EUROPEAN JOURNAL OF CANCER 45 (2009) 1460–1465

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Prevalence of patients with colorectal cancer requiring follow-up or active treatment

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ARTICLE INFO

Article history:
Received 2 December 2008
Received in revised form 7 January 2009
Accepted 13 January 2009
Available online 11 February 2009

Keywords:
Prevalence
Colorectal cancer
Recurrence
Cancer registry

ABSTRACT

Introduction: The objective of this study was to estimate prevalence of colorectal cancers requiring care or follow-up.

Materials and methods: Prevalence was observed in 2005 on the population-based digestive cancer registry of Burgundy (France). Total and 5-year partial prevalences were calculated. The prevalence of patients requiring follow-up was estimated using non-mixture cure models. The prevalence of patients with recurrence was estimated using annual recurrence rates.

Results: Total prevalence was 262,244 cases in France. The mean variation in 5-year partial prevalence between successive 5-year periods was +8.0%. Time to cure was estimated to be 9.3 years, suggesting that follow-up is needed over a 10-year period, corresponding to 71.7% of prevalent cases. In 2005, 5.4% of prevalent cases had recurrent cancer requiring treatment.

Conclusion: This study underlines the burden of colorectal cancer on the health system. Prevalence of patients requiring follow-up or treatment provides interesting information in addition to classic indicators.

1. Introduction

Although the incidence of colorectal cancer and related mortality is well documented world-wide, little is known about its prevalence. Total prevalence is a crucial public health indicator, and as such it is usually reported in most publications.[1] To estimate the magnitude of the problem for health care planning, 5-year partial prevalence is sometimes also calculated.[2,3] It provides an approximation of the number of cases requiring both intensive follow-up and active treatment for recurrence. This empirical method could, however, possibly over- or underestimate the real proportion of patients requiring care. For the purpose of planning health care requirements, other breakdowns of prevalence are of interest, in particular, the prevalence of patients requiring follow-up and that of patients requiring treatment for local recurrence or distant metastasis. Population-based cancer registries with long-standing registration, active follow-up of the occurrence and management of colorectal recurrences and of life status are the most appropriate tools for calculating non-biased and detailed prevalence statistics. The aim of this study was to provide, besides total and partial prevalence, estimations based on new approaches to prevalence: the prevalence of the patients requiring follow-up or active treatment.

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0959-8049/$ - see front matter
doi:10.1016/j.ejca.2009.01.012

2. Materials and methods

2.1. Patients

The Digestive Cancer Registry of Burgundy (France) records all digestive tract cancers diagnosed in the Côte-d'Or and the Saône-et-Loire (1,052,000 inhabitants according to the 1999 census). Cancer registration began in 1976 in the Côte-d'Or area and in 1982 in the Saône-et-Loire area. Information is routinely collected from pathology laboratories, university hospitals, local hospitals, private surgeons, oncologists, gastroenterologists and general practitioners (the French National Health Service) to identify patients treated outside the area and monthly reviews of death certificates were done. No case is recorded through death certificates alone, but these are used to identify missing cases. Because information is obtained from numerous sources, we assumed that nearly all newly diagnosed cases have been recorded. The quality and comprehensiveness of registration are certified every 4 years by an audit of the National Institute for Health and Medical Research (INSERM) and of the National Public Health Institute (InVS). A total of 17,182 incident cases, over a 30-year period, were registered. Among them, 57.3% were under 75 years, and males represented 55.3% of all cases. Cancer location was defined according to the International Classification of Diseases for Oncology.[4] Three subsites were defined: proximal colon cancer (C18.0 to C.18.4), distal colon cancer, including the recto sigmoid junction (C18.5 to C18.7 and C19), and rectal cancer (C20). Follow-up consisted of active surveys on eventual metachronous metastases, local recurrences and vital status. The last follow-up was conducted in 2008 with patients diagnosed in 2005. Information about recurrence was obtained from all clinicians (general practitioners and specialists) involved in the management and the follow-up of these patients. The recurrence status was unknown on 1st January 2008 for 4.8% of registered cases, and vital status was unknown for 1.4% of registered cases.

