MAYO CLINIC

The Increasing Incidence of Young-Onset Colorectal Cancer: A Call to Action

Dennis J. Ahnen, MD; Sally W. Wade, MPH; Whitney F. Jones, MD; Randa Sifri, MD; Jose Mendoza Silveiras, MD; Jasmine Greenamyer, MPH; Stephanie Guiffre, MPA; Jennifer Axilbund, MS; Andrew Spiegel, JD; and Y. Nancy You, MD, MHSc

Abstract

In the United States, colorectal cancer (CRC) is the third most common and second most lethal cancer. More than one-tenth of CRC cases (11% of colon cancers and 18% of rectal cancers) have a young onset (ie, occurring in individuals younger than 50 years). The CRC incidence and mortality rates are decreasing among all age groups older than 50 years, yet increasing in younger individuals for whom screening use is limited and key symptoms may go unrecognized. Familial syndromes account for approximately 20% of young-onset CRCs, and the remainder are typically microsatellite stable cancers, which are more commonly diploid than similar tumors in older individuals. Young-onset CRCs are more likely to occur in the distal colon or rectum, be poorly differentiated, have mucinous and signet ring features, and present at advanced stages. Yet, stage-specific survival in patients with young-onset CRC is comparable to that of patients with later-onset cancer. Primary care physicians have an important opportunity to identify high-risk young individuals for screening and to promptly evaluate CRC symptoms. Risk modification, targeted screening, and prophylactic surgery may benefit individuals with a predisposing hereditary syndrome or condition (eg, inflammatory bowel disease) or a family history of CRC or advanced adenomatous polyps. When apparently average-risk young adults present with CRC-like symptoms (eg, unexplained persistent rectal bleeding, anemia, and abdominal pain), endoscopic work-ups can expedite diagnosis. Early screening in high-risk individuals and thorough diagnostic work-ups in symptomatic young adults may improve young-onset CRC trends.

 ■ Mayo Clin Proc. 2014;89(2):216-224

From the Department of Veterans Affairs, Eastern Colorado Healthcare System, and Division of Gastroenterology, University of Colorado School of Medicine, Denver (D.J.A.); Wade Outcomes Research and Consulting, Salt Lake City, UT (S.W.W.); University of Louisville School of Medicine, and Colon Cancer Prevention Project, Louisville, KY (W.F.J.); Department of Family and Community Medicine, Thomas Jefferson University, Philadelphia, PA (R.S.); Colon Cancer Alliance, Washington, DC (J.M.S., J.G., S.G.); Clinical Cancer Genetics & Prevention, The Johns Hopkins Hospital, Baltimore, MD (J.A.); Global Colon Cancer Alliance, Bala Cynwyd, PA (A.S.); and University of Texas, MD Anderson Cancer Center, Houston (Y.N.Y.).

Colorectal cancer (CRC), the third most common and second most lethal cancer in the United States, is also the leading cause of cancer-related deaths among nonsmokers.[1] The American Cancer Society estimated that 143,460 new CRC cases and 51,690 CRC deaths occurred in 2012.[2,3] Despite these sobering statistics, the Centers for Disease Control and Prevention reported statistically significant decreases in CRC incidence and mortality from 1999 through 2008 for both men and women and in virtually all racial and ethnic groups.[4] These decreases are partially attributed to population-based CRC screening, which was first recommended in 1977 and became a Healthcare Effectiveness Data and Information Set performance measure in 2003.[5-7]

Although average-risk screening is generally recommended to begin at 50 years of age, more than one-tenth of CRC cases (11% of colon cancers and 18% of rectal cancers) occur in younger individuals, and incidence and mortality are increasing significantly in this age group.[5,8-16] We describe incidence and mortality trends, clinical characteristics, and outcomes of CRC in individuals younger than 50 years (young-onset CRC). We aim to raise awareness of young-onset CRC and to instruct primary care physicians (PCPs) in how to help reduce the burden of young-onset CRC.

YOUNG-ONSET CRC INCIDENCE AND MORTALITY

In Americans younger than 50 years, CRC incidence per 100,000 individuals ranges from 0.85 (ages 20-24 years) to 28.8 (ages 45-49 years).[17] Although these rates are substantially lower than those in older age groups, the incidence has increased significantly in younger individuals and decreased in older individuals (Figure 1).[18] The national 1987-2006 Surveillance, Epidemiology, and End Results (SEER) data (Figure 2, A-C) reveal increased colon and rectal cancer incidence

Mayo Clin Proc. ■ February 2014;89(2):216-224 ■ http://dx.doi.org/10.1016/j.mayocp.2013.09.006
www.mayoclinicproceedings.org ■ © 2014 Mayo Foundation for Medical Education and Research

in all 5-year age groups between 20 and 49 years, with the sharpest increases among individuals 40 to 44 years old (10.7 per 100,000 population in 1988 and 17.9 per 100,000 population in 2006).[19]

In the National Cancer Database, a hospital-based cancer registry capturing 70% of all incident cancers in the United States, young-onset CRC incidence increased from 1998 to 2007 (annual percent change [APC], 2.1%; 95% CI, 1.1%-3.1%), whereas later-onset incidence decreased (APC, −2.5%; 95% CI, −3.0% to −2.0%).[10] As in SEER, young-onset rectal cancer incidence (APC, 3.9%; 95% CI, 3.1%-4.7%) increased more rapidly than young-onset colon cancer (APC, 2.7%; 95% CI, 2.0%-3.3%). Compared with later-onset disease, young-onset CRC was more common among nonwhite individuals and among those who were either uninsured or Medicaid insured.

