

Combined Macroscopic Type and IPCL Pattern for Predicting Pathological Invasion Depth in Superficial Esophageal Squamous Neoplasia: A Retrospective Study with Internal Validation

Jihua Dai

Beijing Friendship Hospital

Rui Guo

Beijing Friendship Hospital

Xin Rong

Beijing Friendship Hospital

Bing Yue

Beijing Friendship Hospital

Rui Xu

Beijing Friendship Hospital

Junxiong Wang

Beijing Friendship Hospital

Zhen He

Beijing Friendship Hospital

Huihong Zhai

nxykdx1009@163.com

Beijing Friendship Hospital

Guangyong Chen

Beijing Friendship Hospital

Research Article

Keywords: Superficial esophageal squamous neoplasia, Invasion depth, Macroscopic type, Intrapapillary capillary loop, Internal validation

Posted Date: October 6th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10886975/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background

Accurate pretherapeutic estimation of invasion depth is essential for selecting appropriate treatment for superficial esophageal squamous neoplasia (SESN). We aimed to evaluate endoscopic predictors of pathological muscularis mucosae/submucosal (MM/SM) invasion and to develop an internally validated model combining macroscopic type with intrapapillary capillary loop (IPCL) pattern.

Methods

This retrospective, single-center, lesion-based model-development study included 304 SESN lesions treated by endoscopic submucosal dissection at Beijing Friendship Hospital between January 2020 and October 2025. Pathological depth was dichotomized as epithelium/lamina propria mucosae (EP/LPM) versus MM/SM invasion. Logistic regression was used to evaluate predictors, and a parsimonious model combining macroscopic type and IPCL pattern was assessed by receiver operating characteristic analysis and internally validated using 1000 bootstrap resamples.

Results

Among 304 lesions, 235 (77.3%) were EP/LPM and 69 (22.7%) were MM/SM. In multivariable analysis, IPCL B2 pattern was independently associated with MM/SM invasion (odds ratio [OR] 6.25, 95% confidence interval [CI] 2.80–13.97; $P < 0.001$). Compared with 0-IIb lesions, both 0-IIa lesions (OR 8.77, 95% CI 2.65–29.01; $P < 0.001$) and 0-IIc lesions (OR 23.28, 95% CI 9.71–55.82; $P < 0.001$) had higher odds of MM/SM invasion. The combined model achieved an apparent area under the curve (AUC) of 0.915 (95% CI 0.877–0.953), with sensitivity of 84.06%, specificity of 91.91%, and accuracy of 90.13% at the Youden-optimal cut-off. Bootstrap internal validation showed minimal optimism, with an optimism-corrected AUC of 0.913, Brier score of 0.089, calibration intercept of -0.015, and calibration slope of 0.970.

Conclusions

Macroscopic type and IPCL pattern were complementary predictors of pathological MM/SM invasion in SESN. A simple model combining these two features showed strong discrimination and acceptable optimism-corrected performance, but external validation is required before routine clinical use.

Trial registration:

Not applicable.

Background

Esophageal squamous cell carcinoma (ESCC) remains a major global malignancy and has a substantial disease burden in China [1, 2]. With advances in endoscopic detection and minimally invasive treatment, superficial esophageal squamous neoplasia (SESN) can often be managed by endoscopic resection when the lesion is confined to the epithelium or lamina propria mucosae [3–5]. However, invasion into the muscularis mucosae or submucosa is associated with a higher risk of lymph node metastasis or non-curative resection and may require additional treatment after endoscopic submucosal dissection (ESD) [4–6]. Accurate pretherapeutic depth assessment is therefore central to treatment selection and patient counseling.

Macroscopic morphology is routinely documented according to the Paris classification [7], whereas magnifying endoscopy with narrow-band imaging (ME-NBI) and the Japan Esophageal Society (JES) intrapapillary capillary loop (IPCL) classification provide a standardized vascular framework for estimating invasion depth [8–13]. Type B2 vessels are an important marker of deeper invasion, but they can be hard to read in heterogeneous lesions, which has prompted work to refine how the B2-vessel area and its morphology are assessed [9, 13, 14]. Lugol chromoendoscopy and the pink-color sign (PCS) remain useful for detecting and characterizing squamous neoplasia [15–17]. In practice these features overlap, and no single finding reliably captures the risk of MM/SM invasion.

Paris 0-II subtypes are routinely documented during endoscopic assessment, but their value as categorical predictors of MM/SM invasion has not been fully evaluated in simple, clinically interpretable models. Previous prediction studies in superficial esophageal squamous carcinoma have addressed adverse pathological outcomes, including lymph node metastasis or lymphovascular invasion [18] and deeper submucosal infiltration [19]. However, model performance reported only in the development dataset can be optimistic if internal validation is not performed [20, 21].

