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Verification of the increase in concomitant dysplasia and cancer with the size of sessile serrated lesions

Authors
Daisuke Ohki[1], Yosuke Tsuji[1,2], Hiroyuki Hisada[1], Hideki Nakagawa[1], Satoru Mizutani[1], Kaori Oshio[1], Junichi Sato[1], Dai Kubota[1], Rina Cho[1], Yuko Miura[1], Hiroya Mizutani[2], Yoshiki Sakaguchi[1], Yu Takahashi[1], Seiichi Yakabi[1], Naomi Kakushima[1], Nobutake Yamamichi[1], Tetsuo Ushiku[3], Mitsuhiro Fujishiro[1]

Institutions
1 Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
2 Next-Generation Endoscopic Computer Vision, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Japan
3 Department of Pathology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

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Corresponding author
Dr. Yosuke Tsuji, Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, 113-0033 Tokyo, Japan
ytsujitky@g.ecc.u-tokyo.ac.jp

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ABSTRACT

Background and study aims This study aimed to evaluate the relationship between sessile serrated lesion (SSL) size and the comorbidity rate of SSL with dysplasia (SSLD) and cancer in SSL (SSL-cancer).

Patients and methods This retrospective, single-center analysis identified SSL cases that underwent endoscopic resection between January 2015 and December 2022. The prevalence of SSL, SSLD, and SSL-cancer and their annual trends were assessed. The tumor diameter was stratified as 0 to 5 mm, 6 to 9 mm, 10 to 19 mm, and ≥ 20 mm in size. Furthermore, the frequency of SSL-D/SSL-cancer was determined in each group.

Results The prevalence of SSL was 2.9% (1328/45799). This prevalence was 1.8% (112/6192) in 2015 and 4.2% (230/5500) in 2022, indicating an increasing trend over time. A total of 1825 lesions were assessed: 1751 (96.0%), 55 (3.0%), 14 (0.8%), and 5 (0.3%) of lesions were SSL, SSL with low-grade dysplasia, SSL with high-grade dysplasia and SSL-cancer, respectively. Stratifying the SSLs by size: 0 to 5 mm, 5 to 9 mm, 10 to 19 mm, and ≥ 20 mm, SSLD and SSL-cancer rates were 2.3% (10/429), 2.4% (16/674), 5.3% (31/584), and 11.8% (16/136), respectively. SSLD and SSL-cancer were observed in 2.4% (26/1103) of small SSLs < 10 mm.

Conclusions In cases of SSL, the rate of SSLD and SSL-cancer increased as the lesion diameter increased. A certain rate of SSLD and SSL-cancer was observed even in small SSLs less than 5 mm.

Introduction

Sessile serrated lesions (SSLs) have recently been recognized as precancerous lesions that can lead to colorectal cancer via the serrated pathway. It has been reported that 20% to 30% of all colorectal cancers occur via the serrated pathway [1, 2].

The diagnostic criteria for colorectal serrated lesions have been classified into hyperplastic polyps (HPs), SSL, SSL with dys-

plasia (SSLD), traditional serrated adenoma (TSA), and unclassified serrated adenoma following the revision of the World Health Organization (WHO) classification in 2019 [3].

The prevalence of SSLs is expected to be increasingly reported compared with that before because the 2019 WHO classification revised the definition of a serrated lesion to be one with ≥ 1 unequivocal architecturally distorted serrated crypt. The prevalence of SSL has been reported to vary in recent reports between 2% and 10% [4, 5, 6, 7, 8]. A prospective study from Japan indicated that the prevalence of SSL was approximately 5% [9]. The proportion of SSLD and cancer in SSL (SSL-cancer) in patients with SSL has been reported as follows: approximately 5% to 14% for SSLD and 0.9% to 1.3% for SSL-cancer [10, 11, 12]. In cases in which SSL was accompanied by dysplasia, the rate of subsequent progression was high [13, 14].

Regarding endoscopic findings, in recent years, there have been some reports revealing that SSLD and SSL-cancer can be endoscopically differentiated from SSLs [15, 16]. SSL manifests as JNET type 1 according to the Japan narrow-band imaging (NBI) expert team (JNET) classification and exhibits a type II or type II open-pit pattern according to Kudo's classification using crystal violet staining. Accompanied by dysplasia or carcinoma, lesions manifest redness, with double elevation and nodules. Moreover, magnified NBI (M-NBI) of the same area may show neoplastic patterns (JNET 2A/2B/3) and neoplastic pit patterns (IIIL/IV/Vi irregularities) using crystal violet staining [17]. On the other hand, it has been reported that both SSL and HP manifested JNET type 1 and were difficult to differentiate [18]. Similarly, regarding SSLD or carcinoma, it remains controversial whether even lesions < 1 cm in size can be reliably differentiated preoperatively.

