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Predictive factors for the coexistence of colorectal lateral spreading tumors and colorectal polyps, and risk factors for malignancy

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Abstract

Background Colorectal laterally spreading tumors (LSTs) are precancerous lesions with potential for malignant transformation. The coexistence of LSTs with colorectal polyps may indicate increased risk for early colorectal cancer, yet the associated clinicopathological risk factors remain poorly defined.

Methods This retrospective study included 229 patients diagnosed with LSTs from January 2020 to March 2024 at a single center. Patients were divided into the polyp group ($n=139$) and the non-polyp group ($n=90$) based on the coexistence of colorectal polyps. The polyp group was further subdivided into malignant group ($n=62$) and non-malignant group ($n=77$). Clinicopathological characteristics were compared, and binary logistic regression was used to identify predictive factors for coexistence and for malignancy in LSTs with colorectal polyps.

Results Female (OR = 0.330, 95%CI: 0.186–0.586; $P<0.001$) was associated with a decreased risk, while age > 75 years (OR = 4.293, 95%CI: 1.060–17.376; $P=0.041$) was associated with an increased risk for the coexistence of colorectal polyps with LSTs. The area under the receiver operating characteristic curve (AUC) for the predictive model was 0.703 (95%CI 0.633–0.773; $P<0.001$). LSTs diameter ≥ 2 cm (OR = 4.574, 95%CI: 1.754–11.933; $P=0.002$) and G-M morphological type (were associated with increased risk, while NG-FE morphological type (OR = 0.182, 95%CI: 0.039–0.845; $P=0.030$) was associated with decreased risk for malignancy in LSTs coexisting with colorectal polyps. The AUC for this predictive model was 0.873 (95%CI: 2.788–27.530; $P<0.001$).

Conclusion Males and individuals > 75 years may be at higher risk of LSTs coexisting with colorectal polyps. LST diameter ≥ 2 cm and the G-M morphological type are potential independent risk factors for malignant transformation, though further validation is needed. These results emphasize the necessity of endoscopic screening and early intervention for males, those older than 75 years, with LST dimeter ≥ 2 cm, and with the G-M morphological type.

Clinical trials Not applicable.

Keywords Laterally spreading tumor, Colorectal cancer, Colorectal polyps, Malignant risk

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Introduction

Colorectal cancer (CRC) ranks third globally in cancer incidence and is the second leading cause of cancer-related death [1]. CRC arises through the adenoma-carcinoma sequence, typically originating from either polypoid or non-polypoid lesions [2–6]. Colorectal polyps are masses of colonic tissue that protrude into the lumen and are classified as neoplastic or non-neoplastic (including hamartomatous and inflammatory polyps) [7, 8]. While most preventive strategies have focused on polypoid lesions, non-polypoid lesions, including laterally spreading tumors (LSTs), also contribute significantly to early-stage CRC [8–11]. LSTs are non-polypoid neoplasms first described by Ohno [12], characterized by lateral expansion over the mucosal surface with diameters >10 mm. Endoscopically, they are classified into granular (G-type) and non-granular (NG-type) forms, with subtypes such as homogeneous (G-H), nodular mixed (G-M), pseudo-depressed (NG-PD), and flat elevated (NG-FE) [5, 13, 14]. Some LST subtypes, especially G-M and NG-PD, have been associated with higher malignant potential [14], and contribute to 5.8% of early colorectal cancer cases [13, 15].

In clinical practice, LSTs often coexist with colorectal polyps. According to a large-scale international case-control study, the likelihood of patients with LSTs having concurrent colorectal polyps ranges from 8.4% to 52.5% [16]. Zhao's study [10] found that among 120 cases (46.3%) with colonic polypoid lesions, 79 cases (30.5%) had cancerous polyps, and 7 cases (2.7%) had colorectal cancer at other locations, suggesting a strong association between LSTs and malignancy. However, the pathological features of the associated LSTs were not further described. Currently, the primary endoscopic treatment options for LSTs include endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), and several modified techniques based on EMR and ESD [17, 18]. Given the variable malignant potential of LSTs, precise risk stratification is essential for effective management. Accurate risk stratification of LST malignancy facilitates the selection of optimal treatment strategies, reduces procedure-related complications, and guides postoperative surveillance protocols. Other studies [19] have suggested that LSTs associated with right-sided colon polyps significantly increase the malignancy risk. Current evidence reveals inconsistencies in the clinicopathological characteristics and malignancy risk factors of LSTs, underscoring the need for further research to provide robust theoretical support. Understanding the clinical characteristics and risk factors associated with LSTs coexisting with colorectal polyps could inform tailored endoscopic strategies, reduce malignancy rates, and optimize postoperative surveillance, ultimately improving patient outcomes.

Due to the fact that LSTs account for 5.8% of early colorectal cancer and their coexistence with polyps ranges from 8.4% to 52.5% [13, 16], further investigating the risk stratification is in need. However, few studies have systematically examined the predictive factors for this coexistence or for malignant transformation in LSTs, and current evidence remains fragmented and inconclusive. To address this gap, the present study retrospectively investigates clinical and endoscopic predictors of synchronous polyps in patients with LSTs, and identifies independent risk factors associated with malignant transformation. These findings aim to inform individualized endoscopic treatment strategies and long-term surveillance planning.

Methods

Patients

Patients were categorized into the polyp group ($n = 139$) and the non-polyp group ($n = 90$) based on the coexistence of colorectal polyps. The polyp group was further subdivided into malignant ($n = 62$) and non-malignant ($n = 77$) groups based on LST histology (Fig. 1). As this was an exploratory retrospective study, no a priori sample size calculation was conducted. To assess the adequacy of our sample, a post hoc power analysis was performed using G*Power 3.1 software. Based on a two-tailed test with $\alpha = 0.05$, the available sample size ($N = 229$) provided over 80% power to detect an odds ratio (OR) of 2.5 or greater in binary logistic regression models, which is considered a moderate-to-large effect size and clinically relevant in colorectal neoplasia studies. The study recorded age, gender, history of colorectal polyps (i.e., colorectal polyps detected in previous colonoscopies), as well as the diameter, location, and degree of dysplasia of LSTs and polyps. Serum tumor biomarkers, including carcinoembryonic antigen (CEA), cancer antigen (CA) 19 – 9, CA 125 were also documented. Medical data was extracted from the electronic medical record system. Missing data were present in fewer than 5% of all variables, primarily affecting tumor marker values (e.g., CA19-9, CA125). Given the low rate of missingness and the assumption that the data were missing completely at random (MCAR), listwise deletion was employed for statistical analysis. This approach was chosen to maintain consistency across analyses without introducing imputation-related bias. Sensitivity analyses were not conducted due to the minimal extent of missing data. All statistical models were based on complete case analysis.

