Journal of Gastroenterology and Hepatology
JGHF
doi:10.1111/jgh.16764

ORIGINAL ARTICLE - GASTROENTEROLOGY (CLINICAL)

Long-term outcomes of endoscopic resection of superficial esophageal squamous cell carcinoma in late-elderly patients

Katsunori Matsueda,* Seiji Kawano,* Keisuke Fukui,† Shoichiro Hirata,* Takuya Satomi,* Shoko Inoo,* Kenta Hamada,* Yoshiyasu Kono,* Masaya Iwamuro,* Yoshiro Kawahara‡ and Motoyuki Otsuka*

*Department of Gastroenterology and Hepatology, Okayama University Hospital, ‡Department of Practical Gastrointestinal Endoscopy, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, †Faculty of Societal Safety Sciences, Kansai University, Osaka, Japan

Key words
endoscopic resection, esophageal cancer, late-elderly patient, long-term outcome.

Accepted for publication 24 September 2024.

Correspondence
Katsunori Matsueda, Department of Gastroenterology and Hepatology, Okayama University Hospital, Okayama, 2-5-1 Shikata-cho, Kita-Ku, Okayama 700-8558, Japan.
Email: rge43gs@yahoo.co.jp

Declaration of conflict of interest: The authors declare that they have no conflict of interest.
Financial support: This study did not receive any funding.

Abstract

Background and Aim: As the population ages, the number of elderly patients with superficial esophageal squamous cell carcinoma (ESCC) is increasing. We aimed to clarify the indications for endoscopic resection (ER) in late-elderly patients with ESCC in terms of life expectancy.

Methods: Patients aged ≥75 years who underwent ER for ESCC at our institution from January 2005 to December 2018 were enrolled. Clinical data, including the Eastern Cooperative Oncology Group performance status, American Society of Anesthesiologists physical status (ASA-PS), Charlson comorbidity index, and prognostic nutritional index (PNI), were collected at the time of ER. The main outcome measure was overall survival (OS).

Results: Two hundred eight consecutive patients were enrolled. The patients' median age was 78 years (range, 75–89 years). The 5-year follow-up rate was 88.5% (median follow-up period, 6.6 years). The 5-year OS rate was 79.2% (95% confidence interval [CI], 72.2–84.8), and 5-year net survival standardized for age, sex, and calendar year was 1.04 (95% CI, 0.98–1.09). In the multivariate analysis, an ASA-PS of 3 (hazard ratio, 2.45; 95% CI, 1.16–5.17) and PNI of <44.0 (hazard ratio, 2.73; 95% CI, 1.38–5.40) were independent prognostic factors. When neither of these factors was met, the 5-year OS rate was 87.8% (95% CI, 80.0–92.9), and 5-year net survival was 1.08 (95% CI, 1.02–1.14).

Conclusions: ER for ESCC in late-elderly patients may improve life expectancy. ER is recommended in patients with a good ASA-PS and PNI.

Introduction

Japan has one of the largest aging societies worldwide. In 2021, the average life expectancy increased to 81.5 years for men and 87.6 years for women.[1] Late-elderly people (age of ≥75 years) accounted for 14.9% of Japan's total population in 2021, and this figure is expected to reach 25.6% by 2065.[2] As the population ages, the number of elderly patients with esophageal cancer (EC) is increasing. In Japan, the number of EC-related deaths in late-elderly people increased 1.79 times in 2021 compared with 2001 (from 3300 to 5900).[3]

Although advanced EC is associated with poor survival,[4] EC can be cured by endoscopic resection (ER), surgical resection, or chemoradiotherapy if diagnosed at an early stage.[5–11] ER, including endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), is a safer and less invasive procedure that better preserves esophageal function compared with surgical resection or chemoradiotherapy. A favorable prognosis can be expected after ER,[6,11] even in elderly patients.[12–15] Thus, ER is important for preventing EC-related mortality. However, elderly patients tend to have more comorbidities, a shorter life expectancy, and a poorer general condition than non-elderly patients. In addition, the higher risk of death from various causes in elderly patients raises concerns regarding the true usefulness of endoscopic treatments for superficial esophageal squamous cell carcinoma (ESCC) because no studies have examined whether ER improves the life expectancy of late-elderly patients with ESCC.

