A novel risk score model of esophageal stricture for patients undergoing endoscopic submucosal dissection

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Background and purpose Endoscopic submucosal dissection (ESD) is a promising technique for superficial esophageal lesions. However, stricture is a frequent adverse complication. This study was performed to develop a precise and convenient score prediction model for esophageal strictures after ESD, and compare its efficacy with a previously published predictive model.
Methods This study enrolled clinical data of patients who underwent esophageal ESD for superficial esophageal lesions. Possible risk factors for esophageal stricture were identified by univariate and multivariate logistic regression analysis. Then we developed a prediction model according to the Framingham system for the first time and presented a convenient table containing the risk probability for each patient. In addition, we validated our score model and the previously published model in our center.
Results A total of 838 patients were enrolled in this study and 6 variables, including age, surgery time, location of the lesion, circumference of the lesion, longitudinal resection length, and depth of infiltration were comprised in the score model. The total score ranged from 0 to 16 points and the risk probability was presented in one concise table for each patient. Areas under receiver-operator characteristic curves for the prediction model were 0.715 in derivation group and 0.804 in validation group.
Conclusion We designed and validated a prediction score model for esophageal stricture after ESD, which can be applied conveniently to stratify the stricture risk after esophageal ESD and may facilitate appropriate clinical decision-making for these patients. Eur J Gastroenterol Hepatol 35: 1362–1369

Introduction

Endoscopic submucosal dissection (ESD) has become the first-line therapy for removing superficial esophageal diseases, including cancer, precancerous lesions and other diseases confined to the submucosa [1]. Although ESD is a minimally invasive treatment compared with conventional surgery, post-ESD esophageal stricture has arisen as the most concerning adverse event which lead to malnutrition and poor quality of life for patients [2,3]. The occurrence of esophageal stricture after ESD could rise to 70–80% when the extent of circumferential resection is more than 60% and in patients undergoing resection of the whole circumference, risk of esophageal stricture is almost 100% [4].

So far, researches have focused on identifying the risk factors of esophageal stricture after ESD, and several high-risk factors have been recognized including circumferential extension, histological depth, and longitudinal resection length [5–7]. However, there is only two clinical prediction model for postoperative esophageal stricture thus far, and they did not take longitudinal resection length into account and only based on data from a single center [8]. In addition, it only divided patients into three groups, rather than provide the probability for every patient. Moreover, with the increasing usage of NBI and more choices of ESD procedures, other risk factors, such as intrapapillary capillary loops (IPCL), Tatami sign and ESD knives, should also be considered. Therefore, we investigated the characteristics of lesions and ESD procedures in patients who underwent esophageal ESD, then established and validated a novel risk prediction model of post-ESD stricture according to the Framingham system which can easily estimate the stricture risk of each patient [9]. We believe the risk prediction model may guide stricture prevention and management.

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Keywords: endoscopic submucosal dissection, esophageal strictures, prediction score model, risk factors, the Framingham system

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Materials and methods

Study design and patients

In order to establish a scoring method for post-ESD esophageal stricture, we conducted this retrospective study following three steps: (1) identifying clinically significant

risk factors of esophageal stricture after ESD, (2) developing a risk prediction model for stricture, and (3) validation of the model and quantification of the fibrosis. The study population consisted of 869 patients who underwent esophageal ESD at the First Affiliated Hospital of Nanjing Medical University between January 2018 and June 2021. The indications for esophageal ESD are lisThe patients were excluded if (1) ESD was not completed (n = 2), (2) the follow-up duration after ESD was less than 1 year (n = 6), (3) additional surgery or chemoradiotherapy was performed after ESD (n = 15), (4) the necessary data were missing (n = 8). Finally, 838 patients were enrolled in the study. Enrolled patients were randomly divided into the derivation and validation sets in a 7:3 ratio. The patient enrollment flowchart is shown in Fig. 1. The study was conducted in accordance with the Declaration of Helsinki and has been approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (2022-SR-468). Written informed consent for ESD was obtained from each patient before the procedure.

