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Tip-in endoscopic mucosal resection for large colorectal sessile polyps

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Abstract

Background Tip-in endoscopic mucosal resection (EMR) is a modified EMR technique using which en bloc resection of large colorectal sessile polyps can be performed; however, its usefulness for colorectal sessile polyps of > 20 mm has not been reported. This study examined treatment outcomes of tip-in and conventional EMR for large colorectal sessile polyps of ≥ 20 mm.

Methods This was a retrospective case–control study conducted at a single tertiary center in Japan. Subjects included those with large colorectal sessile polyps of ≥ 20 mm, excluding pedunculated-type polyps, who underwent endoscopic resection between January 2010 and January 2019. The primary outcome was endoscopic treatment outcomes when using tip-in and conventional EMR, and the secondary outcome was the local recurrence rate after endoscopic treatment.

Results Forty-three colorectal lesions were treated using tip-in EMR and 83 using conventional EMR. Tip-in EMR had a significantly higher en bloc resection rate (90.7% vs. 69.8.%), and significantly shorter treatment duration (6.64 ± 0.64 min vs. 10.47 ± 0.81 min) than conventional EMR. However, for lesions > 30 mm, en bloc resection rate was 50.0% and 52.6% for tip-in and conventional EMR, respectively, indicating no significant difference. Perforation rates with tip-in and conventional EMR were 4.6% and 3.6%, respectively, indicating no significant difference. Local recurrence was examined in 80 cases who were followed up for > 6 months after endoscopic resection; recurrence rate was 0% and 7.0% in tip-in and conventional EMR cases, respectively, without significance difference.

Conclusions Tip-in EMR showed high en-block resection rate, particularly in polyps of < 30 mm, and no residual tumor was found. This technique is a potential endoscopic treatment alternative for large colorectal sessile polyps of ≥ 20 mm.

Keywords Tip-in endoscopic mucosal resection · Large colorectal sessile polyp · Recurrence · Pre-cut

In 1973, Deyle et al. [1] reported the strip biopsy technique as an endoscopic treatment method for colorectal tumors, and since then, the technique has been modified, and endoscopic mucosal resection (EMR) is widely used as a minimally invasive treatment method for colorectal adenomas and early colorectal cancers [2–5]. However, conventional EMR has a risk of piecemeal resection for colorectal polyps ≥ 20 mm, and the risk of local recurrence is also reportedly high [6, 7]. According to the European Society of Gastrointestinal Endoscopy (ESGE) clinical guidelines, endoscopic submucosal dissection (ESD) is recommended for adenomas ≥ 20 mm and when superficial invasive cancer is suspected [8] because the size limit for en bloc resection is 20 mm [9].

In recent years, tip-in EMR, which is a modified EMR technique, has been reported as an effective treatment technique for large colorectal sessile polyps [10]. Tip-in EMR is a simple technique applying conventional EMR, and this technique may enable reliable resection of large colorectal sessile polyps in a short duration. However, no studies have examined the effectiveness of tip-in EMR. Therefore, this study aimed to comparatively examine treatment outcomes of tip-in and conventional EMR for large colorectal sessile polyps of ≥ 20 mm.

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Materials and methods

Study design

This was a retrospective case–control study conducted at the St. Marianna University School of Medicine, Kanagawa, Japan, in accordance with the Declaration of Helsinki. The local ethics committee of our hospital approved the study protocol. All authors had access to study data and approved the final draft of the manuscript.

Patients

Study subjects included consecutive patients aged ≥ 18 years who underwent endoscopic resection for large colorectal polyps (≥ 20 mm) at our hospital from January 2010 to January 2019. Cases in which resection was performed via ESD or hybrid ESD as well as pedunculated-type polyp cases were excluded.