The CRC mortality trends mirror incidence trends. Age-adjusted young-onset CRC mortality rates in 2005-2009 ranged from 0.2 per 100,000 population (ages 20-24 years) to 7.7 per 100,000 population (ages 45-49 years).[20] The mortality rate for those with young-onset CRC remained stable between 1975 and 2004, then increased by approximately 2% annually through 2009.[21] By contrast, the age-adjusted mortality rate in older individuals decreased by 2% to 3% annually between 1992 and 2009.[22]

WHY IS YOUNG-ONSET CRC INCREASING?

Drivers of increasing young-onset CRC incidence are not well understood. In the absence of rigorous epidemiologic studies, it is noteworthy that young-onset CRC incidence increased, whereas CRC risk factors, such as sedentary lifestyle, obesity, and diabetes mellitus, were common or increasing.[23-25] Each 5-unit increase in body mass index is associated with an estimated 13% to 18% increase in CRC risk.[3,26] Diabetes mellitus has been associated with up to a 38% (summary relative risk 95% CI, 1.26-1.51) increase in colon cancer risk and a 20% increase in rectal cancer risk (95% CI, 1.09-1.31).[27] Similarly, regular physical activity is associated with a 24% to 31% reduction in CRC risk.[28] These risk factors alone do not explain the observed trends in young-onset CRC because they are common or increasing in older age groups in which CRC incidence decreased.

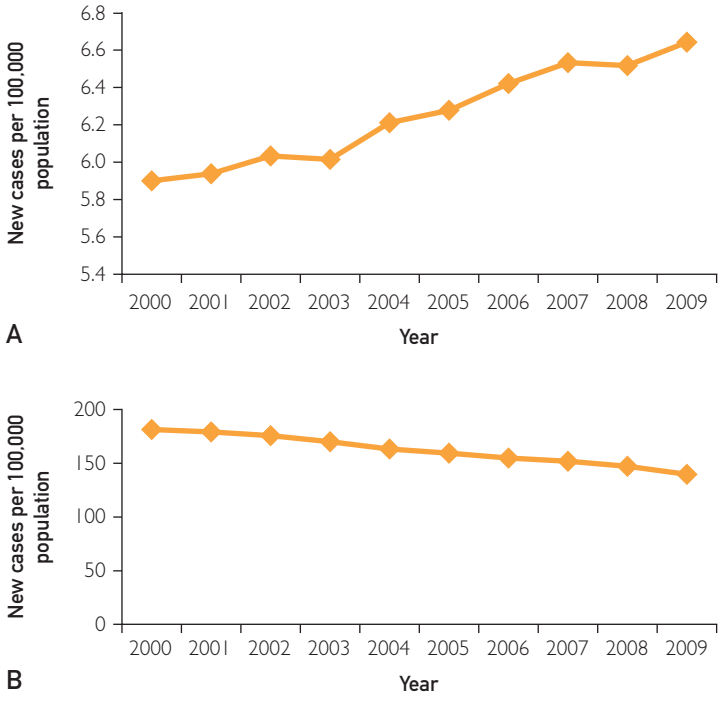

FIGURE 1. Surveillance, Epidemiology, and End Results age-adjusted colorectal cancer incidence per 100,000 individuals in those younger than 50 years (A) and those 50 years or older (B).

Screening for CRC in average-risk individuals is credited as the largest single driver of decreasing CRC incidence and mortality overall. From 1990 to 2010, screening adherence increased to approximately 65% for individuals 50 to 70 years old, with concurrent decreases in CRC incidence.[5,29] Average-risk screening is generally only recommended for individuals after 50 years of age. The fact that routine screening is largely confined to those older individuals might partially explain age-related disparities in CRC incidence and mortality trends. Additional epidemiologic research is needed, however, to better understand these trends.

DISTINCTIVE BIOLOGY AND GENETICS OF YOUNG-ONSET CRC

Single-institution and population-based studies have found distinctive tumor location, stage at presentation, and histologic features in young-onset CRC.[10,30-33] These tumors occur more often than later-onset tumors in the distal colon and the rectum (69.0% vs 57.7%, $P<.001$).[10] In individuals 35 to 39 years of age, 32% of CRC