Only a few studies to date have indicated that a patient factor, such as comorbid disease, is a predictor of good long-term ESD outcomes in elderly patients with ESCC.[14,16,17] In clinical practice, however, it is often difficult to determine whether to perform ER in late-elderly patients with ESCC. Various factors should be considered, including the patient's background, the lesion malignancy, the wishes of the patient and their family, the risk of adverse events, and medical and economic perspectives.

In the present study, we examined the effect of ER on life expectancy in late-elderly patients with ESCC compared with the survival of the general Japanese population. We also analyzed prognostic factors to identify patients who are suitable to undergo ER for ESCC.

Methods

Study design and setting. This retrospective cohort study was conducted at Okayama University Hospital, Japan. The study

protocol was approved by the Institutional Review Board of Okayama University Hospital on September 1, 2023 (No. 2310-006), and the study was performed in accordance with the Declaration of Helsinki.

Participants. Records from consecutive patients aged ≥75 years who underwent ER for superficial ESCC at our institution from January 2005 to December 2018 were retrieved from our pathology and endoscopy database.

Data collection and definitions of patients and lesions. Patient demographic and clinical data at the time of ER were collected and calculated as prognostic factors, including age, sex, Eastern Cooperative Oncology Group performance status (ECOG-PS),[18] American Society of Anesthesiologists physical status (ASA-PS), Charlson comorbidity index (CCI),[16] and prognostic nutritional index (PNI).[19] The PNI was calculated using the following formula: PNI = 10 × serum albumin concentration (g/dL) + 0.005 × lymphocyte count (/mm^3).[19]

Lesions were classified as primary, metachronous, or residual/locally recurrent. Primary lesions were treated by ER in patients with no history of EC. Metachronous lesions were defined as lesions detected >2 months after previous EC treatment.[20] Residual/locally recurrent lesions were defined as those found at the scar of the previous ER that resulted in a positive-margin resection on histologic examination. The presence of remnant esophagus was determined after esophagectomy. All lesions were histologically confirmed as SCC according to the Japanese Classification of Esophageal Cancer.[21,22] If multiple lesions were resected on the same day or within 2 months, lesion characteristics were based on the findings of the most advanced lesion in terms of depth and size.

Indication for ER. The indication for ER was determined according to EC practice guidelines[23,24] and according to the patient's fitness for surgery, comorbidities, and preference for ER. ESD was indicated for most patients. Patients with mucosal defects extending more than three-quarters of the esophageal circumference received steroid therapy to prevent post-ER stricture.

Sedation method. Sedation methods included intravenous sedation or general anesthesia. Depending on the lesion and the patient's condition, the attending physician selected the appropriate sedation method. When intravenous anesthesia was not appropriate, then general anesthesia was chosen in the operating.

Histological evaluation. The resected specimen was sectioned at 2-mm intervals. Histological assessments were performed according to the Japanese Classification of Esophageal Cancer.[21,22]

ER resection results. En bloc resection was defined as resection of a lesion in a single piece, and piecemeal resection was defined as resection of a lesion in multiple pieces. R0 resection was defined as no histologic involvement of the horizontal margin and vertical margin (VM) by the tumor after en bloc resection.

Perforation was defined as an endoscopically visible hole during the procedure, and pneumomediastinum was defined as the presence of air in the mediastinum without perforation as evaluated by computed tomography. Post-ER bleeding was defined as postprocedural bleeding from the ulcer with hematemesis and/or melena requiring emergency endoscopy. Postprocedural pneumonia was defined by the presence of fever or cough and an infiltrative shadow on chest roentgenography or computed tomography. Stricture was defined as a stenotic lesion treated with endoscopic dilation. Treatment-related death was any death resulting from adverse events.

