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The Association Between Anatomic Site and Survival in Malignant Melanoma. An Analysis of 12,353 Cases from The Swedish Cancer Registry

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Abstract—*The relationship between site and survival in cutaneous malignant melanoma was investigated by a follow-up of* 12,353 *Swedish patients diagnosed in* 1960–1982. *In males, the poorest prognosis was found for tumors located on the scalp–neck region* (5-*year relative surival rate, RS* 51%), *followed by the lower extremity* (*RS* 66%) *and trunk* (*RS* 68%). *Among females, the poorest prognosis was noted for tumors located on the external ear* (5-*year RS* 71%), *trunk* (*RS* 78%) *and scalp–neck* (*RS* 78%). *The prognosis varied considerably between the sites of the head–neck region—for eyelid and facial lesions the prognosis was good, but for external ear and scalp–neck tumors it was poor. Multivariate analysis taking into account age and year of diagnosis showed the highest relative hazards* (*RH*) *for female lesions of the trunk* (1.40) *and male scalp–neck tumors* (1.65), *with the upper extremity used as reference* (*RH* = 1.00). *Except for lesions of the trunk, no significant differences in RH were found between the various sites after* 4 *years of observation.*

INTRODUCTION

THE BIOLOGICAL BEHAVIOR of malignant melanoma has received considerable interest in recent years. Most studies, with few exceptions [1, 2], have been carried out on patients registered at a hospital database. Several investigations have shown a strong correlation between a deeper level of invasion or increasing tumor thickness and a poorer prognosis [3–5]. The association between survival and clinical variables such as sex, age and anatomic site has, however, remained equivocal [6–11]. The discrepancies between results might to a large extent be due to the use of small and often selected patient materials, dissimilarities in the grouping of patients, short or incomplete follow-up and inadequate correction for causes of death other than malignant melanoma.

We used the Swedish Cancer Registry as a basis for a recent study to elucidate the relationship between sex and age at diagnosis and relative survival in malignant melanoma. The analysis revealed sex differences in the survival pattern, with a higher female survival, and a poorer prognosis with increasing age at diagnosis, most marked in male patients [12]. The purpose of the present study was to investigate the possible relationship between the anatomic site of the primary cutaneous malignant melanoma and relative survival in the same nationwide material of patients with long-term and almost complete follow-up. The possible confounding effect of age, sex and year of diagnosis in this context was paid special attention.

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MATERIALS AND METHODS

The Cancer Registry

The Swedish National Cancer Registry was started in 1958. All physicians are under obligation to report to the Registry any diagnosis of a malignant disease made on clinical grounds, based on surgically removed tissues, biopsies, cytologic specimens or autopsies [13]. The pathologists and cytologists also have to report separately any diagnosis of a malignant disease made on pathologic and cytologic specimens. Nearly 100% of all diagnoses of cancer in Sweden are reported in this way. In 95% of the cases the Registry receives notifications from both the clinician and the pathologist or cytologist [14]. The registry contains information about sex, age, location, time of diagnosis and eventually date of

death. The diagnoses are coded according to the International Classification of Diseases.

Every Swedish citizen is easily identified by a unique ten-digit national registration number (NRN). Through this number the Cancer Register is linked yearly with the National Causes of Death Register [15] and dates and causes of death are entered into the Cancer Register file. In the present study we also linked the Cancer Register with a register—updated until 1978—of living persons covering the total Swedish population. By these combined means we were able to reveal patients who were given an erroneous NRN at notification and thus could not be identified either in the Death Register or in the register of living persons.

Patients

All patients with a first malignant melanoma diagnosed between 1 January 1960 and 31 December 1982 were collected from the Cancer Register, a total of 13,171 cases. The average time of follow-up was 5 years, 8 months and the median time was 4 years. Omitted from the survival analyses were cases in which the diagnosis was made for the first time at autopsy (n = 504) and patients lost to follow-up (n = 314). The loss of patients to follow-up was due to an incomplete NRN (n = 72), to non-entry of patients in the Death Register and also in the Population Register covering all living persons (n = 228), or other different reasons (n = 14). Thus the proportion of patients with no follow-up was 2.5% and a total of 12,353 patients was left for analysis.

Statistical methods

The observed survival rates (OS) for all causes of death were calculated by means of the actuarial or life-table method [16], and the specific mortality from malignant melanoma was estimated by calculating the relative survival rate (RS) [17, 18]. RS is the ratio between the observed survival in the patient group and the expected survival rate in the general population, which was obtained from Swedish population tables by age (5-year intervals), sex and calendar year. The risk of dying from malignant melanoma per year was calculated as the complement of the annual relative survival rate [19]. The standard errors (S.E.) of the survival rates were calculated from Greenwood's formula [20] and the 95% confidence interval was used to show the uncertainty of the estimates.

