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Chapter 1

Colonoscopy Screening for Colorectal Cancer — Overview of the Literature

Carlos Eduardo Pinzon-Florez, Oscar Andres Gamboa-Garay and Diana Marcela Diaz-Quijano

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Abstract

Objective: The aim of our chapter was to perform a systematic review of the clinical practice guidelines, randomized clinical trials, and prospective studies, using total colonoscopy for screening this population for colorectal cancer (CRC) and to evaluate the effectiveness of diagnosis and safety.

Methods: We included clinical practice guidelines, systematic reviews, and primary studies with more than 25 participants, and only those reporting the evaluation of colonoscopy as screening test for colorectal cancer and adenoma were included in this chapter. Analysis was performed for three outcomes: accuracy of colonoscopy as a screening test, reduction of colorectal cancer incidence and prevalence, and identification of adverse events of the procedure.

Results: For screening colonoscopy, evidence was of moderate quality. The evidence results suggest tentatively an even stronger reduction in distal colorectal cancer incidence and mortality. The colonoscopy significantly reduces the mortality for CRC. These studies suggest a 17% to 30% lower risk of incident colorectal cancer and 64% death from colorectal cancer after screening colonoscopy vs other screening diagnosis tests.

Conclusions: Colonoscopy is a feasible and safe method for screening CRC for proximal locations in asymptomatic people; however, these findings must be in contrast with the cost of the procedure, accessibility opportunities, and complications.

Keywords: Colonoscopy, Screening, Colorectal cancer, Adenoma, Fecal occult blood test (MeSH terms)

1. Introduction

1.1. Epidemiology of colorectal cancer

1.1.1. The colorectal cancer worldwide

Colorectal cancer is a disease typical of the regions with the largest urban and industrial development, which has changed consumption patterns and life. Worldwide, the rate of age-adjusted incidence (APR) of 17.2 cases per 100,000, ranking fourth in incidence among all types of cancer in both sexes, is presented, with a higher incidence rate in men than in women, APR of 20.3 and 14.6 cases per 100,000, respectively, for a total of 663,000 cases in men and 571,000 cases in women (1). About 60% of these cases occur in developed regions; the highest incidence rates are found in Australia, New Zealand, and Western Europe and the lowest in Africa (excluding South Africa) and South-Central Asia, with intermediate rates in Latin America (1).

Worldwide, the mortality rate adjusted for age (TAE) of colorectal cancer is 8.2 cases per 100,000, being the fifth leading cause of cancer death in both sexes, following lung, breast, stomach, and liver cancer. In men, it is 9.6 cases per 100,000 and for women, it is 7.0 cases per 100,000 (being the fourth most common type in both men and women). Nearly 608,000 deaths per year from colorectal cancer are presented, accounting for 8% of all cancer deaths. Unlike the cases of incidence, the highest mortality rates in both sexes are presented in Central and Eastern Europe (20.1 per 100,000 for men, 12.2 per 100,000 for women) and lower mortality rates are presented in Central Africa (3.5 per 100,000 for men and 2.7 per 100, 000 for women) (1).

The diagnosis is made predominantly with the location of polyps, 92% of them in situ and 40 % of cases are diagnosed at 60 years of age, 30 % at 50, and 30 % at 70. The rest 95 % of diagnoses shows adenocarcinoma type as the predominant pathology, being 80 % of sporadic nature, over the diagnosis of hereditary familial problem like. Less than 3% of patients are under 40 years (2).

Colon and rectal cancer have been associated with various risks, such as chronic ulcerative colitis; sclerosing cholangitis; certain inherited problems; a number of aspects related to eating habits, such as low-residue diet rich in saturated fats, diabetes, obesity, lack of physical activity, low intake of fruits and vegetables, smoking, and alcohol intake; ethnicity; and other genetic factors. However, only age has been measured in quantitative terms to establish the burden attributable to mortality. It is also necessary to specify, through additional studies, the burden of risk factors such as familial adenomatous polyposis, hereditary polypoid colorectal cancer, inflammatory bowel disease, sclerosing cholangitis, and others (2, 3).

Due to many factors, probably related to health technologies and early detection of the problem, among others, in the last 20 years, overall survival increased from 42 to 62 %. According to data in Globocan 2008, the five-year survival can be 72 % in men and 61 % in women (1, 2).