ESD indications, procedure and histopathologic evaluation

According to clinical practice of ESD in the USA, we conducted esophageal ESD for high-grade dysplasia to well or moderately-differentiated Paris 0-II lesions. Absolute indications include m1-m2 involvement with ≤2/3 of the esophageal circumference and expanded indications include m3 or sm <200 μm involvement, any size, clinically N0 [10]. We assess the esophageal lesions very carefully via white light endoscopy, NBI endoscopy, EUS and CT scan. ESD was performed according to a standard ESD procedure. Briefly, the protocol consisted of the following 4 steps: (1) marking dots around the lesion, (2) submucosal injection, (3) mucosal incision and submucosal dissection outside of the marked region, and (4) retrieval of the specimen. Resected specimens were stretched to their approximate lengths as in the living body, pinned to identify the horizontal margin, fixed in formalin solution, step sectioned at 1-mm or 2-mm intervals and then assessed microscopically. The histopathologic diagnosis followed the WHO classification criteria. We check the pathological result and suggest patients with lesions invading submucosa more than 200 μm, with positive resection margin, with lymphovascular infiltration or poorly differentiated to accept additional surgery and chemoradiotherapy. However, some patients refuse to accept additional surgery and chemoradiotherapy because of advanced age, weak body, poverty, and other reasons.

Candidates for predictive stricture after ESD

We reviewed the medical records, endoscopic findings, and histopathologic reports of all the patients enrolled in this study to collect demographic information, lesion

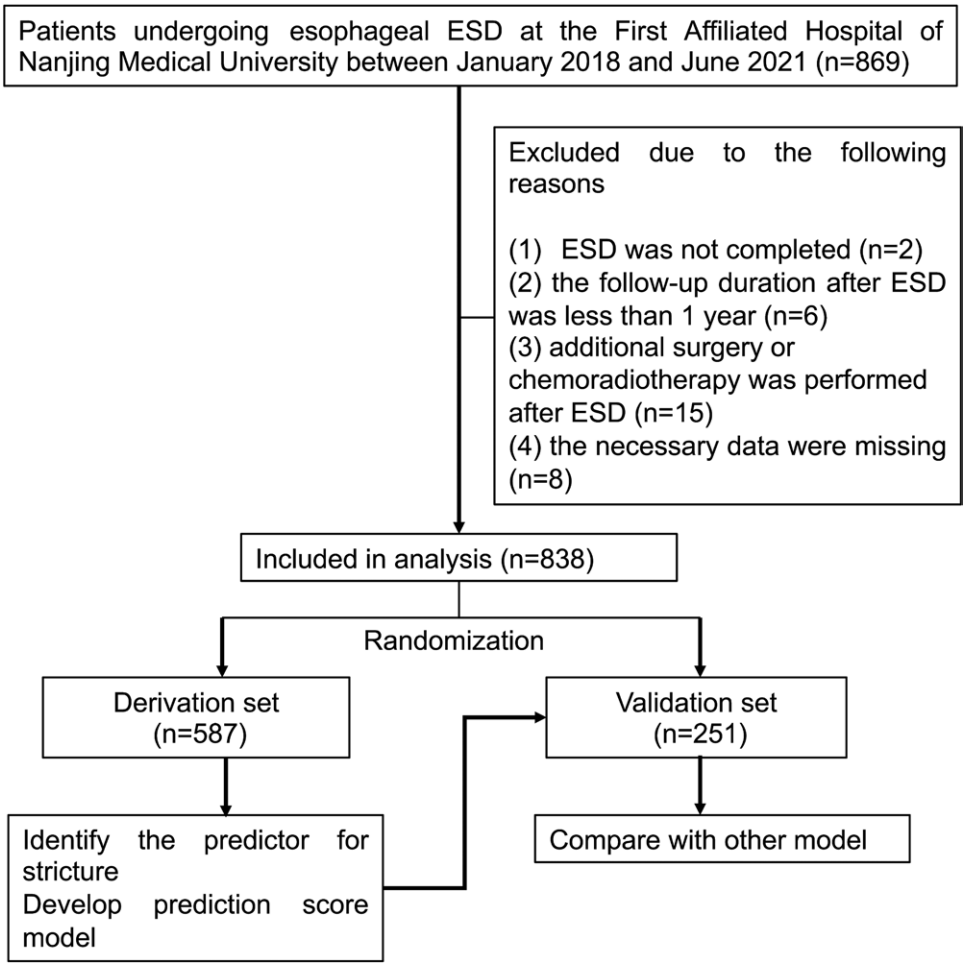

Fig. 1. Study flowchart of risk factor selection and model construction.

