Colorectal cancer as a health care problem: evaluation of the current diagnostic options

Beata Kasztelan-Szczerbińska, Halina Cichoż-Lach, Maria Słomka

Department and Clinic of Gastroenterology with Endoscopic Unit, Medical University, Lublin, Poland

Abstract: Colorectal cancer (CRC) is one of the most frequent malignancies in Western countries. The lifetime risk of developing CRC is estimated at 5–6%. Available data indicate that the epidemiologic situation in Poland leaves a lot to be desired. Approximately 8000 patients die of CRC each year in Poland and outcomes of the disease treatment expressed as the 5-year survival rate are among the worst in Europe, not exceeding 25%. Colorectal cancer is a disease which requires activities promoting early diagnostics and wide-scale prevention due to the fact that it meets the pathologic criteria suitable for the population screening tests. Different screening tests are used in routine medical practice and their use depends on their availability to a patient, according to the principle of superiority of any screening over no screening. This article reviews different screening methods according to their practical value assessed on the basis of the best available evidence.

Key words: colorectal cancer, diagnostic screening tests, early detection and prevention

INTRODUCTION

Colorectal cancer (CRC) is one of the most common neoplasms in developed countries. The lifetime risk of developing CRC is estimated at approximately 5–6% [1]. The world CRC morbidity in 2002 was 1,023,151 [2], which confirms the reports regarding it as a serious social issue. Recently, initial reports on slight reduction in new cases observed in the USA were published. It is probably associated with promotion of preventive screening tests, polypectomies performed and the changing diet and lifestyle of the American society [2]. However, CRC still remains one of the main health problems in the countries of Western and Central Europe and North America, therefore, it still requires continuation of wide-scale activities aiming at early diagnosis and prevention of the disease.

Epidemiology

The epidemiologic situation in Poland leaves a lot to be desired. The CRC annual incidence rate in Poland amounts to 30–35 cases per 100,000 and unfortunately increases by approximately 2.5% a year [3]. It is the second neoplastic cause of death among males and females. Annually, about 8000 patients die of CRC in Poland and the treatment outcomes measured with the 5-year survival rate are among the worst in Europe, not exceeding 25% [3].

Colorectal cancer and recommendations for population screening tests

Colorectal cancer is a disease which requires activities promoting early diagnosis and wide-scale prevention due to the fact that it meets the pathologic criteria suitable for population screening tests. Colorectal cancer is a common disease with high mortality and morbidity rates. Relatively long oncogenesis (usually 5–10 years) and occurrence of benign precursor lesions indicating cancer risk representa therapeutic window for the use of the appropriate treatment. The epidemiological data shows that treatment started at the early stages of the disease – Dukes' stage A, B1, B2, provides the 5-year survival of over 90%, 85% and 70%, respectively, whereas with progression of the disease and metastases, the odds for recovery fall to 5% [1]. Systematic removal of neoplastic precursor lesions from the large intestine is a form of primary prevention and will probably result in decreased CRC morbidity and mortality in the future. The first reports supporting those hopes have just been coming from the USA [1].

Recommendations for screening tests aiming at early detection of CRC consider a potential risk of developing CRC, which is estimated on the basis of the following parameters: age, malignancy in the family medical history, CRC or colorectal adenoma diagnosis and non-specific inflammatory bowel diseases in the medical history [4]. Subjects without predispositions other than age represent a population with low risk of CRC development. This group shall be covered with

Correspondence to:
Assoc. Professor Halina Cichoż-Lach, MD, PhD, Katedra i Klinika Gastroenterologii z Pracownią Endoskopową, Uniwersytet Medyczny, ul. Jaczewskiego 8, 20-090 Lublin, Poland, phone/fax: +48-081-724-45-35, e-mail: lach.halina@wp.pl
Received: January 10, 2008. Accepted in final form: February 10, 2008.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2008; 118 (4): 224-227
Translated by Izabela Jastrzębska, MD, PhD

screening tests from the age of 50. Current standards of CRC screening tests, based on recommendations of the American Cancer Society, were published in 2006 by Martinez et al. [5] Those recommendations include almost all diagnostic methods known to date, and their use depends on their availability in particular regions and countries, according to the principle saying that any screening is better than no screening. However, according to the calculations, the best and the most cost-effective screening method is colonoscopy [1]. It focuses the opportunities of early diagnosis and therapy (polypectomy = primary prevention), and when performed, dependent on the recommendations, each 5–10 years, is in fact a less expensive alternative to other tests which should be performed more frequently. It is often essential to verify their results by colonoscopy which increases costs.