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1.2. Colonoscopy and screening

For about two decades, multiple reports of epidemiological studies have concluded that the introduction of endoscopic procedures is effective for strippage of premalignant lesions. The number of countries that have included colonoscopy and sigmoidoscopy as screening strategies for CRC has increased; however, the cost of implementation and potential adverse events limited its use for those in the middle- and low-income population (1-3).

It is clear that in populations at high risk of colorectal cancer (hereditary familial polyposis, ulcerative colitis or Crohn's disease), the screening test of choice is colonoscopy (4-5). Likewise in early detection in the general population, testing fecal occult blood is implemented and after a positive result, confirmatory colonoscopy and treatment is performed, which seeks to remove the precancerous lesion or cancer in situ. Colonoscopy does not fully meet the criteria on being a screening test for CRC because it is expensive; however it has some advantages because it can include treatment of polyp lesions and early cancer; unfortunately, only few studies of controlled trials have been conducted to analyze the performance of colonoscopy as a screening test for CRC. With regard to sigmoidoscopy, the advantages presented are the evaluation of the proximal colon, and only sigmoidoscopy can assess the distal colon, where most cancers occur [6]. Compared to testing fecal occult blood, colonoscopy has a major role in terms of reducing the incidence and mortality of CRC (7); Winawer and colleagues demonstrated a decrease in CRC incidence – 70 to 90 % – in a cohort of 1400 patients after polypectomy compared with controls based on symptoms and physical examination (8,9). In a study in Olmsted County, a decline in annual mortality of 25.2/100,000 to 21.4/100,000 followed the increase at subsequent rate of polypectomies (10).

The objective of this chapter is to review the literature and make some conclusion about total colonoscopy for screening CRC and the complication rate of screening colonoscopy in this setting, particularly bleeding, perforation, and death.

2. Methods

The purpose of this review is to evaluate the effectiveness and safety of colonoscopy as a screening test for adenoma, advanced adenoma, and colorectal cancer. For safety outcome, we evaluated bleeding, perforation, and death.

An asymptomatic person is defined as a person over 40 years and less than 75 years old without abdominal pain, rectal bleeding, weight loss, or changes in bowel habits.

Early and late adenomas were defined as adenomas smaller than 10 mm and greater than 10 mm, respectively, both of villous adenoma histology or high-grade dysplasia.

2.1. Data source and search strategy

We made a literature search in MEDLINE, EMBASE, the Cochrane Library, CINAHL, and LILACS from 1966 to February 2015. On the other hand, we made a search of guidelines in the

websites of the developer groups NICE, New Zealand Group, SIGN, North America Centers, IETS in Colombia, and CENETEC in Mexico, using the following keywords: ''screening colonoscopy,'' "colonoscopy," "colorectal cancer," "polyps," and ''screening colorectal cancer.'' The types of secondary studies were systematic reviews of the literature and clinical practice guidelines. The primary study types were controlled clinical trial, observational cohort, and case-control studies. Studies published in Spanish and English were the only ones selected. Likewise, additional searches were made from bibliographies of studies identified in the initial search.

2.2. Study selection

The clinical practice guidelines that were rated with 2 older AGREE (11) 60% quality in the domain of methodology were included. Systematic reviews of the literature described colonoscopy as a screening strategy. For primary studies such as controlled trials and observational analytical studies of moderate to high quality, we included the checklists of SIGN (12).

Exclusion criteria was studies evaluating colonoscopy in high-risk population of CRC, other studies evaluating screening tests without comparison with colonoscopy, likewise studies that do not contemplate the outcomes of interest for this chapter and not to report measures were considered effect with confidence intervals

3. Results

3.1. Evidence that exists for screening colorectal cancer

Screening is the examination of asymptomatic individuals or healthy individuals in order to classify them as likely or unlikely to have a disease (6).

The standard screening test is colonoscopy, but there are alternatives such as flexible sigmoidoscopy, computed tomography colonography (CTC or virtual colonoscopy) (7), fecal occult blood test (FOBT) or stool analysis, and also, evidenced by the literature, combined sigmoidoscopy and FOBT; the alternatives also include barium enema and endoscopy capsule; however, there are insufficient epidemiological studies that support these types of screening (8-15).

The optimal strategy of screening for colorectal cancer is selected considering the following criteria: age of onset and age range in individuals at average risk for this condition.

