ORIGINAL RESEARCH ARTICLE

Can surveillance colonoscopy be discontinued in an elderly population with diminutive polyps?

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Abstract:
Objectives: Surveillance colonoscopy after endoscopic resection (ER) for adenomatous polyps reduces the incidence and mortality of colorectal cancer (CRC). However, its significance in the elderly population is uncertain. The study aimed to determine whether surveillance colonoscopy should be discontinued in the elderly population. Methods: We enrolled 105 patients who underwent baseline colonoscopy between January 2004 and December 2009 and were subsequently followed-up over 5 years in our institution. All had diminutive colorectal polyps and were aged <80 years at baseline colonoscopy and ≥80 years at follow-up in May 2018. Patients who had undergone colectomy or who had inflammatory bowel disease, familial adenomatous polyposis, Lynch syndrome, and no diminutive polyps were excluded. The cumulative incidence of the target lesion was evaluated. Histopathological diagnoses included low-grade dysplasia (LGD), high-grade dysplasia (HGD), and carcinoma. Results: The target lesion was detected in 15% (16/105) of the patients. There was no invasive carcinoma; however, two HGDs were detected. There were three lesions that had increased from previously detected diminutive lesions, all of which were LGDs. There were no target lesions detected after 84 years of age, and the cumulative incidence was 0.20. The cumulative incidence was significantly higher in the group with HGD than in the group with no target lesions at baseline colonoscopy. There was no HGD after age 79 years, and the cumulative incidence was 0.019. Conclusion: Surveillance colonoscopy for patients with diminutive polyps may be discontinued after age 79 years.

Keywords:
surveillance colonoscopy, elderly population, discontinuing surveillance, colorectal cancer, diminutive polyp

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Introduction

The National Polyp Study Workgroup has reported that endoscopic resection (ER) for adenomatous polyps reduces the incidence and mortality of colorectal cancer (CRC) by 76%-90% and 53%, respectively[1,2]. Surveillance colonoscopy should be performed until 3 years after ER of newly diagnosed polyps[3]. Several studies have shown that colonoscopy reduces the incidence of CRC[4-9].

Although there is general consensus regarding the utility of colonoscopy, the optimal interval for surveillance colonoscopy after ER for adenomatous polyps and CRC is unclear and varies among regions. In the United States[10] and Europe[11], the subsequent risk of advanced adenoma and CRC is stratified according to the number, size, and histology of the resected tumor at baseline colonoscopy, and the surveillance interval for each risk is defined in each guideline. In Japan, the decision whether to follow US or Euro-
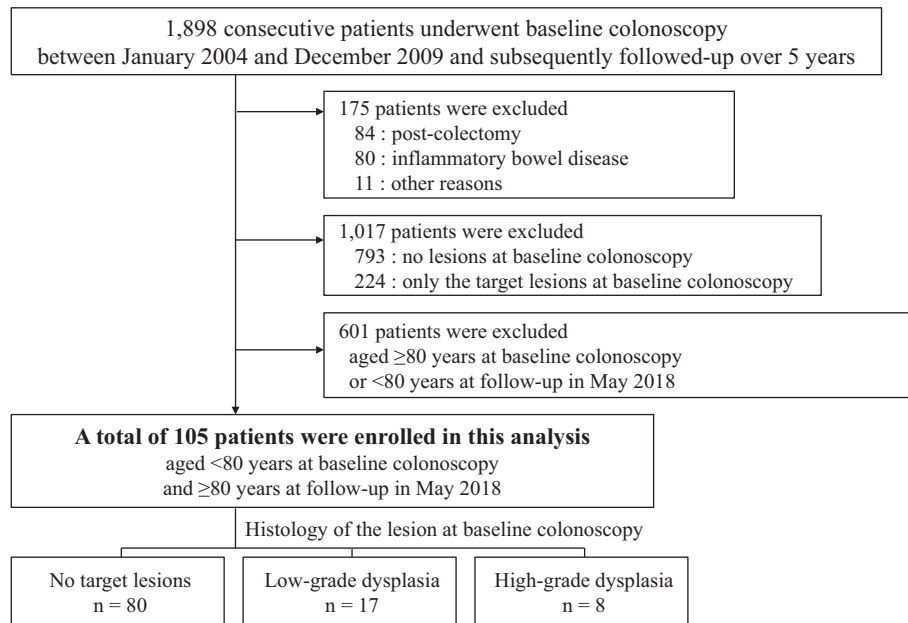
1,898 consecutive patients underwent baseline colonoscopy
between January 2004 and December 2009 and subsequently followed-up over 5 years

