Table 1. Clinicopathological characteristics of delayed bleeding cases

No.	Age	Gender	Resection method	Prophylactic clip	Interval[a] (days)	Location	Lesion size (mm)	Macroscopic type	Histopathology
1	61	F	EMR	Used	1	Transverse	25	Other	Carcinoma
2	56	M	EMR	Not	7	Ascending	25	Other	Carcinoma
3	80	M	EPMR	Not	1	Rectum	20	Other	Adenoma
4	70	M	EPMR	Not	10	Sigmoid	30	Other	Adenoma
5	71	M	EPMR	Not	7	Sigmoid	60	Other	Carcinoma
6	79	M	EPMR	Not	1	Sigmoid	20	Other	Adenoma
7	74	M	EPMR	Not	1	Cecum	50	Sessile	Adenoma
8	68	M	EPMR	Not	2	Cecum	40	Other	Carcinoma
9	59	M	EPMR	Not	1	Transverse	25	Other	Carcinoma
10	65	M	EPMR	Not	3	Transverse	30	Other	Carcinoma
11	61	M	EPMR	Not	3	Ascending	35	Other	Carcinoma
12	65	M	EPMR	Not	5	Rectum	25	Other	Carcinoma
13	52	F	PO	Not	1	Ascending	50	Other	Carcinoma
14	49	M	PO	Used	14	Sigmoid	28	Sessile	Carcinoma
15	64	M	EMR	Used	2	Transverse	40	Sessile	Carcinoma
16	54	M	EPMR	Not	7	Descending	20	Sessile	Adenoma
17	45	M	EMR	Not	2	Rectum	20	Sessile	Carcinoma

[a]Between ER and the onset of delayed bleeding.

Table 2. Comparison of patients with and without delayed bleeding

	Total	Delayed bleeding		*P* value
		Yes	No	
Number of patients	375	17	358	
Age, years (mean ± SD)	63.3 ± 12.3	63.3 ± 10.0	63.3 ± 12.4	NS
Gender (male/female)	240/135	15/2	225/133	0.04
Hypertension (+/−)	83/292	6/11	77/281	NS
Current use of anticoagulant drugs (+/−)	6/369	1/16	5/353	NS
Current use of antiplatelet drugs (+/−)	10/365	0/17	10/348	NS

NS, not significant.

1.5% ($P = 0.04$); hypertension (+/−), 7.2/3.8% ($P = 0.18$); current use of anticoagulant (+/−), 16.7/4.3% ($P = 0.24$); and current use of antiplatelet (+/−), 0/4.9% ($P = 0.53$). There was no delayed bleeding in one patient using both anticoagulant and antiplatelet drugs. There was virtually no difference between the two groups of patients with and without delayed bleeding in terms of mean age, but the delayed bleeding rate in males was significantly higher than in females.

Tumor-related Factors and Delayed Bleeding

A complete comparison of lesions with and without delayed bleeding is summarized in Table 3. As for tumor-related factors, our comparison of the incidence of delayed bleeding included the following results: tumor location (colon/rectum), 3.9/5.2% ($P = 0.81$); macroscopic type (sessile/other), 2.7/5.4% ($P = 0.59$); histopathological findings (adenoma/carcinoma), 3.8/4.4% ($P = 0.76$); resection method (*en bloc* resection/piecemeal resection), 3.1/5.3% ($P = 0.29$); and placement of prophylactic clips (used/not used), 1.7/6.1% ($P = 0.04$). There were no statistically significant differences between lesions with and without delayed bleeding except that the delayed bleeding rate was significantly higher in those cases without prophylactic clip placement.

Table 3. Comparison of lesions with and without delayed bleeding

	Total	Delayed bleeding		*P* value
		Yes	No	
Number of lesions	403	17	386	
Location (colon/rectum)	306/97	12/5	262/124	NS
Lesion size, mm (mean ± SD)	27.1 ± 9.6	31.9 ± 12.2	26.8 ± 9.5	NS
Macroscopic type (sessile/other[a])	182/221	5/12	177/209	NS
Histopathology (adenoma/carcinoma)	132/271	5/12	127/259	NS
Resection method (*en bloc*/piecemeal)	194/209	6/11	188/198	NS
Prophylactic clip placement (used/not used)	174/229	3/14	171/215	0.04

NS, not significant.
[a]Flat, depressed or recurrent.

DISCUSSION

In this study, the risk factors for delayed bleeding after ER were assessed in a group of patients specifically with large colorectal tumors which differed from previous reports. The delayed bleeding rate in male patients and those patients who did not receive prophylactic clip placement was significantly higher ($P = 0.04$).

A number of studies have attempted to identify the factors involved in the occurrence of delayed bleeding after ER, and various factors such as large size, sessile type, right-side location, hypertension and prior anticoagulation therapy have been proposed as being associated with an increased risk of delayed bleeding (15,25–31). This is the first large-scale study to assess these contributing factors in patients specifically with large colorectal tumors.

Delayed bleeding after ER is a clinically serious problem because it can lead to emergency endoscopic hemostasis, intensive patient care monitoring and/or the need for blood transfusions (12,15). Various studies have reported delayed bleeding in 0.3–6.1% of POs (12,15,28,32). In one recent investigation of 6617 POs by Watabe et al. (25), the rate of post-PO bleeding was 0.57%, but the mean size of polyps was only 5.6 mm. Our overall rate of delayed bleeding was higher undoubtedly because the mean size in this study was considerably larger at 27.1 ± 9.6 mm. The results of other studies have also indicated that polyp size was an important risk factor for bleeding both during and after a procedure (15,25–27,33,34), although there was no significant difference between cases with and without delayed bleeding for tumors ≥20 mm according to the results of our study.

In terms of patient-related factors, the delayed bleeding rate was significantly higher in males than females ($P = 0.04$). We could not elucidate from their medical records a possible reason why there was a gender-based difference in patients with delayed bleeding, however, because there was no available evidence regarding any lifestyle differences between male and female patients with delayed bleeding. Watabe et al. (25) concluded that hypertension was a significant risk factor for delayed bleeding, but there was no correlation between hypertension and delayed bleeding in our study. Neither could we find a correlation between the current use of anticoagulant and/or antiplatelet drugs and delayed bleeding.

In contrast, the delayed bleeding rate was significantly lower in the group of patients with prophylactic clip placement ($P = 0.04$). Application of hemostatic clips has been proven safe and effective for managing delayed bleeding following ER (35–37). Hachisu reported on 29 patients treated with prophylactic clipping following PO and delayed bleeding was not detected in any of them (38). A recent study indicated that prophylactic clip placement for the closure of mucosal defects in cases of gastric EMR reduced delayed bleeding (39), but it is still unclear whether or not such clip placement decreases the occurrence of delayed bleeding after ER for colorectal tumors. Although the study by Shioji et al. (12) indicated that clipping did not decrease the occurrence of delayed bleeding, we believe that their study population ($n = 413$) was too small to justify such a conclusion as 76.9% of the polyps were <10 mm (mean size, 7.8 mm). As a result, the efficacy of prophylactic clip placement for the prevention of delayed bleeding in large colorectal tumors remains uncertain and should be determined by analyzing a high-risk group.

The study by Friedland and Soetikno (40) reported that there were no bleeding episodes after resection of 41 polyps up to 10 mm in size followed immediately by prophylactic application in 21 patients receiving the long-term anticoagulation drug warfarin. Although it was a small single-center retrospective study, their findings indicated that prophylactic clip placement in a high-risk group of patients on anticoagulation medication could be effective against delayed bleeding. Our study group also involved high-risk patients because of the large mean size of the resected tumors. Hemoclips were applied to cases of immediate bleeding in our study and we were unable to separate such cases from the prophylactic clip placement cases. Although cases with

immediate bleeding would logically be expected to have a higher risk of delayed bleeding, the rate of delayed bleeding in the entire group in which clipping was performed was significantly lower. This is the first study demonstrating the efficacy of prophylactic clipping in preventing delayed bleeding for colorectal tumors $\geq$20 mm.

