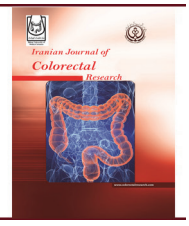
Mini Review

Iran J Colorectal Res 2023;11(2):65-67.

Iranian Journal of Colorectal Research



Early-onset Colorectal Cancer Screening: What's New and What Should We Do?

Budhi Ida Bagus*[1*], *PhD

[1]*Department of Surgery, Sebelas Maret University, Indonesia*

Corresponding author:
Budhi Ida Bagus, PhD;
Department of Surgery, Sebelas Maret University, Indonesia. **Tel:** +62 8122013921
Email: budhi_suryaadnyana@yahoo.com

Received: 2023-05-14
Revised: 2023-06-23
Accept: 2023-06-23

Abstract

Colorectal cancer (CRC) is the third largest cause of death from cancer-related causes in the United States. Screening programs lower the incidence and mortalities of CRC in those aged 50 and above with an average risk for the disease. On the other hand, the incidence of CRC in people younger than 50 years of age (early-onset colorectal cancer, or eoCRC) has recently increased substantially. Epidemiologic studies of eoCRC suggest that the cancer is most prevalent in the distal colon and rectum and is associated with several modifiable risk factors, such as diabetes, obesity, diet, sedentary lifestyle, alcohol intake, and smoking. The data covering the potential risk factors of prior antibiotic exposure and alterations to the microbiome or direct carcinogen exposure are still being gathered. Delayed diagnosis or more aggressive tumor biology may lead to aggressive clinicopathologic characteristics of eoCRC observed at presentation. When matched for stage, the outcomes of patients with eoCRC are comparable to those of patients with later-onset CRC; nevertheless, the overall mortality rate is higher due to a higher frequency of advanced illness at a younger presentation, which results in more life years lost.

Keywords: Colorectal neoplasms, Early detection of cancer, Incidence

Please cite this paper as:
Ida Bagus B. Early-onset Colorectal Cancer Screening: What's New and What Should We Do?. *Iran J Colorectal Res*. 2023;11(2):65-67. doi: 10.30476/ACRR.2023.99839.1183.

Introduction

Colorectal cancer (CRC) is the third largest cause of death from cancer-related causes in the United States. In the mid-1990s, screening for CRC was made mandatory for all persons aged 50 or older. As a result, the incidence of CRC and the death rate associated with later-onset CRCs (loCRCs) in people over 50 have steadily reduced over the past two decades. On the other hand, several studies have pointed to a worrying trend in which the occurrence of CRC in people younger than 50 years old has been steadily rising (1, 2).

It has been shown in several epidemiological studies that the incidence of early-onset colorectal cancer (eoCRC) has been steadily climbing, and that there are links between modifiable risk factors and eoCRC. However, the underlying etiology of the rising incidence of eoCRC has not yet been established. In the case of eoCRC, relatively few studies have been published that inform any molecular or somatic genetic abnormalities; studying these differences enables one to see the occurrence of eoCRC through a new lens (3). The discovery of

putative molecular pathways that drive the formation or propagation of eoCRC can not only throw fresh light on pathogenic mechanisms, but it also has the potential to disclose an etiologic cause of eoCRC and guide risk stratification to target at-risk patients and reduce its incidence (4).

Rising Incidence of Early-onset Colorectal Cancer (eoCRC)

Since the implementation of screening for persons at average risk aged 50 or older in the mid-1990s, the incidence and mortality rate of CRC have progressively decreased. The incidence of CRC and its associated mortality have continued to decrease in people over 50 and overall. The most recent trends show that the average annual percentage change (AAPC) in the incidence of CRC was -0.7 in people between the ages of 50 and 65 from 2007 to 2016, and -4.0 in people aged 65 or older. In contrast, the number of eoCRCs has been on the rise. This observation is susceptible to either of two interpretations, depending on several factors. It is clear from the epidemiology that the increase in eoCRC instances is not caused by genetic evolution but by environmental factors (3, 5). The apparent rise could impact people of all ages within the community; however, the preventative effects of screening colonoscopy mean that an increase in CRC is not seen in older patients who are checked. This results in an apparent increase in eoCRC patients purely because this group is not examined. If, on the other hand, environmental exposure favorably impacts younger groups over older populations, this results in a genuine increase in the number of eoCRC patients while having no impact on older populations (6).

The existence of non-modifiable and well-established risk factors for CRC is what prompts high-risk screening. The existence of a genetic or hereditary cancer syndrome, a personal history of adenoma, and a personal history of inflammatory bowel disease are all factors that should warrant faster colonoscopy schedules for CRC screening. Other risk factors include a family history of CRC, a family history of advanced adenoma, a personal history of adenoma, and a personal history of advanced inflammatory bowel disease. Some studies have indicated that 25% of the already diagnosed cases of eoCRC could have been avoided if only the family history were recognized as a risk factor and high-risk screening was started sooner (5, 7). A history of abdominal or pelvic radiation treatment for a previous malignancy, as well as cystic fibrosis, are additional risk factors that have earned conditional recommendations for the commencement of early screening. The incidence of eoCRC is anticipated to decrease due to better awareness and stricter adherence to screening criteria for high-risk persons; however, this will not totally abate the rising incidence of early-onset colorectal cancer. The identification of additional risk factors that significantly contribute to eoCRC will be essential to thoroughly understand and address the surge in incidence that has been documented (8).

