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Conditional net survival: Relevant prognostic information for colorectal cancer survivors. A French population-based study

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ABSTRACT

Background: Traditionally, survival estimates have been reported as survival from the time of diagnosis. A patient's probability of survival changes according to time elapsed since the diagnosis and this is known as conditional survival. The aim was to estimate 5-year net conditional survival in patients with colorectal cancer in a well-defined French population at yearly intervals up to 5 years.
Methods: Our study included 18,300 colorectal cancers diagnosed between 1976 and 2008 and registered in the population-based digestive cancer registry of Burgundy (France). We calculated conditional 5-year net survival, using the Pohar Perme estimator, for every additional year survived after diagnosis from 1 to 5 years.
Results: The initial 5-year net survival estimates varied between 89% for stage I and 9% for advanced stage cancer. The corresponding 5-year net survival for patients alive after 5 years was 95% and 75%. Stage II and III patients who survived 5 years had a similar probability of surviving 5 more years, respectively 87% and 84%. For survivors after the first year following diagnosis, five-year conditional net survival was similar regardless of age class and period of diagnosis.
Conclusions: For colorectal cancer survivors, conditional net survival provides relevant and complementary prognostic information for patients and clinicians.

1. Introduction

Colorectal cancer is a major health problem in most industrialized countries. In France, it is the third most common cancer and the second leading cause of cancer death [1,2]. Results from the EUROCARE study, involving 29 European countries, indicated that France stood among countries with the highest survival in Europe [3].

Survival estimates are traditionally reported as survival from the time of colorectal cancer diagnosis (5-year survival for example). However, 25% of patients with colorectal cancer resected with curative intent have metastatic recurrence within five years [4]. Therefore, these survival estimates are not necessary applicable to patients who have already survived a period of time after the initial diagnosis and treatment [5]. There are too pessimistic, because there are also based on patients who die within the first years. For colorectal cancer survivors, there is a need for further information that could help to update their prognosis in the years following diagnosis. Conditional survival analysis is a method for estimating the survival rate, for patients who have already survived for a certain period of time after diagnosis. It's a more useful and clinically relevant measure of patient's changing risk of death over time. These estimates give important information to clinicians to determine appropriate surveillance strategies and to patients to help them to resume a normal social life after cancer.

Several studies have previously published results on conditional survival from colorectal cancer [6–16]. Few of them include detailed data of patients and his tumour (stage at diagnosis, location) and none have a 33-year period study. Furthermore, these studies used different relative survival methods to calculate conditional survival. The aim of these methods was to remove deaths due to the other causes of mortality than cancer, therefore providing an estimation of net survival. But it was recently demonstrated that these models generated biased survival estimates [17,18]. The newly described Pohar Perme estimator, used in our study, has been shown to provide unbiased net survival estimates [19]. To our knowledge, it is the first study providing an estimate of conditional

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survival using an unbiased Pohar Perme estimator and detailed data over a 33-year period.

The aim of this study was to estimate 5-year net conditional survival at yearly intervals up to 5 years, in patients with colorectal cancer in a well-defined population in France, using data from the Digestive cancer registry of Burgundy (France).

2. Patients and methods

2.1. Patients

The Burgundy (France) population-based digestive cancer registry includes all digestive tract cancers occurring in the resident population of two well-defined areas (Côte d'Or and Saône-et-Loire). It covers a resident population of 1,052,000 inhabitants. Information is collected from public and private pathology laboratories, the University hospital (including the regional cancer institute), local hospitals and specialists in private practice (surgeons, gastroenterologists, oncologists, and radiotherapists). Administrative information was also used: the hospital administrative database, the Regional Health services database and death certificates. No cases were registered through death certificates alone given the questionable quality of this source of information, but these were used to identify missing cases. Due to the involvement of the entire medical profession, it can be assumed that virtually all newly diagnosed cases of colorectal cancer are recorded. The quality and comprehensiveness of the registry are certified every 4 years by an audit of the National Public Health Institute (InVS), the National Cancer Institute (INCa) and the National Institute for Health and Medical Research (INSERM).

For this study, all cases of colorectal cancer registered by the Digestive Cancer Registry of Burgundy, between 1976 and 2008 were included. Colon and rectal cancers were defined in accordance with the International Classification of Diseases for Oncology, 3nd revision (ICD-0-3), codes C18-C20 [20] and registered according to the standard guidelines for Cancer Registration in Europe provided by the European Network of Cancer Registries [21]. Anal cancer cases (C21) were not included.

