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ORIGINAL ARTICLE

Retrospective Study

Development and validation of a predictive model for the pathological upgrading of gastric low-grade intraepithelial neoplasia

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Abstract

BACKGROUND

The discrepancy between endoscopic biopsy pathology and the overall pathology of gastric low-grade intraepithelial neoplasia (LGIN) presents challenges in developing diagnostic and treatment protocols.

AIM

To develop a risk prediction model for the pathological upgrading of gastric LGIN to aid clinical diagnosis and treatment.

METHODS

We retrospectively analyzed data from patients newly diagnosed with gastric LGIN who underwent complete endoscopic resection within 6 months at the First Medical Center of Chinese People's Liberation Army General Hospital between January 2008 and December 2023. A risk prediction model for the pathological progression of gastric LGIN was constructed and evaluated for accuracy and

clinical applicability.

RESULTS

A total of 171 patients were included in this study: 93 patients with high-grade intraepithelial neoplasia or early gastric cancer and 78 with LGIN. The logistic stepwise regression model demonstrated a sensitivity and specificity of 0.868 and 0.800, respectively, while the least absolute shrinkage and selection operator (LASSO) regression model showed sensitivity and specificity values of 0.842 and 0.840, respectively. The area under the curve (AUC) for the logistic model was 0.896, slightly lower than the AUC of 0.904 for the LASSO model. Internal validation with 30% of the data yielded AUC scores of 0.908 for the logistic model and 0.905 for the LASSO model. The LASSO model provided greater utility in clinical decision-making.

CONCLUSION

A risk prediction model for the pathological upgrading of gastric LGIN based on white-light and magnifying endoscopic features can accurately and effectively guide clinical diagnosis and treatment.

Key Words: Endoscopic resection; Gastric low-grade intraepithelial neoplasia; Early gastric cancer; Pathological upgrade; Prediction model

Core Tip: This study developed and validated a predictive model for the pathological upgrading of gastric low-grade intraepithelial neoplasia using clinical and endoscopic characteristics. The least absolute shrinkage and selection operator (LASSO) regression analysis identified nine key predictors from 30 variables related to pathological upgrading. The LASSO model demonstrated an area under the curve of 0.904, and internal validation with 30% of the data yielded an area under the curve of 0.905, confirming its clinical utility.

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INTRODUCTION

Gastric cancer is one of the most prevalent cancers worldwide, with the fifth-highest mortality rate globally[1]. However, the 5-year survival rate for patients with early gastric cancer (EGC) exceeds 90% following complete lesion resection[2]. Therefore, early diagnosis is crucial for improving prognosis. The progression of gastric cancer involves multiple steps and factors. According to the Correa cascade model[3], it evolves from intestinal metaplasia to atrophy, intraepithelial neoplasia, and eventually adenocarcinoma. Intraepithelial neoplasia is considered a precancerous lesion and is classified into high- or low-grade. Currently, endoscopic treatment is widely recommended for high-grade intraepithelial neoplasia (HGIN). However, although treatment principles for low-grade intraepithelial neoplasia (LGIN) have been proposed[4-6], definitive management guidelines are lacking.

The diagnosis of gastric LGIN is primarily based on endoscopic forceps biopsy (EFB). Retrospective studies indicate that 12.1%-63% of patients diagnosed with LGIN *via* EFB were subsequently found to have HGIN or gastric cancer after endoscopic resection (ER)[7-11]. Discrepancies between EFB and complete resection specimens may result from inappropriate biopsy site selection, small specimen size, or the presence of focal HGIN or cancer within LGIN[12,13]. Although increasing the number of biopsy specimens can improve the accuracy of endoscopic biopsy diagnosis[14,15], it may lead to subepithelial fibrosis, which can affect complete ER and also increase the risk of bleeding. Enlarging biopsy specimen size may be another strategy to improve diagnostic accuracy. However, a previous study showed no significant difference between conventional and jumbo forceps biopsy[15]. EFB is the most important diagnostic tool for gastric mucosal lesions, but this technique may not avail tissue samples that represent the entire lesion. Current guidelines advocate for active endoscopic treatment in patients with LGIN at high risk for pathological upgrading. However, no standardized criteria exist for predicting or diagnosing such cases. Further research into endoscopic features of HGIN and EGC to clarify the typical features of high-risk lesions, and improve the accuracy of the early diagnosis of gastric LGIN, is highly necessary. Some studies have suggested that the pathological upgrading of gastric LGIN may be associated with characteristics observed through white light microscopy, biopsy findings, and magnifying endoscopy (ME)[16-18]. However, no precise and convenient prediction model studies have been conducted. We aimed to construct a practical and efficient risk prediction model by retrospectively analyzing the clinical and endoscopic characteristics of patients with gastric LGIN who underwent pathological upgrading. The findings provide a scientific basis for the clinical management of LGIN.

MATERIALS AND METHODS

Study design and patients

This retrospective study included patients with gastric LGIN diagnosed by initial endoscopic pathology at our center between January 2008 and December 2023, who underwent ER within 6 months. The inclusion criteria were as follows: (1) Age ≥ 18 years; (2) Initial diagnosis of gastric LGIN, which was the only lesion in the stomach; and (3) ME with narrow-band imaging (ME-NBI) and ER performed at our center within 6 months of the initial examination. The exclusion criteria were as follows: (1) History of gastric or esophageal surgery; (2) History of malignant cancer; and (3) Presence of other malignant cancers. The positive group consisted of patients diagnosed with HGIN or EGC after ER, whereas the negative group included patients pathologically diagnosed with LGIN after ER. The model development process is illustrated in Figure 1.

Data acquisition

General clinical data included outpatient ID, sex, age, body mass index, personal history (smoking history, drinking habits, and family history of gastric cancer), long-term use of oral nonsteroidal anti-inflammatory drugs, chief complaints, *Helicobacter pylori* infection status, and treatment information. Laboratory test results included serum carcinoembryonic antigen, carbohydrate antigen 19-9, alpha-fetoprotein, and carbohydrate antigen 125 Levels. Endoscopic imaging features included the following: (1) White light endoscopic features: Lesion location and size; gross morphology of the lesion (including the presence of white coating, ulceration, erosion, congestion, or spontaneous bleeding), and bile reflux observed during endoscopy; and (2) ME-NBI features: Lesion boundary presence, microvascular (MV) pattern, microsurface (MS) pattern, as well as the presence of white opaque substance (WOS), Light blue crest, and white globe appearance. Two experienced endoscopists independently reviewed all endoscopic features in a blinded manner. Biopsy date included intestinal metaplasia, atrophy, acute and chronic inflammatory reactions, LGIN, HGIN, adenocarcinoma and *Helicobacter pylori* infection. Two experienced pathologists reinterpreted all pathological findings, with a senior pathologist confirming any discrepancies.

