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Surgical outcomes and survival of patients over 80 years old who underwent curative resection for gastric cancer

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Purpose: Among patients with gastric cancer who underwent radical gastrectomy, the proportion of patients aged ≥80 years has increased. This study aimed to evaluate surgical outcomes and survival of patients aged ≥80 years who underwent curative resection for gastric cancer and identify independent factors that affect postoperative survival.
Methods: This retrospective study enrolled 1,066 patients aged ≥65 years with gastric cancer who underwent curative resection between January 2014 and December 2018 at a single institution. They were divided into those aged ≥80 years (old-elderly group) and 65–79 years (young-elderly group). Their clinicopathological characteristics and surgical outcomes were compared.
Results: Of the 1,066 patients, 136 (12.8%) were 80 years or older. Higher American Society of Anesthesiologists (ASA) physical status classification and more advanced cancers were observed in the old-elderly group than in the young-elderly group. No significant difference in postoperative complications was found between the groups. At a median follow-up of 49.1 months, the 5-year overall survival rate after surgery for the old-elderly group was lower than that for the young-elderly group (75.6% *vs*. 87.0%, P < 0.001). However, the 5-year disease-specific survival rate was comparable between the groups (90.1% *vs*. 92.2%, P = 0.324). ASA physical status classification, pathologic stage, and surgical approach were independent predictors of overall survival.
Conclusion: Old-elderly patients aged ≥80 years had comparable postoperative outcomes and disease-specific survival to the young-elderly group, suggesting that curative gastrectomy can be considered a viable option for octogenarian patients with gastric cancer.
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Key Words: Gastrectomy, Octogenarians, Stomach neoplasms, Survival

INTRODUCTION

Gastric cancer is the fifth most common cancer worldwide and the 4th leading cause of cancer-related death [1]. It is one of the most commonly diagnosed cancers in Korea, which comprised 10.8% of all new cancer occurrences in 2020, and the age-specific incidence showed a gradual increase in gastric cancer incidence with age [2]. According to the National Statistical Office, life expectancy in South Korea has continuously increased over the past 50 years, and in 2019, the average life expectancy of Koreans reached 83.3 years [3]. When stratified by age, individuals who had reached 80 years of

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age had a life expectancy of 9.53 years. In accordance with the increasing life expectancy, the number of elderly patients with gastric cancer in South Korea has also increased. The Korean Central Cancer Registry data showed that the proportion of patients aged >80 years gradually increased from 6.7% to 11.7% over the last 2 decades [4].

Because elderly patients often have various underlying medical conditions and are vulnerable to stress caused by the surgical procedure, the risk of postoperative complications is higher and the life expectancy after surgical treatment is relatively shorter than younger patients with gastric cancer [5-8]. However, the survival benefits and the quality of life after surgical treatment cannot be overlooked even among elderly patients who fulfill the indications for radical gastrectomy. Therefore, the risk factors for gastrectomy in elderly patients should be investigated to establish a guideline for selecting the appropriate elderly patients apt for surgical treatment.

In this study, we evaluated the survival rates of patients aged ≥80 years who underwent surgical resection to analyze the safety of gastric cancer surgery in elderly patients and identify prognostic factors for survival after radical surgical treatment in elderly patients with gastric cancer.

METHODS

This study was approved by the Institutional Review Board of Kyungpook National University Chilgok Hospital (No. 2023-05-017), and the need for informed consent was waived.

Data collection

Data of patients with gastric cancer aged >65 years who underwent radical gastrectomy at Kyungpook National University Chilgok Hospital from January 2014 to December 2018 were retrospectively analyzed. Clinicopathological data included sex, body mass index (BMI), American Society of Anesthesiologists physical status (ASA PS) classification, and pathologic stage (pStage) according to the 8th edition of the American Joint Committee on Cancer Classification. Treatment data included the extent of surgery, surgical approach, extent of lymph node dissection, combined resection, residual tumor, and adjuvant chemotherapy. The postoperative outcomes included postoperative mortality, postoperative complications classified according to the Clavien-Dindo (CD) classification, overall survival (OS), and disease-specific survival (DSS) [9].

Patients were divided into the group aged ≥80 years (old-elderly group) and the group aged 65–79 years (young-elderly group). Clinicopathological data and surgical outcomes including survival were compared between the 2 age groups.

