Original Article

A diagnostic test: diagnostic value of gastrointestinal endoscopy narrow-band imaging (NBI) for colorectal laterally spreading tumor (LST) and submucosal invasion

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Background: Endoscopic ultrasonography is an effective endoscopic examination method for determining the depth of colorectal cancer invasion. Narrow-band imaging (NBI) techniques increase the contrast of vascular structures and more clearly highlight subtle structures on mucosal surfaces, thereby improving the accuracy of endoscopic assessment. This study investigated the diagnostic efficacy of NBI in colorectal laterally spreading tumor (LST) and its submucosal invasion.

Methods: A total of 224 patients with colorectal LST admitted to the Affiliated Hospital of Putian University from January 2015 to December 2021 were enrolled in this study. The patients were divided into NBI and endoscopic ultrasonography groups according to the different examination methods they received. Subsequently, the clinicopathological characteristics of the patients were collected, and the rates of submucosal invasion of the four subtypes (LST-G-H, LST-G-NM, LST-NG-F, LST-NG-PD) were compared between the two groups. Also, the accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of judging the depth of LST lesions of the two examination methods were compared, taking the results of pathological tissue examination as the gold standard.

Results: This study enrolled 224 patients with LST (mean onset age: 57.98±6.48 years), including 123 males and 101 females. In terms of tumor location, 21 cases were located in the cecum, 22 cases in the ascending colon, 38 cases in the transverse colon, 11 cases in the descending colon, 12 cases in the descending sigmoid junction, 23 cases in the sigmoid colon, and 97 cases in the rectum. The sizes of the tumors ranged from 18.81 to 52.88 mm. Moreover, there were 21 cases of lesion infiltration into the submucosa, and the infiltration rate was 9.38%. Furthermore, the accuracy of NBI in diagnosing colorectal LST was significantly higher than that of endoscopic ultrasonography (87.05% *vs.* 57.14%); NBI was more accurate than endoscopic ultrasonography in the preoperative diagnosis of LST lesion depth in the rectal, non-rectal, granular (LST-G), non-granular (LST-NG), <40, and ≥40 mm groups.

Conclusions: Gastrointestinal NBI has a superior accuracy rate and value than endoscopic ultrasonography in diagnosing colorectal LST, tumor lesion depth, and submucosal invasion. Therefore, gastrointestinal NBI deserves to be promoted in clinical work.

Keywords: Endoscopy; narrow-band imaging (NBI); laterally spreading tumor (LST); submucosal invasion

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Introduction

According to statistics, the incidence of colorectal cancer ranks third among all malignant tumors after lung and breast cancers (1). The prognosis of colorectal cancer is highly correlated with the tumor stage, and the 5-year survival rate of most patients with early colorectal cancers is more than 90% (2). Colorectal laterally spreading tumors (LSTs) are morphologically classified as flat lesions in early colorectal cancer (3); the characteristic growth pattern of colorectal LST is lateral along the intestinal wall rather than vertical. Compared with hyperplastic polyps that are similar to the lesions in size, LST is less likely to develop submucosal invasion (4). It has been reported that LST accounts for 15% of colorectal tumors in outpatient colonoscopy results (5), and the incidence of submucosal invasion ranges from 2.6% to 12.3% (6). Due to its flat morphology, LST detection by colonoscopy is difficult. Therefore, improving the diagnostic accuracy of colorectal LST and submucosal invasion is essential for the prevention and treatment of colorectal cancer.

At present, the identification of superficial and deep submucosal invasion is the key to the preoperative endoscopic assessment of the depth of early colorectal cancer. Briefly, methods that can effectively evaluate the lesion and invasion depth of early colorectal cancer include white-light endoscopy, magnifying chromoendoscopy, endoscopic ultrasonography, and narrow-band imaging (NBI) (7,8). Among them, endoscopic ultrasonography is an effective endoscopic examination method for determining the depth of colorectal cancer invasion (9). Ultrasound probes can be inserted through the biopsy channel of the endoscope, so the lesions can be further assessed using endoscopic ultrasonography after routine endoscopy, and the endoscopy process can be greatly simplified. However, there are some limitations for rare lesions, which need to be combined with pathological results (10).

NBI is an electronic chromoendoscopy technique for the observation of subtle structures on mucosal surfaces and capillary morphology, which is widely used in the diagnosis of colorectal lesions. NBI techniques increase the contrast of vascular structures and more clearly highlight subtle structures on mucosal surfaces, thereby improving the accuracy of endoscopic assessment (11). At present, there are many studies on the application value of NBI in esophageal and gastric cancers (12,13); however, there are few reports on LST. Hence, this study investigated the diagnostic efficacy of NBI in colorectal LST and its submucosal invasion by retrospectively analyzing the clinical data of 224 patients to provide reference for the clinical application of NBI. We present the following article in accordance with the STARD reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2566/rc).