The resection method for SSL is selected according to lesion size and situation, including cold snare polypectomy (CSP), endoscopic mucosal resection (EMR), and endoscopic submucosal dissection (ESD). However, it is currently unclear whether ESD is necessary for en bloc resection of large SSLs. Recently, methods such as piecemeal CSP have been reported. There is a report showing that the local recurrence rate did not differ between EMR and piecemeal CSP for SSLs ≥ 20 mm (6 months: 4.3% versus 4.6%, 18 months: 2.0% versus 1.2%) [19]. Another previous report indicated that piecemeal CSP was performed for SSLs excluding lesions suspected of dysplasia endoscopically, without recurrence after a median observation period of 7 months [19, 20]. In the same study, ESD was performed for lesions with suspected dysplasia.

Cancer comorbidities increase with the size of adenomatous lesions [21, 22, 23]. In addition, diagnosis of cancerous areas in small lesions can be made using magnified NBI endoscopy and chromoendoscopy with crystal violet staining. Therefore, it is acceptable to resect many small lesions using CSP. However, large lesions may not allow accurate localization of cancerous areas, [24] for which en bloc resection using ESD is recommended.

With regard to SSL, there are a few reports which suggest that the incidence of SSLD and SSL-cancer differs depending on the size of the lesion [25], but data are still lacking.

This study aimed to evaluate the relationship between SSL lesion size and the comorbidity rate for dysplasia and cancer.

Patients and methods

Study design

This was a single-center, retrospective, observational study. Data on SSL cases that underwent endoscopic resection (ER) at the University of Tokyo Hospital between January 2015 and December 2022 were collected from electronic medical records. The inclusion criteria were lesions resected using colonoscopy at our hospital with a pathological diagnosis of SSL, SSLD, or SSL-cancer. When multiple endoscopies were performed per year, they were combined into a single annual examination.

The retrospective analysis of each patient's medical record was comprehensively approved by our Ethics Committee (Ethics Review No. 2058), and written informed consent was waived. The study was conducted in accordance with the principles of the Declaration of Helsinki. All patients were guaranteed the opportunity to decline participation through opting out.

Pathological diagnostic criteria, pathology specimen handling and measurement methods

Histological examinations were performed by several skilled pathologists according to the Japanese Society for Cancer of the Colon and Rectum (JSCCR) classification for cases up to 2018 and according to the 2019 WHO classification after 2019.

In the JSCCR classification, SSL had two or more of the following features in more than 10% of the serrated area: 1) dilated crypt; 2) irregularly branching crypt; and/or 3) dilation of the base of the crypt which often has a boot, L, or inverted T shape.

In the 2019 WHO classification, SSL was defined as a serrated lesion with ≥ 1 unequivocal architecturally distorted serrated crypt. A distorted crypt was defined as one that showed at least one of the following characteristics: 1) horizontal growth along the muscularis mucosae; 2) dilation of the crypt base; 3) serration extending into the crypt base; or 4) asymmetrical proliferation. SSLD was defined as having "intestinal dysplasia" with the cytologic features seen in conventional colorectal adenomas, or "serrated dysplasia" characterized by nuclei that are also atypical but rounder with prominent nucleoli, eosinophilic cytoplasm, and increased mitotic activity.

SSLD and SSL-cancer were defined as follows. In Japan, intramucosal carcinoma is treated as cancer in daily clinical practice. However, according to the WHO 2019 criteria, intramucosal carcinoma is included in the category of dysplasia in SSL. Considering the usual clinical practice in Japan, and as previously reported [25], we further divided SSLDs into two categories. We classified SSL-Tis cancer as "SSL with high-grade dysplasia" and those with weak atypia were classified as "SSL with low-grade dysplasia." The coexistence of invasive carcinoma in SSL was classified as "SSL-cancer."

As for SSLD and SSL-cancer, the slides were reevaluated according to the WHO 2019 classification by one gastrointestinal pathologist again for the current study.

