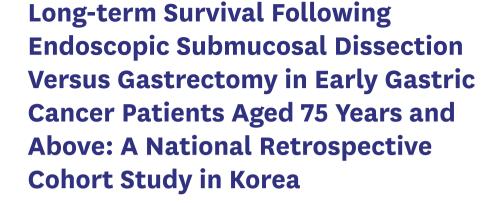


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ABSTRACT

Purpose: Despite a growing older adult population, few studies have compared the long-term outcomes of endoscopic submucosal dissection (ESD) with those of gastrectomy. This study examines long-term survival among older patients with early gastric cancer (EGC) treated with ESD versus gastrectomy.

Materials and Methods: This retrospective cohort study used data from the Korea Clinical Data Utilization Network for Research Excellence. Patients aged ≥75 with stage IA gastric cancer (diagnosed 2014–2015) who underwent ESD or gastrectomy were followed for 5 years. All-cause and cause-specific mortality were assessed using Cox proportional hazard models and propensity score matching.

Results: Of the 442 patients (ESD, 269; gastrectomy, 173), the 5-year overall survival rates were 85.9% for ESD and 80.9% for gastrectomy (P=0.140). In patients aged ≥80, gastrectomy showed higher risks of total (adjusted hazard ratio [aHR], 3.29; 95% CI, 1.70–6.35) and gastric cancer-specific death (aHR, 7.18; 95% CI, 2.08–24.82) compared with ESD. In mucosaconfined lesions, gastrectomy also showed increased gastric cancer-specific mortality (aHR, 6.11; 95% CI, 1.93–19.35). The survival benefit of ESD was comparable to that of gastrectomy among patients aged 75–79 years and those with confined submucosal lesions.

Conclusions: ESD may offer better outcomes than gastrectomy among older patients with stage IA gastric cancer, particularly those aged ≥80 or with mucosa-confined lesions. ESD and gastrectomy may provide similar survival outcomes among patients aged 75–79 years and those with submucosa-confined lesions. These findings support the use of adaptive treatment strategies in older patients with EGC.

Keywords: Stomach neoplasms; Endoscopic mucosal resection; Gastrectomy; Survival rate; Aged



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Conflict of Interest

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

Author Contributions

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INTRODUCTION

In 2022, gastric cancer was the fifth most common cancer and the fifth leading cause of cancer-related deaths worldwide [1]. In Korea, gastric cancer is the fifth most common cancer (age-standardized incidence rate of 26.8 per 100,000 people) and the fourth leading cause of cancer-related deaths (age-standardized mortality rate of 5.7 per 100,000 people) in 2022 [2]. The recent expansion of nationwide gastric cancer screening programs has led to early detection, with the proportion of localized gastric cancers increasing from 53% in 2006 to 63% in 2019 [3-5]. Moreover, the percentage of patients over 70 years of age with gastric cancer in Korea has gradually increased from 28% in 1999 to 37% in 2019.

Endoscopic submucosal dissection (ESD) and radical gastrectomy are the standard treatment options for early gastric cancer (EGC) [5]. ESD is recommended for well or moderately differentiated tumors <2 cm in size and mucosal cancers without ulceration [5]. Although ESD and gastrectomy offer similar overall survival (OS) rates, ESD is less invasive, less expensive, and is associated with faster recovery and better quality of life [6,7]. However, ESD carries a higher risk of synchronous and metachronous lesions and recurrence than does gastrectomy [6,8]. Global guidelines rely on trials conducted among relatively younger patients (45–65 years) and there is limited research comparing long-term ESD versus gastrectomy outcomes in older patients with EGC [9-11]. Furthermore, the Korean Practice Guidelines for Gastric Cancer 2022 reported a comparable survival benefit between ESD and gastrectomy, based on limited studies [5]. These findings underscore the need for further research on survival outcomes, particularly among patients aged ≥75, given the higher prevalence of comorbidities, reduced cardiopulmonary function, and weakened immunity in these patients.

In this study, we assessed the long-term outcomes of ESD versus gastrectomy in older Korean patients with EGC using nationwide data. We analyzed OS and gastric cancer-specific mortality, with subgroup analyses based on age (75–79, ≥80) and tumor invasion depth (mucosa, submucosa) to gain a clearer understanding of treatment effectiveness in this population.

MATERIALS AND METHODS

Data source

We conducted a retrospective cohort study using the linked database from the Korea Clinical Data Utilization Network for Research Excellence (K-CURE) platform [12]. The collaborative staging dataset, sourced from the Korea Central Cancer Registry (KCCR) and collected annually from 52 hospitals and local registries (2012–2019), represents 75% of all gastric cancer cases in Korea, and includes a random sample of 10% of patients stratified by age, sex, and Surveillance, Epidemiology, and End Results summary stage [13]. The dataset features demographic and tumor characteristics, along with detailed pathologic staging information, reviewed by trained cancer registrars using medical records encompassing a period of up to 4 months prior to and following the initial cancer diagnosis to identify the most advanced clinical or pathological stage. Additionally, the KCCR collaborative staging data were linked to the Cancer Public Library database, integrating patient information from Statistics Korea, National Health Insurance Service (NHIS), and Health Insurance Review and Assessment Service (HIRA) [12].