The fact that this also was a single-center retrospective study like the earlier Friedland and Soetikno study is the most notable limitation. A second limitation is that we cannot exclude the possibility of inter-endoscopist bias as to whether or not prophylactic clip placement was performed in individual cases.

The other significant risk factor for delayed bleeding involved male patients in our study compared with female patients. Particularly, in male patients, the delayed bleeding rate in patients without prophylactic clip placement was significantly higher (8.9%) compared with patients with prophylactic clip placement (1.8%) ($P = 0.03$). As indicated above, a recommendation from this study might be that prophylactic clipping should be performed in male patients. In contrast, however, other previously published studies have reported different risk factors for delayed bleeding including sessile type, right-side location, patient hypertension and prior or long-term anticoagulation therapy. In the future, investigation may demonstrate the effectiveness of prophylactic clip placement for patients having such risk factors. We would also have to consider the relationship if any between delayed bleeding and different clipping techniques involving complete closure or exposed vessel clipping. Consequently, the effectiveness of prophylactic clip placement after ER for large colorectal tumors needs to be confirmed in a prospective randomized multicenter trial.

In conclusion, the results of this study indicated that prophylactic clip placement may be an effective method for preventing delayed bleeding after ER for large colorectal tumors.

Authors' Contributions

S.F. and Y.S. conceived study concept and design. S.F. co-wrote the paper and analyzed the data together with T.S. and T.N. and T.M. All authors contributed to endoscopic technical support and discussed the results and commented on the manuscript.

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Conflict of interest statement

None declared.

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ORIGINAL ARTICLE

Safety and efficacy of colorectal endoscopic submucosal dissection in elders: clinical and follow-up outcomes

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Abstract
Purpose Endoscopic submucosal dissection (ESD) has recently been applied to treatment of colorectal neoplasia; however, its safety and efficacy in terms of follow-up outcomes in elders have not been thoroughly examined. The aim of this study is to describe the clinical outcomes of colorectal ESD in elderly patients.
Methods Two groups of patients, elderly (≥75 years of age) and non-elderly (<75 years of age), who underwent colorectal ESD at the National Cancer Center Hospital from February 1998 to December 2010 were retrospectively compared on the following measures: tumor size, procedure time, complication rates, en bloc resection rates, and curative resection rates. We also investigated the follow-up outcomes in non-curative resection cases.
Results Of 614 consecutive patients treated by colorectal ESD, 125 (20.4 %) comprised the elderly group, and 489 patients (79.6 %) comprised the non-elderly group. No significant differences were observed between the two groups in terms of tumor size, procedure time, complication rates, en bloc resection rates, and curative resection rates. Of the patients who underwent non-curative resection, 7/19 (36.8 %) and 47/63 (74.6 %) in the elderly and non-elderly group, respectively, underwent additional treatment. Among the elderly patients who were followed up without additional treatment, no case of local recurrence, residual lesions, or distant metastases was observed during the observation period.
Conclusion Treatment outcomes of colorectal ESD were equivalent in both groups. However, many of the non-curative cases in the elderly patients were followed up without additional treatment. Future studies should focus on the outcome in such patients to confirm the feasibility of colorectal ESD in elderly patients.

Keywords Endoscopic submucosal dissection (ESD) · Colorectal neoplasia · Elderly patients · Colon · Rectum · Laterally spreading tumor (LST)

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Introduction

Colorectal carcinoma is one of the most common cancers worldwide, and its prevalence is steadily increasing in Japan [1]. The increased life expectancy of elderly patients has created a demand for minimally invasive treatments for colorectal cancer in elderly patients [2, 3]. Endoscopic submucosal dissection (ESD), initially developed for early gastric cancer, enables the resection of large superficial tumors en bloc [4, 5]. The advantage of ESD over conventional endoscopic mucosal resection (EMR) is its ability to remove tumors en bloc, regardless of tumor size. Although recent studies have described the effective use of ESD for the treatment of superficial colorectal neoplasia, technical difficulties owing to its thinner wall, tortuous structure, and higher perforation rate in comparison with conventional EMR have been indicated [6–12], and reports on the safety of colorectal ESD in elderly patients are still

limited [13]. In addition, the effectiveness of colorectal ESD, especially follow-up outcomes in elderly patients with non-curative resection, has not been thoroughly examined. Performing additional treatments in elderly patients who have undergone non-curative resection is sometimes difficult due to their general condition. Therefore, the aim of this study is to describe the short-term and follow-up outcomes of non-curative colorectal ESD in elderly patients.

Materials and methods

A total of 614 consecutive patients with 635 colorectal lesions treated by ESD at the National Cancer Center Hospital from February 1998 to August 2010 were retrospectively reviewed. Written informed consent to participate was obtained from all patients who underwent colorectal ESD. We divided them into two groups: an elderly group consisting of patients ≥75 years of age and a non-elderly group consisting of patients <75 years of age. We compared the tumor size (measured by the pathologist after formalin fixation), procedure time, complication rate (perforation and delayed bleeding), en bloc resection rate, and curative resection rate between these two groups. We also investigated the follow-up outcomes of non-curative resection cases.

Inclusion criteria for ESD

For inclusion, the depth of invasion was limited to the mucosa or submucosal superficial (less than 1,000 μm from the muscularis mucosa) as estimated endoscopically as well as by magnification chromoendoscopy. The existence of a non-invasive pattern as determined by magnification chromoendoscopy was helpful in the diagnosis of tumor depth of invasion [14]. Based on extensive clinicopathological analyses, we defined the indications for colorectal ESD as nongranular type laterally spreading tumors (LSTs) larger than 20 mm and granular type LSTs larger than 30 mm because both have a higher submucosal invasion rate and are difficult to treat even by piecemeal EMR [15]. Patients with large villous tumors as well as intramucosal lesions, recurrent lesions, and residual mucosal lesions that showed a non-lifting sign after EMR were also potential candidates for ESD.

Exclusion criteria for ESD

Exclusion criteria included the existence of an invasive pattern [14], as determined by magnification chromoendoscopy, and other invasive cancers and circumferential tumors treated by surgery.

ESD methods

All patients underwent total bowel irrigation with 2–3 L of polyethylene glycol solution the morning of the procedure. Additional polyethylene glycol was administered as necessary. ESD was generally carried out using a single-channel colonoscope with a water-jet system (PCFQ260JI, Olympus Medical Systems, Tokyo, Japan). The margins of the lesions were delineated before ESD using 0.4 % indigo carmine spray dye. For submucosal injection, a mixture of two solutions was prepared before the procedure to create a longer-lasting submucosal fluid cushion. Solution 1 was indigo carmine dye (2 mL of 1 %) and epinephrine (1 mL of 0.1 %) mixed with 200 mL of 10 % glycerol and 5 % fructose in normal saline solution (glycerol; Chugai Pharmaceutical Co, Tokyo, Japan) in a container with the resulting solution. Solution 2 was sodium hyaluronate acid (Mucoup; Johnson & Johnson, Tokyo, Japan) with a smaller amount of indigo carmine dye and epinephrine. During ESD, a small amount of solution 1 was injected into the submucosal layer first to confirm the appropriate submucosal layer elevation. Solution 2 was then injected into the properly elevated submucosal layer, after which a partial marginal incision was performed with a bipolar needle knife (B-knife; Xeon Medical Co, Tokyo, Japan) from the oral side using the endoscope's retroflex position. Using the B-knife reduced the risk of perforation because of its bipolar current electric system. Following the partial marginal incision, a partial submucosal dissection was made using the B-knife. Once again, the solution was injected into the submucosal layer to lift up both the lesion and the submucosal layer from the muscle layer for a safe colorectal ESD. A series of partial marginal incisions followed by partial submucosal dissection was then performed until the lesion was resected completely. An insulation-tipped knife (Olympus Co, Tokyo, Japan) was used after the lesion had rolled up, and the submucosal layer could be directly visualized for safer and faster dissection. We also used a distal attachment that enables fine visualization of the submucosal layer and allows for counter-traction of the submucosal tissue (Fig. 1). The electrosurgical unit used was the ICC 200 (Erbe Elektromedizin, Tübingen, Germany). Intravenous midazolam (2 mg) and pentazocine (15 mg) were administered during all ESD procedures. An additional 2 mg of midazolam was administered whenever indicated based on the judgment of the colonoscopist. Hemo Stat-Y (Pentax, Tokyo, Japan) was used for hemostasis. Carbon dioxide insufflation was used instead of air insufflation to reduce patient discomfort.

