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Advantages of endoscopic submucosal dissection with needle-knife over endoscopic mucosal resection for small rectal carcinoid tumors: a retrospective study

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Abstract
Background Endoscopic submucosal dissection (ESD) is a new, widely accepted method for the treatment of early gastric cancer and was developed to increase the en bloc resection rate. This study aimed to evaluate the efficacy and safety of ESD compared with conventional endoscopic mucosal resection (EMR) for small rectal carcinoid tumors.
Methods A retrospective study was carried out that included 43 patients with small rectal carcinoid tumors (<10 mm). The cohort comprised two groups: Group A ($N = 23$) underwent conventional EMR from January 2004 to August 2005, while group B ($N = 20$) underwent ESD with needle-knife from September 2005 to December 2006. The rate of curative en bloc resection, the procedure time, and the incidence of complications were evaluated.
Results The en bloc resection rate and the rate of completeness of resection of group B were higher than those of group A (100 vs. 87%, 100 vs. 52.5%, respectively). The average operation time required for resection was significantly longer in group B (28.4 ± 17.2 min) compared with group A (12.3 ± 15.4 min) ($p < 0.05$). None of the patients had immediate or delayed bleeding during the procedure. Perforation occurred in one case of group B and the patient recovered after several days of conservative treatment. Three patients had local recurrence after EMR, while no patient experienced recurrence after ESD.
Conclusion ESD, compared with conventional EMR, increased en bloc and histologically complete resection rates and may reduce local recurrence rate for small rectal carcinoid tumors. Increased operation time and complication risks with ESD remain problematic. Further technique and investigation are required to confirm the safety and to assess the long-term prognosis of ESD.

Keywords Rectal carcinoid tumor · Endoscopy · Endoscopic submucosal resection

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With the wide performance of colonoscopy and advances in endoscopy, we are now able to find and diagnose rectal carcinoid tumors at a very early stage [1]. Those that are smaller than 10 mm in diameter and contained within the submucosal layer can be treated by endoscopic resection because they rarely metastasize [2]. However, there is a high risk of incomplete removal or of complications when these tumors are managed by conventional endoscopic mucosal resection (EMR), as most of these tumors are located in the submucosal layer of the rectal wall of the lower portion of the rectum [3]. Incomplete resection of tumors with EMR sometimes results in the need for additional surgery. One-piece resection allows us to make an accurate histological diagnosis as well as to reduce the incidence of unnecessary surgery. The technique of endoscopic submucosal dissection (ESD), being developed for en bloc resection of large lesions in the stomach, has been widely accepted for the treatment of early gastric cancer [4,

5]. Compared with EMR, ESD has the advantages of permitting en bloc and histological complete resection. On the other hand, this method has some disadvantages such as long operating time, high frequency of complications, and the need for a high level of technical skill.

In this retrospective study, we aimed to compare the clinical usefulness of ESD with needle-knife and conventional EMR for treating small rectal carcinoid tumors.

Patients and methods

With the approval of the institutional review board, the selection criteria of the studied cohort were as follows: (1) confirmed histological diagnosis of rectal carcinoid tumors, (2) lesions no larger than 10 mm, (3) the lesions should be contained within submucosal layer, (4) no symptoms of carcinoid syndrome, and (5) no pararectal lymph node and distant metastases found before the procedure. Thus, 43 consecutive patients who underwent endoscopic procedures for rectal carcinoid at Zhongshan Hospital between 2004 and 2006 were enrolled in this study. Endoscopic ultrasonography (EUS) with a high-frequency miniprobe (UM-3R, 20 MHz, Olympus Optical Co., Ltd., Tokyo, Japan) through the biopsy channel of the colonoscopy was performed to evaluate the precise size and the invasion depth of the tumors and to assess whether there had been metastases to the pararectal lymph nodes. Informed consent was obtained from all patients before the procedure was performed.