Study population

We included patients aged ≥75 years who underwent either ESD or gastrectomy for stage 1A gastric cancer (T1N0M0) and were diagnosed between 2014 and 2015. Cancer staging was performed based on clinical or pathological data. Patients with a history of cancer other than gastric cancer who were diagnosed within 2 years prior to gastric cancer diagnosis and those diagnosed with secondary primary cancer within 6 months of their initial gastric cancer diagnosis were excluded. The Institutional Review Board of the National Evidence-based Healthcare Collaborating Agency approved the study protocol (NECAIRB23-007) and waived the requirement for informed consent because of the retrospective nature of the study.

Treatment definition

The treatment group comprised patients with gastric cancer who underwent ESD or gastrectomy. We assessed the initial treatment for gastric cancer after diagnosis. Procedure records, identified using Electronic Data Interchange (EDI) codes, were extracted from the HIRA database. The ESD group included patients who had undergone ESD or endoscopic mucosal resection (EDI: Q7653, QZ933, QX701, QX704, and Q7652). Patients who underwent gastrectomy after the initial ESD treatment were also included in the ESD group. The gastrectomy group included patients who underwent total, partial, distal, subtotal, proximal, wedge, or pylorus-preserving gastrectomy (EDI: Q0251, Q0252, Q0253, Q0254, Q0255, Q0256, Q0257, Q0258, Q0259, Q2533, Q2534, Q2536, Q2537, Q2594, Q2598, and QA536).

Outcome definition

The outcomes of this study were defined as total and gastric cancer-specific deaths within 5 years of the initial treatment. Mortality data, including dates and primary causes of death, were obtained from the Ministry of Statistics database (2012–2020) based on the Korean Classification of Disease (KCD). The primary outcome was total death, whereas the secondary outcome was gastric cancer-specific death (KCD codes starting with "C16"). Deaths from other causes were categorized separately and patients alive at the 5-year follow-up were censored.

Covariates

We included covariates that may have affected the association between treatment effects and outcomes. The covariates included age, sex, and tumor characteristics, such as tumor location (lower, middle, upper, and unknown), tumor size (<2, 2–3, and >3 cm), histologic type (well, moderate, poor, and unknown), and tumor invasion depth (mucosa and submucosa). Data were collected using a collaborative gastric cancer staging system. The tumor invasion depth was determined according to the American Joint Committee on Cancer (AJCC) 8th edition TNM staging system [14], with T1a and T1b representing mucosal and submucosal invasion, respectively.

The insurance fee classification, used as a proxy for income, was derived from NHIS premium data. The premiums are based on wages for insured employees and wealth for the self-employed [15]. The NHIS categorizes premiums into deciles, grouped as low (0: healthcare beneficiary or 1st–3rd deciles), middle (4th–7th deciles), or high (8th–10th deciles).

Data on the hospital type and patient history of primary diagnoses were retrieved from the HIRA database. Hospitals treating gastric cancer were classified as tertiary or other hospitals (general hospitals, hospitals, or clinics). Charlson Comorbidity Index (CCI) scores,



based on primary diagnoses within 2 years preceding the gastric cancer diagnosis, were categorized as <2 or ≥ 2 .

Statistical methods

Baseline characteristics were presented descriptively according to the measured variables. Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were expressed as frequency and percentage. The χ^2 test was used to compare the distribution of the treatment groups according to the selected categorical variables, whereas at test was performed to evaluate continuous variables. The Kaplan-Meier (KM) curve was used to compare the OS between the exposure groups, and the log-rank test was used to test survival differences. Crude cumulative mortality curves for gastric cancer-specific and other causes of mortality were generated, followed by Gray's test to compare the curves between groups. Adjusted cumulative mortality curves for total and gastric cancer-specific deaths were derived using direct standardization to control for a set of confounding variables [16]. Three models assessed the effects of treatment on cause-specific mortality risk. Model 1 estimated the crude hazard ratio (HR) using a cause-specific Cox proportional hazards (PH) model. Model 2 estimated the adjusted HR (aHR) using a cause-specific Cox PH model that controlled for confounding variables, such as age, tumor location, tumor size, histologic type, CCI, insurance fee classification, and hospital type. Model 3 estimated the aHR using a full propensity score (PS) matching method and a cause-specific Cox PH model. Balance was assessed using the standardized mean difference for each variable by comparing the values before and after PS adjustment (Supplementary Fig. 1). Subgroup analyses were conducted according to age and depth of tumor invasion. Statistical significance was set at P<0.05. All analyses were performed using R software 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

