

Short-term outcomes of endoscopic submucosal dissection for superficial cecal tumors: a comparison between extension and nonextension into the appendiceal orifice

Kazuki Boda, Shiro Oka, Shinji Tanaka, Hidenori Tanaka, Kenta Matsumoto, Ken Yamashita, Kyoku Sumimoto, Daiki Hirano, Yuzuru Tamaru, Yuki Ninomiya, Nana Hayashi and Kazuaki Chayama

Abstract

Background: Few studies have investigated the use of endoscopic submucosal dissection (ESD) for cecal tumors extending into the appendiceal orifice. Herein, we assessed the feasibility and safety of ESD for cecal tumors extending into the appendiceal orifice.

Methods: We retrospectively examined the outcomes of ESD for 78 patients with 78 cecal tumors (male/female ratio, 40/38; mean [standard deviation, SD] age, 67 [9] years; mean [SD] tumor size, 32 [15] mm), who underwent ESD at the Hiroshima University Hospital between October 2008 and March 2016. The indication for ESD in cecal tumors extending into the appendiceal orifice was recognition of the distal edge of the lesion in the appendix. They were classified into two groups: patients with cecal tumors extending (Group A: 29 patients, 29 tumors) and not extending (Group B: 49 patients, 49 tumors) into the appendiceal orifice. We compared the outcomes of ESD between both groups.

Results: No significant differences in clinicopathological characteristics were observed between both groups. The rate of severe submucosal fibrosis in Group A (48%) was significantly higher than that in Group B (24%) ($p < 0.05$). The mean (SD) procedure speed in Group A (14 [10] mm²/min) was significantly slower than that in Group B (23 [16] mm²/min) ($p < 0.01$). The *en bloc* resection rates in Groups A and B were 90% and 96%, respectively. There were no significant differences in adverse events reported between both groups.

Conclusions: ESD for cecal tumors with extension into the appendiceal orifice is effective and safe.

Keywords: appendix, cecal tumors, endoscopic submucosal dissection

Received: 13 December 2017; revised manuscript accepted: 28 March 2018

Introduction

Endoscopic submucosal dissection (ESD) has been established as a reliable method for the treatment of superficial colorectal tumors.¹⁻⁹ Currently it is possible to completely resect large tumors and to evaluate tumors pathologically in detail using ESD. Colorectal ESD is technically more difficult than gastric ESD because of the thin intestinal

wall, bending of the intestinal tract, the presence of folds, and poor scope operability. However, recently improved tools have made ESD more feasible and safer than before. Therefore, some high-volume centers have reported on the feasibility and safety of colorectal ESD for lesions with difficult location such as anorectal tumors with hemorrhoids close to the dentate line,¹⁰ colorectal

Ther Adv Gastroenterol

2018, Vol. 11: 1-9

DOI: 10.1177/
1756284818772794

© The Author(s), 2018.
Reprints and permissions:
[http://www.sagepub.co.uk/
journalsPermissions.nav](http://www.sagepub.co.uk/journalsPermissions.nav)

Correspondence to:

Shiro Oka
Department of
Gastroenterology and
Metabolism, Hiroshima
University Hospital,
1-2-3 Kasumi Minami-ku,
Hiroshima, Japan
[oka4683@hiroshima-u.
ac.jp](mailto:oka4683@hiroshima-u.ac.jp)

Kazuki Boda
Department of
Gastroenterology and
Metabolism, Hiroshima
University Hospital,
Hiroshima, Japan

Shinji Tanaka
Department of Endoscopy,
Hiroshima University
Hospital, Hiroshima, Japan

Hidenori Tanaka
Kenta Matsumoto
Ken Yamashita
Kyoku Sumimoto
Daiki Hirano
Yuzuru Tamaru
Yuki Ninomiya

Department of
Gastroenterology and
Metabolism, Hiroshima
University Hospital,
Hiroshima, Japan

Nana Hayashi
Department of Endoscopy,
Hiroshima University
Hospital, Hiroshima, Japan

Kazuaki Chayama
Department of
Gastroenterology and
Metabolism, Hiroshima
University Hospital,
Hiroshima, Japan

