Updates in Screening Recommendations for Colorectal Cancer

Presented by Reid M. Ness, MD, MPH

ABSTRACT

In the past 2 years, several significant changes have been made to the NCCN Guidelines for Colorectal Cancer (CRC) Screening. The age for initiation of screening average-risk adults has been lowered from age 50 to 45 years—without differentiation by age and race—and from age 50 to 45 years for those with second- and third-degree relatives with CRC. For several groups, surveillance intervals have been changed. Patients with 1 or 2 low-risk adenomas at index colonoscopy, on the other hand, can now wait 10 years rather than 5 to 7 years between surveillance examinations. The first surveillance examination following resection of large adenomas or sessile serrated polyps (SSPs) with unfavorable-risk characteristics or that were removed piecemeal should now occur at 6 months. For patients with ≥10 adenomas and SSPs on a single colonoscopy, time to first surveillance was lowered to 1 year.

In an effort to prevent colorectal cancer (CRC), the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) provide recommendations for screening based on a variety of risk factors and patient profiles. In the past 2 years, the NCCN Guidelines for CRC Screening have undergone several significant changes, reflecting recommendations that will spare some patients unnecessary interventions and, in other cases, detect cancers earlier. The updated recommendations were presented at the NCCN 2022 Annual Conference by Reid M. Ness, MD, MPH, Associate Professor of Medicine, Vanderbilt-Ingram Cancer Center, and Chair of the NCCN Guidelines Panel for Colorectal Cancer Screening.

“The first and most significant change in the NCCN Guidelines was a lowering of the initial screening age for average-risk individuals from 50 to 45 years. The second biggest change is the recommendation to extend the surveillance period from 5–7 years to 10 years for patients with only 1 to 2 small tubular adenomas at the index colonoscopy,” Dr. Ness announced.

In other changes, the NCCN Guidelines panel now recommends lowering the age for first screening in persons with second- and third-degree relatives with CRC from 50 to 45 years; shortening the time to first surveillance examination to 6 months following resection of large adenomas or sessile serrated polyps (SSPs) with unfavorable-risk characteristics or that were removed piecemeal; and shortening the time to first surveillance to 1 year for patients found to have ≥10 adenomas or SSPs at a single colonoscopy. However, several other important recommendations remained unchanged, including:

- Age for initiation of screening in persons with affected first-degree relatives with CRC or advanced adenomas/SSPs remains 40 years.
- Surveillance colonoscopy interval in those with only 1 or 2 low-risk SSPs remains at 5 years.
- The surveillance colonoscopy interval following the identification of most high-risk adenomas/SSPs remains at 3 years.
- Initiation of surveillance remains at 8 years for most patients with inflammatory bowel disease, and surveillance intervals remain at 1 to 3 years, depending on measures of underlying CRC risk.

Lowering Screening Age

“The impetus for lowering the initial screening age is based on well-publicized trends in CRC incidence,” Dr. Ness said. Since 1980, there has been a 40% overall decrease in CRC incidence among patients aged ≥50 years in the United States. Unfortunately, this has been accompanied by a more recent increasing incidence of CRC among adults aged 20 to 49 years.1 Because data are lacking on CRC screening in persons aged <50 years, the American Cancer Society and the US Preventive Services Task Force (USPSTF) relied on modeling exercises that demonstrated “small but significant” amounts of life-years gained from CRC screening beginning at age 45 years.23 Cost-effectiveness was not addressed in the analyses, and some experts maintained that “the absolute cost of such a policy change would be unacceptably high,” Dr. Ness said. “Despite these concerns, the panel felt that the cost-to-benefit trade-off was acceptable, and in April 2021, the recommended age to initiate average-risk CRC screening was lowered to 45 years.”
“All CRC screening guidelines in the United States have been brought into accord,” he said. The same recommendation was subsequently made by the USPSTF in May 2021 and the Multi-Society Task Force on CRC Screening in November 2021.3,4