We hypothesized that macroscopic type provides complementary information to IPCL pattern for predicting pathological MM/SM invasion in SESN. This retrospective lesion-based study aimed to develop a simple, clinically interpretable model combining macroscopic type and IPCL pattern and to evaluate both apparent and bootstrap optimism-corrected performance.

Methods

Study design and participants

This was a retrospective, single-center, lesion-based model-development study including consecutive superficial esophageal squamous lesions treated by ESD at Beijing Friendship Hospital between January 2020 and October 2025. Lesions were eligible if pre-treatment endoscopic assessment, including Lugol chromoendoscopy and/or magnifying endoscopic findings, and final pathological depth from the ESD specimen were available. Lesions were excluded if pathological depth could not be confirmed, if key endoscopic variables were missing, or if prior local treatment precluded reliable assessment. The final

analytic cohort comprised 304 lesions. The study was approved by the Ethics Committee of Beijing Friendship Hospital (approval No. BFH20260509004), and the requirement for written informed consent was waived because this was a retrospective analysis of de-identified data.

Reporting followed relevant prediction-model reporting principles, including transparent description of candidate predictors, outcome definition, model development, and validation [21].

Endoscopic variables

Macroscopic type was classified according to the Paris classification as 0-IIa, 0-IIb, or 0-IIc [7]. The pink-color sign (PCS) was recorded as positive or negative after Lugol iodine staining. IPCL pattern was assessed according to the JES classification and categorized as B1 or B2 for the present analysis [9]. When more than one endoscopic feature was present, the predominant or clinically most suspicious area documented before ESD was used for analysis.

Reference standard and outcome definition

The reference standard was the final histopathological assessment of the ESD specimen. Invasion depth was dichotomized as epithelium/lamina propria mucosae (EP/LPM) versus muscularis mucosae/submucosa (MM/SM). The target outcome for model development was MM/SM invasion.

Statistical analysis

Continuous variables are presented as mean $\pm$ standard deviation (SD), and categorical variables as number (%). Group comparisons between the EP/LPM and MM/SM groups were performed using the independent-samples t test or Mann-Whitney U test for continuous variables, and the chi-square test or Fisher exact test for categorical variables, as appropriate.

Univariable logistic regression was performed for each candidate predictor with pathological MM/SM invasion as the dependent variable. Age was rescaled as per 10-year increase, and lesion area was rescaled as per 5-cm² increase to improve interpretability. Macroscopic type was modeled as a nominal categorical variable, with 0-IIb as the reference category. Odds ratios were estimated for 0-IIa versus 0-IIb and 0-IIc versus 0-IIb, and an overall P value for macroscopic type was reported.

Variables with univariable $P < 0.20$ were considered candidates for multivariable logistic regression, together with clinically prespecified endoscopic predictors. To limit overfitting while preserving clinical interpretability, the final diagnostic model for receiver operating characteristic (ROC) analysis and internal validation was defined as the combination of macroscopic type and IPCL pattern, based on their clinical relevance and multivariable associations.

Model discrimination was assessed using the area under the ROC curve (AUC). Sensitivity, specificity, and accuracy were calculated at the optimal cut-off determined by the Youden index. Pairwise

comparisons of AUCs were performed using the DeLong test. Calibration of the final model was assessed using a grouped calibration plot, calibration intercept, calibration slope, and the Brier score.

Internal validation of the final macroscopic type plus IPCL model was performed using 1000 bootstrap resamples. In each bootstrap sample, the final model specification was refitted, and optimism was estimated by comparing model performance in the bootstrap sample with performance when the same fitted model was applied to the original dataset. The average optimism was subtracted from the apparent performance to obtain optimism-corrected estimates of the AUC, Brier score, calibration intercept, and calibration slope.

The dataset was analyzed at the lesion level because the source worksheet recorded lesion-specific pathological depth and endoscopic findings. No imputation was performed; only lesions with complete data for the variables included in the final model were analyzed. All tests were two-sided, and $P < 0.05$ was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA) and R version 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics and group comparisons

A total of 304 lesions were included. Pathological depth was EP/LPM in 235 lesions (77.3%) and MM/SM in 69 lesions (22.7%). Age, sex, smoking history, alcohol history, and lesion area did not differ significantly between the EP/LPM and MM/SM groups (all $P > 0.05$). PCS positivity was more frequent in MM/SM lesions than in EP/LPM lesions (60/69 [87.0%] vs 154/235 [65.5%], $P = 0.001$). Macroscopic type also differed significantly between groups: EP/LPM lesions were predominantly 0-IIb (206/235 [87.7%]), whereas MM/SM lesions were more often 0-IIc (49/69 [71.0%]) or 0-IIa (9/69 [13.0%]) ($P < 0.001$). Likewise, the IPCL B2 pattern was more common in MM/SM lesions than in EP/LPM lesions (52/69 [75.4%] vs 32/235 [13.6%], $P < 0.001$) (Table 1).

