RESEARCH ARTICLE

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Significance of Total Colonoscopy Based on the Outcome of Advanced Colorectal Cancer in Older Individuals

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Abstract

Background: With the increase in Japan's aging population, the number of total colonoscopies (TCS) performed in individuals aged over 80 years is rising. However, TCS carries an increased risk of complications in older individuals, raising concerns about its utility in this population. This study aimed to evaluate the clinical value of TCS in older individuals diagnosed with advanced colorectal cancer (CRC) at our institution. **Materials and Methods:** We conducted a retrospective review of patients aged ≥80 years who underwent TCS between January 2010 and December 2021. Patients diagnosed with advanced CRC were categorized into symptomatic and asymptomatic groups based on the presence or absence of symptoms. The groups were compared in terms of clinical characteristics, pathological features, and long-term outcomes. **Results:** Among 4,130 older patients who underwent TCS, 297 (7.2%) were diagnosed with advanced CRC. Of these, 221 (74%) were symptomatic, and 76 (26%) were asymptomatic. Compared with symptomatic patients, asymptomatic patients had significantly higher body mass index (23.6 vs. 21.5 kg/m^2), serum albumin levels (3.7 vs. 3.5 g/dL), and lower carcinoembryonic antigen (CEA; 3.9 vs. 5.6 ng/mL) and carbohydrate antigen 19-9 (CA19-9; 13.4 vs. 19.7 U/mL) levels (all $p<0.05$). The asymptomatic group also had a higher rate of early-stage disease (68.4% vs. 36.2%) and a greater history of prior TCS (21.1% vs. 5.4%, $p<0.001$). Five-year overall and disease-specific survival rates were significantly higher in the asymptomatic group (68.3% and 88.3%, respectively) compared to the symptomatic group (38.7% and 65.5%) ($p<0.001$). No severe complications, such as perforation, were observed. **Conclusion:** TCS facilitates early detection and improves prognosis in older patients with advanced CRC, supporting its use in appropriately selected individuals.

Keywords: Colorectal cancer- Total colonoscopy- Older patients- Screening

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Introduction

Colorectal cancer (CRC) is one of the most common cancers globally, ranking third in incidence and second in mortality among all cancer types [1]. In Japan, CRC has the highest incidence and second-highest cancer-related mortality rate [2]. Despite its high prevalence, CRC demonstrates a relatively favorable 10-year relative survival rate compared with other malignancies, highlighting the critical role of early detection and screening.

As the life expectancy continues to increase worldwide, the proportion of older individuals is also rising rapidly. In Japan, data from the Ministry of Health, Labour and Welfare's National Database of Health Insurance Claims and Specific Health Checkups (NDB Open Data) have shown a gradual increase in both the number and proportion of total colonoscopy (TCS) procedures performed in individuals aged ≥80 years [3]. Therefore, determining the effectiveness and appropriate application of CRC screening in older adults has become a pressing public health concern. However, evidence supporting the benefits of CRC screening in older individuals remains limited, largely due to their exclusion from previous studies. This exclusion may be attributed to several factors including a higher burden of comorbidities, competing causes of mortality, and an elevated risk of gastrointestinal and non-gastrointestinal complications associated with diagnostic and therapeutic procedures. In some cases, these risks may outweigh the potential benefits of screening [4, 5]. Both fecal immunochemical testing (FIT) and total colonoscopy (TCS) are widely recognized for their effectiveness in reducing CRC incidence and mortality [6-10]. Among these, TCS is considered the gold standard for CRC diagnosis [11, 12], although it is a relatively invasive procedure. Therefore, the decision to perform TCS in older patients should be individualized, based on their overall health status, ability to tolerate the

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procedure, and screening history [13]. The necessity and appropriateness of TCS in older patients remain subjects of ongoing debate. In this study, we aimed to evaluate the clinical value of TCS in older patients by analyzing cases of advanced CRC in patients aged ≥80 years at our hospital. We stratified the patients into symptomatic and asymptomatic groups and compared their clinical backgrounds, pathological characteristics, and prognostic outcomes to evaluate the potential benefits of TCS in this age group.