This study was a retrospective analysis based on anonymized data extracted from the electronic medical records of the First People's Hospital of Lianyungang. Informed consent was waived due to the retrospective nature of the study and the use of de-identified data, which posed no potential harm or impact on patient care, as approved

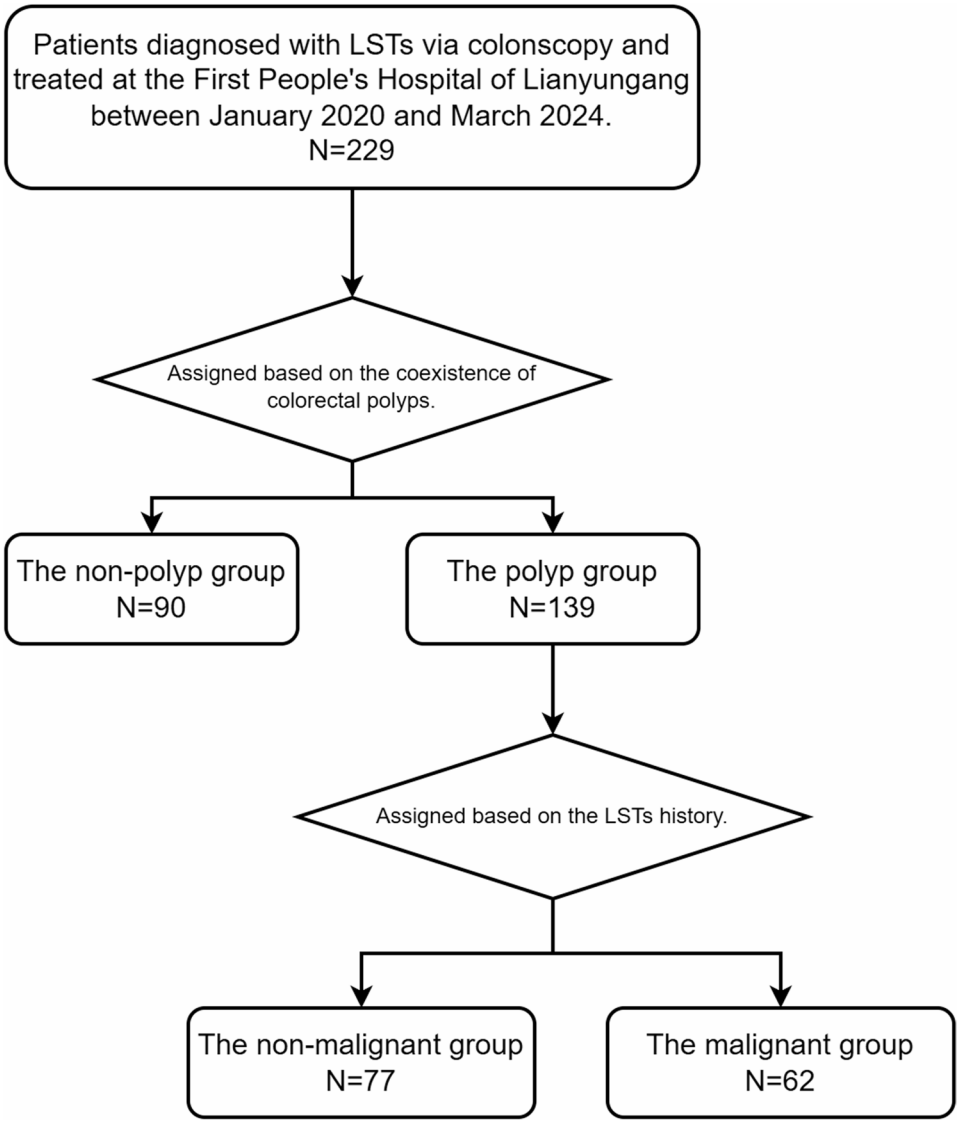

Fig. 1 The flowchart of patient stratification

by the Ethics Committee of the First People's Hospital of Lianyungang (Approval No. KY-20240528001-01). Patient privacy and confidentiality were protected through anonymization of all data, with records stored in a secure, password-protected database accessible only to authorized personnel, adhering to the hospital's data protection policies and the Declaration of Helsinki. This study was not registered in a clinical trial registry due to its retrospective nature and lack of prospective intervention.

Inclusion and exclusion criteria

Patients were eligible for inclusion if they met the following criteria: (1) age ≥ 18 years; (2) presence of LSTs identified during colonoscopy, with morphological classification based on endoscopic appearance; and (3) availability of complete clinical, endoscopic, and histopathological data.

Exclusion criteria were as follows: (1) diagnosis of familial adenomatous polyposis, inflammatory bowel disease, or hereditary nonpolyposis colorectal cancer; and (2) incomplete endoscopic examination of the ileocecal region. The incomplete endoscopic examination was defined as failure to visualize and document both the cecum and the ileocecal valve, based on procedural images and endoscopy reports, due to factors such as inadequate bowel preparation, patient intolerance, or technical limitations. Only patients with documented complete cecal intubation and photographic evidence of the ileocecal valve were included. To ensure consistency in the application of exclusion criteria, all procedural records were independently reviewed by two experienced endoscopists. Coexisting colorectal polyps were defined

as the simultaneous detection of one or more colorectal polyps and an LST during a single colonoscopy session.

Endoscopic criteria of LSTs morphological type

Endoscopic procedures involved high-definition colonoscopy with white light and narrow-band imaging, performed by certified endoscopists using standardized protocols of Olympus CF-HQ290. LST and polyp diameters were independently measured by two experienced endoscopists during endoscopic examination, with the average value recorded. To ensure measurement consistency, LST and polyp diameters were independently measured by two experienced endoscopists. Inter-observer agreement was quantified using the intraclass correlation coefficient (ICC), yielding an ICC of 0.89 (95% CI: 0.85–0.92), which indicates excellent reliability according to established thresholds. The mean of the two measurements was used for analysis.

LST locations were categorized into the ileocecal region, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum. The right colon was defined as the cecum, ascending colon, and the proximal two-thirds of the transverse colon (up to the splenic flexure). The left colon was defined as the distal one-third of the transverse colon (beyond the splenic flexure), descending colon, and sigmoid colon, consistent with standard anatomical delineations used in colorectal cancer research [20]. LSTs were classified into granular and non-granular types morphologically according to the Kudo classification. Granular LSTs include the nodular mixed (G-M) and homogeneous (G-H) subtypes, while non-granular types include the elevated (NG-FE) and pseudo-depressed (NG-PD) subtypes [21].

