Tumori, 95: 665-668, 2009

Strong seasonality in the diagnosis of skin melanoma in Italy: the Italian Network of Cancer Registries (AIRTUM) study

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ABSTRACT

Aim. To evaluate seasonality in the diagnosis of cutaneous melanoma in Italy.

Methods. A total of 16,284 invasive (and 1,235 *in situ*) cutaneous melanomas incident from 1978 to 2002 in 14 cancer registries belonging to the Italian Network of Cancer Registries (AIRTUM) was analyzed. We used the Walter and Elwood test to evaluate seasonality. The monthly distribution of diagnosis was evaluated for sex, skin site, melanoma morphology and period of diagnosis.

Results. The overall monthly diagnosis of invasive melanoma showed a statistically significant excess around the month of June. The same pattern was present for males and females, across age-groups and periods of time. All skin sites showed a cycling trend, melanoma of the head and neck peaked around April, all the others peaked around June. As regards morphologic types, a cyclic trend was evident for superficial-spreading melanomas (peak around July), for not-specified melanomas (June) and for other histotypes (June). Diagnosis of *in situ* melanoma peaked in September.

Conclusions. The present study showed that also in Italy melanoma diagnosis has a seasonal trend, with the peak in early summer. It seemed that summer UV exposure, acting both as a late promoter of malignant melanoma development and also increasing the visibility of pigmented skin lesion, may be relevant to explain such a peak.

Key words: diagnosis, melanoma, population-based, seasonality.

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Received January 19, 2009;
accepted April 28, 2009.

Introduction

Seasonality in cutaneous malignant melanoma (MM) diagnosis has been documented in several western countries, usually with a summertime peak[1-10]. The reasons for such seasonality are still unclear, even though several possible explanations have been suggested. A possible effect of public campaigns for early detection usually carried out during spring-summer has been emphasized[5]. Increased patient awareness and self-detection of suspected lesions due to summer clothing have also been documented[5], and even a short-term promoting effect of UV exposure has been suggested[5]. Although the amplitude of seasonality seems to increase with decreasing latitude[7], sparse data are available for Mediterranean countries[7,11-12].

To contribute to this issue, we analyzed data from a pool of Italian population-based cancer registries.

Materials and methods

Data were retrieved from the Italian Network of Cancer Registries (AIRTUM – www.registri-tumori.it) data base, which collects data from Italian general and specialized population-based cancer registries[13]. The present study focused on cutaneous MM diagnosed from 1978 to 2002. Overall, 16,284 invasive MM were included in the study. *In situ* MM (n = 1,235) were analyzed separately. For the present study, data from the following registries were used: Tuscany (incidence data from 1985 to 2002), Parma (1978-2002), Reggio Emilia (1996-2002), Modena (1988-2002), Ferrara (1991-2002), Sassari (1992-2002), Veneto (1987-2001), Torino (1985-2001), Milano (1999-2002), Latina (1990-2000), Macerata (1991-2000), Genova (1987-2000), Romagna (1986-2002) and Ragusa (1985-2002). Overall, the registries included in the study covered a population of about 10,730,000 inhabitants, which represented 18.8% of the total resident Italian population.

Histologic verification was available for 97.0% of MM (range among registries, 86.4-100%), and the mean incidence of cases known from death certificate only was 0.4% (range among registries, 0-0.9%).

Seasonality was evaluated by means of the Walter and Elwood test for seasonality of a binary outcome with a variable population at risk[14] implemented in the routine 'seast' of the software Stata (www.stata.com). The Walter and Elwood test adjusts for a varying population at risk[14]. The option 'exact', which forces the test to adjust for variable month length, was applied. The test considers observations in each sector (month) arising as moments around a unit circle, with the data corresponding to sector midpoints. The test assumes that within a year there are 12 periods (months) and that in each period n events occur from a population at risk of a certain size. Data may be represented as placed around a unit circle at points corresponding to the periods. The test produces two measures: α as the measure of the amplitude of the cyclic variation, and Θ which gives the direction of the maximum rate[14]. For the latter measure, single months are in counterclockwise position in the circle and correspond to the following mean angle: January 15°, February 45°, March 75°, April 105° and so on up to December 345°.

The monthly distribution of diagnosis was evaluated for invasive MM for: sex (males and females); site (head & neck, upper limb, lower limb, trunk, other, and not specified); morphology (superficial-spreading melanoma (ICDO-3 code = SSM), nodular melanoma, melanoma on malignant lentigo, acral lentiginous melanoma, other, not otherwise specified); period of diagnosis (1978-1982, 1983-1987, 1988-1992, 1993-1997, 1998-2002).