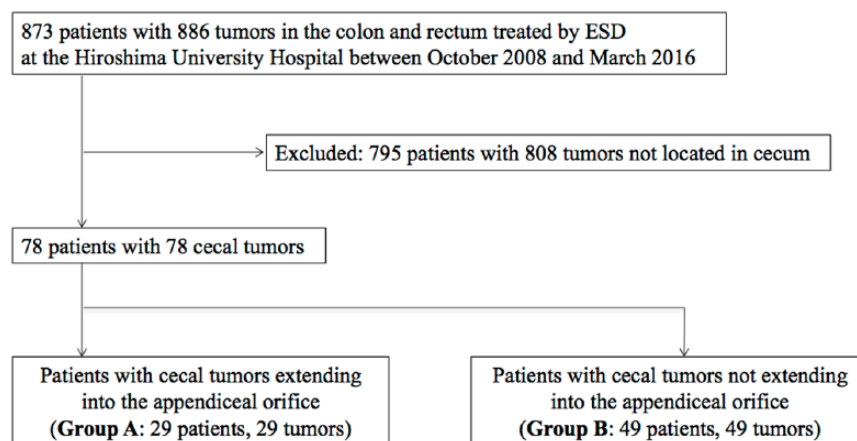


Figure 1. Flow chart of the study.

tumors involving a diverticulum,^{11,12} or cecal lesions involving the ileocecal valve.¹³

In particular, ESD for cecal tumors is difficult because both the scope and tumor are almost perpendicularly oriented, and scope operability is often poor when deep colonic ESD is performed due to the bending of the sigmoid colon. In addition, the working space is narrow and the procedure cannot be performed with the inversed operation of scope. Moreover, for cases with tumor extension into the appendiceal orifice, the ESD procedure is technically more difficult to perform and laparoscopic surgery is often selected as the standard therapy for those tumors.¹⁴ Data are scarce regarding ESD for cecal tumors extending into the appendiceal orifice.^{15,16} Here, we assessed the feasibility and safety of ESD for cecal tumors with extension into the appendiceal orifice.

Methods

Patients

We retrospectively examined the outcomes of colorectal ESD performed at the Hiroshima University Hospital between October 2008 and March 2016. A total of 886 tumors in the colon and rectum in 873 patients, including 78 cecal tumors in 78 patients (male/female ratio, 40/38; mean age, 67 [9] years) were treated by ESD. These patients with cecal tumors were classified into two groups: patients with cecal tumors extending into the appendiceal orifice (Group A: 29 patients, 29 tumors) and patients with cecal tumors not extending into the appendiceal orifice

(Group B: 49 patients, 49 tumors) (Figure 1). The definition of cecal tumors extending into the appendiceal orifice was tumors of which the distal edge in the appendix could not be recognized without using transparent tip hood. We compared the clinicopathological findings and outcomes between the two groups.

The indications for ESD were defined using the criteria proposed by the Japan Gastroenterological Endoscopy Society¹⁷ and the Japanese Society of Gastroenterology as follows.¹⁸ ESD was indicated for tumors that required *en bloc* resection and for which *en bloc* resection using snare endoscopic mucosal resection (EMR) would be difficult,¹⁹ which included laterally spreading tumors of the nongranular type, particularly, the pseudodepressed type, tumors with a type V_I pit pattern, carcinomas with submucosal shallow invasions of less than 1000 μ m, large depressed tumors, and large elevated tumors that were probably malignant, including large nodular lesions such as laterally spreading tumors of the granular type. In addition, ESD was indicated for intramucosal tumors with fibrosis caused by biopsies or peristalsis, local residual early stage carcinomas that developed after endoscopic resection, and sporadic localized tumors associated with chronic intestinal inflammation conditions, including ulcerative colitis. In addition, in our institution, the indication for ESD for cecal tumors with extension into the appendiceal orifice was the recognition of the distal edge of the lesion in the appendix.

The study was performed in accordance with the Declaration of Helsinki. All patients were informed

of the risks and benefits of ESD, and each provided written informed consent for the use of patients' data. This study protocol was approved by the Institutional Review Board of Hiroshima University Hospital (Approval number: E-591, Institutional Review Board registration date: 14 November 2016).

ESD procedure for cecal tumors with extension into the appendiceal orifice

ESD was performed by the two experts (ST or SO) in this series. Carbon dioxide insufflation was used routinely. We performed ESD using a high-resolution video endoscope (CF-H260AZI, PCF-Q260AZI, CF-Q260JI, Olympus, Tokyo, Japan, CF-Y0047 [prototype], or CF-Y0006 [prototype]). In order to overcome the difficulty of ESD for cecal tumors with extension into the appendiceal orifice, we devised some measures: (a) the use of a bell-shaped, small-caliber-tip, transparent tip hood; (b) the use of a splinting tube with a balloon; (c) the use of Dual knife needle-in technique and SB knife Jr.