Histopathological assessment

All resected LSTs and polyps were fixed in 10% neutral-buffered formalin, processed routinely, and embedded in paraffin. Section (4 μm thick) were stained with hematoxylin and eosin (H&E) according to standard protocols. The histopathological classification of LST was based on the 5th edition (2019) WHO Classification of Tumours of the Digestive System [13, 22, 23]. Lesions were categorized into the following subtypes: hyperplastic, tubular adenoma, tubulovillous adenoma, serrated adenoma (including sessile serrated lesion and traditional serrated adenoma), and adenocarcinoma. This classification reflects the latest understanding of colorectal precursor lesions and serrated neoplasia pathways, in which sessile serrated lesions and traditional serrated adenomas are recognized as distinct yet neoplastic entities with malignant potential. High-grade intraepithelial neoplasia and adenocarcinoma were grouped as malignant, whereas hyperplastic and low-grade adenomatous lesions (tubular or serrated) were considered non-malignant.

Colorectal polyps were classified according to the 2019 World Health Organization (WHO) criteria, as summarized by Dornblaser et al. [24]. The major histopathological types included: (1) Hyperplastic polyps: small, distal, non-neoplastic lesions with minimal malignant potential; (2) Sessile serrated lesions (SSLs): proximal flat lesions with serrated crypt architecture and potential for malignant transformation, particularly those with dysplasia; (3) Traditional serrated adenomas (TSAs): rare, distal lesions with serrated and villiform histology, representing high-risk precancerous lesions; (4) Tubular adenomas (TAs): adenomas composed predominantly of tubular glands; (5) Tubulovillous adenomas (TVAs): mixed glandular structures with 25–75% villous features; (6) Adenocarcinomas: polyps with invasion beyond the muscularis mucosae. In patients with multiple polyps, classification was based on the most advanced lesion identified on pathology review. This classification was used to stratify malignant vs. non-malignant polyps in the analysis. Histopathological assessments were conducted by two senior pathologists independently, using hematoxylin and eosin staining on formalin-fixed paraffin-embedded sections. Discrepancies were resolved by consensus with a third pathologist, ensuring quality control. The pathologists were blinded to patients' clinical and endoscopic information during histological review to minimize bias.

Statistical analysis

Data were analyzed using SPSS version 24 (SPSS Inc., Chicago, IL, USA). Categorical variables were compared using the Chi-square test or Fisher's exact test. Normally distributed continuous variables were expressed as the mean ± standard deviation (SD) and analyzed using the independent samples t-test. Non-normally distributed continuous variables were compared using the Mann-Whitney U test. A two-tailed P-value < 0.05 was considered statistically significant. Variables with $P < 0.05$ were entered into a binary logistic regression model to identify predictors of LSTs coexisting with colorectal polyps and independent risk factors for malignancy. Binary logistic regression was chosen to identify predictors of binary outcomes due to its ability to estimate odds ratios (OR) and adjust for multiple covariates. Results are interpreted as ORs with 95% confidence intervals (CI), where an OR > 1 indicates increased risk, and $P < 0.05$ signifies statistical significance after verifying model assumptions. Prior to binary logistic regression, we tested multicollinearity (all VIF < 5), assessed linearity using Box-Tidwell test ($p > 0.05$ for all), and evaluated model fit via Hosmer–Lemeshow test ($p > 0.05$), confirming model validity. As a sensitivity analysis, false discovery rate (FDR) correction was applied post-hoc to the p-values of significant variables in the logistic regression models to assess robustness against multiple testing.

Results

Baseline clinicopathological characteristics

A total of 229 patients were included, with 90 in the non-polyp group and 139 in the polyp group (Table 1). Baseline comparisons revealed no significant differences in prior colorectal polyps (P = 0.22), diameter (P = 0.321), location (P = 0.547), or morphological type (P = 0.256) between the groups. We categorized patients into two age groups using 75 years as the threshold, consistent with major colorectal cancer screening guidelines. Specifically, the U.S. Preventive Services Task Force (USPSTF) recommends routine screening up to age 75 and advises that decisions for those aged 76–85 should be individualized, rather than universally continued or stopped [25]. Patients aged ≥ 75 years (P = 0.041) and male (P < 0.001) were more prevalent in the polyp group. Tubular adenomas were the predominant pathological subtype of LSTs, particularly in the polyp coexistence group (P = 0.034). LSTs were most commonly located in the ascending colon (24.9%) and rectum (23.6%), with no significant differences in tumor markers CEA (P = 0.069), CA 19 – 9 (P = 0.598), or CA 125 (P = 0.541) between groups.

Table 1 Clinicopathological characteristics of patients with LSTs in the coexistence and non-coexistence groups with colorectal polyps. [(n (%)]

	Total	Non-polyp group	Polyp group	OR (95% CI)	*p* value
	n = 229	*n* = 90	*n* = 139		
Gender					<0.001†
Male	123(53.7)	32 (35.6)	91 (65.5)	Reference	
Female	106(46.3)	58 (64.4)	48 (34.5)	0.291(0.164–0.502)	
Age (year)					0.041†
<50	36(15.7)	20(22.2)	16(11.5)	Reference	
50 ~ 75	175(76.4)	66 (73.3)	109(78.4)	2.064(0.973–4.243)	
>75	18(7.9)	4 (4.4)	14 (10.1)	4.375(1.185–13.71)	
History of polyps					0.220†
Yes	25(10.9)	7(13.3)	18(14.4)	Reference	
No	204(89.1)	83(86.7)	121(85.6)	0.567(0.219–1.359)	
Location					0.547†
Ileocecal part	32(14.0)	14(15.6)	18 (12.9)	Reference	
Ascending colon	57(24.9)	25(27.8)	32 (23)	0.996(0.428–2.423)	
Transverse colon	33(14.4)	9 (10.0)	24 (17.3)	2.704(0.701–5.959)	
Descending colon	17(7.4)	6 (6.7)	11 (7.9)	1.426(0.438–4.657)	
Sigmoid colon	36(15.7)	12 (13.3)	24 (17.3)	1.556(0.571–3.969)	
Rectum	54(23.6)	24 (26.7)	30 (21.6)	0.972(0.424–2.408)	
LST Morphological type					0.256†
G-H	64(27.9)	23(25.6)	41(29.5)	Reference	
G-M	87(38.0)	40(44.4)	47(33.8)	0.659(0.345–1.290)	
NG-FE	57(24.9)	22(24.4)	35(25.2)	0.893(0.437–1.824)	
NG-PD	21(9.2)	5(5.6)	16(1.5)	1.795(0.568–4.896)	
LST Pathological subtypes					0.034†
Hyperplastic	24(10.5)	15 (16.7)	9 (6.5)	Reference	
Tubular	136(59.4)	45 (50.0)	91 (65.5)	3.370(1.353–7.870)	
Tubulovillous	42(18.3)	19 (21.1)	23 (16.5)	2.018(0.701–5.683)	
Serrated adenoma	1 (0.4)	1 (1.1)	0 (0.0)	-	
Adenocarcinoma	26(11.4)	10 (11.1)	16 (11.5)	2.667(0.854–7.825)	
LST diameter (cm)					0.321†
< 2	106(46.3)	38 (42.2)	68 (48.9)	Reference	
≥ 2	123(53.7)	52 (57.8)	71 (51.1)	0.763(0.449–1.291)	
Tumor marker	Mean ± SD	Mean ± SD	Mean ± SD		
CEA	2.69 ± 4.68	1.93 ± 1.46	3.16 ± 5.81	-	0.069‡
CA19-9	10.31 ± 7.00	9.97 ± 6.58	10.51 ± 7.28	-	0.598‡
CA125	10.01 ± 5.81	10.33 ± 6.11	9.81 ± 5.64	-	0.541‡

