

Colorectal cancer : controverses

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«Ne soyez ni obstinés dans le maintien de ce qui s'écroule, ni trop pressés dans l'établissement de ce qui semble s'annoncer».

Henri (dit Benjamin) Constant de Rebecque (1767-1830)

Colorectal cancer is seen as a major public health problem in the West. Incidence is more than 45/100,000 inhabitants/year in the United States (1) and 40/100,000 inhabitants/year in Belgium (2). Since 1986 a decline in the incidence of colorectal cancer

(-1%/year) has been noted in the United States. The only factor recognised by R.L. Nelson *et al.* as contributing to this decline has been the increasing use of endoscopic polypectomy (3). While incidence measured over a whole lifetime may appear to be relatively low (3%), it rises rapidly after the age of 50, increasing tenfold between the ages of 50 and 80 from 50/100,000 to 500/100,000 inhabitants/year (1). In terms of mortality, colorectal cancer is in second place after lung cancer for men and after breast cancer for women. It represents 13-15% of all cancers. Mortality remains high : about 60% of patients die of their illness within 5 years.

Progress has been made in understanding the origin of colorectal cancer. For many years now, epidemiology has recognised two principal factors : 1. Genetics, 2. Diet and lifestyle.

The discovery of the APC gene in familial polyposis in 1991 and that of genetic anomalies involved in the syndrome known as "Hereditary Non Polyposis Colon Cancer" (HNPCC) by H.T. Lynch in 1966 (4) have clinical applications in both illnesses. However, they are the source of only a small number of cancers (1% and 5%) (6,7). In the future, the study of the molecular biology of colon polyps (prevalence : 25 to 50% of patients between the ages of 50 and 80) will perhaps make it possible to distinguish polyps capable of developing cancers from others. In colorectal cancer, molecular biology has described genetic anomalies linked to differences in sensitivity to adjuvant treatment (5,6).

External factors (such as diet, lifestyle and medication) affecting the genesis or the development of colorectal cancer are emerging (7,8). Unfortunately, changing the habits of a population is a difficult task, as shown by the failure of campaigns aimed at reducing the levels of tobacco use or obesity (3).

Early detection of colorectal cancers improves the prognosis. The excision of precursor neoplastic polyps reduces the incidence of mortality due to colorectal cancer (3). Three exhaustive recent reviews (9,10,11) analyse the technical and economic problems involved in these practices. Unfortunately, there is no "gold standard" for detection methods, as the results achieved by radiography with barium enema and by colonoscopy are broadly similar for lesions of more than 5mm, and depend to a great extent on the skill of examiners (12,13,14). The results achieved by virtual colonoscopy are comparable to those of traditional examinations, but may be less dependent on examiners. It remains to be demonstrated that compliance to virtual colonoscopy is superior and less expensive (15,16,17).

The choice of subjects to screening is a political, social, and economic decision. At present it is generally agreed that people with increased risk of developing colorectal cancer should be examined either because of their family history or because of their own medical history. In practice it is particularly important to screen patients aged over 50 presenting symptoms.

Treatment of colorectal cancer is surgery. In rectum cancer, the total excision of the mesorectum (TME) reduces the local recurrence rate and improves survival rates without increasing post-operative morbidity (18,19). However, results differ from one surgical team to another (5 to 15% of local recurrence ?) (20, 21).

In recent years the contribution of adjuvant treatments (chemotherapy in case of colon cancer, radiochemotherapy in rectum cancer) has been the subject of controlled studies dealing with Dukes C cancers (22). The presentation of the results of these studies sometimes leads to confusion. An interesting idea is calculating the number of patients needed to treat to improve one patient (NNT = Number Needed to Treat) (23).

In 1990 Moertal *et al.* (24) have shown that 5-Fluorouracil + Levamisole association significantly improved survival ($p = 0.006$) after 3.5 years in 32 patients out of 304 with colon cancer, compared to a similar untreated group. In this study the NNT was 10.5 and the treatment was well tolerated. In cancer of the rectum, a Swedish study (25), using pre-operative radiotherapy of 25 Gy in 5 days, shows a improved survival in 1 patient out of 10 (NNT = 10). As morbidity due to this treatment is minimal, it seems to have advantages over heavier doses.

Practitioners should encourage patients to take part in controlled trials, without exposing them to the dangers of some molecules (NNH = Number Needed to Harm). The physiopathology of colorectal tumors should be the subject of further research, whose results may make it possible to better target patients to be treated, in other words, to reduce the NNT and the NNH (23).

Monitoring, more or less intensive, after surgical curative treatment is not very useful (26,27). A complete pre- or post-operative examination of the colon should ensure that there are no synchronous lesions. Subsequently, operated patients constitute a group with an increased risk of subsequent lesions justifying re-examination of the colon every 3 to 5 years. More frequent checking is aimed primarily at analysing the results of a surgical team and at lessening the anxiety of some patients.

Conclusions

Progress has been made in recent years in understanding the physiopathology of colorectal cancer. These studies could improve the identification of at risk patients and the choice of candidates for adjuvant surgical treatment.

At present it is probable that the declining mortality of colorectal cancer is due to early diagnosis and to polypectomy.

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