ER curability was assessed by the histological results and classified into low-risk and high-risk cancers according to the risk of metastasis.[6,11,25,26] Low-risk cancers were defined as those pathologically confined to the epithelial (EP), lamina propria (LPM), or muscularis mucosa (MM) layers without lymphovascular involvement (LVI) because such cancers have a low risk of metastasis. High-risk cancers were defined as those pathologically invading the submucosa or those with LVI.

Additional treatment. When the ER results diagnosed low-risk cancer and showed a negative VM, we opted for follow-up without additional treatment. When the ER results diagnosed high-risk cancer or a positive VM, additional treatment such as surgery, chemoradiotherapy (CRT), or radiotherapy (RT) was considered.

Follow-up and collection of long-term outcome data. Upper gastrointestinal endoscopy was routinely performed 2 months after ER. Subsequently, in patients with low-risk cancers exhibiting pathological EP or LPM invasion without LVI, only surveillance esophagogastroduodenoscopy was repeated every 6–12 months. All other patients were followed up with tumor marker studies, upper gastrointestinal endoscopy, and computed tomography every 4–6 months for 2–3 years and every 6 months thereafter to detect local recurrence and metachronous EC, lymph node metastases, or distant metastases.

The long-term outcomes of ER were evaluated by overall survival (OS), disease-specific survival (DSS), cause of death, metachronous EC, and metastasis. The patients' vital status and other follow-up data as of December 31, 2023, were examined by inspection of the institutional medical records, linked to Okayama Cancer Registry data, or by contacting the patient or the patient's family or primary physician.

Statistical analysis. To estimate the hazard caused by EC, we estimated the 5-year net survival after ER standardized for age, sex, and calendar year. The net survival is the cumulative probability of surviving to an arbitrary time point since cohort entry after adjusting for other causes of death in the background general population. For application of the Pohar–Perme estimator using the "relsurv" R package,[27] we used age-, sex-, and calendar year-specific population life tables in Japan.[28]

The cutoff values for age, ASA-PS, PNI, and CCI were defined using receiver operating characteristic curves. We evaluated the difference in OS among subgroups according to patient background and lesion factors using the log-rank test. A *P* value of

<0.05 was considered statistically significant. A multivariate Cox proportional hazards model was applied to examine the effect of patient background and lesion factors on OS. In the multivariate analysis, we included age, sex, ECOG-PS, ASA-PS, CCI, and PNI as patient factors and endoscopic curability as a lesion factor because these variables were considered possible contributors to prognosis. We also identified patients suitable to undergo ER for ESCC using the prognostic factors extracted from the multivariate analysis. All analyses were performed using JMP 17 software (SAS Institute Inc., Cary, NC, USA).

Results

Patients. Among 610 patients with ESCC who underwent ER, 208 patients aged ≥75 years at the time of ER were enrolled. The patients' characteristics (185 men and 23 women; median age, 78 years) are summarized in Table 1. Approximately 96% of patients had an ECOG-PS of 0 or 1, and 82% had an ASA-PS of 1 or 2 (ASA-PS 1/2). A total of 69% of patients had a CCI of <3. Regarding comorbidities, 42% of the patients had cancers in other organs, with 18% having oral and laryngopharyngeal cancer. The median PNI was 47.1 (range, 32.7–58.2).

Table 1 Patients' background characteristics

Characteristic	Total (*n* = 208)
Age, years	78 (75–89)
Sex	
Male	185 (89)
Female	23 (11)
Eastern Cooperative Oncology Group performance status	
0 or 1	199 (96)
2–4	9 (4)
American Society of Anesthesiologists physical status	
1 or 2	170 (82)
3	38 (18)
Comorbidities and history (some overlap)	
Cardiovascular disease	29 (14)
Cerebrovascular disease	14 (7)
Respiratory functional disorder	18 (9)
Liver disease	22 (11)
Chronic renal failure	6 (3)
Diabetes mellitus	50 (24)
Cancer of other organs	88 (42)
Oral and laryngopharyngeal cancer	38 (18)
Charlson comorbidity index	
0	53 (25)
1	44 (21)
2	47 (23)
3	30 (14)
4	16 (8)
5	12 (6)
≥ 6	6 (3)
Serum albumin, g/dL	4.0 (2.5–4.9)
Prognostic nutritional index	47.1 (32.7–58.2)
Regular intake of antithrombotic agents	60 (29)

Data are presented as median (range) or *n* (%).