Definitions of endoscopic features

Gross tumors observed under white light endoscopy were classified according to the Paris classification as follows: Polypoid (type 0-I), non-polypoid (type 0-IIa/0-IIb/0-IIc), or excavated (type 0-III). Erosion was defined as a superficial mucosal defect, whereas ulceration was defined as a deep mucosal defect with discontinuity of the muscularis propria. Spontaneous bleeding referred to minor mucosal bleeding caused by ventilation or slight touch. Atrophy in white light endoscopy was characterized by thin gastric mucosa, shallow gastric pits, alternating red and white mucosa, flattening or disappearance of the plicae, and exposure of mucosal blood vessels. It may also be accompanied by mucosal granules or nodules. According to the vessel-plus-surface classification system[19,20], the regular MV pattern refers to uniformly distributed microvessels that form open or closed loops (polygonal) with symmetrical distribution. The irregular MV pattern refers to microvessels with diverse appearances, such as open or closed loops (polygonal), serpentine, branching, and singular patterns. The absence of the MV pattern indicates a WOS obstructing the observation of microvessels beneath the mucosal epithelium. The regular MS pattern shows a uniform (linear, curved, oval, or circular) marginal crypt epithelium with homogeneous morphology, symmetrical distribution, and regular arrangement. The irregular MS pattern refers to the irregular (linear, curved, oval, circular, or villous) marginal crypt epithelium with heterogeneous morphology, asymmetrical distribution, and irregular arrangement. If the marginal crypt epithelium is not fully visualized, the MS pattern is considered absent.

Statistical analysis

Normally distributed data were represented as the mean ± SD and compared using the independent sample *t*-test. Data with a non-normal distribution were represented as the median and interquartile range (Q1, Q3) and compared using the Wilcoxon rank-sum test. Count data were expressed as the number of cases (%) and compared using the χ^2-test. Logistic stepwise regression analysis and the least absolute shrinkage and selection operator (LASSO) regression algorithm were used to select predictor variables, construct the model, generate a nomogram, and calculate the C-index, R2, and Brier values for each model. The Hosmer-Lemeshow goodness-of-fit test (HL test) was performed, and cross-calibration curves were drawn (repeated 1000 times). Internal validation of the prediction model was conducted by randomly selecting 30% of the data. Receiver-operating characteristic (ROC) curves were plotted for both the training and validation sets to calculate the area under the curve (AUC) and 95% confidence interval (CI). *P* values were calculated to evaluate the accuracy in comparison with the AUC of the training set. The clinical applicability of the model was assessed using decision curve analysis (DCA) by calculating the net benefit (NB) within a threshold probability range. The NB values of each predictive model were compared in one figure. - Statistical analysis was performed using R 4.4.1 software (with the following data packages: Mice, glm, lrm, rms, MASS, pROC, ggDCA, rmda, logistf, glmnet, and corrplot). Statistical significance was set at $P < 0.05$.

RESULTS

Baseline characteristics

Table 1 presents the baseline characteristics of the patients. A total of 171 patients were enrolled in the study. After ER, 93

Table 1 Baseline characteristics of patients with positive and negative pathologic upgrade, *n* (%)

	Group	Negative (*n* = 78)	Positive (*n* = 93)	Statistics	*P* value
General characteristics	Sex, male/female	47/31	74/19	7.648	0.006
	Age, years	59.33 ± 12.45	61.85 ± 9.90	-1.44	0.151
	BMI, kg/m^2	23.2 [21.6, 25.2]	24.4 [22.7, 25.9]	3040.5	0.069
	Smoker	22 (28.21)	37 (39.78)	2.517	0.113
	Alcohol drinker	28 (35.90)	35 (37.63)	0.055	0.815
	13C+	8 (10.26)	8 (8.60)	0.214	0.644
	Taking aspirin	4 (5.13)	5 (5.38)	< 0.001	1
	CEA, μg/L	1.64 [1.20, 2.89]	2.23 [1.58, 3.02]	2732.5	0.025
	CA199, U/mL	8.25 [5.05, 11.58]	9.44 [5.79, 13.98]	3011	0.179
	AFP, μg/L	2.72 [2.16, 3.80]	2.58 [1.92, 3.54]	3683.5	0.169
	CA125, U/mL	9.40 [7.63, 10.80]	9.03 [6.74, 12.95]	2395.5	0.936
White light endoscopy characteristics	Size	1.85 ± 1.16	2.52 ± 1.37	15.448	< 0.001
	Location			1.801	0.772
	Cardia	5 (6.41)	9 (9.68)		
	Fundus	1 (1.28)	2 (2.15)		
	Corpus	10 (12.82)	16 (17.20)		
	Horns	18 (23.08)	21 (22.58)		
	Antrum	44 (56.41)	45 (48.39)		
	Atrophy	21 (26.29)	43 (46.24)	6.757	0.009
	Biopsy cores	2.0 (1.0,3.0)	2.0 (1.0,3.0)	3499.000	0.678
	White coating	11 (14.10)	28 (30.11)	6.172	0.013
	Ulceration	1 (1.28)	12 (12.90)	8.156	0.004
	Erosion	37 (47.44)	52 (55.91)	1.222	0.269
	Congested lesion	41 (52.56)	59 (63.44)	2.067	0.151
	Bleeding	5 (6.41)	11 (11.83)	1.468	0.226
	Paris classification			0.663	0.416
	I/III	7 (8.97)	12 (12.90)		
	II	71 (91.03)	81 (87.10)		
	Surface roughness	43 (55.13)	59 (63.44)	1.218	0.270
	Bile reflux	8 (10.26)	9 (9.68)	0.016	0.900
Biopsy pathology	Intestinal metaplasia	44 (56.41)	79 (84.95)	17.109	< 0.001
	Atrophy	7 (8.97)	30 (32.26)	13.563	< 0.001
	Chronic inflammation	78 (100.00)	92 (98.92)	< 0.001	1
	Acute inflammation	30 (38.46)	39 (41.94)	0.213	0.645
	HP in pathology	10 (12.82)	14 (15.05)	0.175	0.675
ME characteristics	ME	76 (97.44)	79 (84.95)		
	Demarcation line	54 (69.23)	65 (69.89)	2.738	0.098
	MV			51.627	< 0.001
	Regular	63 (80.77)	20 (25.32)		
	Irregular/absent	13 (16.67)	59 (74.68)		
	MS			11.115	0.001

Regular	24 (31.58)	7 (8.86)		
Irregular/absent	52 (68.42)	72 (91.14)		
White opaque substance	17 (21.79)	35 (37.63)	8.36	0.004
Light blue crest	15 (19.23)	38 (40.86)	13.85	< 0.001
White globular appearance	0	4 (4.30)	3.95	0.047

BMI: Body mass index; CEA: Carcinoembryonic antigen; CA: Carbohydrate antigen; AFP: Alpha fetoprotein; HP: *Helicobacter pylori*; ME: Magnifying endoscopy; MV: Microvascular; MS: Microsurface.

