymphatic and vascular invasion were significantly higher in the elderly group (64.7% *vs*. 46.7%, *p*=0.049; 58.8% *vs*. 40.8%, *p*=0.047; and 61.8% *vs*. 41.6%, *p*=0.030, respectively).

Postoperative complications. The details of the postoperative complications are shown in Table III. The overall complication rate did not significantly differ (*p*=0.699). Anastomotic leakage was the most frequently observed complication in both groups. There were significant differences between the groups in the anastomotic leakage rates, being lower in the non-elderly group (4.8% *vs*. 17.6%, *p*=0.009). 30-Day mortality was confirmed in two patients because of respiratory disease and cardiovascular disease, respectively, in the non-elderly group (0.5%) and was not observed at all in the elderly one.

Survival analyses. The median follow-up time was 50.2 months (range=0.3-122.0 months). The OS curves are shown in Figure 1. The OS curve for the elderly group was inferior to that of the younger one, although the OS rates at 5 years after surgery of 59.8% *vs*. 66.7% respectively, were not statistically significantly different (*p*=0.103).

The CSS curves are shown in Figure 2. The CSS curve for the elderly group was inferior to that of the younger group;

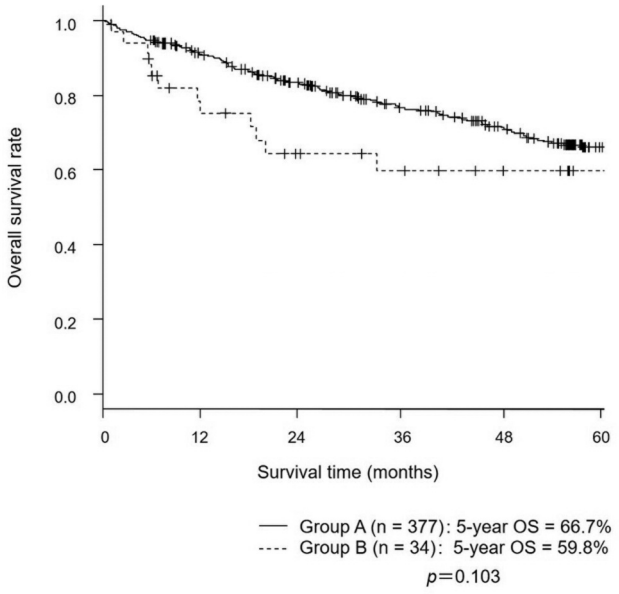

Figure 1. *Overall survival of non-elderly (group A) and elderly (group B) patients in the study groups.*

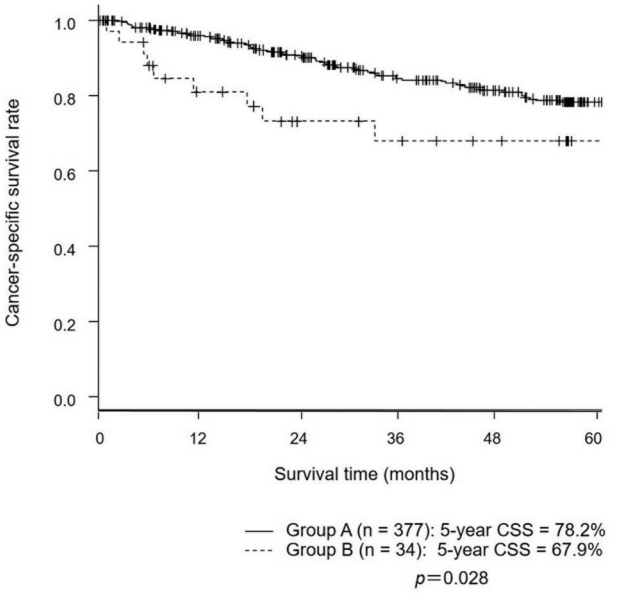

Figure 2. *Cancer-specific survival in non-elderly (group A) and elderly (group B) patients in the study groups.*