2.2. Data analysis

The population data used for calculating incidence and prevalence rates were obtained from the Institut National de Statistiques et des Etudes Economiques (INSEE). All rates were calculated by gender and age group. For the purpose of comparison with other countries, rates were age-standardised by the direct method using the world standard population.

2.2.1. Incidence, total and partial prevalence

Total prevalence was the observed number of patients registered with colorectal cancer and alive on 31st December 2005. Five-year partial prevalence was the observed number of cases diagnosed for less than 5 years at the end-point date and still alive at that date. As an example, it was calculated for the patients diagnosed in the 1976–1980 period and still alive on 31st December 1981. This calculation was repeated for the periods 1981–1985, 1986–1990, 1991–1995, 1996–2000 and 2001–2005. Between 1976 and 2005, the mean variations in 5-year period incidence and 5-year partial prevalence rates by gender were estimated using a Poisson regression adjusted on age. Prevalence at the national level was estimated by applying the age-specific prevalence rates to the whole French population, according to 5-year age group and gender.

2.2.2. Prevalence of patients requiring follow-up

Five-year partial prevalence does not account for patients diagnosed beyond 5 years and who present an excess mortality compared to the general population. The patients requiring follow-up were quantified using a parametric non-mixture relative survival cure model with a Weibull distribution.[5] Relative survival is the ratio of the observed survival to the expected survival in a general population with a similar gender and age distribution. It reflects excess mortality relative to background mortality. Time to cure was defined as the time between diagnosis and the moment at which excess mortality reaches zero, i.e. the population is considered statistically cured.[6] The number of deaths in excess that would occur between diagnosis and statistical cure was estimated. As cure is asymptotic, the population was defined as statistically cured when fewer than 10% of the patients who were expected to die from their cancer were still alive. This threshold of 10% was considered clinically relevant. Thus, among all the patients who were expected to die from cancer, cure occurred at the moment when 9 patients of 10 had died.

2.2.3. Prevalence of patients requiring treatment for recurrence

Recurrence rate is usually clinically considered negligible 10 years after diagnosis. The annual recurrence rates were available up to 10 years after diagnosis from the registry data between 1976 and 1986. They were applied to the number of prevalent patients diagnosed between December 1995 and December 2005 according to the delay since diagnosis. As an example, the 4-year recurrence rate was applied to the observed number of patients diagnosed 4 years before 2005 (i.e. in 2002). In 2005, the number of prevalent patients requiring care because of recurrence was the sum of all iterations. The type of treatment for recurrence was known for prevalent cases in the area. The number of patients who had undergone surgery for cure, palliative treatment (surgery, chemotherapy and/or radiotherapy), or best supportive care for their recurrence was calculated.

Data were analysed using Stata 10.0™ software.[7]

3. Results

3.1. Incidence and survival

World age-standardised incidence rates were higher in males than in females. Overall age-standardised incidence rates for 100,000 inhabitants were 40.0 in males and 23.4 in females, the sex-ratio being 1.7. The trend in incidence over the study period is presented by gender in Fig. 1. The mean variation in the incidence rates between successive 5-year periods was +1.2 [+0.3; +2.2] with a greater variation in males: +2.0% [+0.7; +3.3] than in females: +0.3% [–1.1; +1.7]. The trend in incidence varied according to the subsite. The mean variation in incidence rates between 5-year periods was +8.4% ([6.4–10.4], $p < 0.001$) for proximal colon cancers, –0.8% ([–2.2; 0.6], NS) for distal colon cancers and –2.7% ([–4.6; –0.8], $p = 0.006$) for rectal cancers.