Histological assessment

All specimens were fixed in 10 % buffered formalin and cut into 2-mm slices. Specimens were then examined

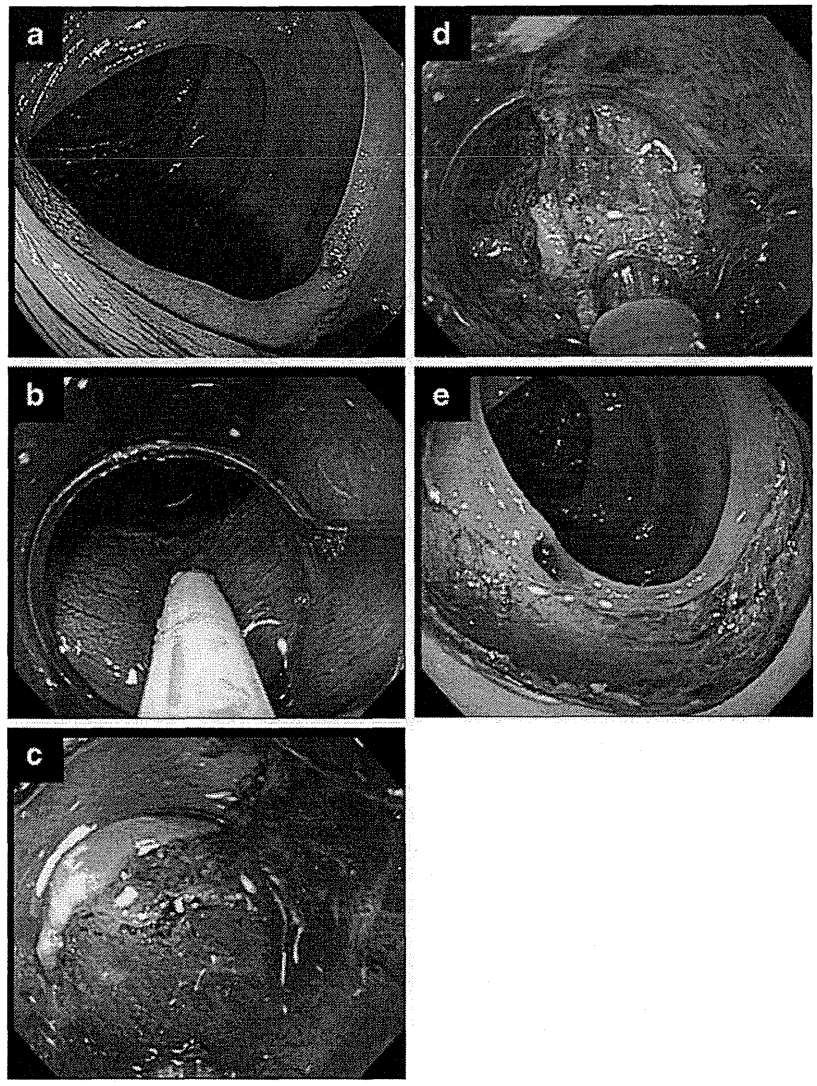

Fig. 1 **a** Nongranular type LST (40 mm in size) located in the ascending colon. **b** Injection of glycerol solution (10 % glycerol and 5 % fructose in normal saline solution) and sodium hyaluronate acid solution into SM layer. **c** Blue-colored submucosal layer clearly visualized using indigo carmine dye and distal attachment for counter-traction. **d** Submucosal dissection using a bipolar needle knife after partial circumferential incision. **e** Ulcer bed after successful en bloc resection

microscopically for depth of invasion, and their histological types and lateral and vertical resection margins were determined. A resection was considered tumor-free when both the lateral and vertical margins of the specimen were negative for tumor cells, irrespective of the histological features of the tumor. A resection was considered to be curative when the following criteria were met: the lateral and vertical margins of the specimen were free of cancer; submucosal invasion was less than 1,000 μm from the muscularis mucosae; and no lymphatic invasion, vascular involvement, or poorly differentiated components were detected. Histological diagnoses were based on the Japanese classification system for cancer of the colon and rectum and the Vienna classification system.

Follow-up

Endoscopic examinations were conducted for individuals with non-curative resections, who were followed up without additional treatment. Piecemeal resection cases were scheduled at 6 months after ESD, and en bloc resection cases were scheduled at 12 months after ESD [16]. After the first endoscopic examination, annual follow-up endoscopic examinations were scheduled. Contrast-enhanced computed tomography (CT) was also performed annually for patients with non-curative resections, who were followed up without additional treatment. The following information was retrospectively collected from medical records: date of the most recent endoscopy; date of the most recent CT scan; and the presence of residual tumors, local recurrence, or distant metastasis.

Statistical analysis

All variables in this study are described as mean±standard deviation (SD). For comparing baseline characteristics between the two groups, we used a *t* test for continuous

Table 1 Patient and tumor characteristics

	Elderly patients	Non-elderly patients	*p* value
Patients (*n*)	125 (20.4 %)	489 (79.6 %)	<0.0001
Lesions (*n*)	134	501	
Age (years), mean±SD	78.3±3.0	61.8±8.6	
Sex ratio			
Male/female	71:54	287:202	0.71
Tumor location			
Cecum or colon	104/134 (77.6 %)	363/501 (72.5 %)	0.21
Rectum	30/134 (22.4 %)	138/501 (27.5 %)	
Macroscopic type			
LST-NG	53/134 (39.6 %)	187/501 (37.3 %)	0.82
LST-G	59/134 (44 %)	238/501 (47.5 %)	
Protruded	7/134 (5.2 %)	31/501 (6.2 %)	
Depressed	4/134 (3.0 %)	11/501 (2.2 %)	
Residual/local recurrence	11/134 (8.2 %)	30/501 (6.0 %)	
SMT	0/134 (0 %)	4/501 (0.8 %)	
Histology			
Adenoma	33/134 (24.6 %)	100/501 (20 %)	0.35
Intramucosal cancer[a]	69/134 (51.5 %)	283/501 (56.5 %)	
SM superficial cancer[b]	15/134 (11.2 %)	53/501 (10.6 %)	
SM deep cancer	17/134 (12.7 %)	54/501 (10.8 %)	
Others	0/134 (0 %)	10/501 (2.0 %)	

[a]Submucosal invasion less than 1,000 μm from the muscularis mucosae

[b]Submucosal invasion 1,000 μm or more from the muscularis mucosae

variables, a chi-square test and Fisher exact tests as appropriate for dichotomous variables. All statistical analyses were performed using SPSS for Windows (SPSS, Release 6.0; SPSS Inc., Chicago, IL, USA, 1993). The *p* values are two sided, and $p<0.05$ was used to determine statistical significance.