We analyzed the data of 23,733 patients diagnosed with gastric cancer between 2012 and 2019 (**Fig. 1**). Among them, 3,527 patients with stage IA primary adenocarcinoma diagnosed

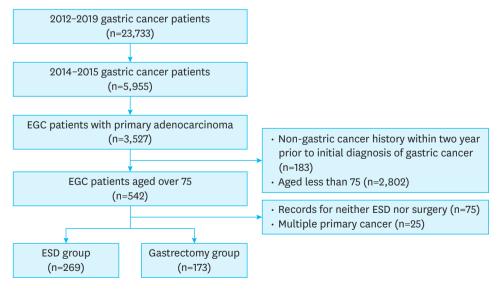


Fig. 1. Flow chart depicting the selection of the ESD and gastrectomy groups. EGC = early gastric cancer; ESD = endoscopic submucosal dissection.



between 2014 and 2015 were identified. The exclusion criteria were patients with a history of non-gastric cancer within 2 years before gastric cancer diagnosis (n=183), those under 75 years of age (n=2,802), those who had not undergone ESD or gastrectomy (n=75), and those diagnosed with a different type of cancer within 6 months of gastric cancer diagnosis (n=25). The final study population included 442 patients: 269 who initially underwent ESD, and 173 who underwent gastrectomy.

Table 1 compares the baseline characteristics of the ESD and gastrectomy groups. Significant differences were found in tumor location, size, depth of invasion, and histological type; however, no significant differences were observed in age, sex, CCI score, insurance classification, or hospital type. The ESD group had smaller tumors, more mucosa-confined lesions, more cases of well-differentiated histology, and a higher proportion of lower-third gastric tumors than the gastrectomy group.

Figs. 2 and **3** compare the 5-year OS between the ESD and gastrectomy groups using a KM curve. No significant difference was observed in OS (P=0.140), although the ESD group exhibited a slightly higher survival rate than the gastrectomy group in the first year, with 5-year OS rates of 85.9% and 80.9%, respectively (**Fig. 2**). Subgroup KM analyses (**Fig. 3**) revealed better 5-year OS in the ESD group among patients aged ≥80 (79.3% vs. 62.0%;

Table 1. Comparison of baseline characteristics between the ESD and gastrectomy groups

Variables	Value	ESD (n=269)	Gastrectomy (n=173)	P-value
Age (yr)	75-79	182 (67.7)	123 (71.1)	0.511
	≥80	87 (32.3)	50 (28.9)	
Sex	Female	102 (37.9)	81 (46.8)	0.079
	Male	167 (62.1)	92 (53.2)	
Tumor location	Lower	189 (70.3)	94 (54.3)	<0.001
	Middle	51 (19.0)	65 (37.6)	
	Upper	9 (3.3)	6 (3.5)	
	Unclassified	20 (7.4)	8 (4.6)	
Tumor size (cm)	Mean±SD	1.98±2.76	2.95±1.76	<0.001
	<2	166 (61.7)	51 (29.5)	<0.001
	2-3	69 (25.7)	58 (33.5)	
	>3	34 (12.6)	64 (37.0)	
Tumor invasion depth	Mucosa (T1a)	214 (79.6)	75 (43.4)	<0.001
	Submucosa (T1b)	51 (19.0)	95 (54.9)	
	Others	4 (1.5)	3 (1.7)	
Histologic type	Well	155 (57.6)	33 (19.1)	<0.001
	Moderate	95 (35.3)	86 (49.7)	
	Poor	10 (3.7)	38 (22.0)	
	Unknown*	9 (3.3)	16 (9.2)	
CCI	Mean±SD	0.94±1.09	1.13±1.22	0.096
	<2	206 (76.6)	123 (71.1)	0.239
	≥2	63 (23.4)	50 (28.9)	
Insurance fee classification	Low (0-3)	42 (15.6)	28 (16.2)	0.599
	Middle (4-7)	65 (24.2)	47 (27.2)	
	High (8–10)	158 (58.7)	93 (53.8)	
	Missing	4 (1.5)	5 (2.9)	
Type of hospital	Tertiary hospital	210 (78.1)	134 (77.5)	0.973
	Others	59 (21.9)	39 (22.5)	
Status at the 5th year	Survived	231 (85.9)	140 (80.9)	0.055
	Gastric cancer-specific death	9 (3.3)	15 (8.7)	
	Other causes of death	29 (10.8)	18 (10.4)	

Values are presented as number (%).