Highlight box

Key findings

- Gastrointestinal NBI has a superior accuracy rate and value than endoscopic ultrasonography in diagnosing colorectal LST, tumor lesion depth, and submucosal invasion.

What is known and what is new?

- At present, the identification of superficial and deep submucosal invasion is the key to the preoperative endoscopic assessment of the depth of early colorectal cancer.
- This study investigated the diagnostic efficacy of NBI in colorectal LST and its submucosal invasion by retrospectively analyzing the clinical data of 224 patients to provide a basis for the clinical application of NBI.

What is the implication, and what should change now?

- NBI is superior to endoscopic ultrasonography for the diagnosis of LST and the accuracy of lesion depth. Therefore, gastrointestinal endoscopy-NBI is worthy of clinical application due to its better diagnostic value for colorectal LST and submucosal invasion.

Methods

General information

Patients with LST who were admitted to the Affiliated Hospital of Putian University from January 2015 to December 2021 were selected, and their clinicopathological characteristics including gender, age, lesion location, lesion morphology, lesion size, and pathological type were collected. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics committee of the Affiliated Hospital of Putian University. Individual consent for this retrospective analysis was waived. A total of 224 patients were enrolled in this study based on the inclusion and exclusion criteria (14). Subsequently, the included patients were divided into NBI and endoscopic ultrasonography groups according to the different examination methods they received.

The inclusion criteria were as follows: (I) both males and females, aged 18–90 years old; (II) received colonoscopy and were diagnosed with colorectal LST according to

the diagnostic criteria of LST (15), including (i) diameter greater than 10 mm, (ii) a superficial lesion that grew laterally but not vertically, (iii) granular (LST-G) and non-granular (LST-NG); and (III) signed the informed consent. Patients were excluded based on the following criteria: (I) had a previous history of acute myocardial infarction (within 6 months); (II) could not tolerate surgery due to complications such as severe heart, brain, lung, kidney, and blood system disorders; (III) had a previous history of colorectal cancer or surgery; (IV) were pregnant and lactating or had pregnancy intentions; and (V) suffered from inflammatory bowel disease (ulcerative colitis and Crohn's disease) or hereditary polyposis (hereditary non-polyposis colorectal cancer, familial adenomatous polyposis, Peutz-Jeghers syndrome, etc.).

A histopathological assessment of LST was performed based on the criteria for the histologic grading of colorectal cancer (World Health Organization, WHO 2010 edition) and Vienna classification (16). Briefly, histopathological types of LST comprised the following: (I) low-grade intraepithelial neoplasia (low-grade adenocarcinoma and mild/moderate atypical hyperplasia); (II) high-grade intraepithelial neoplasia (high-grade adenocarcinoma, severe atypical hyperplasia, carcinoma *in situ*, carcinoma *in situ* accompanied by suspected invasion, and intramucosal carcinoma); (III) superficial submucosal invasion (depth of submucosal invasion <1,000 μm); and (IV) deep submucosal invasion (depth of submucosal invasion ≥1,000 μm).

Outcome measures

Comparisons of submucosal invasion rates among the four subtypes of LST

Based on the morphological features, LST was divided into the LST-G and LST-NG types. Specifically, LST-G was classified as a granular homogeneous type (LST-G-H) or a nodular mixed type (LST-G-NM) according to the presence or absence of thick nodules; and as a flat-bulge type (LST-NG-F) or pseudo depression type (LST-NG-PD) based on the presence or absence of depression. In short, LST was divided into four subtypes in total. Next, the submucosal invasion rates among the four subtypes were compared.

Efficacy comparison between the two examination methods in the diagnosis of LST

Taking pathological examination results as the gold standard of diagnosis, the accuracy, sensitivity, specificity, and positive/negative predictive values in diagnosing LST were compared between endoscopic ultrasonography and NBI. Notably, a was expressed as a true positive, b as a false negative, c as a false positive, and d as a true negative (positive for colorectal LST and negative for non-colorectal tumors).

Accuracy of the two examination methods in judging the depth of LST

For the tumor location, LST was divided into non-rectal and rectal subgroups, and the accuracy of preoperative assessment of LST depth was compared between endoscopic ultrasonography and NBI. After comparing the preoperative assessment accuracy between the two methods, LST was divided into LST-NG (LST-NG-PD and LST-NG-F types) and LST-G (LST-G-NM and LST-G-H types) subgroups based on morphology. LST was also divided into <40 and ≥40 mm subgroups according to the tumor size, and the accuracy of the preoperative assessment of the two methods was compared.