OR odd ratio, *CI* Confidence interval

† Chi-square test

‡ Student t-test

Risk factors for coexistence of LSTs and polyps

Following the baseline comparison, we explored predictive factors for LST-polyp coexistence. Binary logistic regression analysis identified female gender as associated with a decreased risk (OR = 0.330, 95%CI: 0.186–0.586, $P < 0.001$) and aged > 75 years with an increased risk (OR = 4.293, 95%CI: 1.060–17.376, $P = 0.041$) of LSTs coexistence with colorectal polyps (Fig. 2A). These associations remained significant after FDR correction for multiple testing. The predictive performance of this binary logistic model was further evaluated using a receiver operating characteristic (ROC) curve, yielding an area under the curve (AUC) of 0.703 (95% CI 0.633–0.773; $P < 0.001$), indicating a moderate discriminative ability (Fig. 2B). The moderate discriminative ability suggests a clinically useful but not definitive tool for identifying LST-polyp coexistence.

Risk factors for malignancy in LSTs

To assess malignancy risk, patients were categorized into non-malignant ($n = 139$) and malignant ($n = 90$) groups based on LST histology. Significant differences were observed in tumor location ($P < 0.001$), diameter ($P < 0.001$), coexistence with colorectal polyps ($P = 0.041$), and morphological subtype ($P < 0.001$). Malignant lesions were more frequent in the rectum, in LSTs with a diameter ≥ 2 cm, and in the G-M morphological type (Table 2). Among tumor markers, only CA19-9 levels were significantly higher in the malignant group ($P = 0.003$), while CEA *(*$P = 0.848$) and CA 125 ($P = 0.360$) showed no significant differences.

Binary logistic regression identified LSTs with a diameter ≥ 2 cm (OR = 3.757, 95% CI: 1.774–7.957, $P < 0.001$), coexistence with colon polyps (OR = 3.884, 95% CI: 1.794–8.407, $P < 0.001$), rectal location (OR = 3.449, 95% CI: 1.078–11.030, $P = 0.037$), and the G-M morphological type (OR = 9.578, 95% CI: 3.937–23.301, $P < 0.001$) as independent risk factors for malignancy. Conversely, the NG-FE morphological type was associated with a lower risk (OR = 0.201, 95% CI: 0.056–0.719, $P = 0.014$) for malignancy (Fig. 3A). These associations remained significant after FDR correction for multiple testing. The ROC curve analysis yielded an AUC of 0.859 (95% CI 0.812–0.906; $P < 0.001$), reflecting strong discriminative ability (Fig. 3B). The strong discriminative ability indicates clinically meaningful model for predicting malignancy risk.

Risk factors for malignant lesions in coexistence of LSTs and polyps

To further refine malignancy risk, we analyzed the polyp subgroup. All coexisting colorectal polyps identified in the 139 patients with LST–polyp coexistence were biopsied or resected and underwent histopathological assessment, with their features comprehensively summarized in Table 3. Within the polyp group ($n = 139$), patients were subdivided into the non-malignant ($n = 77$) and the malignant ($n = 62$) groups. Significant differences were noted in age ($P = 0.018$), LST location ($P = 0.006$), LST diameter ($P < 0.001$) and LST morphological type ($P < 0.001$), but not in gender, polyp characteristics, or tumor markers except CA 199 ($P = 0.002$) (Table 3).

Binary logistic regression confirmed LST diameter ≥ 2 cm (OR = 4.574, 95% CI: 1.754–11.933, $P = 0.002$) and G-M morphological type (OR = 8.761, 95% CI: 2.788–27.530, $P < 0.001$) as independent risk factors for malignancy, while NG-FE morphological type reduced

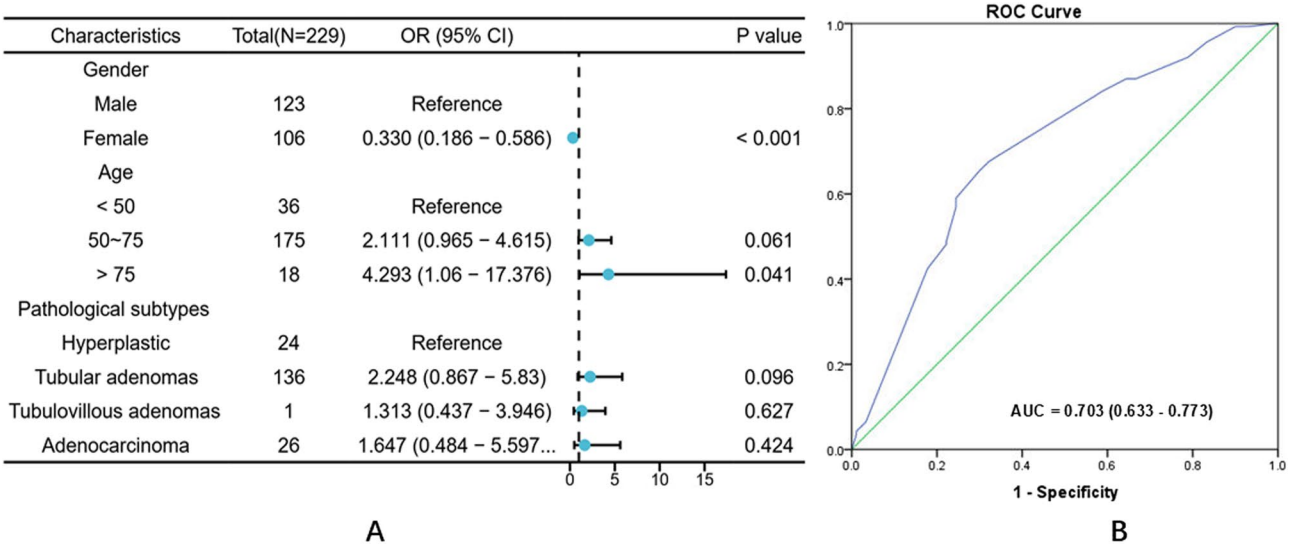

Fig. 2 Risk factors for coexistence of LSTs and polyps. **A** Forest plot of binary logistic regression analysis results showed that female was associated with a decreased risk, while those aged > 75 years was at higher risk of LSTs coexistence with colorectal polyps. **B** ROC curve of the binary logistic regression model indicated a moderate discriminative ability of the model. OR, odd ratio; CI, confidence interval; ROC, receiver operating characteristic