Indication criteria for conventional and tip-in EMR

In all cases, detailed observation was performed using dye-spraying magnifying endoscopy 1–2 months before the procedure date on an outpatient basis. Only lesions that satisfied the following conditions were included: those with lesions ≥ 20 mm; those endoscopically diagnosed as adenoma, sessile serrated adenoma/polyp (SSA/P), and mucosal or SM1 cancer; and those in which en bloc resection was judged to be possible. If the lesion was ≥ 20 mm and had a stalk, then polypectomy was planned. If it was judged that en bloc resection by snare was difficult for colorectal sessile lesions, then ESD or hybrid ESD was performed. H260AZI or H290AZI (Olympus Co., LTD, Tokyo, Japan) was used for magnifying endoscopy. For magnifying endoscopic observation, the pit pattern classification by Kudo et al. [11] was used. If cancer was suspected by magnifying endoscopic observation using indigo-carmine, then additional observation using 0.05% crystal violet staining was performed to determine if the cancer exhibited an invasive or a non-invasive pattern, which can be an indicator of submucosal (SM) deeply invasive cancer, according to the report by Matsuda et al. [12]. When a case was diagnosed with SM deeply invasive cancer, endoscopic treatment was not indicated, the case was referred to a surgeon for consultation. Endoscopic treatment was performed at admission and at approximately 1 month after detailed examination.

Endoscopic procedure

Treatment was performed by six endoscopists who had an experience of > 2000 colonoscopy cases each. Endoscopes used were H260AZI or H290AZI (Olympus Co., LTD, Tokyo, Japan), which were the same types as those used for observation. Since 2014, CO_2 gas has been used in all cases during colonoscopy treatment for pain relief by air insufflation [13]. For local injection, either saline or Glyceol® (Chugai Pharmaceutical Co., Tokyo, Japan) was directed used by the endoscopist, and ESG-100 (forced coagulation mode 20 W, pulse cut mode 20 W) (Olympus Co., LTD, Tokyo, Japan) was used as a high-frequency device. For tip-in EMR, 15-mm snare master, 20-mm spiral snare, or 25-mm snare master (Olympus Co., LTD, Tokyo, Japan) was used. After a sufficient local injection, the snare tip was projected by 1–2 mm and a mucosal incision was created on the oral side of the lesion. After this, while fixing the snare tip to the submucosal layer, the snare was expanded while gradually pulling the scope. Once the lateral margin of the lesion was completely secured, the snare was closed while de-airing, and resection was then performed (Figs. 1, 2). After resection, the resection margin was precisely observed using magnifying endoscopy to confirm the absence of any residual tumor, and the wound was closed using clips where possible. After resection, once it was confirmed that there were no symptoms such as abdominal pain or fever, meal was started on the day of resection, and the patient was discharged the following day.

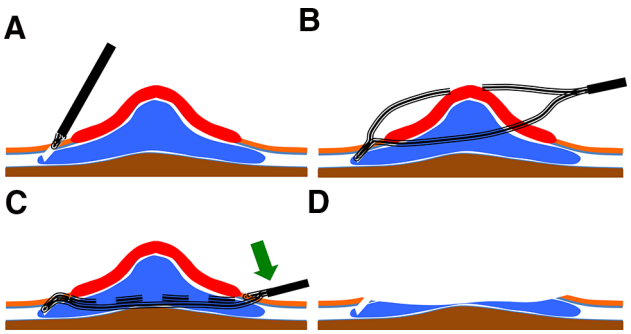

Fig. 1 Tip-in EMR. **A** Following a sufficient local injection into the submucosal layer, project the snare tip 1–2 mm, and create a mucosal incision on the oral side of the lesion. **B** Fixing the snare tip to the submucosal layer, expand the snare while pulling the scope. **C** After confirming that the whole lesion enters within the snare, strangle the snare. **D** Apply electric current and resect the lesion

