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Incidence and survival in patients with cutaneous melanoma by morphology, anatomical site and TNM stage: A Danish Population-based Register Study 1989–2011

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ABSTRACT

Introduction: The incidence of melanoma of the skin has risen in Denmark in recent decades, the increase being steeper from 2004. It is unclear whether this represents a true rise in incidence or whether it is caused by an increased awareness of the condition.
Methods: To assess whether the increase was characterised by early-stage melanomas and a higher proportion of melanomas with superficial spreading morphology, we studied all skin melanoma patients registered in the Danish Cancer Register 1989–2011 (n = 27,010) and followed up for death through 2013. Trends in age-standardised incidence by sex, subsite and morphology, relative survival, TNM stage distribution and stage-specific relative survival from 2004 were analysed.
Results: The incidence of melanoma more than doubled over 23 years. A steeper increase from 2004 was driven mainly by superficial spreading tumours, but the proportion of nodular melanomas in patients 50 years of age and over also increased significantly. The largest increase occurred for stage I tumours and for tumours on the trunk. From 1989–1993 to 2009–2011 the 5-year relative survival increased at 12% and 6% points for male and female patients, respectively.
Interpretation: Greater awareness, and thus lower stage at diagnosis (mediated by a large skin cancer prevention campaign from 2007), might explain part of the increase, but the increase in nodular melanoma also points to a genuine increase in the risk of melanoma.

1. Introduction

The incidence of cutaneous melanoma has risen considerably during recent decades in Caucasian populations around the world [1,2]. In Denmark, it is now the most frequent cancer type in women and the second most frequent in men aged 15–34 years [3].

Exposure to ultraviolet (UV) radiation is the leading cause of melanoma; other factors include age, skin type, numbers of naevi, genetic susceptibility, and family history of melanoma [4]. The reported increase in incidence suggests an increase in risk behaviour in terms of excessive recreational exposure to sunlight.

The increasing incidence of melanoma in several European regions, even among young people, has to some extent been attributed to an increasing number of thin lesions [1,5,6]. The most common and most rapidly increasing morphological subtype is the superficial spreading melanoma [5–10], a type associated with thinner tumours and intense, intermittent UV exposure [10]. The increasing incidence has involved both trunk and limbs [5,6,10,11], and among women the proportion of melanomas diagnosed on the trunk has recently increased in both Denmark and other Northern European countries [11–14], contrasting with previous years' characteristic pattern of higher incidence on the lower extremities.

In order to reduce incidence rates and deaths from melanoma in Denmark, a skin cancer prevention campaign, "Reduce your sun", was launched in 2007, targeting behaviour in the sun and promoting awareness of changes in moles. Meanwhile, the increasing incidence trend contrasts with stable melanoma

Abbreviations: ASR, age-standardised incidence rate; EAPC, estimated annual percentage change; ICSS, International Cancer Survival Standard; NOS, melanoma not otherwise specified; SSM, superficial spreading melanoma; UV, ultraviolet radiation.

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mortality, and it has therefore been questioned whether the recent incidence increase represents a true increase in risk, or whether it is due to better detection, greater awareness, and potential over-diagnosis [15–21].

This study therefore investigates the time trends in incidence and survival of melanoma of the skin among all patients diagnosed between 1989 and 2011 in the Danish population, including information about morphology and anatomical subsite and, from 2004, also TNM stage.

2. Materials and methods

2.1. Register data

Data on all persons in Denmark recorded in the Danish Cancer registry with a diagnosis of primary malignant melanoma of the skin (ICD-10 = C43) between January 1, 1989 and December 31, 2011 were obtained from the NORDCAN database (version 6.1) [3]. Morphology was classified according to ICD-O-3 [22] and categorised into five subgroups: superficial spreading melanoma (M-8743), nodular melanoma (M-8721), lentigo maligna melanoma (M-8742), melanoma not otherwise specified (M-8720) (NOS), and the remaining cutaneous melanomas (M-8730, M-8740, M-8741, M-8744, M-8745, M-8760, M-8761, M-8772, M-8780, M-8790). On the basis of topography codes, tumour locations were grouped into head and neck (C44.0–44.4), trunk (C44.5), upper limb and shoulder (C44.6), lower limb and hip (C44.7), overlapping regions and non-specified regions (NOS) (C44.8–44.9). Missing subsite was included in the latter category. Only the first invasive melanoma diagnosed for each person was included. From 2004, TNM information on cancer stage–reported either by clinicians or pathologists according to the Union for International Cancer Control version 6 [23]–was included in the Danish Cancer Register [23].

