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Skeletal Muscle Depletion: A Risk Factor for Pneumonia following Gastric Endoscopic Submucosal Dissection in Elderly Patients

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Keywords
Pneumonia · Gastric neoplasm · Elderly · Endoscopic submucosal dissection · Sarcopenia

Abstract
Introduction: Endoscopic submucosal dissection (ESD) is an effective treatment for gastric neoplasms in elderly patients; however, it involves several adverse events, including pneumonia. This study aimed to investigate whether skeletal muscle depletion (SMD) was associated with the development of pneumonia in elderly patients who underwent gastric ESD. ***Methods:*** This retrospective observational cohort study included 157 patients (≥80 years) who had undergone gastric ESD. The skeletal muscle cross-sectional area was measured by CT, and the value of the third lumbar vertebra skeletal muscle index (L3 SMI) was evaluated. The SMD was defined as an L3 SMI value ≤38.0 cm^2/m^2 for women and ≤42.0 cm^2/m^2 for men. Pneumonia was also diagnosed using CT to identify all included patients. ***Results:*** Among 157 patients, 66 (42.0%) showed SMD. In the SMD group, the incidence of pneumonia was 21.2%, whereas it was 7.7% in the non-SMD group ($p = 0.018$). The longest hospitalization duration was 19 days. Antibiotics were administered in 61.9% of the patients. Procedure time was not significantly different between the groups (72 ± 54 min vs. 62 ± 44 min, $p = 0.201$). On multivariate analysis, SMD was an independent risk factor for the development of pneumonia (odds ratio = 3.16, 95% confidence interval, 1.18–8.50, $p = 0.023$). ***Conclusions:*** SMD was not a rare entity in patients aged ≥80 years with gastric neoplasms. SMD was a significant risk factor for pneumonia related to gastric ESD in elderly patients.

Introduction

Gastric cancer is one of the most common malignancies, accounting for approximately 780,000 deaths (8.2% of all deaths), which was ranked as the third highest rate of cancer-related mortality worldwide in 2018 [1]. This malignancy usually develops in elderly patients. Endoscopic submucosal dissection (ESD) is now widely accepted as a less invasive treatment than surgery for the

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treatment of early gastric cancers in elderly patients [2–5]. However, some adverse events such as bleeding, perforation, and pneumonia are receiving much attention because the development of these events can lead to clinically worse outcomes that need additional treatment [6, 7]. Several risk factors for gastric ESD-related pneumonia have been recently reported. For instance, aging, a history of diabetes mellitus, cerebrovascular disease or chronic obstructive pulmonary disease, delirium, abnormal preoperative pulmonary function tests (PFTs), and extended procedure times have been identified as risk factors in some reports [8–13]. However, the demographic and baseline characteristics of patients in these reports included a variety of ages, and the definition of ESD-related pneumonia was different.

Based on our clinical practice, elderly frail patients tend to develop ESD-related pneumonia more compared to young patients. Therefore, it is important to investigate the risk factors of ESD-related pneumonia in elderly patients.

Sarcopenia has been defined as the loss of skeletal muscle mass and strength that occurs with advancing age [14]. Sarcopenia is related to other conditions or diseases, including gastrointestinal disease, liver disease, heart failure, and several types of malignancies [15]. Sarcopenia is a syndrome associated with the risk of harmful outcomes, such as decreased physical activity and quality of life and increased mortality [16–20]. Sarcopenia can also be used to predict the prognosis of patients with several types of digestive organ cancers [21, 22].

Recent studies have revealed that the incidence of aspiration pneumonia is high in elderly patients with sarcopenia due to skeletal muscle mass depletion, and thus they have a high potential for impairment of swallowing and expectoration [23]. Skeletal muscle depletion (SMD) is also involved in malnutrition and decreased immunity, both of which increase the risk of infection [24, 25]. The relationship between SMD and ESD-related pneumonia in elderly patients with gastric neoplasms remains unclear. We therefore retrospectively evaluated that relationship.

Materials and Methods

Patients

This single-center retrospective study was approved by the Institutional Review Board of Gifu University Hospital, Gifu, Japan (Approval No. 2018-153). Between January 2013 and September 2018, 828 patients underwent gastric ESD for the treatment of gastric neoplasms at Gifu University Hospital. Patients under the age of 80 years, those with lesions in the gastric tube and gastric remnant, and the ones with missing data necessary for calculating skeletal muscle index such as body weight were excluded.