175 patients were excluded
 84 : post-colectomy
 80 : inflammatory bowel disease
 11 : other reasons

1,017 patients were excluded
 793 : no lesions at baseline colonoscopy
 224 : only the target lesions at baseline colonoscopy

601 patients were excluded
 aged ≥80 years at baseline colonoscopy
 or <80 years at follow-up in May 2018

A total of 105 patients were enrolled in this analysis
aged <80 years at baseline colonoscopy
and ≥80 years at follow-up in May 2018

Histology of the lesion at baseline colonoscopy

| No target lesions
n = 80 | Low-grade dysplasia
n = 17 | High-grade dysplasia
n = 8 |

Figure 1. Patient enrollment flowchart.

pean guidelines is uncertain because management for diminutive adenomas has not been established (i.e., whether to resect or to conduct follow-up)[12-15]. Therefore, in the current Japanese guideline, surveillance colonoscopy is recommended within 3 years after ER[16].

The population is aging rapidly, particularly in developed countries, resulting in an increased need for colonoscopy for preventing CRC. However, an increase in the number of colonoscopies causes an increase in medical expenses and shortages in medical resources; colonoscopy itself causes a relatively heavy physical burden in the elderly population. The appropriateness and timing of discontinuing surveillance colonoscopy in the elderly population should be considered in terms of necessity, safety, and cost-effectiveness. Although the US and European guidelines recommend discontinuation of routine surveillance colonoscopy after age 75 years[10,11], several studies on the benefits and disadvantages of discontinuing surveillance colonoscopy and the appropriate age to discontinue surveillance have reported conflicting results[17-23].

Therefore, we aimed to determine whether surveillance colonoscopy should be discontinued in the elderly with diminutive polyps. By evaluating the incidence of colorectal neoplasia, we determined the cutoff age at which clinicians can discontinue surveillance.

Methods

Patient Enrollment

Of the 1,898 consecutive patients who underwent baseline colonoscopy between January 2004 and December 2009, in whom the target lesions were resected and who were subsequently followed-up over 5 years at Hiroshima University Hospital, those with post-colectomy, inflammatory bowel disease, and no diminutive polyps were excluded, and 706 patients with diminutive colorectal polyps were recruited. Thereafter, those aged ≥80 years at baseline colonoscopy and <80 years at follow-up in May 2018 were excluded. Finally, we enrolled 105 patients (aged <80 years at baseline colonoscopy and ≥80 years at follow-up in May 2018). The patient recruitment flowchart is shown in Figure 1. Patients with diminutive (≤5 mm) adenomatous polyps in the colorectum were followed-up with annual surveillance colonoscopy without resection[24].

The study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by Hiroshima University's Institutional Review Board.

Colonoscopy

Although annual surveillance colonoscopy after baseline colonoscopy was performed in principle, the surveillance interval was determined according to each individual patient's preferences, comorbidities, and systemic conditions. All patients underwent colonoscopies at least three times during the follow-up period, and each surveillance interval was more than one year.

Colonoscopy was performed with a high-resolution video endoscope with magnification (EC-450ZH, EC-450ZW, or EC-L590ZW, FUJIFILM, Tokyo, Japan; or CF-Q240ZI, CF-H260AZI, PCF-Q260AZI, CF-HQ290I, PCF-H290ZI, or CF-HQ290ZI, Olympus, Tokyo, Japan). All colorectal lesions were investigated via magnification with indigo carmine. If the lesion showed irregular pit patterns[25,26], further

Table 1. Clinical Characteristics of the Enrolled Patients.