Table 1
Clinicopathologic and endoscopic characteristics according to pathological invasion depth

Variable	EP/LPM (n = 235)	MM/SM (n = 69)	P value
Age, years, mean $\pm$ SD	61.88 $\pm$ 8.47	61.70 $\pm$ 7.73	0.871
Male sex, n (%)	166 (70.6)	53 (76.8)	0.394
Smoking history, yes, n (%)	119 (50.6)	42 (60.9)	0.174
Alcohol history, yes, n (%)	128 (54.5)	37 (53.6)	> 0.999
Lesion area, cm ² , mean $\pm$ SD	4.11 $\pm$ 5.39	4.56 $\pm$ 6.25	0.550
Pink-color sign positive, n (%)	154 (65.5)	60 (87.0)	0.001
Macroscopic type, n (%)			< 0.001
0-IIa	11 (4.7)	9 (13.0)	
0-IIb	206 (87.7)	11 (15.9)	
0-IIc	18 (7.7)	49 (71.0)	
IPCL B2 pattern, n (%)	32 (13.6)	52 (75.4)	< 0.001
<i>EP/LPM, epithelium/lamina propria mucosae; MM/SM, muscularis mucosae/submucosa; IPCL, intrapapillary capillary loop. Binary variables are shown as one-line positive/yes categories.</i>			

Logistic regression analysis

In univariable logistic regression, PCS positivity (OR 3.51, 95% CI 1.66–7.43; $P = 0.001$), IPCL B2 pattern (OR 19.40, 95% CI 10.00–37.63; $P < 0.001$), and macroscopic type overall ($P < 0.001$) were associated with pathological MM/SM invasion. With 0-IIb as the reference category, both 0-IIa lesions (OR 15.32, 95% CI 5.26–44.65; $P < 0.001$) and 0-IIc lesions (OR 50.98, 95% CI 22.63–114.85; $P < 0.001$) had higher odds of MM/SM invasion (Table 2).

Table 2
Univariable and multivariable logistic regression for pathological MM/SM invasion

Variable	Univariable OR (95% CI)	P value	Multivariable OR (95% CI)	P value
Age (per 10-year increase)	0.97 (0.70–1.34)	0.870		
Male sex (vs female)	1.38 (0.74–2.57)	0.316		
Smoking history (yes vs no)	1.52 (0.88–2.62)	0.136	1.34 (0.60-3.00)	0.473
Alcohol history (yes vs no)	0.97 (0.56–1.66)	0.901		
Lesion area (per 5-cm ² increase)	1.07 (0.86–1.33)	0.549		
Pink-color sign (positive vs negative)	3.51 (1.66–7.43)	0.001	2.41 (0.85–6.86)	0.098
IPCL pattern (B2 vs B1)	19.40 (10.00-37.63)	< 0.001	6.25 (2.80-13.97)	< 0.001
Macroscopic type overall		< 0.001		< 0.001
0-IIa vs 0-IIb	15.32 (5.26–44.65)	< 0.001	8.77 (2.65–29.01)	< 0.001
0-IIc vs 0-IIb	50.98 (22.63-114.85)	< 0.001	23.28 (9.71–55.82)	< 0.001
<i>OR, odds ratio; CI, confidence interval; IPCL, intrapapillary capillary loop. Macroscopic type was modeled as a nominal categorical variable with 0-IIb as the reference category. Variables with univariable P < 0.20 were considered for multivariable regression.</i>				

Smoking history, PCS positivity, IPCL pattern, and macroscopic type met the prespecified $P < 0.20$ screening criterion for multivariable analysis. In the multivariable model, IPCL B2 pattern remained independently associated with MM/SM invasion (OR 6.25, 95% CI 2.80-13.97; $P < 0.001$). Compared with 0-IIb lesions, both 0-IIa lesions (OR 8.77, 95% CI 2.65–29.01; $P < 0.001$) and 0-IIc lesions (OR 23.28, 95% CI 9.71–55.82; $P < 0.001$) had higher odds of MM/SM invasion. PCS positivity was not independently associated with MM/SM invasion after adjustment (OR 2.41, 95% CI 0.85–6.86; $P = 0.098$), and smoking history was likewise not significant (OR 1.34, 95% CI 0.60-3.00; $P = 0.473$).

