

ORIGINAL RESEARCH ARTICLE

## Comparison of the histopathological characteristics of large colorectal laterally spreading tumors according to growth pattern

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### Abstract:

**Objectives:** Colorectal laterally spreading tumors (LSTs) are widely recognized owing to their structural characteristics. This study aims to clarify the histopathological characteristics of large colorectal LSTs according to growth pattern. **Methods:** We studied 297 colorectal LSTs measuring  $\geq 20$  mm in diameter. The LSTs were classified into four types: granular homogenous type (LST-G-H), granular nodular mixed type (LST-G-M), non-granular flat elevated type (LST-NG-F), and non-granular pseudo-depressed type (LST-NG-PD). Retrospectively collected data were examined to compare the histopathological characteristics of LSTs according to the growth pattern. **Results:** LST-G-M lesions (142 lesions) were most common, followed by LST-NG-F (74 lesions), LST-G-H (61 lesions), and LST-NG-PD (20 lesions). The mean tumor diameter of LST-G lesions ( $38.5 \pm 17.2$  mm) was significantly greater than that of LST-NG lesions ( $26.3 \pm 7.0$  mm,  $P < 0.001$ ). In particular, 45% of LST-G-M lesions were  $\geq 40$  mm in diameter. Adenomas accounted for 54% of LST-G-H lesions compared with only 10% of LST-NG-PD lesions. Pathological T1 carcinomas accounted for 55% of LST-NG-PD lesions and were not found among LST-G-H lesions. **Conclusions:** The biological malignancy of colorectal LSTs differs considerably depending on the growth pattern even among large lesions and therefore should be considered when selecting treatment regimens.

### Keywords:

large colorectal laterally spreading tumors, growth pattern, histopathological characteristics, biological malignancy

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### Introduction

Laterally spreading tumors (LSTs) are defined as colorectal tumors measuring  $\geq 10$  mm in diameter that mainly grow horizontally rather than vertically<sup>1-3)</sup>. This term describes the growth pattern of colorectal tumors rather than the macroscopic classification<sup>4)</sup> and is a widely acknowledged “nickname.”

Colorectal LSTs are classified into two categories: LSTs of granular type (LST-G), characterized by a granular or nodular tumor surface, and LSTs of non-granular type (LST-NG), which have a flat, smooth surface<sup>3)</sup>. LST-G lesions are subclassified into two types: homogenous type (LST-G-H) and nodular mixed type (LST-G-M)<sup>3)</sup>. LST-NG lesions are subclassified into two types: flat elevated type (LST-NG-F) and pseudo-depressed type (LST-NG-PD)<sup>3)</sup>. Apart from dif-

ferent growth patterns, LST-G and LST-NG lesions have also been reported to have different histopathological characteristics, including gene mutation patterns and biological malignancy<sup>5-8</sup>).

This study aims to clarify growth-pattern-related differences in the histopathological characteristics of large colorectal LSTs measuring  $\geq 20$  mm in diameter. In addition, we discuss differences in development and progression between LST-G and LST-NG lesions.

## Methods

### Subjects

We studied 297 consecutive colorectal LSTs (286 patients) that measured  $\geq 20$  mm in diameter and were evaluated endoscopically, resected endoscopically or surgically, and diagnosed histopathologically in our hospital from March 2008 through August 2016. LSTs associated with familial adenomatous polyposis or inflammatory bowel diseases, such as ulcerative colitis, were excluded from the study.

This study was performed in accordance with the Declaration of Helsinki. The ethical committee approval of our hospital was obtained. Because this study was an observational study of retrospectively collected data, it was difficult to explain the study to all patients and obtain written informed consent. Information about the study was therefore officially disclosed in a poster form at our hospital after the study had been approved by the ethics review committee. Informed consent was then obtained on an opt-out basis from patients to ensure that patients had an opportunity to refuse to participate in the study.

### Endoscopic examination

As premedication for endoscopic examination, scopolamine butylbromide (10 mg) or glucagon (0.5 mg) was injected intramuscularly to suppress intestinal peristalsis before colonoscopy in patients with no contraindications. The endoscopic diagnosis of colorectal LSTs was based on the appearance on white-light endoscopy and on chromoendoscopy with 0.4% indigo carmine dye.