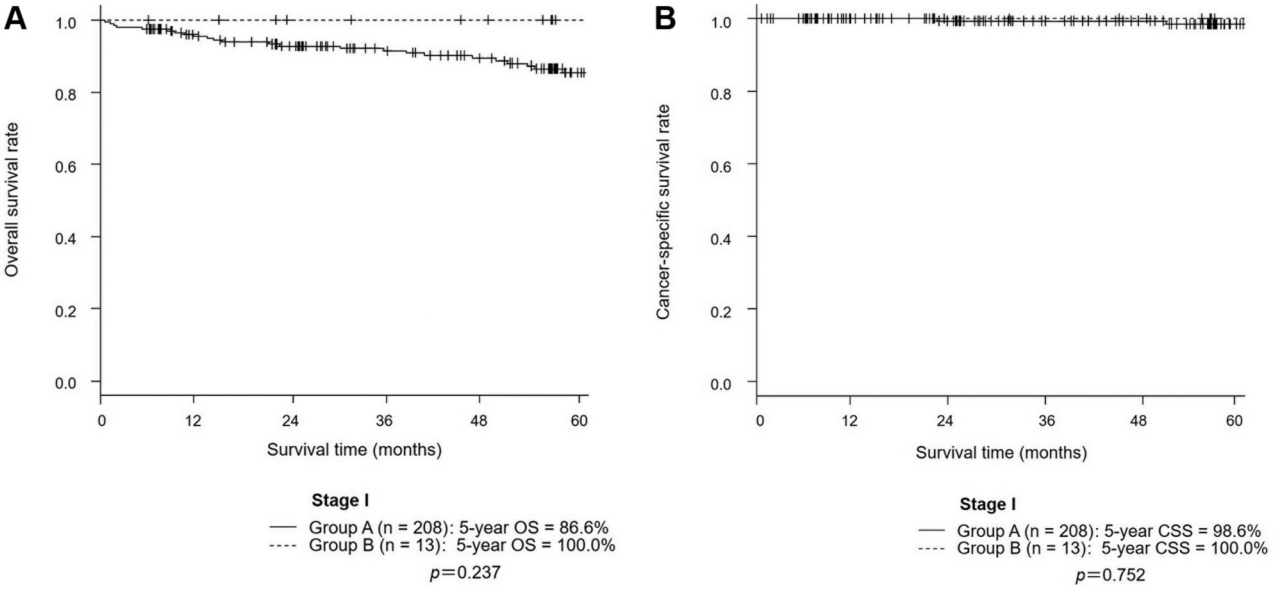

Figure 3. *Overall (A) and cancer-specific (B) survival non-elderly (group A) and elderly (group B) patients with early gastric cancer.*

this was reflected in the significantly lower CSS rate at 5 years after surgery (67.9% *vs*. 78.2%, respectively; p=0.028).

Regarding early gastric cancer, the OS and CSS rates at 5 years after surgery for the elderly group were similar to those of the younger group (100.0% *vs*. 86.6%, p=0.237; and 100.0% *vs*. 98.6%, p=0.752; Figure 3). Regarding advanced gastric cancer, the OS and CSS rates at 5 years after surgery for the elderly group were inferior to those for the younger group (34.3% *vs*. 44.7%, p=0.045; and 44.7% *vs*. 54.7%, p=0.050, respectively; Figure 4).

Reasons for death and recurrence patterns. During the follow-up period, 82 patients (20.0%) died of gastric cancer, and 50 (12.2%) died of other causes (Table IV). The most