An endoscope was attached to a bell-shaped, small-caliber-tip, transparent tip hood (ST Hood, Fujifilm, Tokyo, Japan or ST Hood short type, Fujifilm) in order to facilitate good field visualization and allow stable dissection. We used a splinting tube with a balloon (ST-CB1, Olympus) to improve scope operability if scope operability was poor due to the bending of the sigmoid colon.²⁰ We mainly used a Dual knife (Olympus) or Dual knife J (Olympus) with an electrosurgical generator (ESG-100, Olympus). The needle length of a Dual knife is 1.5 mm in a needle-out state and the tip measures only 0.3 mm in a needle-in state. With a Dual knife J, it is 0.1 mm, in the needle-in state, thereby ensuring even safer dissection. In a situation where the scope and muscular layer are almost perpendicularly oriented, the risk of perforation is high in a needle-out state, so we dissected safely in a needle-in state. When the lesion moves with the act of breathing or the scope operability is poor, we used the SB knife Jr (Sumitomo Bakelite, Tokyo, Japan), which allows safe dissection simply by opening and closing the scissors without moving the knife itself. We mixed equal volumes of 0.4% sodium hyaluronate (Muco Up, Johnson & Johnson, New Brunswick, NJ, USA) and 10% glycerin solution, and added a small amount of indigo carmine (0.2 ml per 20 ml sodium hyaluronate + glycerin). Endoscopic

hemostasis was achieved with hemostatic forceps (Coagrasper, Olympus). The pulse-cut slow-mode setting (25 W) was used for mucosal incisions, and the forced coagulation mode (25 W) was used for submucosal dissection. We used the pulse-cut fast-mode setting (30 W) and soft coagulation (40 W) with the SB knife Jr. Basically, mucosal incision and initial dissection were performed from the side of the appendiceal lumen to prevent very deep dissection into the appendiceal orifice. When there was inadequate space for mucosal incision on the side of the appendiceal lumen, the mucosal incision and the submucosal dissection were started from the periphery of the tumor, and finally continued into the appendiceal orifice sufficiently. These procedures are shown in Figure 2. This tumor was a cecal tumor of size 10 mm and growth type 0–Is. Although a part of the tumor extended into the appendiceal orifice, its edge could be recognized in the appendix. Therefore, we performed an ESD after explaining the risks and benefits of the procedure to the patient. The histological features of the tumor are shown in Figure 2(m). The tumor was an intramucosal carcinoma. Although the tumor extended into the appendix, the horizontal and vertical margins were negative.

Outcomes of ESD

We evaluated the clinicopathological characteristics of cases, procedure time, *en bloc* resection rate, histological complete resection rate, curative (R0) resection rate, and adverse events.

The procedure speed was calculated by dividing the area of the resected specimen by the procedure time (mm^2/min). The approximate area of the resected specimen (mm^2) was calculated as follows: $3.14 \times 0.25 \times \text{long axis diameter (mm)} \times \text{short axis diameter (mm)}$.^{21,22} Poor scope operability was defined as situations in which paradoxical movement of the endoscope, poor control with adhesions, and lesion motion with heart beats or breathing occurred, as reported previously.²³ Endoscopically, the degree of submucosal fibrosis was classified as no fibrosis, mild fibrosis, and severe fibrosis.²⁴ Delayed bleeding was defined as a decrease in hemoglobin levels by 2 g/dL or more compared with the last preoperative level, or any apparent bleeding or massive melena.²⁵ A histologically complete resection was defined as a histopathologically complete *en bloc* resection with negative tumor margins. A curative (R0) resection was determined using the Japanese