It should be emphasized here that a Program of Colonoscopic Screening Tests for early detection of CRC has been carried out in Poland since October 2000. The Program is financed by the Ministry of Health and Welfare from their own resources. Endoscopic centers from all Poland participate in the Program and the number of centers joining in increases over the years. Colonoscopic diagnostics is currently available in every large city. According to the current recommendations, the surveillance covered the asymptomatic population at anaverage risk of CRC, at the age of 50–65 who are to undergo tests every 10 years, and pindividuals of high risk groups:

1) CRC in a family medical history: tests each 5 years when over 40 years
2) persons with hereditary nonpolyposis colorectal cancer (HNPCC), a.k.a. Lynch syndrome or familial adenomatous polyposis documented in the family medical history: tested since the age of 25 each 2–3 years. For this group of people, it is essential to confirm in the Genetic Outpatient Clinic that they belong to HNPCC families, on the basis of the so-called Amsterdam criteria and genetic tests, if necessary.

The National Screening Test Program is designed to improve the epidemiological situation in Poland by increasing the percentage of neoplastic colorectal lesions detected ar their early stages, the 5-year survival rate after surgical treatment, and in the future it will probably result in the reduction in the CRC morbidity and treatment costs. It seems the tests performed in Poland are optimal and will bring marked effects in the future. It is of importance to ensure active participation of all physicians in promoting the Program which is feasible in most major centers in Poland.

A less elaborate endoscopic method due to its limited range is sigmoidoscopy. It enables the detection of 70–85% of cases of CRC in its most common location. It has been shown that patients with advanced distal adenomas are also exposed to 6–10% risk of advanced proximal adenomas [6-8]. Therefore, each diagnosed distal adenoma requires endoscopic examination of the entire large intestine. Supplementation of sigmoidoscopy with stool examination also increases the sensitivity of both methods [9].

Stool examination is commonly used in everyday practice given its non-invasiveness and relative simplicity. Fecal occult blood tests (FOBT) require repetition every year. Results of randomized studies showed that examination by this method performed each two years is less effective [1]. A meta-analysis of randomized controlled trials from the Cochrane database showed reduced mortality caused by CRC among patients undergoing FOBT by 16%. When adjusted for screening attendance in individual studies, reduction in mortality reached 23% [10]. In practice, 2 types of FOBT are used: chemical test (guaiacol, Hemoccult II, Hemoccult II Sensa) and immunochemical (HemeSelect, FlexSure OBT) [11]. The former detects the heme peroxidase activity and may generate false positive results with improper diet (meat, some vegetables and fruit, e.g. turnip, radish) and with use of particular drugs (non-steroidal anti-inflammatory drugs), and false positive results with large doses of vitamin C. Therefore, a 3–5 day abstinence from particular food and drugs prior to the chemical test is recommended. However, it does not distinguish bleeding from the upper and lower part of the gastrointestinal tract either. Sensitivity of the immunochemical test is higher because it detects the presence of human globin in the stool and does not require diet or pharmacological restrictions. Recently, a new immunochemical test (InSure) appeared on the American market, technically less complicated, requiring only two stool samples (3 samples in the previous ones). Another type of the diagnostic tests is the assessment of rectal mucus taken per rectum by a physician with a finger (ColorectAlert). Large intestine epithelium cells continuously secrete various mucins, e.g. high-molecular, glycated glycoproteins. During carcinogenesis, the synthesis is disturbed, both in respect of structure and expression, and inappropriate mucins could potentially be a CRC marker. The galactose oxidase Schiff's test based on the concept and detecting disaccharide-acetyl-d-galactosamine is simple and inexpensive (15 USD). It does not require dietetic restrictions and there is no need of taking stool samples. Performed during surgery, it could increase the number of screening tests in patients in whom screening should be performed. However, further clinical studies are essential in subjects with low CRC risk to assess the usefulness of the screening test. A highly appraised genetic test is PreGenPlus, available on the American market since 2003 and detecting K-ras, p53, APC, Bat-26 mutations in stool. It requires only one stool sample and the assessment is done in the laboratory. However, its price (795 USD) hampers common use, even in the USA.

Screening recommendations also consider a double contrast barium enema, however, this examination has several limitations. in comparison with colonoscopy, its sensitivity significantly depends on the size of colorectal lesions, and it is higher with larger diameter of a polyp, especially those of the sizes >10 mm [12].

Virtual colonoscopy as a non-invasive examination raises hopes in patients who fear endoscopic evaluation. Computer scans show the surface of mucous membrane and the large

intestine lumen. Studies performed in clinical centers in patients with high CRC risk suggest 90% of the test sensitivity for lesions exceeding 1 cm. The results should, however, be confirmed in the common screening test programs [13].

Given that a lot of patients are unwilling to accept colonoscopy, which currently is the best examination method of the large intestine, it is the priority to find a non-invasive, sensitive and specific screening method. The criteria seem to be fulfilled by serological tests, just as cancer markers determined in the diagnostics of other gastrointestinal tract diseases [14,15]. However, at the current stage of research, it still remains a remote future. The search has lasted years and great hopes have been placed in determination of the carcinoembryonic antigen (CEA) discovered in 1969. Consecutive analyses showed that it was not suitable for screening since it was found that each case of CRC detected by CEA assessment was associated with 250 false negative results and 60% of CRC cases were overlooked [16]. It was found useful only for monitoring of recurrence in patients after CRC surgery.