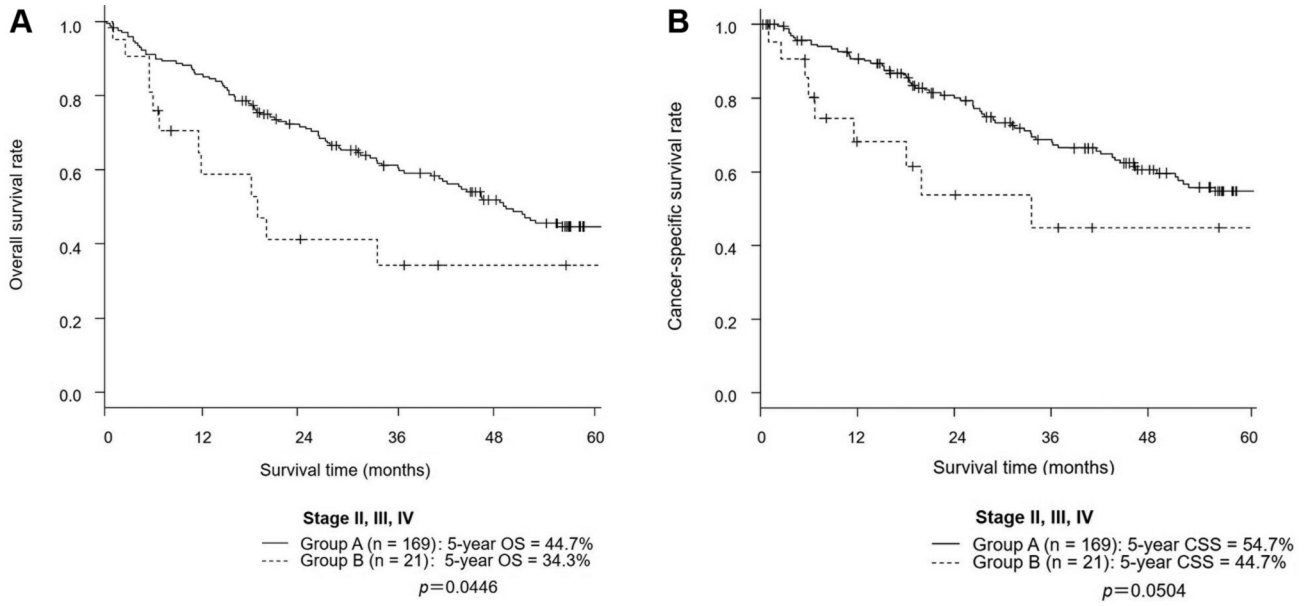

Figure 4. *Overall (A) and cancer-specific (B) survival non-elderly (group A) and elderly (group B) patients with advanced gastric cancer.*

Table IV. *Postoperative outcomes [n (%)] for the whole cohort and according to age.*

Variables		All patients (n=411)	<80 years (n=377)	≥80 years (n=34)	*p*-Value
Cause of death	Gastric cancer	82 (20.0%)	73 (19.4%)	9 (26.5%)	0.369
	Other disease	50 (12.2%)	47 (12.5%)	3 (8.8%)	0.784
	Unknown	3 (0.7%)	3 (0.8%)	0 (0.0%)	>0.99
Recurrence site	Peritoneal dissemination	33 (8.0%)	30 (8.0%)	3 (8.9%)	0.746
	Hematogenous metastasis	31 (7.5%)	30 (8.0%)	1 (2.9%)	0.497
	Lymph node	10 (2.5%)	8 (2.1%)	2 (5.9%)	0.197
	Locoregional	1 (0.2%)	0 (0.0%)	1 (2.9%)	0.083
	Unknown	3 (0.7%)	2 (0.5%)	1 (2.9%)	0.229

common sites of recurrence were the peritoneum (19.0%), hematogenous sites (8.0%), lymph nodes (7.5%), and local recurrences (2.5%), in order of frequency. There were no significant differences between two groups in the reasons for recurrence or death patterns.

Discussion

In the present study, we retrospectively investigated whether or not gastrectomy for patients ≥80 years old with gastric cancer was safe and feasible compared with non-elderly patients. Although our study showed similar findings for elderly and non-elderly patients in the short-term outcomes of gastrectomy, the long-term survival was worse in elderly patients, especially for those with advanced gastric cancer, than in non-elderly patients. Our results therefore suggest that gastrectomy for gastric cancer is a safe option with similar benefits in the short term, regardless of the age of the patient, but surgical indications for elderly patients with advanced gastric cancer should be carefully considered.

In the present study, the short-term results were not significantly different between elderly and non-elderly patients. Some authors reported similar results. For example, Nakanoko *et al*. (14) evaluated 41 patients ≥80 years old and 430 patients <80 years old who underwent gastrectomy for gastric cancer and found no significant difference in the incidence of postoperative complications (12.8% *vs*. 9.8%). Similarly, Kim *et al*. (15) analyzed 31 elderly patients and 404 younger patients and reported that postoperative complications at rates of 16.1% and 11.9%, respectively (p=0.565).