Pathology specimen handling methods were as follows. Polyps were fixed in 10% formalin as soon as they were removed and remained in place overnight. ESD and EMR specimens were fixed by attaching them to a cork to prevent them from being overextended. After fixation, the specimen was split at 2- to 3-mm intervals, paraffinized, and a tissue specimen was prepared. The size of the tumor was measured under the microscope and noted in the pathology report.

Endoscopic resection

In the present study, ER included CSP, EMR, or ESD. The method that was used for resection depended on lesion size and endoscopic findings, for which the final decision was made by the endoscopist. At our hospital, we attempted en bloc resection of lesions as much as possible, without selecting planned endoscopic piecemeal mucosal resection and piecemeal CSP.

Our institution's polyp resection policy is to remove all detected polyps > 5 mm. Polyps < 5 mm are also basically resected if detected, but some endoscopists follow up JNET type 1 polyps < 5 mm in the distal colon and rectum.

The video processor units EVIS LUCERA SPECTRUM, EVIS LUCERA ELITE, EVIS X1 (Olympus Corporation, Tokyo, Japan), and a single-channel lower gastrointestinal endoscope (PCF-H290ZI, PCF-H290I, PCF-PQ260L, PCF-H290TI, CF-HQ290ZI, PCF-Q260AZI, and PCF-Q260AI) were used.

Disposable high-frequency snare SnareMaster Plus (Olympus Co.), Captivator COLD (Boston Scientific), and COLD SNARE (MC Medical) were used for resection. IN addition, disposable high-frequency knife DualKnife, DualKnife J (KD-655Q or KD-655L, Olympus Co.) and IT-nano knife (KD-612L, Olympus Co.) were used for dissection. For local injection, MucoUP (Boston Scientific, Tokyo, Japan) or K smart (Olympus Co.), a sodium hyaluronate solution, was used for ESD. In addition, saline was used for EMR.

Evaluation items

In this study, we performed both patient- and lesion-based analyses.

In regard to the patient-based analysis, the evaluation items were age at diagnosis, sex, histological diagnosis, tubular adenoma comorbidity rate, TSA comorbidity rate, colorectal cancer (CRC) comorbidity rate, and endoscopic indication. With respect to patient-based analysis, information about the most malignant lesions was used when multiple SSLs were resected during a single session. If the grade of malignancy was the same, lesions with larger tumor diameters were used. If the tumor diameter was also the same, deeper lesions were used. We also calculated the combined prevalence of SSL, SSLD, and SSL-cancer and evaluated their annual trends. The number of patients with serrated polyposis syndrome (SPS) in the overall population was also evaluated. SPS was defined as ≥ 5 serrated polyps/lesions proximal to the rectum, all ≥ 5 mm in size, with at least two ≥ 10 mm in size or > 20 serrated polyps/lesions of any size distributed throughout the large bowel, with ≥ 5 proximal to the rectum, according to the WHO 2019 classification.

Regarding lesion-based analysis, the following parameters were used: histological diagnosis, tumor diameter, location, gross type, ER method, and histopathological margins of the resected specimen. Gross types were defined as follows: 0-Is and 0-Ip types as protruded types and 0-IIa and 0-IIb as flat types. If lesions were mixed, such as 0-IIa + Is lesions, the type of the more predominant component was used.

The proximal colon was defined as the area proximal to the splenic flexure (the transverse colon, ascending colon, and cecum), whereas the distal colon was defined as the area distal to the splenic flexure (the descending colon, sigmoid colon, and rectum). Lesions that were biopsied only for diagnostic purposes and those that were not resected were excluded. Lesions resected using cold forceps polypectomy (CFP) were also excluded because their sizes were not mentioned in the pathology report. Tumor diameter was stratified as 0 to 5 mm, 5 to 9 mm, 10 to 19 mm, and ≥ 20 mm. The frequency of SSL-D/SSL-cancer was determined in each group.

Results

Characteristics of histopathologic lesions

The patient-based analysis showed 1328 patients with SSL during the observation period (2015–2022), with 1259 (94.8%) for SSL, 51 (3.8%) for SSL with low-grade dysplasia (SSL with LGD), 13 (1.0%) for SSL with high-grade dysplasia (SSL with HGD) and five (0.4%) for SSL-cancer. Age at diagnosis was 63.1 ± 13.0 years in patients with SSL, 66.6 ± 14.0 years in those with SSL with LGD, 71.7 ± 9.8 years with SSL with HGD and 75.0 ± 3.2 years in those with SSL-cancer, with age increasing as the pathologic grade increased. Fourteen of the patients fell into the diagnosis of SPS.