Surgical procedure and postoperative surveillance

Patients underwent standard radical gastrectomy with D1+ or more lymphadenectomy according to the gastric cancer treatment guidelines from Korea and Japan [10,11]. During the follow-up period, patients were monitored at intervals of every 3 months in the first year after surgery, every 6 months for up to 3 years, and annually thereafter. At each visit, routine laboratory tests, including tumor marker assessments, were conducted, and abdominopelvic computed tomography scans were performed every 6 months to assess the disease status. Patient survival was ascertained by reviewing medical records from follow-up visits or by telephone contact. The OS was defined as the duration from surgery to death, irrespective of the cause, or until the last follow-up visit. The DSS was defined as the time from index surgery to gastric cancer-related death. Patients were followed until death or April 2022.

Statistical analysis

Data were analyzed using the chi-square test for categorical variables and the Student t-test for continuous variables. The OS and DSS were estimated with the Kaplan-Meier method, and the difference between the 2 groups was assessed using a log-rank test. We used the Cox regression model to conduct univariate and multivariate analyses, aiming to identify independent prognostic factors for the OS and DSS in all patients and each respective group. In the multivariate analysis, variables were selected using the backward conditional elimination method. In all analyses, P-values of <0.05 were considered statistically significant. We conducted the statistical analyses using IBM SPSS Statistics for Windows ver. 26 (IBM Corp.).

RESULTS

Patient demographics and clinicopathological characteristics

Between 2014 and 2018, 1,066 patients aged ≥65 years underwent gastrectomy with curative intent for gastric cancer, including 136 patients (12.8%) aged ≥80 years and 930 (87.2%) aged 65–79 years. The patient characteristics for each group are listed in Table 1. The mean age values of each group were 71.6 and 82.1 years, respectively. A significant difference in sex distribution was found, with the old-elderly group including more female patients (41.2% *vs.* 30.2%, P = 0.010). ASA PS classification was significantly higher in the old-elderly group (P < 0.001).

Operative characteristics, including the extent of surgery, surgical approach, and extent of lymph node dissection, were comparable between the 2 groups. No significant differences were found between the groups regarding postoperative complications. Pathologic stage was significantly different between the groups, with the old-elderly group having a more advanced disease than the young-elderly group (P = 0.025).

Table 1. Clinicopathological characteristics of patients

Characteristic	Young-elderly group	Old-elderly group	P-value
No. of patients	930	136	
Sex			0.010
Male	649 (69.8)	80 (58.8)	
Female	281 (30.2)	56 (41.2)	
Age (yr)	71.6 ± 4.2	82.1 ± 2.2	<0.001
Body mass index (kg/m^2)	23.7 ± 3.3	23.3 ± 3.3	0.167
ASA PS classification			<0.001
I	257 (27.6)	20 (14.7)	
II	615 (66.1)	98 (72.1)	
III	58 (6.2)	18 (13.2)	
Surgical extent			0.457
Partial (DG, PG, PPG)	723 (77.7)	112 (82.4)	
Total gastrectomy	158 (17.0)	19 (14.0)	
Extended surgery	49 (5.3)	5 (3.7)	
Surgical approach			0.653
Laparoscopic	357 (38.4)	55 (40.4)	
Open	572 (61.6)	81 (59.6)	
Lymph node dissection			0.702
Less than D2	232 (24.9)	36 (26.5)	
D2 or more	698 (75.1)	100 (73.5)	
Pathologic stage[a]			0.025
IA	538 (57.8)	61 (44.9)	
IB	79 (8.5)	11 (8.1)	
IIA	89 (9.6)	12 (8.8)	
IIB	59 (6.3)	12 (8.8)	
IIIA	57 (6.1)	14 (10.3)	
IIIB	57 (6.1)	11 (8.1)	
IIIC	51 (5.5)	15 (11.0)	
Adjuvant chemotherapy	164 (17.6)	10 (7.4)	0.002
Death during follow-up	120 (12.9)	31 (22.8)	0.002
Postoperative complication[b]			0.942
None	618 (66.5)	89 (65.4)	
I	175 (18.8)	30 (22.1)	
II	106 (11.4)	14 (10.3)	
IIIa	21 (2.3)	2 (1.47)	
IIIb	3 (0.3)	0 (0)	
IV	1 (0.1)	0 (0)	
V	6 (0.6)	1 (0.7)	

Values are presented as number only, number (%), or mean ± standard deviation.
ASA PS, American Society of Anesthesiologists physical status; DG, distal gastrectomy; PG, proximal gastrectomy; PPG, pylorus-preserving gastrectomy.
[a]Pathologic stages were described according to the 8th edition of the American Joint Committee on Cancer Classification.
[b]Severity of postoperative complications was assessed according to the modified Clavien-Dindo grading system.

