Early Detection of and Screening for Colorectal Neoplasia

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There are approximately one million new cases of colorectal cancer (CRC) per year worldwide, with substantial associated morbidity and mortality. The long natural history of colorectal neoplasia affords the opportunity to use preventive measures to improve survival in this disease. Currently screening for adenomatous polyps and early-stage cancers is the best methodology for improving survival. The increasing knowledge of CRC pathogenesis and its natural history is allowing the development of new tools to identify patients who will benefit most from colon cancer screening and the defining of appropriate surveillance intervals. The guidelines for screening for colorectal neoplasia have recently been substantially revised by several organizations based on developing technologies and a growing body of data on the efficacy of CRC screening. (Gut and Liver 2009;3:69-80)

Key Words: Colon cancer screening; Fecal occult blood testing; Colonoscopy; Computed tomographic colonography; Adenoma

INTRODUCTION

Cancers of the colon and rectum (CRC) are a major cause of cancer-associated morbidity and mortality worldwide. CRC is the fourth most common newly diagnosed internal cancer overall in the United States, after cancers of the lung, prostate, and breast, and currently constitutes 10% of new cancers in both men and women. In 2008, there were an estimated 149,000 new CRC cases in the United States and 51,000 related deaths (a rate second only to that of lung cancer). Globally, CRC is the fourth most common cancer in men and the third most common in women, accounting for approximately one million new cases per year. While there is at least a 25-fold variation in the occurrence of CRC worldwide, many countries where CRC mortality was previously low have reported substantial increases during the past decade. CRC has become one of the most common cancers in a number of Asian countries, for example. Despite evidence that 5-year survival is 90% when CRC is diagnosed at an early stage, less than half of cases are diagnosed when the cancer is still localized.

Rapid growth of knowledge about the molecular and biologic characteristics of epithelial cancers has provided useful insights into the pathogenesis of colonic neoplasia. New insights also have been gained in regard to primary prevention. Because CRC arises over long periods as the result of interactions between genetic predisposition and environmental insults, it has become possible to identify pre-neoplastic and early neoplastic lesions with the hope of improving survival rates. More complete knowledge of CRC pathogenesis and its natural history, especially in high-risk groups, is allowing the development of new tools to identify those who will benefit most from colon cancer screening and in defining proper surveillance intervals. During the past year guidelines for screening for colorectal neoplasia have been substantially revised by several organizations based on developing technologies, and a growing body of data regarding the efficacy of CRC screening. This review will focus on evolving concepts and an evidence-based approach to CRC screening.

PRINCIPLES OF SCREENING

Cancer prevention has been traditionally categorized as primary or secondary. Primary prevention refers to the identification of genetic, biologic, and environmental fac-
tors that are etiologic or pathogenetic and subsequent alteration of their effects on tumor development. Although several areas of study have been identified that may lead to primary prevention of CRC, available data do not yet provide a firm basis for the practical application of primary preventive measures in most cases. The goal of secondary prevention (which includes screening) is to identify existing preneoplastic and early neoplastic lesions and to treat them thoroughly and expeditiously. The assumption is that early detection improves prognosis. Screening an asymptomatic population for any disease is worthwhile if the disease represents a major health problem, effective therapy is available if the disease is found, a sensitive and specific screening test is available that is readily acceptable to patients and physicians, and the screening test is cost-effective.

The long natural history of colonic neoplasia, and mucosal progression through defined phenotypic changes (the adenoma to carcinoma pathway) associated with identifiable genetic alterations fundamental to this process, makes CRC feasible. The challenge has been to develop effective, easily administered, and cost-effective screening tests for the disease. Current evidence strongly suggests that screening for CRC reduces related mortality. Direct evidence for this is available from prospective trials of fecal occult blood testing (FOBT), indirectly for colonoscopy and polypectomy (versus historical controls) from the National Polyp Study and from a recent case-control trial. These findings have resulted in recommendation by numerous organizations, including the evidence-based United States Preventive Services Task Force (USPSTF), that screening for CRC should be performed in all persons aged 50 years to 75 years (see below).

Previous studies reviewed by the USPSTF indicated that CRC screening is likely to be cost effective (<$30,000 per additional year of life gained in the United States) regardless of the strategy chosen. A more recent decision analysis commissioned by the USPSTF used microsimulation models from the Cancer Intervention and Surveillance Modeling Network to assess life-years gained and colonoscopy requirements for screening strategies. This group concluded that their findings support colorectal cancer screening with colonoscopy every 10 years, annual screening with a sensitive FOBT, or flexible sigmoidoscopy every 5 years with a midinterval FOBT from age 50 to 75 years. This was part of the basis for recent modifications to the USPSTF guidelines.

The willingness of both patients and physicians to comply with recommendations for screening programs has a major impact on the effectiveness (and cost effectiveness) of CRC screening. Compliance by both the population at large and health care providers has historically has been poor, and interventions to increase screening adherence have been disappointing. The key questions of “who, how, and how often” to screen remain a source of debate.

GUIDELINES

In 2008 new guidelines on screening and surveillance for early detection of colorectal cancer and adenomatous polyps was issued jointly by the American Cancer Society and the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology (Table 1). This update of previous guidelines is notable in that it grouped screening tests into those that primarily detect cancer (annual FOBT including those that are guaiac-based or immunochemical tests, and stool DNA tests and colonoscopy and polypectomy (versus historical controls) in all persons aged 50 years to 75 years (see below). Because of the long average time between adenoma development and cancer diagnosis. Routine screening was therefore not recommended for adults age 76 to 85 years, and screening was not recommended at all in adults older than 85 years of age. These guidelines also indicated that for all populations there is insufficient evidence to assess the benefits and harms of screening with CT colonography or fecal DNA testing.

In 2008 an Asia Pacific Working Group on Colorectal Cancer published consensus recommendations for colorectal cancer screening. This group concluded that the incidence, anatomical distribution and mortality of CRC among Asian populations are not different compared with Western countries. They concluded that screening for colorectal cancer should be started at age 50 years. FOBT (guaiac-based and immunochemical), flexible sigmoidoscopy and colonoscopy were recommended for CRC screening. Double contrast barium enema and CT colonography are not preferred. In resource-limited countries FOBT is the first choice for CRC screening.