characteristics, and procedure-related details. The medical records included age, sex, smoking, drinking, comorbidities, and family history. Lesion characteristics were identified including lesion number, location, circumference, longitudinal resection length, histopathology, depth of infiltration, R0 resection, thickness of specimen, blood vessels, IPCL classification and vessel carcinoma embolus. We also focused on the procedure-related details, including procedure time, clips number, muscular injury, lift sign, pink color sign, Tatami sign, and the usage of knives. R0 resection was defined as complete dissection of lesion with no residual lesion at both longitudinal and transversal resection margin. All patients had a follow-up endoscopy examination within six months after undergoing ESD. Esophageal stricture was recognized as narrowing of the esophageal lumen to the extent that an ordinary endoscope (diameter 9.8 mm) could not pass, accompanying patients' difficulty in consuming solid food.

Model development and validation

Enrolled patients were randomized into the derivation or the validation group at a 7:3 ratio. We used the univariate analysis on the derivation group to identify the significant risk factors for esophageal stricture after ESD. Then, only candidate predictors with $P < 0.10$ in univariate analysis were included in multivariate binary logistic regression. We assigned points proportional to β regression coefficient values for each risk factor according to The Framingham Study risk score system. The specific steps were as follows: (1) We organized the risk factors into meaningful categories and determine reference values. For dichotomous variables, we distinguished them with 0 and 1, and for the continuous data that is not normally distributed, we divide it into several grades according to median and quartile; (2) The least risky state of each predictor was assigned 0 as the base category, and the less healthy the state is, the higher the score it gets; (3) We computed how far each category of each risk factor is from the base category in terms of regression units; (4) We determined a constant value corresponding to 1 point in the scoring tool; (5) The distance of each risk factor state was divided by the constant and rounded to the nearest whole number to keep the score simple. Individual risk estimates were the total points of their individual risk factors and the probability was calculated for each total point using the equation $\mathrm{p} = \frac{1}{1+\exp\left(-\sum_{i=0}^{p}\beta iXi\right)}$. In addition, $\sum_{i=0}^{p}\beta iXi \approx \beta 0 + \beta 1X1\mathrm{REF} + \beta 2X2\mathrm{REF} + \ldots + \beta 6X6\mathrm{REF} + \mathrm{B}\,(\text{total point})$. Optimal cutoff points were determined on the basis of maximum Youden index values of the receiver operating characteristic (ROC) method. Then, the model was validated using the validation set. Finally, we validated the previously published prediction model in our center.

Statistical analysis

Continuous variables were described using the median and interquartile range, and categorical variables were presented as absolute values and percentages. The Student t-tests and chi-square tests (or Fisher exact tests) were used for comparison between groups. Logistic regression analysis was performed to evaluate the association of stricture with risk factors. Associations were presented using odds ratios (ORs) and 95% confidence intervals (95% CIs). The ability of the prediction model to estimate the risk of developing perforation was assessed using the area under the ROC curve. Pearson correlation was used for correlation analysis. A *P*-value <0.05 was considered as statistically significant. All the statistical analyses were performed using SPSS (version 26.0; SPSS, Inc, Chicago, IL, USA).

Results

Predictors of esophageal stricture after ESD

A total of 838 patients fulfilled the inclusion criteria and were enrolled in the final analysis, among whom 587 patients were in the derivation cohort and 251 patients in the internal validation cohort. In the derivation cohort, 130 patients (22.1%) developed stricture by the time of follow-up. Demographic information, lesion characteristics and surgery details of derivation cohort were presented in Tables 1–3. The univariate analysis was conducted, which revealed that the risk of stricture was significantly associated with age, cardiovascular disease, lesion location, circumference, longitudinal resection length, histopathology, infiltration depth, R0 resection, venous cancerous embolus, surgery time, pink color sign, and the usage of KD-611L knife. Then we performed a multivariate logistic regression analysis and found that the independent predictors of stricture after esophageal ESD in the derivation cohort were age ($P = 0.022$, OR = 1.752, 95% CI 1.085–2.829), surgery time ($P = 0.008$, OR = 2.002, 95% CI 1.199–3.34), location of upper thoracic part ($P = 0.001$, OR = 2.639, 95% CI 1.494–4.661), circumference of the lesion ($P = 0.014$, OR = 2.7, 95% CI 1.224–5.953), longitudinal resection length ($P < 0.001$, OR = 1.273, 95% CI 1.147–1.414), and depth of infiltration ($P = 0.004$, OR = 1.487, 95%CI 1.132–1.953) (Table 4). We also found that length was positively correlated with circumferential ($r = 0.2297$, $P < 0.001$).