Variables	n = 105 (%)
Age at baseline colonoscopy, year, mean ± SD (range)	74 ± 3 (68-79)
Age at observation colonoscopy, year, mean ± SD (range)	83 ± 2 (80-89)
Sex, male	79 (75)
Follow-up period, month, mean ± SD	104 ± 28
Use of low-dose aspirin	18 (17)
Incidence of the target lesion	16 (15)
Histology of the lesion at baseline colonoscopy	
No target lesions	80 (76)
LGD	17 (16)
HGD	8 (8)

SD, standard deviation; LGD, low-grade dysplasia; HGD, high-grade dysplasia

magnification with crystal violet was performed. The size of the lesion was measured using a biopsy forceps or a measuring device. All colonoscopies required intubation to the cecum, performed by endoscopists with an experience of ≥1,000 total colonoscopies.

Evaluation

The target lesion indicated for ER was defined according to the guidelines stipulated by the Japanese Society of Gastroenterology[16] as follows: adenoma ≥6 mm in size, flat and depressed lesion, and lesion with type V pit pattern regardless of tumor size. Histopathological diagnosis was classified as low-grade dysplasia (LGD), high-grade dysplasia (HGD), and carcinoma according to the World Health Organization classification system[27]. HGD corresponds to intramucosal carcinoma according to the criteria in the Japanese Classification of Colorectal, Appendiceal, and Anal Carcinomas[28].

Clinicopathological features of the target lesion detected during surveillance colonoscopy (including newly detected lesions and lesions increased in size from previously detected diminutive lesion) and the cumulative incidence of the target lesion as well as their differences between the groups categorized by the lesion at baseline colonoscopy (no target lesion, LGD, and HGD) were evaluated. The cumulative incidences of carcinoma and HGD were also evaluated.

Continuous variables were expressed as mean ± standard deviation (SD). The cumulative incidence of the target lesion was calculated using the Kaplan-Meier method. Comparisons between the groups were made using the log-rank test. JMP version 14.0 (SAS institute Inc., Cary, NC, USA) was used for statistical analysis, and a *P*-value <0.05 was considered statistically significant.

Results

The clinical characteristics of the enrolled patients are shown in Table 1. The mean age at baseline colonoscopy

and observation colonoscopy was 74 and 83 years, respectively, and the mean follow-up period was 104 months. There were no patients with carcinoma at baseline colonoscopy. The target lesion was detected in 15% (16/105) of the patients. Table 2 shows the clinicopathological features of the 16 target lesions detected via surveillance colonoscopy. There was no invasive carcinoma, whereas two HGDs were detected within 36 months after the baseline colonoscopy. There were three lesions that increased from previously detected diminutive lesions, all of which were LGDs. There were no other lesions that developed during the subsequent follow-up period after resection of the target lesions detected at surveillance colonoscopy. There was no relationship between the lesions at baseline colonoscopy and the lesions detected at surveillance colonoscopy.

The cumulative incidence of the target lesion is shown in Figure 2. There were no target lesions detected after age 84 years, for a cumulative incidence of 0.20 (95% confidence interval (CI), 0.12-0.32). Figure 3 shows the cumulative incidence of the target lesion categorized by histology at baseline colonoscopy. The cumulative incidence was significantly higher in the group with HGD than that in the group with no target lesions at baseline colonoscopy. The cumulative incidence of HGD at age 79 years was 0.019 (95% CI, 0.005-0.073), and no HGDs occurred subsequently at follow-up patients at age 80 (n = 103), 82 (n = 61), and 84 (n = 32) years, respectively (Figure 4). There were no adverse events associated with baseline and surveillance colonoscopies.