ESD = endoscopic submucosal dissection; SD = standard deviation; CCI = Charlson Comorbidity Index.

^{*}Unknown cases include signet ring cell carcinoma.



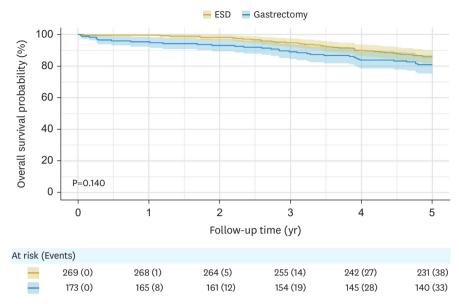


Fig. 2. Comparison of the 5-year overall survival between the ESD and gastrectomy groups. ESD = endoscopic submucosal dissection.

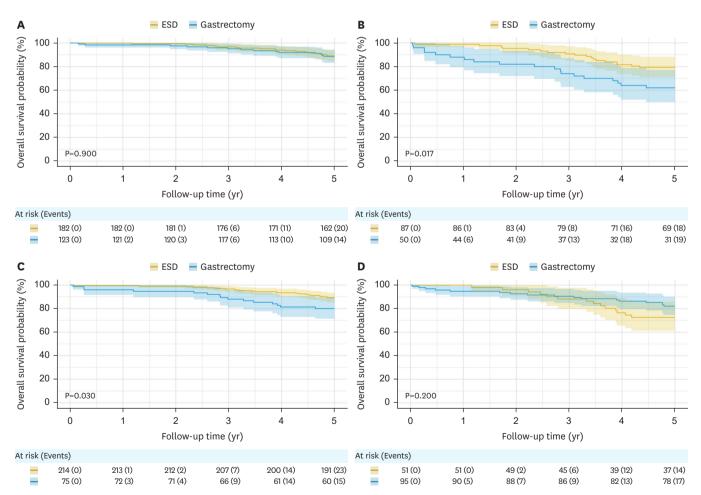


Fig. 3. Comparison of the 5-year overall survival between the ESD and gastrectomy groups. Based on age: (A) 75-79 and (B) ≥80; and tumor invasion depth: (C) mucosa and (D) submucosa. ESD = endoscopic submucosal dissection.



Table 2. Overall and cause-specific death risk comparison using Cox PHs models

Cause of death	Model 1*		Model 2 [†]		Model 3 [‡]		
	HR	95% CI	aHR	95% CI	aHR	95% CI	
All causes							
ESD	Reference		Reference		Reference		
Gastrectomy	1.42	0.89-2.27	1.81	1.03-3.16	1.65	0.93-2.94	
Gastric cancer							
ESD	Ref	Reference		Reference		Reference	
Gastrectomy	2.7	1.18-6.17	3.54	1.37-9.14	4.55	1.67-12.40	
Other causes							
ESD	Reference		Reference		Reference		
Gastrectomy	1.02	0.57-1.84	1.22	0.59-2.51	0.96	0.44-2.07	

PH = proportional hazard; HR = hazard ratio; CI = confidence interval; aHR = adjusted hazard ratio; ESD = endoscopic submucosal dissection.

P=0.017) and for mucosa-confined lesions (89.3% vs. 80.0%; P=0.030). Furthermore, gastric cancer-specific mortality rates were significantly higher in the gastrectomy group overall (P=0.015), as well as within the subgroups aged \geq 80 (P=0.002) and those with mucosa-confined lesions (P=0.002) (Supplementary Fig. 2).

The mortality risk was compared between the ESD and gastrectomy groups (**Table 2**). After adjusting for confounding variables, the gastrectomy group showed a higher risk of total death in model 2 (aHR, 1.81; 95% CI, 1.03–3.16). Moreover, the risk of gastric cancerspecific mortality was significantly higher in the gastrectomy group (model 2: aHR, 3.54; 95% CI, 1.37–9.14; model 3: aHR, 4.55; 95% CI, 1.67–12.40). Compared with the ESD group, the gastrectomy group exhibited a higher 5-year adjusted cumulative mortality rate for total death (13.2%; 95% CI, 9.0–17.3 vs. 21.8%; 95% CI, 14.3–29.2) and for gastric cancer-specific death (3.2%; 95% CI, 0.9–5.4 vs. 10.4%; 95% CI, 4.3–16.5) (**Supplementary Fig. 3**).