Materials and Methods

Study Population and Design

This retrospective study was conducted at Toho University Medical Center, Omori Hospital, Tokyo, Japan. Data were extracted from the hospital's endoscopy management system for all TCS performed between January 2010 and December 2021. The target population included patients aged 18−100 years. The 12-year study period was divided into two-year intervals to evaluate trends in the proportion of TCS procedures performed in patients aged ≥80 years, relative to the total number of TCS procedures.

Patients aged ≥80 years diagnosed with advanced CRC during the study period were included in the analysis. Advanced CRC was defined as tumors invading the muscularis propria or deeper (≥T2 stage). For patients who underwent multiple procedures related to the same clinical event, only the initial TCS was included in the analysis. Patients were excluded if they or their family members declined to participate. This study was approved by the Ethics Committee of the Faculty of Medicine, Toho University (approval number: T2024-2073).

The patients were divided into two groups based on the presence or absence of symptoms at the time of diagnosis. The symptomatic group included patients with clinical symptoms such as abdominal pain, bloating, hematochezia, altered bowel habits, or weight loss. The asymptomatic group included patients without subjective symptoms, including those with positive FIT results. The clinical backgrounds, pathological characteristics, and long-term outcomes of the two groups were compared.

Case Definition

Diagnosis of CRC was primarily based on histopathological confirmation. However, patients with clear clinical evidence of advanced CRC in the absence of histological confirmation were also included. Clinical data were extracted from medical records and included the following variables: age at diagnosis, sex, body mass index (BMI), alcohol and tobacco use, family history of CRC, prior colonoscopy, use of antithrombotic agents, laboratory parameters (hemoglobin, serum albumin, carcinoembryonic antigen [CEA], carbohydrate antigen 19-9 [CA19-9]), tumor location, clinical stage, histological type, gross morphology, treatment strategy, and survival outcomes. The tumor location was classified as either right-sided (cecum to transverse colon) or left-sided (descending colon to rectum). Disease staging was performed in accordance with the 8th edition of the Union for International Cancer Control (UICC) TNM classification system and categorized as stage I/II (IIA–IIC), stage III (IIIA–IIIC), or stage IV (IVA–IVC). The observation period was defined as the time from diagnosis to the last recorded follow-up or death, with a maximum follow-up duration of 60 months ending in December 2024. The treatment modalities were categorized as surgery alone, surgery with chemotherapy, chemotherapy alone, or palliative care. Palliative care included colostomy or ileostomy creation, colorectal stenting, and non-curative surgery for stage IV disease.

Statistical Analysis

Categorical variables were summarized as frequencies and percentages, while continuous variables were expressed as means or medians with interquartile ranges (IQRs), depending on data distribution. Comparisons between categorical variables were performed using the chi-squared (χ^2) test. For continuous variables, either the Student's t-test or the Wilcoxon signed-rank test was applied, as appropriate based on normality. Survival analysis was conducted using the Kaplan–Meier method. Overall survival and disease-specific survival were compared between the groups using the log-rank test. A two-tailed p-value of ≤0.05 was considered statistically significant. All statistical analyses were conducted using the R software, version 4.2.2 (released October 31, 2022).

Results

Number of TCS and Proportion of Older Patients

Between January 2010 and December 2021, 42,060 TCS procedures were performed at our institution. Of these, 4,130 procedures (9.8%) were performed in patients aged ≥80 years. The number of older patients undergoing TCS has steadily increased over time, rising from 435 (7.4%) in 2010–2011 to 762 (10.9%) in 2020–2021 (Figure 1). Among the 4,130 patients aged ≥80 years, 297 (7.2%) were diagnosed with advanced CRC. No TCS-related complications were observed.