3.2. Volume of evidence

For this issue, three clinical practice guidelines were included that scored highly in methodology dimension with the AGREE2 checklist: quality assurance in colorectal cancer screening and diagnosis of the IARC (5) Screening for Colorectal Cancer, US Preventive Services Task Force (USPSTF) recommendation statement (17), and a clinical practice guideline for the early

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detection, diagnosis, treatment, following, and rehabilitation of patients with colorectal cancer of the Colombian Ministry of Health (18).

The review process identified 22 systematic reviews of which six were contained in guidelines previously described (19-24). Of the 16 remaining systematic reviews, two publications were discarded because they did not have clarity in the average-risk population (25; 26) and five for lack of data for the average-risk population (27-31).

The remaining nine studies were scored with the GRADE system. According to screening strategies, four publications analyzed fecal occult blood test (32-35) and two conducted a systematic review of colonoscopy (36), two studies evaluated colonoscopy and compared it with CTC (virtual colonoscopy) (37; 38) and another study evaluated only the CTC (39), and the last review examined capsule endoscopy (40). The American GPC (17) includes a strategy of screening using FOBT, sigmoidoscopy, or colonoscopy beginning at age 50 and ending at age 75.

3.3. Colonoscopy

Colonoscopy is undoubtedly useful in the case of positive fecal occult blood test. The European guide (16) describes that there is limited evidence on the effectiveness of colonoscopy screening to reduce colorectal cancer incidence and mortality. Recent studies suggest that colonoscopy may not be as effective in the right colon and in other segments of the colon and rectum. It also indicates that there is limited evidence suggesting that the interval for colonoscopy should be less than 10 years and may even extend to 20 years. The American guide includes colonoscopy as one method of screening for patients with a 10-year interval (17).

Three of the nine appointed guides as a strategy to colonoscopy screening at intervals of 10 years (18, 22, 24). These recommendations on the ability of colonoscopy as a screening strategy in asymptomatic individuals are not supported by controlled clinical trials; only case-control studies suggest that colonoscopy screening is associated with a low incidence of colorectal cancer (OR 0.46 95 % CI: 0.36.9 to 0.57) and that it decreases colorectal cancer mortality (OR 0.44: 95 % CI: 0.31 to 0.62) (13). The Australian guide suggests that for diagnostic confirmation, in the presence of a positive fecal occult blood test, colonoscopy is indicated, in order to perform biopsies of lesions and therapeutic removal of adenomas (20). The meta-analysis of Niv et al. (38) included ten prospective cohort studies with a total of 68,324 participants in which the procedure was completed by 97%. Colorectal cancer was found in 0.78 % of cases (95 % CI: 0.13 to 2.97): 77 % of CRC patients were in stages I and II. Advanced adenomas occurred in 5 % of cases (95 % CI 4–6 %).

The study of Niv et al. (38), found during the update, concludes that colonoscopy is a feasible method of screening for average-risk individuals; however, the GRADE rating was low for all three outcomes reported: colorectal cancer screening, drilling complications, and bleeding complications because the authors did not present the search strategy. The primary results are contradictory, and no evidence of homogeneity is presented. The study of Brenner Hermann et al. (6) includes four randomized clinical trials, eight case-control studies, and four cohort studies; the result for randomized clinical trial studies reports reduction in overall colorectal

cancer mortality in 22–31 %; in meta-analysis, the pooled risk reduction for incidence was estimated to be 18 % (CI 95 % 11–25%) and for mortality from colorectal cancer 28 % (CI 95 % 20–35 %). The result of observational studies for distal colorectal cancer was strong in reduced incidence and mortality, reduction of 64 % (CI 95 % 50–74 %) in incidence colorectal rates and 66 % (38–81 %) in reduced mortality rates for cancer (6). In this study, it was shown that colonoscopy is much more effective in reducing the incidence and mortality of distal colorectal cancer.

Complications were analyzed in five studies, with the following results: piercing, 0.01 % (95 % CI 0.006 to 0.02) and bleeding, 0.05 % (95 % CI: 0.02 to 0.09). No studies evaluating the effectiveness of virtual colonoscopy in reducing colorectal cancer mortality (13, 24, 40) were found.

3.4. Sigmoidoscopy and colonoscopy

The Colombian guide (18) indicates that screening with flexible sigmoidoscopy and colonoscopy can reduce mortality, and both strategies – sigmoidoscopy and colonoscopy – would fare as diagnostic tools. The European GPC appoints only sigmoidoscopy as the strategy to reduce the incidence and mortality when this strategy is part of an organized screening program.