Table 2 summarizes the characteristics of the 208 lesions. The pathological diagnoses were EP/LPM, MM, SM1 (cancer invading ≤200 μm into the submucosa), and SM2 (cancer invading >200 μm into the submucosa) in 177, 23, 4, and 4 lesions, respectively. LVI was identified in eight (4%) lesions. The cases of VM1 (cancer cells present at the margin, $n = 1$) and VMX (status of margin unable to be assessed, $n = 1$) were both identified in SM2 cancers.

The ER results (three EMR and 205 ESD) are summarized in Table S1. Of the 208 lesions, en bloc resection and R0 resection were achieved in 100% and 85% of cases, respectively. Adverse events included six (3%) cases of intraprocedural perforations, four (2%) cases of pneumomediastinum, no cases of post-ER bleeding, five (2%) cases of pneumonia, and 23 (11%) cases of stricture. No treatment-related death occurred. Regarding sedation method, 206 (99%) patients were sedated using intravenous anesthesia, while two (2%) patients were sedated by general anesthesia. There was no significant difference in adverse events after esophageal ER between intravenous and general anesthesia.

All patients with perforation or pneumomediastinum were treated with immediate endoscopic clipping or conservative

Table 2 Histologic lesion diagnosis

Characteristic	Total (*n* = 208)
Lesion type	
Initial lesion	134 (64)
Metachronous lesion	74 (36)
Residual/locally recurrent lesion	0 (0)
Esophagus status	
Normal	204 (98)
Remnant esophagus	4 (2)
Location	
Cervical/upper thoracic	23 (11)
Middle thoracic	125 (60)
Lower thoracic/abdominal	60 (29)
Tumor size, mm	16 (4–65)
Macroscopic type	
Flat	206 (99)
Non-flat	2 (1)
Histologic tumor depth (depth of invasion)	
EP/LPM	177 (85)
MM	23 (11)
SM1	4 (2)
SM2	4 (2)
Lymphovascular invasion	
Negative	200 (96)
Positive	8 (4)
Horizontal margin	
Negative	179 (86)
Positive or unclear	29 (14)
Vertical margin	
Negative	206 (99)
Positive or unclear	2 (1)

Data are presented as *n* (%) or median (range).
EP, cancer limited to the epithelium; LPM, cancer invading the lamina propria; MM, cancer invading the muscularis mucosa; SM, cancer invading the submucosa; SM1, cancer invading into the submucosa up to 0.2 mm; SM2, cancer invading into the submucosa more than 0.2 mm.

Table 3 Long-term outcomes (n = 208)

Results	
Follow-up period, years	6.6 (0.4–16.1)
Metachronous esophageal cancer	33 (16)
Local recurrence	0 (0)
Metastasis	1 (0.4)
Death	52 (25)
Cause of death	
Esophageal cancer	1 (2)
Oral and laryngopharyngeal cancer	6 (12)
Other organ malignancy	12 (23)
Other causes	24 (46)
Treatment-related death	0 (0)
Unknown	9 (17)

Data are presented as median (range) or n (%).

management, while patients with pneumonia were successfully treated with conservative management alone, including intravenous antibiotics and fasting. All patients with stricture were managed with endoscopic dilation, and none required surgery.

Of the 208 lesions, 14 were classified as high-risk cancers, and additional treatment was performed in four (29%) (surgery, n = 2; and CRT/RT, n = 2). There were no deaths related to the additional treatment.