The cohort was divided into two groups according to the method of endoscopic resection. The conventional EMR method was performed on 23 lesions between January 2004 and August 2005 (group A) and ESD with needle-knife was performed on 20 lesions between September 2005 and December 2006 (group B). Since September 2005, all small rectal carcinoid tumors were resected by ESD in our endoscopy center instead of by conventional EMR. All patients were hospitalized for the endoscopic treatment. Pethidine, hydrochloride, and propofol were given intravenously for sedation with monitoring of cardiorespiratory function during the endoscopic procedure.

EMR was performed with the use of a single-channel colonoscope (CF-Q260, Olympus). Briefly, after injection of submucosal saline containing 0.0025% epinephrine into the base of the lesion, the lesion was tightened with a high-frequency electrosurgical snare. Electronic current was then applied to resect the lesion. For EMR with a cap-fitted panendoscope (EMRC), a transparent cap was attached to the tip of colonoscope, and saline was injected into submucosal layer to elevate the lesion. The lesion was then aspirated, tightened around with a snare, and finally resected with the aid of electrocautery. Lesions larger than 5 mm were resected by EMRC. The artificial ulcer was always carefully trimmed with argon plasma coagulation (APC) after EMR.

ESD was also performed with the use of a single-channel colonoscope (CF-Q260, Olympus). A short transparent cap was attached to the tip of colonoscope to provide a constant endoscopic view and to apply tension to the connective tissue for submucosal dissection. The tip of the needle-knife (KD-10Q-1, Olympus) was bent to cut mucosa and to dissect the rectal submucosal layer. ESD was performed as follows (Fig. 1). (1) Marker dots were made approximately 5 mm away from the lesion. (2) Using a 23-gauge disposable needle, several milliliters of submucosal injection solution (100 ml saline + 5 ml indigo carmine + 1 ml epinephrine) were injected around the lesion to lift it off the muscularis propria layer. (3) The mucosa was then incised outside the marker dots using the needle-knife. (4) The submucosal connective tissue beneath the lesion was gradually dissected from the muscularis propria layer with the needle-knife. Solution was injected repeatedly during the dissection if necessary. Finally, the lesion was resected completely from the muscularis propria layer with the needle-knife. Exposed vessels on the artificial ulcer were coagulated with APC to prevent delayed bleeding. No other knives or EMR techniques were used during ESD.

Patients were allowed to take a small amount of water immediately after the treatment. If there was no complications, patients were permitted to take soft food the next day and were discharged within 1 week. Abdominal radiography was routinely taken after the treatment to check for any perforation. All patients were scheduled to be followed up by standard colonoscopy and EUS every 3 months within the first year after treatment to confirm the healing of the artificial ulcer and assess any residual tumor; thereafter, it was performed annually to diagnose local recurrence and other lesions. Biopsy specimens were taken from any ulcerative lesion identified during the follow-up examinations to histologically confirm the presence of residual tumor and local recurrence. Abdominal and pelvic CT was also carried out to assess pararectal lymph nodes and distant metastases if necessary.

The en bloc resection rate, histologically complete resection rate, the time required for resection, complications (procedure-related bleeding, perforation), and residual/local recurrence of the resected lesion were evaluated. An en bloc resection was defined as a one-piece resection. A complete resection was considered a resection with a tumor-free margin in which both the lateral and basal margins were free of tumor cells, and an incomplete resection was diagnosed when the tumor extended into the lateral or basal margin or the margins were indeterminate due to artificial burn effects. Patients with incomplete

