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Is melanoma survival influenced by month of diagnosis?

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ABSTRACT

Background: Despite being a well-documented phenomenon, seasonal variation in the incidence of cutaneous melanoma is poorly understood, and data on the seasonality of melanoma survival are scarce. We sought to explore the seasonal variation in melanoma incidence and survival in Belgium and to assess the characteristics and outcomes of cases diagnosed during the seasonal peak.

Methods: All cases of invasive cutaneous melanoma—patients over 15 years of age and registered by the Belgian Cancer Registry (BCR) from 2004 to 2009—were included ($n = 9782$). Monthly variations in incidence were estimated by the ratio of the number of cases diagnosed each month to that diagnosed in January ($R_{month/January}$) using Nam's method. The observed and relative 5-year survival rates were adjusted on patient and tumour characteristics using Cox proportional hazards regression models and generalised linear models with a Poisson error structure, respectively.

Results: A peak in melanoma incidence was observed in June ($R_{June/January} = 1.64$, 95% confidence interval (CI) = 1.54–1.73). The 5-year observed survival (OS) and relative survival (RS) rates were significantly higher for patients diagnosed in June compared with other months ($OS_{June} = 84\%$, 95%CI = 81–86 versus $OS_{Othermonths} = 79\%$, 95%CI = 78–80; $RS_{June} = 93\%$, 95%CI = 90–95 versus $RS_{othermonths} = 87\%$, 95%CI = 86–88). After adjustment, the 5-year OS remained significantly higher for patients diagnosed in June (hazard $ratio_{June} = 0.78$, 95%CI = 0.62–0.98); however, the 5-year RS was no longer significantly different for patients diagnosed in June compared with other months (relative excess $risk_{June} = 1.16$, 95%CI = 0.73–1.84).

Conclusions: This study demonstrated a seasonal variation in melanoma incidence in Belgium with a peak in June for the period 2004–2009. When adjusted for patient and tumour characteristics, patients diagnosed in June had higher observed survival rates, but relative survival rates did not differ. Our findings do not support an influence of season of diagnosis on melanoma prognosis.

1. Introduction

Over recent decades, the worldwide incidence of cutaneous melanoma has risen faster than that of any other cancer [1], increasing from 3% to 7% per year in Caucasians; this represents a doubling in rate every 10–20 years [2]. In Belgium, world standardised incidence rates for cutaneous melanoma increased from 8.5 per 100,000 person-years in 2004 to 10.8 in 2011 in males and from 11.8 per 100,000 person-years in 2004 to 15.2 in 2011 in females, ranking this cancer as the eighth most common in men and the sixth most common in women in this country [3,4]. Since melanoma incidence is increasing dramatically, it is important to identify the factors that may influence this rise.

Seasonal variation in cutaneous melanoma incidence is a well-documented phenomenon, with several studies [5–17] showing an incidence peak in summer. Some hypotheses have been proposed: such as the effect of prevention campaigns [14], seasonal variation

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in clothing habits [15,16], seasonal change in medical care, or a short-term effect of ultraviolet radiation exposure [11,16,17]. However, seasonal variation in melanoma incidence is still poorly understood, and has not yet been studied in Belgium. Moreover, few studies explored the effect of seasonal variation on survival. Only two recent studies [6,18] have investigated variation in melanoma fatality by season of diagnosis, with conflicting results.

The objectives of this study were to explore a potential seasonal variation in cutaneous melanoma incidence and survival in Belgium between 2004 and 2009, and to assess the characteristics and outcomes of cases diagnosed during the seasonal peak.

2. Materials and methods

2.1. Study population and data collection

The Belgian population is spread over three regions (Flanders, Wallonia and Brussels-Capital), which represent respectively 57.8%, 32.4% and 9.8% of the inhabitants [19]. The Belgian Cancer Registry (BCR) comprehensively collects data on all new cancer cases diagnosed in Flanders since 1999 and in the three Belgian regions since 2004. Data are collected from the oncological care programmes (clinical network) and from all pathology laboratories (pathology network) in Belgium. A complete description of the data registration and data collection has been reported elsewhere [3].