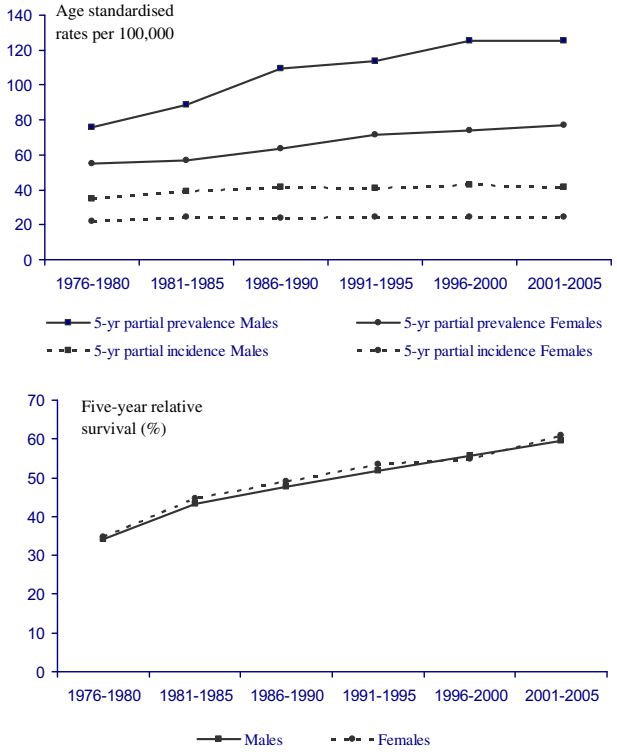

Fig. 1 – Trends in age-standardised 5-year partial prevalence, age-standardised 5-year incidence and 5-year relative survival.

Five-year relative survival increased from 34.2% (1976–1980) to 59.6% (2001-2005) in males. The corresponding values in females were 34.7% and 61.0% (Fig. 1). The overall relative survival rates were 51.4% [50.5–52.4] at 5 years and 45.0% [43.9–46.1] at 10 years. Five-year relative survival rose from 34.4% [31.1–37.7] for the 1976–1980 period of diagnosis to 59.6% [57.3–61.8] for the 2001–2005 period. The dramatic increase in 5-year relative survival rates was similar whatever the subsite was. For proximal colon cancers, they rose from 32.2% (1976–1980) to 58.0% (2001–2005) corresponding to a 5-year mean variation of +13.0% ([10.3–15.6], $p < 0.001$). For distal colon cancers, they rose from 36.2% to 62.3% (+14.2%, [12.1–16.2], $p < 0.001$) and for rectal cancers from 32.5% to 59.7% (+15.0% [12.2–17.7], $p < 0.001$) between the same periods.

3.2. *Total prevalence*

Overall 5108 patients, in this population of one million inhabitants, with a previous diagnosis of colorectal cancer, were alive on 31st December 2005. Age-standardised total prevalence rates were 244.9 per 100,000 inhabitants in males and 152.6 per 100,000 inhabitants in females. Proximal colon cancers represented 28% of total prevalent cases, whereas distal colon cancers and rectal cancers represented 49% and 23%, respectively. Applying age-specific prevalence rates by sex for the Burgundy area in 2005 to the French population yielded an estimated 143,125 males and 119,119 females alive with a history of colorectal cancer. Among total prevalent cases, 46.3% were diagnosed during the 5 years prior to the end-point date, 25.4% were diagnosed 5–10 years prior to that

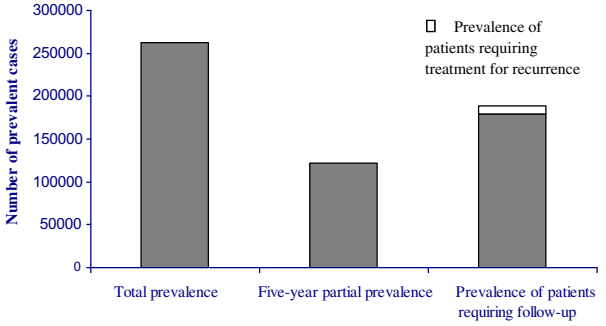

Fig. 2 – Colorectal cancer prevalence in France on 31st December 2005.

date, 23.3% were diagnosed 10–20 years and 5.0% were diagnosed 20–30 years, of which 1.2% were diagnosed 30 years prior to the end-point date (Fig. 2).