Patients with stage ≥II comprised 47.1% of the old-elderly group and 33.7% of the young-elderly group. The old-elderly group was significantly less likely to have received adjuvant chemotherapy (7.4% *vs.* 17.6%, P < 0.001).

Survival outcomes

The median follow-up duration for all patients was 49.1 months (range, 0.2–98.2 months). The median follow-up durations for the old-elderly and young-elderly groups were 34.4 months (range, 0.3–98.2 months) and 52.6 months (range, 0.2–98.0 months), respectively (P < 0.001). In this study, 151 deaths (14.2%) occurred, of which 72 deaths (47.7%) were due to disease recurrence during the follow-up.

A significant difference in OS was found between the 2 groups, favoring the young-elderly group (P < 0.001, Fig. 1A). The 5-year OS rates were 85.1% and 70.7% in the young-elderly and old-elderly groups, respectively. When stratified by the pStage, the difference in OS was shown only in stage II (Fig. 1B–D). However, no significant differences in the DSS were found between the 2 groups, including all stages or stratified by each

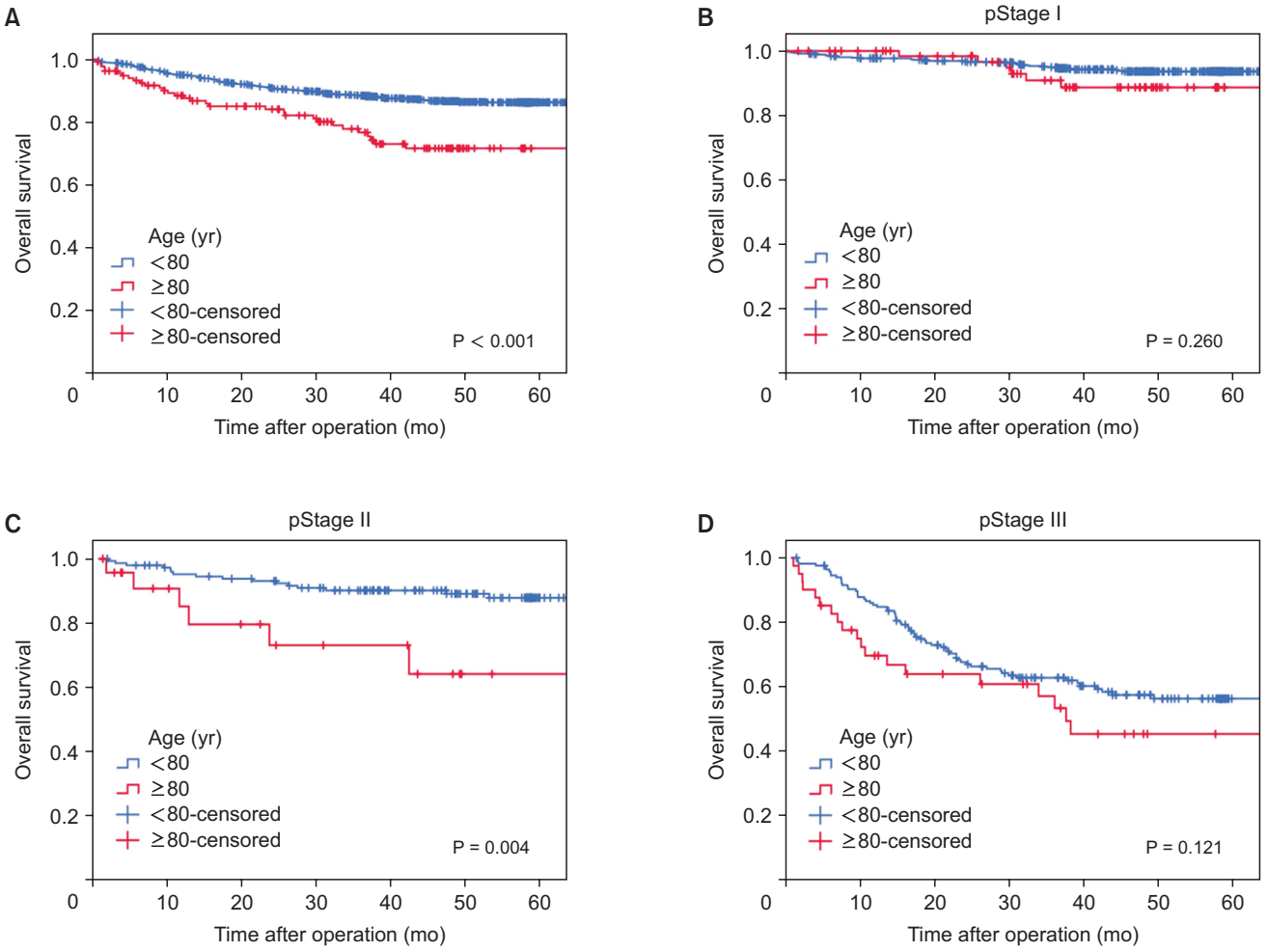

Fig. 1. Comparison of overall survival between the old-elderly and the young-elderly groups stratified by pathologic stage. (A) All pathologic stages (stages I–III, P < 0.001). (B) Stage I (P = 0.260). (C) Stage II (P = 0.004). (D) Stage III (P = 0.121, log-rank test).

stage (Fig. 2).