Model discrimination and internal validation

The final diagnostic model combined macroscopic type and IPCL pattern. In apparent performance analysis, the model achieved an AUC of 0.915 (95% CI 0.877–0.953), with sensitivity of 84.06%, specificity of 91.91%, and accuracy of 90.13% at the Youden-optimal cut-off. Its AUC was significantly higher than that of macroscopic type alone (0.870, 95% CI 0.821–0.919; DeLong $P = 0.003$) and IPCL pattern alone (0.809, 95% CI 0.753–0.864; DeLong $P < 0.001$), whereas the difference between

macroscopic type alone and IPCL pattern alone was not statistically significant ($P = 0.079$) (Tables 3 and 4; Fig. 1).

Table 3
Apparent diagnostic performance of individual models and the combined model

Model	Optimal cut-off	Sensitivity, %	Specificity, %	Accuracy, %	AUC (95% CI)
Macroscopic type	0.450	84.06	87.66	86.84	0.870 (0.821–0.919)
IPCL pattern	0.619	75.36	86.38	83.88	0.809 (0.753–0.864)
Macroscopic type + IPCL	0.446	84.06	91.91	90.13	0.915 (0.877–0.953)
<i>AUC, area under the receiver operating characteristic curve; CI, confidence interval; IPCL, intrapapillary capillary loop. Cut-offs were selected using the Youden index.</i>					

Table 4
Pairwise comparison of ROC curves using the DeLong test

Comparison	z statistic	P value
Macroscopic type + IPCL vs macroscopic type	2.942	0.003
Macroscopic type + IPCL vs IPCL pattern	4.239	< 0.001
Macroscopic type vs IPCL pattern	1.759	0.079
<i>IPCL, intrapapillary capillary loop; ROC, receiver operating characteristic.</i>		

Bootstrap internal validation with 1000 resamples showed minimal optimism. The apparent AUC was 0.915, and the optimism-corrected AUC was 0.913. The apparent Brier score was 0.085, and the optimism-corrected Brier score was 0.089. The optimism-corrected calibration intercept was -0.015 , and the optimism-corrected calibration slope was 0.970, suggesting limited overfitting. The grouped apparent calibration plot showed acceptable agreement in the low-risk range, mild underestimation in the intermediate-risk range, and mild overestimation in the high-risk range. Figure 2 presents grouped apparent calibration, whereas Table 5 reports optimism-corrected calibration metrics.

Table 5
Bootstrap internal validation of the final macroscopic type plus IPCL model

Metric	Apparent value	Optimism-corrected value
AUC	0.915	0.913
Brier score	0.085	0.089
Calibration intercept	0.000	-0.015
Calibration slope	1.000	0.970
Bootstrap iterations	1000	1000
<i>AUC, area under the receiver operating characteristic curve. The final model specification was refitted in 1000 bootstrap resamples to estimate optimism-corrected performance.</i>		

Discussion

In this retrospective lesion-based model-development study, macroscopic type and IPCL pattern provided complementary information for predicting pathological MM/SM invasion in SESN. When macroscopic type was modeled as a nominal categorical variable, both 0-IIa and 0-IIc lesions showed higher odds of MM/SM invasion than 0-IIb lesions, with the strongest association observed for 0-IIc lesions. IPCL B2 pattern also remained independently associated with MM/SM invasion after adjustment. A parsimonious model combining macroscopic type and IPCL pattern showed strong apparent discrimination and maintained similar performance after bootstrap internal validation, with limited evidence of overfitting.

Morphology and microvascular architecture reflect different aspects of tumor behavior, which may explain why the two features carried complementary information. ME-NBI and the JES IPCL classification are widely used for depth estimation, and type B vascular patterns have repeatedly been linked to deeper invasion [8–13]. Interpretation of B2-vessel patterns is nonetheless sensitive to lesion heterogeneity, image quality, and the size and morphology of the B2-vessel area, all of which remain areas of active refinement [9, 13, 14]. Our results indicate that a simple, routinely recorded macroscopic descriptor adds useful information to vascular assessment without the need for a more complex model.

PCS positivity was associated with MM/SM invasion on univariable analysis but lost significance after adjustment for macroscopic type and IPCL pattern. This does not make Lugol-based assessment unimportant: Lugol chromoendoscopy and PCS remain valuable for lesion detection, boundary recognition, and characterization of squamous neoplasia during routine endoscopy [15–17]. In our data, however, PCS added no independent predictive information beyond the two retained variables, so we kept it out of the final model while recognizing its descriptive value.