We assessed the patients' baseline characteristics, including age, sex, BMI, presence of comorbidities, pulmonary function, Eastern Cooperative Oncology Group Performance Status (ECOG-PS), and performance status according to the American Society of Anesthesiologists (ASA-PS) [26, 27]. The presence of comorbidities was evaluated using the Charlson comorbidity index (CCI). When assessing the CCI, 2 points for the presence of solid tumors were not counted because all patients in this study had cancer. PFTs were performed using a spirometer (CHESTAC-8800; Chest, Tokyo, Japan). Patients who showed a forced expiratory volume in 1 s as percentage of forced vital capacity (FEV1%) <70% or predicted vital capacity (%VC) <80% were defined as having an obstructive or restrictive disorder, respectively [28, 29]. A mixed-type respiratory disorder was defined when patients had both obstructive and restrictive disorders [29].

Indications and Protocol for ESD

The indications for ESD were based on the Japanese guidelines for gastric cancers [30]. Within the ESD protocol, PFTs were examined approximately 1 month before admission. On the day of admission, blood samples were obtained for assessing complete blood counts and general chemistry, and chest radiography was performed to exclude preoperative lung diseases. After these examinations revealed no problems, ESD was performed on the admission day. ESD was performed using an endoscope with a water-jet function (EVIS GIF-Q260J; Olympus, Tokyo, Japan), with a dual knife (KD-650; Olympus Medical Systems Co., Ltd., Tokyo, Japan) or the FlushKnife BTS (FUJIFILM Co., Tokyo, Japan). A VIO electrosurgical generator (VIO 300D; ERBE, Tubingen, Germany) was used for all ESD procedures. An overtube and endotracheal tube were not placed in any of the patients. Both diazepam and pentazocine were used for conscious sedation. During the ESD procedure, CO_2 insufflation was used. Prophylactic antibiotics were not administered. During the procedure, the suction of saliva from the mouth was performed by nurses as necessary. One day after ESD, CT was performed for all patients regardless of the presence of symptoms. Patients without any adverse events 7 days after ESD were discharged.

Lesion Characteristics

Tumor location was classified as upper, middle, or lower third of the stomach. Macroscopic type, tumor size, depth, histologic type, ulcerative findings, and lymphovascular involvement were pathologically determined. The depth of submucosal invasion was categorized based on the distance from the lowest portion of the muscularis mucosae as SM1 (<500 μm) and SM2 (≥500 μm) [30]. The histologic type was categorized as a differentiated or undifferentiated type based on the major histologic features of each lesion [31].

Definition and Evaluation of ESD-Related Pneumonia

ESD-related pneumonia was defined as a newly detected lobar consolidation or interstitial infiltrates by the 1-day post-ESD CT. Radiologists detected lesions without any clinical information about ESD. Clinicopathologic features of pneumonia, including distribution of consolidation or infiltration, body temperature, and white blood cell counts, were evaluated 1 day after ESD.