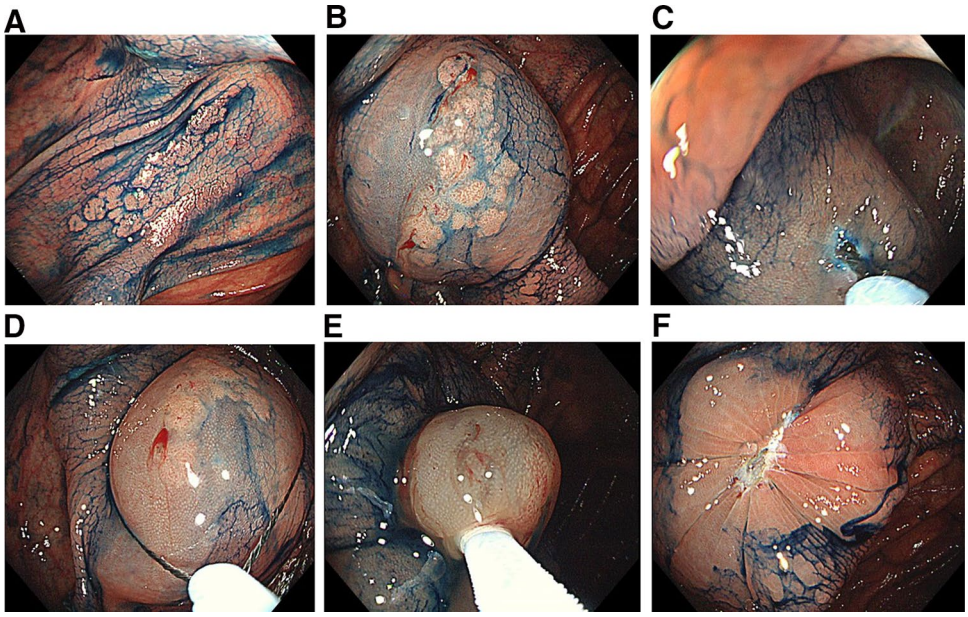

Fig. 2 Tip-in EMR using 15-mm snare master. **A** A 20-mm flat elevated lesion is detected in the ascending colon. **B** Submucosal injection of saline was performed thrice. **C** By projecting the tip of the snare by 2 mm, a mucosal incision is made on the oral side of the lesion. **D** Snare is expanded, and the margin of the lesion is confirmed to be well within the snare. **E** Snaring is performed to confirm that the muscle layer is not involved. **F** En bloc resection of the entire lesion is performed, and it is confirmed that there is no residual lesion

Histological assessment

All resected specimens were formalin-fixed, cut into 2-mm thick sections. Pathological evaluations followed the Japanese Society for cancer of the Colon and Rectum guidelines 2016 [14] and Vienna classification [15]. If both lateral and vertical margins were pathologically negative, then it was defined as R0 resection. Moreover, if tumor cells were identified at the horizontal surgical edge, then it was defined as a lateral margin positive.

Follow-up after endoscopic resection

In case of endoscopic piecemeal resection (EPMR), colonoscopy was performed after 6 months to 1 year, in general, to confirm that there was no residual recurrence. If R0 resection was achieved, then surveillance colonoscopy was performed after 1 year post endoscopic resection. For colorectal cancer with the depth of invasion of SM1, computed tomography (CT) was performed every half a year and colonoscopy once a year, following the Japanese Society for cancer of the Colon and Rectum guidelines, 2016 [14]. For SM deep cancer, additional surgery was recommended as non-curative resection.

Data analysis

Patient data were retrospectively collected using the endoscopy database NEXUS® (FUJIFILM Holdings Co., Tokyo, Japan) and electronic medical records. The primary outcome was endoscopic treatment outcomes when using tip-in and conventional EMR, and the secondary outcome was the local recurrence rate after endoscopic treatment. Endoscopic treatment duration was defined from the start time of injection to the submucosal layer to the completion of resection. In addition, local recurrence after endoscopic treatment was examined only in cases that were followed up for > 6 months.

Statistical analysis

Results are presented as median and average for continuous variables. χ^2-test and Fisher's exact test were used to compare categorical data, and Student's *t* test was used to compare continuous data. $P < 0.05$ was considered to indicate statistical significance. Statistical analyses were conducted using SPSS software (version 22.0; IBM Corp., Armonk, NY, USA).

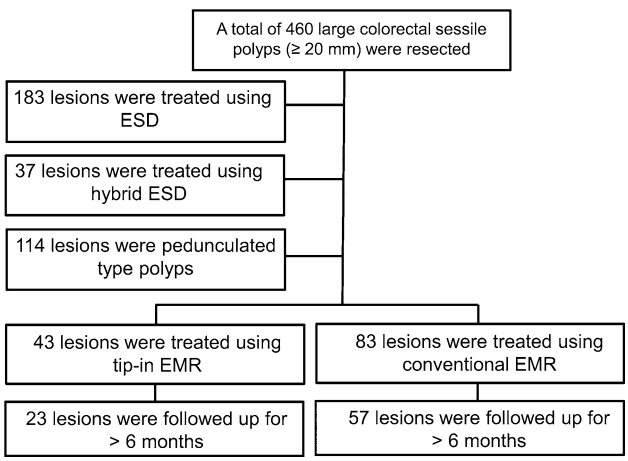

Fig. 3 Flow chart of patient enrolment

Results

Figure 3 shows a chart of patient enrolment. During the study period, endoscopic resection was performed on 460 large colorectal polyps of > 20 mm. Of these, 126 lesions were resected using tip-in or conventional EMR. Moreover, 80 cases were followed up for > 6 months after endoscopic resection. Patient and clinical characteristics are summarized in Table 1. There was no significant difference between the two groups in terms of sex, age, lesion location, macroscopic type, tumor diameter, and pathological findings.

