
Screening, Diagnosis, and Investigations for Colorectal Cancer in the Elderly

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Shingo Tsujinaka and Yutaka J. Kawamura

Take Home Pearls

- Screening strategies in the elderly should be tailored to comorbid conditions and life expectancy.
- Colonoscopy in the elderly carries certain risks, regional safety data, and completion rates need to be taken into account when developing a screening strategy for a given population.
- The role of computed tomographic colonography remains uncertain.

2.1 Introduction

The incidence of colorectal cancer (CRC) increases with age. In the United States, a new diagnosis of CRC occurs in 24% in patients aged 64–74 years, 27% in those aged 75–84 years, and 12% in those aged 85 years or older (Day et al. 2011b). The US Preventive Services Task Force (USPSTF) recommended screening for CRC using fecal occult blood tests, sigmoidoscopy, or colonoscopy, beginning at the age of 50 years and continuing until age 75 years. The USPSTF recommends against routine screening for colorectal cancer in adults aged 76–85 years with individual consideration and recommends against any screening for those 85 years or older (2008). These distinctive recommendations may be attributable to unique characteristics of elderly

S. Tsujinaka (✉) • Y.J. Kawamura
Department of Surgery,
Jichi Medical University, Saitama Medical Center,
1-847, Amanumacho, Omiya, Saitama-shi,
Saitama 330-8503, Japan
e-mail: tsujinakas@omiya.jichi.ac.jp; kawamura@omiya.jichi.ac.jp

patients with more comorbid medical conditions, potential cognitive impairment resulting in informed consent difficulty, potential higher incidence of logistical problems (i.e., transportation), and shorter life expectancy compared with younger individuals (Lin et al. 2006). Some clinicians may have concerns in screening or diagnostic colonoscopy with regard to the possibility of inadequate bowel preparation, lower completion rate, and increased risk of adverse events (Lin et al. 2006).

This chapter highlights the efficacy and effectiveness, and the complex issues relative to CRC screening and subsequent investigative procedures.

2.2 Fecal Occult Blood Testing (FOBT)

2.2.1 Overview

FOBT is currently the most widely prescribed screening modality. Patients with positive FOBT results should undergo a follow-up complete colonoscopy, and previous trials have demonstrated that 15–33% reduction in colorectal cancer mortality can be achieved when positive FOBT results were followed by colonoscopy (Mandel et al. 1993; Hardcastle et al. 1996; Kronborg et al. 1996). Recommended tests for CRC screening in average-risk individuals beginning at age 50 years by guideline organizations include colonoscopy every 10 years as the most preferred modality, followed by annual fecal occult blood tests (FOBT), flexible sigmoidoscopy every 5 years, or annual FOBT plus flexible sigmoidoscopy every 5 years as alternatives (Davila et al. 2006).

FOBT can be typically performed with use of a guaiac-based test (G-FOBT) targeting peroxidase-like activity of hem or hemoglobin in feces, or immunochemical-based test (I-FOBT) using hemoglobin-specific antibodies (Davila et al. 2006). G-FOBT is highly sensitive but frequently affected by peroxidase-containing foods and dietary heme from red meat; 3-day food restrictions are necessary to avoid false-positive results. I-FOBT is more specific but less sensitive compared with G-FOBT; therefore, a combination of I-FOBT and G-FOBT should also be advocated to improve diagnostic accuracy (Allison et al. 1996; Greenberg et al. 2000).

2.2.2 FOBT Screening in the Elderly

Although FOBT screening is deemed to be effective in early detection, it may not benefit patients with short life expectancies since its benefit does not appear immediately (Walter and Covinsky 2001). This is reflected by the results from previous trials on FOBT aimed for reduction in mortality from CRC; the cancer-specific survival curves between the screened and unscreened patients did not differ significantly until at least 5 years after the initial screening (Mandel et al. 1993; Hardcastle et al. 1996; Kronborg et al. 1996). Cancers destined to result in death within 5 years of diagnosis may be too aggressive for patients to benefit from early detection and treatment, suggesting the elderly patients with estimated life expectancy of less than 5 years would not derive survival benefit from cancer screening (Walter and Covinsky 2001). The

benefit of positive FOBT results from asymptomatic tumors must be weighed against immediate burdens of downstream procedures (i.e., colonoscopy) and treatments (i.e., endoscopic resection or surgical bowel resection) (Kistler et al. 2011).

2.3 Colonoscopy for Colorectal Cancer Screening in the Elderly

2.3.1 Overview

Colonoscopy is the preferred and the most common modality for CRC screening (Davila et al. 2006; Wexner et al. 2006). In order to achieve adequate inspection of the colonic mucosa, cathartic bowel preparation is necessary. When bowel preparation is given, it should be tolerable, safe, and effective, regardless of the age of the candidate.