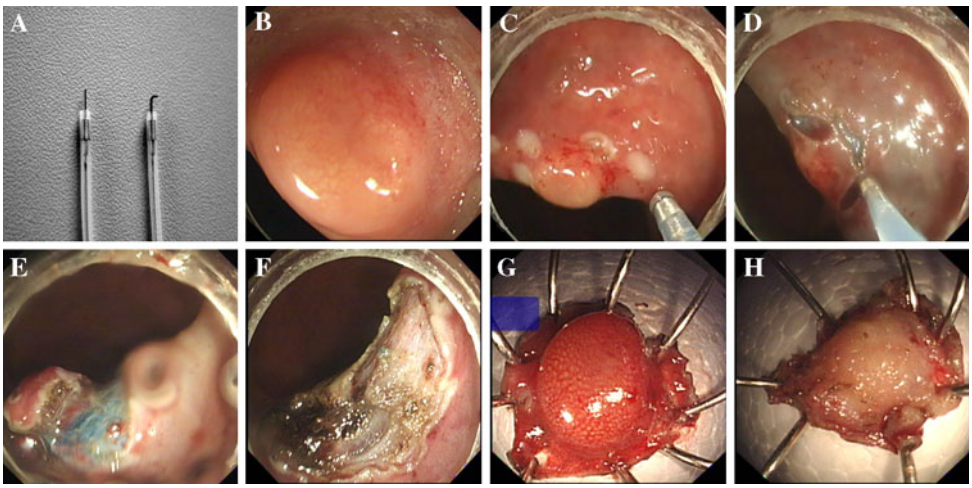

Fig. 1 The small rectal carcinoid tumor resected by ESD with needle-knife. **A** Needle-knife for ESD. **B** Endoscopic view of rectal carcinoid tumor. **C** The outline of the carcinoid tumor marked by the needle-knife. **D** The mucosa was incised outside the marker dots after several milliliters of solution were injected into the submucosal layer. **E** Solution was injected repeatedly during the dissection. **F** The wound dealt with APC after resection. **G** The specimen was stretched along its edge with needles and pinned onto a plate. **H** The base of the resected specimen. With complete resection of the lesion in one piece, the size of the resected specimen was 12 × 10 mm

resections were recommended for further endoscopic resection until the margins were tumor-free or for surgical intervention. The time required was measured from the time point of marking to resection of the lesion. Procedure-related bleeding was classified as immediate or delayed. Immediate bleeding was defined as large amounts of bleeding during the procedure and difficult hemostasis. Delayed bleeding was defined as clinical evidence of bleeding as evidenced by melena at 0–30 days after ESD which requires endoscopic treatment. The incidence of perforation as seen during colonoscopy or based on the free air on a plain abdominal radiography or a CT image after the procedure was recorded. Residual/local recurrence of the lesion was determined histopathologically by using biopsy specimens in follow-up endoscopy and EUS without further treatment.

Statistical analysis

Quantitative data are expressed as the mean and standard deviation (SD) values. Statistical significance was evaluated using Fisher's exact test or Student's *t* test as appropriate. *p* Values (two-tailed) of less than 0.05 were considered statistically significant.

Results

A total of 43 patients with small rectal carcinoid tumors were treated by endoscopic resection. Table 1 summarizes the clinical characteristics of those patients. No difference in clinical characteristics between groups A and B were observed. The mean ages of group A and group B were 50.3 ± 13.6 and 47.6 ± 18.5 years, respectively. The mean tumor size of group A was 6.7 mm (range = 3–10, SD = 2.1), while that of group B was 7.2 mm (range = 4–10, SD = 1.9).

The en bloc resection rate of group B was 20/20 (100%) and that of group A was 20/23 (87%). The rate of complete resection for group B was 100% (20/20), significantly different from that of group A at 52.2% (12/23) ($p < 0.05$). Among those 11 (47.8%) incomplete resection lesions in group A, 8 had positive basal margins and 3 had indeterminate margins. Histopathological evaluation revealed that both the lateral and basal margins of the specimens were free of tumor cells in all lesions of group B (Fig. 2). As indicated in Table 1, the time required for resection was significantly longer in group B compared with group A (28.4 ± 17.2 vs. 12.3 ± 15.4 min, respectively, $p < 0.05$).

Bleeding and perforation are two major complications of endoscopic resection. None of the patients in either group had immediate or delayed bleeding during the procedure. Minor bleeding occurred in all of the cases, but hemostasis was achieved by nonsurgical endoscopic treatment, i.e., hot biopsy forceps electrocoagulation, argon plasma coagulation (APC), and hemoclipping. None of the patients required blood transfusion.