Clinical Characteristics of Older Patients with Advanced CRC

Table 1 summarizes the clinical characteristics of 297 patients aged ≥80 years who were diagnosed with advanced CRC. The median age was 84 years (range: 80–99 years), and 46.5% of the patients were male. The median BMI was 21.8 kg/m² (interquartile range [IQR]: 19.8–24.7). A family history of CRC was present in 5.7% of the patients, and 9.4% had a history of prior colonoscopy. The median serum albumin level was 3.6 g/dL. The median tumor marker levels were 5.1 ng/mL for CEA and 17.4 U/mL for CA19-9. The tumor was right-sided in 46.1% of the cases, and 44.4% were diagnosed at stage I or II.

Comparison Between Asymptomatic and Symptomatic Groups

Of the 297 older patients diagnosed with advanced CRC, 76 (26%) were asymptomatic and 221 (74%) were symptomatic. Table 2 compares clinical characteristics of

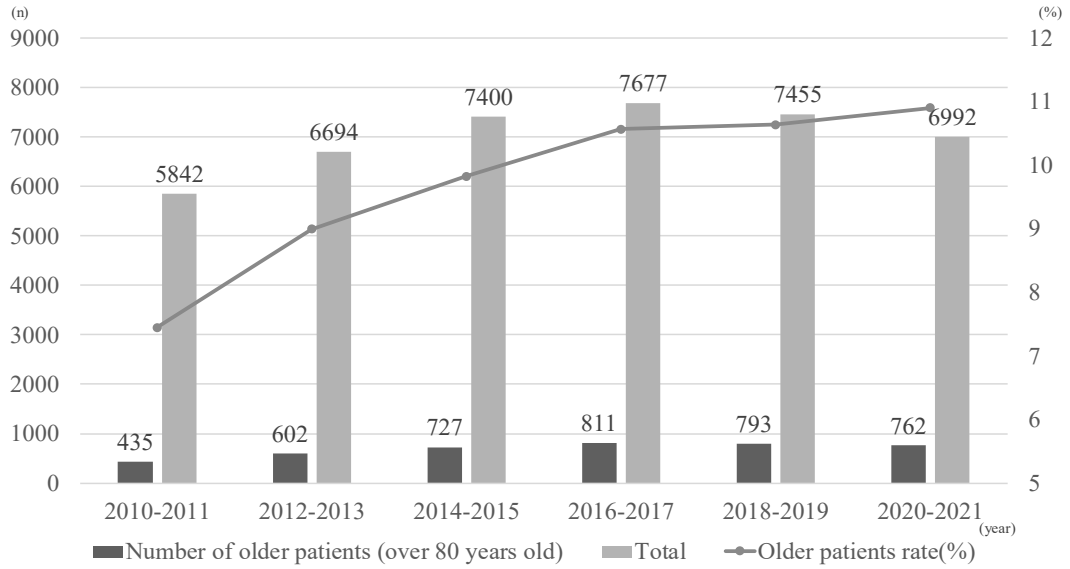

Figure 1. Number of TCS and Proportion of Older Patients. The annual number of total colonoscopies performed at our institution from 2010 to 2021 and the proportion of the procedures conducted in patients aged 80 years or older.

Table 1. Clinical Characteristics of Older Patients with Advanced Colorectal Cancer

	Total (n=297)
Age- year (median [range])	84 (80–99)
Male sex- n (%)	138 (46.5)
BMI-kg/m^2 (median [IQR])	21.8 (19.8–24.7)
Alcohol- n (%)	104 (35.0)
Current or ex-smoker- n (%)	133 (44.8)
CRC FH- n (%)	17 (5.7)
CS history- n (%) [a]	28 (9.4)
Antithrombotic drugs use- n (%)	69 (23.2)
Blood Test	
Hb (g/dL) (median [IQR])	10.8 (8.9–12.4)
Alb (g/dL) (median [IQR])	3.6 (3.1–3.9)
CEA (ng/mL) (median [IQR]) [b]	5.1 (2.8–14.4)
CA19-9 (U/mL) (median [IQR]) [c]	17.4 (8.43–35.2)
Cancer site	
Right colon- n (%)	137 (46.1)
Left colon- n (%)	160 (53.9)
Cancer stage	
I, II -n (%)	132 (44.4)
III- n (%)	107 (36.0)
IV- n (%)	58 (19.5)
TCS-related complications- n (%)	0 (0)