Long-term ER outcomes. The follow-up data are summarized in Table 3. The median follow-up period was 6.6 years, and the 5-year follow-up rate was 88.5%. The OS and net survival rates are shown in Figure 1. The 3- and 5-year OS rates were 88.6% (95% confidence interval [CI], 83.4–92.4) and 79.2% (95% CI, 72.2–84.8), respectively. The 5-year net survival standardized for age, sex, and calendar year was 1.04 (95% CI, 0.98–1.09). The 3- and 5-year DSS rates were 100% and 99.3% (95% CI, 95.2–99.9), respectively.

No patient developed local recurrence, whereas 33 (16%) patients developed metachronous EC. All patients who received treatment for metachronous EC were treated with ER, and all of these lesions were intramucosal SCCs. Fifty-two patients died during the follow-up period, among whom one (2%) died of the index EC (pathologic LPM invasion with LVI, i.e. high-risk cancer) although the patient did not receive additional surgery due to advanced age and cerebrovascular disease. Eighteen (35%) patients died of other organ malignancies, predominantly oral and laryngopharyngeal cancers (six patients, 12%).

Based on the receiver operating characteristic analysis, we defined the cutoff values for age, ASA-PS, PNI, and CCI as 77 years, 3, 44.0, and 3, respectively. The univariate analysis showed that ECOG-PS 2–4, ASA-PS 3, CCI $\geq$ 3, and PNI $<$ 44.0 were significantly associated with OS (Table 4).

In the multivariate analysis, an age of $\geq$77 years (hazard ratio, 2.04; 95% CI, 1.03–4.01), ASA-PS 3 (hazard ratio, 2.45; 95% CI, 1.16–5.17), and PNI $<$ 44.0 (hazard ratio, 2.73; 95% CI, 1.38–5.40) were independent prognostic factors for poor OS (Table 5).

The extracted prognostic factors for OS, including ASA-PS and PNI, were combined for further investigation (Fig. 2). If both ASA-PS 1/2 and PNI $\geq$ 44.0 were met, the 5-year OS was favorable at 87.8% (95% CI, 80.0–92.9), and net survival was 1.08 (95% CI, 1.02–1.14). Otherwise (ASA-PS 3, PNI $<$ 44.0, or both), the 5-year OS was significantly shorter at 60.7% (95% CI, 46.3–73.5) ($P < 0.001$), and the net survival was 0.95 (95% CI, 0.84–1.07).

Adverse events according to ASA-PS and PNI. The incidence of adverse events, such as perforation (3.0% *vs* 2.2%, P = 0.77 and 3.1% *vs* 2.8%, P = 0.91), pneumomediastinum (1.5% *vs* 4.4%, P = 0.21 and 1.5% *vs* 2.2%, P = 0.73), pneumonia (2.0% *vs* 4.4%, P = 0.34 and 4.6% *vs* 1.7%, P = 0.19), or stricture (11.6% *vs* 11.1%, P = 0.93 and 6.2% *vs* 13.4%, P = 0.12), had no significant difference between the ASA-PS 1/2 versus ASA-PS 3 and PNI $<$ 44.0 versus PNI $\geq$ 44.0, respectively.

Discussion

In this retrospective cohort study, we found favorable long-term outcomes after ER in late-elderly patients with superficial ESCC. The 5-year net survival standardized for age, sex, and calendar year was 1.04 (95% CI, 0.98–1.09). ASA-PS and PNI were significant prognostic factors for OS, and when the two factors were met (ASA-PS 1/2 and PNI $\geq$ 44.0), the 5-year survival rate was 87.8% (95% CI, 80.0–92.9), and net survival was 1.08 (95% CI, 1.02–1.14).