None in group A suffered from perforation, whereas one case (5%) in group B had perforation. The perforation occurred on 2 days after we performed the ESD procedure. The patient complained of a little abdominal distention without abdominal pain. The perforation was very small and could not be found during ESD. Routine abdominal radiography showed pneumoretroperitoneum. After 5 days of conservative treatment with discontinuation of oral intake and intravenous use of antibiotics, the patient

Table 1 Clinical characteristics and treatment outcomes of patients in groups A and B

	Group A (EMR) ($n = 23$)	Group B (ESD) ($n = 20$)	p value
Gender, M/F	14/9	12/8	
Age (mean ± SD) (years)	50.3 ± 13.6	47.6 ± 18.5	
Tumor size (mean ± SD) (mm)	6.7 ± 2.1	7.2 ± 1.9	
No. of patients with en bloc resection	20 (87.0%)	20 (100%)	0.28
No. of patients with complete resection	12 (52.2%)	20 (100%)	<0.05
Procedure time (mean ± SD) (min)	12.3 ± 15.4	28.4 ± 17.2	<0.05
No. of patients with bleeding			
Immediate	0	0	
Delayed	0	0	
No. of patients with perforation	0	1(5%)	
No. of patients with local recurrence	3 (13.0%)	0	0.28
No. of patients with metastases	0	0	

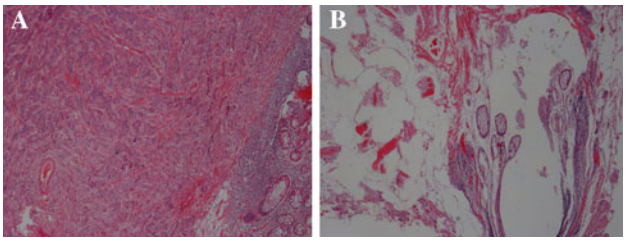

Fig. 2 Histopathological view of a carcinoid tumor resected with ESD (hematoxylin and eosin stain). **A** The tumor was within the submucosa of the rectum (×40). **B** The basal margin was free of tumor invasion (×40)

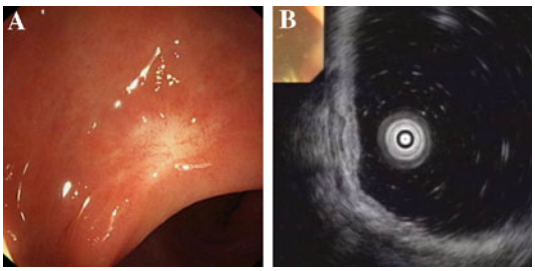

Fig. 3 Follow-up 12 months after a carcinoid tumor was resected with ESD. **A** The artificial ulcer was healed with scar formation. **B** EUS showed no tumor residue or local recurrence

recovered without further endoscopic or surgical intervention.

The average follow-up period after treatment was 42.6 ± 26.1 months in group A and 18.7 ± 10.6 months in group B. There were three cases in group A of local recurrence evaluated by colonoscopy and EUS during follow-up, while none of the patients in group B had recurrence during follow-up (Fig. 3). Although the follow-up period of group A was longer than that of group B, all three recurrent cases in group A were found within 1 year, which means that the recurrence rate was still comparable to that of group B since the minimum follow-up time of group B was longer than 12 months. All three locally recurrent lesions were successfully treated with curative intent. One patient underwent transanal surgery and the other two were treated by ESD. During the follow-up period, no metastases were found and there was no treatment-related death in either group.