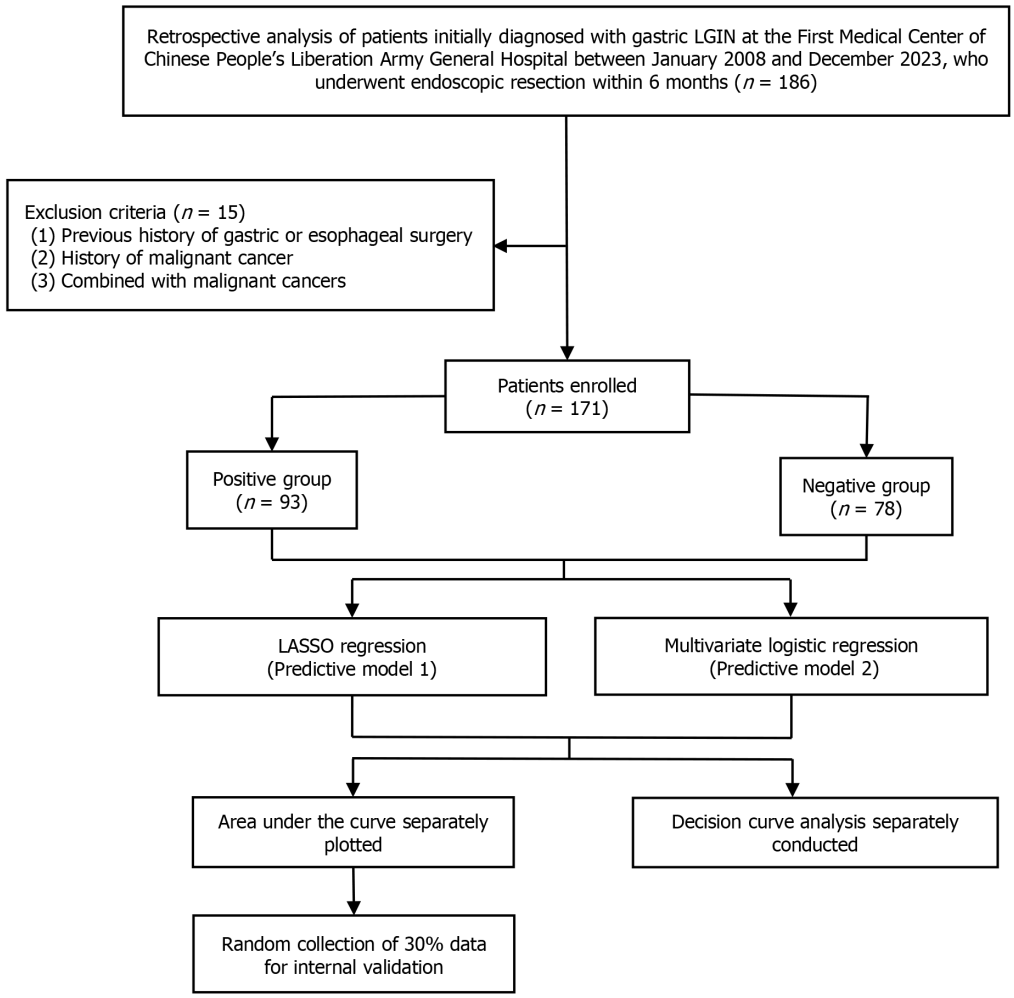

Figure 1 Study flowchart. LGIN: Low-grade intraepithelial neoplasia.

patients were pathologically confirmed to have been upgraded to the positive group, with 35 (37.63%) of them exhibiting focal cancer. Seventy-eight patients were diagnosed with LGIN after surgery. The median time interval from the initial diagnosis by white light endoscopy to completion of ER was 1.7 months in the positive group and 1.2 months in the negative group (P = 0.134). Compared to the negative group, a higher proportion of patients in the positive group were males (P = 0.006) and had elevated serum carcinoembryonic antigen levels (P = 0.025). They also had larger lesions observed under white light endoscopy (P < 0.001), atrophy (P = 0.009), white coating on the mucosal surface (P = 0.013), and surface ulceration (P = 0.004). Intestinal metaplasia (P < 0.001) or atrophy (P < 0.001) were more frequently observed in endoscopic biopsies and often revealed an irregular or absent MV pattern (P < 0.001) and MS pattern (P = 0.001), white opaque substance (P = 0.004), and light blue crests (P < 0.001).

Construction of the prediction models

Multivariate logistic regression analysis: Variables showing statistical differences in the univariate analysis were subjected to a stepwise logistic regression (backward) analysis to identify the optimal model. The predictors included sex (male) (odds ratio (OR): 2.499, 95%CI: 0.973-6.812, P = 0.057), presence of ulceration under white light microscopy (OR: 14.372, 95%CI: 1.199-534.717, P = 0.032), MV irregularity/absence (OR: 8.539, 95%CI: 3.687-21.259, P < 0.001), MS irregu-

larity/absence (OR: 3.659, 95%CI: 1.234-12.251, $P = 0.019$), presence of white opaque substance (OR: 1.769, 95%CI: 0.731-4.330, $P = 0.205$), light blue crest (OR: 1.801, 95%CI: 0.723-4.530, $P = 0.205$), and pathological intestinal metaplasia (OR: 4.344, 95%CI: 1.594-13.015, $P = 0.004$). The statistical results are presented in Table 2. A nomogram is shown in Figure 2. The presence of ulceration under white light endoscopy ($P = 0.032$), MV irregularity/absence ($P < 0.001$), MS irregularity/absence ($P = 0.019$), and intestinal metaplasia ($P = 0.004$) were identified as independent risk factors for pathological upgrading of LGIN.

LASSO regression model: LASSO regression analysis was performed on the 30 variables associated with pathological upgrading. Male sex, lesion size, presence of ulceration, clear boundary observed under magnification endoscopy, MV irregularity/absence, MS irregularity/absence, light blue crest appearance, intestinal metaplasia, and atrophy were identified as the most important predictors with non-zero coefficients (Figure 3). A nomogram is shown in Figure 4.