Superficial ESCC is usually not immediately fatal, but it can eventually progress to advanced EC. This progression can cause several adverse events, such as stenosis, which can ultimately lead to death from EC. The natural history of superficial ESCC should be considered when determining the indication for ER in late-elderly patients. The period required for superficial ESCC to progress to advanced EC is reportedly 4–5 years.[29] Guanrei *et al*.[29] investigated the natural history of 90 patients with untreated superficial ESCC with a long follow-up period (median [range] of 49.5 [19–78] months) and found that 52 (58%) patients' lesions remained superficial. By contrast, eight (9%) patients' lesions progressed to advanced EC, and 27 (30%) patients died of EC with an average survival time of 53.2 months. Based on the limited information regarding the natural history of ESCC, most superficial lesions are likely to remain in the early stage for a few years; however, some superficial lesions progress to advanced EC over several years, leading to death. In the present study, distant metastases from high-risk cancer developed within a few years in one patient and became lethal only 2 months later. It is difficult to predict which superficial lesions will progress to advanced EC; therefore, we recommend identifying late-elderly patients with ESCC who are expected to achieve good long-term outcomes after ER. The present study demonstrated the most favorable long-term prognosis for late-elderly patients with a low ASA-PS and high PNI; ER of ESCC should be performed in such patient.

The ASA-PS and PNI were found to be independent predictors in the multivariate analysis. By contrast, the CCI was not useful for assessment of the prognosis, although it has been used as a preoperative prognostic marker for patients with ESCC undergoing ER.[14,17,30,31] The discrepancy has three possible explanations. First, only the most severe comorbidity is adopted as an evaluation item in the ASA-PS classification, and the ASA-PS is scored

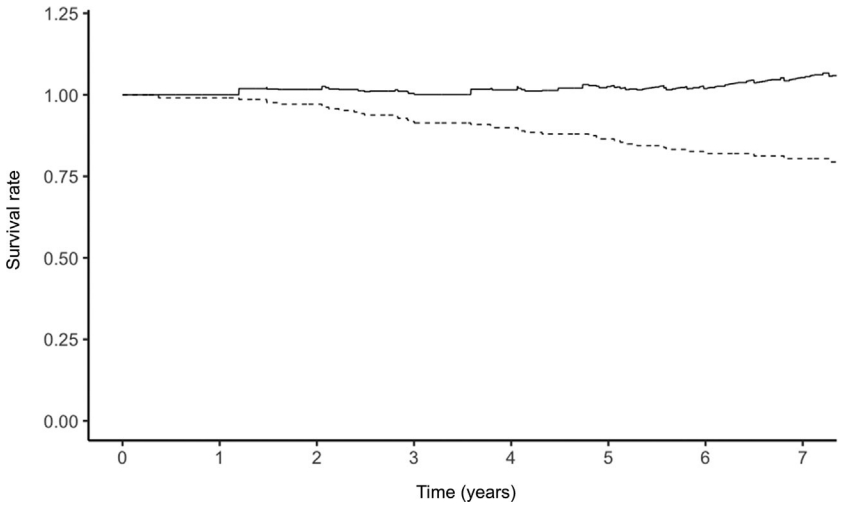

Figure 1 Overall survival (OS) and net survival of patients in this study. Net survival was the cumulative probability of surviving to an arbitrary time point since cohort entry after adjusting for other causes of death in the general population. The 3- and 5-year OS rates were 88.6% (95% confidence interval [CI], 83.4–92.4) and 79.2% (95% CI, 72.2–84.8), respectively. The 5-year net survival was 1.04 (95% CI, 0.98–1.09). —, Net survival; - -, Overall survival.

Table 4 Association between overall survival and patient and lesion factors by univariate analysis using log-rank test (*n* = 208)

Factors	Patients, n	Five-year overall survival rate, % (95% confidence interval)	*P*-value
Patient			
Age, years			0.178
<77	75	87.0 (76.7–93.1)	
≥77	133	74.3 (64.6–82.1)	
Sex			0.175
Male	185	78.5 (71.0–84.4)	
Female	23	86.2 (58.2–96.5)	
Eastern Cooperative Oncology Group performance status			0.001
0 or 1	199	80.2 (73.2–85.8)	
2–4	9	43.8 (11.4–82.5)	
American Society of Anesthesiologists physical status			<0.001
1 or 2	170	83.8 (76.2–89.4)	
3	38	59.6 (42.5–74.6)	
Charlson comorbidity index			<0.001
0–2	144	84.8 (76.7–90.5)	
≥3	64	66.2 (52.3–77.8)	
Prognostic nutritional index			<0.001
≥44.0	152	85.8 (78.4–91.0)	
<44.0	56	55.2 (36.4–72.7)	
Lesion			
Curability			0.795
Low-risk cancer	194	80.2 (73.2–85.8)	
High-risk cancer	14	64.8 (30.8–88.4)	