CRC FH, Family history of colorectal cancer; CS, history of colonoscopy; Hb, Hemoglobin; Alb, Albumin; CEA, Carcinoembryonic antigen; CA19-9, Carbohydrate antigen 19-9; TCS, Total colonoscopy; [a], Information was unavailable for 119 patients; [b], Information was unavailable for 3 patients; [c], Information was unavailable for 5 patients.

these two groups. The median age was 83 years (range: 80–96 years) in the asymptomatic group and 84 years (range: 80–99 years) in the symptomatic group. There were no significant differences in alcohol consumption (38.1% vs. 33.9%, p=0.51), smoking history (43.4% vs. 45.2%, p=0.78), family history of CRC (6.6% vs. 5.4%, p=0.73), or the use of antithrombotic agents (23.7% vs. 23.1%, p=0.27). Compared to symptomatic patients, asymptomatic patients had a significantly higher BMI (23.6 vs. 21.5 kg/m², p<0.05) and serum albumin level (3.7 vs. 3.5 g/dL, p<0.001), indicating a better nutritional status. A history of colonoscopy was more common in the asymptomatic group (21.1% vs. 5.4%, p<0.001). Hemoglobin levels did not differ significantly between the groups (10.8 vs. 10.7 g/dL, p=0.39). Tumor marker levels were significantly lower in the asymptomatic group for both CEA (3.9 vs. 5.6 ng/mL, p<0.001) and CA19-9 (13.4 vs. 19.7 U/mL, p<0.001). Right-sided colon cancer was significantly more frequent in the asymptomatic group (60.5% vs. 41.2%, p<0.05). Early-stage disease (stage I/II) was more common in the asymptomatic group (68.4%) than in the symptomatic group (36.2%). In contrast, advanced-stage disease was more frequent in the symptomatic group: stage III (40.3% vs. 23.7%) and stage IV (23.2% vs. 7.9%, p<0.001), suggesting earlier detection in asymptomatic patients.

Treatment and Prognosis

The treatment modalities and survival outcomes of the 258 patients with available follow-up data are summarized in Table 3. Surgery was the most frequently performed treatment in both groups. In the asymptomatic group, 83.0% of patients underwent surgery, 14.1% received postoperative chemotherapy, and 7.0% received palliative care only. In the symptomatic group, 68.4% of patients underwent surgery, 14.4% received postoperative chemotherapy, no patient received chemotherapy alone, and 28.9% received palliative care only (p<0.05). Long-term follow-up data were available for 228 patients (60 in the asymptomatic group and 168 in the symptomatic group). The median follow-up duration was 36 months (range: 1–60 months). The 5-year overall survival rate

Table 2. Comparison of Clinical Characteristics Between Asymptomatic and Symptomatic Older Patients with Advanced Colorectal Cancer