Results

A total of 614 consecutive patients with 635 colorectal lesions were treated by colorectal ESD. Of these patients, 125 (20.4 %) were in the elderly group and 489 (79.6 %) were in the non-elderly group. There were no significant differences between the two groups with respect to gender ratio, tumor location, macroscopic tumor type, or histology (Table 1). No significant differences were observed between the two groups with respect to resected specimen size, procedure time, complication rate, en bloc resection rate, or non-curative resection rate (Table 2). Of the patients who underwent non-curative resection, 7/19 (36.8 %) in the elderly group and 47/63 (74.6 %) in the non-elderly group underwent additional treatment. Significantly fewer people in the elderly group underwent additional treatment. Among the 12 patients in the elderly group and the 16 in the non-elderly group who were followed up without surgery for a median of 46 and 27.5 months, respectively, there was no case of local recurrence, residual lesions, or distant metastasis observed during the study period. Among the seven elderly patients who underwent additional surgery

Table 2 Clinical outcomes of colorectal ESD

	Elderly patients	Non-elderly patients	*p* value
Tumor size			
Long axis (mm), mean±SD	35.2±17.4	36.3±18.5	0.54
Short axis (mm), mean±SD	30.9±15.6	29.5±15.4	0.34
Procedure time (min), mean±SD	104.7±77.0	102.7±72.2	0.79
Complication rate	3.7 % (5/134)	4.2 % (21/501)	0.19
Perforation rate	2.2 % (3/134)	2.6 % (13/501)	0.24
Postoperative bleeding rate	1.5 % (2/134)	1.6 % (7/501)	0.30
En bloc resection rate	93.3 % (125/134)	88.1 % (443/501)	0.085
Non-curative resection rate	14.2 % (19/134)	12.6 % (63/501)	0.62

Table 3 Outcomes of additional surgical treatment

	Elderly patients	Non-elderly patients
Additional surgical treatment [patients (*n*)/lesions (*n*)]	7/7	42/42
Residual lesions (%)	0/7 (0)	6/42 (14.3)
Lymph node metastases (%)	0/7 (0)	2/42 (4.8)
Distant metastases (%)	0/7 (0)	2/42 (4.8)

for non-curative lesions, no residual lesions or lymph node metastases were observed in the resected specimens. In contrast, of the 42 non-elderly patients who underwent additional surgery for non-curative lesions at the National Cancer Center Hospital, 6 (14.3 %) had residual tumors and 2 (4.8 %) had lymph node metastases in the resected specimens; distant metastases were confirmed in two patients (4.8 %; Table 3).

Discussion

The results of our study show that the short-term outcome of colorectal ESD in elderly patients was comparable to that in non-elderly patients, suggesting that colorectal ESD is technically feasible in both groups of patients. In this study, many of the non-curative cases in elderly patients were followed up without additional treatment; the most common reason for which was request for the same by the patient and family (Table 4). The evaluation of risk as determined by histological assessment of resected specimens, mostly en bloc, might have influenced patient and family choice. In the non-curative cases followed up without additional treatment, local recurrences, residual lesions, or distant metastases were not observed in either group during the study period. Considering that the mortality rates for surgical treatment have been reported as 1.7–10.1 % in elderly patients [17–20], it seems acceptable to follow-up non-curative cases in the elderly group without additional treatment. Nevertheless, the follow-up periods are still limited. According to a previous report, the mean post-operative hospital stay for laparoscopic colorectal resection was 7.2 days [21], while that for colorectal ESD in the patients of this study was 4.0 days. The short hospitalization period is a significant advantage of ESD, not only cost-wise but also in terms of avoiding functional decline in elderly patients [22]. Of the elderly patients who underwent additional surgery, no residual lesions, lymph node metastases, or distant metastases were observed upon follow-up. However, of the non-elderly patients who

Table 4 Non-curative cases followed up without additional treatment in elderly patients

Case	Age (years)	Sex	Tumor location	Macroscopic type	Reasons for non-curative treatment	Reasons for follow-up without additional treatment	Follow-up duration (M)	Vital status
Case 1	78	M	Rectum	Is	pSM 7,000 μm	Underlying disease (Parkinson's disease)	108	Living
Case 2	76	M	Rectum	IIa+IIc (LST-NG)	pSM 3,700 μm	Request of patient and family	7	Deceased (chronic heart failure)
Case 3	76	M	Ascending colon	IIa+IIc (LST-NG)	pSM 3,000 μm	Request of patient and family	57	Living
Case 4	75	F	Transverse colon	IIa+IIc (LST-NG)	pSM 500 μm poorly differentiated component	Request of patient and family	59	Living
Case 5	77	M	Sigmoid colon	IIa+IIc (LST-NG)	pSM 1,000 μm	Request of patient and family	76	Living
Case 6	75	F	Ascending colon	IIa+IIc (LST-NG)	pSM 1,300 μm	Request of patient and family	61	Living
Case 7	76	M	Rectum	IIa+IIc (LST-NG)	pSM 2,300 μm	Request of patient and family	60	Living
Case 8	75	F	Ascending colon	Is+IIa (LST-G)	pSM 2,000 μm	Request of patient and family	59	Living
Case 9	79	M	Rectosigmoid colon	IIa+IIc (LST-NG)	pSM 2,500 μm	Underlying disease (leukemia)	12	Deceased (leukemia)
Case 10	81	M	Rectum	IIa (LST-NG)	pSM 1,750 μm	Request of patient and family	42	Living
Case 11	77	M	Rectum	Is+IIa (LST-G)	pSM 6,000 μm	Underlying disease (depression)	46	Living
Case 12	76	M	Cecum	Is+IIa (LST-G)	pSM 1,300 μm	Request of patient and family	8	Living

underwent additional surgery, residual tumors were found in 14.3 %, lymph node metastases in 4.8 %, and distant metastases in 4.8 %. This discrepancy between elderly and non-elderly patients might indicate differences in the clinicopathological characteristics of colorectal cancer between young and elderly patients. Chou et al. reported that younger patients with colorectal cancer have more aggressive histopathological characteristics and poorer prognoses compared to older patients [18]. By collecting more data on the follow-up outcomes of non-curative cases, it may become possible to propose different strategies for elderly and non-elderly patients. In the current study, there was no significant difference between these two groups with respect to perforation rates, a finding discordant with other reports [23, 24]. All cases of perforation were successfully managed endoscopically, with no occurrence of panperitonitis in elderly patients. It can be assumed that mortality for panperitonitis is higher in elderly than non-elderly patients [25]. Even though we have reported less experience performing ESDs, fewer than 50 cases had independent risk factors for complications [6]. It is therefore feasible to perform colorectal ESD at high-volume centers, even in elderly patients.

Limitations of the present study include its single-center design, small number of patients followed up without additional treatment, and a short follow-up period. At this point, it is difficult to recommend a strategy for treating non-curative cases of colorectal ESD in elderly patients who have a higher risk of surgery-associated complications. Further follow-up studies that focus on mortality and complication rates are necessary to confirm the feasibility of colorectal ESD in elderly patients.

Conclusion

Treatment outcomes for colorectal ESD in elderly patients were equivalent to those in non-elderly patients. However, many of the non-curative cases in elderly patients were followed up without additional treatment. Thus, future studies should collect more information on treatment outcomes in such patients in order to confirm the feasibility of colorectal ESD in elderly patients.

Conflicts of interest All authors have no conflicts of interest or financial ties to disclose.

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INTERNAL MEDICINE

□ CASE REPORT □

Solitary Metastatic Colon Cancer Showing a Small Depressed Configuration

Hidetsugu Yamagishi, Taku Sakamoto, Takahisa Matsuda, Takeshi Nakajima and Yutaka Saito

Abstract

We herein present a case of IIc-like metastatic lung cancer that was detected early. A 65-year-old man presented with diarrhea and difficulty walking. Colonoscopy demonstrated a depressed lesion in the descending colon. However, the appearance of the lesion by endoscopy with a magnifying objective was not compatible with early colon cancer. Therefore, we performed diagnostic endoscopic mucosal resection to allow for an examination of the whole lesion. A histological examination demonstrated lung cancer metastasis to the colon. Only 1.6% of lung cancers metastasize to the large intestine, and metastatic colorectal cancer is not usually detected at an early stage. In the present case, however, endoscopy and a histological examination revealed alterations in the mucosal configuration of the lesion, which were unusual for early colon cancer.

Key words: colonoscopy, metastatic colon cancer

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Introduction

Gastrointestinal tract metastasis from a malignant tumor is rare, and the large intestine, in particular, is thought to be comparatively less prone to metastasis. Metastatic gastrointestinal tumors account for 1.9% of all metastatic alimentary canal tumors and 0.1-1.0% of malignant colorectal tumors (1). Among gastrointestinal tract tumors, metastasis from primary lung cancer accounts for only 0.19% of all cases (2). Such metastases are commonly detected in the small intestine (3) and have a higher predilection for occurrence in the jejunum than in the ileum. In addition, multiple (rather than solitary) lesions tend to occur in such metastases. Gastrointestinal tract metastasis is generally manifested by ileus or gastrointestinal bleeding at an advanced stage. We herein present a case of IIc-like colon metastasis from lung cancer that was detected at an early stage.