On the basis of the colonoscopic findings, the LST-G lesions were subclassified into two categories: LST-G-H lesions, characterized by multiple granules or nodules of similar sizes on the tumor surface, and LST-G-M lesions, characterized by nodules of different sizes on the tumor surface (Figure 1a, 1b)<sup>3</sup>. The LST-NG lesions were subclassified into two categories: LST-NG-PD lesions, characterized by a poorly demarcated, shallow tray-like depression in the center of the tumor, and LST-NG-F lesions, characterized by a flat tumor with no depression (Figure 1c, 1d)<sup>3</sup>. The growth patterns of the LSTs in our study were subclassified by 20 at-

tending endoscopists. The endoscopic pictures were reviewed by at least two experienced colonoscopists who had over 10 years of experience in colonoscopy and belonged to our hospital to determine the final subclassification of the LSTs.

For colorectal LSTs associated with findings suggesting submucosal or deeper invasion on colonoscopic examination, including chromoendoscopy, the pit pattern of the lesions was diagnosed on magnifying endoscopy, and the depth of invasion was additionally evaluated on endoscopic ultrasonography<sup>9-11</sup>. Lesions that were considered to locally invade the mucosa or slightly invade the submucosa on the basis of the colonoscopic findings and were evaluated to be resectable endoscopically were resected by endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). Lesions with deep invasion of the submucosa or of the muscularis propria or deeper were surgically treated by colectomy with lymph-node dissection.

### Histopathological evaluation

All resected specimens were fixed in 10% formalin solution and thinly sliced to prepare specimens. All specimens were stained with hematoxylin and eosin and then histopathologically evaluated by a pathologist to assess the LST diameter, histological type, and depth of tumor invasion. If tumor invasion was confined to the mucosa on histopathological examination, tumor *in situ* (adenoma and pTis carcinoma) was diagnosed. If the tumor invaded the submucosa, pathological stage 1 (pT1) carcinoma was diagnosed<sup>12</sup>. pT1 cancer with a submucosal invasion depth of less than 1000  $\mu\text{m}$  was defined as pT1a cancer, and pT1 cancer with a submucosal invasion depth of 1000  $\mu\text{m}$  or more was defined as pT1b cancer<sup>12</sup>. For lesions that underwent piecemeal resection by EMR or ESD, the tumor diameter was measured at the time of endoscopic examination, using a blue rubber disc with a diameter of 1 cm if the tumor diameter was difficult to accurately evaluate in the resected specimens.

