Predicting lymph node metastasis for endoscopic resection of superficial esophageal squamous cell carcinoma

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ABSTRACT

Objective: The aims of this study were to identify risk factors for lymph node metastasis and develop a reliable risk stratification system.

Methods: Between May 2001 and December 2015, 262 patients who underwent endoscopic resection or surgery for superficial esophageal squamous cell carcinoma were enrolled. We evaluated possible predictive factors for lymph node metastasis: age, gender, tumor length, tumor area, circumferential spread, tumor location, gross appearance, depth of invasion, tumor differentiation, and lymphovascular invasion.

Results: The incidence of lymph node metastasis was 14.5% (38/262). In multivariate analysis, tumor size (>15 mm), depth of invasion (submucosal invasion), and lymphovascular invasion were significantly associated with lymph node metastasis. These factors were included in the risk stratification system and assigned scores; the total risk stratification system score was 0 to 6. The area under the receiver operating characteristic curve for predicting lymph node metastasis was 0.869 (95% confidence interval, 0.813-0.926). The high-risk group (risk stratification system score ≥ 3) exhibited a significantly higher risk of lymph node metastasis than the low-risk group (score <3) (26.5% vs 1.6%). There was no lymph node metastasis in patients with a risk stratification system of 0. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the risk stratification system were 94.7%, 55.4%, 26.5%, 98.4%, and 61.1%, respectively.

Conclusions: We developed a risk stratification system that should facilitate the identification of patients with a high or low risk of lymph node metastasis. This may aid the precise selection of patients who can undergo endoscopic resection. (J Thorac Cardiovasc Surg 2019;157:397-402)

Receiver operating characteristic curves of the RSS.

Central Message

Tumor size, LVI, and submucosal invasion were independent risk factors for LNM in patients with SESCC.

Perspective

We developed a simple RSS for the prediction of LNM, and it may be helpful in clinical practice by facilitating the precise selection of patients who can undergo ER. Also, we propose that if any of these risk factors do not apply to a tumor after ER, careful observation can be recommended.

See Editorial Commentary page 403.

Esophageal cancer is the eighth most common malignancy in the world.¹ In Korea, the detection rate of superficial esophageal squamous cell carcinoma (SESCC) during screening endoscopy has increased with the introduction of new endoscopic techniques, such as magnifying

endoscopy and narrow-band imaging endoscopy.² SESCC, defined as mucosal or submucosal esophageal cancer regardless of the presence or absence of lymph node metastasis (LNM), is associated with a better outcome because of its presentation at an early cancer stage.^{3,4} Surgical resection of the esophagus is considered the standard treatment for patients with SESCC. However, esophagectomy is associated with high morbidity and mortality rates.⁵⁻⁷ Furthermore, surgery

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Abbreviations and Acronyms

CI	= confidence interval
ER	= endoscopic resection
LNM	= lymph node metastasis
LVI	= lymphovascular invasion
NPV	= negative predictive value
OR	= odds ratio
ROC	= receiver operating characteristic
RSS	= risk stratification system
SESCC	= superficial esophageal squamous cell carcinoma

cannot be performed in patients with an advanced age or multiple comorbidities.⁸

Nowadays, endoscopic resection (ER) is widely used for the treatment of SESCO because it is minimally invasive and maintains the patient's quality of life. Several studies have reported that LNM of esophageal cancer can be detected by computed tomography, positron emission tomography, or endoscopic ultrasound. However, the accuracy of these methods is insufficient to completely exclude the presence of LNM.⁹⁻¹¹ ER is a local treatment that does not include lymph node dissection. Thus, it is important to be able to predict LNM before ER because appropriate management of SESCO with LNM involves surgery or chemoradiotherapy.

Of the current indications for ER of SESCO, only the depth of tumor invasion is defined as a criterion.³ Yet, LNM is a key factor predicting the prognosis of SESCO. Therefore, we aimed to investigate the risk factors for LNM in SESCO and develop a reliable risk stratification system (RSS) for the prediction of LNM to establish the appropriate treatment strategy for SESCO.