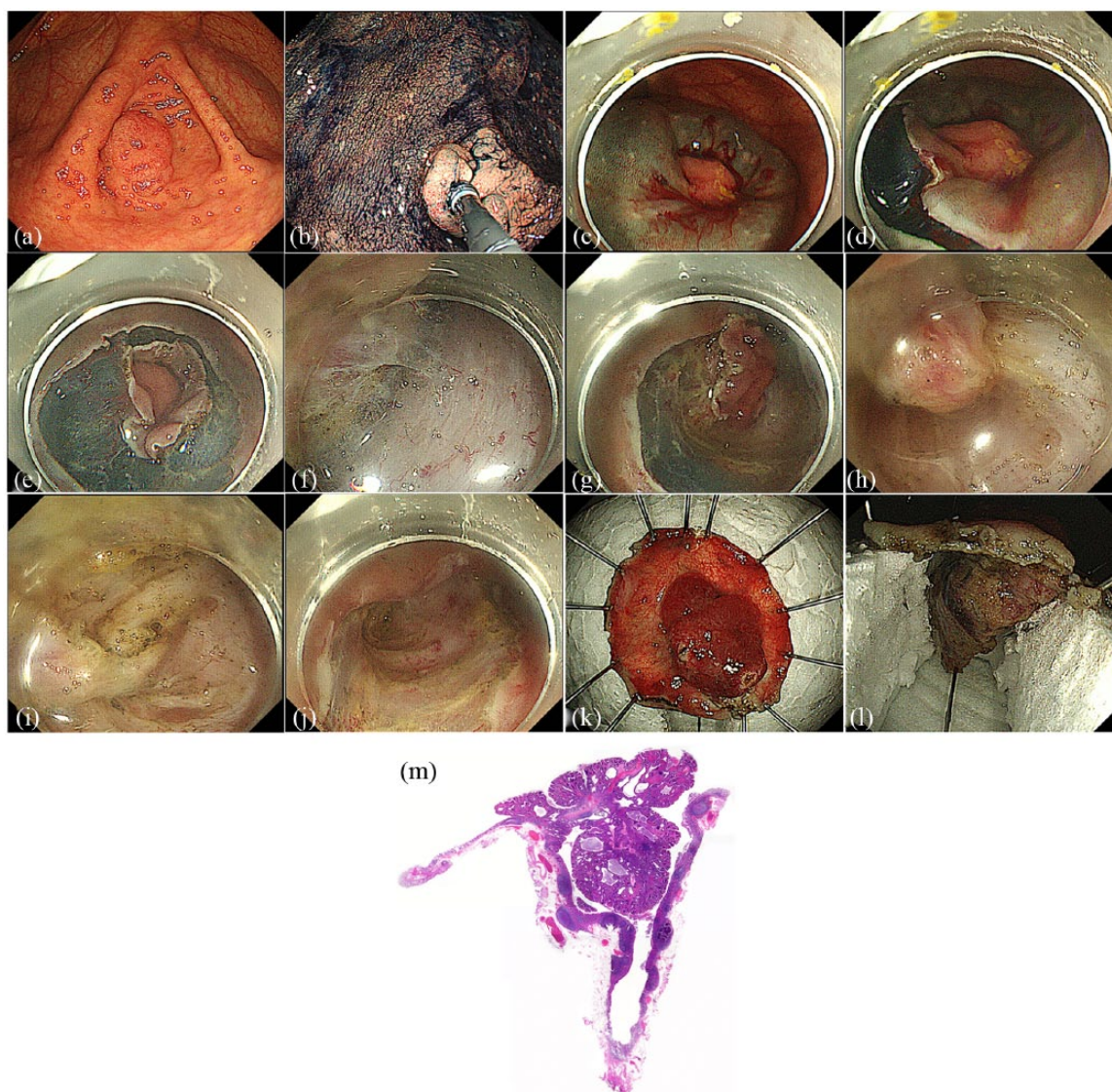


Figure 2. Endoscopic submucosal dissection procedure.

(a) The tumor was a cecal tumor of size 10 mm and growth type 0–Is. (b) A part of the tumor extended into the appendiceal orifice, but its edge could be recognized in the appendix. (c) The tumor did not lift after submucosal injection. (d, e) We started an incision around the tumor because there was inadequate space to make an incision on the appendiceal side. (f, g, h) After complete circumferential incision, we dissected the submucosal layer using the needle-in technique. The risk of perforation was high if we had dissected in a needle-out state because our scope and muscular layer both were almost perpendicularly oriented. (i) We were able to dissect sufficiently into the appendiceal lumen. (j, k, l) The ulcer bed and the resected specimen became conical in shape. (m) The histological features of the resected tumor (Loupe view of hematoxylin and eosin).

Society for Cancer of the Colon and Rectum guideline criteria, which involved satisfying all four of the following characteristics: a well/moderately differentiated or papillary carcinoma; no vascular invasion; a submucosal invasion depth < 1000 μm ; grade 1 budding.²⁶ At 1 year after ESD, follow-up colonoscopies were performed on the patients who underwent histologically complete resections of high-grade dysplasias and T1 carcinomas that met the curative

criteria. For patients with piecemeal high-grade dysplasias and those with tumors that had histologically positive horizontal margins, follow-up colonoscopies were performed at 3–6 months after ESD, and further colonoscopies were performed 1 year later. For patients who had undergone ESD for T1 carcinomas that did not meet the curative criteria, blood tests, including the carcinoembryonic antigen level, and computed tomography of the abdomen and

pelvis were performed every 6 months postoperatively for the first 3 years and every 12 months thereafter, and follow-up colonoscopies were performed every year.

