A long-term follow-up study on the prognosis of endoscopic submucosal dissection for colorectal laterally spreading tumors

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Background and Aims: Colorectal laterally spreading tumors (LSTs) are divided into homogeneous (LST-G-H), nodular mixed (LST-G-M), flat elevated (LST-NG-F), and pseudodepressed (LST-NG-PD) subtypes. We hypothesized that based on the rates of advanced histology, the recurrence rates of the LST-NG-PD and LST-G-M groups may be higher than those of the other subgroups.

Methods: Endoscopic submucosal dissection (ESD) was performed in 156 patients with a total of 177 LSTs. The clinicopathological features and long-term prognosis of ESD according to specific subtype were investigated.

Results: LSTs were most commonly found in the rectum, and the highest percentage of rectal lesions was observed in the LST-G-M group (71.1% vs overall 55.4%, $P = .032$). The LST-G-M lesions were larger (60 ± 22 mm vs 40 ± 33 mm, $P = .034$) than the LST-G-H lesions. The LST-G-M group also demonstrated more high-grade intraepithelial neoplasias (32.2% vs 10.8%, $P = .003$) and submucosal carcinomas (13.6% vs 1.5%, $P = .010$) compared with the LST-G-H group. The LST-NG-PD group exhibited the highest incidence of submucosally invasive cancer (16.7%). The overall perforation rate was 2.3%. The perforation rate in the LST-NG group was higher than that in the LST-G group (5.7% vs 0.8%, $P = .047$). All recurrences (7.7%) were found by colonoscopy without any detection of cancers, and no difference was found among the subtypes.

Conclusions: No significant differences were observed among subgroups with 44.4 ± 16.3 months of follow-up. Considering that all recurrences were discovered by colonoscopy and most could be cured by repeated ESD, the LSTs of all subgroups require more intensive follow-up compared with smaller adenomatous lesions. (Gastrointest Endosc 2016;83:800-7.)

A colorectal laterally spreading tumor (LST) is a flat and broad-based lesion, 1 cm or greater in diameter that extends laterally and circumferentially along the colorectal wall rather than perpendicular to it.[1] It should receive considerable attention because of its high malignant potential.[2–5] Endoscopic submucosal dissection (ESD) is the standard treatment for LSTs.[6,7] In 2008, Kudo et al[8] divided LSTs into 4 subtypes based on different surface morphologies. Considerable medical literature shows that the risk of containing advanced histology significantly increases in some LST subgroups. For example, malignant transformation and premalignant lesions (high-grade intraepithelial neoplasia/carcinoma in situ [HGIN/CIS]) were reported frequently in the LST pseudodepressed (LST-NG-PD) and LST nodular mixed (LST-G-M) groups.[9–13] The proportion of submucosa-massive lesions also reportedly increases in the LST-NG-PD group.[13,14] We hypothesized that based on rates of advanced histology, the recurrence

Abbreviations: CIS, carcinoma in situ; ESD, endoscopic submucosal dissection; HGIN, high-grade intraepithelial neoplasia; LST, laterally spreading tumor; LST-G-H, laterally spreading tumor homogeneous; LST-G-M, laterally spreading tumor nodular mixed; LST-NG-F, laterally spreading tumor flat elevated; LST-NG-PD, pseudodepressed laterally spreading tumor.

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rates of the LST-NG-PD or LST-G-M group may be higher than those of the other subgroups. In this study, we performed a retrospective analysis of the outcome and a prospective analysis of the long-term prognosis of LST patients undergoing ESD and assessed the clinicopathological features of the different subtypes of LSTs.

MATERIALS AND METHODS

General information

A retrospective analysis of LST patients with ESD was carried out at our hospital from January 2003 to December 2007. During this initial period, no international accepted guidelines were available for the treatment of colorectal LSTs or large polyps. Polypoid and nonpolypoid lesions were discovered by colonoscopy. Hot biopsy, polypectomy, EMR, or piecemeal EMR were used for lesions smaller than 30 mm with no routine staining. Lesions larger than 30 mm were identified by ESD after staining and observation by a senior endoscopist (E.-D.Y.). Surgery was performed instead of ESD when one of the following situations occurred: (1) a nonlifting sign after submucosal injection; (2) an invasive type V pit pattern; and (3) a biopsy-confirmed local canceration.[15] LSTs are defined as lesions greater than 10 mm in diameter. However, all patients included in this study had lesions larger than 30 mm because smaller LSTs were not stained and treated with ESD at our hospital at that time.