Table 2 Clinicopathological characteristics of patients in the malignant and non-malignant groups of LSTs. [n (%)]

	Total	Nonmalignant	Malignant	OR (95%CI)	*p* value
	n = 229	*n* = 139	*n* = 90		
Gender					0.206†
Male	123(53.7)	70(50.4)	53(58.9)	Reference	
Female	106(46.3)	69(49.6)	37(41.1)	0.708(0.415–1.206)	
Age (year)					0.074†
< 50	36(15.7)	27(19.4)	9(10.0)	Reference	
50 ~ 75	175(76.4)	104(74.8)	71(78.9)	2.048(0.891–4.763)	
> 75	18(7.9)	8(5.8)	10(11.1)	3.750(1.054–12.48)	
Coexisting with polyps					0.041†
Yes	139(60.7)	77(55.4)	62(68.9)	Reference	
No	90(39.3)	62(44.6)	28(31.1)	0.561(0.324–0.972)	
History of polyps					0.428†
Yes	25(10.9)	17(12.2)	8(8.9)	Reference	
No	204(89.1)	122(87.8)	82(91.1)	1.428(0.614–3.320)	
Location					<0.001†
Ileocecal part	32(14.0)	23(16.5)	9(10.0)	Reference	
Ascending colon	57(25.0)	38(27.3)	19(21.1)	1.278(0.523–3.131)	
Transverse colon	33(14.4)	22(15.8)	11(12.2)	1.278(0.463–3.756)	
Descending colon	17(7.4)	14(10.1)	3(3.3)	0.730(0.218–2.709)	
Sigmoid colon	36(15.7)	24(17.3)	12(13.3)	1.278(0.484–3.625)	
Rectum	54(23.6)	18(12.9)	36(40.0)	5.111(1.910–12.83)	
Morphological type					<0.001†
G-H	64(27.9)	52(37.4)	12(13.3)	Reference	
G-M	87(38.0)	27(19.4)	60(66.7)	9.630(4.425–21.43)	
NG-FE	57(24.9)	50(36.0)	7(7.8)	0.607(0.236–1.675)	
NG-PD	21(9.2)	10(7.2)	11(12.2)	4.767(1.723–14.16)	
LST diameter (cm)					<0.001†
< 2	106(46.3)	85(61.2)	21(23.3)	Reference	
≥ 2	123(53.7)	54(38.8)	69(76.7)	5.172(2.824–9.439)	
Tumor marker	Mean ± SD	Mean ± SD	Mean ± SD		
CEA	2.69 ± 4.68	2.64 ± 5.94	2.77 ± 1.86	-	0.848‡
CA19-9	10.31 ± 7.00	9.00 ± 5.69	12.12 ± 8.19	-	0.003‡
CA125	10.01 ± 5.81	9.69 ± 5.83	10.47 ± 5.78	-	0.360‡

OR Odd ratio, *CI* Confidence interval

† Chi-square test

‡ Student t-test

risk (OR = 0.182, 95% CI: 0.039–0.845, $P = 0.030$) of malignancy in LSTs coexisting with colorectal polyps (Fig. 4A). FDR correction for multiple testing confirmed the associations. The ROC curve showed an AUC of 0.873 (95% CI 0.814–0.931, $P < 0.001$) (Fig. 4B), indicating strong predictive power of the model.

Discussion

While colorectal LSTs are frequently observed to coexist with polyps during endoscopy, the clinical implications and malignancy risk of such coexistence remain poorly understood. However, few studies have specifically examined the clinical characteristics of patients with coexisting lesions or systematically investigated the malignant risk factors associated with LSTs. To address this gap, we conducted a retrospective analysis to identify the malignant risk factors in colorectal LSTs. Our findings aim to establish effective preoperative evaluation criteria and provide evidence-based guidance for optimizing treatment strategies and prognostic assessments. This study revealed that male gender and advanced age (>75 years) correlated with an increased likelihood of LSTs coexisting with colorectal polyps. However, neither factor independently increased the malignancy risk of LSTs. Interestingly, when evaluating the malignancy risk of LSTs in patients with coexisting colorectal polyps, male gender remained statistically insignificant. In contrast, univariate analysis indicated that age was a significant predictor of advanced histology in LSTs. The predictive model for LST–polyp coexistence (AUC = 0.703) indicates moderate discrimination—useful for risk screening but insufficient for clinical decision-making alone. The malignancy model (AUC

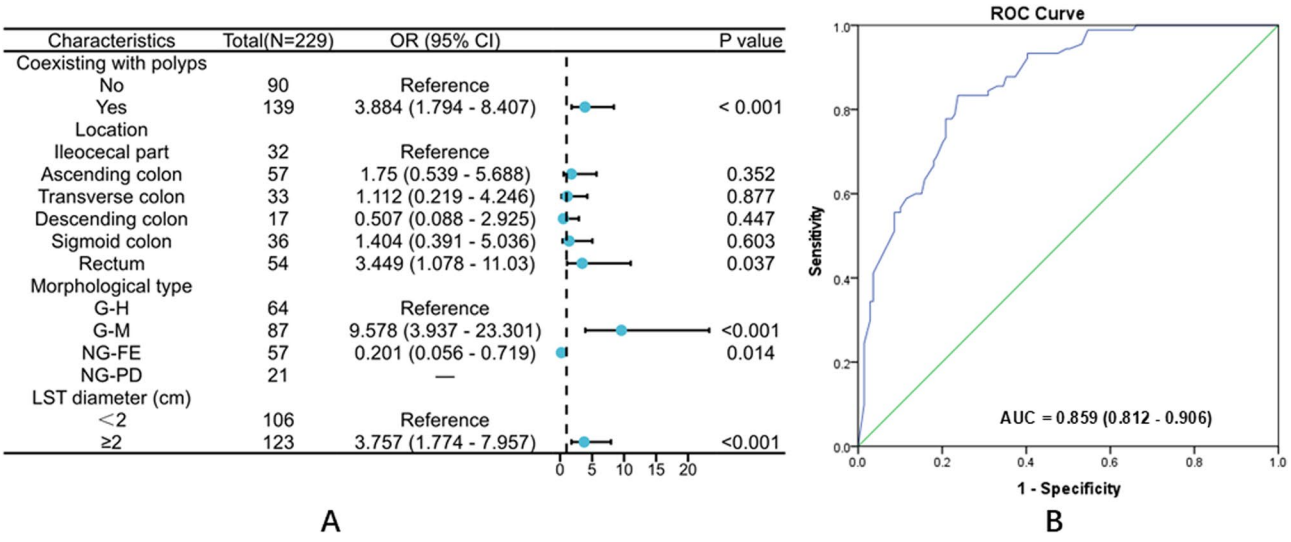

Fig. 3 Risk factors for malignant lesions in LSTs. **A** Forest plot of binary logistic regression analysis results revealed that LSTs with a diameter ≥ 2 cm, coexistence with colon polyps, rectal location, and the G-M morphological type are independent risk factors for malignancy, while the NG-FE morphological type was a protective factor. **B** ROC curve of the binary logistic regression model suggested a strong discriminative ability of the model. OR, odd ratio; CI, confidence interval; ROC, receiver operating characteristic