Case Report

A 65-year-old man presented with diarrhea, numbness, pain in both lower extremities, and difficulty walking. A barium enema examination indicated transverse colon stenosis, and computed tomography (CT) revealed nodular shadows in the liver. Both advanced colon cancer and metastatic liver cancer were diagnosed.

Colonoscopy showed no lesions in the transverse colon, but it did reveal a depressed lesion (3 mm) in the descending colon (Fig. 1). After indigo carmine dye spraying, the tumor and its margin became clearer (Fig. 2), and macroscopic type 0-IIc cancer was identified. Narrow-band imaging revealed slightly irregular and loose microcapillary vessels (Fig. 3). Crystal violet staining showed a small round pit pattern of Kudo's Type IIIs (Fig. 4). The endoscopic diagnosis was early colon cancer. We performed an endoscopic mucosal resection of the lesion.

A histological evaluation revealed a poorly differentiated adenocarcinoma in the submucosa (Fig. 5). The neoplastic cells appeared to have invaded the lamina propria stroma; the duct epithelium was unaffected. Vascular invasion was confirmed (Fig. 6 and 7). We suspected a metastatic rather than primary tumor based on the histology of the tumor and the fact that the tumor cells were negative for caudal-type homeobox-2, prostate-specific antigen and chromogranin A, and positive for thyroid transcription factor-1 (Fig. 8). We strongly suspected metastasis from lung cancer.

The presence of lung cancer was confirmed by CT, which

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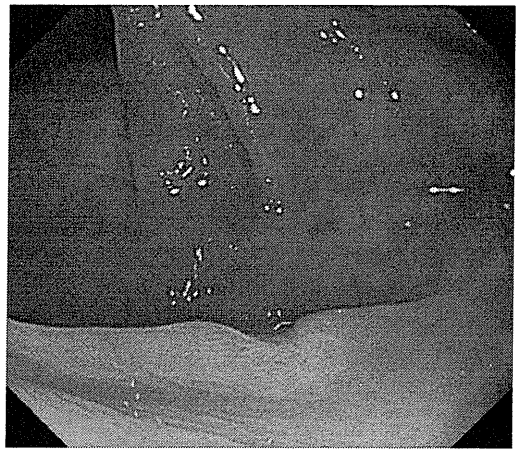

Figure 1. **Colonoscopy showed a depressed lesion in the descending colon.**

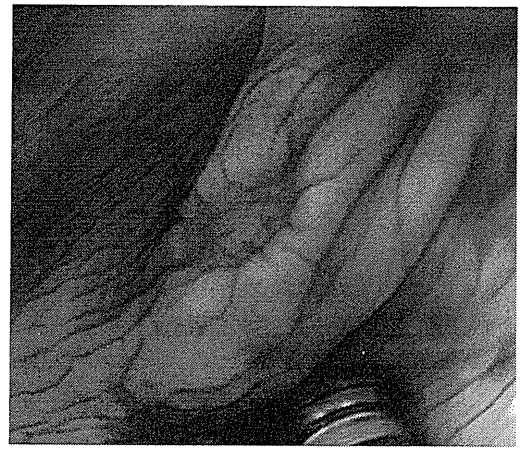

Figure 2. **Indigo carmine dye spraying.**

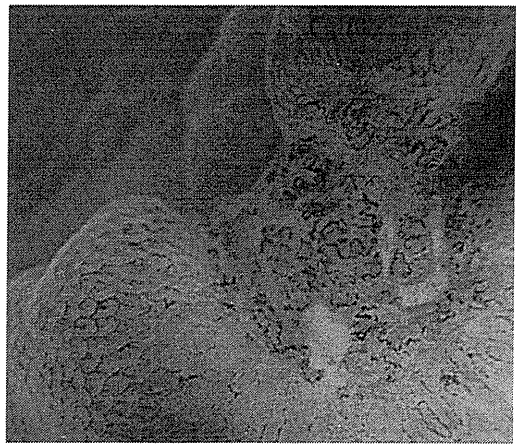

Figure 3. **Narrow-band imaging (NBI) showed normal vessels around the depressed area. There were slightly irregular vessels and loose microcapillary vessels in the depressed area.**

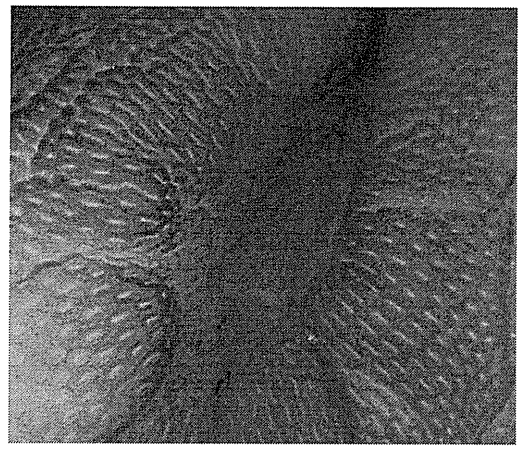

Figure 4. **Crystal violet staining revealed a normal pit pattern around the depressed area. The depressed area consisted of small irregular pits.**

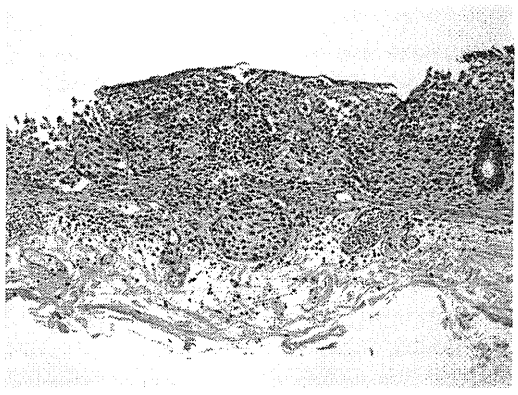

Figure 5. **Histology of the resected specimen showed poorly differentiated adenocarcinoma in the submucosa (Hematoxylin and Eosin staining, ×100).**

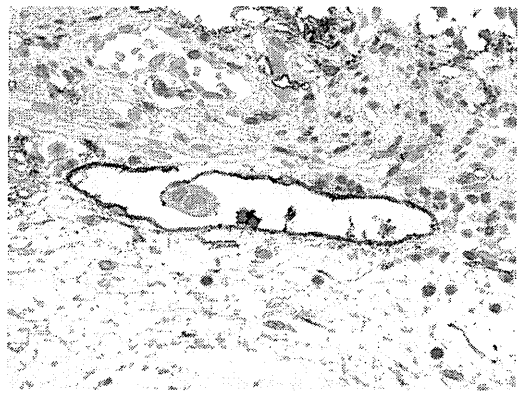

Figure 6. **Lymphatic invasion (D2-40, ×400).**

also revealed liver and bone metastases (Fig. 9 and 10). We diagnosed the patient with primary lung cancer based on the pathological examination and CT. The patient was transferred to the terminal care unit for the prophylactic control of pain and symptoms.

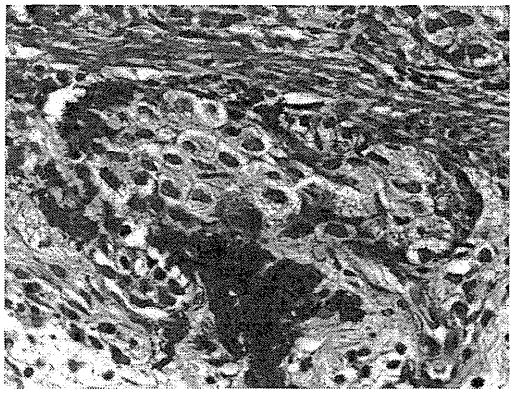

Figure 7. Venous invasion (Victoria blue-Hematoxylin and Eosin staining, ×400).