Adenoma coexisting elsewhere in the colon was present in 46.0% of the patients (611/1328), CRC in 7.0% (93/1328), and TSA in 2.5% (33/1328). **Supplementary Table 1** presents the results of patient-based histopathological types.

The lesion-based analysis showed 1825 lesions overall, 1751 (96.0%) with SSL, 55 (3.0%) with SSL with LGD, 14 (0.8%) with SSL with HGD and 5 (0.3%) with SSL-cancer. All four types of SSLs were more frequently observed in the proximal colon than in the distal colon (SSL: 1251/1751 [71.4%]; SSL with LGD: 47/55 [85.5%]; SSL with HGD: 12/14 [85.7%] and SSL-cancer: 5/0 [100%]). The rates of complete resection with the tumor-free margin were 867 of 1751 (49.5 %) for SSLs, 24 of 55 (43.6 %) for SSLs with LGD, nine of 14 (64.3 %) for SSLs with HGD, and three of five (60.0%) for SSL-cancer ▶ **Table 1** presents the results for each lesion-based histopathological type analysis.

Annual trends in SSL prevalence

During the entire observation period, 1328 patients with SSL were confirmed, and 45,799 lower endoscopies were performed during the same period, with a prevalence of 2.9%. ▶ **Table 2** presents the changes in prevalence by year. The prevalence was 1.8% (112/6192) in 2015 and 4.2% (230/5500) in 2022, indicating an increasing trend over time.

▶ **Table 1** Characteristics of each lesion by histopathology type.

	SSL	SSL with LGD	SSL with HGD	SSL-cancer (%)	Total
N (%)	1751 (96.0)	55 (3.0)	14 (0.8)	5 (0.3)	1825
Mean tumor size (mm)	9.5 ± 6.2	13.9 ± 9.5	12.9 ± 6.9	15.8 ± 7.1	9.7 ± 6.4
Location: proximal/distal (% proximal)	1251/500 (71.4)	47/8 (85.5)	12/2 (85.7)	5/0 (100)	1315/510 (72.1)
Morphology: flat type/protruded type (% flat type)	1469/282 (83.9)	44/11 (80.0)	7/7 (50.0)	3/2 (60.0)	1523/302 (83.5)
Resection methods: CSP/EMR/ESD	724/851/176	18/19/18	3/8/3	0/3/2	745/881/199
Margin (total): negative/X/positive (% negative)	867/795/89 (49.5)	24/27/4 (43.6)	9/4/1 (64.3)	3/0/2 (60.0)	903/826/96 (49.4)
Margin (cancer): negative/X/positive (% negative)	n/a	n/a	n/a	5/0/0 (100)	

SSL, sessile serrated lesion; SSL with LGD, SSL with low-grade dysplasia; SSL with HGD, SSL with high-grade dysplasia; CSP, cold snare polypectomy; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; CRC, colorectal cancer; M, intramucosal; SM, submucosal.

▶ **Table 2** Prevalence of SSL: time trend.

Year	SSL	Number of colonoscopies	Prevalence
2015	112	6192	1.8
2016	138	6557	2.1
2017	133	6094	2.2
2018	145	5730	2.5
2019	174	5554	3.1
2020	188	4553	4.1
2021	208	5619	3.7
2022	230	5500	4.2
Total	1328	45799	2.9

SSL, sessile serrated lesion.

Characteristics of lesions for each endoscopic resection method

During the observation period, CSP was performed for 745 lesions, EMR for 881 lesions, and ESD for 199 lesions. CFP and diagnostic biopsies were performed on 50 lesions, which were excluded from analysis as described above. ▶ **Table 3** presents the results of each ER method. The mean tumor diameter was 6.3 ± 2.7 mm (CSP); 9.5 ± 3.4 mm (EMR); and 22.8 ± 8.9 mm (ESD). The rates of complete resection with histopathological margin free were as follows: 27.7% (206/745) in CSP; 60.8% (536 /881) in EMR; and 80.9% (161/199) in ESD. Of the 745 CSP cases, SSL with LGD was confirmed in 18 (2.4%) and SSL with HGD in 3 (0.4%).