2.2. Data set

For all cases information about age, gender, subsite, treatment and stage at diagnosis was routinely collected. Details on patient survival were ascertained from death certificates, the National Register of French Residence (RNIPP), registers of place of birth and whenever necessary from practitioners. Life status at January 2012 was known for 90.5% of the cases.

Patients were categorized into age as follows: under 65 years, 65–74 years, 75–84 years and over 85 years. Patients over 85 were not included in the analysis by age group because of the difficulty in providing reliable estimates. Tumour sites were grouped into 3 anatomical subsites: the right colon (C18.0 to C18.4), left colon and rectosigmoid junction (C18.5 to C18.7, C19) and rectum (C20). Colonic subsite was unknown for 122 cases (0.7%). The stage of disease at diagnosis was classified according to the UICC classification [22]: stage I (T1/2 N0 M0), stage II (T3/4 N0 M0), stage III (all T N1/2 M0), and stage IV (all T, N, M1). Patients with visceral metastases and those not resected were classified under the heading 'advanced' stage. The stage at diagnosis was unknown for 225 patients (1.2%). The date of the primary diagnosis was categorized into three periods of 8 years: 1976–1983, 1984–1991, 1992–1999 and one of 9 years, 2000–2008. Treatment was divided into surgery with curative intent, i.e. macroscopic resection of all malignant tissue and no microscopic evidence of spread into the surgical margin (R0 resection), and other treatment (failure to resect all malignant tissue, palliative treatment).

2.3. Statistical analyses

Net survival is defined as the survival that would be observed if cancer was the only possible cause of death. The recently described Pohar Perme estimator has been shown to estimate unbiased net survival and thus to provide information that is not affected by deaths unrelated to the cancer [19]. The expected mortality rates (necessary for this estimator) were calculated from life-tables defined by age, sex, year of diagnosis, and Department of residence (French administrative area). These life-tables were provided by the National Statistics Institute. We calculated net survival at the time of diagnosis using this new Pohar Perme estimator. Thus the most recent advances in methodology for the estimation of net survival were used.

Conditional survival is defined as the probability of surviving an additional y years on the condition that the patient has survived x years. It is calculated by dividing the net survival at $(x+y)$ years after diagnosis by the net survival at x years after diagnosis. We calculated conditional 5-year net survival corresponding to the probability of surviving an additional 5 years considering death related to cancer only. For example, to compute 5-year conditional net survival for a patient who has already survived 3 years, net survival at 5 + 3 years is divided by net survival at 3 years. The 95% confidence intervals of the annual conditional survival rates were estimated. The variance of the conditional probability is given by a variation of the usual "Greenwood formula" for unconditional survival. Analyses were performed using R 2.14 software©.

3. Results

Between 1976 and 2008, 18,300 cases of colorectal cancer were registered and included in this present study. Patients' characteristics are given in Table 1. There was a slight male predominance (54%), which tended to increase over time. The mean age was 71.6 years. There was a minor variation in the proportion of patients in the different age groups over time. The proportion of patients over 85 years increased slightly. There was also a minor increase in the proportion of TNM stage I and a decrease in advanced stages. There was a dramatic decrease in operative mortality from 11% (1976–1983) to 5% (2000–2008) and an increase in resectability for cure from 64% to 70%.

Table 2 presents 5-year conditional net survival at yearly intervals up to 5 years after diagnosis according to sex, age group, subsite, period of diagnosis and treatment (resection for cure vs. other treatment). The overall probability of surviving an additional 5 years ranged from 51% at diagnosis to 89% for those who survived 5 years after diagnosis. Conditional survival in men and women increased with every succeeding year survived with a year-by-year similar probability of surviving an additional 5 years. Age was an important determinant of 5-year net survival expectancy at diagnosis. It varied between 58% in patients under 65 years to 46% in those aged 75–84 years. Among patients who survived at least 1 year the conditional probability of surviving an additional 5 years was similar at the yearly intervals for all age groups (Table 2). Patients who survived 1 year after diagnosis had a 64–66% chance of a further 5 years of survival according to the age group. For those who survived 5 years after diagnosis, survival varied between 85% and 87%. Concerning the site of the cancer, rectal cancers were noted to have the poorest 5-year survival probability at diagnosis (48% vs. 52% for left colon and for right colon). By year 5, a gap between survival in right and left colon cancer appeared and the gap with regard to rectal cancer persisted.