Model testing and evaluation

Precision and stability of the measurement: The nomogram was self-verified. The C-index for the prediction nomogram was 0.896 (95%CI: 0.846-0.947) for the logistic stepwise regression model. The ROC curve yielded an AUC value of 0.896 (95%CI: 0.846-0.947) for the logistic stepwise regression model (Figure 5A). A random selection of 30% of the data was used as the validation set, resulting in an AUC of 0.908 (Figure 5B). After performing 1000 cross-validation replicates, the Brier value of the model was 0.131. The HL test yielded a P value of 0.428, indicating no significant difference between the predicted and actual values, confirming the model's good fit (Figure 5C). The AUC for the LASSO regression model was 0.904 (95%CI: 0.856-0.951), indicating high predictive accuracy (Figure 6A). A random selection of 30% of the data was used for internal validation, yielding an AUC of 0.905, further confirming the model's robustness and reliability (Figure 6B). Repeated cross-validation analysis showed a Brier value of 0.124, and the HL test P value was 0.957, suggesting superior stability and a closer approximation to actual values compared to the logistic stepwise regression model (Figure 6C).

Reassessment of clinical utility: DCA was used to assess the clinical applicability of both models. The decision curve is shown in Figure 7. Within the threshold probability (80%), both models exhibited superior NB compared to surgical and follow-up interventions. Overall, the LASSO model demonstrated a higher NB than the stepwise logistic regression model.

DISCUSSION

In this retrospective study, we analyzed a cohort of 171 patients with gastric LGIN diagnosed by biopsy at our center over the past 16 years, who voluntarily underwent ER within 6 months. Postoperative pathology confirmed LGIN in 78 cases, while 93 cases were upgraded to HGIN or EGC, resulting in a pathological upgrade rate of 54.39% (93/171). We compared the general clinical characteristics, white light endoscopy findings, and ME features between these two groups. Logistic stepwise regression and LASSO regression analyses were employed to develop a predictive model for pathological upgrading of gastric LGIN. The LASSO model demonstrated superior prediction accuracy and greater clinical applicability.

We aimed to examine the general clinical characteristics, white light endoscopic features, endoscopic biopsy findings, and ME-NBI characteristics of patients in relation to pathological stability or upgrading. Variables found to predict pathological upgrading included male sex ($P = 0.057$), presence of ulcer on white light endoscopy ($P = 0.032$), MV irregularity/absence ($P < 0.001$), MS irregularity/absence ($P = 0.019$), presence of a WOS ($P = 0.205$), presence of light blue crest ($P = 0.205$), and presence of intestinal metaplasia in biopsy pathology results ($P = 0.004$). The AUC for this model was 0.896, and internal validation using a randomly selected 30% sample yielded an AUC value of 0.908. Based on the P values obtained, the presence of ulcers on white light endoscopy, intestinal metaplasia in biopsy pathology, MV irregularity or disappearance on ME-NBI, and MS irregularity or disappearance were identified as independent risk factors for pathological upgrading of gastric LGIN. Lesions exhibiting these characteristics should be closely monitored, with prompt intervention when necessary. LASSO regression analysis was used to address the potential collinearity among predictor variables. The optimal combination of predictors included male sex, lesion size, white light endoscopy features, clear boundary under ME-NBI, MV irregularity/absence, MS irregularity/absence, light blue crest, intestinal metaplasia, and atrophy in biopsy pathology. This model exhibited an AUC of 0.904 with an internal validation AUC of 0.905, demonstrating superior prediction accuracy compared with the logistic regression model. DCA revealed a higher NB for clinical intervention based on the LASSO model, indicating its greater clinical applicability.

Both models identified the presence of ulceration on white light endoscopy, MV and MS irregularity or absence, the presence of light blue crest, and intestinal transformation in biopsy pathology as common predictors, emphasizing the importance of these factors in predicting the pathological upgrading of gastric LGIN. These findings align with recent advancements in research on the endoscopic features of gastric HGIN and EGC[21-24]. Despite the limited accuracy of white light endoscopy and conventional biopsy for diagnosing gastric intraepithelial neoplasia, our analysis demonstrates that ulceration on white light endoscopy and intestinal metaplasia observed during endoscopic biopsy are significant clinical indicators for predicting pathological upgrading of LGIN. There are notable regional disparities in the development of digestive endoscopy technologies. In countries and regions where ME and NBI are less prevalent, routine white light endoscopy can serve as an initial screening tool for high-risk lesions, guiding patients toward advanced endoscopy techniques and improving diagnostic rates for gastric HGIN and EGC.

Table 2 Stepwise logistic regression of predictors for pathologic upgrade in gastric low-grade intraepithelial neoplasia

	Coef	SE (coef)	OR (95%CI)	*P* value
Intercept	-4.223	0.808	0.015 (0.002-0.066)	1.757^{-10}
Sex, male	0.916	0.478	2.499 (0.973-6.812)	0.057
Ulceration, yes	2.665	1.343	14.372 (1.199-534.717)[1]	0.032
MV, irregular/absent	2.145	0.436	8.539 (3.687-21.259)	< 0.001
MS, irregular/absent	1.297	0.564	3.659 (1.234-12.251)	0.019
White opaque substance, yes	0.570	0.442	1.769 (0.731-4.330)	0.205
Light blue crest, yes	0.589	0.454	1.801 (0.723-4.530)	0.205
Intestinal metaplasia, yes	1.469	0.516	4.344 (1.594-13.015)	0.004

[1]Correction for sparse data.

Coef: Coefficient; SE: Standard error; OR: Odds ratio; CI: Confidence interval; MV: Microvascular; MS: Microsurface.