Table 2 shows endoscopic outcomes, which were defined as the primary outcome measure for this study. En bloc resection rate was 90.7% with tip-in EMR and 69.8% with conventional EMR, indicating significantly higher rate with tip-in EMR ($P = 0.008$). The mean treatment duration was 6.64 ± 0.64 min for tip-in EMR and 10.47 ± 0.81 min for conventional EMR, indicating significantly shorter duration for tip-in EMR ($P = 0.005$). In addition, the lateral margin positive rate by pathological evaluation after resection was 32.6% in tip-in EMR cases and 53.0% in conventional EMR cases, indicating significantly lower rate using tip-in EMR ($P = 0.038$). Perforation, observed as a complication, occurred in two lesions (4.6%) in tip-in EMR cases and in three (3.6%) in conventional EMR cases, but the difference was not significant ($P = 0.556$). All cases with perforation were successfully sutured using hemoclips, and additional surgical intervention was not required. Post-procedural bleeding was not observed in either group.

En bloc resection rates by size and location are shown in Table 3. En bloc resection rates for lesions of 20–24 and 25–29 mm by tip-in EMR were 96.4% and 100%, respectively, which were significantly higher than those by conventional EMR of 80.3% and 53.8%, respectively ($P = 0.045/P = 0.023$); however, the rates for lesions > 30 mm by tip-in EMR was 50.0%, which were not significantly different ($P = 0.623$) compared with those by conventional EMR of 52.6%. En bloc resection rates that lesions located in colon and rectum by tip-in EMR were 90.0% and 100%, respectively, which were significantly higher than those by conventional EMR of 69.3% and 45.4%, respectively ($P = 0.030/P = 0.037$); however, the rates that lesions located in cecum by tip-in EMR was 83.3%, which were not significantly different ($P = 0.375$) compared with those by

Table 1 Clinical characteristics of patients

Characteristics	Tip-in EMR ($N = 43$)	Conventional EMR ($N = 83$)	*P*-value
Sex			
Female	21 (48.8%)	33 (39.8%)	0.571
Male	22 (51.2%)	50 (60.2%)	
Age			
Average ± SD	69.9 ± 11.6	68.9 ± 11.8	0.669
Location			
Cecum	6 (14.1%)	10 (12.0%)	0.782
Colon	30 (69.7%)	62 (74.7%)	0.554
Rectum	7 (16.2%)	11 (13.3%)	0.788
Macroscopic type			
Is	11 (25.6%)	28 (33.7%)	0.968
IIa	26 (60.4%)	42 (50.6%)	
Is + IIa	5 (11.6%)	12 (14.4%)	
IIa + IIc	1 (2.4%)	1 (1.3%)	
Macroscopic type			
LST-G	5 (11.6%)	13 (15.7%)	0.602
(Sub classification)			
LST-NG	27 (62.8%)	42 (14.5%)	
Tumor size (mm)			
Average ± SD	22.9 ± 4.1	24.3 ± 5.6	0.149
Pathology			
Adenoma	29 (67.4%)	63 (75.9%)	0.310
SSA/P	13 (30.2%)	16 (19.2%)	0.166
Mucosal cancer	1 (2.4%)	4 (4.9%)	0.660

EMR Endoscopic mucosal resection, *LST-G* laterally spreading tumor granular type, *LST-NG* laterally spreading tumor nongranular type, *SSA/P* sessile serrated adenoma/polyp

Table 2 Clinical outcomes

	Tip-in EMR ($N = 43$)	Conventional EMR ($N = 83$)	*P*-value
En bloc resection rate	39 (90.7%)	58 (69.8%)	0.008
Treatment duration[a] (mean ± SD: min)	6.64 ± 0.64	10.47 ± 0.81	0.005
Lateral margin positive	14 (32.6%)	44 (53.0%)	0.038
Complication			
Perforation	2 (4.6%)	3 (3.6%)	0.556
Delayed bleeding	0 (0%)	0 (0%)	1.000