The patients' survival was constantly compared with a comparable survival probability in the general population. The proportion of expected life lost was obtained as the ratio between the loss in length of life due to disease and the estimated expected length of life of the matched general population [18, 21].

To study the effect of the location of the malignant melanoma after taking into account year of diagnosis, sex and age, a Cox model [22] was used. Analyses of relative hazards were made for men and women separately, for both sexes combined, and also a generalized version was estimated in which the effects of the explanatory variables were allowed to vary with time in such a way that they remained constant within 4-yearly intervals. Age was included as a continuous variable. As the effect of this variable was found to be nonlinear, a second-order term was included for age in addition to the linear term. A likelihood-ratio test was used in the Cox model when testing for the overall effect of anatomic site.

RESULTS

Distribution by age and sex

The distribution of malignant melanomas by site, sex and age is shown in Table 1. The most frequent location was the trunk (n = 4048), followed by the lower (n = 3234) and upper extremity (n = 1670). In men the most common anatomic site was the trunk, followed up to the age of 70 years by the lower extremity and after that age by the face. In women younger than 70 years the lower extremity was the predominant site, but after this age the most frequent site was the face. The second most frequent site up to the age of 60 was the trunk. The mean and median ages of male and female patients were calculated for each site. It was found that tumors of the face, eyelid and external ear occurred mainly in older patients, whereas the patients with tumors of the trunk and lower extremity were somewhat younger (Table 2).

Site unspecified and multiple sites

The group of patients with malignant melanomas of unspecified sites accounted for 1185 (9.6%) of all patients. The relative survival rates for men and women in the site unspecified group were compared with those for all men and women respectively (Fig. 1). The difference in RS between the female groups of patients was small, indicating that there had been no selection of patients, with respect to survival, to the site unspecified group. The male site unspecified group had a slightly more favorable prognosis in the midpart of the follow-up period than all men, but the cumulative RS did not differ markedly over the whole period of follow-up, and bias due to selection is unlikely to have occurred.

The patients with malignant melanoma located on multiple sites had the poorest survival. The 5-year RS was 31.7% for men and 42.7% for women (Fig. 1). The risk of dying was highest during the first year after diagnosis, when the peak values were 32.3% (men) and 29.6% (women). The reason for the poor prognosis was probably that many patients

Table 1. Distribution of patients with a newly diagnosed malignant melanoma by sex, age and tumor site according to the ICD classification. Data reported to the Swedish Cancer Registry in 1960–1982

Site	<40 years				40–49				50–59			
	Male		Female		Male		Female		Male		Female	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Eyelid	2	0.2	3	0.2	5	0.5	2	0.2	8	0.6	5	0.4
External ear	16	1.7	10	0.8	11	1.2	6	0.5	28	2.1	14	1.1
Face	44	4.6	42	3.2	37	3.9	44	3.9	74	5.5	95	7.2
Scalp–neck	52	5.5	36	2.7	30	3.2	25	2.2	39	2.9	23	1.7
Trunk	428	45.0	370	27.9	501	53.1	324	28.5	754	56.4	297	22.6
Upper extremity	99	10.4	176	13.2	110	11.6	167	14.7	132	9.9	230	17.5
Lower extremity	194	20.4	544	40.9	144	15.3	457	40.2	137	10.3	525	40.0
Multiple sites	6	0.6	4	0.3	5	0.5	5	0.4	15	1.1	5	0.4
Sites unspecified	111	11.6	144	10.8	101	10.7	107	9.4	149	11.2	120	9.1
All sites	952	100.0	1329	100.0	944	100.0	1137	100.0	1336	100.0	1314	100.0

Site	60–69				≥70				All ages					
	Male		Female		Male		Female		Male		Female		Both sexes	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Eyelid	6	0.4	5	0.4	11	1.0	19	1.2	32	0.6	34	0.5	66	0.5
External ear	34	2.6	21	1.6	56	4.9	37	2.4	145	2.5	88	1.3	233	1.9
Face	137	10.4	197	15.1	282	24.5	496	31.7	574	10.1	874	13.1	1448	11.7
Scalp–neck	47	3.6	42	3.2	62	5.4	43	2.7	230	4.0	169	2.6	399	3.2
Trunk	628	47.6	222	17.0	339	29.5	185	11.8	2650	46.5	1398	21.0	4048	32.8
Upper extremity	166	12.6	237	18.2	112	9.7	241	15.4	619	10.8	1051	15.8	1670	13.5
Lower extremity	159	12.0	461	35.3	190	16.5	423	27.0	824	14.5	2410	36.2	3234	26.2
Multiple sites	11	0.8	2	0.2	10	0.9	7	0.4	47	0.8	23	0.4	70	0.6
Site unspecified	132	10.0	117	9.0	88	7.6	116	7.4	581	10.2	604	9.1	1185	9.6
All sites	1320	100.0	1304	100.0	1150	100.0	1567	100.0	5702	100.0	6651	100.0	12,353	100.0