3.3. *Five-year partial prevalence*

The age-standardised 5-year partial prevalence rates on 31st December 2005 were 125.2 per 100,000 inhabitants in males and 76.9 per 100,000 inhabitants in females. The estimated number of cases at the national level was 122,048. Trends in 5-year partial prevalence rates over the study period are presented by gender in Fig. 1. Five-year prevalence rates regularly increased with the period of diagnosis. Age-standardised 5-year partial prevalence rates for 100,000 inhabitants increased from 75.8 (1976–1980) to 125.2 (2001–2005) in males and from 55.0 (1976–1980) to 76.9 (2001–2005) in females. The mean variation in partial prevalence rates by successive 5-year periods was +8.0% ([6.7–9.4%], $p < 0.001$). It was +8.9% [+7.1 to +10.8] in males and +6.9% [+4.9; +9.0] in females. The mean variation in partial prevalence rates by successive 5-year periods was +13.8% for proximal cancers ([11.2–16.3], $p < 0.001$). It was +6.1% ([4.3–7.9], $p < 0.001$) for distal cancers and +3.9% ([1.3–6.4], $p < 0.001$) for rectal cancers.

3.4. *Prevalence of patients requiring follow-up*

Time to cure was 9.3 years [8.3–10.4]. Overall 84.7% of the excess mortality due to colorectal cancer occurred in the 5 years following diagnosis and 15.3% occurred between 5 years and time to cure. At the national level, the estimated number of excess death between 5 and 9.3 years was 13895. Because of the excess mortality until cure, patients need to be followed up for disease recurrence over the 10 years following diagnosis. Overall, 71.7% of prevalent cases were diagnosed during the 10 years prior to the end-point date, corresponding to 188,314 subjects at the national level.

3.5. *Prevalence of patients with recurrence*

At the national level, the estimated 10-year prevalence for patients who were initially treated with a curative intent was 169,658. The annual rates of recurrence and the estimated number of recurrences in 2005 by 1-year period are presented in Table 1. Overall, recurrence occurred during the year 2005 in 9235 of these 10-year partial prevalent cases (5.4%). These

Table 1 – Number of recurrences in 2005 among 10-year prevalent cases.

Time from diagnosis (years)	Number of prevalent cases[a]	Annual rate of recurrence (%)[b]	Number of recurrences
1	27,145	11.4	3095
2	27,060	12.5	3393
3	22,497	6.1	1377
4	18,544	3.1	579
5	16,915	2.5	423
6	15,269	1.1	163
7	12,368	0.8	99
8	10,960	0.6	68
9	9569	0.3	25
10	9331	0.1	14
Total	169,658		9235

a Observed number of prevalent patients initially treated for cure.
b Observed from the available database.

patients had resection for cure in 49.3% of cases (67.7% for local recurrences and 45.6% for distant metastasis), palliative treatment (surgery, chemotherapy or radiotherapy) in 40.8% of cases and best supportive care in 9.9% of cases.

4. Discussion

Prevalence is one of the most useful measures of cancer burden. However, it includes patients who are followed up without receiving any treatment, patients who receive medical treatment because of recurrence and patients who can be considered cured. The interest of this study lies in the fact that it reports on the prevalence of patients requiring follow-up and on that of patients with recurrent colorectal cancer.

Our data offer a solid basis for the calculation of different prevalence rates. Because information was obtained from all the available medical sources, including pathology laboratories, as well as administrative sources, we assume that nearly all newly diagnosed cases were recorded. Follow-up data were also nearly complete with information on survival at the endpoint date in nearly 99% of the cases. Nevertheless, some limitations have to be considered. Prevalence data are limited to a 30-year period. Patients diagnosed before 1976 and still alive were not recorded. Survivors (1.2%) were diagnosed 30 years ago, indicating that the underrating of prevalence due to the cases diagnosed before the start of the registry was very small. The estimation of colorectal cancer prevalence at the national level was based on the hypothesis that there was no difference between the age- and sex-specific prevalence rates in the covered area and those in France as a whole. This is supported by the high degree of concordance between the incidence and survival of colorectal cancer in Burgundy and estimations made at the national level.[8–10]