	Asymptomatic group (n=76)	Symptomatic group (n=221)	p-value
Age-year (median [range])	83 (80–96)	84 (80–99)	0.23
Male sex- n (%)	36 (47.4)	102 (46.5)	0.86
BMI-kg/m^2 (median [IQR])	23.6 (20.3−25.5)	21.5 (19.6−24.5)	0.01
Alcohol- n (%)	29 (38.1)	75 (33.9)	0.51
Current or ex-smoker- n (%)	33 (43.4)	100 (45.2)	0.78
CRC FH- n (%)	5 (6.6)	12 (5.4)	0.73
CS history- n (%) [a]	16 (21.1)	12 (5.4)	<0.001
Antithrombotic drugs use- n (%)	18 (23.7)	51 (23.1)	0.27
Blood Test			
Hb (g/dL) (median [IQR])	10.8 (9.5−12.7)	10.7 (8.8−12.3)	0.39
Alb (g/dL) (median [IQR])	3.7 (3.5−4.0)	3.5 (3.0−3.8)	<0.001
CEA (ng/mL) (median [IQR]) [b]	3.9 (2.4−8.3)	5.6 (3.0−22.2)	<0.001
CA19-9(U/mL) (median [IQR]) [c]	13.4 (8.0−20.35)	19.7 (8.6−44.1)	0.002
Cancer site			
Right colon- n (%)	46 (60.5)	91 (41.2)	
Left colon- n (%)	30 (39.5)	130 (58.8)	0.004
Cancer stage			
I, II- n (%)	52 (68.4)	80 (36.2)	
III- n (%)	18 (23.7)	89 (40.3)	
IV- n (%)	6 (7.9)	52 (23.2)	<0.001
TCS-related complications- n (%)	0 (0)	0 (0)	

CRC FH, Family history of colorectal cancer; CS, history of colonoscopy; Hb, Hemoglobin; Alb, Albumin; CEA, Carcinoembryonic antigen; CA19-9, Carbohydrate antigen 19-9; TCS, Total colonoscopy; [a], Information was unavailable for 119 patients; [b], Information was unavailable for 3 patients; [c], Information was unavailable for 5 patients.

was significantly higher in the asymptomatic group than in the symptomatic group (68.3% vs. 38.7%, p<0.001). Similarly, the 5-year disease-specific survival rate was significantly higher in the asymptomatic group (88.3% vs. 65.5%, p<0.001). The Kaplan–Meier survival curves are presented in Figure 2. The asymptomatic group had significantly better overall survival (hazard ratio [HR]=0.37, 95% confidence interval [CI]: 0.23–0.60) and disease-specific survival (HR=0.25, 95% CI: 0.11–0.54) compared to the symptomatic group.

Discussion

As the global life expectancy increases, the burden of

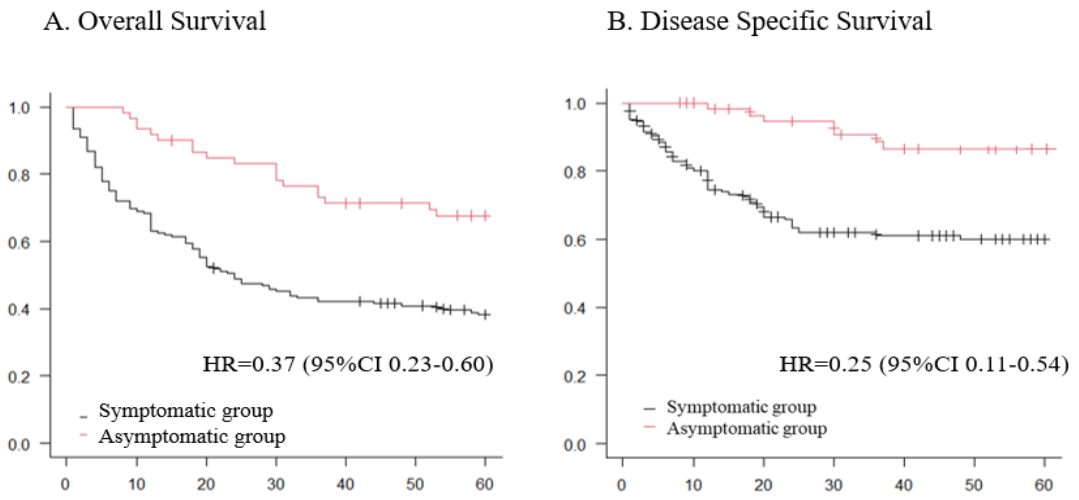

Figure 2. Kaplan–Meier Analysis of Survival According to Symptom Status in Older Patients with Advanced Colorectal Cancer. Kaplan–Meier curves comparing (a) overall survival and (b) disease-specific survival between asymptomatic and symptomatic patients aged ≥80 years with advanced colorectal cancer. The asymptomatic group showed significantly better outcomes for both