Internal validation supported the stability of the two-predictor model within this dataset. The apparent AUC fell only marginally after bootstrap optimism correction, from 0.915 to 0.913, and the optimism-

corrected Brier score, calibration intercept, and calibration slope all pointed to acceptable performance and limited overfitting. With a moderate sample size and only 69 MM/SM events, a random split-sample approach would have shrunk both the development and validation sets and risked unstable estimates; bootstrapping let us estimate optimism while keeping every observation for model development [20, 21]. Internal validation does not, however, establish generalizability, and the model should be externally validated before broader clinical use.

The model is best used as a pre-ESD risk-stratification aid rather than a standalone decision rule. Lesions with higher-risk combinations, such as 0-IIc morphology and an IPCL B2 pattern, may warrant closer pretherapeutic review, repeat magnifying endoscopy, and more cautious treatment planning, and the predicted risk may help frame discussions with patients about deeper invasion and the possibility of non-curative resection. A low predicted risk, together with otherwise favorable findings, may reinforce confidence in endoscopic treatment. In all cases the model should complement, not replace, expert endoscopic judgment and final pathology.

This study has several limitations. First, it was retrospective and conducted at a single tertiary center, which may limit generalizability because case mix, referral patterns, endoscopic expertise, and pathological assessment may differ across institutions. Second, the analysis was lesion-based; if some patients contributed more than one lesion, within-patient correlation may not have been fully accounted for. Third, endoscopic variables were derived from available clinical records and images, and formal blinded multi-observer assessment was not performed; therefore, interobserver reproducibility could not be evaluated. Fourth, the outcome was dichotomized as EP/LPM versus MM/SM invasion. This distinction is clinically practical for pre-ESD risk stratification, but it does not distinguish finer levels of submucosal invasion. Fifth, although bootstrap internal validation was performed, the model has not yet been externally validated. Finally, calibration was assessed using grouped apparent calibration and optimism-corrected summary metrics; larger independent datasets are needed to evaluate calibration more precisely across the full range of predicted risk.

Conclusions

Macroscopic type and IPCL pattern are complementary endoscopic predictors of pathological MM/SM invasion in SESN. A simple model combining the two showed strong discrimination and held up well after bootstrap internal validation. Combining macroscopic and microvascular assessment may therefore be a practical way to stratify risk before ESD, though external validation is needed before routine use.

Abbreviations

AUC

area under the receiver operating characteristic curve

CI

confidence interval
EP/LPM
epithelium/lamina propria mucosae
ESCC
esophageal squamous cell carcinoma
ESD
endoscopic submucosal dissection
IPCL
intrapapillary capillary loop
JES
Japan Esophageal Society
ME-NBI
magnifying endoscopy with narrow-band imaging
MM/SM
muscularis mucosae/submucosa
OR
odds ratio
PCS
pink-color sign
ROC
receiver operating characteristic
SESN
superficial esophageal squamous neoplasia.

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of Beijing Friendship Hospital (approval No. BFH20260509004), with a waiver of written informed consent because only de-identified clinical and pathological data were analyzed.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

No funding was received for this study.

Author Contribution

HZ and GC designed and supervised the study throughout, and critically reviewed and revised the manuscript for important intellectual content. JD and XR collected the data. RX and BY performed the pathological slide review and pathological assessment. ZH and JW performed the endoscopic procedures and treatments. RG performed the statistical analysis and drafted the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

Availability of data and materials

The datasets analyzed during the current study are not publicly available because they are derived from clinical records. De-identified data may be available from the corresponding author on reasonable request and with ethics committee approval.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209–49. 10.3322/caac.21660.
2. Conway E, Wu H, Tian L. Overview of risk factors for esophageal squamous cell carcinoma in China. *Cancers (Basel)*. 2023;15(23):5604. 10.3390/cancers15235604.
3. Ishihara R. Endoscopic diagnosis and treatment of superficial esophageal squamous cell cancer: present status and future perspectives. *Curr Oncol*. 2022;29(2):534–43. 10.3390/curroncol29020048.
4. Ishihara R, Arima M, Iizuka T, Oyama T, Katada C, Kato M, et al. Endoscopic submucosal dissection/endoscopic mucosal resection guidelines for esophageal cancer. *Dig Endosc*. 2020;32(4):452–93. 10.1111/den.13654.
5. Park CH, Yang DH, Kim JW, Kim JH, Kim JH, Min YW, et al. Clinical practice guideline for endoscopic resection of early gastrointestinal cancer. *Clin Endosc*. 2020;53(2):142–66. 10.5946/ce.2020.032.