2.3.2 Method of Bowel Preparation

A standard method of bowel cleansing is an ingestion of polyethylene glycol (PEG). Since PEG is nondigestible, nonabsorbable, and iso-osmolar with plasma, it only purges colonic luminal contents without affecting the physiologic conditions including body weights, blood pressures, and electrolytes (Day et al. 2011b; Juluri et al. 2011). The drawback of PEG is requirement of large volume of its solution (standard, 4 l; low volume, 2 l) and poor palatability. The former issue raises a particular concern to the elderly patients because inability to consume the prescribed treatment may affect the preparation quality (Thomson et al. 1996), although the estimated shortfall is considered to be relatively small with the reported mean volume consumption ranges from 91% to 93% (Belsey et al. 2007). The split dosing of PEG solution has been shown to be as effective as the whole dose protocol (El Sayed et al. 2003; Belsey et al. 2007; Cohen 2010); therefore, it may improve noncompliance rate in the elderly patients.

The common complaints in the elderly patients associated with PEG include dizziness, fecal incontinence, abdominal pain, and nausea (Day et al. 2011b). Also, there are case reports of adverse events such as pulmonary aspiration, pancreatitis, ischemic colitis, and dysnatremia in patients with impaired thirst sensation, suggesting the importance of adequate hydration during bowel preparation in these individuals (Day et al. 2011b).

The alternative method is the use of sodium phosphate (NaP). NaP consists of a low-volume laxative that osmotically draws plasma water into the bowel lumen to promote bowel cleansing (Wexner et al. 2006). NaP may be contraindicated for elderly patients because it can result in potentially fatal fluid shift and electrolyte disturbances (Curran and Plosker 2004; Lichtenstein et al. 2007). Also, patients taking angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, diuretics, and nonsteroidal anti-inflammatory agents may have more adverse effects to bowel preparation for colonoscopy (Lichtenstein et al. 2007). In elderly patients, NaP appeared to be more

tolerated than PEG but had significantly more complications with electrolyte disturbances, with comparable quality of preparation (Thomson et al. 1996; Seinela et al. 2003). Furthermore, the recent prospective, randomized trial revealed that bowel cleansing for colonoscopy using NaP induced tenfold likelihood of mucosal inflammation than that of PEG (Lawrance et al. 2011). This finding may give further caution to the selection of cathartic agents for colonoscopy in the elderly.

2.3.3 Complications During Colonoscopy

Colonoscopy-specific complications may potentially be fatal to the elderly patients who are generally vulnerable to invasive procedure, and there has been controversy over whether increased age is an independent risk factor (Day et al. 2011b). A recent systematic review with meta-analysis (Day et al. 2011a) demonstrated that pooled incidence of adverse events per 1,000 colonoscopies in patients 65 years of age and older was as follows: 26.0 [95% CI, 25.0–27.0] for cumulative gastrointestinal (GI) adverse events, 1.0 [95% CI, 0.9–1.5] for perforation, 6.3 [95% CI, 5.7–7.0] for GI bleeding, 19.1 [95% CI, 18.0–20.3] for cardiovascular (CV)/pulmonary complications, and 1.0 [95% CI, 0.7–2.2] for mortality rate. Furthermore, among octogenarians, adverse events per 1,000 colonoscopies were as follows: 34.9 [95% CI, 31.9–38.0] for cumulative GI adverse events, 1.5 [95% CI, 1.1–1.9] for perforation, 2.4 [95% CI, 1.1–4.6] for GI bleeding, 28.9 [95% CI, 26.2–31.8] for CV/pulmonary complications, and 0.5 [95% CI, 0.06–1.9] for mortality rate. These data indicate that patients 80 years of age and older have greater risk of cumulative GI adverse events and perforation compared with patients younger than 80 years of age. The incidence of GI bleeding and CV/pulmonary complications tended to be higher in octogenarians without statistical significance.

Although colonoscopy is generally considered a safe procedure, these results should be integrated to discussions when considering colonoscopy, including informed consent process, clinical decision making, and refining population-based screening policies in the elderly (Day et al. 2011a).

2.3.4 Completion Rate of Colonoscopy

Completion rate in performing total colonoscopy is reportedly very high over 90% (Day et al. 2011b); however, it appears to be lower in octogenarians with a mean of $84.7\% \pm 11.7\%$ (Day et al. 2011a). Some studies included increased age as the factors predictive of failed colonoscopy or technical difficulty with prolonged cecal intubation (Lukens et al. 2002; Schmilovitz-Weiss et al. 2007; Lee et al. 2008), while some did not show that age directly associate with adjusted completion rate (Nelson et al. 2002; Arora and Singh 2004; Karajeh et al. 2006) and the procedural failure was rather affected by the higher prevalence of bowel stricture because of diverticular disease and/or malignancy (Karajeh et al. 2006) or poorer bowel preparation (Nelson et al. 2002) in the elderly.