MATERIALS AND METHODS**Patients and Data Collection**

We retrospectively reviewed the medical records of all patients who underwent ER or esophagectomy for esophageal cancer at Severance and Gangnam Severance Hospital, Seoul, South Korea, from May 2001 to December 2015. We excluded those patients who received neoadjuvant chemotherapy or chemoradiotherapy as SESCO treatment. We excluded patients with insufficient data for a full pathologic analysis. However, patients who underwent ER and received additional surgery because of noncurative resection were included and analyzed according to the final pathology results. Thus, 262 patients were eligible for inclusion in our study. Patients enrolled in our study underwent endoscopic ultrasound, computed tomography, or positron emission tomography to determine the possibility of LNM. Endoscopic findings of the tumors were classified according to the Paris classification.¹² Nonprotruding or nonexcavated type tumors were classified as flat type, and protruding or excavated type tumors were classified as nonflat type. The Institutional Review Board of Gangnam Severance Hospital waived the need for approval of this study (Institutional Review Board No. 3-2017-0185).

Histopathologic Examination

Surgical specimens were fixed in formaldehyde, and the tumor tissue and surrounding normal tissue were serially cut perpendicularly at 2- to 5-mm intervals. The size of tumor, tumor histology, depth of invasion, and presence of lymphovascular invasion (LVI) were evaluated according to the Japanese Classification of Esophageal Carcinoma.¹³ Mucosal cancer was divided into 3 subtypes according to the extent of invasion: m1, intraepithelial carcinoma; m2, cancer invading the lamina propria; and m3, cancer in contact with or invading the muscularis mucosa. Submucosal invasion was defined as a tumor extending beyond the muscularis mucosa. The location of tumor was classified according to the guidelines of the American Joint Committee on Cancer.¹⁴ The upper esophagus extended from the thoracic inlet to the level of the tracheal bifurcation, the mid-esophagus extended from the tracheal bifurcation to the distal esophagus just above the esophagogastric junction, and the lower esophagus contained the intra-abdominal portion of the esophagus and the esophagogastric junction.

Statistical Analysis

The chi-square test or Fisher exact test was used to compare categorical parameters. The Student *t* test was used to compare continuous variables. The factors with 2-sided *P* values less than .05 in univariate analysis were included in a multivariate logistic regression analysis. Multivariate logistic regression analysis with backward stepwise selection was used to identify independent factors for predicting LNM. The Youden Index was used to identify the optimal cutoff value in the receiver operating characteristic (ROC) curve that maximized sensitivity and specificity. To define simple integer-based point scores for each predictive factor, the score of each valuable was weighted according to the beta coefficients obtained in the multivariate logistic regression model. To generate the scoring model, the beta coefficients were rounded to the nearest whole number. The total risk score for each patient was calculated by summing the scores of the individual risk factors. The Hosmer–Lemeshow test was used to confirm the goodness of fit. We obtained a calibration plot to confirm the agreement between the predicted probability and the actual probability based on the development model. The statistical calculations were performed using SPSS version 18.0 for Windows software (SPSS Inc, Chicago, Ill).

RESULTS**Clinicopathologic Characteristics**

The clinicopathologic characteristics of the 262 patients (243 male; median age, 63.5 years; range, 35-83 years) are shown in Table 1. Among these patients, 81 (30.9%) underwent ER and 181 (69.1%) underwent esophageal surgery. According to the gross appearance, 106 patients (40.5%) had a flat type tumor and 156 patients (59.5%) had a nonflat type tumor. The median tumor size was 18 mm (range, 0.5-70 mm). According to the depth of tumor invasion, 129 patients (49.2%) had mucosal cancer and 133 patients (50.8%) had submucosal cancer. Regarding the tumor histology, 23 patients (8.8%), 83 patients (31.7%), 137 patients (52.3%), and 19 patients (7.3%) had carcinoma in situ, well-differentiated, moderately differentiated, and poorly differentiated tumors, respectively. LVI was found in 35 patients (13.4%). LNM was diagnosed in 38 patients (14.5%).

Risk Factors for Lymph Node Metastasis in Superficial Esophageal Squamous Cell Carcinoma

Table 2 shows comparisons of the clinicopathologic findings according to the presence or absence of LNM.