6. Yamashina T, Ishihara R, Nagai K, Matsuura N, Matsui F, Ito T, et al. Long-term outcome and metastatic risk after endoscopic resection of superficial esophageal squamous cell carcinoma. *Am J Gastroenterol*. 2013;108(4):544–51. 10.1038/ajg.2013.8.
7. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon. *Gastrointest Endosc*. 2003;58(6 Suppl):S3–43. 10.1016/S0016-5107(03)02159-X
8. Ishihara R, Matsuura N, Hanaoka N, Yamamoto S, Akasaka T, Takeuchi Y, et al. Endoscopic imaging modalities for diagnosing invasion depth of superficial esophageal squamous cell carcinoma: a systematic review and meta-analysis. *BMC Gastroenterol*. 2017;17(1):24. 10.1186/s12876-017-0574-0.
9. Oyama T, Inoue H, Arima M, Momma K, Omori T, Ishihara R, et al. Prediction of the invasion depth of superficial squamous cell carcinoma based on microvessel morphology: magnifying endoscopic classification of the Japan Esophageal Society. *Esophagus*. 2017;14(2):105–12. 10.1007/s10388-016-0527-7.
10. Mizumoto T, Hiyama T, Quach DT, Sanomura Y, Urabe Y, Oka S, et al. Magnifying endoscopy with narrow-band imaging in estimating the invasion depth of superficial esophageal squamous cell carcinomas. *Digestion*. 2018;98(4):249–56. 10.1159/000489490.
11. Hatta W, Koike T, Ogata Y, Kondo Y, Ara N, Uno K, et al. Comparison of magnifying endoscopy with blue light imaging and narrow band imaging for determining the invasion depth of superficial esophageal squamous cell carcinoma by the Japanese Esophageal Society's intrapapillary capillary loop classification. *Diagnostics (Basel)*. 2021;11(11):1941. 10.3390/diagnostics11111941.
12. Fu D, Zhao H, Lan W, Li Y. Diagnostic accuracy of JES classification for prediction of invasion depth in superficial esophageal squamous carcinoma: meta-analysis. *J Coll Physicians Surg Pak*. 2024;34(3):336–42. 10.29271/jcpsp.2024.03.336.
13. Lin X, Lin X, Liang W, Deng W, Liu W. Accuracy and influencing factors of type B2 vessels in predicting the invasion depth of superficial esophageal squamous cell carcinoma under narrow-band imaging magnifying endoscopy. *Discov Oncol*. 2024;15(1):335. 10.1007/s12672-024-01215-6.
14. Yoshida M, Mori K, Urabe Y, Hirasawa D, Sasaki F, Takeuchi M, et al. Evaluating the usefulness of considering the size and morphological type of type B2 vessel area based on Japan Esophageal Society classification in estimating tumor invasion depth in superficial esophageal squamous cell carcinomas: study protocol for a prospective observational study (Japan BEES study). *BMC Gastroenterol*. 2024;24(1):50. 10.1186/s12876-024-03138-6.
15. Shimizu Y, Omori T, Yokoyama A, Yoshida T, Hirota J, Ono Y, et al. Endoscopic diagnosis of early squamous neoplasia of the esophagus with iodine staining: high-grade intra-epithelial neoplasia turns pink within a few minutes. *J Gastroenterol Hepatol*. 2008;23(4):546–50. 10.1111/j.1440-1746.2007.04990.x.
16. Takahashi M, Shimizu Y, Ono M, Suzuki M, Omori S, Yoshida T, et al. Endoscopic diagnosis of early neoplasia of the esophagus with narrow band imaging: correlations among background coloration and iodine staining findings. *J Gastroenterol Hepatol*. 2014;29(4):762–8. 10.1111/jgh.12477.

17. Ishihara R, Kanzaki H, Iishi H, Nagai K, Matsui F, Yamashina T, et al. Pink-color sign in esophageal squamous neoplasia, and speculation regarding the underlying mechanism. *World J Gastroenterol*. 2013;19(27):4300–8. 10.3748/wjg.v19.i27.4300.
18. Tao Y, Chen S, Yu J, Shen Q, Ruan R, Wang S. Risk factors of lymph node metastasis or lymphovascular invasion for superficial esophageal squamous cell carcinoma: a practical and effective predictive nomogram based on a cancer hospital data. *Front Med (Lausanne)*. 2022;9:1038097. 10.3389/fmed.2022.1038097.
19. Cui Y, Luo Z, Wang X, Liang S, Hu G, Chen X, et al. Analyzing risk factors and constructing a predictive model for superficial esophageal carcinoma with submucosal infiltration exceeding 200 micrometers. *BMC Gastroenterol*. 2024;24(1):350. 10.1186/s12876-024-03442-1.
20. Steyerberg EW, Harrell FE Jr, Borsboom GJ, Eijkemans MJ, Vergouwe Y, Habbema JDF. Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. *J Clin Epidemiol*. 2001;54(8):774–81. 10.1016/S0895-4356(01)00341-9.
21. Collins GS, Reitsma JB, Altman DG, Moons KGM. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. *Ann Intern Med*. 2015;162(1):55–63. 10.7326/M14-0697.