Statistical analysis

Statistical analysis was performed using SPSS 22.0 statistical software (IBM Corp., Armonk, NY, USA). Measurement data were expressed as the mean ± standard deviation or quartiles, and the *t*-test was used for comparison between groups. Enumeration data were expressed as the rate (%) or constituent ratio, and the χ^2 test was used for comparison between groups. $P<0.05$ (two-sided) was considered statistically significant.

Results

Clinicopathologic characteristics

A total of 224 LST patients (mean onset age: 57.98±6.48 years) were enrolled in this study, including 123 males and 101 females. There were 21 cases of lesions in the cecum (9.38%), 22 in the ascending colon (9.82%), 38 in the transverse colon (16.96%), 11 in the descending colon (4.91%), 12 in the descending sigmoid junction (5.36%), 23 in the sigmoid colon (10.27%), and 97 in the rectum (43.30%). As for lesion morphology, 159 cases were diagnosed as LST-G-NM (70.98%), 20 cases as LST-G-H (8.93%), 38 cases as LST-NG-F (16.96%), and seven cases as LST-NG-PD (3.13%). The lesions ranged from 18.81 to 52.88 mm in size, with a mean size of 34.93 mm.

Table 1 Clinicopathologic characteristics

Clinicopathologic characteristics	Total (n=224)
Gender	
Male	123 (54.91%)
Female	101 (45.09%)
Age (years)	57.98±6.48
Lesion location	
Cecum	21 (9.38%)
Ascending colon	22 (9.82%)
Transverse colon	38 (16.96%)
Descending colon	11 (4.91%)
Descending sigmoid junction	12 (5.36%)
Sigmoid colon	23 (10.27%)
Rectum	97 (43.30%)
Lesion morphology	
LST-G-H	20 (8.93%)
LST-G-NM	159 (70.98%)
LST-NG-F	38 (16.96%)
LST-NG-PD	7 (3.13%)
Lesion size (mm)	34.93 (18.81, 52.88)
Pathological type	
Low-grade intraepithelial neoplasia	20 (8.93%)
High-grade intraepithelial neoplasia	32 (14.29%)
Superficial submucosal invasion	151 (67.41%)
Deep submucosal invasion	21 (9.38%)

Measurement data were expressed as the mean ± standard deviation or quartiles; enumeration data were expressed as case (%). LST-G-H, granular homogeneous type; LST-G-NM, nodular mixed type; LST-NG-F, flat-bulge type; LST-NG-PD, pseudo depression type; LST, laterally spreading tumor.

Based on the tumor types, 20 cases were diagnosed as low-grade intraepithelial neoplasia, 32 cases as high-grade intraepithelial neoplasia, 151 cases as superficial submucosal invasion, and 21 cases as deep submucosal invasion (*Table 1*).

Submucosal invasion rate

Of the 224 LST cases included in this study, 21 cases developed into submucosal invasion, including 16 LST-G-NM types (accounting for 10.1% of the total morphological type), three LST-NG-F types (7.9% of the total morphological type), one granular homogeneous type (5% of the total morphological type), and one LST-NG-PD type (14.3% of the total morphological type) (*Table 2*).

Table 2 Submucosal invasion rate of four subtypes among the subjects

Morphology	Total (n=224)	Cases of submucosal invasion (n=21)	Rate (%)
LST-G-H	20	1	5.0
LST-G-NM	159	16	10.1
LST-NG-F	38	3	7.9
LST-NG-PD	7	1	14.3

Enumeration data were expressed as case (%). LST-G-H, granular homogeneous type; LST-G-NM, nodular mixed type; LST-NG-F, flat-bulge type; LST-NG-PD, pseudo depression type; LST, laterally spreading tumor.

Comparison of the diagnostic efficacy of the two methods

To compare the diagnostic efficacy of NBI and endoscopic ultrasonography, the results of pathological tissue examination were considered the gold standard for diagnosis. The outcomes showed that the accuracy of NBI and endoscopic ultrasonography in the diagnosis of colorectal LST was 87.05% (195/224) and 57.14% (128/224), respectively, and the difference between the two methods was statistically significant (P<0.05) (*Table 3*). In addition, the sensitivity, specificity, positive predictive value, and negative predictive value of NBI in the diagnosis of LST were markedly higher than those of endoscopic ultrasonography (P<0.05).