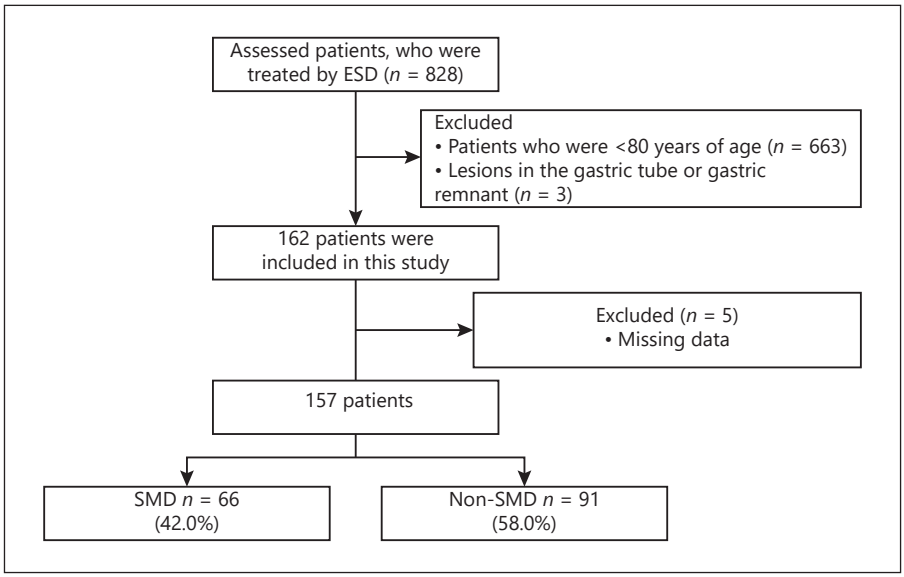

Fig. 1. A study flowchart of the patients who underwent ESD. ESD, endoscopic submucosal dissection; SMD, skeletal muscle depletion.

Evaluation of Skeletal Muscle Mass

The volume of skeletal muscle mass was evaluated using CT images taken 1 day after ESD. The muscles in the third lumbar vertebra (L3) region were analyzed using SYNAPSE VINCENT software (version 3.0; Fujifilm Medical, Tokyo, Japan). The cross-sectional area of the muscle (cm^2) at the L3 level computed from each image was normalized by the square of the height (m^2) to obtain the L3 skeletal muscle index (SMI, cm^2/m^2) [32]. SMD was defined based on a guideline for sarcopenia according to the Japan Society of Hepatology [33]. The SMD was defined as an L3 SMI value ≤38.0 cm^2/m^2 for women and ≤42.0 cm^2/m^2 for men. These values were strongly correlated with low skeletal muscle mass [34].

Statistical Analysis

Categorical variables are reported as percentages. Continuous variables that were not normally distributed are expressed as the median ± range, whereas continuous variables that were normally distributed are expressed as the mean ± standard deviation. Categorical variables were compared between the 2 groups (SMD group vs. non-SMD group) using Fisher's exact test. Continuous variables were compared using *T* tests or Mann-Whitney *U* tests. Differences were considered statistically significant at $p < 0.05$.

Risk factors for ESD-related pneumonia were assessed using a multivariate logistic regression model adjusted for covariates, and odds ratios (ORs) and 95% confidence intervals (CIs) were determined. In addition to SMD, covariates including procedure time and diabetes mellitus were chosen based on a priori clinical judgment and previous research [8–13]. The 95% CI of the OR was used to assess the statistical significance at the level of $\alpha = 0.05$.

Receiver operating characteristic curve analysis was used to establish the optimal cutoff value of SMI that can be used to predict ESD-related pneumonia. Analyses were conducted using EZR software (version 3.51; Saitama Medical Center, Jichi Medical University, Saitama, Japan). The software is a graphic user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) that has been modified to include frequently used biostatistical functions [34].

Table 1. Demographic and clinical characteristics of the 157 patients (aged ≥80 years) with gastric cancer treated by ESD

Age, median (range), years	83 (80–94)
Sex, *n* (%)	
Male	118 (75.2)
Female	39 (24.8)
BMI, kg/m^2	22.3±3.4
Location of the lesion, *n* (%)	
Upper	30 (19.1)
Middle	52 (33.1)
Lower	75 (47.8)
CCI, *n* (%)	
0	69 (43.9)
1	55 (35.0)
2	18 (11.5)
3	11 (7.0)
4	2 (1.3)
5	2 (1.3)
Comorbidities (with overlap) categorized by CCI, *n* (%)	
Diabetes mellitus	28 (16.5)
Malignancy without metastasis	26 (15.3)
Cerebrovascular diseases	19 (11.2)
Myocardial infarction	14 (8.2)
Chronic lung diseases	12 (7.1)
Peptic ulcers	8 (4.7)
Cognitive impairment	7 (4.1)
Connective tissue diseases	6 (3.5)
Moderately renal dysfunction	3 (1.8)
Heart failure	2 (1.2)
Diabetic nephropathy	2 (1.2)
Lymphoma	1 (1.0)
Peripheral vascular diseases	1 (1.0)
Psychiatric disorder (depression)	1 (0.6)

ESD, endoscopic submucosal dissection; CCI, Charlson comorbidity index.