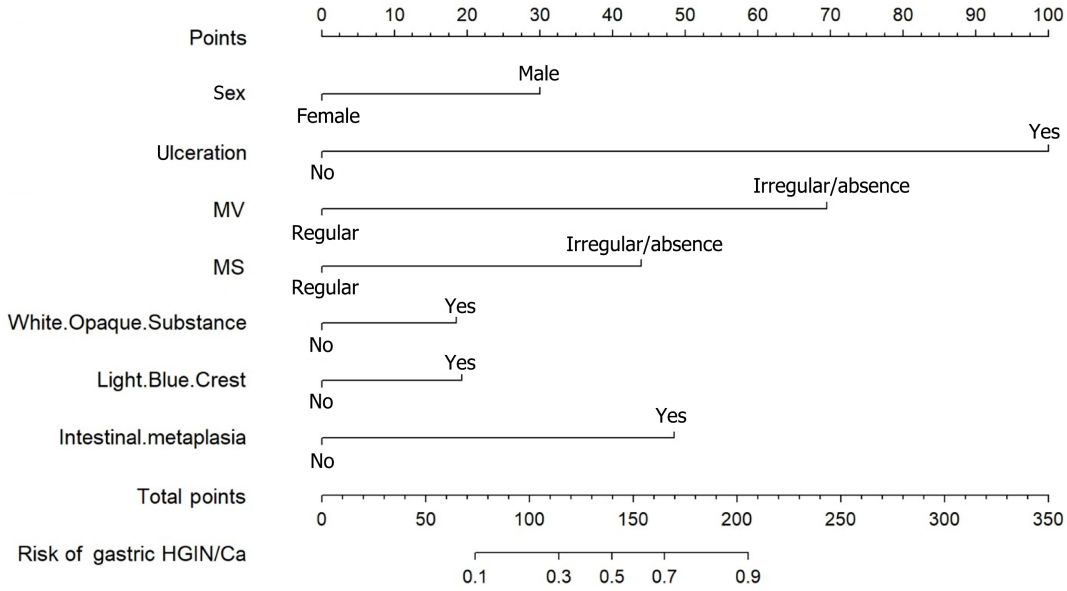

Figure 2 Nomogram of the stepwise logistic regression model. An individual patient's value is located on the axes for each variable, and a line is drawn upward to determine the number of points received for each variable value. The sum of these numbers is located on the Total Points axis, and a line is drawn downward to the Risk of Pathological Progression axis to determine the risk probability of high-grade intraepithelial neoplasia/cancer. MV: Microvascular; MS: Microsurface; HGIN: High-grade intraepithelial neoplasia; Ca: Cancer.

Observational studies of ME for gastric HGIN and EGC have long been a focus of endoscopic research. Tumor cells induce vascular and structural changes as they grow[25,26], and these subtle alterations can be visualized through ME-NBI, thereby enhancing early detection rates of gastric cancer. In 2013, Maki *et al*[27] from Fukuoka University in Japan proposed that ME-NBI could significantly enhance diagnostic efficiency for EGC by observing changes in gastric mucosal MV and MS patterns, achieving an impressive diagnostic accuracy of 92%. However, some studies have reported abnormal MV and MS patterns in 34.89% and 39.53% of patients with LGIN after ER, respectively[24]. Therefore, relying solely on MV and MS abnormalities may not accurately predict the risk of pathological progression. A 2022 Japanese study demonstrated that combining MV and MS patterns achieved an accuracy rate of 82.1% for diagnosing gastric cancer, surpassing the accuracy of evaluating MV (76.4%) or MS (73.6%) alone[28]. Consequently, integrating MV and MS patterns observed through ME-NBI along with biopsy pathological features may offer a more comprehensive approach for predicting pathological upgrades in lesions.

This study had some limitations. First, it was retrospective in nature, and to minimize recall bias, we excluded data with significant missing values or questionable authenticity, which may have introduced selectivity bias. Second, the quality of the endoscopic images used for retrospective analysis could affect the accuracy of assessment by endoscopists. Third, our sample size was relatively small. Future multicenter, large-scale prospective studies are needed to further validate the predictive efficiency and clinical applicability of this model.

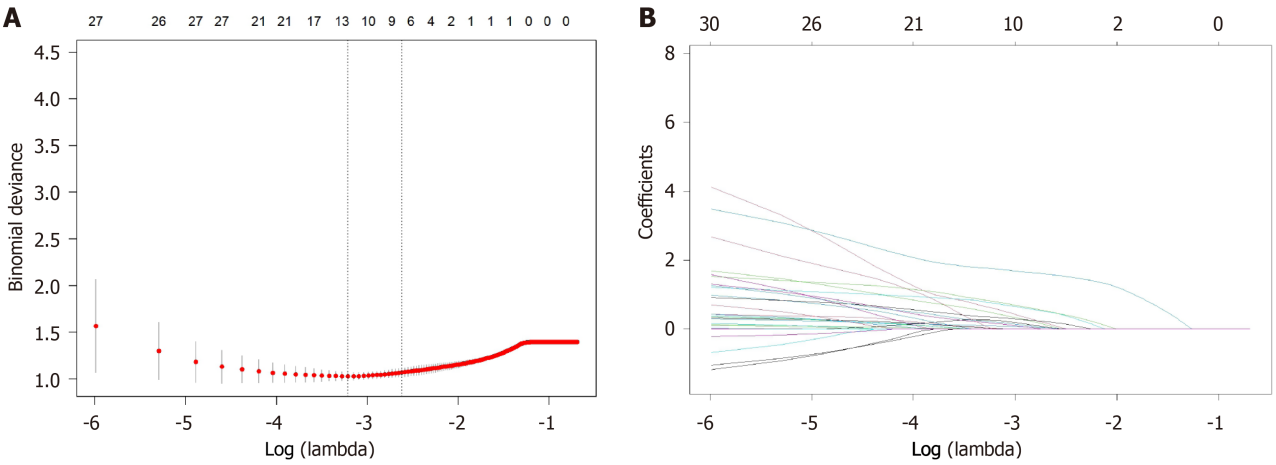

Figure 3 Demographic and clinical feature selection using the least absolute shrinkage and selection operator binary logistic regression model. A: Optimal parameter (lambda) selection in the least absolute shrinkage and selection operator (LASSO) model used five-fold cross-validation through minimum criteria. The partial likelihood deviance (binomial deviance) curve was plotted *vs* log (lambda). Dotted vertical lines were drawn by the optimal values using the minimum criteria and the 1 SE of the minimum criteria (the 1-SE criteria); B: LASSO coefficient profiles of the 30 candidate features.