Results

The overall monthly diagnosis of invasive MM showed a statistically significant excess from the cyclic variation with the maximum around the month of June (represented by Θ values between 150 and 180) (Figure 1 and Table 1). The same pattern was present for males and females (Table 1). No differences from this early summer peak were evidenced either across age groups or across periods of time of diagnosis, except for 1978-1982, for which very few cases were available (Table 1). According to the site of MM onset, all main sites showed a cyclic trend: MM of the head and neck peaked around April, all the others peaked around June (Table 1).

Sex and site-specific results were similar to the mean value for both sexes together for upper limb (males $\Theta = 182.3$, $P = 0.02$, females $\Theta = 176.7$, $P < 0.001$) and for lower limb ($\Theta = 181.0$, $P = 0.036$, females $\Theta = 191.2$, $P < 0.001$), slightly different for head and neck (males $\Theta = 90.8$, $P < 0.001$, females $\Theta = 108.6$, $P < 0.001$) and especially for trunk (males $\Theta = 162.2$, $P < 0.001$, females $\Theta = 138.3$, $P < 0.001$), which showed an anticipated peak in May for females.

As regards MM morphologic types, a cyclic trend was evident for superficial-spreading melanomas (peak around July), for not otherwise specified melanomas (June) and for other histotypes (June), whereas no statistically significant cyclic trend was evidenced for nodular, acral, or lentigo melanomas.

The excess in June and July did not fill up the deficit in August. In fact, the mean incidence rate of the period June-August was significantly higher (1.09 cas-

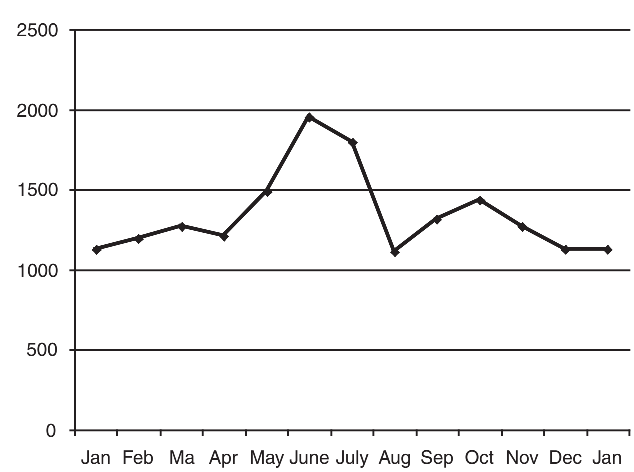

Figure 1 - Italian network of cancer registries (AIRTUM). Skin melanoma: Number of melanoma diagnosis according to the month of diagnosis, 1978-2002.

Table 1 - Italian Network of Cancer Registries (AIRTUM). Cutaneous melanoma, number of monthly mean diagnosis, amplitude (α) and direction (Θ) of the cyclic annual variation

	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec	Total	α	Θ	*P*
All invasive	1128	1193	1272	1209	1485	1949	1798	1113	1313	1433	1267	1124	16284	0.169	173.1	**
In situ	98	84	94	90	127	111	107	70	93	145	135	81	1235	0.062	256.8	**
Sex																
Males	560	594	602	548	707	911	842	523	585	672	575	546	7665	0.152	165.8	**
Females	568	599	670	661	778	1038	956	590	728	761	692	578	8619	0.186	178.5	**
Age (yr)																
0-44	293	321	325	316	376	462	461	272	338	373	341	296	4174	0.131	172.2	**
45-64	410	439	463	442	571	758	716	416	507	519	487	417	6145	0.197	177.2	**
65+	425	433	484	451	538	729	621	425	468	541	439	411	5965	0.167	168.8	**
Period																
1978-82	11	6	10	8	8	13	8	11	4	10	9	9	107	0.061	104.9	ns
1983-87	72	59	55	67	83	116	92	68	68	75	54	60	869	0.219	173.3	*
1988-92	201	201	225	222	244	355	307	196	233	264	245	192	2885	0.156	180.4	**
1993-97	323	359	411	377	476	638	569	303	398	481	386	346	5067	0.187	169.8	**
1998-02	521	568	571	535	674	827	822	535	610	603	573	517	7356	0.158	173.1	**
Morphology																
Nodular	119	117	104	110	125	141	133	104	88	113	99	100	1353	0.118	128.2	ns
SSM	318	392	434	391	496	610	657	357	467	507	438	348	5415	0.200	184.0	**
Lentigo	32	35	36	30	47	50	49	27	42	32	36	32	448	0.154	161.6	ns
ALM	7	11	8	11	10	11	10	7	7	7	14	7	110	0.128	105.2	ns
Other	147	158	159	157	193	278	230	143	161	176	144	126	2072	0.228	163.9	**
NOS	505	480	531	510	614	859	719	475	548	598	536	511	6886	0.151	173.6	**
Subsite																
Head&neck	163	164	146	137	165	205	178	89	131	171	153	131	1833	0.092	97.4	**
Upper limb	134	142	173	157	197	279	259	175	183	155	177	155	2186	0.241	179.2	**
Trunk	357	397	408	371	465	577	531	310	355	462	422	359	5014	0.118	155.0	**
Lower limb	268	300	319	323	387	577	529	366	405	397	317	271	4465	0.278	188.8	**
NOS	200	190	226	221	271	311	301	173	239	248	198	208	2786	0.157	165.1	**