Table 5 Association between overall survival and patient and lesion factors by multivariate analysis using Cox proportional hazards model (n = 208)

	Patients, *n*	Deaths, *n*	Hazard ratio	95% confidence interval
Age, years				
<77	75	14	1	1.03–4.01
≥77	133	38	2.04	
Sex				
Female	23	4	1	0.69–12.4
Male	185	48	2.92	
Eastern Cooperative Oncology Group performance status				
0 or 1	199	47	1	0.94–11.9
2–4	9	5	3.35	
American Society of Anesthesiologists physical status				
1 or 2	170	29	1	1.16–5.17
3	38	23	2.45	
Charlson comorbidity index				
0–2	144	28	1	0.83–3.67
≥3	64	24	1.75	
Prognostic nutritional index				
≥44.0	152	31	1	1.38–5.40
<44.0	56	21	2.73	
Curability				
Low-risk cancer	194	48	1	0.34–3.95
High-risk cancer	14	4	1.16	

according to the severity for each patient. However, the CCI system contains many evaluation items, including comorbidities and malignancy, and all scores for these items are summed. Thus, the CCI is likely to be higher than the ASA-PS. In our study, 31% (64/208) of patients had a CCI of ≥3, whereas only 18% of patients had an ASA-PS of 3 (indicating severe systemic disease). Second, a history of malignancy is classifiable by the CCI but not the ASA-PS. Patients with ESCC are more likely to have malignancies in other organs,[32] especially oral and laryngopharyngeal cancer, which are attributed to field cancerization.[33] In the present study, 88 (42%) patients had a history of cancers in other organs, among which the major malignancy was oral and laryngopharyngeal cancer (43%, 38/88). This fact, specific to patients with ESCC, is another reason that the CCI was higher than the ASA-PS. Third,

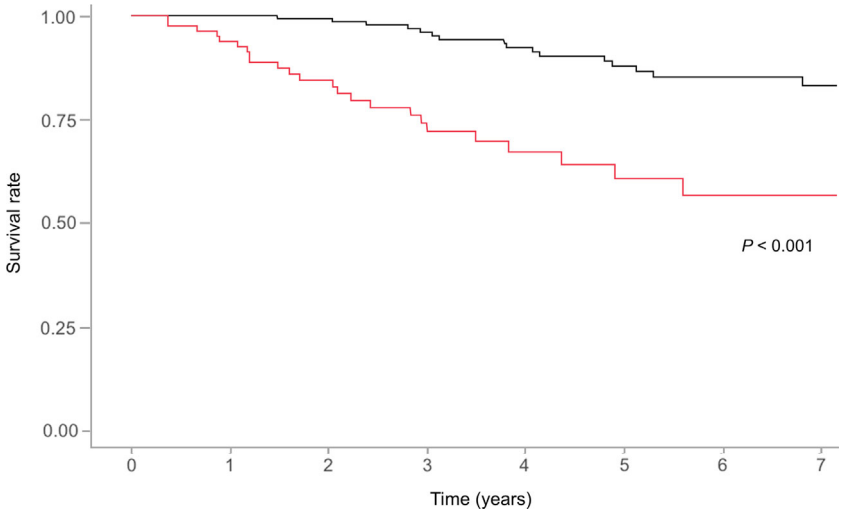

Figure 2 Comparison of overall survival (OS) of patients with and without poor prognostic background factors: American Society of Anesthesiologists physical status (ASA-PS) of 3 and prognostic nutritional index (PNI) of <44.0. The 5-year OS of patients with either ASA-PS 3, PNI < 44.0, or both, and that of patients with neither were 60.7% (95% confidence interval [CI], 46.3–73.5) and 87.8% (95% CI, 80.0–92.9), respectively, and the 5-year net survival was 0.95 (95% CI, 0.84–1.07) and 1.08 (95% CI, 1.02–1.14), respectively. —, Patients with neither ASA-PS nor PNI <44; —, Patients with either ASA-PS, PNI <44, or both.