2.3.5 Japanese Perspectives on Colonoscopy

There have been a number of studies conducted by Japanese colonoscopists in an effort to improve cecal intubation rate, cecal intubation time, total examination time, and disease detection rate and to reduce complication rate and patient discomfort (Kondo et al. 2007; Tsutsumi et al. 2007; Horiuchi et al. 2008; Harada et al. 2009; Takeuchi et al. 2010). In one randomized controlled trial, the efficacy of the transparent hood attached to the colonoscope was assessed (Kondo et al. 2007). The overall cecal intubation rate was 96.4%, 94.3%, and 95.3% in the transparent hood, short hood, and no-hood groups, respectively ($p=0.58$). Only a history of abdominal surgery had a significantly negative impact on successful cecal intubation in the multivariate analysis. Increased age (70 years of age or older) was not independently associated with completion of cecal intubation. However, the average cecal intubation time in patients aged 70 years or older was 13.5, 16.0, and 20.0 min in the transparent hood, short hood, and no-hood groups, respectively ($p=0.04$). The use of the transparent hood was attributed to a 17% reduction in cecal intubation time ($p=0.003$). This trial also showed that the use of the transparent hood was effective for trainee endoscopists in shortening cecal intubation time in difficult case such as elderly (70 years of age or older) and female patients. In another similar randomized trial (Harada et al. 2009), the mean cecal intubation time was significantly shorter in the hood group (10.2 min) than in the no-hood group (13.4 min). The proportion of examinees who answered comfortable was 35.9% in the hood group and 27.6% in the no-hood group ($p=0.04$), and those who answered intolerable was 18.0% in the hood group and 25.4% in the no-hood group ($p=0.037$). However, the cecal intubation rate did not differ between the hood group (96.5%) and the no-hood group (95.0%). Additionally, in a large retrospective study, the completion rate was 96.8% in patients less than 80 years of age compared with 92.7% in those aged 80 years or older (Tsutsumi et al. 2007). Furthermore, two studies showed very low complication rate in very old patients, 0.9% (bleeding after polypectomy) in octogenarians (Tsutsumi et al. 2007) and 1.7% (oxygen administration due to deep sedation) in nonagenarians (Horiuchi et al. 2008). The authors believe that these encouraging evidences have optimal roles in improved screening colonoscopy for the elderly population.

2.4 Current Issues in Colorectal Cancer Screening in the Elderly: The Net Benefit or the Net Burden?

Emerging literatures regarding benefits and burdens from CRC screening in the United States have impacted on the significance of existing screening strategy. In the setting where fewer than 60% of patients receive a colonoscopy within 1 year after positive FOBT result, elderly adults tend to have low rate of follow-up colonoscopy compared to younger patients (Kistler et al. 2011). A longitudinal study determining the frequency of downstream outcomes during 7 years of follow-up was conducted

targeting 212 patients 70 years or older with a positive FOBT result at four Veteran Affairs facilities (Kistler et al. 2011). Fifty-six percent of patients received follow-up colonoscopy, detecting 34 significant adenomas and 6 cancers. In contrast, 46% of those without colonoscopy died of other causes (43 of 94), while three died of CRC within 5 years after FOBT. This study also showed that 87% of patients with the worst life expectancy experienced a net burden from screening (26 of 30) as did 70% with average life expectancy (92 of 131) and 65% with the best life expectancy (35 of 51). Thus, it is reasonably assumed that patients with the best life expectancy would benefit from screening more than those with the worst (Kistler et al. 2011), and this has been verified by the multi-modeling analyses (Ko and Sonnenberg 2005; Lin et al. 2006). One study compared the risk and benefits of screening in patients aged 70–94 years with differing health status using three screening strategies including annual fecal occult blood tests, flexible sigmoidoscopy every 5 years, or colonoscopy every 10 years (Ko and Sonnenberg 2005). One cancer-related death would be prevented by screening 42 healthy men aged 70–74 years with colonoscopy, 178 healthy women aged 70–74 years with fecal occult blood tests, 431 women aged 75–79 years in poor health with colonoscopy, or 945 men aged 80–84 years in average health with fecal occult blood tests. These results indicate that the potential benefits and risks of screening vary in elderly patients of different life expectancies (Ko and Sonnenberg 2005). The other showed that the prevalence of colonic neoplasia increased with age; however, screening colonoscopy in elderly patients (patients 80 years of age and older) resulted in only 15% of the expected gain in life expectancy in younger patients (patients 50–54 years of age), even when adjusted for life expectancy (Lin et al. 2006).