Statistical analysis

The Student's *t* test and the Mann–Whitney *U* test were used to compare the distribution of continuous variables by outcome, and the Pearson chi-squared test or Fisher's exact probability test were used to examine the association between categorical variables and outcomes. $p < 0.05$ was considered to be statistically significant. All statistical analyses were performed using JMP version 10 (SAS Institute Inc., Cary, NC, USA).

Results

Comparison of clinicopathological characteristics between Group A and Group B are shown in Table 1. The mean and standard deviation (SD) tumor size in Group A was 32 (16) mm and that in Group B was 33 (15) mm. Seven (24%) patients in Group A and five (10%) patients in Group B had undergone appendectomy in the past; the difference between both groups was not significant. Likewise, there were no significant differences between the two groups in sex ratio, mean age, ratio of anticoagulants and/or antiplatelets use, growth type, and histology.

Comparison of outcomes related to ESD between Group A and Group B are shown in Table 2. The rate of severe submucosal fibrosis in Group A (48%) was significantly higher than that in Group B (24%) ($p < 0.05$). The mean procedure time in Group A was 117 (127) min and that in Group B was 82 (52) min, and the difference was not significantly different. The mean (SD) procedure speed in Group A (14 [10] mm²/min) was significantly slower than that in Group B (23 [16] mm²/min) ($p < 0.01$). The *en bloc* resection rate, histological complete resection rate, and R0 resection rate were 90%, 86%, and 86%, respectively, in Group A and 96%, 88%, and 84%, respectively, in Group B, and were not significantly different between both groups. Two (7%) patients in Group A and five (10%) patients in Group B underwent additional surgery. Perforation during the procedure occurred in two (7%) patients in Group A and one (2%) patient in Group B. All cases underwent ESD for tumors with severe submucosal fibrosis in the early period of the

introduction of ESD and none of the patients required surgery. Delayed bleeding occurred in one (3%) patient in Group A and two (4%) patients in Group B. None of them required transfusion. There were no significant differences in adverse events between the two groups. The mean follow-up duration was 27 (14) months (range 7–62 months) and no local recurrence was found.

Discussion

ESD for cecal tumors with extension into the appendiceal orifice is technically difficult because the field visualization and scope operability are often poor and the scope and tumor are almost perpendicularly oriented. Thus, laparoscopic surgery has often been selected as the standard therapy for those tumors.¹⁴ Recently, there have been reports about endoscopic full-thickness resection for appendiceal adenoma.^{27–29} However, the number of cases was small and the feasibility and safety were unclear. Moreover, endoscopic full-thickness resection cannot achieve *en bloc* resection of large tumors. However, our data revealed that ESD for cecal tumors with extension into the appendiceal orifice was clinically effective and safe. An endoscope attached to a bell-shaped, small-caliber-tip, transparent tip hood such as the ST Hood or ST Hood short type facilitated good field visualization even in the appendiceal lumen. We also used a single-use splinting tube with a balloon to improve poor scope operability due to the bending of the sigmoid colon in deep colonic ESD.²⁰ We used single-use splinting tubes for five cases in this study. In the situations where the scope and muscular layer were almost perpendicularly oriented, we used the Dual knife needle-in technique or SB knife Jr.³⁰ Recently, Ritsuno and colleagues³¹ reported that S-O clip-assisted ESD was safe and fast for *en bloc* resection of large superficial colorectal tumors because the S-O clip allows the direct visualization of the cutting line during ESD and can be used at any location without withdrawing the endoscope.

In the present study, there was no local recurrence during the follow-up duration. However, Eun Mi Song and colleagues³² reported that the recurrence rate after endoscopic resection for cecal polyps involving appendiceal orifice was high (15.6%), and that polyps involving 75% or more of the appendiceal orifice circumference were an independent risk factor for recurrence in their study regarding endoscopic resection for cecal polyps involving the appendiceal orifice.

Table 1. Comparison of clinicopathological characteristics between Group A and Group B.