SSM, superficial-spreading melanoma; ALM, acral lentiginous melanoma; NOS, not otherwise specified; ns, not significant.
*≤0.01; **<0.001.

es/100,000 subjects/year; 95% CI, 1.05-1.12) than that of the other months (0.85; 95% CI, 0.83-0.87).

The analysis was carried out separately for 1,235 *in situ* MM. For these tumors, a statistically significant cyclic trend peaking in October was documented. Only some of the Registries contributed with *in situ* MM. To exclude a possible selection bias, for registries that provided *in situ* MM we repeated the analysis also for invasive MM, and again the summer peak was evidenced (data not shown).

Discussion

The present descriptive study, carried out on a huge population-based case series, confirmed that also in Italy there was seasonality in the diagnosis of MM, with a peak of new diagnoses around June. This summer peak was present for males and females and through all the analyzed age groups. As evidenced in the US, there was a substantial seasonal variation in the diagnosis of almost all morphology types, except for nodular MM[3].

The peak in early summer was not explained as a consequence of an anticipated medical attendance before a holiday period. In Italy, in August there is the modal value of holidays, and in this month also most of the health services reduce their activity. The peak of diagnosis in early summer is much greater than the loss in August, and other explanations than just a 'holiday effect' need to be considered.

The effect of public campaigns for MM early detection (e.g., http://www.skincancerday.it) was one of the proposed explanations for this summer peak. The effect should have been enhanced during recent years according to the diffusion of such public health campaigns usually performed at the beginning of summer[5]. However, although these campaigns have increased over time, the summer peak was evidenced in the 80's, when the popularity and attention on skin MM and its early diagnosis was less than today.

In other studies, the early diagnosis effect was supported by a higher percentage of thinner MM[7-8] and by a better survival for MM diagnosed in summer than for those detected in other seasons[8]. Unfortunately, information on Breslow thickness and Clark level was not available in the present case series, and no evaluation of the relationship between seasonality and stage at diagnosis was possible. However, early diagnosis should be effective for both invasive and not yet invasive MM, but the summer peak was not documented for *in situ* MM[15], which on the contrary showed a peak of diagnosis in Autumn. Therefore, it seems that different explanations seem to work for invasive and *in situ* MM[15].

Increased patient awareness and self-detection of suspected lesions due to summer clothing has also been considered relevant among the possible explanations for the summer peak in diagnosis[10]. Data on site of MM were also analyzed for gender, assuming a difference in summer clothing and in the willingness to get a tan and to sunbathe between males and females. Although better visibility with less clothing during spring and early summer may be important, present data analyzed for subsites and gender did not confirm such an explanation. In fact, all the skin subsites, except for head and neck, showed the same summer peak. On the contrary, we would have expected a more evident effect for usually unexposed body sites (e.g., trunk) and also some differences between males and females (e.g., for lower limbs).

Another possible explanation of the summer peak may include the effect of intense sun exposure on the visibility, and consequently on the detectability of a melanocytic proliferation. An increased pigmentation in melanocytic nevi after intense UV exposure has been documented[16-17] as the proliferation and activation of epidermal melanocytes[16]. Therefore, intense sun exposure that occurred in summer may alert the patient himself or the physician about a pigmented lesion. If this was the case, and if a quite long exposure was necessary, then detectability of suspicious lesions would be more likely to occur at the end rather than at the beginning summer. On the one hand, this was true only for *in situ* MM, which peaked in October. On the other hand, a short-term UV-induced darkening effect may contribute to explain the peak of invasive MM.

Among the other possible explanations for the summer peak in MM diagnosis, there was also the possible effect of UV radiation as a promoting factor for the progression of MM during the late stages of development of the disease[5,9]. This hypothesis would also be in accord with the peak evidenced for invasive but not for *in situ* MM.

In conclusion, the present study confirmed that also in Italy MM diagnosis had a seasonal trend, with the peak in early summer. Presumably, seasonality is multifactorial in a disease which has been demonstrated to be pathogenetically heterogeneous. Among the other possible explanations, it seemed that summer UV exposure – acting both as a late promoter of MM development and also increasing the visibility of pigmented skin lesion – may be relevant to explain such a peak.

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