Colorectal Cancer — An Update for Primary Care Nurse Practitioners

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ABSTRACT

The picture of colorectal cancer (CRC) is changing. Our understanding of factors that drive the growth of CRC, the image of a CRC patient, and our approach to treating CRC is all evolving. This article will bring the picture into clearer focus. We will start with an update of the pathogenesis of CRC, review screening methods, look at a meta-analysis of risk factors, then follow with new information about the concern of younger patients developing CRC. We finish with a look at a new treatment option. With this more focused view, nurse practitioners can screen more effectively for colorectal cancer.

Keywords: cancer risk, cancer screening, colorectal cancer, early detection, nurse practitioner

INTRODUCTION

The impact of colorectal cancer (CRC) is substantial; it ranks as the third most common cancer for both men and women,[1] as well as the second most common cause of cancer deaths for men and third for women in the United States.[2] It is estimated that 135,430 people will be diagnosed with CRC and 50,260 people will die from CRC in 2017.[2] That is a sobering thought because CRC remains one of the most preventable cancers.[2,3] CRC almost always develops slowly over many years from benign growths in the colon or rectum. With appropriate screening, lesions can be identified and removed before they become malignant.[3,4] Siegel et al[5] report that recent declines in CRC incidence rates are likely driven by an increase in colonoscopy screenings. They report that in adults 50 to 75 years old, colonoscopy use has increased from 19% in 2000 to 55% in 2013.[5] Despite that increase, only 65% of adults in the United States are following current screening recommendations. CRC treatment contributes approximately $14 billion annually to health care costs, and screening and early detection could help control that cost.[4]

PATHOGENESIS OF CRC

CRC can occur randomly (sporadic), from inherited mutations in cancer-related genes (hereditary) or from chronic inflammatory bowel diseases, such as Crohn's disease or ulcerative colitis. Sporadic tumors account for most of CRC at about 94%, inherited mutations account for 5%, and inflammatory bowel diseases for 1%.[6] In the sporadic group, about 25% of tumors occur in patients who have a family history of CRC (familial) but no identified familial genetic CRC syndrome, indicating possible unidentified cancer-related genes.[1]

Sporadic CRCs typically develop along 1 of 3 proposed genetic and morphologic pathways. The first is the chromosomal instability or suppressor pathway, accounting for about 70% of sporadic CRCs. This pathway is characterized by genetic alterations that interfere with tumor suppressor genes (such as APC, KRAS, and p53) that activate pathways critical for carcinogenesis. These tumors are also described as having microsatellite stability or intact DNA mismatch repair systems. Second is the microsatellite instability (MSI) or mutator pathway, accounting for about 15% of sporadic CRCs. This pathway is activated by disruption of the DNA mismatch repair genes (MMR deficiency). The mismatch repair system is responsible for proofing newly created DNA, identifying and repairing replication errors. When this system is inactivated, DNA mutations increase rapidly, allowing malignant

cell lines to grow. The BRAF gene is an oncogene and can direct cell growth. It is often mutated in MSI tumors, facilitating malignant cell growth. These tumors often arise in the proximal colon and have increased mucin production, signet ring cells, and low-grade differentiation. The third is the CpG island methylator phenotype (CIMP) or serrated pathway, which causes tumor suppressor genes to switch off, allowing growth of malignant cell lines. This accounts for 30%–40% of sporadic CRC. These tumors are also often found in the proximal colon, occur more often in females, and have poor differentiation.[1,3,6–9]

Hereditary CRC can be subdivided into those with or without colon polyps. The syndromes characterized by polyps include familial adenomatous polyposis (FAP), MYH-associated polyposis, Peutz-Jeghers syndrome, Juvenile Polyposis syndrome, phosphatase and tensin homolog (PTEN), and hamartoma tumor (Cowden) syndrome. Those commonly without polyps are referred to as hereditary nonpolyposis CRC (Lynch syndrome). The 2 most common are hereditary nonpolyposis CRC and FAP; both are autosomal dominant. FAP develops most often from the chromosomal instability pathway. This syndrome results in the development of hundreds to thousands of polyps in the colon and rectum beginning in adolescence. If untreated, 100% of those affected will develop CRC by the age of 40 years. Prophylactic subtotal colectomy followed by annual rectal endoscopy is recommended for affected individuals, but can be delayed until the polyp burden becomes too high to be safely managed by colonoscopy. Hereditary nonpolyposis CRC develops most often from the MSI pathway and is associated with increased risk of CRC, synchronous and metachronous CRCs, along with endometrial, ovarian, gastric, small bowel, urinary tract, brain and biliary cancers. National Comprehensive Cancer Network guidelines recommend that these individuals begin annual or biennial screening colonoscopy at age 20–25 years, or 10 years before the age at diagnosis of youngest family member (whichever comes first).[10–13]

The pathway of development of CRC from inflammatory bowel disease is not yet well understood. Chronic inflammation plays a role in the development of CRC, and this is certainly important in the development of CRC in inflammatory bowel disease. The chromosomal instability pathway and the MSI pathway also play important roles, but at different times and frequencies than in sporadic CRC.[14]

All the pathways described earlier cause focal changes that develop into benign polyps. These typically grow slowly, may remain benign, or may take decades to develop into malignancies. The 2 types of polys with the most potential for malignant transformation are adenomas and sessile serrated polyps. Tubulovillous and villous adenomas have the greatest malignant potential and account for 60%–70% of CRC. Sessile serrated polys account for 25%–35% of CRC. They are flat, may not bleed, and grow in a way that can be difficult to detect during colonoscopy.[3,4]

Our understanding of these pathways is rapidly increasing, facilitating development of more targeted and effective treatments, as well as the development of more sensitive and specific screening methods to detect early CRC and even developing benign and precursor polyps[3,4] (see Figure).

Another field of emerging study important to the understanding of CRC pathogenesis and treatment is the gut microbiota. The gut microbiota likely plays an important role in the development of CRC, a role in protecting from the development of CRC, as well as a role in determining the response to treatment of CRC. It is not within the scope of this article to present an in-depth discussion of the gut microbiota, but to note the developing field of research that will likely enhance our understanding of CRC as well as give us new targets for detection, prevention, and treatment. For a more in-depth review, please refer to Drewes et al.[15]

SCREENING FOR CRC

Screening remains the most important means to prevent CRC. The primary care nurse practitioner should be knowledgeable about CRC screening guidelines and apply them appropriately to patients. There are several reliable resources for screening guidelines, including the National Cancer Institute, National Comprehensive Cancer Network, American Society for Clinical Oncology, American Cancer Society, Centers for Disease Control and Prevention,