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Brief communication

Age-specific incidence of all neoplasms after colorectal cancer

Fabio Levi MD, MSc [a,*], Lalao Randimbison ScD [a], Rafael Blanc-Moya MD [a], Carlo La Vecchia MD, MSc [b,c]

[a] Department of Medicine and Community Health, Vaud Cancer Registry and Cancer Epidemiology Unit, Institute of Social and Preventive Medicine (IUMSP), Lausanne University Hospital, Lausanne, Switzerland
[b] Department of Epidemiology, IRCCS-Istituto di Ricerche Farmacologiche "Mario Negri", Milan, Italy
[c] Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

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ABSTRACT

Purpose: Patients diagnosed with a specific neoplasm tend to have a subsequent excess risk of the same neoplasm. The age incidence of a second neoplasm at the same site is approximately constant with age, and consequently the relative risk is greater at younger age. It is unclear whether such a line of reasoning can be extended from a specific neoplasm to the incidence of all neoplasms in subjects diagnosed with a defined neoplasm.
Methods: We considered the age-specific incidence of all non–hormone-related epithelial neoplasms after a first primary colorectal cancer ($n = 9542$) in the Vaud Cancer Registry data set.
Results: In subjects with a previous colorectal cancer, the incidence rate of all other epithelial non–hormone-related cancers was stable around 800 per 100,000 between age 30 and 60 years, and rose only about twofold to reach 1685 at age 70 to 79 years and 1826 per 100,000 at age 80 years or older. After excluding synchronous cancers, the rise was only about 1.5-fold, that is, from about 700 to 1000. In the general population, the incidence rate of all epithelial non–hormone-related cancers was 29 per 100,000 at age 30 to 39 years, and rose 30-fold to 883 per 100,000 at age 70 to 79 years. Excluding colorectal cancers, the rise of all non–hormone-related cancers was from 360 per 100,000 at age 40 to 49 years to 940 at age 70 to 79 years after colorectal cancer, and from 90 to 636 per 100,000 in the general population (i.e., 2.6- vs. 7.1-fold).
Conclusions: The rise of incidence with age of all epithelial non–hormone-related second cancers after colorectal cancer is much smaller than in the general population. This can possibly be related to the occurrence of a single mutational event in a population of susceptible individuals, although alternative models are plausible within the complexity of the process of carcinogenesis.

Introduction

Patients with a specific neoplasm tend to have a subsequent excess risk of the same neoplasm. In terms of relative risk, such an excess risk is greater at younger age, whereas in absolute terms, the incidence of a second neoplasm at the same site is approximately constant with age [1].

Thus, women diagnosed with a breast cancer tend to have high and approximately constant subsequent breast cancer rates [2], and subjects diagnosed with head and neck [3,4], colorectal cancer [5,6], basal cell carcinoma, [7] or melanoma [8] of the skin tend to have high and constant subsequent incidence of the same neoplasm, respectively. These age distributions contrast with the well-known rise with a power function of age of the incidence of non–hormone-related epithelial neoplasms in the general population [9].

Such a rise of cancer incidence with a power function of age has been interpreted, within the multistage theory of carcinogenesis, as an indicator that the process of carcinogenesis involves the accumulation of several stochastic somatic changes [10]. It is possible therefore that the constant incidence rate with age of second primary cancers is explained by the occurrence of a single mutational event in a population of susceptible individuals, within the simple multistage theory [11,12].

It is however unclear whether such a line of reasoning can be extended from the setting of second cancers at the same site as the primary tumor to the setting of second cancers at other anatomic sites. To test this hypothesis, we have considered the age-specific incidence of all epithelial non–hormone-related neoplasms after a first primary colorectal cancer in the Vaud Cancer Registry data set [6], and contrasted that age function with the age-specific rates of all epithelial non–hormone-related cancers in the same population.

The authors declare no conflict of interest.

* Corresponding author. Department of Medicine and Community Health, Vaud Cancer Registry, Cancer Epidemiology Unit, Institute of Social and Preventive Medicine (IUMSP), Lausanne University Hospital, Route de la Corniche 10, 1010 Lausanne, Switzerland. Tel.: +41 21 314 73 11; fax: +41 21 314 73 17.
E-mail address: fabio.levi@chuv.ch (F. Levi).

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Materials and methods

Data for the present study were derived from the Vaud Cancer Registry data set, which includes information concerning incident cases of malignant neoplasms occurring in the Swiss canton of Vaud (about 713,000 inhabitants, according to the December 2010 National Census) [6]. The Registry adheres to the rules of registration for the first and second primary cancers of the International Agency for Research on Cancer [13] and has been included in the International Agency for Research on Cancer's Cancer Incidence in Five Continents volumes since 1982 [14]. Within colon, separate primary sites (i.e., second cancers) in the same patient were considered for left colon (International Classification of Diseases for Oncology, First Edition [ICD-O-1] topography code 153.1–153.3, 153.7) and right colon (ICD-O-1 153.0, 153.4–153.6). Within colorectum, in the same patient, up to three colorectal primaries could be registered, two for colon and one for rectum (ICD-O-1 154.0–154.1) [6].

Population-based incidence data have been available since 1974, and the present report includes data until 2010. The main information available comprises demographic characteristics of the patient, primary site, and histologic type of the tumor according to the standard ICD-O-1 (ICD-O-1 and both ICD-O-1 and ICD-O-3 since 2005) [15,16].

Passive and active follow-up were recorded, and each subsequent item of information concerning an already registered case was used to complete the record of that patient. Information from the death certificate was added to the registration file.