TABLE 1. Patient clinicopathologic characteristics

Characteristics	No. of patients (n, %)
Gender	
Male	243 (92.7)
Female	19 (7.3)
Age (y, median [range])	64 (35-83)
Pretreatment evaluation	
Computed tomography	262 (100)
Endoscopic ultrasound	252 (96.2)
Positron emission tomography	250 (95.4)
Treatment modality	
ER	81 (30.9)
Surgery	181 (69.1)
Retrieved lymph node (median [range])	37 (0-108)
Tumor location within esophagus	
Upper	19 (7.3)
Middle	77 (29.4)
Lower	166 (63.4)
Tumor type on gross examination	
Flat	106 (40.5)
Nonflat	156 (59.5)
Tumor size (mm, median [range])	18 (0.5-70)
Proportion of circumferential extension	
<1/4	55 (21.0)
1/4-2/4	105 (40.1)
2/4-3/4	66 (25.2)
≥3/4	36 (13.7)
Depth of invasion	
Epithelium	23 (8.8)
Lamina propria	59 (22.5)
Muscularis mucosa	47 (17.9)
Submucosa	133 (50.8)
Differentiation	
Carcinoma in situ	23 (8.8)
Well differentiated	83 (31.7)
Moderately differentiated	137 (52.3)
Poorly differentiated	19 (7.3)
TNM stage*	
Stage I	254 (96.9)
Stage II	8 (3.1)
LVI	
Absence	227 (86.6)
Presence	35 (13.4)
LNM	
Absence	224 (85.5)
Presence	38 (14.5)

ER, Endoscopic resection; *TNM*, tumor, node, metastasis; *LVI*, lymphovascular invasion; *LNM*, lymph node metastasis. *Quoted from American Joint Committee on Cancer 8th edition.

Tumor size (originally a continuous variable) was divided at 15 mm, which was the value showing the highest area under the curve during ROC curve analysis. Univariate analysis showed that these variables were significantly associated with the presence of LNM: tumor size

($P < .001$), circumferential extension ($P = .005$), gross appearance ($P = .004$), depth of invasion ($P < .001$), tumor differentiation ($P < .001$), and LVI ($P < .001$). On the contrary, age ($P = .069$), gender ($P = .744$), and tumor location ($P = .397$) were not significantly associated with LNM. In multivariate logistic regression, tumor size (odds ratio [OR], 3.417; 95% confidence interval [CI], 1.280-9.122; $P = .014$), depth of invasion (OR, 15.757; 95% CI, 3.577-69.402; $P < .001$), and LVI (OR, 8.699; 95% CI, 3.494-21.657; $P < .001$) were significantly associated with LNM (Table 3).

Risk Stratification System for Prediction of Lymph Node Metastasis in Superficial Esophageal Squamous Cell Carcinoma

We assigned a risk score to each predictor that showed a significant association with LNM in the multivariate analysis. Tumor size of more than 15 mm was assigned 1 point, submucosal invasion was assigned 3 points, and the presence of LVI was assigned 2 points (Table 4). We analyzed LNM by summing these 3 scores; the final total scores ranged from 0 to 6. Because submucosal invasion was determined to be the most powerful risk factor of LNM, the patients were classified into 2 groups according to depth of invasion. In each group, the LNM rate was examined by subdividing the group according to LVI and tumor size. There was no LNM in patients with mucosal cancer and a tumor size less than 15 mm. In patients with submucosal cancer, the LNM rate was almost double when the tumor size was at least 15 mm, compared with less than 15 mm, regardless of the presence or absence of LVI (LVI (–): 20.3% vs 10.0%, LVI (+): 76.2% vs 37.5%) (Table 5). LNM relative to tumor size and depth of invasion in SESCC was further analyzed (Table 6). If the depth of invasion was less than the muscularis mucosa, there was no LNM, irrespective of the tumor size. In contrast, if the tumor exhibited submucosal invasion, there was a possibility of LNM even if the tumor size was 15 mm or less (14.6%).