Comparison of the accuracy between the two methods in judging the depth of LST

The lesion locations, morphologies, and sizes are shown in *Table 4*. In the rectal group, the accuracy of NBI in judging the depth of colorectal LST before surgery was considerably higher than that of endoscopic ultrasonography (87.63% *vs.* 56.70%) (P<0.001). In the non-rectal group, NBI was significantly more accurate than endoscopic ultrasonography in the preoperative judgment of colorectal LST (86.61% *vs.* 57.48%) (P<0.001). However, there were no significant differences in the accuracy of NBI and endoscopic ultrasonography in judging the depth of

Table 3 Comparison of diagnostic efficacy between the two methods

Methods	Diagnostic efficacy				
	Accuracy	Sensitivity	Specificity	Positive predictive value	Negative predictive value
NBI	87.05 (195/224)	89.07 (163/183)	78.05 (32/41)	94.77 (163/172)	61.54 (32/52)
Endoscopic ultrasonography	57.14 (128/224)	60.11 (110/183)	43.90 (18/41)	82.71 (110/133)	19.78 (18/91)
χ^2	49.810	40.494	10.045	11.617	25.375
P	<0.001	<0.001	0.002	0.001	<0.001

Enumeration data were represented as the rate (%) or constituent ratio. NBI, narrow-band imaging.

Table 4 Comparison of the accuracy of the two examinations in diagnosing the depth of laterally spreading tumor

Classification	Group	Methods	Accurate	Inaccurate	Accuracy (%)
LST location	Rectal	NBI	85	12	87.63[A]
		Endoscopic ultrasonography	55	42	56.70[B]
	Non-rectal	NBI	110	17	86.61[C]
		Endoscopic ultrasonography	73	54	57.48[D]
LST morphology	LST-NG	NBI	154	25	86.03[E]
		Endoscopic ultrasonography	106	73	59.22[F]
	LST-G	NBI	41	4	91.11[G]
		Endoscopic ultrasonography	22	23	48.89[H]
LST size	<40 mm	NBI	122	10	92.42[I]
		Endoscopic ultrasonography	95	37	71.97[J]
	≥40 mm	NBI	78	14	84.78[K]
		Endoscopic ultrasonography	33	59	35.87[L]

Enumeration data were represented as case (%). P (A and B) <0.001, P (C and D) <0.001, P (A and C) =0.823, P (B and D) =0.907; P (E and F) <0.001, P (G and H) <0.001, P (E and G) =0.364, P (F and H) =0.211; P (I and J) <0.001, P (K and L) <0.001, P (I and K) =0.069, P (J and L) <0.001. NBI, narrow-band imaging; LST, laterally spreading tumor; LST-G, laterally spreading tumor-granular group; LST-NG, laterally spreading tumor non-granular group.

LST between the rectal and non-rectal groups (P=0.823, P=0.907).

As for LST morphology, in the LST-G group, the accuracy of NBI in diagnosing the depth of colorectal LST preoperatively (91.11%) was higher than that of endoscopic ultrasonography (48.89%) (P<0.001). In the LST-NG group, the accuracy of NBI in judging the depth of colorectal LST preoperatively (86.03%) was higher than that of endoscopic ultrasonography (59.22%) (P<0.001). The accuracy of NBI and endoscopic ultrasonography in judging the depth of LST between the LST-G and LST-NG groups was not significantly different (P=0.364, P=0.211).

As for lesion size, the accuracy of NBI in judging the depth of colorectal LST preoperatively in the <40 mm group (92.42%) was higher than that of endoscopic ultrasonography (71.97%) (P<0.001). In the ≥40 mm group, the accuracy of NBI in diagnosing the depth of colorectal LST preoperatively (84.78%) was higher than that of endoscopic ultrasonography (35.87%) (P<0.001). There was a marked difference in the accuracy of endoscopic ultrasonography in judging the depth of LST between the <40 and ≥40 mm groups (P<0.001), and the accuracy in the ≥40 mm group was substantially lower than that in the <40 mm group (35.87% *vs.* 71.97%); however, there was no significant difference in the accuracy of NBI between the

two groups (P=0.069).

Discussion

LST is a flat colorectal tumor lesion that generally grows laterally along the superficial and circumferential intestinal walls rather than vertically along the deep intestinal wall. In recent years, more attention has been paid to flat colorectal lesions, as they have a higher malignant potential and incidence of submucosal invasion than bulge lesions (17). The objective of the present study was to analyze the diagnostic efficacy of NBI and conventional endoscopic ultrasonography to facilitate better clinical diagnosis and treatment of LST and submucosal invasion.