Discussion

This study reports the incidence of target lesions in an elderly population with diminutive polyps during surveillance colonoscopy at a high-volume center. Studies on the diagnostic yield of CRC and necessity of colonoscopy in the elderly population have yielded conflicting results. In a study of previously screened patients aged ≥70 years, Hare-

Table 2. Clinicopathological Features of the Target Lesions Detected via Surveillance Colonoscopy.

No.	Detected lesion at surveillance colonoscopy									At baseline colonoscopy	
	Age (year)	Sex	Size (mm)	Location	Macroscopic type	Histology	Increased lesion*	Period to detect (month)	Subsequent follow-up period (month)	No. of lesion**	Worst histology
1	75	M	8	A/C	0-Is	LGD	No	25	76	1	-
2	75	M	6	S/C	0-Is	LGD	No	21	64	10	LGD
3	76	M	6	D/C	0-Isp	LGD	No	58	61	3	HGD
4	76	M	10	Rb	0-IIa	HGD	No	15	138	3	-
5	77	M	6	T/C	0-Is	LGD	No	70	51	5	HGD
6	78	F	7	T/C	0-Isp	LGD	No	31	52	1	-
7	78	M	10	S/C	0-Isp	LGD	Yes	78	38	4	LGD
8	79	M	6	S/C	0-Is	LGD	No	54	37	5	-
9	79	M	6	A/C	0-Is	LGD	No	35	63	2	LGD
10	79	M	7	S/C	0-Is	HGD	No	36	105	3	-
11	80	F	6	S/C	0-Isp	LGD	Yes	123	28	3	HGD
12	81	M	6	S/C	0-Is	LGD	No	62	45	3	-
13	82	M	6	S/C	0-Is	LGD	No	97	28	2	-
14	82	M	6	S/C	0-Is	LGD	No	51	59	6	LGD
15	83	M	7	T/C	0-Isp	LGD	Yes	110	22	3	-
16	84	M	12	T/C	0-IIa	LGD	No	127	11	1	-

LGD, low-grade dysplasia; HGD, high-grade dysplasia

* Lesion increased in size compared with previously detected diminutive lesion

** Including resected target lesions and left in situ diminutive polyps
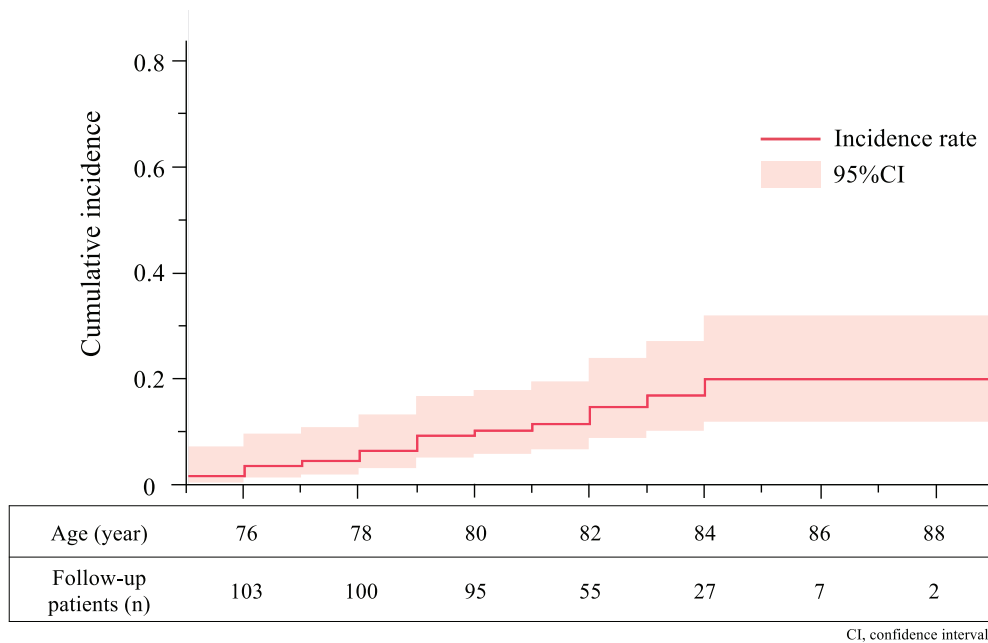
Figure 2. Cumulative incidence of the target lesion. There was no incidence of the target lesion after age 84 years, and the cumulative incidence was 0.20.