Because half of all patients who present with CRC before age 50 years do so before they even reach 45 years of age, NCCN also recommends that those presenting with symptoms suggestive of a possible diagnosis for rectal cancer, such as iron deficiency and rectal bleeding, be evaluated with colonoscopy in a timely fashion, he added.5 In addition, the NCCN Guidelines panel considered whether the initial screening age should be lowered for average-risk non-Hispanic Black individuals, but determined that the model was reassuring in that 45 years of age is appropriate for all sex- and race-based groups.6

**Extending Surveillance Period to 10 Years**

“The recommendation to extend the surveillance period after the finding of a low-risk adenoma is based upon very strong cohort data,” Dr. Ness said (Figure 1). These data come from a meta-analysis of 8 cohort studies that evaluated the risk of CRC in 10,139 persons with low-risk adenomas on index colonoscopy compared with persons with normal baseline colonoscopies. In the former group, the investigators found a small but statistically significant increase in future advanced adenomas (relative risk, 1.55; \( P = .0001 \)).7 The pooled 5-year cumulative incidence of advanced adenomas was 3.3% for the no-adenoma group, 4.9% for the low-risk adenoma group, and 17.1% for patients with advanced adenomas at baseline.

Combined data from the Nurses’ Health Study and the Health Professional Follow-Up Study, which followed 122,899 patients for a median of 10 years after colonoscopy, showed that the hazard ratios (HRs) for patients with 1 or 2 small tubular adenomas was not significantly increased over those with no polyps at baseline.8 A prospective cohort study from Kaiser Permanente Northern California published in 2020 followed 64,422 patients for 8 years.9 The investigators found that the HRs for CRC incidence and death in patients with low-risk adenomas at baseline were not significantly different from those of patients with normal findings. In contrast, patients with high-risk adenomas at baseline had a significant increase in age-adjusted CRC after 5 years.

“Although the guidelines recommend extending the surveillance period for patients with 1 to 2 low-risk adenomas, we did not extend the surveillance period for patients with only low-risk SSPs on index colonoscopy, secondary to a perceived paucity of data. Nonetheless, there are current studies...”

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**Figure 1.** NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Colorectal Cancer Screening: personal history of polyph found at colonoscopy (CSCR-4). Version 1.2022. © 2022 National Comprehensive Cancer Network, Inc. All rights reserved. These guidelines and this illustration may not be reproduced in any form without the express written permission of NCCN®. To view the most recent and complete version of these NCCN Guidelines, go to NCCN.org.
that could lead to our extending the surveillance period recommendation in the near future,” Dr. Ness said.

The guidelines panel reviewed how serrated polyp size and location affected risk. The Nurses’ Health Study and Health Professionals Follow-Up Study showed that the HR for metachronous CRC associated with small serrated polyps was 1.25—not significantly different than that for patients without baseline polyps—whereas large, serrated polyps carried an HR of 3.35. Interestingly, neither the number nor location of these polyps significantly affected the risk of metachronous CRC. However, in a study from Li et al9 of 233,393 patients, serrated polyps in the rectosigmoid colon did not increase CRC risk, whereas both small and large polyps in the proximal colon did significantly increase risk.

“We kept the recommended surveillance interval for patients with ≥3 low-risk adenomas and SSPs, and most higher-risk adenomas and SSPs, at 3 years. We also continue to recommend consideration of genetic testing for a polyposis syndrome in all patients with ≥10 adenomas or SSPs on a single colonoscopy or with a lifetime cumulative incidence of at least 20. In contrast, the guidelines now recommend that any person with ≥10 polyps at colonoscopy who does not have a polyposis syndrome have repeat colonoscopy within 1 year,” he said.