Prediction model for esophageal stricture after ESD

A clinical scoring prediction model for esophageal stricture after ESD was further developed in order to better predict stricture before it happened. Points were assigned to each risk factor based on the β-coefficient in logistic regression analysis of the derivation cohort (Table 5). According to the Framingham system, we organized the risk factors into categories and determine reference values for each. Then the constant B was set as 0.427, and $\sum_{i=0}^{p}\beta iXi \approx -4.47 + 0.252{*}1.5 + 0.427{*}(\text{total point})$. The points of the 6 risk factors were as follows: age, ≥65 years old (1point); surgery time, ≥1 h (2 points); ≥2/3 circumference of the lesion (2 points); lesion location in the upper thoracic part (2 points); depth of infiltration, limited to the epithelium (M1, 0 point), confined to lamina propria mucosa (M2, 1 point), confined to muscularis mucosa (M3, 2 points), and infiltrated into the submucosal layer (SM, 3 points); and longitudinal resection length, 1–2 cm (0 point); 3–4 cm (1 point); 5–6 cm (2 points); 7–8 cm

Table 1. Univariate analysis of patients' characteristics

					95% CI	
	Non-stenosis (n = 458)	Stenosis (n = 128)	*P* value	OR	Lower	Upper
Age, median (range), y	64 (15–86)	67 (46–90)	0.046	1.061	1.034	1.089
Sex			0.422	1.189	0.779	1.815
Male	328	87				
Female	130	41				
Current or past smoking, n (%)	167 (36.5)	42 (32.8)	0.446	0.851	0.562	1.289
Current or past drinking, n (%)	151 (33.0)	39 (30.5)	0.593	0.891	0.583	1.361
Comorbidity, n (%)						
Hypertension	158 (34.5)	43 (33.6)	0.849	0.961	0.635	1.454
Diabetes mellitus	41 (9.0)	12 (9.4)	0.883	1.052	0.536	2.067
Cardiovascular disease	14 (3.1)	9 (7.0)	0.041	2.399	1.013	5.677
Stroke	15 (3.3)	5 (3.9)	0.728	1.201	0.428	3.368
COPD	7 (1.5)	3 (2.3)	0.539	1.546	0.394	6.067
Gout	2 (0.4)	2 (1.6)	0.171	3.619	0.505	25.948
Esophagitis	3 (0.7)	2 (1.6)	0.324	2.407	0.398	14.565
Family history of esophageal cancer, n (%)	36 (7.9)	15 (11.7)	0.250	1.556	0.823	2.942
Hepatitis	18 (3.9)	4 (3.1)	0.672	0.789	0.262	2.373
Tuberculosis	7 (1.5)	2 (1.6)	0.978	1.023	0.210	4.984
Appendectomy	27 (5.9)	3 (2.3)	0.107	0.383	0.114	1.284
Cholecystectomy	24 (5.2)	2 (1.6)	0.074	0.287	0.067	1.231

Table 2. Univariate analysis of lesion characteristics

					95% CI	
	Non-stenosis	Stenosis	*P* value	OR	Lower	Upper
Lesion number			0.885	1.043	0.592	1.836
Single	395	110				
Multiple	62	18				
Location						
Neck part	4	4	0.052	3.661	0.903	14.848
Upper thoracic part	63	35	<0.001	2.360	1.473	3.779
Middle thoracic part	342	107	0.035	1.728	1.035	2.887
Lower thoracic part	269	82	0.277	1.252	0.834	1.880
Abdominal part	15	5	0.728	1.201	0.428	3.368
Circumference of the lesion, n (%)			<0.001	5.422	2.736	10.743
<2/3	442	107				
≥2/3	16	21				
Longitudinal resection length, medium (range), cm	5 (1–12)	7 (1–16)	<0.001	1.411	1.294	1.539
Histopathology			<0.001	0.815	0.675	0.985
LGIN	84	11				
HGIN	142	22				
Carcinoma	167	91				
Other	28	2				
Depth of infiltration			<0.001	1.960	1.602	2.398
M1	365	62				
M2	51	28				
M3	23	20				
SM	19	18				
R0 resection			0.005	4.358	1.438	13.207
No	6	7				
Yes	452	121				
Thickness of specimen	2(1–9)	2(1–8)	0.432	1.104	0.893	1.365
Blood vessel-rich			0.626	0.593	0.071	4.972
No	452	127				
Yes	6	1				
IPCL classification			0.053	1.504	0.779	2.095
A	143	28				
B1	274	82				
B2	41	18				
Venous cancerous embolus			<0.001	6.040	1.941	18.798
No	453	120				
Yes	5	8				