= 0.859) exhibits strong discrimination and may inform endoscopy prioritization, pending external validation. Previous studies [19] have identified right colon polyps as a significant risk factor for predicting the malignancy of LSTs. Consistently, our findings indicate that LSTs are more likely to have advanced histology when coexisting with colorectal polyps. However, we did not find a significant association between the location or morphology type of colorectal polyps and the malignancy risk of LSTs. This discrepancy may be due to the heterogeneous nature of colorectal polyps, which complicates comprehensive statistical analysis. Further research is needed to explore the potential interactions between polyp subtypes and LST progression.

Previous studies [15, 26] have indicated that LST patients are typically around 65 years old and predominantly male, aligning with our findings. Similarly, a retrospective study by Shen et al. [19] demonstrated that males and individuals aged between 50 and 75 have a higher incidence of colorectal polyps and LSTs, though these factors did not influence the malignancy risk. Other studies [27–29] have identified male gender and advanced age as risk factors for colorectal polyps, which may explain the significant differences observed in our study when LSTs coexist with polyps. We also found that patents ≥ 50 years (including those ≥ 75 years) are at a higher risk of malignant LST, suggesting that even patients ≥ 75 should alert the risk of colorectal cancer, though the USPSTF recommends routine screening up to age 75 [25]. However, further research is needed to determine whether elderly patients with LSTs have a higher likelihood of harboring advanced histology.

Serum tumor markers serve as valuable adjuncts in the diagnosis and prognostic evaluation of colorectal cancer (CRC). A meta-analysis reported that carcinoembryonic antigen (CEA) has a sensitivity of 46% and a specificity of 89% for CRC diagnosis [30]. In contrast, carbohydrate antigen 19 – 9 (CA 19 – 9) demonstrates a lower sensitivity of approximately 30% but a higher specificity of 92%. Recent research suggests that the combined use of multiple tumor markers may improve diagnostic accuracy and prognostic stratification [31]. In the present study, serum tumor markers, including CA 19 – 9 and CEA, were measured. Univariate analysis showed no significant association with LST-polyp coexistence (P >0.05), consistent with their exclusion from multivariate models based on a P < 0.05 threshold in baseline comparisons. Regardless of the coexistence of colonic polyps, CA 19 – 9 levels were significantly elevated in the malignant LST group compared to the non-malignant group. The significant CA 19 – 9 elevation in the malignant group suggests a potential role in malignancy risk, warranting further investigation with adjusted models in larger cohorts [32]. However, given the relatively small sample size and the retrospective design, these findings should be interpreted with caution. Further large-scale studies are needed to validate these results and explore the potential utility of CA 19 – 9 as a predictive biomarker for LST malignancy.

To further clarify the malignant potential of different LST morphological subtypes, we analyzed their distribution and associated malignancy risk. In our cohort, G-M was the most prevalent subtype (38.0%), followed by G-H (27.9%), NG-FE (24.9%), and NG-PD (9.2%). Consistent with previous studies [15, 17, 33–35], both

Table 3 Clinicopathological characteristics of malignant and non-malignant LSTs coexisting with colorectal polyps. [(n (%)]

	Total	Nonmalignant	Malignant	OR(95% CI)	*p* value
	n **= 139**	***n*** **= 77**	***n*** **= 62**		
Gender					0.353†
Male	91 (65.5)	53(68.8)	38(61.3)	Reference	
Female	48 (34.5)	24(31.2)	24(38.7)	1.395(0.685–2.856)	
Age (year)					0.018†
< 50	16(11.5)	14(18.2)	2(3.2)	Reference	
50 ~ 75	109(78.4)	57(74)	52(83.9)	9.333(1.631–49.41)	
> 75	14 (10.1)	6(7.8)	8(12.9)	9.333(1.631–49.41)	
Location of LSTs					0.006†
Ileocecal part	18 (12.9)	12(15.6)	6(9.7)	Reference	
Ascending colon	32 (23.0)	17(22.1)	15(24.2)	1.765(0.507–5.728)	
Transverse colon	24 (17.3)	15(19.5)	9(14.5)	1.200(0.340–3.939)	
Descending colon	11 (7.9)	9(11.7)	2(3.2)	0.444(0.079–2.799)	
Sigmoid colon	24 (17.3)	16(20.8)	8(12.9)	1.000(0.269–3.326)	
Rectum	30 (21.6)	8(10.4)	22(35.5)	5.500(1.430–17.16)	
LST diameter (cm)					<0.001†
<2	68 (48.9)	52(67.5)	16(25.8)	Reference	
≥ 2	71 (51.1)	25(32.5)	46(73.2)	5.980(2.855–12.04)	
Morphological type of LST					<0.001†
G-H	41(29.5)	31(40.3)	10(16.1)	Reference	
G-M	47(33.8)	10(13.0)	37(59.7)	11.47(4.051–31.90)	
NG-FE	35(25.2)	29(37.7)	6(9.7)	0.641(0.196–1.971)	
NG-PD	16(1.5)	7(9.0)	9(14.5)	3.986(1.247–14.12)	
History of polyps					0.124†
Yes	18(14.4)	13(16.9)	5(8.1)	Reference	
No	121(85.6)	64(83.1)	57(91.9)	2.316(0.781–6.146)	
Location of polyps					0.841†
Right colon	54(38.8)	31(40.3)	23(37.1)	Reference	
Left colon	32(23.0)	16(20.8)	16(25.8)	1.348(0.542–3.232)	
Rectum	17(12.2)	9(11.7)	8(12.9)	1.198(0.410–3.684)	
Right colon + left colon	0(0.0)	0(0.0)	0(0.0)	-	
Right colon + rectum	5(3.6)	4(5.2)	1(1.6)	0.337(0.027–2.332)	
Left colon + rectum	5(3.6)	2(2.6)	3(4.8)	2.022(0.383–11.96)	
3 sites	26(18.7)	15(19.5)	11(17.7)	0.988(0.368–2.489)	
Polyp size (cm)					0.139†
< 1	90(64.7)	54(70.1)	36(58.1)	Reference	
≥ 1	49(35.3)	23(29.9)	26(41.9)	1.696(0.841–3.492)	
Number of polyps					0.377†
≤ 2	84(60.4)	44(57.1)	40(64.5)	Reference	
> 2	55(39.6)	33(42.9)	22(35.5)	0.733(0.364–1.432)	
Pathological subtypes of polyps					0.102†
Hyperplastic polyps	55(39.6)	36(46.8)	19(30.6)	Reference	
Sessile serrated lesions	0(0.0)	0(0.0)	0(0.0)	-	
Traditional serrated adenomas	0(0.0)	0(0.0)	0(0.0)	-	
Tubular adenomas	80(57.5)	40(51.9)	40(64.5)	1.895(0.945–3.74)	
Tubulovillous adenomas	4(2.9)	1(1.3)	3(4.8)	5.684(0.778–75.48)	
Adenocarcinomas	0(0.0)	0(0.0)	0(0.0)	-	
Distance between polyp and LSTs					0.804†
close	89(64.0)	50(64.9)	39(62.9)	Reference	
far	50(36.0)	27(35.1)	23(37.1)	1.092(0.539–2.187)	
Tumor marker	Mean ± SD	Mean ± SD	Mean ± SD		
CEA	3.16 ± 5.81	3.43 ± 7.86	2.87 ± 1.66	-	0.594‡