Univariate analysis revealed that worse OS was associated with age ≥80 years, extended surgery, advanced pStage, adjuvant chemotherapy, severe complication, open approach, D2 or more lymph node dissection, and male sex. The multivariate analysis demonstrated that age of ≥80 years (HR, 2.058; 95% CI, 1.342–3.157), extended surgery (HR, 2.210; 95% CI, 1.338–3.651), pStage II (HR, 1.780; 95% CI, 1.022–3.098), pStage III (HR, 5.831; 95% CI, 3.724–9.130), adjuvant chemotherapy (HR, 1.516; 95% CI, 1.009–2.279), and severe complications (HR, 2.990; 95% CI, 1.684–5.308) were independent prognostic factors for worse OS (Table 2).

The DSS was negatively associated with surgical extent, lymph node dissection of D2 or more, advanced pStage, adjuvant chemotherapy, male sex, and open approach. In the multivariate analysis, only extended surgery (HR, 3.153; 95% CI, 1.691–5.880), pStage III (HR, 11.064; 95% CI, 4.905–24.958), and adjuvant chemotherapy (HR, 1.981; 95% CI, 1.166–3.364) were independently related to worse DSS (Table 3).

Of the 151 death events, 72 patients (47.7%) died of gastric cancer and 79 (52.3%) died of other causes. Only 10 of 31 death events (32.3%) in the old-elderly group were related to gastric cancer. The other 21 deaths (67.7%) in the old-elderly group were attributable to causes other than gastric cancer, and the exact causes of death were mostly unknown. In the young-elderly group, 58 patients of 120 death events (48.3%) died from causes other than gastric cancer.

DISCUSSION

This study demonstrated that the old-elderly group tended to have more advanced disease but was less likely to have adjuvant chemotherapy after curative resection. The incidence of early postoperative complications was comparable between the 2 age groups despite the worse physical status and more advanced disease in the old-elderly group. The old-elderly group had