Table 2. Baseline characteristics of the SMD and non-SMD groups

	SMD (n = 66)	Non-SMD (n = 91)	p value
Age, years	83 (80–94)	82 (80–93)	0.62‡
Sex male/female, male (%)	50/16 (75.8)	68/23 (74.7)	1¶
BMI, kg/cm^2	20.6±2.9	23.6±3.1	<0.001§
SMI, cm^2/m^2	35.8±4.0	47.3±5.4	<0.001§
ECOG performance status, n (%)			
0–1	66 (100)	91 (100)	1¶
2–4	0 (0.0)	0 (0.0)	1¶
ASA-PS, n (%)			
I	6 (9.1)	9 (9.9)	0.34¶
II	41 (62.1)	65 (71.4)	0.34¶
III	19 (28.8)	17 (18.7)	0.34¶
≥IV	0 (0.0)	0 (0.0)	0.34¶
Taking antithrombotics, n (%)	17 (25.8)	25 (27.5)	0.86¶
PFTs			
FEV1%	69.9±13.5	67.8±9.2	0.25§
%VC	95.7±19.7	108.0±17.0	<0.001§
Normal	27 (35.0%)	34 (36.7%)	0.75¶
Obstructive type	25 (41.7%)	53 (58.9%)	0.046¶
Restrictive type	9 (15.0%)	3 (3.3%)	0.014¶
Mixed type	5 (8.3%)	1 (1.1%)	0.038¶
CCI, n (%)			
0	22 (33.3)	47 (51.6)	0.14¶
1	27 (40.9)	28 (30.8)	0.14¶
2	8 (12.1)	10 (11.0)	0.14¶
3	6 (9.1)	5 (5.5)	0.14¶
4	1 (1.5)	1 (1.1)	0.14¶
5	2 (3.0)	0 (0.0)	0.14¶
Comorbidities, n (%)			
Diabetes mellitus	12 (18.2)	14 (15.4)	0.67¶
Cancer of the other organs	14 (21.2)	9 (9.9)	0.066¶
Cerebrovascular diseases	9 (13.6)	7 (7.7)	0.29¶
Chronic lung diseases	10 (15.2)	6 (6.6)	0.11¶
Myocardial infarction	4 (6.1)	8 (8.8)	0.76¶

SMD, skeletal mass depletion; SMI, skeletal mass index; ECOG, Easter Cooperative Oncology Group; ASA-PS, American Society of Anesthesiologists Physical Status; PFTs, pulmonary function tests; FEV1%, forced expiratory volume in 1 s as percentage of forced vital capacity; %VC, predicted vital capacity; CCI, Charlson comorbidity index. ‡ Mann-Whitney U test. ¶ Fisher's exact test. § Student's t test.

Results

Baseline Characteristics of the Enrolled Patients

Among the 828 patients who underwent ESD for gastric cancer, 663 patients were excluded due to age (<80 years old), 3 were excluded due to lesions in the gastric tube or gastric remnant, and 5 were excluded due to a lack of data. Of the remaining 157 patients, 66 (42.0%) were diagnosed with SMD. The patient flow is shown in Figure 1.

The patients' baseline characteristics are summarized in Table 1. The patients consisted of 118 men (75.2%) with a median age of 83 years (range 80–94 years). The median CCI value was 1 (0–5), while the mean BMI was 22.4 ± 3.3 kg/m^2.

Comparison of Baseline Characteristics and Clinical Outcomes of Patients with and without SMD

As listed in Table 2, the SMD group had significantly lower BMI (20.6 ± 2.9 vs. 23.6 ± 3.1, $p < 0.001$) and SMI (35.8 ± 4.0 vs. 47.3 ± 5.4, $p < 0.001$). All patients had an ECOG-PS of 0–1, and ASA-PS was not significantly different in each group. In PFTs, the incidence of obstructive impairment was high in the non-SMD group (58.9 vs. 41.7%, $p = 0.046$), but that of restrictive and mixed-type