Discussion

Rectal carcinoid tumors are rare but primary carcinoids may be discovered in the rectum more often nowadays with the advent of screening colonoscopy. The reported incidence of rectal carcinoid tumors is 17–27% of all gastrointestinal carcinoids, and the majority of rectal carcinoid tumors are small, with 86% being less than 1 cm in diameter [6]. In general, metastasis correlates with the size of the rectal carcinoid tumor [7]. Carcinoids smaller than 1 cm in diameter only occasionally exhibit malignant potential, and tumors larger than 2 cm are almost always invasive, metastatic, or both. The important features associated of rectal carcinoids with metastatic risk are involvement of the muscularis propria, size greater than 2 cm, and the presence of mitotic figures. Invasion into muscularis propria carries the strongest statistical risk. As for the treatment of rectal carcinoid tumors, tumor size and depth of invasion are considered to be the main determinants of appropriate treatment. Therefore, it is important to diagnose the depth of invasion and to measure the tumor size preoperatively. EUS is an ideal for examination of the tumor in that it allows direct determination of the depth of invasion and tumor size by the sonographic image. Tumor diameter on EUS and the depth of invasion correlated to some extent [8–10]. Considering the guidelines of Soga [11] for the treatment of rectal carcinoid tumors, local excision or endoscopic excision is considered curative for

lesions smaller than 10 mm with the extremely low risk of metastases.

As a minimally invasive technique, endoscopic resection may benefit patients diagnosed with rectal carcinoid tumors. It offers the promise of localized treatment of these tumors, with relatively few complications and low mortality. Various endoscopic resection procedures such as endoscopic polypectomy, strip biopsy, aspiration resection, and band-snare resection have been described as effective treatments for rectal carcinoid tumors [12–14]. However, complete resection of carcinoid tumors of the rectum is difficult with conventional polypectomy because about 75% of the tumors extend into the submucosa [9]. Polypectomy may not provide adequate resection margins and additional surgical intervention may be needed.

For submucosal lesions such as rectal carcinoid tumors, endoscopic treatment requires special techniques for deeper resection to achieve clear margins. This can be achieved by lifting the lesion with either submucosal injection of saline solution as in conventional EMR or direct submucosal dissection as in ESD. The use of ESD in the treatment of rectal carcinoids is substantial for the following two reasons: First, since the rectum is fixed in the retroperitoneum, the endoscope can be maneuvered more easily than it can in other organs of gastrointestinal tract. Second, panperitonitis is less likely to occur, even if the muscle layer is torn. ESD, developed from the EMR method, is a new form of endoscopic treatment that has the advantage of making large en bloc resection possible, allows precise histological staging, and may prevent disease recurrence better than the standard EMR method [15, 16]. ESD enables us to treat rectal carcinoid tumors and has revolutionized the management of diseases of the lower digestive tract. However, ESD involves some risks because of its technical features and it also takes a long time to perform.

In this study, en bloc resection of rectal carcinoid tumors was achieved with ESD in all 20 lesions (100%) on which it was attempted, and the rate of complete resection was 100%, while the rate for one-piece resection with tumor-free margins was only 52.2% with EMR. This is a big improvement compared with conventional methods. The risk of local recurrence after EMR varies between 2 and 35% [17]. In this study there were three cases (13%) with local recurrence in the EMR group during follow-up, but no patient in the ESD group had local recurrence. Careful follow-up is necessary to detect any local recurrence as complete removal may be possible in repeat procedures. Further studies are required to assess the efficacy of this technique, long-term recurrence rates, and patient survival.

Bleeding and perforation are the two main complications of ESD. Because the perforation is usually small, it can be found and managed with metallic clips in an experienced endoscopist's hands, but massive bleeding during ESD sometimes is difficult to deal with. Compared with perforation, the prevention and handling of bleeding is more important. Once bleeding occurs during ESD, hemostasis may take a long time and the endoscopic view may be affected; blind hemostasis may eventually lead to perforation. Sometimes when massive bleeding is encountered, one has no choice but to stop the ESD procedure. During ESD, immediate minor bleeding is not uncommon and can be treated successfully by grasping the bleeding vessels with hot biopsy forceps and coagulating them [18]. Direct coagulation with the needle-knife can be done for small vessels in the submucosa during ESD. Metallic clips are often deployed for more brisk bleeding, but they may have an effect on the next ESD procedure [19]. In this study, no patient had immediate or delayed bleeding during either the EMR or the ESD procedure.