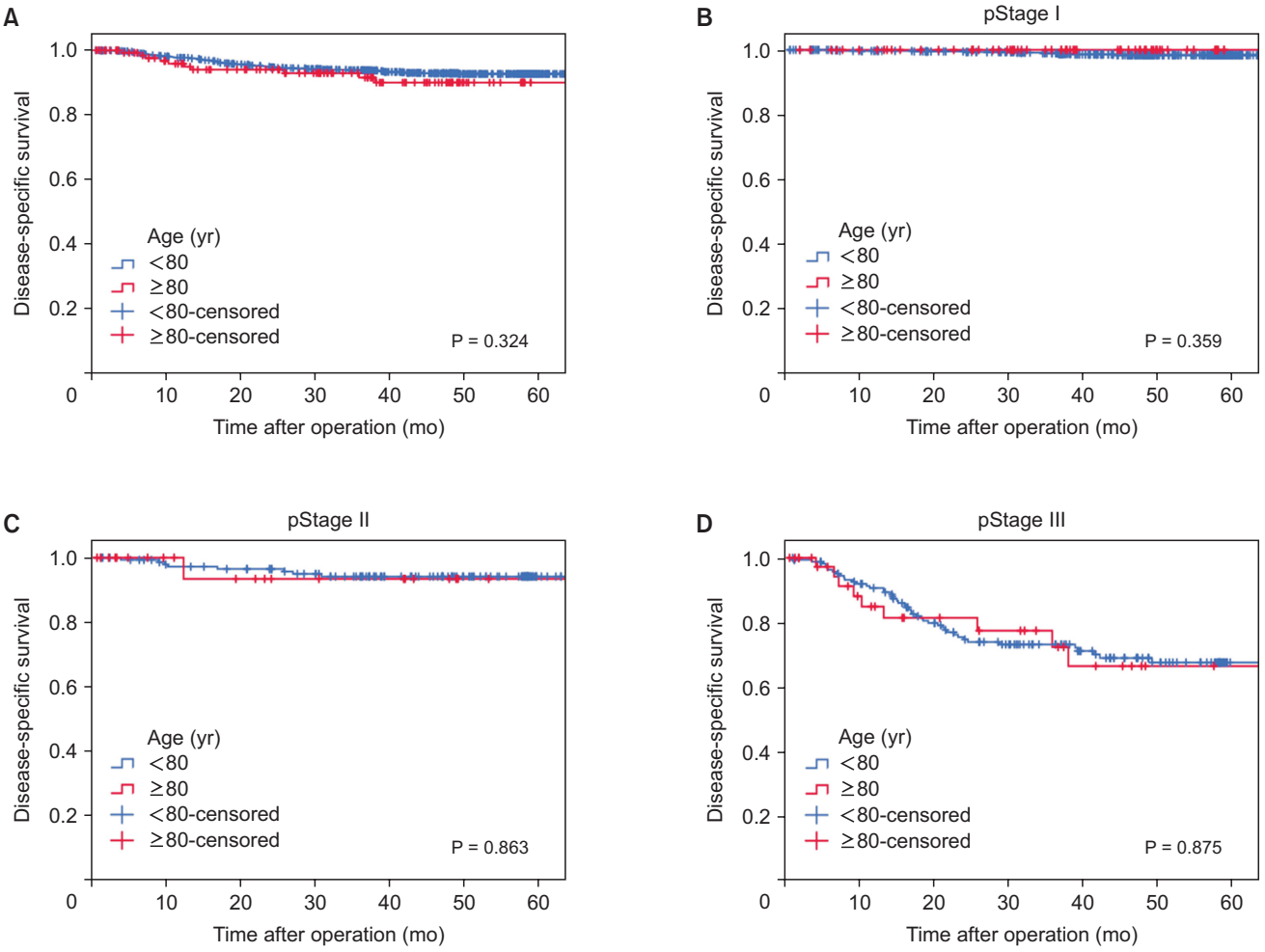

Fig. 2. Comparison of the disease-specific survival between the old-elderly and the young-elderly groups stratified by pathologic stage. (A) All pathologic stages (stages I–III, P = 0.324). (B) Stage I (P = 0.359). (C) Stage II (P = 0.863). (D) Stage III (P = 0.875, log-rank test).

worse OS than the young-elderly group, whereas the DSS was comparable between the groups, which reflected the finding that nearly half of the deaths were related to causes other than gastric cancer.

The increasing life expectancy worldwide is leading to a rise in the proportion of elderly individuals, increasing the number of elderly populations diagnosed with cancer [12]. Surgical treatment of these geriatric patients requires careful consideration of functional changes due to aging, underlying diseases, comorbidity risks, and concerns about the quality of life after treatment. Geriatric patients may have slow or difficult recovery after surgery due to underlying conditions, and a high risk of complications after surgery can lead to high mortality rates. In addition, alternative treatment methods may be considered for geriatric patients to avoid a decline in their quality of life following aggressive surgical treatment.