Table 3 (continued)

	Total	Nonmalignant	Malignant	OR(95% CI)	*p* value
	n = 139	*n* = 77	*n* = 62		
CA19-9	10.51 ± 7.28	8.51 ± 4.90	12.73 ± 8.74	-	0.002‡
CA125	9.81 ± 5.64	9.36 ± 5.41	10.31 ± 5.89	-	0.362‡

OR, odd ratio; CI, confidence interval

† Chi-square test

‡ Student t-test

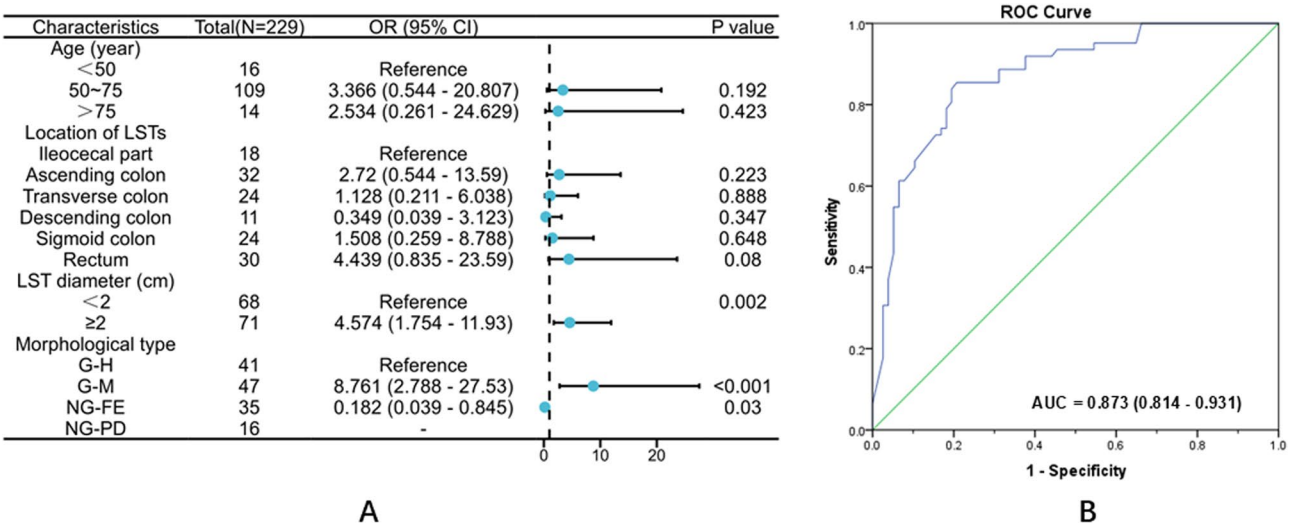

Fig. 4 Risk factors for malignant lesions in LSTs coexisting with colon polyps. **A** Forest plot of binary logistic regression analysis results showed that LSTs with a diameter ≥ 2 cm and G-M morphological type were risk factors for malignancy, whereas NG-FE morphological type was a protective factor for malignancy in LSTs coexisting with colorectal polyps. **B** ROC curve of the binary logistic regression model indicated a strong discriminative ability of the model. OR, odd ratio; CI, confidence interval; ROC, receiver operating characteristic

G-M and NG-PD subtypes were associated with significantly higher rates of submucosal invasion and advanced histology. Prior reports have shown that G-M lesions, characterized by irregular nodular surfaces, are more likely to harbor precancerous changes and submucosal carcinoma compared to the more uniform G-H subtype [34]. Likewise, NG-PD lesions, although less common, are frequently underrecognized and carry a high risk of deep invasion, as highlighted by Kudo et al. [36]. Our findings corroborate these observations, reinforcing the need for heightened endoscopic vigilance toward G-M and NG-PD subtypes. The slightly lower prevalence of NG-PD in our cohort may be attributable to differences in study population, diagnostic thresholds, or regional disease patterns. Interestingly, we also observed that among patients with coexisting colorectal polyps, the G-H subtype maintained a relatively low malignancy risk, while NG-FE showed lower malignancy risk in patients without polyp coexistence. This nuanced interaction may reflect sample size limitations and warrants further investigation. These results underscore the clinical importance of LST morphological classification in malignancy risk stratification. Future research might focus on integrating these endoscopic subtypes into preoperative risk assessment models and exploring their molecular underpinnings, such as KRAS or BRAF mutations, to inform tailored surveillance and treatment strategies.

The anatomical location of LSTs has been widely studied across different populations. Studies from Japan and Italy have shown that LSTs predominantly occur in the proximal colon [37]. However, other studies [36, 38] have pointed out that granular lesions are most frequently found in the rectum and proximal colon, while non-granular lesions are more commonly located in the transverse colon. In our study, 53.3% (122/229) of LSTs were found in the proximal colon. Within the malignant group, LSTs were mostly frequently observed in the distal colon, particularly the rectum. This observation may be related to the longer fecal retention time in the distal colon, which could contribute to mucosal alterations and tumor progression. Yusuke Horiuchi et al. [39] indicated that rectal NG-PD tumors exhibit a high proportion of submucosal invasive lesions, and that non-granular tumors (both NG-PD and NG-FE) in the rectum carry a higher malignancy risk than those in the colon. Additionally, previous studies have reported that invasive cancer is rarely found in G-H lesions [34, 40, 41], further supporting the notion that tumor location plays a crucial role in the malignancy

risk assessment. On the other hand, we found that the rectum also had the high proportion of LST cases, and among patients with coexisting colorectal polyps, the proportion remained high (36.5%). Rectal location remained a significant risk factor in multivariate analysis, while coexistence with colon polyps did not significantly impact malignancy risk. These findings have important clinical implications, suggesting that LSTs located in the rectum carry an elevated malignancy risk. This underscores the necessity of careful endoscopic evaluation and potential early intervention for rectal LSTs, particularly those with high-risk morphological features.