Table 3 summarizes the subgroup analyses by age (75–79 vs. ≥80) and tumor invasion depth (mucosa vs. submucosa). Among patients aged ≥80, gastrectomy was associated with significantly higher risks of total death (model 3: aHR, 3.29; 95% CI, 1.70–6.35) and gastric cancer-specific death (model 3: aHR, 7.18; 95% CI, 2.08–24.82) than ESD following PS adjustment. The adjusted 5-year cumulative mortality rates for total as well as gastric cancerspecific mortality were higher in both the ESD and gastrectomy groups among patients aged ≥80 than among those aged 75–79 years (**Supplementary Fig. 3**). After controlling for confounding variables, gastrectomy carried higher risks of total death (model 3: aHR, 2.69; 95% CI, 1.33–5.46) and gastric cancer-specific death (model 3: aHR, 6.11; 95% CI, 1.93–19.35) for mucosa-confined lesions. Among patients who underwent gastrectomy, the adjusted 5-year cumulative mortality rates were similar for lesions confined to the mucosa (22.0%; 95% CI, 11.4–32.6) and submucosa (20.9%; 95% CI, 11.7–30.1). In contrast, among patients who underwent ESD, the adjusted 5-year cumulative mortality rate was higher for submucosal lesions (21.4%; 95% CI, 11.0–31.9) than for mucosa-confined lesions (10.6%; 95% CI, 6.5–14.7) (**Supplementary Fig. 3**).

^{*}Crude Cox PHs model.

[†]Cox PHs model controlling for age, tumor location, tumor size, histologic type, CCI, insurance fee classification, and hospital type.

[‡]Full propensity score-matched model controlling for age, tumor location, tumor size, histologic type, CCI, insurance fee classification, and hospital type.



Table 3. Overall and cause-specific death risk comparison between the gastrectomy and ESD (reference) groups based on the age category and tumor invasion depth

Subgroups	Cause of death	of death Model 1*		Model 2 [†]		Model 3 [‡]	
		HR	95% CI	aHR	95% CI	aHR	95% CI
Age category (yr)							
75-79	All causes	1.05	0.53-2.07	1.13	0.48-2.67	0.98	0.39-2.47
	Gastric cancer	1.20	0.32-4.45	1.48	0.27-8.25	0.91	0.24-3.53
	Other causes	1.00	0.45-2.22	1.16	0.43-3.15	1.01	0.32-3.14
≥80	All causes	2.16	1.13-4.11	2.35	1.06-5.19	3.29	1.70-6.35
	Gastric cancer	5.41	1.72-16.99	9.04	2.11-38.75	7.18	2.08-24.82
	Other causes	1.20	0.50-2.86	1.03	0.35-2.97	1.67	0.59-4.74
Tumor invasion depth							
Mucosa (T1a)	All causes	2.02	1.05-3.87	2.35	1.12-4.94	2.69	1.33-5.46
	Gastric cancer	4.58	1.63-12.88	5.27	1.65-16.89	6.11	1.93-19.35
	Other causes	1.10	0.44-2.80	1.13	0.38-3.40	1.31	0.43-4.02
Submucosa (T1b)	All causes	0.63	0.31-1.27	1.01	0.44-2.33	0.53	0.26-1.10
	Gastric cancer	0.91	0.22-3.81	1.47	0.26-8.27	0.83	0.15-4.67
	Other causes	0.55	0.24-1.25	0.90	0.34-2.40	0.47	0.22-1.01

ESD = endoscopic submucosal dissection; HR = hazard ratio; CI = confidence interval; aHR = adjusted hazard ratio; CCI = Charlson Comorbidity Index. *Crude Cox PHs model.

DISCUSSION

This study evaluated treatment outcomes in older patients with EGC who underwent ESD or gastrectomy. Our findings revealed that the ESD group exhibited better OS and a lower risk of gastric cancer-specific death than the gastrectomy group, particularly among patients aged ≥80 years and those with mucosa-confined lesions. Among patients aged 75–79 years and those with submucosa-confined lesions, the risks of total and gastric cancer-specific deaths were comparable between the ESD and gastrectomy groups.

To the best of our knowledge, 3 meta-analyses have compared OS following ESD versus gastrectomy for gastric cancer [6,7,17]. Two of these meta-analyses focused on the overall patient population with EGC and found comparable survival benefits between ESD and gastrectomy [6,7]. In contrast, Liu et al. limited their investigation to older patients with EGC and reported worse OS after ESD. Their pooled analysis yielded a HR of 2.81 (95% CI, 2.20–3.58) for all-cause mortality in the ESD group compared with gastrectomy [17]. It is important to emphasize that this pooled estimate was not adjusted for prognostic or demographic confounders, and the authors acknowledge that OS may have been affected by differences in baseline patient characteristics or death from other causes in older populations [17]. Nevertheless, Lue et al. and the studies they reviewed consider ESD a viable alternative to gastrectomy for older patients with EGC, considering their age, overall health, comorbidities, and nutritional status [18-22].