Table 3. Comparison of Treatment Modalities and Survival Outcomes Between Asymptomatic and Symptomatic Older Patients with Advanced Colorectal Cancer

	Total	Asymptomatic (n=71)	Symptomatic (n=187)	p-value
Treatment				
Surgery- n (%)	157 (60.9)	56 (78.9)	101 (54.0)	
Surgery and chemotherapy- n (%)	37 (14.3)	10 (14.1)	27 (14.4)	
Chemotherapy- n (%)	5 (1.9)	0 (0)	5 (2.7)	
Palliative therapy- n (%)	59 (22.9)	5 (7.0)	54 (28.9)	0.003
5-year survival rate				
OS (%)		68.3	38.7	<0.001
DSS (%)		88.3	65.5	<0.001

OS, Overall Survival; DSS, Disease-Specific Survival

CRC among older individuals has become a significant public health concern. Despite this, individuals aged ≥80 years are often excluded from CRC screening programs and clinical trials due to concerns related to frailty, comorbidities, and procedural risks [14]. This study provides novel evidence supporting the clinical utility of TCS in this underrepresented population. We demonstrated that older asymptomatic individuals diagnosed with advanced CRC through TCS had significantly more favorable clinical profiles and improved survival outcomes compared to their symptomatic counterparts [15, 16].

A key finding of this study is the considerable survival advantage observed in the asymptomatic group. The five-year overall survival rate was 68.3% and the disease-specific survival rate was 88.3%. These outcomes are notable, given the advanced age of the cohort, and are comparable to those reported in younger populations undergoing routine screening [17, 18]. Importantly, the asymptomatic group presented more frequently with early-stage disease and right-sided tumors, which are typically more challenging to detect because of their slower progression and lack of obvious symptoms [19]. These findings highlight the importance of proactive screening in relatively healthy older individuals who may have a significant disease without overt clinical signs [20-22].

Biologically, the asymptomatic group exhibited a higher body mass index and serum albumin levels, along with lower levels of tumor markers, such as CEA and CA19-9. These findings indicate better general health and nutritional status, reinforcing previous reports identifying nutritional indicators as significant prognostic factors for CRC [23]. Malnutrition and cancer-related cachexia have consistently been linked to reduced treatment tolerance, increased postoperative complications, and shorter survival [24-26]. These results suggest that nutritional assessment may help guide clinical decisions, such as recommending colonoscopic screening for older individuals with good nutritional status, while prioritizing alternative evaluations (e.g., for other comorbidities or using CT-based examinations) in those with poor nutritional status.

Although curative surgery was common in both groups, it was performed more frequently in asymptomatic patients. These patients also required palliative care less often than symptomatic patients, who generally had more advanced-stage disease and worse functional status. Although the use of chemotherapy was limited in both groups, likely because of concerns regarding toxicity and frailty in this age group, the ability to undergo curative surgery remains a major determinant of improved outcomes [14]. According to the Comprehensive Survey of Living Conditions by the Ministry of Health, Labour and Welfare, approximately 30% of individuals aged ≥75 years and 20% of those aged ≥85 years undergo CRC screening [27]. In this study, the most common reason for undergoing colonoscopy in the asymptomatic group was a positive fecal occult blood test. These findings suggest that fecal occult blood testing remains a useful screening tool in older adults who are in sufficiently good health to attend medical facilities and undergo follow-up colonoscopy.

Notably, the rate of prior colonoscopy was significantly higher in the asymptomatic group, suggesting that regular surveillance may contribute to earlier detection or even cancer prevention through polypectomy. These findings are consistent with those from large cohort studies that have demonstrated reduced CRC incidence and mortality in individuals with a history of colonoscopy [28-30]. In aging populations, screening strategies that incorporate endoscopic history, functional capacity, and life expectancy may enhance both efficiency and effectiveness.