wood et al. concluded that surveillance colonoscopy remains important in elderly patients because the incident rate of carcinoma increased more sharply with age, whereas that of neoplasia increased slowly[17]. Stevens et al. also argued against discontinuing screening colonoscopy in the elderly[18]. Meanwhile, it was reported that the mean extension of life
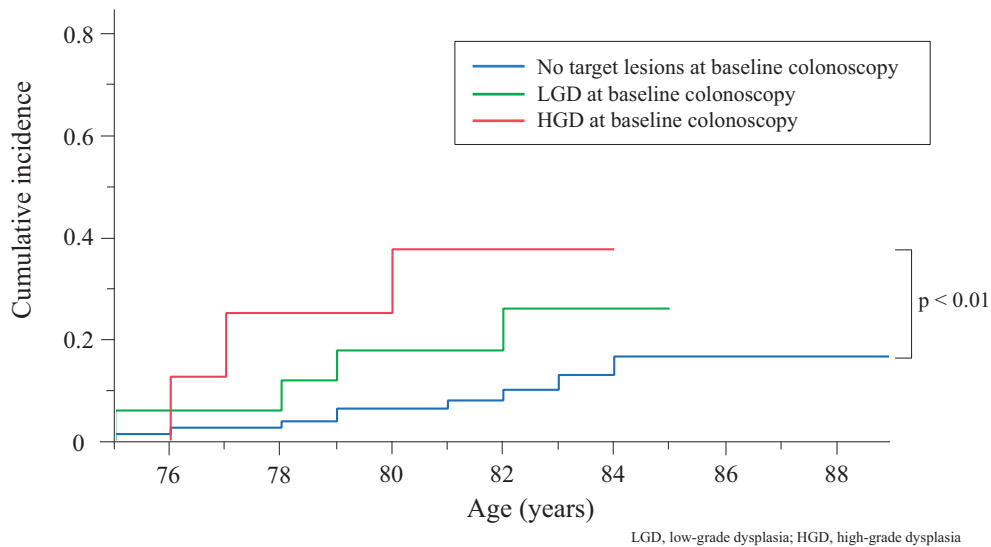
Figure 3. Cumulative incidence of the target lesion categorized by the lesion at baseline colonoscopy. The cumulative incidence was significantly higher in the group with HGD than that in the group with no target lesions at baseline colonoscopy.
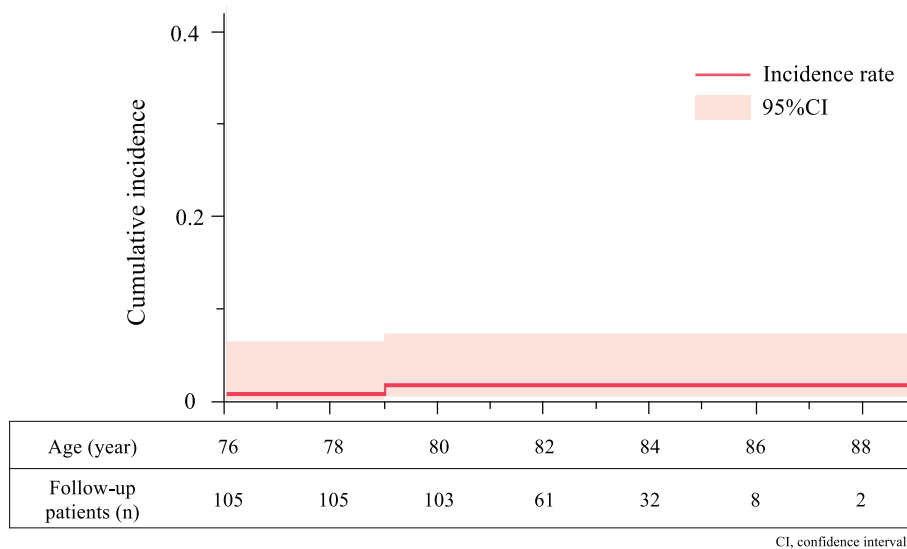