Perforation during ESD can be managed in many cases conservatively if it is found immediately and closed during the procedure if there was good bowel preparation [20, 21]. When there is perforation into the retroperitoneal space, it has been reported that the pressured air from the tip of the endoscope can cause subcutaneous emphysema, pneumoretroperitoneum, pneumomediastinum, and pneumoscrotum [22]. Endoscopic closure of a perforation with endoclips has been attempted because the rectal lumen is thought to be comparatively clean and the perforation is usually small during ESD. One patient in the present study suffered perforation with pneumoretroperitoneum after ESD, and the condition was successfully managed without additional surgery.

As for the endoscopic treatment of small rectal carcinoid tumors, Ono et al. [23] reported that endoscopic submucosal resection with a ligation device (ESMR-L) provided a significantly deeper vertical resection margin and, theoretically, a high rate of curative resection. The same group recently reported a retrospective study of 61 patients with satisfactory results achieved [24]. Moon et al. [25] reported that endoscopic submucosal resection with double ligation (ESMR-DL) for the treatment of small rectal carcinoid tumors showed no histopathological evidence of tumor involvement at the resection margins, no immediate or late complications, and no local recurrence in any patient. The difference among ESD, ESMR-L, and ESMR-DL with respect to the benefit of endoscopic treatment of rectal carcinoids therefore needs to be further evaluated, especially regarding the vertical resection margin, complication, and local recurrence.

In conclusion, ESD is a feasible method for the treatment of small rectal carcinoid tumors and has advantages over EMR with regard to achieving en bloc and complete resection. This treatment modality also has an acceptable rate of complications which can be adequately managed

endoscopically. Further investigation is required to confirm the safety and assess the long-term prognosis of this method.

Disclosures Ping-Hong Zhou, Li-Qing Yao, Xin-Yu Qin, Mei-Dong Xu, Yun-Shi Zhong, Wei-Feng Chen, Li-Li Ma, Yi-Qun Zhang, Wen-Zheng Qin, Ming-Yan Cai, and Yuan Ji have no conflicts of interest or finanicial ties to disclose.