3.5. Computed tomography colonography (virtual colonoscopy) versus colonoscopy

Pickhardt and colleagues (37) evaluated the sensitivity of CTC and colonoscopy for the detection of colorectal cancer. The research group indicates that although most studies argue that the test performance can be improved in line with the prevalence of the disease, the sensitivity of CTC remained independent of the prevalence. The evaluation of the quality design of this study was low in all outcomes, through the use of a single database and in relation to the population, including only two studies of the average-risk population and age higher than 50 years; in addition, the evidence is indirect. The evidence presented by the Blue Cross and Blue Shield Association (39) was rated low because it only included two studies of individuals at average risk and a description of their results does not show confidence intervals. The study of El-Maraghi (40) lacks clear criteria for inclusion and description of homogeneity tests, key in systematic reviews.

3.6. Capsule endoscopy versus colonoscopy

The objective of the study from the Medical Advisory Secretariat (41) was to determine the effectiveness and safety of capsule endoscopy in identifying colorectal cancer and adenomatous polyps in the average-risk population greater than 50 years old and as a screening strategy. They conclude that although capsule endoscopy is a noninvasive method and has lower sensitivity and specificity and accuracy than colonoscopy, its ability in detecting colorectal cancer has not been studied. The qualifying result of the outcomes of sensitivity, specificity, detection of polyps greater than or equal to 6 mm, and detection of any polyp independent of size was low due to the lack of reporting of homogeneity tests.

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3.7. Screening intervals

The European guide (16) indicates that in the case of choosing colonoscopy because of the prevalence, there is a case for screening individuals under age 50 or adults over 75 years or more, due to comorbidities that may outweigh the benefits of the examination. The American guide (42) supported this age of completion of screening; it believes that screening can be studied in the age range of 76–84 years and recommends its accomplishment in individuals 85 years or older.

4. Discussion

For colonoscopy screening test, the meta-analysis of Niv et al. (38), performed with cohort studies, suggests that colonoscopy is a possible and desirable CRC screening method in asymptomatic individuals; however, it is not clearly described how the critical evaluation of the articles was performed nor how the reference to the possible publication bias is made. Colonoscopy no randomized controlled trials that indicate the incidence and mortality from colorectal cancer. Evidence from observational studies suggests that this test could reduce the incidence and mortality from colorectal cancer, according to the National Polyp Study (43, 44) and the Italian multicenter study (45), and although it is a highly sensitive technique (26), the evidence is insufficient to exclude or include colonoscopy as the first-line screening strategy (17,25,41). As an additional point, colonoscopy requires specific training by the clinician, is more expensive than other screening tests, presents greater risk of complications during the test, and increases the likelihood of injury in cases in which polypectomy is performed.

Virtual colonoscopy is a highly specific test, particularly for polyps <9mm; however, the sensitivity varies widely, even for large polyps. The low efficiency of studies to explain the variability of the sensitivity requires rethinking and further study of this test, before recommending it for everyday use in the assessment of polyps (46).

Sigmoidoscopy, colonoscopy, barium enema, and even virtual colonoscopy are up-to-date diagnostic tools for which a greater number of studies evaluating the effectiveness of these methods as the primary screening tests in asymptomatic persons are required (13, 24, 42).

There is a possible overrepresentation of the state of health of the people attending for colonoscopy in analytical observational studies, which may incur information bias. Furthermore, it is possible confounding by these context variables that influence the development of a colonoscopy as well as the incidence of CRC, such as family history, diet, and physical activity.

5. Conclusion

We conclude that colonoscopy may be offered as a CRC screening tool for the high-risk population as well as the asymptomatic population since the diagnostic yield for polyps and

cancer is high. These results have to be evaluated with further research and weighed against the cost, accessibility, quality of life of patients, and possible serious complications.

Author details

Carlos Eduardo Pinzon-Florez[1*], Oscar Andres Gamboa-Garay[1,2] and Diana Marcela Diaz-Quijano[1]

*Address all correspondence to: carlos.pinzon1@unisabana.edu.co

1 Health Research Group. Universidad de La Sabana, Colombia

2 Analyses Research Group. National Cancer Institute. Bogota, Colombia

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