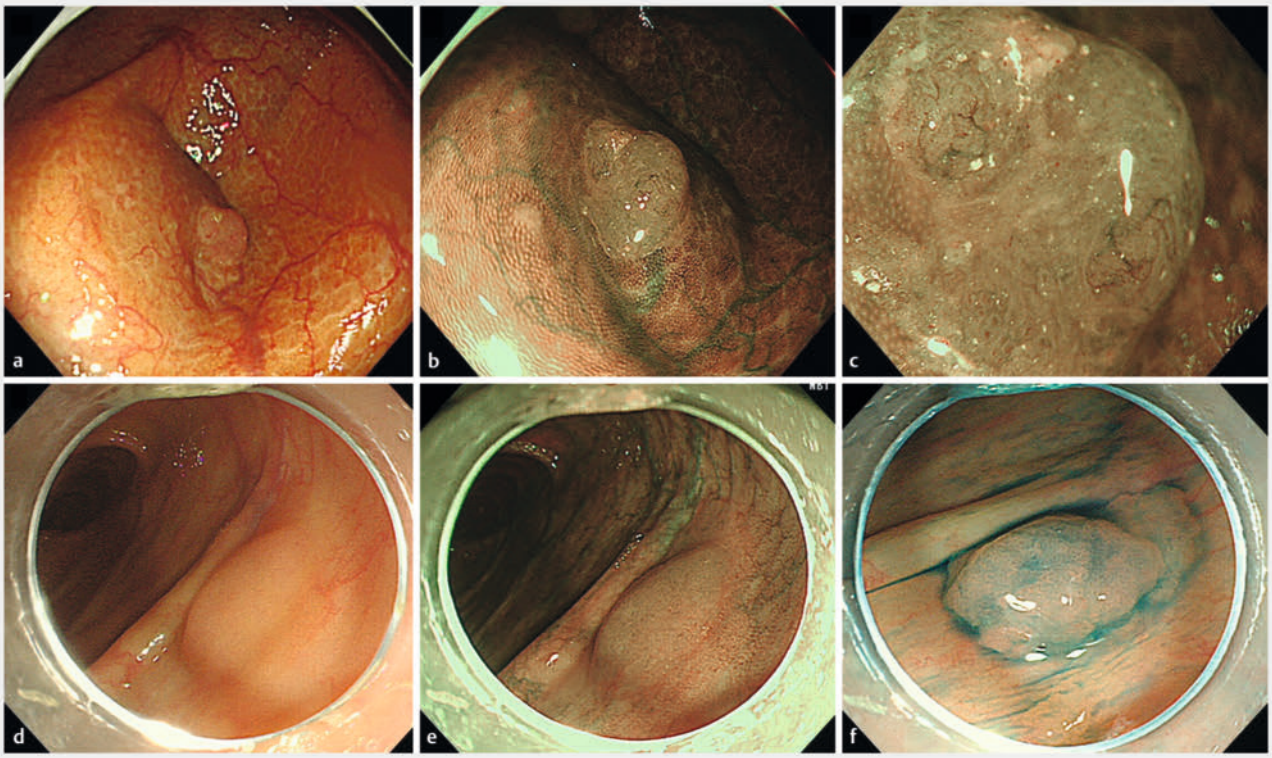
Clinical features of SSL with HGD and SSL-cancer

During the observation period, SSL with HGD and SSL-cancer was observed in 19 patients. The characteristics of the lesions are listed in **Supplementary Table 2**. Of the 19 lesions, 14 (73.7%) were SSL with HGD and five (26.3%) were submucosal invasive cancer. Of the 19 lesions, six (31.6%) were < 10 mm in diameter and three (15.8%) underwent CSP. All three lesions re-

▶ **Table 3** Characteristics of each lesion by resection method.

	CSP	EMR	ESD
N	745	881	199
Mean tumor size (mm)	6.3 ± 2.7	9.5 ± 3.4	22.8 ± 8.9
Pathology: SSL/SSL with LGA/SSL with HGD/SSL-cancer	724/18/3/0	851/19/8/3	176/18/3/2
Location: proximal/distal (%proximal)	457/288 (61.3)	678/203 (77.0)	180/19 (90.5)
Morphology: flat type /protruded type (% flat type)	607/138 (81.4)	727/154 (82.5)	189/10 (95.0)
Margin (total): negative/X/positive (% negative)	206/527/12 (27.7)	536/69/276 (60.8)	161/23/15 (80.9)

SSL, sessile serrated lesion; SSL with LGD, SSL with low-grade dysplasia; SSL with HGD, SSL with high-grade dysplasia; CSP, cold snare polypectomy; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.