medical progress has improved treatment outcomes for specific diseases in recent years, achieving a better prognosis of solid cancer, even with distant metastasis, and an increase in controllable comorbidities. Improvements in the treatment of malignancies and comorbidities may have changed the effect of the CCI on the prognosis. These background factors may explain why the ASA-PS had a stronger association with the life prognosis than the CCI in elderly patients, although the CCI still affected OS. We consider that the ASA-PS is a simple and useful index to comprehensively evaluate the risk of death from causes unrelated to EC in elderly patients with ESCC treated by ER.

The PNI is a significant prognostic factor for patients who undergo ESD for ESCC,[30,31] and it was significantly associated with OS in the present study. Considering the results of this study and previous reports, the PNI is an important factor for predicting the prognosis of elderly patients undergoing ER for ESCC. In the real-world setting, some patients with ESCC are likely to have an impaired nutritional status due to alcoholic liver cirrhosis attributed to heavy drinking, which may also influence the OS of those undergoing ER. Indeed, the 5-year OS rate of patients with liver cirrhosis was significantly lower than that of patients without liver cirrhosis in one study.[34] Recent studies have revealed the importance of the PNI in the long-term outcomes of several comorbidities.[35–38] To improve the prognoses of patients with ESCC treated with ER, the total management of comorbid diseases and the nutritional status should be emphasized. The present study indicates the need to evaluate the ASA-PA and PNI in determining whether to perform ER and the importance of more carefully determining the indications for esophageal ER in patients with a high ASA-PS or low PNI.

After standardization for age, sex, and calendar year in our study, the net survival of patients was better than the survival of the general Japanese population. In particular, when ASA-PS 1/2 and PNI ≥ 44.0 were met, the 5-year survival rate was 87.8% and net survival was 1.08 (95% CI, 1.02–1.14). In clinical practice, it is often difficult to determine whether to perform ER in elderly patients. This study suggests that ER is useful in patients with a good ASA-PS and PNI.

Onodera *et al.*[19] reported that the incidence of postoperative complications for gastrointestinal diseases was higher in patients with a low PNI than in those with a high PNI. ASA-PS also has strong independent associations with postoperative medical adverse events and mortality across surgical procedures.[39] Here, there was no significant difference in adverse events after esophageal ER between low versus high ASA-PS and low versus high PNI. Furthermore, no patient died of adverse events related to esophageal ER. Similar results were demonstrated in a previous study using the ASA-PS classification by adjusting the baseline characteristics using a propensity analysis.[40] Considering these results, performing ER do not seem to affect survival even in patients with a high ASA-PS or low PNI, unless they have serious comorbidities. Therefore, ER for ESCC would be a safe and feasible minimally invasive treatment method regardless of comorbid diseases and nutritional status.

This study has several limitations. First, it was a single-center retrospective study. In addition, this study did not include a control group in which patients did not receive ER for ESCC due to the patient's condition (i.e. age, underlying diseases) and preference. Thus, selection bias may exist. Further prospective trials are required for validation. Second, we had no information on height, weight, body mass index, or sarcopenia. A meta-analysis revealed that preoperative sarcopenia in patients with EC is associated with OS after esophagectomy.[41] Thus, these factors would have been valuable in the present study.

In conclusion, ER in late-elderly patients with ESCC may improve the life expectancy by preventing EC mortality. ER is recommended in patients with a good ASA-PS and PNI.

Acknowledgments

This work was supported in part by Grants-in-Aid from the Ministry of Education, Culture, Sports, Science and Technology, Japan (22H02828 to M.O.).

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Endoscopic resection results and sedation method.