The proportion of patients aged ≥71 years has increased from 9.1% in 1995 to 28.8% in 2019 among patients who underwent gastric cancer surgery in Korea according to the nationwide survey results [13]. Similar to the characteristics of geriatric patients with cancer in the previous literature [14-16], old-elderly patients showed a higher ASA PS classification and higher pStage than the young-elderly group and received less aggressive treatment in the present study.

Several studies have shown that early postoperative complications or mortality occur more frequently in elderly patients after radical gastrectomy [14-17]. Wakahara et al. [15] reported that the rate of severe complications of CD grade ≥IIIa was 10.5% in the elderly group, higher than that in the control group. Takeshita et al. [14] reported that the postoperative mortality rate was 1.9% in the elderly group and was significantly higher than 0.7% in the non-elderly group. In this study, the incidence of severe postoperative complications (CD grade ≥III) in the old-elderly group was 2.2%, which was comparable to the young-elderly group despite the higher ASA PS classification and presence of more comorbidities. It is also

Table 2. Predictors of overall survival

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (yr)				
65–79	Reference		Reference	
≥80	2.236 (1.505–3.321)	<0.001	2.058 (1.342–3.157)	0.001
Sex				
Male	Reference			
Female	0.648 (0.445–0.942)	0.023		
Body mass index (kg/m^2)				
<25	Reference			
≥25	0.882 (0.621–1.253)	0.484		
ASA PS classification				
I	Reference			
II	1.098 (0.753–1.601)	0.627		
III	1.535 (0.830–2.839)	0.172		
Surgical approach				
Laparoscopic	Reference			
Open	3.324 (2.179–5.073)	<0.001		
Surgical extent				
Partial (DG, PG, PPG)	Reference		Reference	
Total gastrectomy	2.223 (1.537–3.217)	<0.001	1.359 (0.927–1.990)	0.116
Extended surgery	4.305 (2.650–6.993)	<0.001	2.210 (1.338–3.651)	0.002
Lymph node dissection				
Less than D2	Reference			
D2 or more	3.288 (1.929–5.605)	<0.001		
Severe complications[a)]	3.778 (2.139–6.671)	<0.001	2.990 (1.684–5.308)	<0.001
Pathologic stage				
I	Reference		Reference	
II	2.217 (1.329–3.698)	0.002	1.780 (1.022–3.098)	0.042
III	8.870 (6.152–12.789)	<0.001	5.831 (3.724–9.130)	<0.001
Adjuvant chemotherapy	3.564 (2.570–4.943)	<0.001	1.516 (1.009–2.279)	0.045

Variables were selected using backward conditional elimination method in the multivariate analysis.
HR, hazard ratio; CI, confidence interval; ASA PS, American Society of Anesthesiologists physical status; DG, distal gastrectomy; PG, proximal gastrectomy; PPG, pylorus-preserving gastrectomy.
[a)]Severe complication is defined as grade III or higher according to the Clavien-Dindo grading system.

comparable to the complication rate reported in overall patients with gastric cancer in previous studies, and much smaller than those reported in elderly patients with gastric cancer [18-21]. This might be attributable to the careful selection of eligible patients for surgery in the old-elderly group. Furthermore, this result is from a relatively large-volume center specializing in gastric cancer treatment. Nonetheless, this study suggests that the risk of complications after surgery is not unconditionally high in carefully selected elderly patients.

Previous studies have shown that radical surgical treatment in patients aged 75–80 years who had gastric cancer could achieve oncologic outcomes similar to the younger population; however, the results were not completely consistent [14-17]. Wakahara et al. [15] and Tan et al. [20] reported that the OS between the 2 age groups (≥75 years *vs.* <75 years) were not significantly different. However, Takeshita et al. [14] and Kim et al. [16] showed that the group aged ≥80 years had significantly poorer OS, whereas the DSS was comparable to that in the younger group, which was consistent with our study results. This difference might be due to the different cutoff values used to define the elderly group as those aged ≥80 years were more likely to encounter non-cancer-related death events. The higher proportion of patients with early disease stage could be another reason because these patients were less likely to die of gastric cancer. This study revealed that the old-elderly group had worse OS than the young-elderly group, mainly due to noncancerous reasons. This pattern was particularly evident in patients with earlier disease stages (stages I and II), in which only 1 of 12 death events resulted from gastric cancer progression. However, the DSS was not affected by age group in our study and in previous publications [16], suggesting that the therapeutic effect of surgery for cancer is the same regardless of age.