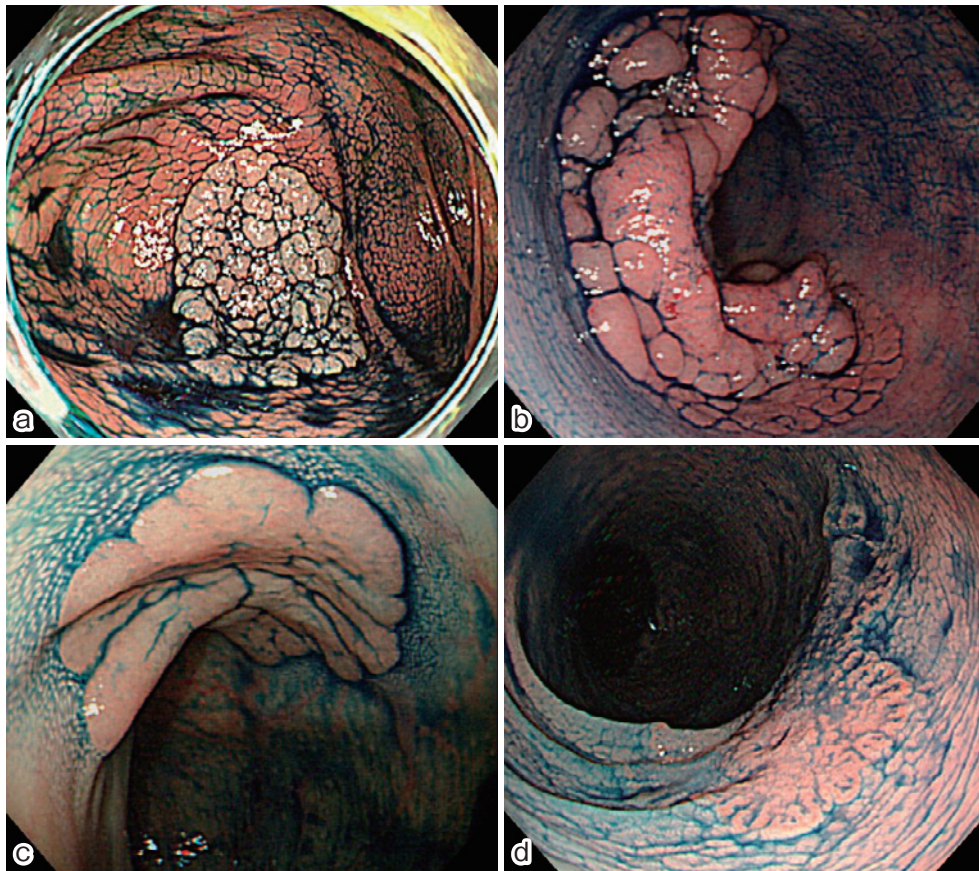
### Statistical analysis

Chi-squared tests and Fisher's exact test were used to compare proportions. T tests were used to compare continuous variables between groups. P values of less than 0.05 were considered to indicate statistical significance. Continuous variables are expressed as mean values with standard deviations. All statistical analyses were performed with the use of STATA 14 software (Houston, TX, USA).

## Results

### Demographic data

Among the 286 patients (297 lesions), 9 had multiple LSTs measuring  $\geq 20$  mm in diameter: 2 of the patients had



**Figure 1.** Chromoendoscopic images of four types of laterally spreading tumors (LST) according to their growth pattern.

- (a) LST-G-H: LST-granular homogenous type.
- (b) LST-G-M: LST-granular nodular mixed type.
- (c) LST-NG-F: LST-non-granular flat elevated type.
- (d) LST-NG-PD: LST-non-granular pseudo-depressed type.

3 lesions, and 7 had 2 lesions. The mean age was 69.3 years, with no difference between males and females (Table 1). The numbers of lesions according to the LST subclassification were 142 LST-G-M lesions, which were most common, followed by 74 LST-NG-F lesions, 61 LST-G-H lesions, and 20 LST-NG-PD lesions. As for the histopathological diagnosis, there were 95 adenomas, 173 pTis carcinomas, and 29 pT1 carcinomas. Among pT1 carcinomas, 15 lesions were pT1a cancer, and 14 lesions were pT1b cancer. There were no advanced carcinomas invading the muscularis propria or deeper regions. As for the treatment regimens, the largest proportion of LSTs was treated by ESD, followed by EMR and colectomy. Among the lesions treated by EMR, only 21 underwent *en bloc* resection, and the other 69 underwent piecemeal resection. Ten of the lesions treated by ESD underwent piecemeal resection. Among the 15 lesions (15 patients) resected by colectomy, 3 were pT1 carcinomas. Two of these lesions were LST-G-M tumors accompanied by lymph-node metastasis.

#### **Locations and sizes of LSTs**

The locations of LSTs differed significantly according to the lesion subclassification ( $P = 0.0001$ , Table 2). LST-G-H and LST-G-M lesions were frequently found in the rectum and the region from the ascending colon to the cecum. LST-NG lesions were most commonly found in the transverse colon. In particular, more than half of all LST-NG-PD lesions arose in the transverse colon.

The LSTs were classified into three subgroups according to the tumor diameter: lesions with a diameter of 20 to 29 mm, those with a diameter of 30 to 39 mm, and those with a diameter of  $\geq 40$  mm. The frequencies of the three groups differed significantly according to lesion subclassification ( $P = 0.0001$ , Table 3). The most common tumor diameter of LST-G-H, LST-NG-F, and LST-NG-PD lesions was 20 to 29 mm. As the tumor diameter increased, the numbers of lesions decreased. In contrast, the number of LST-G-M lesions increased as the tumor diameter increased, and nearly half of all LST-G-M lesions were  $\geq 40$  mm in diameter. The

mean tumor diameter of LST-G lesions ( $38.5 \pm 17.2$  mm) was significantly greater than that of LST-NG lesions ( $26.3 \pm 7.0$  mm;  $P < 0.001$ ).