Table 3. Comparison of clinical outcomes between SMD and non-SMD groups

	SMD (n = 66)	Non-SMD (n = 91)	p value
Procedure time, min	56 (10–235)	51 (10–218)	0.40‡
Macroscopic type, *n* (%)			
Elevated	29 (43.9)	52 (57.1)	0.23¶
Flat/depressed	13 (19.7)	16 (17.6)	0.23¶
Mixed	24 (36.4)	23 (25.3)	0.23¶
Tumor size, mm	15 (4–53)	15 (1–55)	0.62‡
Tumor depth, *n* (%)			
Mucosa	56 (84.8)	75 (82.4)	0.58¶
Submucosa, SM1	5 (7.6)	11 (12.1)	0.58¶
Submucosa, SM2	5 (7.6)	5 (5.5)	0.58¶
Histologic type, *n* (%)			
Differentiated	61 (93.8)	83 (92.2)	0.63¶
Undifferentiated	2 (3.1)	4 (4.4)	0.63¶
Neuroendocrine tumor	2 (3.1)	1 (1.1)	0.63¶
Nonneoplastic	0 (0.0)	2 (2.2)	0.63¶
Ulcerative finding, *n* (%)	3 (4.6)	2 (2.2)	0.65¶
Lymphovascular involvement, *n* (%)	9 (13.8)	10 (11.1)	0.46¶
Delayed bleeding, *n* (%)	4 (6.1)	2 (2.2)	0.24¶
Delayed perforation, *n* (%)	1 (1.5)	0 (0.0)	0.42¶
Pneumonia, *n* (%)	14 (21.2)	7 (7.7)	0.018¶

SMD, skeletal muscle depletion; SM1, tumor infiltration into the submucosal layer <500 μm from the muscularis mucosae; SM2, tumor infiltration into the submucosal layer ≥500 μm from the muscularis mucosae. ‡ Mann-Whitney U test. ¶ Fisher's exact test.

Table 4. Clinicopathologic features of the 21 patients with ESD-related pneumonia

Age, median (range), years	83 (80–91)
Sex, *n* (%)	
Male	14 (66.7)
Female	7 (33.3)
BMI, kg/m^2	20.7±2.1
Male	20.8±1.8
Female	20.4±2.7
CCI, *n* (%)	
0	7 (33.3)
1	7 (33.3)
2	3 (14.3)
3	3 (14.3)
4	0 (0.0)
5	1 (4.8)
Location of the pneumonia, *n* (%)	
Left lobe	12 (57.1)
Right lobe	4 (19.0)
Bilateral	5 (23.8)
Procedure time, min	65 (12–235)
Temperature, °C	38.2±0.7
White blood cell counts, /μL	10,290 (5,380–17,080)
Antibiotics use, *n* (%)	13 (61.9)
Prolongation of admission, *n* (%)	5 (23.8)
Days of prolonged admission	4 (1–68)

ESD, endoscopic submucosal dissection; CCI, Charlson comorbidity index.

impairment was high in the SMD group (15.0 vs. 3.3%, p = 0.014, and 8.3 vs. 1.1%, p = 0.038, respectively). There were no significant differences between the SMD and non-SMD groups with respect to age, sex, CCI, and comorbidities.

The comparison of clinical outcomes between the SMD and non-SMD groups is summarized in Table 3. Procedure time (mean procedure time for ESD was 65 ± 47 min), macroscopic type, tumor size, tumor depth, histologic type, presence of ulcerative findings, and lymphovascular involvement were not significantly different in each group. Four patients (6.1%) and 1 patient (1.5%) developed delayed bleeding and delayed perforation, respectively, in the SMD group, while there were 2 (2.2%) and 0 (0.0%), respectively, in the non-SMD group. Of the enrolled 157 patients, 21 (13.4%) developed ESD-related pneumonia. Of the 21 patients, 14 (21.2%) were in the SMD group and 7 (7.7%) were in the non-SMD group (p = 0.018) (shown in Table 3).

Clinicopathologic Features of ESD-Related Pneumonia

The clinicopathologic features of the 21 patients who developed ESD-related pneumonia are summarized in Table 4. BMI was 20.7 ± 2.1. Seven patients (33.3%) had a CCI score of 0, and the other 14 (66.7%) had a CCI ≥1. Pneumonia developed in the left lobe in 12 patients (57.1%), the right lobe in 4 patients (19.0%), and bilateral lobes in 5 patients (23.8%). The median procedure time was 65 (12–235) minutes. Body temperature was 38.2 ± 0.7°C, and white blood cell counts 1 day after ESD were 10,290 (5,380–17,080)/μL. Antibiotics were administered to 13 patients (61.9%). Five patients (23.8%) needed prolongation of admission. The median duration of additional hospital stay was 4 (range 1–68).