Variables	Cecal lesion	
	Group A	Group B
Number of patients, <i>n</i>	29	49
Number of tumors, <i>n</i>	29	49
Sex		
Male, <i>n</i> (%)	19 (66)	21 (43)
Female, <i>n</i> (%)	10 (34)	28 (57)
Age, years, mean (SD)	67 (8.3)	66 (10)
Use of anticoagulants and/or antiplatelets		
Yes, <i>n</i> (%)	4 (14)	7 (14)
No, <i>n</i> (%)	25 (86)	42 (86)
Previous appendicectomy		
Yes, <i>n</i> (%)	7 (24)	5 (10)
No, <i>n</i> (%)	22 (76)	44 (90)
Tumor size, mm, mean (SD)	32 (16)	33 (15)
Growth type		
LST-G, <i>n</i> (%)	19 (66)	24 (49)
LST-NG, <i>n</i> (%)	7 (24)	15 (31)
Polypoid, <i>n</i> (%)	3 (10)	10 (20)
Histology		
SSA/P, <i>n</i> (%)	1 (4)	1 (2)
Low-grade dysplasia, <i>n</i> (%)	12 (41)	19 (39)
High-grade dysplasia, <i>n</i> (%)	12 (41)	17 (35)
T1 carcinoma (< 1000 μm), <i>n</i> (%)	0 (0)	5 (10)
T1 carcinoma (≥ 1000 μm), <i>n</i> (%)	4 (14)	7 (14)
Group A, patients with cecal tumors extending into the appendiceal orifice; Group B, patients with cecal tumors not extending into the appendiceal orifice. LST-G, laterally spreading tumor of the granular type; LST-NG, laterally spreading tumor of the nongranular type; SSA/P, sessile serrated adenoma/polyp; SD, standard deviation.		

Although it was mainly caused by the high rates of endoscopic piecemeal mucosal resection in their series (23.7%) due to the difficulty of procedure, it was also possible that a part of tumor remained in the appendiceal lumen. It is important to detect the minute amounts of residual tumor tissue that surround the resected ulcer or ulcer bed after

ESD, and to evaluate and confirm the pathological horizontal margin carefully even when an *en bloc* resection has been achieved.

No patients in this study experienced acute appendicitis after ESD. However, there are some case reports about acute appendicitis after EMR.^{33,34}

Table 2. Comparison of outcomes related to endoscopic submucosal dissection between Group A and Group B.

Variables	Cecal lesion		p value
	Group A	Group B	
Operability of scope			
Good, n (%)	18 (62)	31 (63)	NS
Poor, n (%)	11 (38)	18 (37)	
Use of a single-use splinting tube			
Yes, n (%)	3 (10)	2 (4)	NS
No, n (%)	26 (90)	47 (96)	
Submucosal fibrosis			
None or mild, n (%)	15 (52)	37 (76)	< .05
Severe, n (%)	14 (48)	12 (24)	
Procedure time, min, mean (SD)	117 (127)	82 (52)	NS
Procedure speed, mm ² /min, mean (SD)	14 (10)	23 (16)	< .01
Resection status			
<i>En bloc</i> , n (%)	25 (90)	47 (96)	NS
Piecemeal, n (%)	4 (10)	2 (4)	
Discontinued procedure, n (%)	0 (0)	0 (0)	
Histological complete resection			
Complete, n (%)	24 (86)	43 (88)	NS
Incomplete, n (%)	5 (14)	6 (12)	
Endoscopic curability			
R0 resection, n (%)	24 (86)	41 (84)	
Non-R0 resection, n (%)	5 (17)	8 (16)	
Follow up, n (%)	3 (10)	3 (6)	NS
Additional surgical resection, n (%)	2 (7)	5 (10)	
Adverse events			
Delayed bleeding, n (%)	1 (3)	2 (4)	
Intraoperative perforation, n (%)	2 (7)	1 (2)	
Conservative therapy, n (%)	2 (7)	1 (2)	NS
Surgery, n (%)	0 (0)	0 (0)	
Local recurrence, n (%)	0 (0)	0 (0)	NS
Group A, patients with cecal tumors extending into the appendiceal orifice; Group B, patients with cecal tumors not extending into the appendiceal orifice. NS, not significant; SD, standard deviation.			

Furthermore, Jacob and colleagues¹⁵ reported that 2 out of the 76 patients who underwent ESD for tumors near the appendiceal orifice experienced acute appendicitis after ESD, and that one case might have been caused by the clips used for closure of the ulcer bed during ESD. Therefore, it is important to explain to patients before ESD about the possibility of appendicitis and to prevent unnecessary clipping for the ulcer bed around the appendiceal orifice after ESD. Moreover, in the event of increased inflammatory response after ESD, the use of antibiotics should be considered.