Table 2. The median and mean ages (years, with standard deviation, S.D.) at the time of diagnosis of patients with malignant melanoma, by sex and tumor site

Site	Men			Women		
	Median Age	Mean Age	(S.D.)	Median Age	Mean Age	(S.D.)
Eyelid	60.5	61.6	(14.0)	72.0	67.6	(16.4)
External ear	65.0	63.2	(17.1)	67.0	63.8	(16.6)
Face	69.0	66.4	(15.7)	71.0	69.1	(14.5)
Scalp–neck	58.5	55.8	(18.0)	60.0	56.2	(16.8)
Trunk	55.0	53.9	(13.9)	50.0	50.4	(15.9)
Upper extremity	57.0	55.8	(15.2)	58.0	56.5	(15.9)
Lower extremity	56.0	54.3	(17.9)	53.0	53.1	(16.1)
Multiple sites	58.0	58.8	(14.4)	57.0	54.6	(19.4)
Site unspecified	55.0	53.9	(15.0)	53.0	53.4	(17.2)

classified as having multiple primary cutaneous melanomas in fact had metastatic disease at the time of diagnosis.

The site unspecified and multiple site groups were excluded from further analyses.

Anatomic site and survival in men

Among men, the relative survival rate was lowest for those whose malignant melanoma was located on the scalp–neck, intermediate for those with lesions of the trunk, lower extremity and external ear, and highest for those with lesions involving the face, upper extremity and eyelid (Fig. 2; Table 3). A stable RS—indicating that those who have survived represent a cured fraction—was found after about 6 years for melanomas located on the lower extremity, after 7 years on the upper extremity, and after 8 years on the scalp and neck; patients with trunk

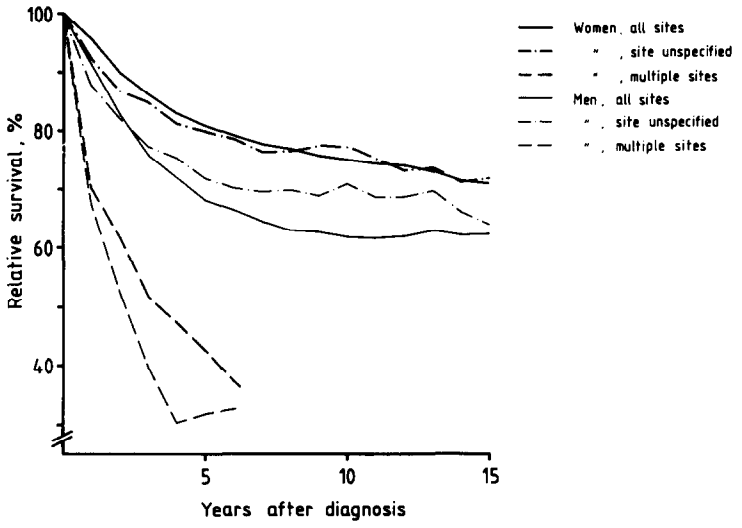

Fig. 1. Relative survival rates (RS) by sex for all malignant melanoma patients and for those classified as 'site unspecified' and 'multiple sites' respectively.

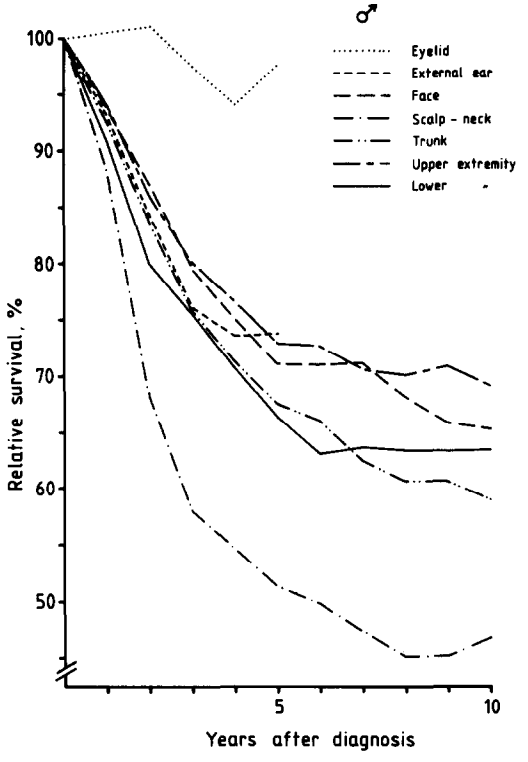

Fig. 2. Relative survival rates (RS) for men with malignant melanoma in Sweden 1960–1982, by tumor site.

melanomas were seemingly cured after about 10 years of survival.