▶ **Fig. 1** Endoscopic findings of SSL with **a–c** low-grade dysplasia and **d–f** SSL with high-grade dysplasia (intramucosal cancer). **a** White-light imaging of the I–I lesion approximately 5 mm in the cecum. **b** Narrow-band imaging of the lesion. **c** Narrow-band imaging combined with magnifying lesion endoscopy. Mucus and dust adhere to the surfaces of the lesions. Dilated vessels and crypts are observed on the surfaces of the lesions. **d** White-light imaging of a IIa lesion approximately 7 mm in the ascending colon. A PCF-PQL scope is used because the patient has difficulty inserting the scope. **e** Narrow-band imaging of the lesion. **f** Chromoendoscopy of lesions. Dilated crypts are observed on the surface of the lesions.

sected with CSP had indeterminate or positive margins, but no local recurrence was observed in colonoscopy during the median follow-up period of 32 months. One lesion had a small tumor diameter of 6 mm, and deep submucosal invasion with 1100 µm was observed. The average tumor diameter of SSL with HGD was 12.9 ± 6.9 mm, and that of submucosal invasive cancer was 15.8 ± 7.1 mm. Of the five submucosal invasive cancer lesions, invasion depth of ≥ 1000 µm was found in three (60.0%), lymphovascular invasion in four (80%), and budding grade 2 in one (20.0%).

Dysplasia/cancer comorbidity rate by SSL size

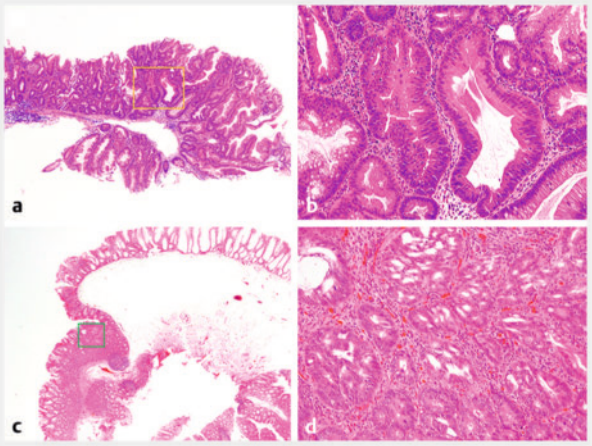
The frequency of SSLD and SSL-cancer when stratified by size is listed in ▶ **Table 4**. The rates of SSLD and SSL-cancer were as follows: 2.3% (10/429) in 0 to 5 mm; 2.4% (16/674) in 6 to 9 mm; 5.3% (31/584) in 10 to 19 mm; and 11.8% (16/136) in > 20 mm.

Typical endoscopic images of SSL with low-grade dysplasia and SSL with HGD (intramucosal cancer) from 0 to 9 mm each are shown in ▶ **Fig. 1**, and pathological images are shown in ▶ **Fig. 2**. As for the lesions > 10 mm, nodules or double elevation and reddish color tended to be observed. Regarding the smaller lesions (0–9 mm), double elevation was found in some lesions, but it was difficult to accurately predict whether there was concomitant dysplasia or cancer component. **Supplementary Table 3** shows whether or not SSL-cancer/SSLDs < 10 mm has endoscopic findings of reddish area and double elevation.

Discussion

To the best of our knowledge, there are few reports about rates of SSLD and SSL-cancer comorbidity according to the size of SSLs [25]. In adenomas, the rate of advanced neoplasia has been reported to increase with size [21, 22, 23]. The rate carcinoma reported from Japan was 0.5% for diminutive polyps (0–5 mm), 3% for small polyps (6–9 mm), and 25.2% for large polyps (> 10 mm) [26]. The present study revealed that the proportion of SSLD and SSL-cancer increased with increasing size (▶ **Table 4**) although the frequency of SSLD and SSL-cancer was not as high as that of advanced neoplasia of adenomas. Murakami et al. also reported that the frequency of dysplasia or carcinoma increases as the size of SSL increases (0.9% in < 5 mm; 7.6% in 6 to 10 mm; 9.9% in 11 to 15 mm; 12.4% in 16 to 20 mm; 15.3% in > 21 mm) [25]. The rate of SSLD and SSL-cancer < 5 mm was lower than in our study.

