Colorectal cancer screening

Jean-François Colin, Robert Vanheuverzwyn

Department of Gastroenterology, Cliniques Universitaires UCL Saint-Luc, 10 avenue Hippocrate, 1200 Bruxelles.

Key words : colorectal cancer, screening, colonoscopy.

Introduction

Colorectal cancer (CCR) is the second cause of cancer death in developed western world. Most colorectal cancers are probably preventable through screening.

Screening is the search for cancer and precancerous lesions in asymptomatic patients. In general screening of a disease is useful if :

1. The disease is common with a high morbidity and/or mortality.
2. Early diagnosis improves prognosis
3. The benefit of screening is superior to its costs
4. Screening is acceptable, possible and efficient.

There is no doubt that colorectal cancer fullfil the two first conditions. The third one is a socio-economic choice. In this review, our aim is to analyse the fourth condition.

Colorectal cancer screening is defined as testing asymptomatic persons for the presence of colorectal cancer or adenomatous polyps. Almost all colorectal cancers arise from adenomatous polyps that develop over a period of years. During this period, polyps can be detected and removed. Endoscopic polypectomy seems to be the main reason for the decrease of CCR mortality incidence (1-3).

Who should be screened ?

People aged 50 years and older have an average-risk if they have no risk factors for colorectal cancer other than age. The lifetime risk of colorectal cancer approaches 6% in both men and women. Sporadic cancers constitutes about 75% of CCR. Their incidence start to increase at 50 years, and by the age of 50 to 80, the incidence is increased by ten folds (from 50/100000 to 500/100000 resident per year). Therefore, it is logic to suggest screening to subjects aged more than 50 years (4-5).

Family past history contributed to the high CCR incidence. The incidence is multiplied by a factor of two if one parent of first degree had a CCR or a polyp in the colon superior to 1cm. (15-20% of the population) ; the incidence is multiplied by four if both parents had been affected (1-3% of the population) and by about twenty in the hereditary nonpolyposis colorectal cancer (HNPCC) syndrome (1-5% of the population). In the HNPCC syndrome, it is advised to begin the screening at 25 years or five years before the age of appearance of a CCR in the family (5-8).

Among the personnal past history, a CCR multiplies the risk of a new cancer by two, a solitary adenoma > 1 cm or a villous adenoma multiplies the risk by three, and the multiple adenomas > 1 cm or the multiple villous adenomas multiplies the risk by six.

In inflammatory bowel diseases of the colon, it is admitted that the risk of CCR becomes significative in patients with pancolitis after twenty years of evolution and in patients with left colitis after thirty years of evolution (3-4). Because of the difficulties in early CCR diagnosis in these patients, systematic screening is still a controversial subject.

Table I. — **Colorectal cancer : choice of subjects to screen**

Population	%	Relative risk	Cumulative risk 0-74 yr
General	75%	1	3.5%
Family history			
1 parent + C.C.R.	15-20%	2	6.4%
2 parents + C.C.R.	1-3%	4	10.4%
Adenoma > 1 cm		2	
F.A.P.	< 1%		> 90% 75 yr
H.N.P.C.C.	1-5%		> 60% 75 yr
Personal history			
Colorectal cancer	< 1%	2	
Adenoma	< 1%		
> 1 cm or villous	< 1%	3	
> 1 cm multiple	< 1 %	6	
I.B.D.	< 1%		
Diffuse > 20 yr		10 ?	20-30% ?
Left > 30 yr		10 ?	12%

Screening strategies

All screening techniques reduce significantly the incidence of CCR in the examined population. In subjects where the risk of CCR is increased, it is logic to use the more performant techniques.

In average-risk patients (75% of the population, RR = 1) the faecal occult blood tests (FOBT) are

Correspondence and request for reprints : Vanheuverzwyn R., Service de Gastroentérologie, Cliniques Universitaires UCL Saint-Luc, 10 avenue Hippocrate, 1200 Bruxelles.
Session of june 17, 2000.

feasable and useful. Actually only the guaiac-based FOB tests, in particular Haemoccult, had been used in many series. The detection of faecal hematoporphyrin is a sensitive method but less specific (animals porphyrins). By specifically detecting human haemoglobin, immunological tests avoid the problem of dietary interference. These tests are more specific for the colon because the breakdown of haemoglobin occurs in the stomach and the small bowel (9).

In some studies, the FOBT is positive in 1-2% of the population aged more than 40 years. In around 10% of positive subjects , a polyp of more than 10mm is found, and in 6-8% of the positive subjects a CCR is detected. Several recent studies with Hemoccult-II (without rehydratation) provide convincing evidence validating this screening method. An overall 15-33% reduction of CCR mortality was observed in these studies with an annual FOBT, and 15-22% reduction if the FOBT was performed biannually. To obtain these results, fifty percent of the recruited population should be screened. The sensitivity of this method will be improved if testing is repeated, requiring strict compliance (10-13).