### Histopathological diagnosis

The proportions of adenomas, pTis carcinomas, and pT1 carcinomas differed significantly among the subgroups ( $P = 0.0001$ , Table 4). Adenomas were most common among the

LST-G-H lesions, pTis carcinomas were most common among the LST-G-M and LST-NG-F lesions, and pT1 carcinomas were most common among the LST-NG-PD lesions. In particular, pT1 carcinomas accounted for 55% of all LST-NG-PD lesions and were more common among such lesions than among LSTs with other growth patterns. None of the LST-G-H lesions were pT1 carcinomas. Among the LSTs that were adenomas, the most common histological type was tubular adenoma among LST-NG lesions and tubulovillous adenoma among LST-G lesions. In particular, tubulovillous adenoma accounted for 74% (25 of 34 lesions) of all LST-G-M lesions.

We examined the relations of the growth patterns of the LSTs to the tumor diameter and histopathological diagnosis (Table 5). Among the LST-G-H lesions, adenomas accounted for 69% of lesions that were 20 to 29 mm in diameter. An increase in tumor diameter was accompanied by an increase in the proportion of pTis carcinomas, but none of the LST-G-H lesions were pT1 carcinomas. Among the LST-G-M lesions, adenomas accounted for nearly half of the lesions with a diameter of 20 to 29 mm. As the tumor diameter increased, the proportions of pTis and pT1 carcinomas increased, and 21% of the LST-G-M lesions with a diameter of  $\geq 40$  mm were pT1 carcinomas. Among the LST-NG-F lesions, an increase in tumor diameter was associated with an increased proportion of pTis carcinomas. However, only three LST-NG-F lesions with a diameter of 20 to 29 mm were pT1 carcinomas. Among the LST-NG-PD lesions, carcinomas accounted for 86% of the lesions with a diameter of 20 to 29 mm, half of which were pT1 carcinomas. An increase in the tumor diameter was accompanied by an increasing proportion of pT1 carcinomas, but the number of lesions decreased.

**Table 1.** Demographic Data of the Study Subjects (286 Patients with 297 LSTs).

Age (years), mean [SD]	69.3 [10.1]
Sex male:female	146:140
Growth pattern of LSTs,	
Granular type	203 (68)
Homogenous type	61
Nodular mixed type	142
Non-granular type	94 (32)
Flat elevated type	74
Pseudo-depressed type	20
Histology	
Adenoma	95 (32)
pTis carcinoma	173 (58)
pT1 carcinoma	29 (10)
pT1a carcinoma	15
pT1b carcinoma	14
Initial treatment	
EMR	90 (30)
En bloc resection	21
Piecemeal resection	69
ESD	192* (65)
En bloc resection	182
Piecemeal resection	10
Colectomy	15 (5)

SD, standard deviation LSTs, laterally spreading tumors n (%)

EMR, endoscopic mucosal resection ESD, endoscopic submucosal dissection

\*, Three patients underwent additional colectomy.

## Discussion

Improved diagnostic accuracy enabled by progress in colonoscopic equipment and improved methods for bowel

**Table 2.** Relation between Growth Pattern of Colorectal LSTs and Tumor Location.

	LST-G-H (n = 61) n (%)	LST-G-M (n = 142) n (%)	LST-NG-F (n = 74) n (%)	LST-NG-PD (n = 20) n (%)
Rectum	14 (23)	52 (37)	4 (5)	2 (10)
Sigmoid	4 (7)	21 (15)	6 (8)	3 (15)
Descending	0	5 (4)	13 (18)	1 (5)
Transverse	3 (5)	12 (8)	24 (33)	11 (55)
Ascending	21 (34)	32 (22)	21 (28)	1 (5)
Cecum	19 (31)	20 (14)	6 (8)	2 (10)