A total of 15,764 cutaneous melanomas were registered by the BCR during the period 1999–2009. Since the BCR has collected data on all new cancer cases diagnosed in the three Belgian regions only since 2004, we excluded cases diagnosed before 2004 ($n = 5633$), in order to have a comprehensive evaluation of the three regions in the analyses. We further excluded cases under 15 years of age ($n = 32$), leaving 9782 cases defined as invasive cutaneous melanoma by the International Classification of Diseases (10th revision) (C43.X) [20]. Patients with metachronous or synchronous tumours were included. Characteristics of patients (age, sex, geographical region, number of primary cancers) and tumours (year of diagnosis, histological type, anatomical site, Breslow thickness, ulceration, lymph-node invasion, distant metastasis) were included as potential covariates in the analyses. Histological type was coded according to the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) [21]. Five histological groups were defined: superficial spreading melanoma (SSM, ICD-O-3: 8743), nodular melanoma (NM, 8721), lentigo maligna melanoma (LMM, 8742), melanoma not otherwise specified (NOS, 8720), and others (specified types). Information about Breslow thickness, ulceration, lymph-node invasion and distant metastasis was retrieved from the TNM staging, which was coded using the TNM Classification 6th edition [22]. Breslow thickness was categorised as $\leq$1.00, 1.01–2.00, 2.01–4.00, or >4.00 mm.

Data on the number of dermatological consultations in Belgium over the period 2006–2009 were obtained from the Inter Mutualistic Agency (IMA) database, which collects health insurance data in Belgium [23].

3. Statistical analyses

3.1. Incidence analyses

Monthly variations in cutaneous melanoma incidence over 2004–2009 were estimated using the ratio of the number of cases diagnosed each month to the number of cases diagnosed in January ($R_{\text{month/January}}$). Confidence intervals (CIs) were calculated using Nam's method [24]. The characteristics of melanoma cases diagnosed during the seasonal peak were compared with those diagnosed during the other months of the year using Pearson's chi-squared tests. Potential confounders were taken into account in multivariable logistic regression models estimating odds ratios (ORs) of melanoma diagnosis during the seasonal peak compared with the other months.

3.2. Survival analyses

To compare the outcomes of cases diagnosed during the seasonal peak with those of cases diagnosed during the other months of the year, survival analyses were performed to estimate observed and relative survival rates. We calculated survival time from the incidence date until date of death or date of last known vital status derived from the Belgian Crossroads Bank for Social Security on August 1, 2011. First, we analysed unadjusted observed survival (OS) using the Kaplan–Meier method. Cox proportional hazards regression models were then used to estimate adjusted hazard ratios (HRs) and 95%CIs. Unadjusted relative survival (RS) rates were calculated as the ratio of OS in the studied population to expected survival in a comparable group from the Belgian population, which was matched to the study population with respect to a set of main factors influencing cancer survival. Expected survival rates were obtained by applying the Ederer II method [25] on the Belgian population life-tables stratified by age, sex, and calendar period. Finally, we used Poisson regression to model the excess mortality due to melanoma and estimate the effect of seasonal variation after controlling for potential confounding factors [26].

In the BCR database, when month of diagnosis was unknown the reported incidence date was systematically coded 1st July. Since it was not possible to distinguish these cases from those that were truly diagnosed on 1st July, we excluded all cases with an incidence date of 1st July from incidence and survival analyses. Then, sensitivity analyses including these cases were conducted to appraise their impact on our findings. Missing values were taken into account by creating an extra "missing" category for each variable of interest, and we checked that our findings were not substantially modified when using multiple imputation techniques [27]. In all analyses, prognostic factors with a P-value <0.25 were retained in the multivariable models. All analyses were performed using the SAS software (version 9.1, SAS Institute, Cary, NC).

Table 1
Number of incident cases of cutaneous malignant melanoma (CMM) by month of diagnosis during 2004–2009 in Belgium and $R_{\text{month/January}}$* (95%CI).

Incidence cases of CMM			Dermatological consultations (2006–2009)	
Month	Total	$R_{\text{month/January}}$[a] (95%CI)	N	CMM/100 000
January	680	1.00	752.836	66
February	713	1.05 (0.99–1.11)	725.001	70
March	747	1.10 (1.04–1.16)	801.468	64
April	797	1.17 (1.11–1.24)	751.346	73
May	935	1.38 (1.30–1.45)	757.689	89
June	1112	1.64 (1.54–1.73)	797.967	96
July	799	1.21 (1.15–1.28)	620.332	91
August	847	1.25 (1.18–1.32)	637.708	91
September	864	1.27 (1.20–1.34)	730.790	80
October	860	1.26 (1.20–1.34)	792.775	79
November	732	1.08 (1.02–1.14)	728.706	69
December	696	1.02 (0.97–1.08)	641.292	78
Total	9782		8737.910	79

[a] Ratio of the number of cases diagnosed each month to that diagnosed in January.

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