Classification of LSTs

LSTs were divided into 2 subtypes according to endoscopic features: LST-G with nodules or granules distributed evenly or not on the surface of the lesion and LST-NG with a smooth surface and no nodules or granules. In 2008, Kudo et al,[8] further divided the former subtype into homogeneous (LST-G-H) and nodular mixed (LST-G-M), and the latter subtype was divided into flat-elevated (LST-NG-F) and pseudodepressed (LST-NG-PD) (Fig. 1). In this study, 2 experienced endoscopists blindly reviewed the endoscopic images of the LST cases. The LSTs were stained, underwent ESD, and were divided into 4 subtypes according to the Kudo et al classification. Consensus was reached by discussion when disagreement arose.

Endoscopic submucosal dissection

All patients were given a complete explanation of the procedure and provided signed written informed consent before the procedure. A needle-knife (KD-10Q; Olympus, Tokyo, Japan) was used in the procedure only during the initial period of ESD at our hospital. A hook-knife and an insulated-tip knife were gradually adopted for incision and separation, and a transparent hood (ST hood) was started to be placed on the top of the endoscope in 2005. We initially chose to snare the lesion after circumferential mucosal incision with a needle-knife in some patients, which is now called a simplified or hybrid ESD,[16] as an introductory step to a full ESD. Indigo carmine (0.4%) or methylene blue (0.5%) was used for the preoperative staining. The surface structures and the type of the openings of colonic crypts were observed before the lesion margin was determined by common electronic colonoscopy or magnifying colonoscopy. Repeated submucosal injections (100 mL of 0.9% saline solution containing 0.4% indigo carmine and 0.0001% epinephrine) were carried out to lift the lesion with an injection needle (NM-4L-1; Olympus). A high-frequency generator (ICC-200; ERBE, Tübingen, Germany) was used for all ESD procedures (Endocut E3, 45-60 W for marginal incisions; forced coagulation E1, 40 W for submucosal dissection). An incision was made along the margin of the lesion by an insulated tip knife assisted by a needle-knife before the submucosal separation. ESDs were performed without intravenous sedation or analgesia. The lesion was pulled open gravitationally by changing the patients' body position without the assistance of an ST hood in some of the cases. Careful hemostasis was observed in visible vessels at the base of the mucosal defect, and hemoclips were used when bleeding or perforation occurred during the operation.

Histopathological assessment

Excised specimens were paraffin embedded and sectioned perpendicularly at 2-mm intervals. Pathological diagnosis was made after hematoxylin and eosin staining and microscopic observation. Assessment criteria included lesion size, invasive depth, presence of fibrotic scar, lymphatic and vascular involvement, and lateral and basal margins with residual adenoma or tumor tissue. En bloc resection is defined as a tumor removed in a single piece. En bloc R0 resection is histologically defined as a tumor removed as a single piece without adenomatous tissue or residual carcinoma at the lateral or deep margins. HGIN/CIS is defined as a lesion with the morphological characteristics of high-grade dysplasia or adenocarcinoma confined to the glandular epithelium or invading the lamina propria without submucosal invasion.[17] Submucosal carcinoma is defined as carcinoma that invades the muscularis mucosa into the submucosa.[17]

Follow-up

This study was approved by the Committee on the Ethics of Biomedicine Research of the Second Military Medical University, Shanghai, China. All of the patients signed the informed consent form for follow-up. All LST patients undergoing ESD were required to undergo follow-up colonoscopy regularly and sign the informed consent form for follow-up. The local recurrence rate, incidence of new primary tumors/polyps in other areas, and overall/disease-specific survival were assessed and analyzed prospectively.

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