LSTs, laterally spreading tumors LST-G-H, laterally spreading tumor granular homogenous type

LST-G-M, laterally spreading tumor granular nodular mixed type

LST-NG-F, laterally spreading tumor non-granular flat elevated type

LST-NG-PD, laterally spreading tumor non-granular pseudo-depressed type

**Table 3.** Relation between Growth Pattern of Colorectal LSTs and Tumor Diameter.

	LST-G-H (n = 61) n (%)	LST-G-M (n = 142) n (%)	LST-NG-F (n = 74) n (%)	LST-NG-PD (n = 20) n (%)
20 - 29 mm	29 (48)	36 (25)	57 (77)	14 (70)
30 - 39 mm	22 (36)	43 (30)	14 (19)	5 (25)
≥40 mm	10 (16)	63 (45)	3 (4)	1 (5)

LSTs, laterally spreading tumors LST-G-H, laterally spreading tumor granular homogenous type  
 LST-G-M, laterally spreading tumor granular nodular mixed type  
 LST-NG-F, laterally spreading tumor non-granular flat elevated type  
 LST-NG-PD, laterally spreading tumor non-granular pseudo-depressed type

**Table 4.** Relation between Growth Pattern of Colorectal LSTs and Histological Diagnosis.

	LST-G-H (n = 61) n (%)	LST-G-M (n = 142) n (%)	LST-NG-F (n = 74) n (%)	LST-NG-PD (n = 20) n (%)
Adenoma	33 (54)	34 (24)	26 (35)	2 (10)
TA	14	7	21	2
TVA	15	25	4	0
TSA	3	2	1	0
SSA/P	1	0	0	0
pTis carcinoma	28 (46)	93 (65)	45 (61)	7 (35)
pT1 carcinoma	0 (0)	15 (11)	3 (4)	11 (55)

LSTs, laterally spreading tumors TA, tubular adenoma  
 LST-G-H, laterally spreading tumor granular homogenous type TVA, tubulovillous adenoma  
 LST-G-M, laterally spreading tumor granular nodular mixed type TSA, traditional serrated adenoma  
 LST-NG-F, laterally spreading tumor non-granular flat elevated type SSA/P, sessile serrated adenoma /polyp  
 LST-NG-PD, laterally spreading tumor non-granular pseudo-depressed type

**Table 5.** Relations of Growth Pattern of Colorectal LSTs to Tumor Diameter and Histological Diagnosis.

	Histology	Tumor diameter		
		20-29 mm n (%)	30-39 mm n (%)	40 mm ~ n (%)
LST-G-H (n = 61)	Adenoma	20 (69)	8 (36)	5 (50)
	pTis carcinoma	9 (31)	14 (64)	5 (50)
	pT1 carcinoma	0	0	0
LST-G-M (n = 142)	Adenoma	17 (47)	11 (25)	6 (9)
	pTis carcinoma	19 (53)	30 (70)	44 (70)
	pT1 carcinoma	0	2 (5)	13 (21)
LST-NG-F (n = 74)	Adenoma	21 (37)	5 (36)	0
	pTis carcinoma	33 (58)	9 (64)	3 (100)
	pT1 carcinoma	3 (5)	0	0
LST-NG-PD (n = 20)	Adenoma	2 (14)	0	0
	pTis carcinoma	6 (43)	1 (20)	0
	pT1 carcinoma	6 (43)	4 (80)	1 (100)

LSTs, laterally spreading tumors LST-G-H, laterally spreading tumor granular homogenous type  
 LST-G-M, laterally spreading tumor granular nodular mixed type  
 LST-NG-F, laterally spreading tumor non-granular flat elevated type  
 LST-NG-PD, laterally spreading tumor non-granular pseudo-depressed type

preparation has led to the detection of many flat lesions in addition to conventionally detected polypoid lesions. Flat colorectal LSTs are associated with a characteristic growth pattern and a low incidence of invasive cancer for a given

large size and can therefore usually be resected by minimally invasive endoscopic procedures<sup>1,6,13,14</sup>. In Japan, ESD has been rapidly disseminated as an endoscopic technique for the resection of large colorectal tumors, especially LSTs, and good treatment outcomes have been reported<sup>15-18</sup>. ESD was the procedure most often selected for the resection of LSTs measuring  $\geq 20$  mm in diameter in our study. ESD for colorectal tumors has been commonly performed in a part of some countries in East Asia, including Japan. However, ESD is accepted to be performed only in hospitals that meet the official standards to secure the certainty and safety in Japan.