In the present study, in SSL cases, SSLD and SSL-cancer were observed in 2.4% of lesions with diminutive polyps, indicating



▶ **Fig. 2** Histopathological findings of SSL with **a,b** low-grade dysplasia and **c,d** SSL with high-grade dysplasia (intramucosal cancer). **a** SSL with low-grade dysplasia (hematoxylin-eosin stain×40). The area enclosed by the orange squares represents the dyplastic component. Orange squares, magnified 200 ×, represent **b**. **b** A higher-power image of the dysplastic component (hematoxylin-eosin stain×200). **c** SSL with high-grade dysplasia (intramucosal cancer) (hematoxylin-eosin stain×20). The area enclosed by the green squares represents the high-grade dysplasia (inrramucosal cancer) component. The green squares, magnified 200 ×, are denoted as **d**. **d** A higher-power image of the high-grade dysplasia (inrramucosal cancer) component (hematoxylin-eosin stain×200).

that the rate of SSLD and SSL-cancer in patients with diminutive SSL polyps was higher than that in those with adenomas. There is also a report from Japan indicating that a diminutive polyp suspected to be an HP turned out to be an inapplicable lesion for ER 10 years later [27]. Therefore, even small serrated lesions require attention. With regard to the diminutive SSL polyps, the frequency of dysplasia and cancer remains a matter for further study. In some cases, it is difficult to distinguish the presence of a dysplastic or cancerous component from the endoscopic findings, which implies that resection for diminutive SSL polyps is preferable if possible.

We think that our study is useful in showing that even small SSLs have high malignant potential and should be treated with caution.

The frequencies of SSL, SSLD, and SSL-cancer between 2015 and 2022 were evaluated in this study. Using patient-based analysis, the frequencies of SSL with LGD, SSL with HGD, and SSL-cancer in all patients with SSLs were 3.8%, 1.0% and 0.4%, respectively, whereas using a lesion-based analysis, the frequencies of SSL with LGD, SSL with HGD, and SSL-cancer were 3.0%, 0.8%, and 0.3%, respectively, in agreement with the previous reports [11, 12].

The prevalence of SSL was approximately 2.9% over the entire observation period, consistent with previous reports [6, 7, 9]. The annual trends were 1.8% in 2015, 2.5% in 2018, and 4.2% in 2022, indicating an upward trend over time. Previous reports have shown that the prevalence of SSLs increased over time [4, 5, 8]. One possible reason for this increase over time was that the concept of serrated lesions and their recognition as potentially malignant lesions has been disseminated; endoscopists have become more careful in their search for serrated lesions, and the rate at which they resect lesions they recognize has also increased. In addition, the pathological diagnostic criteria for SSL at our hospital changed from the JSCCR classification to the WHO classification in 2019, which is considered to be one of the reasons for the increased prevalence of SSL.

SSL with HGD (intramucosal cancer) and SSL-cancer was observed in 19 lesions, five of which had submucosal invasion. In addition, three of the five lesions had a depth of invasion ≥ 1000 µm, and four lesions (80.0%) were LVI-positive, suggesting that the SSL-cancer progressed rapidly. Therefore, aggressive endoscopic therapeutic intervention at the precancerous stage would be desirable.

For both SSLD and SSL-cancer, some areas of nodule or double elevation and reddish color were observed for lesions with relatively large tumor diameters. However, SSL with LGD, SSL with HGD, and SSL-cancer accounted for a large proportion of small lesions (< 10 mm), accounting for 36.4% (20/55), 26.3% (5/14), and 20.0% (1/5), respectively. One small lesion each of SSL with low-grade adenocarcinoma and SSL with high-grade adenocarcinoma (intramucosal cancer) is shown in ▶ **Fig. 1**. However, it was considered difficult to accurately predict preoperatively if there was a dysplastic or cancerous component.