Nevertheless, it is importantly advised that the aforementioned estimated life expectancy is based on the populations in the United States; therefore, difference in life years saved by screening may vary in different geographic locations such as Europe, Asia, and other nations (Day et al. 2011b).

Overuse of screening colonoscopy is another issue that may associate with procedural adverse effects and increased expenditures using limited resources (Goodwin et al. 2011). Among 24,071 Medicare patients with a negative initial screening colonoscopy, 46% underwent a repeated colonoscopy in fewer than 7 years, including 46% of patients aged 75–79 years and 33% of those aged 89 years or older. These results clearly did not meet the available universal guidelines (Davila et al. 2006). Moreover, in 43% of patients who had a repeated colonoscopy, there was no clear indication for repeated examination. In their multivariate analyses, interestingly, male sex, more comorbidities, and colonoscopy by a high-volume colonoscopist or in an office setting were associated with higher rates of the early repeated examination without clear indication (Goodwin et al. 2011). To explain this, the authors presumed that patients with multiple comorbidities see more medical providers and thus increasing their opportunities of being recommended for another screening colonoscopy, though it is generally perceived that the presence of comorbid medical conditions reduces the benefit of CRC screening (Day et al. 2011b).

2.5 Potential Role of Computed Tomographic Colonography (CTC)

Although preimaging bowel preparation using cathartic agents is still necessary, computed tomographic colonography (CTC) is currently available as minimally invasive procedure for detection of colonic neoplasia (Heresbach et al. 2011).

A recent meta-analysis assessing the diagnostic value of CTC for screening demonstrated that estimated per patient sensitivity of CTC for greater than or equal to 6-mm polyps and adenomas were 68.1% and 78.6%, with the corresponding specificity of 94.6% or 91.4%, whereas the estimated per patient sensitivity for greater than or equal to 10-mm polyps and adenomas were 83.3% and 87.9%, with the corresponding specificity of 98.7% and 97.6% (de Haan et al. 2011). This meta-analysis concluded that CTC has a high sensitivity for adenomas greater than or equal to 10 mm and has lower sensitivity for adenomas greater than or equal to 6 mm, as compared to colonoscopy (de Haan et al. 2011).

Macari et al. (2011) undertook a retrospective cohort study comparing the frequency of recommendations for additional imaging (RAIs) for extracolonic findings, polyp prevalence among seniors (65 years of age and older) and non-seniors (younger than 65 years of age). The polyp prevalence was similar (14.2% for seniors vs. 13.2% for non-seniors), and the presence of extracolonic findings was significantly more frequent in seniors than in non-seniors (74.0% vs. 55.4%) but without statistical significance in RAIs (6.0% in seniors vs. 4.4% in non-seniors).

Since the tagging technique of residual colonic material allows discriminate high-density stool and fluid from the colonic wall, CT colonography may not require rigorous bowel cleansing compared with colonoscopy (Keedy et al. 2011). As a result, lesser volume of cathartic agents can improve patient adherence and tolerability, and the optimal solutions of those were currently investigated by the American College of Radiology Imaging Network (ACRIN) National CTC Trial (Hara et al. 2011). The polyp detection rate was comparable among PEG, NaP, and magnesium citrate, although NaP had the highest patient compliance and the least residual stool (Hara et al. 2011).

Despite the endorsement as an acceptable option for colorectal cancer screening, the governmental health care system recently decide not to cover CTC for screening purpose in the United States (Heiken 2009; Garg and Ahnen 2010). The reasons for which include radiation exposure, false-negative rates for smaller polyps, the discovery of extracolonic findings leading to excess RAIs, variability in performance, lack of targeted studies, and absence of clear definitions of expertise and certification (Garg and Ahnen 2010). Furthermore, an evident limitation of CTC screening is that so far there is no study demonstrating the efficacy of CTC in reducing the CRC incidence and mortality (Davila et al. 2006).

However, given the lesser invasive nature and having lesser perceived discomfort compared to colonoscopy, CTC may improve compliance rate in CRC screening and provide an important role as an adjunctive screening modality, particularly in the elderly community (McFarland et al. 2009; Heresbach et al. 2011).

Conclusions

It must be reminded that the ideal purpose of screening is to detect and eradicate precancerous or cancerous diseases, thereby that can reduce cancer-related mortality in asymptomatic individuals. Current concepts and evidences support that colonoscopy is the most feasible examination for CRC screening at any ages of patients. Screening colonoscopy in the elderly patients should be performed after careful consideration for indication with full informed consent with regard to potential benefits and risks relative to procedure. Furthermore, health care providers should be aware that increasing screening rates may lead to increase in false-positive results, cancer overdiagnosis, morbidity and mortality from screening procedure and/or downstream treatments, and monetary burden on both patients and health care system.

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