In our study, large colorectal LSTs measuring  $\geq 20$  mm in diameter were studied to determine the histopathological characteristics of LSTs according to their growth pattern. We included only large colorectal LSTs in the study because an increase in tumor size was speculated to be associated with more remarkable variations in growth-pattern-dependent histopathological characteristics. We would like to confirm whether the histopathological characteristics were the same as those of LSTs with a diameter of 10 mm or greater, as reported in previous studies. A previous study of large colorectal LSTs of a diameter of  $\geq 20$  mm was conducted by only Tanaka et al.<sup>19</sup> Uraoka et al.<sup>14</sup> and Yamada et al.<sup>20</sup> classified many colorectal LSTs with a diameter of  $\geq 10$  mm into LST-G and LST-NG to compare the incidence of pT1 carcinomas and performed a multivariate analysis to examine the endoscopic characteristics of carcinomas invading the submucosa. In these studies, however, colorectal LSTs were not subclassified into four types according to the growth pattern to determine histopathological characteristics. In large colorectal LSTs, not only endoscopic resection but also surgery should be considered. We think that our results may be useful for determining the optimal treatment for large colorectal LSTs according to the growth pattern.

The characteristics of the locations and size of LSTs in our study were consistent with the results of previously reported studies<sup>16,21,22</sup>. Miyamoto et al.<sup>21</sup> reported that among LST-G lesions, a particularly high proportion of LST-G-M lesions arose in the rectum, and such lesions accounted for 77% of the LSTs found in the rectum. The mean tumor diameter of LST-G lesions has been reported to be significantly greater than that of LST-NG lesions<sup>17,19,23</sup>. Although we focused on only large LSTs with a diameter of  $\geq 20$  mm, similar results were obtained.

As for the histological types of LSTs that were adenomas, the largest proportions of LST-NG lesions were tubular adenomas. In contrast, the largest proportions of LST-G lesions were tubulovillous adenomas, and this trend was particularly remarkable among LST-G-M lesions, which included many particularly large lesions. Kusaka et al.<sup>24</sup> also pointed out that villous adenoma components are more frequently found in LST-G-M lesions. Generally, the tumor epithelium tends to be taller in tubulovillous adenomas than in tubular adeno-

mas, and differences in histological components may have led to differences in the sizes and growth patterns of the LSTs.

LST-NG lesions have been reported to have a higher biological malignancy, associated with a higher incidence of pT1 carcinomas, than LST-G lesions, even if the tumor diameter is small<sup>17,19,20</sup>. Yamada et al.<sup>20</sup> reported that the rate of pT1 cancer among LST-NG lesions with a diameter of  $\geq 10$  mm was 39.0%, which was higher than that among LST-G lesions (19.3%). In our study, we focused on large LSTs with a diameter of  $\geq 20$  mm, and consistent results were obtained. The reasons for the differences in the biological malignancy of LSTs according to the growth pattern remain unclear. However, some studies have reported that gene mutation patterns differ between LST-G and LST-NG lesions<sup>5-8</sup>. Sakai et al.<sup>7</sup> reported that mutations of the TP53 tumor suppressor gene were expressed when carcinoma invaded the submucosa in patients with LST-G lesions and from the time that carcinoma was still confined to the mucosa in patients with LST-NG lesions. TP53 gene mutations might be linked to cancer progression and might underlie the higher biological malignancy of LST-NG lesions compared with LST-G lesions.