In contrast, the rate of anastomotic leakage was higher in the elderly patients than in the non-elderly ones in the present study (17.6% *vs*. 4.8%, p=0.009). Cardiovascular disease and high ASA scores were previously reported as risk

factors for anastomotic leakage. Kim *et al*. (16) reported that preoperative cardiovascular disease was an independent risk factor for anastomotic leakage (odds ratio=1.826, 95% interval confidence=1.088-3.067; $p<0.001$). In addition, Vural *et al*. (17) reported that a high ASA score (≥3) was significantly associated with an increased rate of postoperative complications compared with a low ASA score (≤2) (odds ratio=2.285, $p=0.033$). In our study, the ratio of preoperative cardiovascular disease to a high ASA score was significantly higher in the older patients than in the younger ones ($p=0.009$ and $p=0.006$, respectively), which may have resulted in the occurrence of anastomotic leakage.

In the present study, the 5-year OS and CSS rates were worse in the elderly patients, especially those with advanced gastric cancer, than in the non-elderly patients. However, some authors have reported different results. Isobe *et al*. reported that the OS and CSS rates in the most elderly (≥85 years old, n=56) and elderly (80-84 years old, n=161) patients at 3 years after gastrectomy for gastric cancer were not significantly different (70.1% *vs*. 68.5%, $p=0.885$; and 73.8% *vs*. 72.6%, $p=0.984$, respectively) (18). Mengardo *et al*. also reported that elderly patients (≥80 years old, n=75) who underwent gastrectomy for gastric cancer had similar 5-year OS and CSS rates to younger patients [70-79 years (n=166), $p=0.107$; and ≤69 years (n=226), $p=0.319$] (19).

However, other authors have reported that a worse ASA score, an advanced pathological stage, and infectious complications are associated with worse long-term outcomes in elderly patients with gastric cancer than those in non-elderly patients (19-21). Mengardo *et al*. found that the 5-year OS rate was significantly lower in elderly patients (>80 years: 16%) than in non-elderly patients [(≤69 years: 38%) and 70-79 years: 48%; $p=0.024$) when analyzing only patients who underwent gastrectomy for gastric cancer with an ASA score of 3-4 (19). Tokunaga *et al*. reported that patients with postoperative intraperitoneal complications (pancreas-related complications, anastomotic leakage, and intra-abdominal abscess) had a worse 5-year OS rate than those without such complications (66.4% *vs*. 86.8%, $p<0.001$) (21). In the present study, the ASA score and pathological stage were worse in elderly patients than in younger ones ($p=0.006$ and 0.072, respectively), and the rate of intra-abdominal complications (anastomotic leakage, abdominal abscess, and pancreatic fistula) was higher in elderly patients than non-elderly patients (20.6% *vs*. 9.8%, $p=0.075$), which may have resulted in worse OS and CSS rates in elderly patients than in younger ones.

Several limitations associated with the present study warrant mention. Therefore, special care must be taken when interpreting our findings. Initially, a relatively small sample of elderly patients (n=34) was enrolled in this study. In addition, the indication of surgery was determined by the operator's preference. This study may therefore have selection bias. For example, advanced gastric cancer was more frequently observed in the elderly patients than in the non-elderly patients. Minimally invasive treatment, such as endoscopic treatment, was likely prioritized over surgical resection for early gastric cancer in elderly patients. Furthermore, surgery was often indicated for advanced cancer with life-threatening symptoms, such as anemia and stenosis, even when considering the risks of surgery. Secondly, the period of this study was relatively long (about 12 years). Steady improvement of operative devices and regimens for chemotherapy during this period may have affected the result. Thirdly, this study may have had selection bias because no standard treatment, such as adjuvant chemotherapy or chemotherapy, has been established for cases of relapse in elderly patients, and the indication of chemotherapy was determined by the physician's preference. This may therefore have affected the results. Given these limitations, the current results need to be tested in other cohort series.

In summary, gastrectomy for gastric cancer is a safe option with similar benefits in the short term regardless of a patient's age; however, surgical indications for elderly patients with advanced gastric cancer should be carefully considered.

Conflicts of Interest

The Authors have no conflicts of interest to declare regarding this study.

Authors' Contributions

KK, KK and TA contributed to the conception and design of the study. KK, KK, TA, IH, KH, MM, YA, YM, KK, MN, MM and YR contributed to the data collection and assembly. All of the Authors contributed to the data acquisition and interpretation of the analyzed data. KK and KK wrote the article. All of the Authors contributed to the critical revision of the article. All of the Authors read and approved the final article.

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