[a]Time from the start of the submucosal injection to the completion of resection

Table 3 En bloc resection rate by size and location

	Tip-in EMR ($N = 43$)	Conventional EMR ($N = 83$)	*P*-value
Size			
20–24 mm	27/28 (96.4%)	41/51 (80.3%)	0.045
25–29 mm	9/9 (100%)	7/13 (53.8%)	0.023
≥ 30 mm	3/6 (50.0%)	10/19 (52.6%)	0.623
Location			
Cecum	5/6 (83.3%)	10/10 (100%)	0.375
Colon	27/30 (90.0%)	43/62 (69.3%)	0.030
Rectum	7/7 (100%)	5/11 (45.4%)	0.037

Table 4 Follow-up outcomes after endoscopic resection

	Tip-in EMR ($N=23$)	Conventional EMR ($N=57$)	P-value
Endoscopic follow-up time (mean ± SD)	2.0 ± 1.41	2.4 ± 1.45	0.910
Follow-up period (mean ± SD: months)	17.1 ± 8.3	34.4 ± 22.0	0.012
Local recurrence rate	0 (0%)	4 (7.0%)	0.495
Duration until recurrence (mean ± SD: months)	–	5.5 ± 4.15	–

conventional EMR of 100%. Furthermore, there were no statistically significant difference found in the en bloc resection rates between the 6 endoscopists ($P=0.811$).

Table 4 shows local recurrence rates that were defined as the secondary outcome. The number of cases that could be followed up for > 6 months was 23 among tip-in EMR cases and 57 among conventional EMR cases. There was no significant difference between tip-in and conventional EMR cases in the number of endoscopic procedures performed after endoscopic resection [2.0 ± 1.41 and 2.4 ± 1.45, respectively ($P=0.910$)]. In contrast, the follow-up period was 17.1 ± 8.3 months for tip-in EMR cases and 34.4 ± 22.0 months for conventional EMR cases, indicating that conventional EMR cases were followed up for a significantly longer period ($P=0.012$). Local recurrence was not observed in any tip-in EMR case (0%) but was seen in four cases (7.0%) of conventional EMR; however, this difference was not statistically significant ($P=0.495$).

Discussion

In the present study, en bloc resection rate with tip-in EMR was significantly higher than that with conventional EMR in large colorectal sessile lesions of ≥ 20 mm. Furthermore, treatment duration was significantly shorter with tip-in EMR. Thus, tip-in EMR is a useful technique in the treatment of large colorectal sessile polyps of ≥ 20 mm.

In large colorectal sessile polyps of ≥ 20 mm, conventional EMR has a risk of EPMR and a high risk of residual recurrence of 7.4–17% [6, 7, 16, 17]. Therefore, the usefulness of ESD in the treatment of colorectal polyps of ≥ 20 mm has been recently reported because it has a higher en bloc resection rate and lower local recurrence rate than EMR [6, 7]. Theoretically, en bloc resection is possible using ESD, regardless of the size, and is also a useful treatment technique for colorectal polyps of ≥ 20 mm.

In a multicenter prospective study that examined treatment outcomes of colorectal ESD in Japan, a high en bloc resection rate of 88–94.5% was reported [18, 19]. This report suggested that colorectal ESD is already a standardized endoscopic treatment technique in Japan. In addition, in recent years, a higher en bloc resection rate of ESD than EMR has been reported not only in Japan but also in other eastern and western countries [20–24], and it has become a widely used treatment technique worldwide. However, because endoscopic maneuvers for the treatment of colorectal ESD are challenging and because the colon wall is thin, there are concerns of complications such as perforation; this is particularly evident when considering the high perforation rate of 1.6–18% [18, 19, 25–32]. Furthermore, there have been reports of cases requiring surgical treatment when perforation occurred [27]. Moreover, the ESGE guidelines state that ESD should be performed only by physicians with a sufficient experience in endoscopic treatment because colorectal ESD is technically difficult and involves disadvantages such as a high cost and long hospitalization periods [8].

In contrast, tip-in EMR is a simplified technique of conventional EMR, in which treatment can be performed in a short period, similar to the conventional method, and does not require sophisticated techniques required for EMR. Furthermore, because the required device and hospitalization period are the same as those of conventional EMR, no additional cost is required in tip-in EMR, which is an additional advantage.