Sources of Data on Early-onset Colorectal Cancer (eoCRC)

The Surveillance, Epidemiology, and End Results (SEER) registries, which account for patients located within specified regions in the United States, are the source of a significant amount of the data used to analyze the trends of eoCRC. Studies collected from international registries in other industrialized nations reveal that the United States follows a pattern comparable to that seen in other countries. It has been difficult to estimate the incidence trend of eoCRC in several parts of the world due to the lack of well-maintained registries. It is interesting to note that certain wealthy nations have experienced a reduction in the incidence of eoCRC (9). In particular, Austria, Italy, and Lithuania indicate a continuing decline in the rates of eoCRC. It is not totally obvious why these countries have a decreasing eoCRC incidence in comparison to other developed countries; nevertheless, Italy and Austria begin CRC screening at the ages of 44 and 40, respectively (7, 10).

Screening of Early-onset Colorectal Cancer (eoCRC)

Changes in the prevalence of early-onset colorectal cancer have spurred the reassessment of established CRC screening recommendations. Because current incidence rates of CRC are greater than historical incidence rates, updated modeling studies that use these rates imply that average risk screening should begin at age 45. While previously, incidence rates of CRC were lowest among adults aged 45–49 (11), the American Cancer Society recently issued a qualified recommendation for a revised threshold to commence CRC screening at the age of 45 years in response to these modern models, which suggested that the threshold should be lowered to 40 years. After some long-term evaluations, the American Gastroenterological Association and the United States Preventative Services Task Force both reaffirmed their previous recommendations regarding the need to begin CRC screening at an earlier age (12).

The possibility of beginning screening for CRC at age 45 has stirred up some debate, particularly concerning the focus of resource allocation on the 35% of at-risk individuals over the age of 50 who are not currently screened in comparison to the opening up of a greater pool of individuals that are aged 45-49 years (13). It would be ideal to understand the biological reason for the epidemiological data showing this rise in eoCR. Then, we could more accurately risk stratify patients in the under-50 age group to pre-symptomatically target screening resources. This would allow us to avoid using age as the sole variable that demarcates and decides

when the onset of at-risk population-wide screening occurs. Last but not least, when the age of 45 years as the screening criterion becomes more widely adopted, this may induce a modification to the definition of eoCRC to that of age 45 or 40 years, or even lower. This is because the incidence of eoCRC increases with age. An informed, targeted approach is one that is applied to higher-risk individuals who are identified as a result of an understanding of the epidemiology and biology of the disease. Broad societal implementation for the entire population for initiating screening at the age of 45 years might be an easier and more uniform message to providers and patients, but it might also constrain resources and be more expensive for society (14, 15).

Conclusion

Currently, no guidelines or evidence support any particular preventative, surveillance, or treatment modality for people diagnosed with eoCRC instead of loCRC. Because of the nature of their younger presentation and potential lifespan remaining, patients diagnosed with eoCRC are more likely to receive aggressive surgical resections (such as metastatic resections), multimodal chemotherapy, and immunotherapy than their older counterparts.

Conflict of interest: None declared.

References

1. Mauri G, Sartore-Bianchi A, Russo AG, Marsoni S, Bardelli A, Siena S. Early-onset colorectal cancer in young individuals. Molecular oncology. 2019;13(2):109-31.
2. Burnett-Hartman AN, Lee JK, Demb J, Gupta S. An Update on the Epidemiology, Molecular Characterization, Diagnosis, and Screening Strategies for Early-Onset Colorectal Cancer. Gastroenterology. 2021;160(4):1041-9.
3. Akimoto N, Ugai T, Zhong R, Hamada T, Fujiyoshi K, Giannakis M, et al. Rising incidence of early-onset colorectal cancer - a call to action. Nature reviews Clinical oncology. 2021;18(4):230-43.
4. A, Carethers JM. Epidemiology and biology of early onset colorectal cancer. EXCLI journal. 2022;21:162-82.
5. Muller C, Ihionkhan E, Stoffel EM, Kupfer SS. Disparities in Early-Onset Colorectal Cancer. Cells. 2021;10(5).
6. Jeong MA, Kang HW. [Early-onset Colorectal Cancer]. The Korean journal of gastroenterology = Taehan Sohwagi Hakhoe chi. 2019;74(1):4-10.
7. Willauer AN, Liu Y, Pereira AAL, Lam M, Morris JS, Raghav KPS, et al. Clinical and molecular characterization of early-onset colorectal cancer. Cancer. 2019;125(12):2002-10.
8. Xi Y, Xu P. Global colorectal cancer burden in 2020 and projections to 2040. Translational oncology. 2021;14(10):101174.
9. Puzzono M, Mannucci A, Grannò S, Zuppardo RA, Galli A, Danese S, et al. The Role of Diet and Lifestyle in Early-Onset Colorectal Cancer: A Systematic Review. Cancers. 2021;13(23).
10. Saraiva MR, Rosa I, Claro I. Early-onset colorectal cancer: A review of current knowledge. World journal of gastroenterology. 2023;29(8):1289-303.
11. Ullah F, Pillai AB, Omar N, Dima D, Harichand S. Early-Onset Colorectal Cancer: Current Insights. Cancers. 2023;15(12).
12. Done JZ, Fang SH. Young-onset colorectal cancer: A review. World journal of gastrointestinal oncology. 2021;13(8):856-66.
13. Garrett C, Steffens D, Solomon M, Koh C. Early-onset colorectal cancer: why it should be high on our list of differentials. ANZ journal of surgery. 2022;92(7-8):1638-43.
14. Siegel RL, Jakubowski CD, Fedewa SA, Davis A, Azad NS. Colorectal Cancer in the Young: Epidemiology, Prevention, Management. American Society of Clinical Oncology educational book American Society of Clinical Oncology Annual Meeting. 2020;40:1-14.
15. Wu CW, Lui RN. Early-onset colorectal cancer: Current insights and future directions. World journal of gastrointestinal oncology. 2022;14(1):230-41.