The optimal cutoff value for LNM was 3 points on the RSS according to the ROC curve analysis (Table E1). Therefore, we divided the patients into 2 groups: a low-risk group (RSS score <3 points) and a high-risk group (RSS score ≥3 points). We noted LNM in 1.6% (2/126) and 26.5% (36/136) of patients in the low- and high-risk groups, respectively. The sensitivity, specificity, positive predictive value, negative predictive value (NPV), and accuracy of the RSS were 94.7% (95% CI, 0.81-0.99), 55.4% (95% CI, 0.49-0.62), 26.5% (95% CI, 0.19-0.35), 98.4% (95% CI, 0.94-0.99), and 61.1% (95% CI, 0.56-0.65), respectively. The RSS showed good discrimination for detecting LNM (area under the curve = 0.869 for the development data) (Figure 1). We confirmed the goodness of fit of the model with the Hosmer–Lemeshow test after establishing the

TABLE 2. Clinicopathologic findings according to presence or absence of lymph node metastasis

Variables	LNM (–) (n = 224) (n, %)	LNM (+) (n = 38) (n, %)	P
Age (y, median [range])	65.0 (35–83)	60.5 (42–72)	.069
Gender			.744
Male	208 (92.9)	35 (92.1)	
Female	16 (7.1)	3 (7.9)	
Tumor size			.001
≤15 mm	105 (46.9)	7 (18.4)	
>15 mm	119 (53.1)	31 (81.6)	
Circumferential extension			.005
<1/4	53 (23.7)	2 (5.3)	
1/4–2/4	89 (39.7)	16 (42.1)	
2/4–3/4	57 (25.4)	9 (23.7)	
≥3/4	25 (11.2)	11 (28.9)	
Location within esophagus			.397
Upper third	15 (6.7)	4 (10.5)	
Middle third	69 (30.8)	8 (21.1)	
Lower third	140 (62.5)	26 (68.4)	
Tumor type on gross examination			.004
Flat	99 (44.2)	7 (18.4)	
Nonflat	125 (55.8)	31 (81.6)	
Depth of invasion			<.001
Mucosa	127 (56.7)	2 (5.3)	
Submucosa	97 (43.3)	36 (94.7)	
Tumor differentiation			<.001
Carcinoma in situ	23 (10.3)	0 (0.0)	
Well differentiated	79 (35.3)	4 (10.5)	
Moderately differentiated	108 (48.2)	29 (76.3)	
Poorly differentiated	14 (6.3)	5 (13.2)	
LVI			<.001
Absence	208 (92.9)	19 (50.0)	
Presence	16 (7.1)	19 (50.0)	

LNM, Lymph node metastasis; LVI, lymphovascular invasion.

development model. The *P* value was .7387. Therefore, the RSS model fitted well without overfitting. The predicted probability and the actual probability were almost identical to the 45-degree line in the calibration plot, indicating that

TABLE 3. Multivariate logistic regression analysis results for factors associated with lymph node metastasis

Variables	OR (95% CI)	P value	Beta
Tumor size			
≤15 mm	Reference		
>15 mm	3.417 (1.280–9.122)	.014	1.229
Depth of invasion			
Mucosa	Reference		
Submucosa	15.757 (3.577–69.402)	<.001	2.757
LVI			
Absent	Reference		
Present	8.699 (3.494–21.657)	<.001	2.163

OR, Odds ratio; CI, confidence interval; LVI, lymphovascular invasion.

TABLE 4. Risk stratification system for lymph node metastasis prediction

Factor	Scores			
	0	1	2	3
Tumor size (mm)	≤15	>15		
Depth of invasion	Mucosa			Submucosa
LVI	Absent		Present	

LVI, Lymphovascular invasion.

the model fitted well (Figure 2). Also, we analyzed post hoc power to demonstrate the predictive power of the development model. The result was 96.91%. Therefore, we regarded the development model was reliable.

DISCUSSION

Several previous studies revealed that the 5-year survivals of patients with esophageal cancer with mucosal and submucosal invasion were 83.5% to 87.6% and 54.9% to 63.6%, respectively.^{15,16} Furthermore, the 5-year survival of patients with submucosal invasion plus LNM was lower (27.0%–43.6%).^{15,16} Therefore, LNM is one of the most important factors associated with a poor prognosis in SESCC, and the opportunity for cure can be reduced in cases of undetected LNM.¹⁷ According to guidelines of the Japanese Esophageal Society for the diagnosis and treatment of esophageal cancer, endoscopic treatment is principally indicated for patients with a low likelihood of LNM in whom the tumor is technically resectable by endoscopy.³ Therefore, it is crucial to know the risk of LNM for the management of SESCC. In the current study, we established an RSS to predict LNM in SESCC. The RSS showed good diagnostic accuracy for discrimination of high- and low-risk groups, and patients with a risk score of 0 had no LNM.