The flexible rectosigmoidoscopy every five years is the best cost-benefit method. The tolerance is variable (2-94%) depending on the information given to the patient. It reduces the CCR mortality by 60% (14). Nevertheless about half the cases of advanced proximal neoplasia will not be detected (15,16). Total colonoscopy has not been studied in randomised studies. Nevertheless the American College of gastroenterology recommends total colonoscopy every ten years despite its risks (17).

Barium enema is usually better accepted, no sedation is required, and compared to colonoscopy, complications (3/10000 versus 85/10000) and mortality (0.3/10000 versus 2/10000) are less encountered. The cost of barium enema is lower than the cost of total colonoscopy. Barium enema has not been evaluated as a screening test in randomized trials. Barium enema is inferior to colonoscopy for the detection of colorectal cancer, small polyps and for recurrent lesions after polypectomy (18-20).

Therefore, there is not a gold standard, and the choice of the examination (barium enema combined with flexible rectosigmoidoscopy, total colonoscopy) will depend on the disponibility and the competence of examiners.

The actual performances of virtual coloscopy are more or less similar to the traditional examination for the lesions of more than 10mmm but would be less examinator-dependant.It remains to show that the compliance is higher and the cost is lower (21-23).

In the future, the research of altered DNA in stool might be evaluable tool for colorectal cancer screening (24).

In patients with high risk of CCR because of their individual or familial past history (25% patients of the population ; RR : 2-6), total examination of the colon every five years is recommended (4,6,25,26).

Conclusions

1. Patients with symptoms suggesting the existence of a polyp or of a CCR must be investigated thouroughly. When history suggests the presence of a high risk of CCR, this must be considered as a symptom.
2. The screening of polyps and cancers could be proposed to the population aged more than fifty years. This decision is a choice of the society. Nowadays, haemoccult (once per year) and/or flexible rectosigmoidoscopy (once every five years) are the best quality-cost ratio.
3. The different procedures of screening must be assessed more precisely and controlled.
4. When a screening is suggested, the subject must be clearly informed about the risks and the benefits of the different procedures, and the necessity to continue the investigations if a test would be positive.
5. In patients with a high risk of colorectal cancer colonoscopy must be recommended every five years.
6. Many questions remain without answers. What is the mecanism of polyp-cancer sequence observed in abount 10% of polyps ? What are the psychologic effect of screening ? Could we develop better screening test ?

References

1. Surveillance, Epidemiology, and End Results (SEER Program 1973-1997). National Cancer Institute. DCPC, surveillance program.
2. NELSON R.L., PERSKY V., TURYK M. Determination of factors responsible for the declining incidence of colorectal cancer. *Dis Colon Rectum*, 1999, **42** : 741-752.
3. WINAWER S.J., FLETCHER R.H., MILLER L., GODLEE F., STOLAR M., MULROW C.D., WOOLF S.H., GLICK S.N., GANIATS T., BOND J., ROSEN L., ZAPKA J.G., OLSEN S., GIARDIELLO F., SISK J., VAN ANTWERP R., BROWN-DAVIS C., MARCINIAK D., MAYER R.J. Colorectal cancer screening : clinical guidelines and rationale. *Gastroenterology*, 1997, **112** : 594-642.
4. BURT R.W. Colon cancer Screening. *Gastroenterology*, 2000, **119** : 837-853.
5. BENHAMICHE A.M. Cancer du côlon : épidémiologie descriptive et groupes à risque élevé. *Gastroenterol. Clin. Biol.*, 1998, **22** : S3-S11.
6. Conclusions et recommandations du Jury de la Conférence de consensus "Prévention, dépistage et prise en charge des cancers du côlon". *Gastroenterol. Clin. Biol.*, 1998, **22** : S275-S288.
7. ST.JOHN J.B., MCDERMOTT F.T., HOPPER J.L., DEBNEY E.A., JOHNSON W.R., HUGHES E.S. Cancer risk in relatives of patients with common colorectal cancer. *Ann. Int. Med.*, 1993, **118** : 785-790.
8. JARVINEN H.J., AARNIO M., MUSTONEN H., AKTAN-COLLAN K., AALTONEN L.A., PELTOMÄKI P., DE LA CHAPELLE A., MECKLIN J. Controlled 15-year trial on screening for colorectal cancer in families with hereditary nonpolyposis colorectal cancer. *Gastroenterology*, 2000, **118** : 829-834.
9. ROCKEY D.C. Primare care : occult gastrointestinal bleeding. *N. Engl. J. Med.*, 1999, **341** : 38-46.
10. MANDEL J.S., CHURCH T.R., BOND J.H., EDERER F., GEISSER M.S., MONGIN S.J., SNOVER D.C., SCHUMAN L.M. The effect of fecal occult-blood screening on the incidence of colorectal canceer. *N. Engl. J. Med.*, 2000, **343** : 1603-1607.
11. FAIVRE J., TAZI M.A., MILAN C., LEJEUNE, DASSONVILLE F., DURAND G. L'étude bourguignonne d'évaluation du dépistage de masse du cancer colorectal par la recherche d'un saignement occulte dans les selles : résultats à 9 ans. *Gastroenterol. Clin. Biol.*, 1999, **23** : A88.
12. HARDCASTLE J.D., CHAMBERLAIN J.O., ROBINSON M., MOSS S., AMAR S., BALFOUR T., JAMES P.D., MANGHAM C.M. Randomised