Dr. Ness acknowledged that there are few data to inform those 2 recommendations. In one study from Harvard, the odds of diagnosing an underlying polyposis syndrome were increased in persons with ≥10 cumulative adenomas.11 In another often-cited article from South Korea, patients with >10 adenomas versus those with 3 to 10 adenomas had a 2.25 elevated risk for advanced colorectal neoplasia.12

Management of Large Polyps

The surveillance interval has been shortened for patients with large (≥1 cm) adenomas and SSPs either with unfavorable-risk factors for local recurrence or removed in piecemeal fashion. The guidelines now recommend the first surveillance colonoscopy at 6 months, rather than 12 months, with the second occurring 12 months later, even without evidence of recurrence at the first surveillance examination. A number of studies support this recommendation,13-15 showing a sizable recurrence rate at 6 months, a much higher risk of recurrence after piecemeal resection than en bloc resection, and an increasing risk of recurrence associated with increasing size of the resected polyp.

Recommendations Based on Family History

Individuals with a first-degree relative with (1) CRC or endometrial cancer who were diagnosed before age 50 years or (2) synchronous or metachronous Lynch syndrome–related cancers regardless of age should undergo genetic evaluation. Otherwise, for persons with a first-degree relative with CRC, the guidelines panel recommends colonoscopy beginning at age 40 years, or 10 years before the earliest familial CRC diagnosis, with surveillance at least every 5 years (Figure 2). This recommendation is based on data published almost 30 years ago from a cohort study of >119,000 adults undergoing their first screening who were then followed for 6.5 years. The study determined the age-adjusted relative risk for CRC for those with a first-degree relative with CRC, and essentially validated the 10-year earlier shift in diagnosis, based on the presence of a family history.16

A more recent long-range case-control study of Utah residents aged 50 to 80 years determined the HR for developing CRC was 1.6 to 2.5 among individuals with a first-degree relative with CRC, with the highest risk seen among those whose relatives were diagnosed before age 40 years.17 Other studies have found a much lower risk for persons with second- and third-degree relatives with CRC.18 After much discussion, the guidelines panel continued to only recommend colonoscopy screening beginning...
at age 45 years for persons with CRC limited to second- and third-degree relatives,” he said (Figure 2).

Finally, for adults with first-degree relatives that have confirmed advanced adenoma or advanced SSPs at any age (Figure 2), the recommendations are similar to those for patients with an affected first-degree relative with CRC. Hong Kong investigators determined the odds of finding adenomas among 200 persons who also had siblings with advanced adenomas compared with 400 adults without an affected sibling. Those with affected siblings had a matched-sex odds ratio of 3.29 for any adenoma and 6.05 for advanced adenomas.

### Screening Modalities and Evaluation of Findings

No significant changes have been made regarding the recommended modalities and strategies for evaluation of screening findings. The panel continues to endorse colonoscopy every 10 years, fecal immunochemical testing every 1 year, multitargeted stool DNA testing every 3 years, CT colonoscopy every 5 years, and flexible sigmoidoscopy every 5 to 10 years.

Summarizing the characteristics of the various diagnostic modalities employed in CRC, Dr. Ness noted that with adherence to the recommended screening intervals, all screening strategies are cost-effective compared with no screening. Nonetheless, to achieve the best results, CRC screening should be done as part of a systematic population-based program that includes direct outreach to patients and in-clinic focused interventions to increase screening rates, reduce mortality, and minimize disparities by race and ethnicity.

### Patients With Inflammatory Bowel Disease

The panel made no significant changes to the recommendations for CRC screening in patients with underlying Crohn’s disease or ulcerative colitis. Surveillance should be started 8 years after the onset of symptoms and be conducted with high-definition, white-light endoscopy or chromoendoscopy with targeted biopsies. Exceptions to this schedule are patients with primary sclerosing cholangitis, who should start yearly surveillance upon diagnosis, and patients with a family history of CRC or advanced neoplasia where age of the family member at diagnosis may supersede the standard recommendations for inflammatory bowel disease, he said.

The frequency of surveillance after initial colonoscopy ranges between 1 and 3 years, depending on personal and family histories, disease activity, and other findings (such as invisible dysplasia and chronic stricture).

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### Disclosures

Dr. Ness has disclosed receiving grant/research support from Guardant Health.

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### References