(4 points); 9–10 cm (5 points); >10 cm (6 points). The sum of points from each risk factor in an individual was adopted as the final total point, which ranged from 0 to 16. Based on the equation of $p = \frac{1}{1+\exp\left(-\sum_{i=0}^{p}\beta iXi\right)}$, we displayed the probability estimations for each total point in Table 6. The ROC curve was used to calculate the maximum Youden index for the total score and we got a cutoff value of 5.5, with an receiver-operator characteristic curves (AUC) of 0.715 ($P < 0.001$, 95% CI 0.663–0.766) (Fig. 2a).

Validation of the risk prediction model

We validated the risk prediction model for esophageal stricture after ESD in the validation cohort, which showed AUC of 0.804 (95% CI 0.744–0.864) (Fig. 2b).

Table 3. Univariate analysis of procedure characteristics

					95% CI	
	Non-stenosis	Stenosis	*P* value	OR	Lower	Upper
Procedure time, median (range), min	50 (10–240)	80 (25–300)	<0.001	1.022	1.017	1.028
Clips number	0 (0–19)	0 (0–18)	0.273	0.933	0.861	1.011
Muscular injury			0.517	1.220	0.668	2.230
No	410	112				
Yes	48	16				
Lift sign			0.176	0.367	0.081	1.662
No	4	3				
Yes	454	125				
Pink color sign			<0.001	1.241	1.204	1.517
No	186	30				
Yes	272	98				
Tatami sign			0.051	1.542	0.997	2.386
No	164	34				
Yes	294	94				
Knife, n (%)						
KD-650Q	442 (96.5)	127 (99.2)	0.106	4.587	0.604	35.001
KD-620LR	6 (1.3)	1 (0.8)	0.626	0.593	0.071	4.972
KD-650L	15 (3.3)	2 (1.6)	0.306	0.468	0.106	2.072
KD-611L	4 (0.9)	5 (3.9)	0.014	4.614	1.221	17.441
IT-knife2	3 (0.7)	1 (0.8)	0.878	1.194	1.123	11.579

Table 4. Multivariate analysis of potential factors for esophageal stricture after ESD

				95% CI	
	SE	*P* value	OR	Lower	Upper
Age	0.245	0.022	1.752	1.085	2.829
Cardiovascular disease	0.495	0.114	2.184	0.828	5.76
KD-611L knife	0.898	0.155	3.582	0.616	20.816
Pink color sign	0.348	0.202	1.561	0.788	3.09
Tatami sign	0.343	0.874	0.947	0.483	1.856
Surgery time	0.261	0.008	2.002	1.199	3.34
Circumference of the lesion	0.403	0.014	2.7	1.224	5.953
IPCL	0.216	0.574	0.886	0.58	1.352
Histopathology	0.152	0.669	1.067	0.792	1.438
Venous cancerous embolus	0.695	0.392	1.814	0.464	7.089
Neck part	0.984	0.982	1.023	0.149	7.034
Upper thoracic part	0.29	0.001	2.639	1.494	4.661
Middle thoracic part	0.325	0.361	0.743	0.393	1.404
Longitudinal resection length	0.053	<0.001	1.273	1.147	1.414
Depth of infiltration	0.139	0.004	1.487	1.132	1.953
R0 resection	0.741	0.896	1.101	0.258	4.711

Table 5. Development of the risk score model to predict esophageal stricture after ESD

Risk factor	Categories	Reference value	β	wij-wiref	D	B	Score
Age	<65	0	0.5	0	0	0.427	0
	≥65	1	0.5	1	0.5	0.427	1
Surgery time	<1h	0	0.794	0	0	0.427	0
	≥1h	1	0.794	1	0.794	0.427	2
Circumference of the lesion	<2/3	0	0.96	0	0	0.427	0
	≥2/3	1	0.96	1	0.96	0.427	2
Upper thoracic part	Yes	0	0.93	0	0	0.427	0
	No	1	0.93	1	0.93	0.427	2
Depth of infiltration	m1	0	0.427	0	0	0.427	0
	m2	1	0.427	1	0.427	0.427	1
	m3	2	0.427	2	0.854	0.427	2
	sm	3	0.427	3	1.281	0.427	3
Longitudinal resection length	1–2	1.5	0.252	0	0	0.427	0
	3 -4	3.5	0.252	2	0.504	0.427	1
	5–6	5.5	0.252	4	1.008	0.427	2
	7–8	7.5	0.252	6	1.512	0.427	4
	9–10	9.5	0.252	8	2.016	0.427	5
	>10	11.5	0.252	10.5	2.646	0.427	6