One of the important uses of population-based statistics is it allows comparison with data collected in other areas of the world. However, it is difficult to interpret these data because the differences in prevalence rates can be attributed to the differences in incidence, in survival, or a combination of the two. Similar calendar periods must be compared because of the influence of incidence and survival trends on prevalence. Differences in colorectal cancer prevalence between France, Italy and Spain, with relatively similar survival, were attributed mainly to the differences in incidence.[11] Incidence ranged in Europe between 28 and 51 per 100,000 inhabitants in men and between 17 and 31 per 100,000 inhabitants in women in the 1993–2005 period.[12] Inversely, large differences in colorectal cancer prevalence between Poland (45 per 100,000) and Sweden (240 per 100,000) were mainly attributed to the differences in cancer survival.[13] In Europe, 5-year relative survival ranged between 42% and 66% in 2004.[14,15] Prevalence rates in this study were close to those reported by the SEER programme.[16] Total prevalence has some specific merits. It is of major importance in the evaluation of the magnitude of the colorectal cancer problem.

The data obtained from this study indicate that there was a dramatic increase in the 5-year partial prevalence (+8% by 5-year periods). The increase in incidence (+1.2% by 5-year periods) explained only a small part of the trend in prevalence, which was thus mainly related to the major increase in survival.[17] Improved survival has been shown to be related to a decrease in operative mortality[18] and to substantial advances in the management of colorectal cancer associated with detection at an earlier stage.[19] These trends indicate that such prevalence estimations need to be performed regularly. The increase in prevalence in this study is an indicator that progress has been made over time in the care of cancer patients. However, the increase in prevalence is associated with increasing demands on the health system. The only way to decrease colorectal cancer prevalence is to reduce the occurrence of the disease by promulgating a healthy diet, and in the short term, by implementing well-organised screening programmes.

Five-year partial prevalence of colorectal cancer is generally considered an estimation of individuals needing medical follow-up. At the population level, survival among cancer patients 5 years after diagnosis is still lower than that reported in the general population with a similar age and sex distribution. This implies that patients cannot be considered cured after 5 years. This is why we attempted to estimate the number of patients who were not cured 5 years after diagnosis, which necessitated the use of cure models. Our results indi-

cate that 5-year partial prevalence underestimates the proportion of patients who will die from their cancer by nearly 15.3%.

Prevalence data should be completed by information on the number of patients presently alive with recurrences that require care.[20] Unfortunately, such data are rarely available at a population level because special surveys are required to obtain them. Our results indicate that a subset of 5.4% of 10-year prevalent cases in 2005 required treatment for recurrences. Considering incidence data alone underestimates the health resources that are necessary to treat colorectal cancer. Because of the high cost of palliative chemotherapy, often with long-term treatment, the prevalence of patients who cannot be treated radically may become a major determinant of the cost of recurrent cancer.[21] Prevalence data should also be completed by information on the cost of health care. This study confirms that 80% of recurrences occur within 3 years after diagnosis. However, late recurrences do occur. These may not be immediately fatal, which explains why cure is reached only after 9.3 years. These results suggest that clinical surveillance is needed over the 10 years following diagnosis so as to implement complementary examinations whenever necessary in order to detect recurrence as early as possible. The population of 10-year prevalent cases is very large, representing 71.7% of all prevalent cases.

For the individual patient, cure of the disease does not mean the recovery of the prior health status. Indeed, curative treatment may induce long-term outcomes on health or individual resentment. As an example, in a FECS/EUROCARE high resolution study, 70% of long-term survivors had intestinal or urinary problems, 10% had incontinence and 10% had a second primary tumour.[22] A US study performed among Medicare patients indicated that 62% of prevalent cases were still receiving some kind of care for their colorectal cancer 20 years after diagnosis.[23] The long-term impact of colorectal cancer management must be investigated in more detail.

Total prevalence appears to be a basic indicator of the burden of colorectal cancer in a given population. The increase in 5-year partial prevalence, mainly related to the improvements in survival, results in an increasing burden of colorectal cancer on health care resources. Other prevalence indicators reinforce the usefulness of prevalence measures. This is particularly the case for the prevalence of patients who need to be followed up and the prevalence of patients requiring treatment because of a recurrence.

Conflict of interest statement

None declared.

Acknowledgement

M. Chauvenet was supported by a grant from the French Foundation for Medical Research (FRM).

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