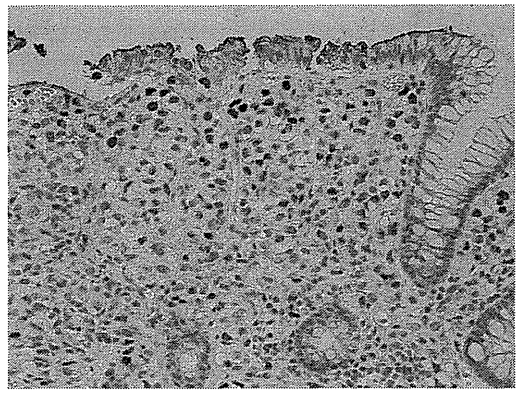

Figure 8. Thyroid transcription factor-1-positive tumor cells (×200).

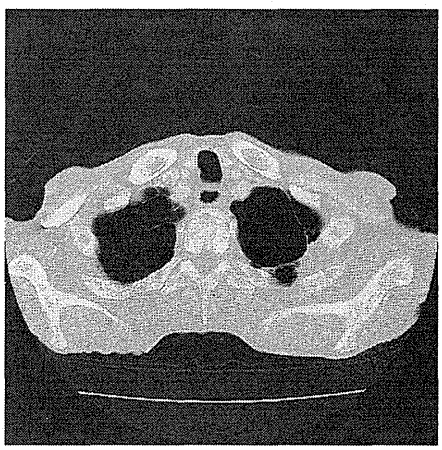

Figure 9. CT scan revealed the lung mass.

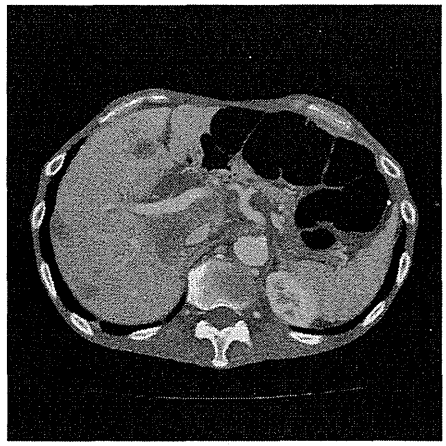

Figure 10. CT scan revealed the presence of multiple hepatic metastases and bone metastasis.

Discussion

The prevalence of lung cancer metastases to the large intestine is 1.6% in autopsy cases in Japan (4). Metastatic colorectal cancer is usually not detected at an early stage. This is probably because gastrointestinal tract metastases do not produce clinical symptoms, such as apoplexy, perforation, or intestinal atresia until the lesion becomes enlarged.

In the current case, our initial diagnosis was early primary colon cancer, which was based on the macroscopic appearance of the lesion during colonoscopy, and a metastatic tumor was not suspected. However, a retrospective analysis and confirmatory endoscopy showed alterations in the mucosal pattern in the lesion, which is not a common feature of early colon cancer. More typical images are seen for Narrow-band imaging (NBI) and pit patterns in cases of early colorectal cancer, but in the present case, the pits in the depressions were considered to correspond to atypical type III cancer. We therefore considered that in the initial lesion, there was little morphological change at the mucosal surface, and that such change was submucosal, because the tumor cells that had infiltrated into the submucosal layer had proliferated towards the epithelial side, thereby causing retraction of the normal non-malignant glandular tubules and making the pits appear small and round.

Furthermore, it was also considered that tumor cell proliferation towards the mucosal surface had led to ulceration, thereby producing 0-IIc-like changes with central depressions. Lung cancer metastasis to the large intestine mainly involves hematogenous spread (5), wherein the tumor cells initially spread to the submucosa and muscularis propria and then subsequently proliferate. Such tumors generally have diffuse infiltrating-type and submucosal tumor-like patterns.

Histopathologically, the neoplastic cells show a medullary proliferation pattern, accompanied by a fibrous stroma. Therefore, it is important to differentiate between endocrine cell carcinoma and metastasis from various organs. We considered that the metastasis might have originated from prostate cancer, but staining for prostate specific antigen (PSA) was negative. Subsequently, we considered metastasis from lung cancer and performed thyroid transcription factor-1 (TTF-1) staining, which is useful for making a differential diagnosis. TTF-1, discovered by Civitareale, shows high organ specificity and it is positive in both squamous cell carci-

noma (5-11%) and adenocarcinoma (62.5-72%) of the lung (6, 7). TTF-1 has also been reported to be expressed in 80-97% of small cell cancers. Therefore, to rule out small cell cancer in the present case, we performed chromogranin A staining, and negative results were obtained.

On the basis of these findings, we diagnosed the patient with lung cancer metastasis to the colon. This case of a IIc-like metastatic lesion from lung cancer is very rare, and the endoscopic appearance and pathological findings reported herein should therefore be important for the differential diagnosis of similar cases.

The authors state that they have no Conflict of Interest (COI).

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ORIGINAL ARTICLE—ALIMENTARY TRACT

The impact of narrow band imaging for colon polyp detection: a multicenter randomized controlled trial by tandem colonoscopy

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Abstract
Background Previous studies have yielded conflicting results on the adenoma detection rate with narrow band imaging (NBI) compared with white light imaging (WLI). To overcome the confounding factors of these studies, we aimed to evaluate the colonic adenoma detection rate with primary NBI versus that with primary WLI by using consistent NBI system, endoscope, and imaging settings, and experienced colonoscopists.
Methods In this multicenter prospective trial, 813 patients were randomized to undergo high-definition, tandem colonoscopy in the right colon with either NBI followed by WLI (NBI–WLI group) or WLI followed by NBI (WLI–NBI group). The NBI settings were fixed at surface structure enhancement level A-5 and adaptive index of hemoglobin color enhancement level 3. All detected polyps were resected or biopsied for histopathological analysis. The primary and secondary outcome measures were the adenoma detection rates and miss rates, respectively, with primary imaging.
Results The NBI–WLI and WLI–NBI groups comprised 389 and 393 patients, respectively, who met the inclusion criteria. The groups did not differ significantly in age, gender, institution, indication for colonoscopy, bowel preparation, or observation time. The adenoma detection rates of primary NBI and WLI were 42.3 and 42.5 %, respectively [difference not significant (NS)]. The adenoma miss rate was significantly less with primary NBI than with primary WLI (21.3 vs. 27.8 %; $p = 0.03$).
Conclusions NBI does not improve the adenoma detection rate during primary colonoscopy; however, it has a lower miss rate for adenoma lesions in the proximal colon than WLI.

Keywords Adenoma detection rate · Colonoscopy · Screening

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Introduction

Early detection and removal of colorectal adenoma lesions by screening colonoscopy are the most effective means of colorectal cancer prevention [1–3]. The adenoma detection rate is an important quality indicator for colonoscopy; moreover, this detection rate is an independent predictor of the risk of colorectal cancer after screening colonoscopy

[4]. Colonoscopy is considered the gold standard for the detection and treatment of colorectal polyps; however, white light imaging (WLI) has an adenoma miss rate of 10–30 % during colonoscopy [5–7]. Various methods, such as pan-colonic dye-spraying [8, 9], wide-angle colonoscopy [10, 11], Third Eye Retroscope colonoscopy [12, 13], and cap-fitted colonoscopy [14] reportedly reduce the adenoma miss rate. Similarly, some researchers have indicated improvements in the adenoma detection rate by performing colonoscopy with narrow band imaging (NBI) [15–21].

NBI is an innovative imaging technology that uses narrow band width filters [22, 23]. The center wavelengths of the dedicated trichromatic optical filters are 540 and 415 nm, with bandwidths of 30 nm. NBI enables endoscopic imaging with a one-touch electrical button and without indigo carmine dye-spraying. It also helps in clearly visualizing the microvascular structure of the organ surface, because the 415-nm light is well absorbed by hemoglobin. Given that the microvascular surface of an adenoma lesion is thicker and more irregular than that of normal mucosa, surface microvascular irregularities are useful landmarks for identifying an early neoplasm in the gastrointestinal tract; such lesions appear brownish during NBI. In addition, lesion detection and diagnosis can be performed simultaneously with NBI.