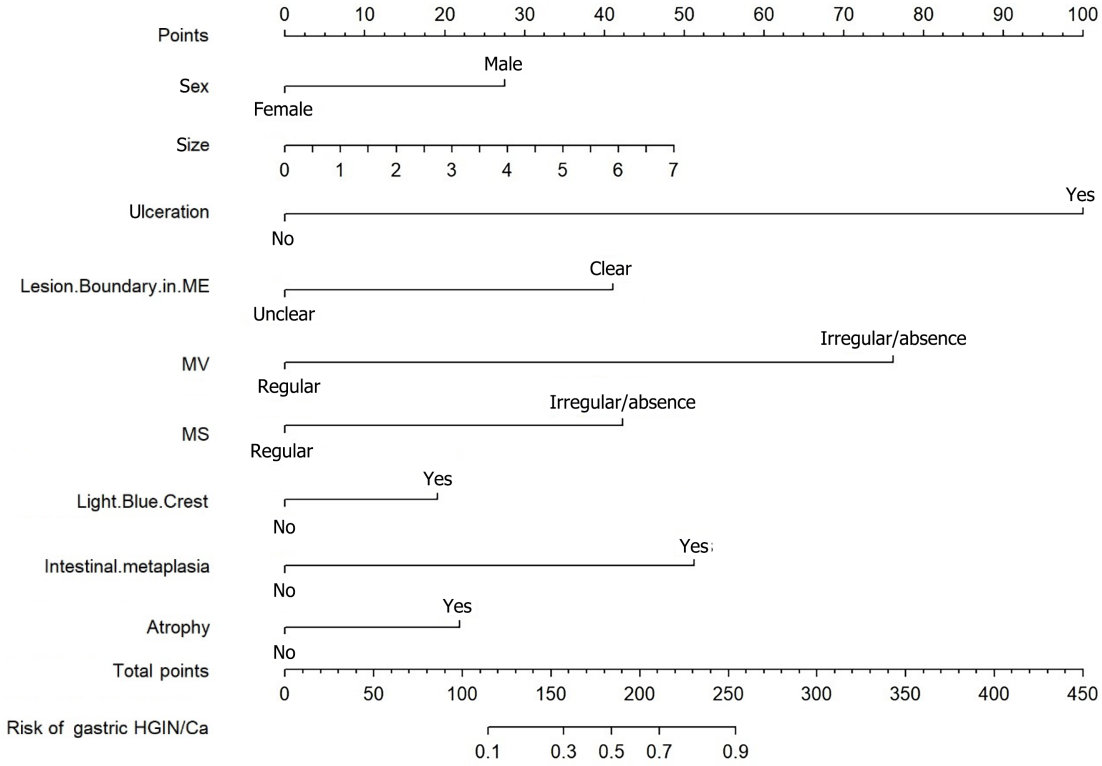

Figure 4 Nomogram of the least absolute shrinkage and selection operator regression analysis model. An individual patient's value is located on the axes for each variable, and a line is drawn upward to determine the number of points received for each variable value. The sum of these numbers is located on the total points axis, and a line is drawn downward to the Risk of Pathological Progression axis to determine the risk probability of high-grade intraepithelial neoplasia/cancer. ME: Magnifying endoscopy; MV: Microvascular; MS: Microsurface; HGIN: High-grade intraepithelial neoplasia; Ca: Cancer.

CONCLUSION

By integrating the characteristics of white light endoscopy, biopsy pathology findings, and ME-NBI features, our predictive model can accurately and quickly assess the risk of pathological upgrading in patients with gastric LGIN, offering valuable guidance for clinical diagnosis and treatment planning. Our research team will continue to validate and optimize this model.

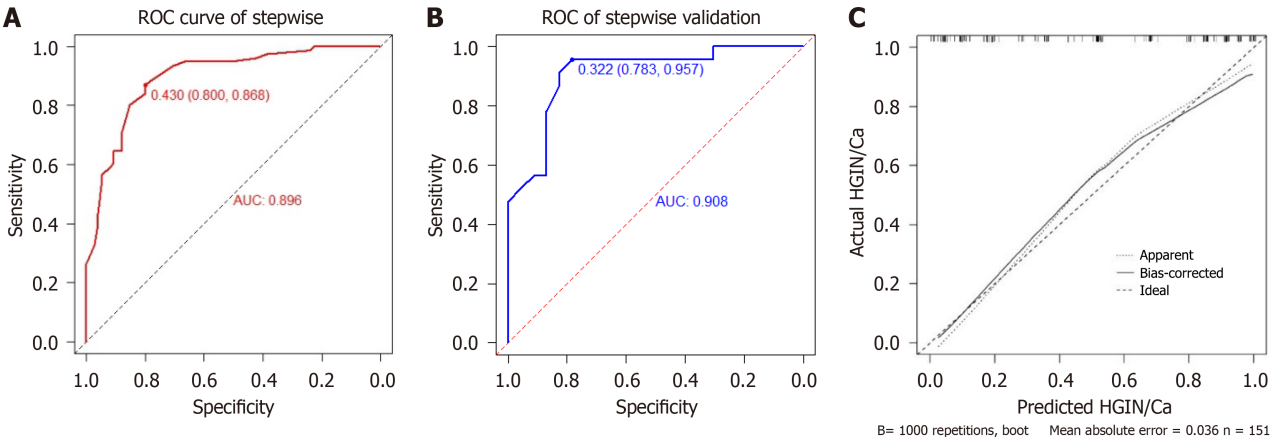

Figure 5 Evaluation of the performance of the nomogram in predicting the risk of pathologic upgrade in patients with gastric low-grade intraepithelial neoplasia in the logistic stepwise regression model. A: The receiver-operating characteristic curve of the nomogram in the training cohort (area under the curve = 0.896); B: The receiver-operating characteristic curve of the nomogram in the internal validation cohort (area under the curve = 0.908); C: The calibration curve. ROC: Receiver-operating characteristic; AUC: Area under the curve; HGIN: High-grade intraepithelial neoplasia; Ca: Cancer.