A previous study indicated that the site of rectum, a diameter of ≥ 2 cm, and a morphology of G-M were related to malignancy [42]. The incidence rates of submucosal invasive cancer in LSTs measuring 10–19 mm, 20–29 mm, and ≥ 30 mm were 4.6%, 9.2%, and 16.5%, respectively [43]. This trend highlights a positive correlation between lesion size and malignant potential. Consistent with these findings, our study demonstrated that LSTs with a diameter ≥ 2 cm are an independent risk factor for malignancy, irrespective of their coexistence with colorectal polyps. This underscores the importance of tumor size in risk stratification and clinical decision-making, reinforcing the need for timely endoscopic intervention in larger LSTs to prevent malignant progression.

Base on the collected variables, we constructed two predictive models. While both models demonstrated statistically significant discrimination, their clinical utility must be interpreted with caution. For instance, an AUC of 0.703 for LST–polyp coexistence represents only moderate accuracy and may be more suitable for identifying at-risk subgroups rather than making definitive clinical decisions. In contrast, the malignancy prediction model (AUC = 0.873) approaches the threshold typically considered acceptable for clinical decision-making (AUC ≥ 0.85), suggesting potential utility in guiding intervention strategies such as the choice between EMR and ESD. However, further validation is required to determine appropriate cutoff values for sensitivity and specificity, and to evaluate model performance in prospective cohorts. Future work should focus on integrating these predictors into a user-friendly clinical risk score or decision-support tool to aid individualized management.

Despite the findings, this study has several limitations that should be acknowledged. First, it was a single-center retrospective analysis, which may introduce selection and information biases due to the reliance on existing medical records without prospective standardization. The single-center setting also restricts the diversity of the patient population and clinical practices, limiting generalizability. In addition, the absence of follow-up outcomes such as recurrence, surveillance results, or patient survival limits the ability to assess long-term prognostic value. Without follow-up data, the clinical significance of the predictive models cannot be fully established, and their utility for guiding clinical decision-making remains uncertain. Future studies might adopt multicenter prospective designs with standardized data collection and long-term follow-up to evaluate recurrence, post-treatment outcomes, and survival. Second, no a priori power calculation was performed. Although a post hoc power analysis confirmed that our sample size ($N = 229$) provided over 80% power to detect an odds ratio ≥ 2.5, smaller but potentially meaningful associations may have gone undetected. Future research might incorporate pre-study sample size estimations based on expected effect sizes to improve statistical robustness. Third, this study did not apply formal multiple testing correction given the exploratory design, which may increase the risk of type I error. Although a post-hoc FDR sensitivity analysis confirmed the robustness of key findings, these results should be interpreted with caution and validated in independent cohorts using more rigorous statistical approaches, such as FDR or Bonferroni correction with appropriate power calculations. Fourth, as our study focused on risk factors within LST patients, a control group without LSTs was not included. This limits the ability to determine whether the identified predictors are specific to LST-associated polyp coexistence or reflect broader population-level trends, potentially affecting the generalizability of our findings. Future studies should include control groups without LSTs to enable more comprehensive comparative analyses and validate whether these risk factors are unique to the LST population. Fifth, important confounding variables such as dietary habits, smoking, alcohol intake, family history, and genetic background were not available and thus could not be controlled for in the analysis. Further prospective studies might collect detailed lifestyle and genetic data to allow adjustment for these potential confounders. Finally, all patients were from a single institution in eastern China. While the findings may be generalizable to similar East Asian populations, external validation in other ethnic and geographic groups is essential to confirm applicability across diverse clinical settings, accounting for potential variations in genetic, environmental, and healthcare system factors. Taken together, these limitations suggest that although the associations observed in this study are statistically significant, they should be interpreted with caution and confirmed through future prospective, multicenter research.

Conclusion

This study indicates that males and patients aged > 75 years may be likely to develop LSTs coexisting with colorectal polyps. LSTs with a diameter ≥ 2 cm and G-M morphological type are independent risk factors

for malignant transformation. From a clinical perspective, our findings may support more personalized decision-making in the management of LSTs. Patients with LSTs ≥ 2 cm or with G-M morphology—both identified as independent malignancy risk factors—may benefit from earlier or more aggressive intervention, such as en bloc resection via ESD rather than piecemeal EMR. Furthermore, these high-risk features could be incorporated into risk-adapted endoscopic surveillance protocols, with shorter follow-up intervals recommended for patients harboring high-risk lesions. Identifying individuals at increased risk of LST–polyp coexistence (e.g., older males) may also help guide screening priorities in clinical practice. In addition, these predictors may serve as the basis for patient counseling and shared decision-making by communicating personalized risk profiles. Future work should aim to develop and validate a risk scoring system or clinical decision-support tool based on these factors. External validation in diverse populations is essential before applying these findings in other clinical settings. What's more, future studies might include control groups without LSTs to enable more comprehensive comparative analyses and adopt multicenter prospective designs with standardized data collection and long-term follow-up to evaluate recurrence, post-treatment outcomes, and survival.

Abbreviations

LST	Laterally spreading tumor
CRC	Colorectal cancer
EMR	Endoscopic mucosal resection
ESD	Endoscopic submucosal dissection
G-M	Granular mixed type
G-H	Granular homogeneous type
NG-FE	Non-granular flat elevated type
NG-PD	Non-granular pseudo-depressed type
CEA	Carcinoembryonic antigen
CA19-9	Carbohydrate antigen 19 – 9
CA125	Cancer antigen 125
AUC	Area under the curve
ROC	Receiver operating characteristic
SD	Standard deviation
OR	Odds ratio
CI	Confidence interval
SPSS	Statistical Package for the Social Sciences
WHO	World Health Organization. USPSTF, U.S. Preventive Services Task Force

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Authors' contributions
QW Y, JF S, ZM Z, SX Z, XY L collected patients' clinical data. QW Y and XY L analyzed and interpreted the patient data. QW Y was a major contributor in writing the manuscript. XY L reviewed the manuscript and acquired funding for this study. All authors read and approved the final manuscript.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was a retrospective analysis based on anonymized data extracted from the electronic medical records of the First People's Hospital of Lianyungang. This study was approved by the Ethics Committee of the First People's Hospital of Lianyungang (Approval No. KY-20240528001-01), and all procedures adhered to the principles of the Declaration of Helsinki. No identifiable personal information of patients was collected or disclosed. As such, informed consent to participate was not required, and was also waived by the ethics committee of the First People's Hospital of Lianyungang.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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