Muto et al. [24] reported the efficiency of NBI for the early detection of superficial cancers in the head and neck region and the esophagus. In the colorectal region, this modality was expected to enable the early detection of adenoma lesions; however, both positive [15–17] and negative [18–21] results have been reported, and some researchers have concluded that there was no improvement in the adenoma detection rate of NBI compared with that of WLI. One reason for these conflicting findings could be a difference between the optical-electronic technologies employed in the video endoscopes in the different NBI systems used [sequential system (LUCERA; Olympus Optical, Tokyo, Japan) vs. non-sequential system (EXERA II; Olympus Optical)]. Further, differences in the endoscope (low-resolution vs. high-resolution) and imaging (surface structure enhancement and index of hemoglobin color enhancement) settings can lead to different findings in the detection of the same lesion [25, 26]. Moreover, the colonoscopist's experience may have a considerable impact on the detection rate: if the colonoscopist does not have sufficient training in the chromoendoscopy of flat and depressed lesions with an NBI system, the usefulness of NBI for adenoma detection may not be evident. Finally, we note that most of the previous studies of NBI used a single-center design.

To overcome the aforementioned confounding factors, we aimed to evaluate the colonic adenoma detection rate achieved with NBI versus that achieved with WLI by using consistent NBI system, endoscope, and imaging settings, and experienced colonoscopists.

Patients and methods

Study population

Consecutive patients who were scheduled to undergo total colonoscopy with NBI at six institutions were considered eligible for inclusion in the study. The study was performed in university settings/academic centers. Patients with a history of surgical colorectal resection or those with inflammatory bowel disease, familial adenomatous polyposis, or hereditary non-polyposis colorectal cancer were excluded.

The institutional medical ethics committees approved the study protocol, which adhered to the tenets of the Declaration of Helsinki, and all patients gave written informed consent for diagnosis and treatment before the procedures. This study was registered in the University Hospital Medical Network Clinical Trials Registry (UMIN 000002934).

This study was supported by the Ministry of Health, Labour and Welfare of Japan, and there are no conflicts of interest between the authors and this or any other organization or company.

Study design

To investigate whether a lesion detected by primary imaging could be identified subsequently by the other type of imaging, or whether a lesion missed by primary imaging could be identified subsequently by the other type of imaging, the enrolled patients were randomized to undergo tandem colonoscopy with either NBI followed by WLI (NBI–WLI group) or WLI followed by NBI (WLI–NBI group).

After the endoscopists had achieved complete colonoscope insertion into the cecum with WLI, they were informed of the patient's allocation. Patients with poor bowel preparation, those with melanosis coli, those with multiple polyps unresectable in a single endoscopic examination, and those with advanced cancer were withdrawn.

We examined only the right colon, including the cecum, ascending colon, and transverse colon, because of a previous report of positive adenoma detection with NBI in this region, and to reduce the patient's discomfort during insertion and withdrawal.

Randomization

Random assignment was performed in each case by an investigator using a computer-aided system on the Medical Research Support website (Kyoto, Japan). A minimization algorithm was used to balance the selection of the primary

examination, according to the following 4 stratification variables: institution, age (<60 and ≥60 years), gender, and indication for colonoscopy.

Endoscopic equipment and setting

All procedures were performed up to the cecum by using a high-definition colonoscope (CF-H260AZI; Olympus Optical). A video endoscope system (EVIS LUCERA SPECTRUM; Olympus Optical) was used without a magnifying system. The NBI settings were fixed at surface structure enhancement level A-5 and adaptive index of hemoglobin color enhancement level 3. Twenty-seven endoscopists, each of whom had performed more than 5000 colonoscopies and more than 500 NBI colonoscopies, participated in this study.

Endoscopic procedure

For bowel preparation, 2–3 L of polyethylene glycol solution was administered in the morning on the day before the procedure. Scopolamine butylbromide (10 mg) was administered in the absence of contraindications, and midazolam (0.03 mg/kg) and/or pethidine hydrochloride (35 mg) was used for conscious sedation only when a patient complained of discomfort or pain. An examiner assessed the quality of bowel preparation according to the extent of mucosal visualization after suction of the fluid residue, as follows: excellent (approximately 100 % mucosal visualization following suction of fluid residue); good (approximately 90 % mucosal visualization); fair (less than 90 % mucosal visualization); poor (large amounts of solid fecal matter were found) [27]. The endoscopists who participated in the study were blinded to the indication for the procedure and and to the findings of previous colonoscopy.

In the NBI–WLI group, the colonoscope was withdrawn from the cecum to the splenic flexure with NBI, reinserted into the cecum, and then withdrawn again to the splenic flexure with WLI; in the WLI–NBI group, the same steps were performed with WLI first and then with NBI. The same endoscopist performed the primary and secondary examinations for the same patient. Patients were maintained in a supine position during NBI–WLI and WLI–NBI examinations, because changing the position did not influence the detection and miss rate [28].

In the primary examination, the endoscopists diagnosed lesions using the image obtained upon the detection of the lesion. At the same time, lesions less than 20 mm in diameter that were diagnosed as adenomas were removed endoscopically, and all lesions that were diagnosed as hyperplastic polyps were biopsied. All endoscopic treatments were performed using WLI. The same procedure was followed for the secondary examination. Adenoma lesions more than 20 mm in diameter were observed with both NBI and WLI and were removed by endoscopic mucosal resection or endoscopic submucosal dissection on another day in the hospital.

We did not use chromoendoscopy during the NBI or WLI because it elevates the adenoma detection rate; however, when observation with chromoendoscopy was diagnostically required, it was performed after the secondary examination.

In the primary examination, all lesions diagnosed as adenomas were removed by hot biopsy, snare polypectomy, endoscopic mucosal resection on the same day, or endoscopic submucosal dissection on another day, and all lesions diagnosed as hyperplastic polyps were biopsied. The location of each lesion was defined according to landmarks such as the hepatic flexure and splenic flexure. The lesion size was estimated by using open endoscopic biopsy forceps and/or a snare. Macroscopically, the lesions were classified according to the Paris classification of superficial gastrointestinal lesions [29]. We measured the total observation time, excluding mucosal washing, the diagnostic time, and the therapeutic time using a stopwatch. A doctor who was not the examiner, or a nurse, operated the stopwatch.

Histologic examination

All resected and biopsy specimens were retrieved, immediately fixed in 10 % buffered formalin solution, and examined histologically by hematoxylin and eosin staining. Experienced gastrointestinal pathologists blinded to the endoscopic diagnosis determined the histopathological diagnosis according to the World Health Organization (WHO) criteria [30]. Only traditional serrated adenoma (TSA) was included in the category of serrated adenoma.

Statistical analysis

The primary outcome measure was the detection rate of non-advanced adenoma lesions [adenoma with low-grade dysplasia (LGD)] and advanced adenoma lesions [adenoma of ≥10 mm or with villous histology in 25 % of polyps or with high-grade dysplasia (HGD) and submucosal invasive cancer] in the primary examination. Assuming an adenoma detection rate of 61 % in the right colon with WLI, from the pilot study at the National Cancer Center Hospital East and an increase of 16 % in the detection rate with NBI [17], the necessary sample number was calculated to be 369 patients in each group, 738 patients in total. Hence, 400 patients were required in each group for the probability of an α error to be 0.05 with a power of 0.80 (reflecting a β error of 0.2). The secondary outcome measure was the

adenoma miss rate in the primary examination; we defined a missed adenoma lesion as one detected only during the secondary examination.

Nominal and ordinal variables are expressed as frequencies and percentages. Continuous variables are expressed as means and standard deviations (age, adenoma lesions per patient) or medians and ranges (withdrawal time). Continuous data were compared by using the Mann–Whitney *U*-test. Pearson's χ^2test or Fisher's exact test was used to analyze categorical data and compare proportions. SPSS version 11 (SPSS, Chicago, IL, USA) was used for the statistical analyses. All statistical tests were two-tailed and significance was defined as $p < 0.05$.