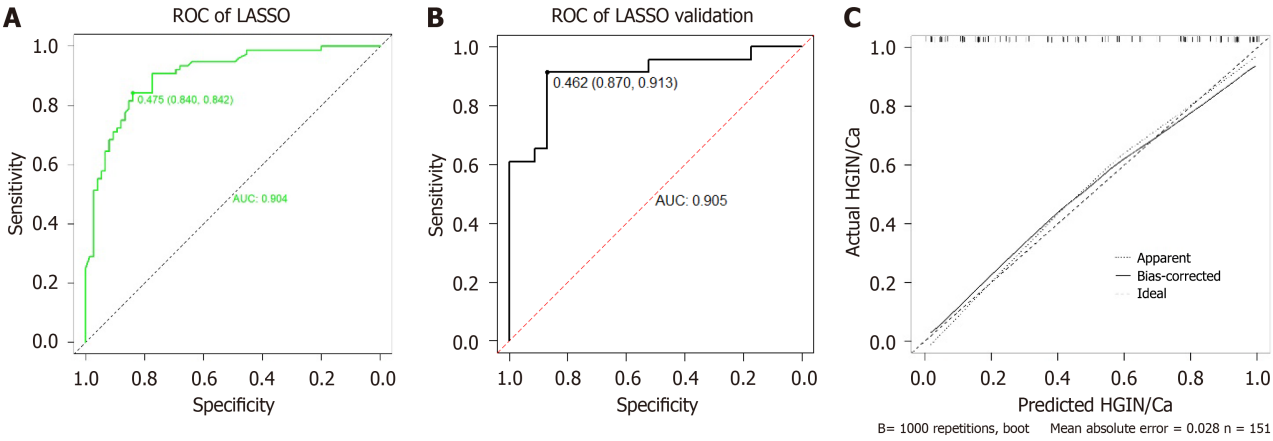

Figure 6 Evaluation of the performance of the nomogram in predicting the risk of pathologic upgrade in patients with gastric low-grade intraepithelial neoplasia in the least absolute shrinkage and selection operator regression model. A: The receiver-operating characteristic curve of the nomogram in the training cohort (area under the curve = 0.904); B: The receiver-operating characteristic curve of the nomogram in the internal validation cohort (area under the curve = 0.905); C: The calibration curve. ROC: Receiver-operating characteristic; AUC: Area under the curve; HGIN: High-grade intraepithelial neoplasia; Ca: Cancer; LASSO: Least absolute shrinkage and selection operator.

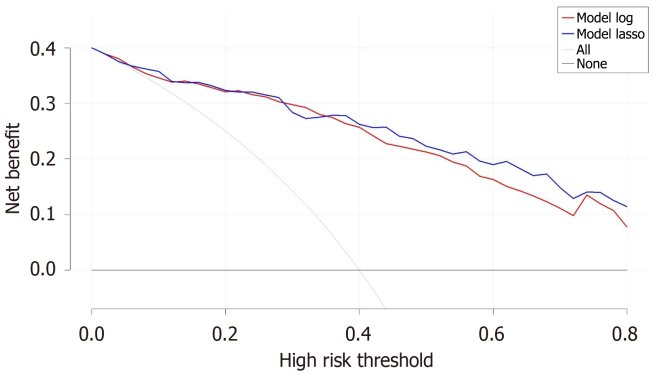

Figure 7 Decision curve analysis on the prediction models. A high-risk threshold of 0.8 was set, above which clinically recommended endoscopic resection was advised. The gray curve represents the net benefit for all patients receiving endoscopic resection, while the black line indicates the net benefit (NB) when all patients were followed up. The red curve represents the NB based on intervention decisions made using a stepwise regression model, and the blue curve represents the NB based on intervention decisions made using the least absolute shrinkage and selection operator model.

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FOOTNOTES

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REFERENCES

1 **Bray F**, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2024; **74**: 229-263 [PMID: 38572751 DOI: 10.3322/caac.21834]

2 **Gotoda T**. A large endoscopic resection by endoscopic submucosal dissection procedure for early gastric cancer. *Clin Gastroenterol Hepatol* 2005; **3**: S71-S73 [PMID: 16013003 DOI: 10.1016/s1542-3565(05)00251-x]

3 **Correa P**, Piazuelo MB. The gastric precancerous cascade. *J Dig Dis* 2012; **13**: 2-9 [PMID: 22188910 DOI: 10.1111/j.1751-2980.2011.00550.x]

4 **Andersen JW**, Jensen TM, Kjær DW, Oppfeldt AM. [The management of gastric polyps]. *Ugeskr Laeger* 2022; **184**: V10210773 [PMID: 35506619]

5 **ASGE Standards of Practice Committee**, Evans JA, Chandrasekhara V, Chathadi KV, Decker GA, Early DS, Fisher DA, Foley K, Hwang JH, Jue TL, Lightdale JR, Pasha SF, Sharaf R, Shergill AK, Cash BD, DeWitt JM. The role of endoscopy in the management of premalignant and malignant conditions of the stomach. *Gastrointest Endosc* 2015; **82**: 1-8 [PMID: 25935705 DOI: 10.1016/j.gie.2015.03.1967]

6 **Dinis-Ribeiro M**, Areia M, de Vries AC, Marcos-Pinto R, Monteiro-Soares M, O'Connor A, Pereira C, Pimentel-Nunes P, Correia R, Ensari A, Dumonceau JM, Machado JC, Macedo G, Malfertheiner P, Matysiak-Budnik T, Megraud F, Miki K, O'Morain C, Peek RM, Ponchon T, Ristimaki A, Rembacken B, Carneiro F, Kuipers EJ; European Society of Gastrointestinal Endoscopy; European Helicobacter Study Group; European Society of Pathology; Sociedade Portuguesa de Endoscopia Digestiva. Management of precancerous conditions and lesions in the stomach (MAPS): guideline from the European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter Study Group (EHSG), European Society of Pathology (ESP), and the Sociedade Portuguesa de Endoscopia Digestiva (SPED). *Endoscopy* 2012; **44**: 74-94 [PMID: 22198778 DOI: 10.1055/s-0031-1291491]

7 **Choi CW**, Kang DH, Kim HW, Park SB, Kim S, Cho M. Endoscopic submucosal dissection as a treatment for gastric adenomatous polyps: predictive factors for early gastric cancer. *Scand J Gastroenterol* 2012; **47**: 1218-1225 [PMID: 22839759 DOI: 10.3109/00365521.2012.666674]

8 **Lim H**, Jung HY, Park YS, Na HK, Ahn JY, Choi JY, Lee JH, Kim MY, Choi KS, Kim DH, Choi KD, Song HJ, Lee GH, Kim JH. Discrepancy between endoscopic forceps biopsy and endoscopic resection in gastric epithelial neoplasia. *Surg Endosc* 2014; **28**: 1256-1262 [PMID: 24310738 DOI: 10.1007/s00464-013-3316-6]

9 **Hwang JW**, Bae YS, Kang MS, Kim JH, Jee SR, Lee SH, An MS, Kim KH, Bae KB, Kim B, Seol SY. Predicting pre- and post-resectional

histologic discrepancies in gastric low-grade dysplasia: A comparison of white-light and magnifying endoscopy. *J Gastroenterol Hepatol* 2016; **31**: 394-402 [PMID: 26474082 DOI: 10.1111/jgh.13195]

10 **Lee JH**, Min YW, Lee JH, Kim ER, Lee H, Min BH, Kim JJ, Jang KT, Kim KM, Park CK. Diagnostic group classifications of gastric neoplasms by endoscopic resection criteria before and after treatment: real-world experience. *Surg Endosc* 2016; **30**: 3987-3993 [PMID: 26694184 DOI: 10.1007/s00464-015-4710-z]