References

1. Ishikawa H, Imanishi K, Otani T, Okuda S, Tatsuta M, Ishiguro S (1989) Effectiveness of endoscopic treatment of carcinoid tumors of the rectum. Endoscopy 21:133–135
2. Matsui K, Iwase T, Kitagawa M (1993) Small, polypoid-appearing carcinoid tumors of the rectum: clinicopathological study of 16 cases and effectiveness of endoscopic treatment. Am J Gastroenterol 88:1949–1953
3. Yoshikane H, Goto H, Niwa Y, Matsui M, Ohashi S, Suzuki T, Hamajima E, Hayakawa T (1998) Endoscopic resection of small duodenal carcinoid tumors with strip biopsy technique. Gastrointest Endosc 47:466–470
4. Oda I, Gotoda T, Hamanaka H (2005) Endoscopic submucosal dissection for early gastric cancer: technical feasibility, operation time and complications from a large consecutive series. Dig Endosc 17:54–58
5. Ono H, Kondo H, Gotoda T, Shirao K, Yamaguchi H, Saito D, Hosokawa K, Shimoda T, Yoshida S (2001) Endoscopic mucosal resection for treatment of early gastric cancer. Gut 48:225–229
6. Modlin IM, Kidd M, Latich I, Zikusoka MN, Shapiro MD (2005) Current status of gastrointestinal carcinoids. Gastroenterology 128:1717–1751
7. Federspiel BH, Burke AP, Sobin LH, Shekitka KM (1990) Rectal and colonic carcinoids: a clinicopathologic study of 84 cases. Cancer 65:135–140
8. Zhou PH, Yao LQ, Zhong YS, He GJ, Xu MD, Qin XY (2004) Role of endoscopic miniprobe ultrasonography in diagnosis of submucosal tumor of large intestine. World J Gastroenterol 10:2444–2446
9. Matsumoto T, Iida M, Suekane H, Tominaga M, Yao T, Fujishima M (1991) Endoscopic ultrasonography in rectal carcinoid tumors: contribution to selection of therapy. Gastrointest Endosc 37:539–542
10. Kameyama H, Niwa Y, Arisawa T, Goto H, Hayakawa T (1997) Endoscopic ultrasonography in the diagnosis of submucosal lesions of the large intestine. Gastrointest Endosc 46:406–411
11. Soga J (2005) Early-stage carcinoids of the gastrointestinal tract: an analysis of 1914 reported cases. Cancer 103:1587–1595
12. Fujimura Y, Mizuno M, Takeda M, Sato I, Hoshika K, Uchida J, Kihara T, Mure T, Sano K, Moriya T (1993) A carcinoid tumor of the rectum removed by strip biopsy. Endoscopy 25:428–430
13. Kobayashi K, Katsumata T, Yoshizawa S, Sada M, Igarashi M, Saigenji K, Otani Y (2005) Indications of endoscopic polypectomy for rectal carcinoid tumors and clinical usefulness of endoscopic ultrasonography. Dis Colon Rectum 48:285–291
14. Jung IS, Ryu CB, Kim JO, Lee JS, Lee MS, Shim CS (2003) Rectal carcinoid treated by EMR. Gastrointest Endosc 58:253
15. Gotoda T, Kondo H, Ono H, Saito Y, Yamaguchi H, Saito D, Yokota T (1999) A new endoscopic mucosal resection procedure using an insulation-tipped electrosurgical knife for rectal flat lesions: report of two cases. Gastrointest Endosc 50:560–563
16. Onozato Y, Ishihara H, Iizuka H, Sohara N, Kakizaki S, Okamura S, Mori M (2006) Endoscopic submucosal dissection for early gastric cancers and large flat adenomas. Endoscopy 38:980–986
17. Gotoda T, Friedland S, Hamanaka H, Soetikno R (2005) A learning curve for advanced endoscopic resection. Gastrointest Endosc 62:866–867
18. Fijishiro M, Yahagi N, Kakushima N (2006) Management of bleeding concerning endoscopic submucosal dissection with the flex knife for stomach neoplasm. Digest Endosc 18:S119–S122
19. Shiba M, Higuchi K, Kadouchi K, Montani A, Yamamori K, Okazaki H, Taguchi M, Wada T, Itani A, Watanabe T, Tominaga K, Fujiwara Y, Hayashi T, Tsumura K, Arakawa T (2005) Risk factors for bleeding after endoscopic mucosal resection. World J Gastroenterol 14:7335–7339
20. Fujishiro M, Yahagi N, Nakamura M, Kakushima N, Kodashima S, Ono S, Kobayashi K, Hashimoto T, Yamamichi N, Tateishi A, Shimizu Y, Oka M, Ogura K, Kawabe T, Ichinose M, Omata M (2006) Endoscopic submucosal dissection for rectal epithelial neoplasia. Endoscopy 38:493–497
21. Tsunada S, Ogata S, Ohyama T, Ootani H, Oda K, Kikkawa A, Ootani A, Sakata H, Iwakiri R, Fujimoto K (2003) Endoscopic closure of perforation caused by EMR in the stomach by application of metallic clips. Gastrointest Endosc 57:948–951
22. Humphreys F, Hewetson KA, Dellipiani AW (1984) Massive subcutaneous emphysema following colonoscopy. Endoscopy 16:160–161
23. Ono A, Fujii T, Saito Y, Matsuda T, Lee DT, Gotoda T, Saito D (2003) Endoscopic submucosal resection of rectal carcinoid tumors with a ligation device. Gastrointest Endosc 57:583–587
24. Mashimo Y, Matsuda T, Uraoka T, Saito Y, Sano Y, Fu K, Kozu T, Ono A, Fujii T, Saito D (2008) Endoscopic submucosal resection with a ligation device is an effective and safe treatment for carcinoid tumors in the lower rectum. J Gastroenterol Hepatol 23:218–222
25. Moon JH, Kim JH, Park CH, Jung JO, Shin WG, Kim JP, Kim KO, Hahn T, Yoo KS, Park SH, Park CK (2006) Endoscopic submucosal resection with double ligation technique for treatment of small rectal carcinoid tumors. Endoscopy 38:511–514