Results

Group characteristics

Between October 2008 and March 2010, 813 patients were enrolled in this study. Of the 813 enrolled patients, 406 and 407 patients were randomly assigned to the NBI–WLI and WLI–NBI groups, respectively (Fig. 1). Three patients were withdrawn just before the primary examination, because of refusal to participate in the study ($n = 1$) and cardiac arrhythmia ($n = 2$). The colonoscope reached the cecum in 809 (99.9 %) of the remaining 810 study patients. Then 27 patients were withdrawn because of poor bowel preparation ($n = 8$), melanosis coli ($n = 6$), multiple polyps unresectable in a single endoscopic examination ($n = 5$), advanced cancer ($n = 4$), duplicated registration ($n = 1$), and other factors ($n = 3$). Finally, we analyzed 389 and 393 patients in the NBI–WLI and WLI–NBI groups, respectively.

The characteristics of the groups are listed in Table 1. The 782 analyzed patients included 553 (70 %) men, and the mean patient age was 63.2 ± 10.1 years. The indications for colonoscopy were polyp surveillance ($n = 553$), screening ($n = 183$), any abdominal symptoms ($n = 45$).and family history of colorectal cancer ($n = 1$). The bowel preparation was described as excellent, good, and fair in 246, 439, and 97 patients, respectively. The groups did not differ significantly in gender, age, indication for colonoscopy, bowel preparation, or institution. No complications occurred with the endoscopic treatment.

Table 2 shows the total observation times of the examinations. The observation times did not differ significantly between the groups.

Detection rates

The numbers of patients with lesions detected by primary NBI and WLI, including adenoma and hyperplastic polyp lesions, were 191 and 187, respectively (Table 3). The detection rate of adenoma lesions did not differ significantly between primary NBI and primary WLI (42.4 vs. 42.5 %). When we compared the detection rates of primary NBI and WLI by adenoma characteristics, the percentages of patients were not significantly different in terms of the number of lesions, non-advanced or advanced adenoma, and polypoid or flat and depressed adenoma.

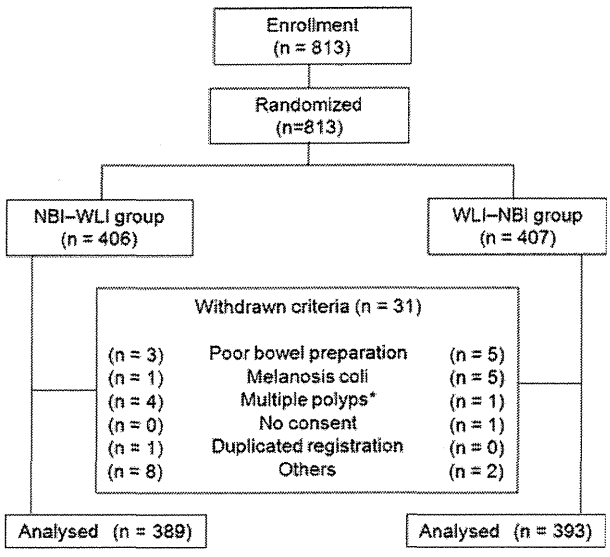

Fig. 1 CONSORT diagram. Overview of the study design. *Multiple polyps* (*asterisk*) many polyps unresectable in a single endoscopic examination, *NBI* narrow band imaging, *WLI* white light imaging

Table 1 Patient characteristics

Characteristic	NBI–WLI group ($n = 389$)	WLI–NBI group ($n = 393$)	p
Male gender	267 (69)	277 (70)	0.57
Mean (SD) age (years)	63.2 (10.2)	63.3 (9.9)	0.58
Indication for colonoscopy			0.67
Polyp surveillance	280	273	
Screening	88	95	
Any abdominal symptom	21	24	
Family history of CRC	0	1	
Bowel preparation			0.25
Excellent	115	131	
Good	219	220	
Fair	55	42	

Data represent the number of patients (%) unless indicated otherwise
NBI narrow band imaging, *WLI* white light imaging, *CRC* colorectal cancer

Table 2 Observation time

Time (s)	NBI–WLI group			WLI–NBI group			Primary imaging			Total		
	NBI	WLI	*p*	WLI	NBI	*p*	NBI	WLI	*p*	NBI	WLI	*p*
Median	210	164	0.67	180	180	0.98	210	180	0.76	190	180	0.78
Range	59–1112	52–1230		60–1200	20–1200		59–1112	60–1200		20–1200	52–1230	

NBI narrow band imaging, *WLI* white light imaging

Table 3 Detection rates of primary NBI and WLI

	Primary NBI ($n = 389$)	Primary WLI ($n = 393$)	*p*
Patients with any lesion	191 (49.1)	187 (47.6)	0.67
Patients with adenoma lesions	165 (42.4)	167 (42.5)	0.98
Mean (SD) no. of lesions per patient	0.79 (1.23)	0.79 (1.27)	0.98
Patients with 1–2 lesions	135 (34.7)	133 (33.8)	0.88
Patients with ≥3 lesions	30 (7.7)	34 (8.7)	
Patients with non-advanced adenoma[a]	106 (27.2)	112 (18.5)	0.59
Patients with advanced adenoma[a]	59 (15.2)	55 (14.0)	
Patients with polypoid adenoma only	30 (7.2)	45 (11.5)	0.06
Patients with flat and depressed adenoma	135 (34.1)	122 (31.0)	

Data represent the number of patients (%) unless indicated otherwise

[a] Advanced adenoma: adenomas ≥10 mm or with villous histology in 25 % of the polyps or with high-grade dysplasia or invasive cancer

Characteristics of the detected adenoma lesions

The total numbers of adenoma lesions detected by primary NBI and WLI were 306 and 310, respectively (Table 4), and those identified by secondary WLI and NBI were 83 and 119, respectively. The adenoma miss rates of primary NBI and WLI were significantly different (21.3 vs. 27.8 %; $p = 0.03$). In terms of location, there was no significant difference in the detection rate. Morphologically, polypoid lesions were detected significantly more often by primary NBI ($p = 0.006$). Further, 4-mm or smaller lesions ($p = 0.04$) and LGD ($p = 0.04$) were detected significantly more often by primary NBI. There was no significant difference in the detection rate for advanced adenoma. Figure 2 shows representative images of polyps detected by one imaging technique and missed by the other.

Discussion

The present study was the first randomized tandem colonoscopy trial in a multicenter setting for comparing the adenoma detection and miss rates of NBI and WLI. The results did not show any objective advantage of NBI over WLI in terms of improved detection of adenoma lesions in primary colonoscopy; however, NBI had a lower adenoma miss rate in the proximal colon than WLI by tandem colonoscopy.

The results of previous randomized trials comparing the adenoma detection rate of colonoscopy with NBI against that of colonoscopy without NBI are controversial. For example, Uraoka et al. [17] reported that the total number of adenoma lesions detected by colonoscopy with NBI was significantly higher than that detected by high-definition colonoscopy alone ($p = 0.02$) and adenomatous lesions in the right colon were identified more often by NBI ($p = 0.02$). Similarly, Inoue et al. [16] noted a significantly higher number of patients with detected diminutive (<5 mm) adenomas ($p = 0.011$) and lesions in the distal colon ($p = 0.02$) in their NBI group than in their control group. On the other hand, Rex and Helbig [18] reported no significant difference in the percentage of patients with adenomas detected by WLI versus NBI ($p = 0.68$). Further, Adler et al. [21] reported no significant difference between their NBI and their control groups in terms of the general adenoma detection rate (0.32 vs. 0.34 %). We attribute these varied results to differences in factors such as the NBI systems, endoscope and imaging settings, and the learning curves among the studies.

Differences in the NBI systems can be explained by differences between the optical-electronic technologies employed in video endoscopes in the previous studies: a sequential system (LUCERA) was used in the studies conducted in Japan and the United Kingdom, whereas a non-sequential system (EXERA II) was used in the other Western studies. Though we used only the LUCERA system in the present study, the present study was also a negative study of the rate of adenoma detection. Hence, we consider that the video endoscope system alone is not a reason for the negative study in the adenoma detection rate of NBI.

Darkness and noise of the viewing screen cause problems in NBI without high-definition colonoscopy, and