After exclusion of basal and squamous cell carcinomas of the skin from the whole database, 9542 patients (5123 males and 4419 females) diagnosed with a first colorectal primary malignancy were abstracted from the Registry's database and followed over the period 1974–2010 for the occurrence of a second epithelial non–hormone-related neoplasms, emigration or death, contributing to a total of 45,900 person-years at risk. Nonmelanomatous skin cancers, germ cell, lymphoid and primary breast, gynecological and male genital neoplasms (i.e., sex–hormone-related cancers) were excluded.

Synchronous cancers were defined as those occurring within 2 months of diagnosis of the first cancer. Metachronous cancers were those occurring 2 months or later since diagnosis of the first one.

We computed and contrasted the age-specific incidence rates of all second non–hormone-related epithelial cancers in subjects with a first epithelial colorectal cancer to those in the general population of the Canton of Vaud. We excluded basal and squamous cell carcinomas of the skin. We ran separate analyses including and excluding colorectal cancer.

Results

There were 591 second primary cancers after a first diagnosis of colorectal cancer. The most common sites of second neoplasms were colorectum (250, 42%), lung (75, 13%), bladder (44, 7%), cutaneous melanoma (36, 6%), and stomach (31, 5%). Of these, 177 were synchronous and 414 were metachronous.

Table 1 and Figure 1A (on a logarithmic scale) give the age-specific incidence rates of all epithelial non–hormone-related cancer patients aged 30 years or older ($n = 588$) after a diagnosis of first colorectal cancer, and in the general population. In subjects with a previous colorectal cancer, the incidence rate of all other cancers was stable around 800 per 100,000 between age 30 and 60 years and rose only about twofold to reach 1685 at age 70 to 79 years and 1826 per 100,000 at age 80 years or older. In the general population, the rate of epithelial non–hormone-related cancers was 29 per 100,000 at age 30 to 39 years and rose 30-fold to 883 per 100,000 at age 70 to 79 years. The difference in all cancer sites between subjects with colorectal cancer and the general population was somewhat greater in men than in women, but the patterns were similar. After exclusion of synchronous cancers, however, the rate ratios became similar in men and women.

Table 1
Incidence of second neoplasms* in patients diagnosed with colorectal cancer and in the general population. Vaud Cancer Registry, Switzerland, 1974–2010

Age (y)	Post colon*		General population*	
	Rate/100,000	Rate ratio (no. of cases) [95% CI†]	Rate/100,000	Rate ratio
Males and females				
30–39	804.7	1‡ (6)	29.2	1‡
40–49	866.2	1.08 (28) [0.72–1.57]	108.6	3.72
50–59	808.8	1.01 (72) [0.79–1.28]	326.4	11.18
60–69	1233.2	1.53 (163) [1.31–1.79]	628.6	21.53
70–79	1684.7	2.07 (223) [1.82–2.38]	882.7	30.23
80+	1825.7	2.27 (96) [1.85–2.77]	852.8	29.21
Males				
30–49	967.0	1‡ (21)	82.9	1‡
50–59	901.3	0.93 (44) [0.67–1.24]	460.9	5.56
60–69	1569.7	1.62 (112) [1.32–1.96]	951.2	11.47
70–79	2445.9	2.52 (151) [2.14–2.98]	1365.2	16.47
80+	1961.8	2.03 (41) [1.45–2.76]	1342.2	16.19
Females				
30–49	719.6	1‡(13)	55.1	1‡
50–59	696.5	0.97 (28) [0.65–1.41]	198.8	3.61
60–69	838.5	1.16 (51) [0.86–1.53]	353.5	6.42
70–79	1019.3	1.42 (72) [1.11–1.80]	545.0	9.89
80+	1735.9	2.41 (55) [1.79–3.13]	617.9	11.21

* Second colorectal cancers included; basal and squamous cell carcinomas of the skin and nonepithelial and hormone-related neoplasms were excluded.
† CI: confidence interval.
‡ Reference category.

When the same analysis was conducted excluding (second) colorectal cancers (Table 2 and Fig. 1B), the pattern was similar in men, but the difference in rate ratios between subjects with a previous colorectal cancer and the general population was apparently smaller in women. Excluding colorectal cancers, the rise of all non–hormone-related cancers was from 360 per 100,000 at age 40 to 49 years to 940 at age 70 to 79 years after colorectal cancer, and from 90 to 636 per 100,000 in the general population (i.e., 2.6- vs. 7.1-fold).

We ran sensitivity analyses excluding synchronous cancers (Table 3). After exclusion of synchronous cancers, the rise was about 1.5-fold, that is, from about 700 to about 1000 per 100,000. Overall, the results were similar after exclusion of second colorectal cancers (besides hormone-related and nonepithelial cancers), with a rise in all cancers combined from 360 per 100,000 at age 40 to 49 years to about 700 at age 70 years or older. As for the overall data set, the differences between men and women became smaller after exclusion of synchronous cancers. In an additional sensitivity analysis, we also split our data set in two periods, that is, 1974 to 1989 and 1990–2010, and again the results were consistent across calendar periods, with incidence of all other cancers after the diagnosis of first colorectal cancer rising only about twofold between age 40 to 49 years and 70 years or older in both periods (from 650 to 1250 per 100,000 in 1974–1989 and from 1000 to 2000 per 100,000 in 1990–2010).

Discussion

We observed that the incidence of several previous neoplasms of the same site is approximately constant with age for a large number of neoplasms [1], contrary to the well-known rise of the incidence of epithelial non–hormone-related cancers with the fourth to fifth power of age [9]. This translates in an approximately 30-fold difference in cancer incidence between age 30 and 80 years, as observed in the general population from major cancer registration systems worldwide (i.e., the SEER data set [17,18]) and in the present data set, too.