The probability of stricture ranged from 0% in score 0 to 100% in score 12. We also examined the efficiency of a previously published prediction model based on five risk factors for esophageal stricture after ESD in our cohort, which included operating time, circumferential range, lesion location, depth of infiltration, and R0 resection. The area under the ROC curve for this score model was 0.653 (95% CI 0.597–0.709; Fig. 2c). In addition, the model

was also internally validated in the derivation group using 10-fold cross-validation, which yielded ten AUC values ranging from 0.63 to 0.79 (coefficient of variation 6%) with an average AUC of being 0.72, indicating its satisfactory generalization capacity. In order to prove if the model quantify the amount of fibrosis, we searched the bougie dilation history of these patients and the information of first bougie's diameter was available in 81 patients. Then we performed correlation analysis and found the model score was inversely correlated with the diameter of the first bougie ($r = -0.5636$, $P < 0.001$). We also construct a formula to guide bougie selection in dilation (diameter(mm) = –0.2771 × score + 9.8).

Discussion

Currently, ESD has become the main therapeutic approach for superficial esophageal lesions with better quality of life than surgical resection. However, esophageal stricture after ESD frequently occurs and can result in severe dysphagia. With the increasing number of patients undergoing ESD as a result of extended indications and technical improvements, the incidence of resection-related post-ESD stricture is also elevated [11]. In our center, the rate could be as high as over 20% consistent with other studies [12,13]. Although previous studies have examined risk factors for stricture, there was only two predictive model. One is nomogram model and the other is score predictive model, which is more convenient to use in clinic. Both of them are from one center and have never been validated in another center. Thus, in this study, we developed a prediction model according to the Framingham system for the first time and presented a convenient table containing the risk probability for each patient. We believe that the estimation of esophageal stricture after ESD would be very helpful for guiding precautionary medical intervention in the clinical setting, which may decrease the incidence of stricture.

Nowadays, more and more studies focused on the risk factors of esophageal stricture after ESD and the conditions of patients, lesions and surgery all influence the incidence of stricture [5,14,15]. Moreover, as the extensive use of narrow-band imaging, our knowledge of lesions' endoscopic manifestations has become much more profound. Most of previous studies had the limitation of not evaluating the lesion characteristics in detail, such as pink color sign and Tatami sign. We added these factors into screening strategy and later analyzed if these characteristics affect outcomes. In order to construct an effective predictive model without missing important risk factors, we reviewed the medical records, endoscopic findings, and histopathologic reports of all the patients enrolled in this study. A total of 42 characteristics of patients, lesions, and surgery procedures were analyzed. Among them, 16 risk factors were significant in univariate analysis. Finally, 6 risk factors, including age, surgery time, location of the lesion, circumference of the lesion, longitudinal resection length, and depth of infiltration, were found to be independent predictors affecting risk of esophageal stricture after ESD in multivariate analysis. In other words, post-ESD esophageal stricture was more likely seen in patients ≥65 y, with surgery time ≥1 h, lesions located in the upper thoracic part, lesions with a circumference ≥2/3, longer longitudinal resection length, and deeper infiltration.

We found that age was a risk factor for stricture and if a patient is older than 65 years, the incidence of esophageal stricture after ESD increased significantly. Old patients are prone to many diseases, including spinal disease and cardiac disease. These diseases could induce esophageal distortion, which may increase the chance of muscular layer injury during ESD and finally induce stricture. Moreover,

Table 6. Total points and estimate of risk of the prediction model

Point total	Estimate of risk	Point total	Estimate of risk
0	1.64%	9	43.81%
1	2.50%	10	54.44%
2	3.78%	11	64.68%
3	5.67%	12	73.73%
4	8.44%	13	81.14%
5	12.38%	14	86.83%
6	17.80%	15	90.99%
7	24.92%	16	93.93%
8	33.72%		