▶ **Table 4** Frequency of each histopathology type when stratified by lesion size.*

Tumor size (mm)	SSL	SSL with LGD	SSL with HGD	SSL-cancer (%)	SSLD + cancer	Total
0–5	419	8 (1.9)	2 (0.5)	0	10 (2.4)	429
6–9	658	12 (1.8)	3 (0.4)	1 (0.15)	16 (2.4)	674
10–19	553	23 (3.9)	6 (1.0)	2 (0.34)	31 (5.3)	584
> 20	120	11 (8.1)	3 (2.2)	2 (1.5)	16 (11.8)	136
Total	1750	54	14	5	73	1823

SSL, sessile serrated lesion; SSLD, sessile serrated lesion with dysplasia; SSL with LGD, SSL with low-grade dysplasia; SSL with HGD, SSL with high-grade dysplasia.
*Two lesions were excluded because they were multi-segmented at specimen collection, and their exact size was unknown.

ER for SSL is performed by selecting CSP, EMR, or ESD according to the size and localization. CSP has been reported to have higher rates of incomplete resection and positive or unknown margins compared with EMR [28]. Reports from Japan indicated that the CSP and EMR margin indeterminate/positive rates were 57% and 38%, respectively [29]. According to the same report, SSL was a risk factor for indeterminate/positive margins. The present results also showed low negative margin rates for CSP and EMR at 27.7% and 60.8%, respectively. The morphological characteristics of SSL may have also contributed to the difficulty in accurately recognizing their edges compared with adenomas. When ER is performed for a lesion in which SSL is considered, it should be performed carefully, such as resection with a large margin.

With regard to the resection method of SSL, CSP for lesions < 10 mm in size, including both diminutive and small polyps, is considered acceptable, similar to what is acceptable for adenoma [30]. However, CSP has a low rate of negative margins with a reported local recurrence rate of 1.4% after CSP for adenomatous lesions [31]. In advanced neoplasia, the local recurrence rate has been reported to be as high as 6%to 13.3% [32, 33]. Moreover, pathologically positive margins have been reported to be a risk factor for local recurrence. Therefore, careful follow-up is required if the pathological evaluation after CSP reveals dysplasia or carcinoma with indeterminate-positive margins.

The frequency of SSLD and SSL-cancer in lesions measuring > 20 mm was 11.8%. Although the frequency of SSLD and SSL-cancer was lower than that for advanced neoplasia of adenomas of the same size, this should be noted. A report from Japan showed that colorectal ESD could be performed safely, had an excellent short-term prognosis, and did not cause local recurrence in the long term [34], suggesting that en bloc resection with ESD may be considered for SSLs > 20 mm. In the same report, en bloc resection was also considered desirable because piecemeal resection and pathologically positive margins increased the risk of local recurrence by eight times. Although some recent reports have shown that piecemeal CSP did not cause local recurrence, the median observation period was not long enough [35]; it was considered necessary to carefully judge its indications.

A limitation of this study is that it was a single-center retrospective analysis. In the future, prospective studies of SSL lesions will be necessary. Second, the quality of the images used in this study was not necessarily high. One of the reasons for this may be that endoscopists did not predict that small lesions, in particular, would be highly atypical. Further assessment would be essential in order to investigate whether dysplasia and cancer could be confirmed preoperatively even in small SSLs with magnifying endoscopy.

Third, polyps of the distal colon and rectum with JNET type 1 were not resected by some endoscopists and were followed up. Therefore, the actual SSL prevalence could be much higher. Fourth, JSCCR classification was used before 2018 and the WHO 2019 classification was used after 2019. However, all slides for SSLD and SSL-cancer were reviewed by a gastrointestinal pathologist, and the WHO 2019 classification was confirmed for these lesions. The gastrointestinal pathologist who read the SSL cases confirmed that most cases of SSL without dysplasia met the diagnostic criteria for both the JSCCR and WHO classifications.

When the JSCCR classification was being used at our hospital, the diagnosis of "serrated lesion" was given to lesions with a dilated or irregular branch at the base of the crypt, but which could not be ruled out as SSA/P. Serrated lesions may be SSLs because the WHO 2019 revised classification has a larger range of lesions to cover. There were only 114 cases of serrated lesions. The effect on prevalence was considered to be small and did not have a significant impact on the direction of the current results.

Conclusions

In conclusion, as with adenomas, the frequency of dysplasia and cancer increases with increasing size in SSL. And SSL has a certain rate of dysplasia and cancer even in diminutive polyps < 5 mm.

Conflict of Interest

The authors declare that they have no conflict of interest.

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