Comparison of ESD-Related Pneumonia Characteristics between the SMD and Non-SMD Groups

A comparison of the characteristics of pneumonia in the SMD and non-SMD groups is summarized in Table 5. In the SMD group, 8 (57.1%), 4 (28.6%), and 2 (14.3%)

Table 5. Comparison of characteristics of ESD-related pneumonia in the SMD and non-SMD groups

	SMD (n = 14)	Non-SMD (n = 7)	p value
Sex, n (%)			
Male	11 (78.6)	3 (42.9)	0.16¶
Female	3 (21.4)	4 (57.1)	0.16¶
Location of the pneumonia, n (%)			
Left lobe	8 (57.1)	4 (57.1)	0.31¶
Right lobe	4 (28.6)	0 (0.0)	0.31¶
Bilateral lobes	2 (14.3)	3 (42.9)	0.31¶
CCI, n (%)			
0	3 (21.4)	4 (57.1)	0.25¶
1	4 (28.6)	3 (42.9)	0.25¶
2	3 (21.4)	0 (0.0)	0.25¶
3	3 (21.4)	0 (0.0)	0.25¶
5	1 (7.1)	0 (0.0)	0.25¶
PFTs			
FEV1%	71.0±15.7	70.3±10.9	0.92§
%VC	90.7±26.8	99.7±23.0	0.48§
Abnormal PFTs*	8 (47.1%)	6 (35.3%)	1.00¶
Procedure time, min	58 (19–235)	75 (12–178)	0.71¶

ESD, endoscopic submucosal dissection; SMD, skeletal mass depletion; CCI, Charlson comorbidity index; PFTs, pulmonary function tests; FEV1%, forced expiratory volume in 1 s as percentage of forced vital capacity; %VC, predicted vital capacity. * Abnormal PFTs are the proportion of patients with obstructive disease or restrictive disease. Data were missing for 4 patients. ¶ Fisher's exact test. § Sudent's t test.

Table 6. Predictors for the development of ESD-related pneumonia

Variable	OR	95% CI	p value
Procedure time	1.00	0.99–1.01	0.45
Diabetes mellitus	2.95	1.02–8.57	0.047
SMD	3.16	1.18–8.50	0.023

ESD, endoscopic submucosal dissection; OR, odds ratio; CI, confidence interval; SMD, skeletal muscle depletion.

patients developed pneumonia in the left, right, and bilateral lobes, respectively, while 4 (57.1%) and 3 (42.9%) in the left and bilateral lobes, respectively, in the non-SMD group (p = 0.31). The CCI was not significantly different between the groups. Patients with abnormal PFTs, including those with obstructive or restrictive disease, were 8 (47.1%) in the SMD group and 6 (35.3%) in the non-SMD group (p = 1.00). The procedure time was 58 (19–235) minutes in the SMD group and 75 (12–178) minutes in the non-SMD group (p = 0.20).

Relationship between ESD-Related Pneumonia and SMD

The results of the multivariate analysis revealed that SMD and diabetes mellitus were independent risk factors for the development of pneumonia (OR = 3.16; 95% CI: 1.18–8.50; p = 0.023; and OR = 2.95; 95% CI: 1.02–8.57; p = 0.047), whereas ESD procedure time (OR = 1.00; 95% CI: 0.99–1.01; p = 0.45) was not an independent risk factor (shown in Table 6). When compared to patients without pneumonia, men with pneumonia had a significantly lower SMI (38.9 ± 6.6 vs. 44.3 ± 7.2, p = 0.0034). As SMI decreased, the probability of developing pneumonia increased among men (shown in Fig. 2a). The optimal cut-off value of SMI for predicting the development of pneumonia was 43.4 in men, with an AUROC of 0.78 (shown in Fig. 2b). In women, the probability of developing pneumonia was not associated with SMI in the present study; the AUROC was 0.57 in women.