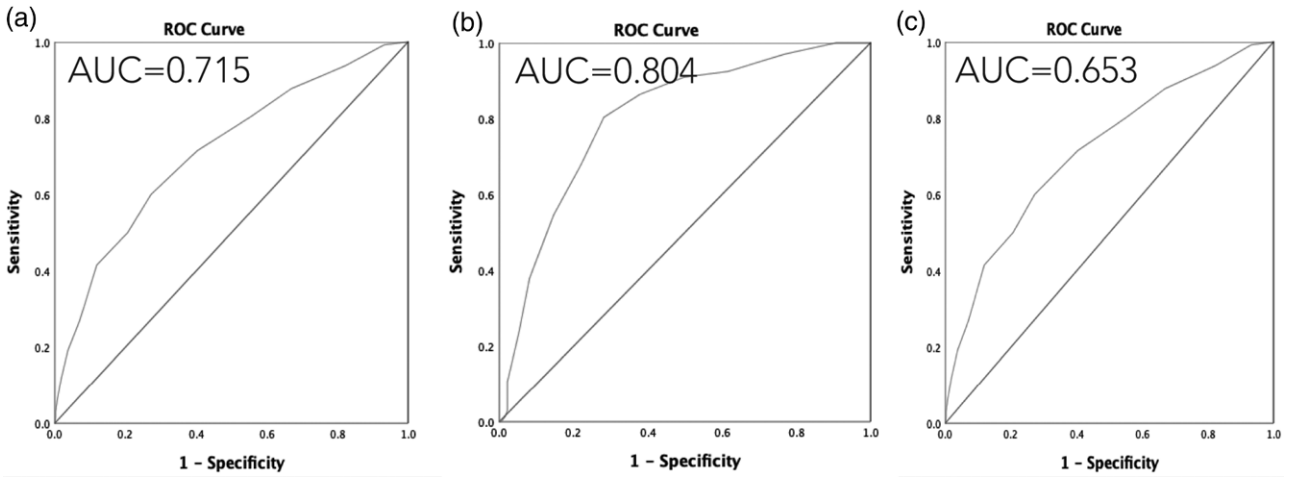

Fig. 2. The receiver operating characteristic curve (ROC) of prediction models. (a) ROC of our model in derivation set; (b) ROC of our model in validation set; (c) ROC of other models in derivation set.

Liu *et al*. have revealed that aging could promote fibrosis by altering lipoprotein and lipid metabolism, which is consistent with our results [16].

We proved that surgery time longer than 1h could be an independent risk factor for esophageal stricture. Clinically, longer surgery time is mainly attributable to a difficult lesion or operators with less experience. In order to avoid confounding factors, we adopt strict personnel training in operation and only those doctors with five or more years of ESD experience could conduct esophageal ESD in our center. In addition, Chen's study also confirmed that surgery time was correlated with post-ESD stricture [6].

We also found that lesions in upper thoracic part increased the likelihood of stricture. It is a common sense that the luminal diameter of the esophagus is different among different levels. Considering the luminal diameter of the upper esophagus is smaller compared with the lower esophagus, it is easy to understand that the smaller diameter may enhance risk of stricture after ESD. Ono *et al*. also revealed the same results, highlighting the necessity for operators to be more cautious when dealing with the narrow space of upper thoracic region [13].

A lesion with circumferential extension ≥2/3 displayed a remarkable ability in prediction postoperative stricture in our study. Shi *et al*. revealed that lesion circumferential extension>3/4 was an independent risk factor [17]. Zhou's study adopted 1/2 and 3/4 of the circumference as a classification to assess risk factors [18]. However, patients with lesion circumferential extension>3/4 only account for a fraction of all the patients. Taken together, circumferential extension ≥2/3 was chosen as risk factor, which was convenient for clinical application.

Many studies have identified longitudinal resection length as an independent risk factor for postoperative stricture and multivariate analysis in our study showed similar results [19,20]. we found that length was positively correlated with circumferential ($r = 0.2297$, $P < 0.0001$). Length and circumferential are two fundamental dimensions of lesions and directly determine fibrosis severity. The mechanisms involved in esophageal stricture after ESD included the immune response and changes in mucosal cells. Longer lesions could induce severer immune response and accelerate fibrosis formation.