Table 3. Prognostic factors of disease-specific survival

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (yr)				
65–79	Reference			
≥80	1.397 (0.716–2.727)	0.327		
Sex				
Male	Reference			
Female	0.545 (0.309–0.963)	0.037		
Body mass index (kg/m^2)				
<25	Reference			
≥25	1.009 (0.615–1.656)	0.972		
ASA PS classification				
I	Reference			
II	0.681 (0.415–1.118)	0.129		
III	0.809 (0.310–2.113)	0.665		
Surgical approach				
Laparoscopic	Reference			
Open	15.962 (5.024–50.715)	<0.001		
Surgical extent				
Partial (DG, PG, PPG)	Reference		Reference	
Total gastrectomy	3.291 (1.939–5.587)	<0.001	1.498 (0.871–2.575)	0.144
Extended surgery	8.560 (4.658–15.729)	<0.001	3.153 (1.691–5.880)	<0.001
Lymph node dissection				
Less than D2	Reference		Reference	
D2 or more	25.869 (3.594–186.196)	0.001	5.645 (0.743–42.867)	0.094
Severe complications[a]	2.383 (0.869–6.534)	0.091		
Pathologic stage				
I	Reference		Reference	
II	4.439 (1.762–11.183)	0.002	2.176 (0.810–5.851)	0.123
III	27.603 (13.606–55.998)	<0.001	11.064 (4.905–24.958)	<0.001
Adjuvant chemotherapy	7.800 (4.881–12.464)	<0.001	1.981 (1.166–3.364)	0.011

Variables were selected using backward conditional elimination method in the multivariate analysis.
HR, hazard ratio; CI, confidence interval; ASA PS, American Society of Anesthesiologists physical status; DG, distal gastrectomy; PG, proximal gastrectomy; PPG, pylorus-preserving gastrectomy.
[a]Severe complication is defined as grade III or higher according to the Clavien-Dindo grading system.

According to the Korean Practice Guidelines for Gastric Cancer, adjuvant chemotherapy is recommended for stage II or III disease after curative gastrectomy to improve survival [22]. Unexpectedly, adjuvant chemotherapy was a poor prognostic factor for both DSS and OS in the present study, and it appears to be related to the advanced disease status as patients with more advanced stages tend to receive adjuvant chemotherapy. In addition, the proportion of patients receiving adjuvant chemotherapy was significantly smaller in the old-elderly group (7.4% *vs.* 17.6%) despite advanced gastric cancer being more frequently observed in the old-elderly group and only 10 patients (15.6%) of the old-elderly group above stage II have received adjuvant chemotherapy in the present study. Many clinicians hesitate to administer adjuvant chemotherapy to elderly patients because of the higher risk of complications, higher incidence of comorbidities, and higher rates of patient refusal [23]. In this study, the comparable DSS between the 2 age groups despite the lower administration of chemotherapy in the old-elderly group suggests that further investigation is needed to determine the survival benefit of adjuvant chemotherapy in the old-elderly patients and whether to follow standard guidelines for this specific age population.

This study has several limitations. This study was a retrospective cohort study in a single institution. This study design might have led to a critical selection bias because only those who were eligible for surgery were included in the analysis. This study cohort excluded patients with poor performance who were unable to undergo surgical treatment, and this selection process could have influenced the relatively favorable results observed in the old-elderly group. The number of patients in the old-elderly group was markedly small, and the heterogeneity of patient demographics and pathologic

staging between the 2 age groups is another limitation of this study, although the heterogeneity has been adjusted in the statistical analysis. Furthermore, loss to followup appeared to happen more frequently in the old-elderly group judging from the shorter median duration of follow-up, which might have affected the survival outcomes. Well-designed prospective studies are required to provide a more optimal dataset for getting more accurate results.

Radical gastrectomy with curative intent is comparably safe and effective in patients aged ≥80 years, and old age alone should not be the exclusion criterion for surgical treatment of a potentially curable disease. Nonetheless, patients eligible for curative surgery must be carefully selected considering surgical risks and survival benefits based on the physical status and cancer stages in each old-elderly patient.

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Conflict of Interest

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

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