Figures

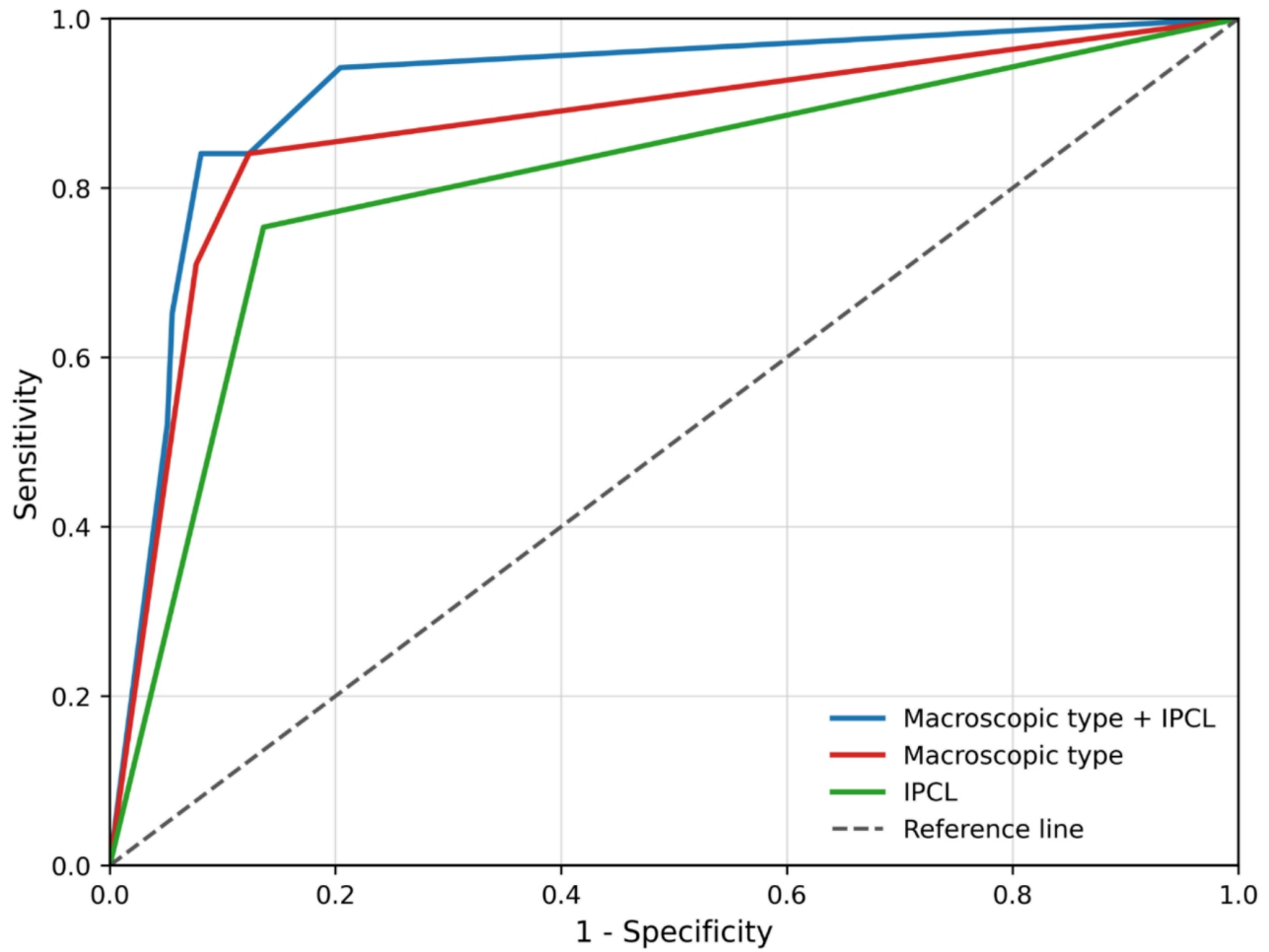


Figure 1

Receiver operating characteristic curves for predicting pathological MM/SM invasion. ROC curves compare macroscopic type alone, IPCL pattern alone, and the combined macroscopic type plus IPCL model for discriminating MM/SM lesions from EP/LPM lesions.