controlled trial of faecal-occult blood screening for colorectal cancer. *Lancet*, 1996, **348** : 1472-1477.
13. KRONBORG O., FENGER C., OLSEN J., JORGENSEN O.D. Randomised study of screening for colorectal cancer with faecal-occult blood test. *Lancet*, 1996, **348** : 1467-1471.
14. SELBY J.V., FRIEDMAN G.D., QUESENBERRY C.P., WEISS N.S. A case-control study of screening sigmoidoscopy and mortality from colorectal cancer. *N. Engl. J. Med.*, 1992, **326** : 653-657.
15. IMPERIALE T.F., WAGNIER D.R., CHING Y.L., LARKIN G.N., ROGGE J.D., RANSOHOFF D.F. Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. *N. Engl. J. Med.*, 2000, **343** : 169-173.
16. LIEBERMAN D.A., WEISS D.G., BOND J.H., AHNEN D.J., GAREWAL H.G., CHEJFEC G. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. *N. Engl. J. Med.*, 2000, **343** : 162-168.
17. REX D.K., JOHNSON D.A., LIEBERMAN D.A., BURT R.W., SONNENBERG A. Colorectal cancer prevention, 2000 : screening recommendations of the American college of Gastroenterology. *Am. J. Gastroenterol.*, 2000, **95** : 868-877.
18. REX D.K., RHAMANI E.Y., HASEMAN J.H., LEMMEL G.T., KASTER S., BUCKLERY J.S. Relative sensitivity of colonoscopy and barium enema for detection of colorectal cancer in clinical practice. *Gastroenterology*, 1997, **112** : 17-23.
19. WAYE J.D. What is the gold standard for colon polyps. *Gastroenterology*, 1997, **112** : 292-294.
20. WINAWER S.J., STEWART E.T., ZAUBER A.G., BOND J.H., ANSEL H., WAYE J.D., HALL D., HAMLIN J.A., SCHAPIRO M., O'BRIEN M.J., STERNBERG S.S., GOTTLIEB L. A comparison of colonoscopy and double contrast barium enema for surveillance after polypectomy. *N. Engl. J. Med.*, 2000, **342** : 1766-1772.
21. FENLON H.M., NUNES D.P., SCHROY P.C., BARISH M.A., CLARKE P.D., FERRUCCI J.T. Comparison of virtual and conventional colonoscopy for the detection of colorectal polyps. *N. Engl. J. Med.*, 1999, **341** : 1496-1503.
22. SONNENBERG A., DELCO F., BAUERFEIND P. Is virtual colonoscopy a cost-effective option to screen for colorectal cancer. *Am. J. Gastroenterol.*, 1999, **94** : 2268-2274.
23. PAPPALARDO G., POLETTINI E., FRATTAROLI F.M., CASCIANI E., D'ORTA C., D'AMATO M., GUALDI G.F. Magnetic resonance colonography versus conventional colonoscopy for the detection of colonic endoluminal lesions. *Gastroenterology*, 2000, **119** : 300-304.
24. AHLQUIST D.A., SKOLETSKY J.E., BOYNTON K.A., HARRINGTON J.J., MAHONEY D.W., PIERCEALL W.E., THIBODEAU S.N., SHUBER A.P. Colorectal screening by detection of altered human DNA in stool : feasibility of a amultitarget assay panel. *Gastroenterology*, 2000, **119** : 1219-1227.
25. PARIENTE A., MILAN C., LAFON J., FAIVRE J. Colonoscopic screening in first-degree relatives of patients with "Sporadic" colorectal cancer : a case-control study. *Gastroenterology*, 1998, **115** : 7-12.
26. RHODES J.M. Colorectal screening in the UK : joint position statement by the British Society of Gastroenterology, the Royal College of Physicians, and the Association of Coloproctology of Great Britain and Ireland. *Gut*, 2000, **46** : 746-748.