These findings have implications for policies and guidelines. While some international recommendations advise discontinuing CRC screening after the age of 75 or 80 years [5], our findings challenge these fixed age limits by demonstrating the meaningful benefits of TCS in carefully selected older individuals. Colorectal cancer screening guidelines vary internationally. In Japan, according to the 2024 guideline, organized FIT screening is recommended to end at age 74; however, for individuals who have not undergone screening for a long period and who maintain good physical function, opportunities may be offered beyond age 74 based on individual circumstances [31]. In contrast, the United States Preventive Services Task Force advises against screening in those aged 86 years or older, while for individuals aged 76–85 years, decisions

are recommended to be individualized based on overall health status and patient preference [13]. In Europe, the upper age limit for screening is generally set at 74 years, with only limited recommendations beyond this age [32]. These differences reflect variations in healthcare systems and population demographics, while also suggesting the need for risk-based screening strategies in older adults that do not rely solely on chronological age. Chronological age alone may not accurately reflect the physiological reserves or the potential to benefit from early detection. Therefore, individualized screening decisions based on comorbidity profiles, cognitive and physical functions, nutritional status, and patient preferences are warranted. Recent improvements in procedural safety and bowel preparation protocols have reduced the risks associated with colonoscopy in older adults [3].

Nevertheless, this study has some limitations. First, this was a retrospective single-center study, which may have limited the generalizability of the findings. In particular, information on prior colonoscopy history relied on entries in electronic medical records, and 119 of 297 cases (approximately 40%) lacked this documentation. Such a substantial proportion of missing data may introduce bias and reduce the reliability of the findings. This limitation should therefore be taken into account when interpreting the results. Second, although most CRC diagnoses are confirmed pathologically, some are based on clinical or imaging findings, introducing potential diagnostic variability. Third, patients without cancer or those with negative colonoscopy results were excluded, precluding an assessment of the full preventive potential of TCS in older individuals. Finally, although no TCS-related complications were reported in this study, this is likely due to underreporting inherent in its retrospective design. In particular, minor adverse events such as post-polypectomy syndrome or mild bleeding may have been overlooked, as it can be difficult to extract such information from electronic medical records. Therefore, this limitation should be taken into account when interpreting the safety of TCS in this population.

Future research should focus on developing risk stratification tools tailored to the older population by incorporating clinical, functional, and social parameters to identify individuals most likely to benefit from screening. Prospective studies evaluating patient-centered outcomes such as quality of life, recovery time, and the ability to maintain functional independence will further inform appropriate screening strategies for older adults.

In conclusion, this study demonstrated that TCS in individuals aged ≥80 years can lead to the early detection of advanced CRC, improved surgical eligibility, and favorable long-term survival outcomes, particularly among asymptomatic patients. These findings support a shift from rigid age-based screening thresholds to personalized risk-based approaches. Expanding access to high-quality colonoscopy in appropriately selected older patients may contribute to further reductions in CRC mortality and improved health outcomes in aging societies.

Author Contribution Statement

T.I. collected the data, performed the statistical analysis, and drafted the manuscript. T. I., M.O., K.H., and J.T. collected clinical data. T.I., T.T., A.F., and T.M. designed the study and edited the manuscript. All the authors have read and agreed to the published version of the manuscript.

Acknowledgements

Ethics approval statement

This study was approved by the Ethics Committee of the Faculty of Medicine, Toho University (approval number: T2024-2073).

Data availability statement

Because of the nature of this research, the participants in this study did not agree that their data would be publicly shared; thus, supporting data were not available.

Patient consent statement

Details of the study protocol, including the right to opt out of participation, are published on the institutional website. All potential participants were provided the opportunity to voluntarily decline enrollment.

Conflict of interest disclosure

The authors declare no conflicts of interest.

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