Jacob and colleagues¹⁵ classified the lesions into four groups according to the relationship between the tumor and appendiceal orifice. ESD was not performed on tumors that deeply entered the appendiceal orifice with edges that could not be observed unless appendectomy was performed prior to ESD in their series. In our institution the indication for ESD in cecal tumors extending into the appendiceal orifice is the recognition of the distal edge of the lesion in the appendix, and this must be definitively observed before ESD. The ST Hood and ST Hood short type are useful in facilitating good visualization and ascertaining how deep the tumor extends into the appendix. If the distal edge of the tumor cannot be observed despite the use of the ST Hood or ST Hood short type, the tumor should be resected by surgery. Five cases underwent surgery for this reason during the same period in the current study. Histologically, in all of these cases, the tumor extended deeply into the appendiceal lumen and surgical resection was reasonable.

This study has some limitations. First, it was a retrospective study of clinical records in a single center. Second, the study data were only from experts in ESD. Third, the number of cases that underwent ESD for cecal tumors extending into the appendiceal orifice was relatively small. Thus, more of these cases are needed to clarify further the indications of ESD for cecal tumors. Finally, this study was not designed to compare ESD with conventional surgery or EMR.

In conclusion, ESD for the cecal tumors with extension into the appendiceal orifice can be performed effectively and safely.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors declare no conflicts of interest in preparing this article.

References

1. Tanaka S, Oka S, Kaneko I, *et al.* Endoscopic submucosal dissection for colorectal neoplasia: possibility of standardization. *Gastrointest Endosc* 2007; 66: 100–107.
2. Tamegai Y, Saito Y, Masaki N, *et al.* Endoscopic submucosal dissection: a safe technique for colorectal tumors. *Endoscopy* 2007; 39: 418–422.
3. Hurlstone DP, Atkinson R, Sanders DS, *et al.* Achieving R0 resection in the colorectum using endoscopic submucosal dissection. *Br J Surg* 2007; 94: 1536–1542.
4. Tanaka S, Oka S and Chayama K. Colorectal endoscopic submucosal dissection: present status and future perspective, including its differentiation from endoscopic mucosal resection. *J Gastroenterol* 2008; 43: 641–651.
5. Saito Y, Fukuzawa M, Matsuda T, *et al.* Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal resection of large colorectal tumors as determined by curative resection. *Surg Endosc* 2010; 24: 343–352.
6. Tanaka S, Tamegai Y, Tsuda S, *et al.* Multicenter questionnaire survey on the current situation of colorectal endoscopic submucosal dissection in Japan. *Dig Endosc* 2010; 22(Suppl. 1): S2–S8.
7. Terasaki M, Tanaka S, Oka S, *et al.* Clinical outcomes of endoscopic submucosal dissection and endoscopic mucosal resection for laterally spreading tumors larger than 20 mm. *J Gastroenterol Hepatol* 2012; 27: 734–740.
8. Oka S, Tanaka S, Saito Y, *et al.* Local recurrence after endoscopic resection for large colorectal neoplasia: a multicenter prospective study in Japan. *Am J Gastroenterol* 2015; 110: 697–707.
9. Boda K, Oka S, Tanaka S, *et al.* Clinical outcomes of endoscopic submucosal dissection for colorectal tumors: a large multicenter retrospective study from the Hiroshima GI Endoscopy Research Group. *Gastrointest Endosc* 2018; 87: 714–722.
10. Tamaru Y, Oka S, Tanaka S, *et al.* Endoscopic submucosal dissection for anorectal tumor with hemorrhoids close to the dentate line: a multicenter study of Hiroshima GI Endoscopy Study Group. *Surg Endosc* 2016; 30: 4425–4431.