Figure 4. Cumulative incidence of HGD. There was no incidence of HGD after age 79 years, and the cumulative incidence was 0.019.

expectancy via screening colonoscopy in patients aged ≥ 80 years was only 15% of the expected gain in younger patients aged 50-54 years, although the prevalence of neoplasia was higher in elderly patients[19]. There are some studies showing low diagnostic yield of CRC in elderly patients who had undergone screening or surveillance examinations[20-23]. As for screening colonoscopy, a prospective cohort study has reported the impact of colonoscopy on preventing CRC in those aged 70-79 years who had not undergone colonoscopy in the previous 5 years[20]. In those aged 70-74 years, the risk of CRC over 8 years was lower in those who underwent colonoscopy group than in those who did not (2.19% vs. 2.62%). By contrast, it was not lower in those aged 75 to 79 years (2.84% vs. 2.97%, respectively). Regarding surveillance colonoscopy, the incidence of CRC in patients aged ≥75 years who underwent surveillance colonoscopy was lower than that in the reference population (aged 50-74 years) (0.24 per 1,000 person-years vs. 3.61 per person-years[22]).

The incidence of adverse events associated with colonoscopy is high in the elderly population[20,22,24-30]. A meta-analysis showed that the incidence rates of adverse events

(per 1,000 colonoscopies) in patients aged ≥65 years were 1.0 for perforation, 6.3 for gastrointestinal bleeding, 19.1 for cardiovascular/pulmonary complications, and 1.0 for mortality[29]. Particularly, in patients aged ≥80 years, the incidence rates were 1.5 for perforation, 2.4 for gastrointestinal bleeding, 28.9 for cardiovascular/pulmonary complications, and 0.5 for mortality. Given that many studies have also reported that the incidence of these serious adverse events and subsequent hospitalization associated with colonoscopy increased with age and comorbidity[20,22,30,31], it is important to consider that the risk may exceed the benefit of colonoscopy in the elderly population. Colonoscopy is not a completely reliable modality because there are some CRCs that are diagnosed within 3 or 5 years after previous colonoscopy without detected cancer, termed post-colonoscopy colorectal cancer (PCCRC). The rate of PCCRC varies from 2.7% to 12.1% according to reports[32-38]. PCCRC is thought to have more rapid growing potential than other CRCs[8], or they are simply missed in previous colonoscopies[39].

The rapid aging of the population and prolonged life expectancy in recent years have led to an increasing number of colonoscopies performed in the elderly population that in turn results in a healthcare burden (increased medical expense and low cost-effectivity). Van Hess et al. evaluated which test should be indicated for preventing CRC at what age from the viewpoint of comorbidity and cost-effectiveness[40]. They suggested that colonoscopy, sigmoidoscopy, and fecal immunochemical test were cost-effective for unscreened patients without any comorbidities until the age of 83, 84, and 86 years, respectively. Meanwhile, in unscreened elderly with moderate and severe comorbidity, CRC screening was cost-effective up to age 83 and 80 years, respectively.

The latest United States[10] and European[11] guidelines have included the indication of colonoscopy for elderly population to prevent CRC. In the European guideline[11], the recommended cutoff age for discontinuing surveillance is 75 years; this also depends on the patient's preferences and comorbidities. In the United States, the United States Preventive Services Task Force determined that screening should not be continued after age 85 years because the risk could exceed the potential benefit[41]. For patients aged 75-85 years, they recommend discontinuation of routine screening with consideration of the comorbidities and findings of a prior colonoscopy. The American Cancer Society made almost the same proposal[42]. Collectively, colonoscopy is infrequently recommended in the elderly population overseas.