A total of 224 patients with LST were included in this study. On the one hand, the mean age of the included patients was older than 57 years, suggesting that individuals older than 57 years were prone to suffer from LST; this finding is consistent with previous literature reports (18). On the other hand, LST mainly occurred in the rectum, followed by the transverse colon, sigmoid colon, ascending colon, cecum, descending colon, and descending sigmoid junction. Furthermore, there were 159 LST-G-NM cases, 20 LST-G-H cases, 38 LST-NG-F cases, and seven LST-NG-PD cases, which was similar to the findings reported by Kim *et al.* (19). Moreover, the diameter of lesions ranged from 18.81 to 52.88 mm, with an average size of 34.93 mm. It is reported that the larger the diameter of lesions, the greater the possibility of submucosal invasion (20). The above-mentioned result suggests that the size of lesions contributes to the clinical evaluation of the risk of submucosal invasion (19).

Kudo *et al.* stated that the correlation between lesion diameter size and submucosal invasion rate was associated with the LST subtype. Specifically, the LST-NG-PD type had the highest invasion rate (37.7%), the LST-G-NM type had a higher submucosal invasion rate (31.7%), while the LST-G-H and LST-NG-F types had lower submucosal invasion rates (21). In this study, the invasion rate of the LST-NG-PD type was the highest (14.9%) while that of the LST-NG-F type was the lowest (7.9%) among the four subtypes. The results of this study verified the conclusion of Kudo *et al.*

Although the overall risk of developing submucosal invasion in LST patients is not high, it is not as optimistic as the overall risk after LST is subdivided into various subtypes according to endoscopic morphology. In fact, different subtypes have different clinicopathologic features and submucosal invasion rates; notably, the LST-NG-PD type has a particularly high submucosal invasion rate (22-24). Therefore, fine differentiation of LST is considerably important for the accurate identification of the nature of the lesion. Based on previous studies and the results of this study, there are significant differences in the clinicopathological features of each LST subtype, and the risk of submucosal invasion of the lesion can be preliminarily assessed according to the LST classification. Also, owing to the limited sample size, there may have been some bias in this study.

In the present study, the accuracy, specificity, sensitivity, negative predictive value, and positive predictive value of NBI in the diagnosis of colorectal LST were significantly higher than those of endoscopic ultrasonography. Also, NBI was more accurate than endoscopic ultrasonography in diagnosing the depth of colorectal LST in the rectal, non-rectal, LST-G, LST-NG, <40, and ≥40 mm groups. Endoscopic ultrasonography is an important means of clinical diagnosis of gastrointestinal tumors, which can be applied to intuitively observe the location, morphology, and depth of invasion of the tumor as well as the relationship between the tumor and the surrounding tissues (25).

Endoscopic ultrasonography can effectively identify intramucosal carcinoma, superficial submucosal invasion, and deep submucosal invasion. Also, with an accuracy of up to 90%, endoscopic ultrasonography not only has good diagnostic accuracy for early lesions but also presents an important guiding significance for selecting the best treatment (26). However, some articles have reported that the pathological subtypes and morphology of LST are diverse, so diagnosis is easily missed during endoscopic ultrasonography (27). Hence, NBI has emerged as a new endoscopic technique.

Compared with endoscopic ultrasonography, NBI enables meticulous observation of the epithelial morphology in the gastrointestinal mucosa and has been widely used to diagnose gastrointestinal diseases in clinical practice (28). When the mucosal capillaries in LST are observed by NBI, the capillary structure is divided into four types (CP I, CP II, CP IIIA, and CP IIIB) based on Sano's capillary pattern classification (29). Therefore, NBI has certain reference significance for selecting the treatment methods of early colorectal lesions. Moreover, NBI is easy to perform and not time-consuming. Several studies have also confirmed that NBI can effectively identify non-neoplastic/neoplastic lesions and determine the depth of invasion of the lesion by observing the capillary morphology on the mucosal

surface of the lesion (30,31). In fact, a study has stated that the NBI technique is more accurate than endoscopic ultrasonography (32). In other words, NBI has important clinical significance for the diagnosis, prognostic evaluation, and treatment options of diseases.

However, there may be some bias in the final results of this study due to sample size constraints. Hence, the conclusions obtained by this study need to be further justified by prospective, large-sample, multicenter studies.

Conclusions

In summary, NBI is superior to endoscopic ultrasonography for the diagnosis of LST and the accuracy of lesion depth. Therefore, gastrointestinal endoscopy-NBI is worthy of clinical application due to its better diagnostic value for colorectal LST and submucosal invasion.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2566/rc

Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2566/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2566/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics committee of the Affiliated Hospital of Putian University. Individual consent for this retrospective analysis was waived.

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