In this study, we observed that ESD offers significant long-term benefits for OS and is associated with reduced gastric cancer-specific mortality in older patients with EGC. Unlike previous single-hospital studies [18-22], our nationwide study assessed data from 52 cancer-related institutions, including major tertiary hospitals across South Korea, thereby providing a comprehensive view of real-world clinical practice. To account for potential variations in ESD and surgical options, we controlled for key confounders, such as age, sex, tumor characteristics (e.g., tumor location, size, and histologic type), and comorbidities based on the CCI and additionally adjusted for hospital type and insurance fee classification. The results showed a lower risk of total and gastric-cancer-specific deaths in the ESD group than in

[†]Cox PHs model controlling for age, tumor location, tumor size, histologic type, CCI, insurance fee classification, and hospital type.

Full propensity score-matched model controlling for tumor location, tumor size, histologic type, CCI, insurance fee classification, and hospital type.



the gastrectomy group. Therefore, ESD should be actively considered for older patients aged ≥ 80 or those with mucosa-confined lesions, following thorough evaluation of comorbidities as well as nutritional status and psoas muscle mass [23]. However, the long-term survival benefit of ESD versus gastrectomy for patients aged ≥ 80 in Korea still remains unreported.

The elevated risk of total and gastric cancer-specific deaths in patients undergoing gastrectomy may be attributed to the invasive nature of the surgery. Moreover, gastrectomy involves general anesthesia and longer procedure times, which increase the risk of complications and mortality, particularly in older patients. Complications such as anastomotic leakage, infections, and cardiopulmonary problems significantly contribute to mortality in older patients undergoing gastrectomy [24,25]. Among patients aged ≥80, the gastrectomy group exhibited lower OS than the ESD group, which was partly linked to age-related post-surgical pneumonia that typically occurred within 30 days [26]. In our study, the gastrectomy group experienced a significantly greater number of rehospitalization days (7–90 days) after the initial procedure than the ESD group (data not shown). These rehospitalizations, primarily related to gastric cancer, were associated with increased administration of antibiotics, including vancomycin, imipenem, meropenem, ertapenem, linezolid, and piperacillin. Consequently, the difference in OS between the 2 groups was greatest in the first-year post-treatment and then gradually narrowed, indicating a procedure-related effect.

For submucosa-confined lesions, the comparative risk of death between gastrectomy and ESD remains unclear (**Table 3**). Patients who underwent ESD may have undergone as having received curative resections despite non-curative outcomes, leading them to opt for additional gastrectomy. Notably, non-curative ESD without further surgery is associated with poor long-term prognosis [27,28]. Thus, the higher probability of lymph node metastasis may have contributed to the increased risk of cancer-specific or overall mortality in these patients.

The strength of our study lies in its nationwide scope and comprehensive dataset, incorporating the cancer registry and insurance claims data, thereby enhancing the generalizability of our findings. The K-CURE platform offers an integrated dataset that links national health insurance claims with the cancer registry, enabling researchers to investigate tumor characteristics in patients with cancer using KCCR data. We selected a dataset that encompassed a comprehensive range of prognostic factors, including the AJCC TNM stage, tumor location, morphological characteristics, histological type, and tumor size. These variables are typically not available in nationwide datasets. Furthermore, to the best of our knowledge, this is the first nationwide study to be conducted, apart from previous observational studies, which were mostly single-center studies. Korea operates a government-led screening program that provides esophagogastroduodenoscopies to adults aged 40 or older; it has over 60% participation, which ensures a well-organized dataset [29]. Moreover, our study included patients who underwent ESD followed by additional gastrectomy in the ESD group, whereas previous studies excluded or grouped these patients into gastrectomy groups. This approach reflects the real-world treatment settings initially assigned to older patients with EGC.

This study had some limitations. First, its retrospective nature and the characteristics of nationwide claims data require operational definitions of certain variables. Unlike hospital data, national datasets lack detailed chronological treatment information, making it challenging to adjust for all potential confounding factors. Second, clinically relevant



prognostic factors such as nutritional status and *Helicobacter pylori* infection history were not available and could only be partially proxied by CCI. Third, comorbidities were assessed only within the 2 years preceding the index gastric cancer diagnosis; thus, the omission of comorbidities recorded 2–5 years earlier may have affected the survival estimates. Extending the lookback window for cancer history and comorbidities beyond 2 years would shift the index year to after 2015, reducing the follow-up duration to less than 5 years. Therefore, to maintain at least 5 years of follow-up, we limited our cohort to patients diagnosed with gastric cancer between 2014 and 2015.

In conclusion, this study highlights that ESD is associated with better survival, particularly among patients aged ≥ 80 years or those with mucosa-confined lesions. Moreover, the survival outcomes of ESD and gastrectomy were comparable among patients aged 75–79 years or and those with submucosa-confined lesions. These findings emphasize the need for tailored treatment decisions for older patients. ESD may be a preferable and less invasive option for patients with stage IA gastric cancer. Given the complexity of treatment in these patient groups, treatment decisions should affect the patient characteristics, tumor pathology, and overall health status. Further studies should investigate additional key prognostic factors to facilitate a more comprehensive risk evaluation and survival analyses.