In Japan, one of the countries with the longest life expectancies, the decision to follow these guidelines is uncertain. Our study revealed that the cumulative incidence of the target lesion slowly increased with age, and the cumulative incidence at age 84 years was 20%. The cumulative incidence of the target lesion was higher in the group with HGD than

that in the group with no target lesions at baseline colonoscopy, which is similar to the reports of previous studies[3,43-45]. Although our results may be helpful for determining the surveillance interval, it is necessary to consider the progression rate of neoplasia and life expectancy in the elderly population. Because the lead time for progression from LGD to carcinoma is around 10 to 20 years[46,47], the possibility that LGD will grow to developed carcinoma and lead to death within the period of life expectancy is considered low. Our study supports this expectation because there were only three lesions that increased from diminutive lesions at baseline colonoscopy during the 78-123 months of follow-up, and their histology was all LGDs.

Despite the fact that the surveillance interval of this study was shorter than those of other studies and there were small differences in age and life expectancy between the cohort in the present study and those in previous studies, the cumulative incidence of CRC in this study was 0%, lower than reported previously (1.0% in patients aged ≥70 years undergoing surveillance colonoscopy[17], 0.24 per 1,000 person-years in patients aged ≥75 years undergoing surveillance colonoscopy[22], and 2.19 to 2.84% in patients aged 70-79 years undergoing screening colonoscopy)[19]. The cumulative incidence of HGD was 1.9%, and no HGDs were found during surveillance colonoscopy after age 79 years. Although the HGDs were detected in a short interval, and they may progress to carcinoma if not resected when detected, the cumulative incidence of CRC was estimated at less than 1.9%. In the present study, although quality indicators such as adenoma detection rate[39] were not assessed, all colonoscopies were performed by experienced endoscopists at least three times during the study period with short intervals. High-quality colonoscopy is thought to contribute to the low incidence of target lesions.

Our finding of a low cumulative incidence of target lesions supports the discontinuation of surveillance colonoscopy in patients without any target lesions by age 79 years. Studies on the existence of PCCRC, high incidence of adverse events associated with colonoscopy, and the problem of cost-effectiveness in the elderly population also support this recommendation, despite differences in investigated regions, healthcare systems, and medical levels.

This study has some limitations. First, this was a single-center retrospective study, and the number of patients was relatively small. In addition, patients who were status post-colectomy were excluded because they have a high risk of metachronous colorectal carcinoma. Surveillance for them should be evaluated in another study. Second, patients enrolled in this study were limited to those with diminutive polyps; therefore, the findings on surveillance colonoscopy in this study are not generalizable to the general population. Nevertheless, the incidence of colorectal carcinoma in the general population cannot be higher than that in this study

population on the basis of the assumption that those with diminutive polyps are at a potentially higher risk of colorectal carcinoma than are those with no diminutive polyps[46,47]. Third, as the results were obtained from patients at an academic hospital, the patient characteristics may be different from those of the general population. The patients may have dropped out due to other serious illness. Fourth, the short interval of surveillance colonoscopy may have allowed for the early detection of lesions before they progressed to carcinoma. Finally, other factors related to CRC such as comorbidity were not evaluated. Nevertheless, we showed the low incidence of target lesion via high-quality surveillance colonoscopy.

In conclusion, there was no incidence of carcinoma and HGD after age 79 years, and the cumulative incidence of the target lesion was quite low. Therefore, surveillance colonoscopy for patients with diminutive polyps may be discontinued after aged over 79 years.

Disclaimer

Shinji Tanaka is one of the Associate Editors of Journal of the Anus, Rectum and Colon and on the journal's Editorial Board. He was not involved in the editorial evaluation or decision to accept this article for publication at all.

Conflicts of Interest

There are no conflicts of interest.

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