Incidence rates per 100,000 were age-standardised to the European population (ASR(E)). Evaluation of the incidence increase used estimated annual percentage change calculated as the fitted slope of the linear trend line in the logarithm of incidence rates.

Relative survival is defined as the observed survival divided by the expected survival in the patient group. Follow-up for death was made through 2013. The observed survival was estimated using the actuarial method and the expected survival by the Ederer II method [24]. The expected survival was estimated from population mortality rates stratified by sex, age and calendar time in 1-year intervals. Relative survival can be interpreted as the survival if death only from the cancer was possible. Since the age distribution of patients differ over time, the stage-specific 5-year relative survival figures were age-standardised with the International Cancer survival Standard as used in the Nordic Cancer Survival Study [25]. For the last period 2009–2011, where patients could not be followed for death for 5 years, the hybrid method was used, supplementing survival experience from previous cohorts where the patients had survived 1 year [26].

2.2. Statistical analysis

Data were analysed using SAS version 9.3 (SAS Institute Inc., Cary, North Carolina, USA). Relative survival was calculated using the STATA program strs [24].

3. Results

In total, 27,010 cases of primary incident invasive cutaneous melanoma were diagnosed between January 1, 1989 and December 31, 2011; cases were reported by age, morphology and subsite (Table 1). Gender-specific incidence trends by subsite are presented in Fig. 1.

A significant increase in the age-standardised incidence rates – 2.3-fold for men and 2.2-fold for women – was seen over the period 1989–2011. A stronger upward trend in incidence was seen from 2004. In 2011 the ASR(E) per 100,000 person-years at risk was 30.5 for men and 35.5 for women. A consistently higher incidence was seen among women (man/woman rate ratio of 0.9) across the entire study period. Among men, the trunk was the most common anatomical site across the entire period 1989–2011, and the incidence on the trunk remained persistently higher among men than among women. Throughout the entire study period the incidence involving the trunk increased 2.7-fold in men and 3.1-fold in women, with the steepest increase from 2004. Among women the most common subsites until 2008 were the lower limb and hip, whereafter the trunk took over.

Table 1
Number, percent distribution and age-standardised incidence, ASR(E), by age-group, morphology and subsite of Danish patients diagnosed with malignant melanoma of the skin stratified by sex and time-periods 1989–2003 and 2004–2011.

	Men						Women					
	1989–2003			2004–2011			1989–2003			2004–2011		
	N	%	ASR(E)	N	%	ASR(E)	N	%	ASR(E)	N	%	ASR(E)
Age												
All ages	6170	100.0	14.9	5904	100.0	23.5	7837	100.0	17.3	7099	100.0	27.8
0–49	1861	30.2	6.3	1454	24.6	9.4	3123	39.8	10.9	2883	40.6	19.2
50–59	1395	22.6	28.3	1048	17.8	35.5	1491	19.0	30.5	1194	16.8	41.1
60–69	1284	20.8	37.2	1593	27.0	64.4	1228	15.7	32.5	1355	19.1	53.0
70–79	1116	18.1	47.3	1162	19.7	87.0	1208	15.4	38.7	883	12.4	55.1
80+	514	8.3	51.6	647	11.0	103.6	787	10.0	38.2	784	11.0	66.7
Subsite												
Head & neck	807	13.1	1.9	763	12.9	2.9	789	10.1	1.4	597	8.4	1.9
Trunk	2883	46.7	7.0	3074	52.1	12.3	2017	25.7	4.8	2332	32.8	9.6
Upper limb & shoulder	711	11.5	1.7	630	10.7	2.5	1334	17.0	2.9	1133	16.0	4.2
Lower limb & hip	786	12.7	1.9	728	12.3	3.0	2847	36.3	6.4	2403	33.8	9.6
NOS & overlapping	983	15.9	2.4	709	12.0	2.8	850	10.8	1.9	634	8.9	2.4
Morphology												
SSM	2399	38.9	5.9	3680	62.3	14.8	3391	43.3	7.8	4756	67.0	19.3
Nodular	611	9.9	1.5	638	10.8	2.5	572	7.3	1.2	610	8.6	2.2
Lentigo	166	2.7	0.4	173	2.9	0.6	284	3.6	0.5	172	2.4	0.5
NOS	2958	47.9	7.1	1319	22.3	5.2	3552	45.3	7.8	1425	20.1	5.4
Remaining	36	0.6	0.1	94	1.6	0.4	38	0.5	0.1	136	1.9	0.5