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SUPPLEMENTARY MATERIALS

Supplementary Fig. 1

Evaluation of propensity score matching between the ESD and gastrectomy groups using absolute standardized mean differences. The subgroups were as follows: (A) overall population, (B) age 75–79, (C) age ≥80, (D) mucosa-confined lesions, and (E) submucosa-confined lesions.

Supplementary Fig. 2

Comparison of the 5-year cause-specific cumulative mortality between the ESD and gastrectomy groups. Among the overall study population: (A) gastric cancer-specific death and (B) other causes of death; among patients aged 75–79 years: (C) gastric cancer-specific death and (D) other causes of death; among patients aged ≥80 years: (E) gastric cancer-specific death and (F) other causes of death; among patients with mucosa-confined lesions: (G) gastric cancer-specific death and (H) other causes of death; and among patients with submucosa-confined lesions: (I) gastric cancer-specific death and (J) other causes of death.

Supplementary Fig. 3

Comparison of the adjusted 5-year cumulative mortality for total and gastric cancer-specific deaths between the ESD and gastrectomy groups. Among the overall population: (A) total death and (B) gastric cancer-specific death; among patients aged 75–79 years: (C) total death and (D) gastric cancer-specific death; among patients aged ≥80 years: (E) total death and (F) gastric cancer-specific death; among patients with mucosa-confined lesions: (G) total death and (H) gastric cancer-specific death; and among patients with submucosa-confined



lesions: (I) total death and (J) gastric cancer-specific death. Variables such as age, tumor location, tumor size, histologic type, CCI, insurance fee classification, and hospital type were controlled for in the analysis. The table in each plot presents the adjusted cumulative mortality rates with 95% CI at the 1st, 3rd, and 5th years of follow-up.

REFERENCES

- 1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2024;74:229-263. PUBMED | CROSSREF
- Park EH, Jung KW, Park NJ, Kang MJ, Yun EH, Kim HJ, et al. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2021. Cancer Res Treat 2024;56:357-371. PUBMED | CROSSREF
- Park SH, Kang MJ, Yun EH, Jung KW. Epidemiology of gastric cancer in Korea: trends in incidence and survival based on Korea Central Cancer Registry Data (1999–2019). J Gastric Cancer 2022;22:160-168.
 PUBMED | CROSSREF
- 4. Luu XQ, Lee K, Jun JK, Suh M, Jung KW, Choi KS. Effect of gastric cancer screening on long-term survival of gastric cancer patients: results of Korean national cancer screening program. J Gastroenterol 2022;57:464-475. PUBMED | CROSSREF
- 5. Kim TH, Kim IH, Kang SJ, Choi M, Kim BH, Eom BW, et al. Korean practice guidelines for gastric cancer 2022: an evidence-based, multidisciplinary approach. J Gastric Cancer 2023;23:3-106. PUBMED | CROSSREF
- 6. Liu Q, Ding L, Qiu X, Meng F. Updated evaluation of endoscopic submucosal dissection versus surgery for early gastric cancer: a systematic review and meta-analysis. Int J Surg 2020;73:28-41. PUBMED | CROSSREF
- 7. Gu L, Khadaroo PA, Chen L, Li X, Zhu H, Zhong X, et al. Comparison of long-term outcomes of endoscopic submucosal dissection and surgery for early gastric cancer: a systematic review and meta-analysis. J Gastrointest Surg 2019;23:1493-1501. PUBMED | CROSSREF
- 8. Xu X, Zheng G, Gao N, Zheng Z. Long-term outcomes and clinical safety of expanded indication early gastric cancer treated with endoscopic submucosal dissection versus surgical resection: a meta-analysis. BMJ Open 2022;12:e055406. PUBMED | CROSSREF
- 9. Sekiguchi M, Oda I, Morita S, Katai H, Yano T, Terashima M, et al. Management of elderly patients with early gastric cancer in Japan. Jpn J Clin Oncol 2022;52:425-432. PUBMED | CROSSREF
- Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018 (5th edition). Gastric Cancer 2021;24:1-21. PUBMED | CROSSREF
- 11. National Comprehensive Cancer Network. NCCN guideline: gastric cancer [Internet]. Plymouth Meeting (PA): National Comprehensive Cancer Network; 2024 [cited 2024 Aug 26]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf.
- 12. Choi DW, Guk MY, Kim HR, Ryu KS, Kong HJ, Cha HS, et al. Data resource profile: the cancer public library database in South Korea. Cancer Res Treat 2024;56:1014-1026. PUBMED | CROSSREF
- Korea Central Cancer Registry. Collaborative stage data user guide [Internet]. Goyang: Korea Central Cancer Registry; 2018 [cited 2024 Jul 15]. Available from: https://kccrsurvey.cancer.go.kr/sub02/ sub02_01.jsp.
- 14. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. The eighth edition AJCC cancer staging manual: continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin 2017;67:93-99. PUBMED | CROSSREF
- 15. Kim YS, Kim J, Kim Y, Kang HT. Disparities in cause-specific mortality by health insurance type and premium: evidence from Korean NHIS-HEALS cohort study, 2002–2019. BMC Public Health 2024;24:1577. PUBMED | CROSSREF
- 16. Denz R, Klaaßen-Mielke R, Timmesfeld N. A comparison of different methods to adjust survival curves for confounders. Stat Med 2023;42:1461-1479. PUBMED | CROSSREF
- 17. Liu F, Wen ZL, Liu XR, Li ZW, Lv Q, Zhang W, et al. Comparison of endoscopic submucosal dissection versus surgery for early gastric cancer in the elderly: a pooled analysis. World J Surg Oncol 2023;21:283. PUBMED | CROSSREF
- 18. Park CH, Lee H, Kim DW, Chung H, Park JC, Shin SK, et al. Clinical safety of endoscopic submucosal dissection compared with surgery in elderly patients with early gastric cancer: a propensity-matched analysis. Gastrointest Endosc 2014;80:599-609. PUBMED | CROSSREF