11 **Zhu LY**, Dai J, Zhao YJ, Xue HB, Ge ZZ, Li XB. Endoscopic resection for gastric epithelial neoplasia: how to solve pathological discrepancy and achieve curative resection? *J Dig Dis* 2013; **14**: 231-237 [PMID: 23297845 DOI: 10.1111/1751-2980.12032]

12 **Maekawa A**, Kato M, Nakamura T, Komori M, Yamada T, Yamamoto K, Ogiyama H, Nakahara M, Kawai N, Yabuta T, Mukai A, Hayashi Y, Nishida T, Iijima H, Tsujii M, Morii E, Takehara T. Incidence of gastric adenocarcinoma among lesions diagnosed as low-grade adenoma/dysplasia on endoscopic biopsy: A multicenter, prospective, observational study. *Dig Endosc* 2018; **30**: 228-235 [PMID: 29094455 DOI: 10.1111/den.12980]

13 **Choi CW**, Kim HW, Shin DH, Kang DH, Hong YM, Park JH, Park SB, Cho M, Lee JH. The risk factors for discrepancy after endoscopic submucosal dissection of gastric category 3 lesion (low grade dysplasia). *Dig Dis Sci* 2014; **59**: 421-427 [PMID: 24366779 DOI: 10.1007/s10620-013-2874-8]

14 **Zhao G**, Xue M, Hu Y, Lai S, Chen S, Wang L. How Commonly Is the Diagnosis of Gastric Low Grade Dysplasia Upgraded following Endoscopic Resection? A Meta-Analysis. *PLoS One* 2015; **10**: e0132699 [PMID: 26182344 DOI: 10.1371/journal.pone.0132699]

15 **Jeon HK**, Ryu HY, Cho MY, Kim HS, Kim JW, Park HJ, Kim MY, Baik SK, Kwon SO, Park SY, Won SH. A randomized trial to determine the diagnostic accuracy of conventional vs. jumbo forceps biopsy of gastric epithelial neoplasias before endoscopic submucosal dissection; open-label study. *Gastric Cancer* 2014; **17**: 661-668 [PMID: 24337434 DOI: 10.1007/s10120-013-0322-2]

16 **Chen Y**, Dang Y, Sang H, Wang X, Chen M, Lu D, Zhang G. Establishment and validation of a model to determine the progression risk of low grade intraepithelial neoplasia. *Surg Endosc* 2021; **35**: 1551-1557 [PMID: 32424624 DOI: 10.1007/s00464-020-07531-6]

17 **Yang L**, Jin P, Wang X, Zhang T, He YQ, Zhao XJ, Li N, Yang GZ, Sheng JQ. Risk factors associated with histological upgrade of gastric low-grade dysplasia on pretreatment biopsy. *J Dig Dis* 2018; **19**: 596-604 [PMID: 30187683 DOI: 10.1111/1751-2980.12669]

18 **Zou L**, Jiang Q, Guo T, Wu X, Wang Q, Feng Y, Zhang S, Fang W, Zhou W, Yang A. Endoscopic characteristics in predicting prognosis of biopsy-diagnosed gastric low-grade intraepithelial neoplasia. *Chin Med J (Engl)* 2022; **135**: 26-35 [PMID: 34873080 DOI: 10.1097/CM9.0000000000001637]

19 **Muto M**, Yao K, Kaise M, Kato M, Uedo N, Yagi K, Tajiri H. Magnifying endoscopy simple diagnostic algorithm for early gastric cancer (MESDA-G). *Dig Endosc* 2016; **28**: 379-393 [PMID: 26896760 DOI: 10.1111/den.12638]

20 **Yao K**, Anagnostopoulos GK, Ragunath K. Magnifying endoscopy for diagnosing and delineating early gastric cancer. *Endoscopy* 2009; **41**: 462-467 [PMID: 19418401 DOI: 10.1055/s-0029-1214594]

21 **Yao K**. The endoscopic diagnosis of early gastric cancer. *Ann Gastroenterol* 2013; **26**: 11-22 [PMID: 24714327]

22 **Lan S**, Lai F, Fang X, Li X, Zhong C, Cao T. Establishment and Evaluation of a Risk Prediction Model for Pathological Escalation of Gastric Low-Grade Intraepithelial Neoplasia. *J Vis Exp* 2024 [PMID: 38436295 DOI: 10.3791/65868]

23 **Sun T**, Ke XQ, Wang M, Wang QZ. Establishment and validation of a clinical diagnostic model for gastric low-grade intraepithelial neoplasia. *Medicine (Baltimore)* 2023; **102**: e35515 [PMID: 37986403 DOI: 10.1097/MD.0000000000035515]

24 **Zhu Y**, Wu K, Wang FY. Efficacy of Magnifying Endoscopy with Narrow-Band Imaging in the Diagnosis of Early Gastric Cancer and Gastric Intraepithelial Neoplasia. *Turk J Gastroenterol* 2024; **35**: 299-306 [PMID: 39113459 DOI: 10.5152/tjg.2024.23116]

25 **Jafari Nivlouei S**, Soltani M, Carvalho J, Travasso R, Salimpour MR, Shirani E. Multiscale modeling of tumor growth and angiogenesis: Evaluation of tumor-targeted therapy. *PLoS Comput Biol* 2021; **17**: e1009081 [PMID: 34161319 DOI: 10.1371/journal.pcbi.1009081]

26 **Jafari Nivlouei S**, Soltani M, Shirani E, Salimpour MR, Travasso R, Carvalho J. A multiscale cell-based model of tumor growth for chemotherapy assessment and tumor-targeted therapy through a 3D computational approach. *Cell Prolif* 2022; **55**: e13187 [PMID: 35132721 DOI: 10.1111/cpr.13187]

27 **Maki S**, Yao K, Nagahama T, Beppu T, Hisabe T, Takaki Y, Hirai F, Matsui T, Tanabe H, Iwashita A. Magnifying endoscopy with narrow-band imaging is useful in the differential diagnosis between low-grade adenoma and early cancer of superficial elevated gastric lesions. *Gastric Cancer* 2013; **16**: 140-146 [PMID: 22592604 DOI: 10.1007/s10120-012-0160-7]

28 **Horiuchi Y**, Hirasawa T, Ishizuka N, Tokura J, Ishioka M, Tokai Y, Namikawa K, Yoshimizu S, Ishiyama A, Yoshio T, Fujisaki J. Additive effect of evaluating microsurface and microvascular patterns using magnifying endoscopy with narrow-band imaging in gastric cancer: a post-hoc analysis of a single-center observational study. *BMC Gastroenterol* 2022; **22**: 125 [PMID: 35296263 DOI: 10.1186/s12876-022-02197-x]

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