When resecting large colorectal sessile polyps of ≥ 20 mm using conventional EMR, the snare can be slippery, which thereby increases the risk of piecemeal resection. However, in tip-in EMR, making a pre-cut on the oral side of the lesion and snaring the lesion while fixing the snare tip can make the snare less slippery. The pre-cut prevents the snare tip from raising, making it possible to resect the lesion while securing sufficient margins including the oral side. This is likely the reason for the significantly higher en bloc resection rate with tip-in EMR than with conventional EMR. Furthermore, because the snare is not slippery in tip-in EMR, snare reapplications are less frequent. Therefore, treatment duration can be significantly shortened compared with that of conventional EMR.

However, when performing tip-in EMR, attention should be paid to avoid complications such as perforation. Perforation may occur when the local injection is not successfully completed at the time of initial mucosal incision or when the snare tip is pulled out too long. Therefore, it is important to perform sufficient local injection to the submucosal layer at the time of mucosal incision and to limit the length of the snare tip to approximately 2 mm. In addition, by first fixing the snare tip and then snaring the lesion, the lesion can be more tightly held in tip-in EMR than in conventional EMR. Therefore, when holding the lesion, there may be a higher risk of involving the muscle layer. Therefore, special attention should be paid to a lesion located on a fold. Thus, to

avoid perforation, it is often necessary to sufficiently inject on the first attempt and to try not to tightly grasp the lesion with the snare at the time of resection. In this study, the en bloc resection rate of tip-in EMR of lesions of 20–29 mm was > 96%; however, for lesions > 30 mm, the rate was as low as 50.0%. Tip-in EMR is a technique that uses a snare, which limits the size of possible resected tissue. Results of the present study indicated that other treatment methods, such as ESD or planned EPMR, were necessary for lesion > 30 mm. Furthermore, en bloc resection rates that lesions located in colon and rectum by tip-in EMR were significantly higher than those by conventional EMR; however, the rates that lesions located in cecum by tip-in EMR were not significantly different compared with those by conventional EMR. The cecum is blind end, the lesion sometimes can be observed at right in front of colonoscopy. For lesion that can be seen in right in front of colonoscopy, resection can be also be achieved by conventional EMR, while directly viewing the oral side of the lesion after local injection. For above reason, en bloc resection rates might be high even with conventional EMR in case of cecum. However, this result might be the small subject sample. Therefore, we believe that, in the future, the resection rate should be examined in a larger subject sample.

Although not statistically significant, there were no local recurrences with tip-in EMR, whereas there were four local recurrences with conventional EMR. The mean interval until recurrence was approximately 6 months, which was a similar result as observed in previous reports that examined recurrence after EPMR [6, 33]. All recurrent cases were managed by endoscopic treatment, and none of the cases required surgical treatment. However, cases in which tip-in EMR was performed, the follow-up period was limited. It is necessary to carefully continue follow-up in patients to determine local recurrence.

There are several limitations to this study. First, this was a retrospective single-center study and was not randomized. Second, the subject sample was small, which could have resulted in underestimation or overestimation in the present study results. Further investigation is needed by multicenter prospective study with a larger subject sample in the future. The third was the effect of the learning curve of endoscopists. The present study was conducted over a long period of 10 years, and included six endoscopists within the study period. During this period, we cannot rule out the possibility that the learning curve of endoscopists affected the results. Forth, operators of the endoscopic treatments were limited to experienced endoscopists because the treatments were for large lesions, which could not be performed by inexperienced endoscopists at our hospital. Therefore, it remains to be determined whether this technique is appropriate for non-expert endoscopists. Finally, 37% of cases could not be followed up by endoscopy after endoscopic resection at our hospital. Therefore, in future, it is necessary to prospectively examine the presence or absence of local recurrence by increasing the number of cases.

In conclusion, the en bloc resection rate for large colorectal sessile polyps of ≥ 20 mm was significantly higher and treatment duration was shorter with tip-in EMR than with conventional EMR. Thus, tip-in EMR is a useful treatment method for large colorectal sessile polyps of ≥ 20 mm. Particularly, in case with polyp size of < 30 mm, en bloc resection rate was high with tip-in EMR. Tip-in EMR is a potential endoscopic treatment alternative for large colorectal sessile polyps of ≥ 20 mm.

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Compliance with ethical standards

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