- 19. Kang S, Lee JH, Kim Y, Park K, Na HK, Ahn JY, et al. Comparison of endoscopic submucosal dissection and surgery for early gastric cancer that is not indicated for endoscopic resection in elderly patients. Surg Endosc 2023;37:4766-4773. PUBMED | CROSSREF
- Miyahara K, Ishida M, Kono Y, Hirata T, Obayashi Y, Gotoda T, et al. Prognosis after curative resection for stage IA gastric cancer in elderly patients: endoscopic submucosal dissection versus surgery. Surg Today 2022;52:1329-1340. PUBMED | CROSSREF
- 21. Kishida Y, Takizawa K, Kakushima N, Kawata N, Yoshida M, Yabuuchi Y, et al. Endoscopic submucosal dissection versus surgery in elderly patients with early gastric cancer of relative indication for endoscopic resection. Dig Endosc 2022;34:497-507. PUBMED | CROSSREF
- 22. Etoh T, Katai H, Fukagawa T, Sano T, Oda I, Gotoda T, et al. Treatment of early gastric cancer in the elderly patient: results of EMR and gastrectomy at a national referral center in Japan. Gastrointest Endosc 2005;62:868-871. PUBMED | CROSSREF
- Ito N, Funasaka K, Fujiyoshi T, Nishida K, Furukawa K, Kakushima N, et al. Scoring system for predicting the prognosis of elderly gastric cancer patients after endoscopic submucosal dissection. Dig Endosc 2023;35:67-76. PUBMED | CROSSREF
- 24. Nelen SD, Bosscha K, Lemmens VEPP, Hartgrink HH, Verhoeven RHA, de Wilt JHW, et al. Morbidity and mortality according to age following gastrectomy for gastric cancer. Br J Surg 2018;105:1163-1170. PUBMED | CROSSREF
- 25. van Kooten RT, Voeten DM, Steyerberg EW, Hartgrink HH, van Berge Henegouwen MI, van Hillegersberg R, et al. Patient-related prognostic factors for anastomotic leakage, major complications, and short-term mortality following esophagectomy for cancer: a systematic review and meta-analyses. Ann Surg Oncol 2022;29:1358-1373. PUBMED | CROSSREF
- 26. Shibata C, Ogawa H, Nakano T, Koyama K, Yamamoto K, Nagao M, et al. Influence of age on postoperative complications especially pneumonia after gastrectomy for gastric cancer. BMC Surg 2019;19:106. PUBMED | CROSSREF
- 27. Eom BW, Kim YI, Kim KH, Yoon HM, Cho SJ, Lee JY, et al. Survival benefit of additional surgery after noncurative endoscopic resection in patients with early gastric cancer. Gastrointest Endosc 2017;85:155-163.e3. PUBMED | CROSSREF
- 28. Kim JH, Kim YI, Ahn JY, Shin WG, Yang HJ, Nam SY, et al. Long-term outcomes of endoscopic resection followed by additional surgery after non-curative resection in undifferentiated-type early gastric cancer: a nationwide multi-center study. Surg Endosc 2022;36:1847-1856. PUBMED | CROSSREF
- Kim YI, Choi IJ. Current status of the gastric cancer screening program in Korea. J Korean Med Assoc 2022;65:250-257. CROSSREF