Discussion

This study clarified the risk factors for ESD-related pneumonia in elderly patients with gastric neoplasms. The results of the present study clearly showed the first evidence that SMD predicts the development of ESD-related pneumonia in elderly patients aged ≥80 years. Sarcopenia is significantly associated with different diseases including frailty or dysphagia [15–25, 35]. Although sarcopenia is defined by both loss of skeletal muscle and strength, our study retrospectively focused on only one of them (volume of skeletal mass). Although there were no significant differences between the SMD and non-SMD groups in ESD procedure time which is known as a risk factor for ESD-related pneumonia [8, 9, 11–13], the patients in the former group easily developed pneumonia. A possible reason why elderly patients with SMD easily develop ESD-related pneumonia is that swallowing function, which is important in preventing erroneous aspiration, may be weakened in patients with sarcopenia. Sarcopenia has been reported to be an independent risk factor for dysphagia among older people [35]. It is also expected that the patient's coughing reflex is compromised when the skeletal muscle function decreases, especially in specific situations, such as under conscious sedation, where some patients who lose skeletal muscle function may easily develop aspiration pneumonia.

In this study, we used a CT scan to diagnose ESD-related pneumonia because the examination is more accurate than chest radiography [36, 37]. Therefore, com-

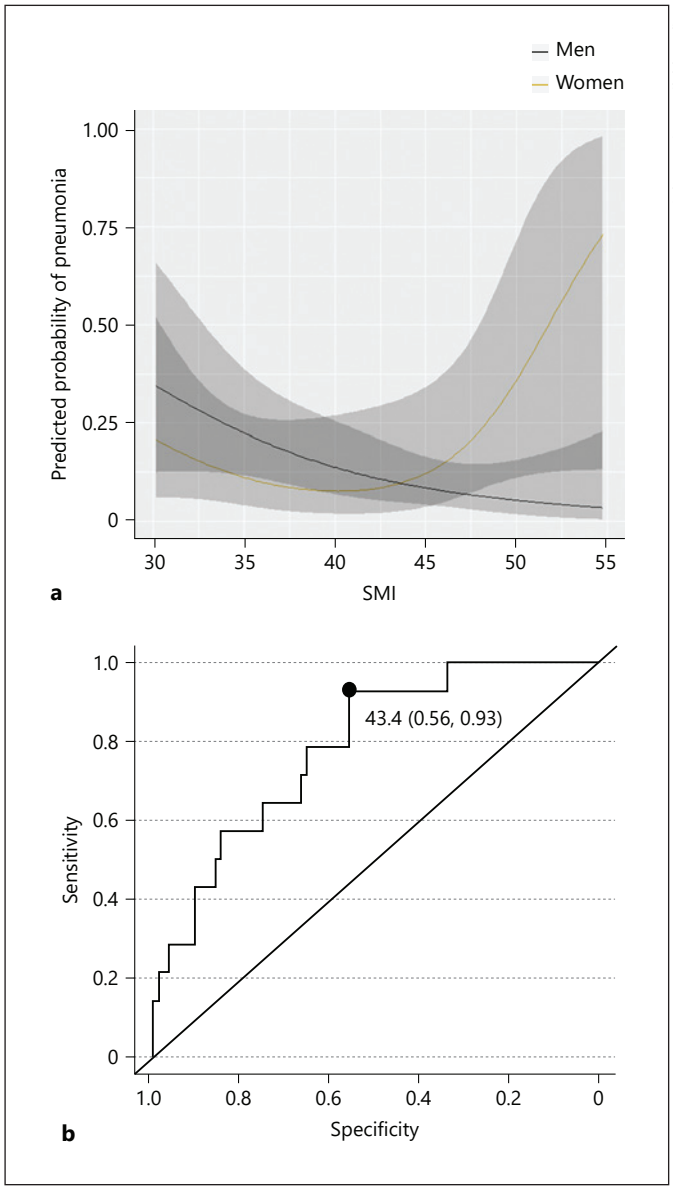

Fig. 2. a Predicted probability of ESD-related pneumonia. Blue line: male. Yellow line: female. **b** Receiver operating characteristic curve of ESD-related pneumonia in men who underwent ESD. ESD, endoscopic submucosal dissection.