Among patients with LST-G lesions, an increase in the tumor diameter of LST-G-H lesions was associated with decreased numbers of lesions. In patients with LST-G-M lesions, however, an increase in the tumor diameter was associated with increased numbers of lesions. In patients with LST-G-H lesions, adenoma was histopathologically confirmed in only more than half of the lesions, even when the tumor diameter reached 20 to 29 mm. As the tumor diameter increased, the incidence of pTis carcinoma increased. However, no invasive carcinoma was found even when the tumor diameter was  $\geq 40$  mm. The rarity of invasive carcinoma in patients with LST-G-H lesions has been reported previously<sup>22,25,26</sup>. In contrast, 76% of the LST-G-M lesions were carcinomas, and an increase in tumor diameter was associated with an increased incidence of pT1 carcinoma. In patients with small LST-G-H lesions, tumor development and cancerization were associated with the development of nodules of various sizes on the tumor surface, and large nodules also formed, suggesting that many LST-G-H lesions transform into LST-G-M lesions with increasing tumor diameter. The appearance of large nodules on LST-G-M lesions has been reported to often indicate the presence of underlying submucosal or deeper invasion<sup>14,20,25,27</sup>.

Among LST-NG lesions, LST-NG-PD lesions have a higher incidence of invasive carcinomas than LSTs with other growth patterns<sup>3,17,22,28</sup>. The incidence of pT1 carcinomas associated with LST-NG-PD lesions was reported to be 12.5% by Kim et al.<sup>22</sup> and 35.7% by Nishiyama et al.<sup>17</sup> In our study, we focused on only large LSTs with a diameter of  $\geq 20$  mm, and 55% of LST-NG-PD lesions were pT1 car-

cinomas. An increase in the tumor diameter of LST-NG-PD lesions was associated with an increase in the incidence of pT1 carcinomas, but the number of lesions decreased dramatically. Horiuchi et al.<sup>28)</sup> reported that all LST-NG-PD lesions were pT1 carcinomas even if the tumor diameter was <20 mm and that no LST-NG-PD lesion had a diameter of  $\geq$  30 mm. These results suggest that the growth pattern of LST-NG-PD lesions is associated with deep invasion at an early phase and with changes in gross appearance.

As for the endoscopic resection technique for colorectal LSTs, the results of our study suggest that piecemeal EMR is an acceptable procedure because most LST-G-H lesions, including large lesions measuring  $\geq$ 20 mm or more in diameter, are confined to the mucosa. However, EMR is inappropriate for the treatment of large LSTs with other growth patterns owing to the risk of pathological T1 carcinoma. In particular, LST-NG-PD lesions are associated with a high incidence of invasive cancer regardless of lesion size and with submucosal or deeper multifocal invasion<sup>14,29)</sup>. The depth of invasion of such lesions has been reported to be difficult to accurately evaluate even after pit pattern analysis on magnifying endoscopy<sup>30)</sup>. Piecemeal EMR should be particularly avoided in large LST-NG-PD lesions because more than half of lesions with a diameter of  $\geq$ 20 mm were pT1 cancer in our study. Treatment, including surgery, should therefore be selected.

Our study had several limitations. It was a retrospective, observational study performed in a single center and included a small number of LST-NG-PD lesions. Among large colorectal LSTs, the number of lesions with pT1 cancer was only 29. Therefore, large LSTs with pT1 cancer could not be subclassified into two groups: pT1a cancer and pT1b cancer. In addition, relatively small LSTs with a diameter of 10 to 20 mm were not included in the analysis, which was considered to be a limitation.

Because we focused on large colorectal LSTs measuring  $\geq$  20 mm in diameter in our study, our results may be useful for determining the optimal treatment for large colorectal LSTs according to the growth pattern. Furthermore, we were able to confirm that factors such as lesion site and the size and incidence of invasive cancer differed among the four types of LST lesions in this study. Particularly in patients with LST-G lesions, we speculated that many LST-G-H lesions could progress to LST-G-M lesions on the basis of the number of lesions and the depth of invasion according to the tumor diameter. Further studies of larger numbers of cases, including small lesions measuring 10 to <20 mm in diameter, are thus needed to confirm the progression patterns of LSTs, particularly LST-NG lesions.

#### Conflicts of Interest

There are no conflicts of interest.

Approval code issued by the institutional review board and the name of the institution(s) that granted the approval B16-161, Ethics Committee of Kitasato University Hospital

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