Our results showed that the independent predictive factors for LNM in patients with SESCC were tumor size, LVI, and depth of invasion. Circumferential extension, gross type, and tumor differentiation were significantly associated with LNM in univariate analysis, but they lost significance in multivariate analysis. Patients with a tumor size less than 15 mm, no LVI, and mucosal cancer exhibited

TABLE 5. Lymph node metastasis rates according to tumor size, depth of invasion, and lymphovascular invasion

Tumor size (mm)	LVI (–) (n, %)	LVI (+) (n, %)
Mucosal invasion (n = 129)		
≤15	0/61 (0.0)	0/3 (0.0)
>15	2/62 (3.2)	0/3 (0.0)
Submucosal invasion (n = 133)		
≤15	4/40 (10.0)	3/8 (37.5)
>15	13/64 (20.3)	16/21 (76.2)

LVI, Lymphovascular invasion.

TABLE 6. Lymph node metastasis rates according to tumor size and depth of invasion

Tumor size (mm)	M1 LNM (n, %)	M2 LNM (n, %)	M3 LNM (n, %)	SM LNM (n, %)
≤15	0/12 (0.0)	0/31 (0.0)	0/23 (0.0)	7/48 (14.6)
>15, ≤30	0/8 (0.0)	0/17 (0.0)	1/17 (5.9)	18/58 (31.0)
>30	0/3 (0.0)	0/11 (0.0)	1/7 (14.3)	11/27 (40.7)

M1, Epithelium; LNM, lymph node metastasis; M2, lamina propria; M3, muscularis mucosa; SM, submucosal.

no LNM (0/61). Our findings are in agreement with those of previous studies showing that LVI and depth of invasion were associated with LNM.¹⁸⁻²² We established an RSS using size, depth of invasion, and LVI to predict LNM in patients with SESCC. According to this RSS, we identified subgroups that should undergo surgery or systemic chemotherapy, not ER. In other studies, 1% to 11% of patients with mucosal invasion, in contrast to 16% to 49% of patients with submucosal invasion, exhibited LNM.²³⁻²⁵ There were only 2 patients with mucosal cancer who had LMN in our study (1.6%, 2/129), both of whom had muscularis mucosa invasion and a relatively large tumor (>15 mm). Although our model had a relatively low specificity (55.4%) and positive predictive value (26.5%), its sensitivity (94.7%) and NPV (98.4%) were high. Therefore, our RSS could be effective for detecting patients at high risk for LNM after noncurative ER (sensitivity, 94.7%), and it should be particularly useful for excluding those at low risk for LNM (NPV, 98.4%). Generally, the definitions for curative ER were en bloc resection, negative horizontal and vertical margins, and no LVI.

Li and colleagues¹⁸ reported a nonsignificant tendency toward an increased likelihood of LNM as tumor length

increased, but these findings were only confined to submucosal tumors. However, several studies showed opposite results.^{8,22} Pech and colleagues²⁶ reported that histologic differentiation was a potential risk factor for LNM. However, we found no significant association between tumor differentiation and LNM. According to the Japan Esophageal Society, the indication for ER of SESCC is a tumor confined within the epithelium or lamina propria mucosa. Lesions reaching the muscularis mucosa or slightly infiltrating the submucosa (up to 200 μm) are amenable to mucosal resection despite the risk of LNM, and these cases represent relative indications.³ Our data suggest that if a tumor has certain characteristics—size less than 15 mm, no LVI, and confined to the mucosa—then the possibility of LNM is extremely low.

Study Limitations

There are some limitations in our study. First, it was a retrospective study, so it was not possible to completely eliminate some potential biases, such as selection, allocation, or measurement bias. Also, lack of external validation may be a limitation of our study. Therefore, further study will be needed to validate our RSS. Second, the sample size was relatively small, which restricted some of the analyses. For example, mucosa and submucosa

FIGURE 1. ROC curves of the RSS. Development data (area under the curve = 0.869, 95% CI, 0.813-0.926).

B = 200 repetitions, boot Mean absolute error = 0.013 n = 262

FIGURE 2. Calibration plot for the development cohorts.