11. Ritsuno H, Sakamoto N, Osada T, *et al.* Large superficial tumor of the colon involving a diverticulum removed by endoscopic submucosal dissection. *Gastrointest Endosc* 2015; 82: 751.
12. Kato M, Uraoka T, Wada M, *et al.* Laterally spreading tumor involving a colon diverticulum successfully resected by endoscopic submucosal dissection. *Gastrointest Endosc* 2016; 84: 191–192.
13. Yoshizaki T, Toyonaga T, Tanaka S, *et al.* Feasibility and safety of endoscopic submucosal dissection for lesions involving the ileocecal valve. *Endoscopy* 2016; 48: 639–645.
14. Dulskas A, Samalavicius NE, Gupta RK, *et al.* Laparoscopic colorectal surgery for colorectal polyps: single institution experience. *Wideochir Inne Tech Maloinwazyjne* 2015; 10: 73–78.
15. Jacob H, Toyonaga T, Ohara Y, *et al.* Endoscopic submucosal dissection of cecal lesions in proximity to the appendiceal orifice. *Endoscopy* 2016; 48: 829–836.
16. Tashima T, Ohata K, Nonaka K, *et al.* Endoscopic submucosal dissection for laterally spreading tumors involving the appendiceal orifice. *Surg Endosc* 2017; 31: 5444–5450.
17. Tanaka S, Kashida H, Saito Y, *et al.* JGES guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. *Dig Endosc* 2015; 27: 417–434.
18. Tanaka S, Saitoh Y, Matsuda T, *et al.* Evidence-based clinical practice guidelines for management of colorectal polyps. *J Gastroenterol* 2015; 50: 252–260.
19. Oka S, Tanaka S, Kanao H, *et al.* Current status in the occurrence of postoperative bleeding, perforation and residual/local recurrence during colonoscopic treatment in Japan. *Dig Endosc* 2010; 22: 376–380.
20. Asayama N, Oka S, Tanaka S, *et al.* Clinical usefulness of a single-use splinting tube for poor endoscope operability in deep colonic endoscopic submucosal dissection. *Endosc Int Open* 2016; 4: E614–E617.
21. Toyonaga T, Man-I M, Fujita T, *et al.* The performance of a novel ball-tipped Flush knife for endoscopic submucosal dissection: a case-control study. *Aliment Pharmacol Ther* 2010; 32: 908–915.
22. Tanaka S, Toyonaga T, Morita Y, *et al.* Feasibility and safety of endoscopic submucosal dissection for large colorectal tumors. *Surg Laparosc Endosc Percutan Tech* 2015; 25: 223–228.
23. Hayashi N, Tanaka S, Nishiyama S, *et al.* Predictors of incomplete resection and perforation associated with endoscopic submucosal dissection for colorectal tumors. *Gastrointest Endosc* 2014; 79: 427–435.
24. Matsumoto A, Tanaka S, Oba S, *et al.* Outcome of endoscopic submucosal dissection for colorectal tumors accompanied by fibrosis. *Scand J Gastroenterol* 2010; 45: 1329–1337.
25. Tajiri H and Kitano S. Complications associated with endoscopic mucosal resection: definition of bleeding that can be viewed as accidental. *Dig Endosc* 2004; 16(Suppl. 1): S134–S136.
26. Watanabe T, Itabashi M, Shimada Y, *et al.* Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2014 for treatment of colorectal cancer. *Int J Clin Oncol* 2015; 20: 207–239.
27. Schmidt A, Bauerfeind P, Gubler C, *et al.* Endoscopic full-thickness resection in the colorectum with a novel over-the-scope device: first experience. *Endoscopy* 2015; 47: 719–725.
28. Al-Bawardy B, Rajan E, Wong Kee Song LM, *et al.* Over-the-scope clip-assisted endoscopic full-thickness resection of epithelial and subepithelial GI lesions. *Gastrointest Endosc* 2017; 85: 1087–1092.
29. Valli PV, Mertens J and Bauerfeind P. Safe and successful resection of difficult GI lesions using a novel single-step full-thickness resection device (FTRD®). *Surg Endosc* 2018; 32: 289–299.
30. Oka S, Tanaka S, Takata S, *et al.* Usefulness and safety of SB knife Jr in endoscopic submucosal dissection for colorectal tumors. *Digest Endosc* 2012; 24: 90–95.
31. Ritsuno H, Sakamoto N, Osada T, *et al.* Prospective trial of traction device-assisted endoscopic submucosal dissection of large superficial colorectal tumors using the S-O clip. *Surg Endosc* 2014; 28: 3143–3149.
32. Eun Mi Song, Hyo-Joon Yang, Hyun Jung Lee, *et al.* Endoscopic resection of cecal polyps involving the appendiceal orifice: a KASID multicenter study. *Dig Dis Sci* 2017; 62: 3138–3148.
33. Kuriyama M. Acute appendicitis as a rare complication after colonoscopy. *Clin J Gastroenterol* 2014; 7: 32–35.
34. Nemoto Y, Tokuhisa J, Shimada N, *et al.* Acute appendicitis following endoscopic mucosal resection of cecal adenoma. *World J Gastroenterol* 2015; 21: 8462–8466.