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REVIEW

Colorectal cancer screening in the familial risk population: Is colonoscopy still the strategy of choice?

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Abstract First-degree relatives of patients with colorectal cancer (CRC) are at high risk of this disease. For this reason, medical organizations and clinical guidelines recommend more intensive screening and surveillance for such first-degree relatives than for the average-risk population. Colonoscopy has been the cornerstone of CRC screening in this setting. Although colonoscopy is the most sensitive technique for the detection of neoplastic lesions (especially non-advanced adenomas), its role is less clear for CRC. In addition, screening colonoscopy has several limitations that may affect the success of a screening campaign, such as poor participant acceptance, the need for skilled endoscopists, participant access to screening colonoscopy, overburdened endoscopy units, potential complications, and procedure-related costs. In addition, recent evidence has cast doubt on the advantage of colonoscopy over other strategies for the detection of advanced neoplastic lesions. Despite being less sensitive in general, other screening methods frequently recommended in the average-risk population may be more acceptable and thus help increase CRC screening uptake. This review discusses recent evidence on the risk of CRC in first-degree relatives, the advantages and disadvantages of each screening technique, participation rates depending on the technique, patient preferences, and barriers to screening.

PALABRAS CLAVE
Colonoscopia de cribado;
Población de riesgo familiar;
Cáncer de colon;
Participación

Cribado del cáncer colorrectal en población de riesgo familiar. Es aún la colonoscopia la estrategia de elección?

Resumen Los familiares de primer grado de pacientes con cáncer colorrectal (CCR) tienen mayor riesgo de CCR que la población general. Por este motivo, las organizaciones médicas recomiendan una vigilancia más intensiva en esta población. Aunque la colonoscopia ha sido considerada la piedra angular de cribado, tiene limitaciones que pueden afectar el éxito de una campaña de cribado, que incluyen: baja aceptación, necesidad de personal entrenado,

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sobrecarga de trabajo, complicaciones y costes relacionados con el procedimiento. Evidencias recientes cuestionan la ventaja de la colonoscopia sobre otras estrategias de cribado para la detección de lesiones neoplásicas avanzadas. Aunque otras estrategias son menos sensibles, pueden ser mejor aceptadas y podrían incrementar la participación del cribado del CCR en los familiares de primer grado.

Esta revisión discute la evidencia actual sobre: riesgo de CCR en familiares de primer grado, beneficios y contrapartidas de cada técnica de cribado, participación de cada estrategia, preferencias y las barreras para la participación.

Introduction

Colorectal cancer (CRC) is the second leading cause of cancer-related death in developed countries and it ranks third among the most common cancers worldwide.[1] Several factors such as age, sex, and family history, have been related to the risk of developing CRC. Family history is the most powerful risk factor after age, particularly when dealing with first-degree relatives (FDR) of a patient with CRC.[2] In addition, the risk of developing CRC is directly related to the number of relatives affected and inversely related to the age of the youngest index case.[2–4]

The risk of developing CRC in these FDRs is 2- to 4-fold higher than that of the average-risk population. For this reason, current practice guidelines recommend more intensive surveillance in this population. Screening starting at the age of 40 years or 10 years before the youngest case affected is universally recommended.[5,6] In FDRs of patients with CRC, the predominant screening strategy is colonoscopy every 5 or 10 years, depending on the number of relatives affected and age at diagnosis, on the basis that it is the most effective procedure to detect and remove pre-malignant lesions or early cancers.[7] However, colonoscopy has various limitations, such as its inherent invasiveness, potential life-threatening complications, the need for skilled endoscopists, subject access to screening colonoscopy, low screening uptake, and procedure-related costs. Finally, it is not an infallible screening method and significant neoplasms may be missed.[8,9] Other screening strategies, including flexible sigmoidoscopy and stool-based tests, are also recommended for a select group of FDRs with the lowest risk of CRC.[5,6] These recommendations are empirically based on the higher risk of CRC in FDRs compared with average-risk participants, but there is limited evidence about what procedure should be recommended at each level of risk, because randomized controlled trials comparing different strategies in this setting are scarce.[7] Because of the scientific vacuum, some guidelines recommend that the screening test should be selected based on a risk/benefit assessment of the procedure, availability of the screening test, and patient preferences.[10] The present review aims to assess the pros and cons of each screening strategy for FDRs of CRC patients, taking into account effectiveness, factors related to participation and patient preferences.

Familial risk of colorectal cancer

Approximately 30% of patients with CRC have a family history of colorectal neoplasia[11] and only 5% show hereditary syndromes conferring an increased risk of CRC. Around 10% of the general population have a family history of CRC.[12,13] Therefore, most FDRs are labeled as individuals at moderate risk for CRC, distinguishing them from subjects with average-risk (general population aged over 50 years without any family history) and high-risk (individuals belonging to families with genetic syndromes described above). In these subjects, environment–genetic background interaction would explain the familial aggregation of cases with CRC, probably due to other genes or low-penetrance polymorphisms.[14]

In the general population, the risk of CRC is approximately 5%,[13] but it is increased when familial aggregation is present. Factors such as age of the index case, kinship, number of affected relatives or tumor location in the index case are associated with different risks.

Published evidence on family risk of CRC can be summarized from three meta-analyses including 27, 33 and 57 studies.[2–4] Age less than 50 years in the index case significantly increases the risk of CRC: relative risk (RR) ranged between 1.84 and 6.83. In another study, relatives of subjects with CRC older than 40 years had a similar risk to those over 50 years with no family history of CRC.[12]

The greater the number of FDRs affected with CRC, the higher the risk of developing CRC (RR = 2.2, ≈4 and 8.5 for 1, 2 or 3 affected relatives, respectively). The existence of second-degree relatives affected with CRC is also a risk factor for this disease (RR = 1.73).[3] Similarly, a meta-analysis that included 13 studies found an increased risk of colorectal adenomas in individuals with a family history of CRC (OR 1.7; 95% CI 1.4–3.5).[15] Regarding CRC location, FDRs of patients with colon cancer have a higher risk of CRC than those with relatives whose tumors are located in the rectum (RR ≈ 2.3 vs. ≈1.9). FDRs of patients with left-sided colon cancer are at greater risk than those of patients with right-sided tumors.[12] In familial CRC, knowledge of the genes involved in etiopathogenesis is scarce. Certain low-penetrance genes or polymorphisms of genes involved in DNA repair processes might explain the presence of cases of familial aggregation that cannot be classified in well characterized hereditary CRC syndromes. Such low-penetrance genetic alterations