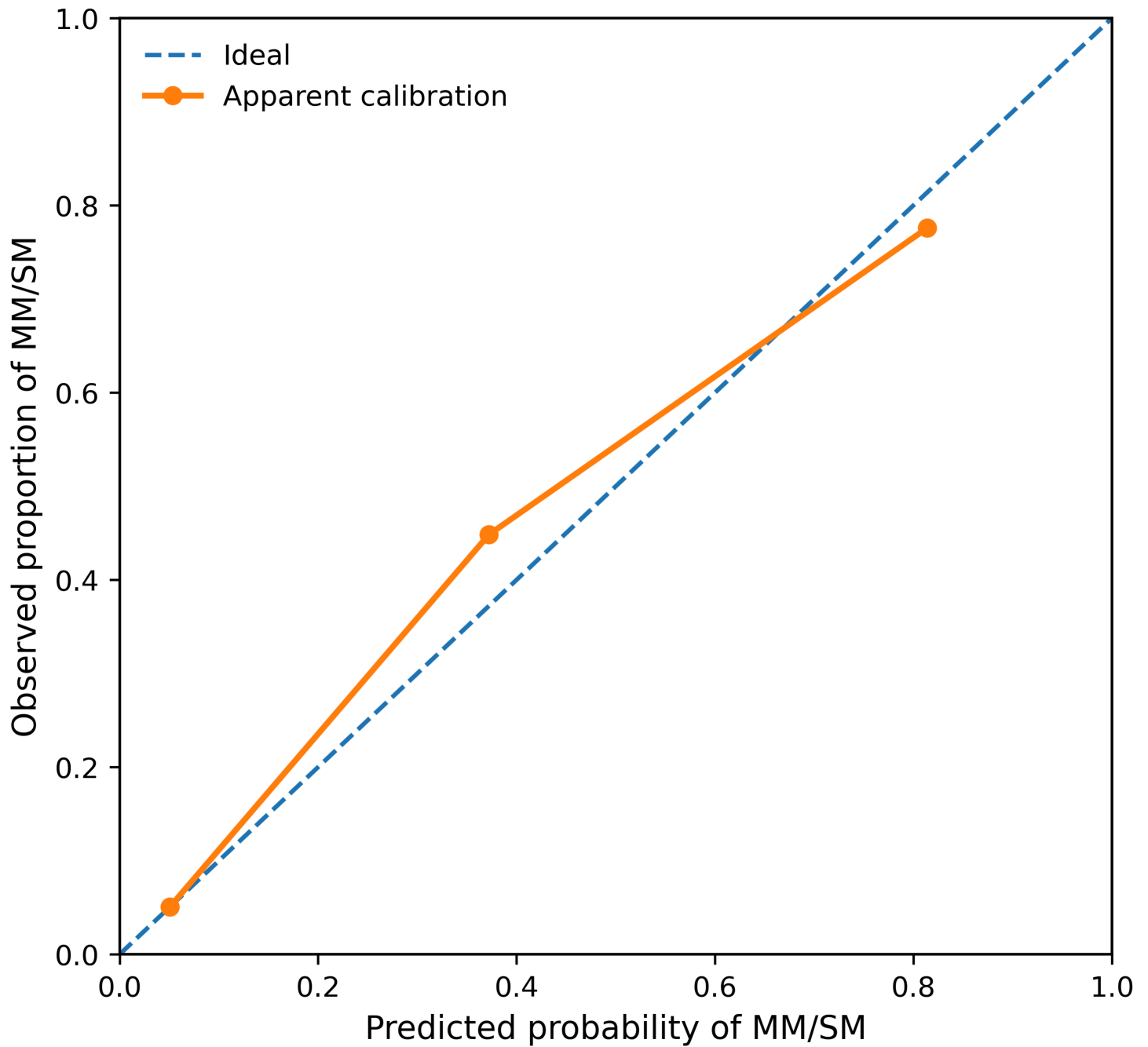


Figure 2

Grouped calibration plot for the final model. The dashed line represents ideal calibration. The grouped apparent calibration curve shows acceptable agreement in the low-risk range, mild underestimation in the intermediate-risk range, and mild overestimation in the high-risk range. This figure presents grouped apparent calibration, whereas optimism-corrected calibration metrics are reported in Table 5.