Ono *et al*. reported that depth of the mucosal lesion may independently predicted postoperative stricture, which is similar with our findings [13]. When the depth of lesion infiltration exceeds m3 or sm1, esophageal stricture more likely occurred after ESD. We all know that there are various immune-related cells and fibroblast cells in the submucosa level and lesion invading submucosa could promote fibrosis formation [21]. So we included depth of lesion as a risk factor in our prediction model.

In this study, we applied the formula $p = \frac{1}{1+\exp\left(-\sum_{i=0}^{p} \beta i Xi\right)}$ to calculate specific proportion for each total point and presented all the results in one table, which is clear and easy to use for clinicians. No score prediction model of esophageal stricture after ESD was published until March 2023 by Xia *et al*. which contained eleven potential risk factors. Compared with our prediction model, the factors screened in Xia's model were much less. At last, five independent risk factors were contained in his model, including the operating time, circumferential range, lesion location, depth of infiltration, and R0 resection, without considering age, surgery time, and longitudinal resection length. Besides risk factors, the reason of our superiority also lies in the reasonable Framingham system. For example, in our study, patients with circumference more than 2/3 get 2 points. However, in Xia's study, only patients with en bloc circumferential get 3 points and only small portion of patients accept en bloc circumferential resection. Moreover, it is a common sense that stricture risk increases as the lesion infiltrated to SM, but Xia *et al*. give patients with a depth of infiltration of SM a score of 0. We give lesions reaching M1, M2, M3, and SM 0, 1, 2, and 3 points separately, which is in accordance with clinical phenomenon. According to Xia's study, the patients were then divided into low risk, intermediate risk, and high risk. However, it did not provide specific proportion for each total point, so we presented the score prediction model and showed specific proportion for each total point. In addition, our model owned AUC of 0.715 (95% CI 0.663–0.766) in derivation cohort and 0.804 (95% CI 0.744–0.864) in validation cohort. Our model was also internally validated in the derivation group using 10-fold cross-validation, which yielded ten AUC values ranging from 0.63 to 0.79 (coefficient of variation 6%) with an average AUC of being 0.72, indicating its satisfactory generalization capacity. The AUC for Xia's model in our center was 0.653 (95% CI, 0.597–0.709), which is lower than our model. However, we also should take it into consideration that model needs re-adjustment when applying to a new population. We appreciate the hard work of Xia and hope that we can cooperate to construct a more precise and stable prediction model for esophageal stricture after ESD in the future.

Up to now, the application of preventive measures has been reported to effectively reduce the incidence of esophageal stricture after ESD. Steroid injection therapy and oral steroid administration are the mainstream. Many other clinical applications have also been developed, such as tissue shielding methods with polyglycolic acid sheet, autologous oral mucosal epithelial sheet transplantation, and stent placement [22–26]. However, it would be better if these preventive procedures are adopted before the stricture happens. So a more efficient prediction model of esophageal stricture is necessary and undoubtedly help to improve the clinical management.

Nowadays, most patients were treated with serial bougie dilation in the context of esophageal stricture and diameter of the first bougie was chosen according to the degree of stricture. Then we considered if our model could predict severity of fibrosis and help in choosing bougies. We searched the bougie dilation history of these patients and the information of first bougie's diameter was available in 81 patients. Then we performed correlation analysis and found the model score was inversely correlated with the diameter of the first bougie ($r = -0.5636$, $P < 0.0001$, diameter(mm) = $-0.2771 \times$ score + 9.8). We therefore proposed that our score model also could be used to guide bougie selection in dilation.

However, this study has several limitations. Firstly, this is a retrospective study with potential unknown biases. Secondly, the prediction model was developed and validated in our hospital. It remains unclear whether this model is applicable to post-ESD patients in other medical centers.

Thirdly, the accuracy of this prediction model needs to be further optimized and appropriately updated with more novel risk factors found from prospective studies in future.

Conclusion

In summary, we designed and validated a model that predicts esophageal stricture after ESD based on age, surgery time, location of the lesion, circumference of the lesion, longitudinal resection length, and depth of infiltration. We believe it can be applied to stratify the risk of post-ESD esophageal stricture and facilitate appropriate clinical management.

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JY designed the study. JY, LG, MHC and HLD collected the data. JY and RRS analyzed the data. JY, ZY and LH drafted the manuscript. YYG and GXZ modified the manuscript. All authors contributed to the article and approved the submitted version.

Conflicts of interest

There are no conflicts of interest.

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