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VIDEO 1. Importance and relevance of our study. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)32010-5/fulltext](https://www.jtcvs.org/article/S0022-5223(18)32010-5/fulltext).

could not be classified into subgroups such as SM1, SM2, and SM3 during the analyses because of insufficient data. Furthermore, the incidence of LNM was low in the low-risk group. Therefore, the statistical power of low-risk group with high-risk features such as larger tumor size and LVI was inadequate. Third, it was impossible to dissect the lymph nodes in patients who had undergone ER. Although imaging studies, such as computed tomography, positron emission tomography, or endoscopic ultrasound, were performed before ER, the lack of histopathologic confirmation by surgical retrieval does not completely eliminate the possibility of LNM. However, when we reanalyzed data except cases of ER, the results were not changed (Tables E2 and E3).

CONCLUSIONS

We found that a tumor size of 15 mm or greater, LVI, and submucosal invasion were independent risk factors for LNM in patients with SESCC (Video 1). Furthermore, we developed a simple RSS for the prediction of LNM using these risk factors. This RSS may be helpful in clinical practice by facilitating the precise selection of patients who can undergo ER. On the basis of these data, we propose that if any of these risk factors do not apply to a tumor after ER, careful observation can be recommended.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: lymph node metastasis, risk stratification system, superficial esophageal squamous cell carcinoma

TABLE E1. Identification of the optimal cutoff value in the receiver operating characteristic curve

Criterion	Predicted probability	Sensitivity (95% CI)	Specificity (95% CI)
0 (≥0)	0	100 (90.7-100.0)	0 (0.0-1.6)
1 (>0)	1.3	100 (90.7-100.0)	27.23 (21.5-33.6)
2 (>1)	3.6	94.74 (82.3-99.4)	54.02 (47.3-60.7)
3 (>2)	9.5	94.74 (82.3-99.4)	55.36 (48.6-62.0)
4 (>3)	22.6	84.21 (68.7-94.0)	72.77 (66.4-78.5)
5 (>4)	45.1	50 (33.4-66.6)	95.54 (91.9-97.8)
6 (>5)	69.7	42.11 (26.3-59.2)	97.77 (94.9-99.3)

CI, Confidence interval.

TABLE E2. Clinicopathologic findings according to presence or absence of lymph node metastasis in surgical cases

Variables	LNM (−) (n = 143) (n, %)	LNM (+) (n = 38) (n, %)	P
Age (y, median [range])	65.0 (45-83)	60.5 (42-72)	.259
Gender			.967
Male	132 (92.3)	35 (92.1)	
Female	11 (7.7)	3 (7.9)	
Tumor size			.001
≤15 mm	66 (46.2)	7 (18.4)	
>15 mm	77 (53.8)	31 (81.6)	
Circumferential extension			.256
<1/4	17 (11.9)	2 (5.3)	
1/4-2/4	55 (38.5)	16 (42.1)	
2/4-3/4	46 (32.2)	9 (23.7)	
≥3/4	25 (17.5)	11 (28.9)	
Location within esophagus			.135
Upper third	5 (3.5)	4 (10.5)	
Middle third	44 (30.8)	8 (21.1)	
Lower third	94 (65.7)	26 (68.4)	
Tumor type on gross examination			.021
Flat	53 (37.1)	7 (18.4)	
Nonflat	90 (62.9)	31 (81.6)	
Depth of invasion			<.001
Mucosa	64 (44.8)	2 (5.3)	
Submucosa	79 (55.2)	36 (94.7)	
Tumor differentiation			.044
Carcinoma in situ	9 (6.3)	0 (0.0)	
Well differentiated	38 (26.6)	4 (10.5)	
Moderately differentiated	85 (59.4)	29 (76.3)	
Poorly differentiated	11 (7.7)	5 (13.2)	
LVI			<.001
Absence	132 (92.3)	19 (50.0)	
Presence	11 (7.7)	19 (50.0)	

LNM, Lymph node metastasis; LVI, lymphovascular invasion.

TABLE E3. Multivariate logistic regression analysis results for factors associated with lymph node metastasis in surgical cases

Variables	OR (95% CI)	P value	Beta
Tumor size			
≤15 mm	Reference		
>15 mm	2.838 (1.069-7.535)	.036	1.043
Depth of invasion			
Mucosa	Reference		
Submucosa	9.941 (2.221-44.503)	.003	2.297
LVI			
Absent	Reference		
Present	7.252 (2.777-18.938)	<.001	1.981

OR, Odds ratio; CI, confidence interval; LVI, lymphovascular invasion.