pared to a previous study using simple chest radiographic images for the diagnosis of pneumonia, or obtaining CT in case pneumonia was suspected, the incidence of pneumonia in our study had to be close to the real incidence. Actually, the reported incidence of pneumonia after ESD was 0.8–4.0%, and that of our study was 13.4% [9–13]. In case thin elderly patients had uncertain fever after ESD, CT should be obtained when it is difficult to diagnose pneumonia just by simple chest radiographic study. For exploration to prevent ESD-related pneumonia, an accurate diagnosis of pneumonia is necessary. CT should have been obtained as a control before ESD in this study. However, we regarded that chest radiography is sufficient for the patients with no symptoms. The depletion of skeletal muscle mass was also evaluated by CT. With the evaluation of skeletal muscle mass, there is a strong correlation between the results when measuring the L3 SMI and performing bioelectrical impedance analysis, which reflects whole-body muscle mass [32, 33]. Therefore, in addition to the diagnosis of ESD-related pneumonia, CT examination is a useful tool for the evaluation of loss of skeletal mass. CT scans were performed within 48 h after admission. Thus, pneumonias in this study were different from hospital-acquired pneumonia. It should be noted that SMD was not an independent risk factor for hospital-acquired pneumonia but ESD-related pneumonia.

Procedure time was previously reported as a risk factor for the development of pneumonia after ESD [8, 9, 11–13]. However, in the multivariate analysis, procedure time was not identified as an independent risk factor in our study. This may be explained by the results of our mean procedure time (65.4 ± 47.4 min), which was shorter than that described in a previous report (90–103 min) [8, 9]. There is a natural concern that longer procedure times increase the risk of ESD-related pneumonia, especially in elderly patients with sarcopenia. Therefore, it is essential to complete the procedure with the least possible delay. Diabetes mellitus was also previously reported as a risk factor in the report as well as in our study [8]. Diabetes mellitus is known to predispose to infection in general, and it may be a predisposing factor for respiratory infections resulting from abnormalities in neutrophil function, such as impaired chemotaxis, phagocytosis, and bacterial killing [38, 39]. In practice, diabetes mellitus is a significant risk factor for aspiration pneumonia [40]. There is no doubt that diabetes mellitus is also a risk factor for ESD-related pneumonia.

As for predicting the risk of ESD-related pneumonia, ROC curve analysis of SMI showed a relatively reliable result in men but not in women. This is associated with a smaller sample size (39 patients) and a lower incidence of the event (7 cases) in women in the present study. These factors may cause low accuracy in the ROC curve analysis in females. This was a retrospective study conducted in a single center with a small sample size, especially for women. This is one of the limitations of the present study, and further multicenter, large-scale studies should be conducted to confirm the results of the present study.

The other limitation is that SMD is not universally defined. We used a cutoff value of SMI according to the criteria of the Japan Society of Hepatology; however, this was originally established for patients with chronic liver disease [33]. Measurement of the L3 SMI is a simple method using CT imaging. However, for institutes where the measurement of the L3 SMI is unavailable, it is difficult to objectively determine the presence of SMD. Additional simple and easy-to-use diagnostic tools, such as grip strength, should be validated to evaluate the loss of skeletal muscle mass.

Finally, it should be emphasized again that 42.0% of elderly patients (≥80 years) with early gastric cancers showed SMD in the present study. This finding suggests that the depletion of skeletal muscle mass is common in elderly patients with gastric cancer. With the aging of the society, SMD should be assessed prior to upper gastrointestinal ESD because the evaluation of SMD may be useful in identifying elderly patients who are at a high risk of developing ESD-related pneumonia. ESD under general anesthesia may prevent ESD-related pneumonia because endotracheal tube should prevent aspiration to the lung from the larynx. However, the efficacy of endotracheal intubation is uncertain. In fact, the incidence of pneumonia of upper gastrointestinal ESD did not differ between ESD under general anesthesia and that in the endoscopy room [41]. The efficacy of general anesthesia to prevent pneumonia is to be evaluated, especially in elderly patients. In conclusion, among elderly patients ≥80 years of age, SMD was a risk factor for gastric ESD-related pneumonia.

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Statement of Ethics

This single-center retrospective study was approved by the Institutional Review Board of Gifu University Hospital, Gifu, Japan (Approval No. 2018-153). Informed consent was obtained from all patients before ESD for clinical research to give them an opt-out agreement.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

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