Great expectations are associated with modern diagnostic methods which are gaining a strong position in oncology. Using proteomics methods enables wide analysis of plasma protein expression and identification of protein configuration typical of a particular neoplastic process. They could potentially serve the function of a cancer biomarker [11]. It was also reported that the nuclear matrix protein composition showed tissue specificity and could function as a kind of "fingerprints" of individual types of cells and tissues. Brunagel et al. [17,18] demonstrated a particular disorder in the nuclear matrix protein composition in CRC and in CRC liver metastases. Despite significant achievements, finding an objective, non-invasive test, with reproducible results, inexpensive and useful in everyday practice, is not an easy task.

In the 21st century, prevention is a milestone in the common understanding of health issues. Colorectal cancer is a social issue in numerous developed countries, particularly in Poland, where the health situation in this respect leaves a lot to be desired. Therefore, measures should be taken to reduce the CRC mortality in the future. Early detection of neoplastic and precursor lesions by screening of an asymptomatic population could improve health situation. Currently, there is no ideal screening method and endoscopic examination, i.e. colonoscopy, remains the most reliable and cost-effective method [19].

REFERENCES

1. Levin B. Colorectal cancer. ACP Medicine, 2005. http: //www.medscape.com/viewarticle/502838.
2. Jemal A, Tiwari RC, Murray T. Cancer statistics 2004. Ca Cancer J Clin. 2004; 54: 8-29.
3. Bielicki D. Epidemiologia i prewencja raka jelita grubego. Gastroenterol w Codziennej Prakt Lek. 2003; 5: 4-8.
4. Winawer SJ, Fletcher R, Rex D. Colorectal cancer screening and surveillance: clinical guidelines and rationale – update based on new evidence. Gastroenterology. 2003; 124: 544-560.
5. Martinez SR, Shawn EY, Hoedema RE, et al. Colorectal cancer screening and surveillance: current standards and future trends. Ann Surg Oncol. 2006; 13: 786-775.
6. Nicholson FB, Korman MG, Stern A, Hansky J. Distribution of colorectal adenomas: implications for bowel cancer screening. MJA. 2000; 172: 428-430.
7. Gondal G, Grotmol T, Hofstad B, et al. Grading of distal colorectal adenomas as predictors for proximal colonic neoplasia and choice of endoscope in population screening: experience from the Norwegian Colorectal Cancer Prevention study (NORCCAP). Gut. 2003; 52: 398-403.
8. Watson AJM. Are proximal colorectal cancers always associated with distal adenomas? Gut. 2003; 52: 317-318.
9. Lieberman DA, Weiss DG. One-time screening for colorectal cancer with combined fecal occult blood testing and examination of the distal colon. Veterans Affairs Cooperative group 380. N Engl J Med. 2001; 345: 555-560.
10. Towler BP, Irwing L, Glasziou P, et al. Screening for colorectal cancer using the faecal occult blood test, hemoccult. Cochrane Database Syst Rev. 2002; 2: CD001216.
11. Ouyang DL, Chen J, Getzenberg RH, et al. Noninvasive testing for colorectal cancer: a review. Am J Gastroenterol. 2005; 100: 1393-1403.
12. A comparison of colonoscopy and double-contrast barium enema for surveillance after polypectomy. National Polyp Study Work Group. N Eng J Med. 2000; 342: 1766.
13. Gluecker T, Dorta G, Keller W, et al. Performance of multidetection computed tomography colonography compared with conventional colonoscopy. Gut. 2002; 51: 2007.
14. Jakimiuk B, Mroczko B, Sznitkowski M. Markery nowotworowe w diagnostyce raka żołądka. Pol Arch Med Wewn. 2005; 2: 799-807.
15. Groblewska M, Mroczko B, Szmitkowski M. Markery nowotworowe raka trzustki (antygeny towarzyszące nowotworom). Pol Arch Med Wewn. 2005; 6: 585-593.
16. Duffy MJ. Carcinoembryonic antigen as a marker for colorectal cancer: is it clinically useful? Clin Chem. 2001; 47: 624-630.
17. Brunagel G, Vietmeier BN, Bauer AJ, et al. Identification of nuclear matrix protein alterations associated with human colon cancer. Cancer Res. 2002; 62: 2437-2442.
18. Brunagel G, Schoen RE, Bauer AJ, et al. Nuclear matrix protein associated with colon cancer metastasis to the liver. Clin Cancer Res. 2002; 8: 3039-3045.
19. Macafee DAL, Scholefield JH. Population based endoscopic screening for colorectal cancer. Gut. 2003; 52: 323-326.