The excess death risk for different locations varied with respect to year and magnitude of maximum values. The highest death risk occurred during the second year after diagnosis for malignant melanomas located on the scalp–neck region (22.8%), followed by the lower extremity (12.4%) and trunk (9.6%). During the third year after diagnosis lesions located on the external ear and face had their highest death risks, of 10.1% and 8.9% respectively, whereas for those on the eyelid there was a peak value of 3.5% during the fourth year.

Multivariate analysis was carried out for men with tumors of specified locations, with adjustments for age and year of diagnosis included in the proportional hazards model. The overall test for site revealed a highly significant difference ($P < 0.001$). The male patients with upper extremity lesions were used as a reference, since they were relatively numerous ($n = 619$) and had an age distribution similar to that of the total material. The highest relative hazard was found for scalp–neck melanomas (1.65, thus indicating a 65% higher death intensity than for upper extremity melanomas) and the lowest for those on the eyelid (0.46) (Table 4). Correction for year of diagnosis had only a minor effect on the relative hazards. Age, however, had a confounding effect regarding melanomas of the eyelid, external ear and face, for which a relatively poor prognosis was found in the univariate analysis and a better prognosis in the analyses with adjustment for the higher mean age in these groups.

The proportional loss of expected length of life was largest for patients with tumors of the scalp–neck region (61.2%), followed by the lower extremity (28.3%) and trunk (27.8%) (Table 5).

Anatomic site and survival in women

Among women the lowest relative survival rates were found in those whose malignant melanoma was located on the external ear, followed by the trunk and scalp–neck region. Upper and lower extremity lesions were associated with a higher RS and the best prognosis was found for facial and eyelid tumors. Compared with the male patients there was a continuous decrease in the relative survival for all sites over the entire period of observation, with the possible exception of scalp–neck

Table 3. Five- and 10-year relative survival (RS) with number of patients (n) in each group and 95% confidence intervals (CI) for men and women, by tumor site

	5 years						10 years					
	Men			Women			Men			Women		
Anatomic site	(*n*)	RS	95% CI	(*n*)	RS	95% CI	(*n*)	RS	95% CI	(*n*)	RS	95% CI
Eyelid	(23)	97.6	80.1–115.0	(16)	75.2	50.2–100.2	(13)	92.3	63.2–121.3	(6)	73.9	33.0–114.9
External ear	(67)	73.6	62.4–84.8	(45)	71.2	58.0–84.5	(33)	67.2	52.0–82.4	(20)	77.0	57.9–96.0
Face	(253)	71.0	64.9–77.2	(450)	85.7	81.2–90.1	(102)	65.3	56.1–74.4	(202)	82.2	75.1–89.2
Scalp–neck	(80)	51.3	43.1–59.6	(93)	77.8	69.6–86.0	(28)	46.8	36.4–57.3	(52)	72.3	61.4–83.2
Trunk	(1227)	67.6	65.3–69.8	(730)	77.7	75.0–80.5	(526)	58.9	55.9–61.9	(327)	67.4	63.5–71.2
Upper extremity	(282)	72.9	68.0–77.8	(553)	83.5	80.3–86.7	(122)	69.1	62.4–75.7	(264)	76.7	72.0–81.4
Lower extremity	(384)	66.4	62.0–70.7	(1338)	81.2	79.1–83.2	(165)	63.4	57.8–69.1	(723)	77.0	74.2–79.7

Table 4. Multivariate analysis of malignant melanoma, taking into account year of diagnosis and age of patient, by tumor site. Relative hazards (RH) with 95% confidence intervals (CI) for men, women and both sexes during the whole period of follow-up. The upper extremity location was used as reference

	Men		Women		Both sexes	
Site*	RH	95% CI	RH	95% CI	RH	95% CI
Eyelid	0.46	(0.25–0.84)	0.84	(0.48–2.32)	0.60	(0.40–0.90)
External ear	0.92	(0.71–1.20)	1.06	(0.77–1.46)	0.96	(0.78–1.17)
Face	0.85	(0.71–1.01)	0.77	(0.66–0.90)	0.81	(0.72–0.91)
Scalp–neck	1.65	(1.33–2.05)	1.15	(0.88–1.51)	1.45	(1.23–1.72)
Trunk	1.19	(1.03–1.38)	1.40	(1.21–1.62)	1.26	(1.14–1.40)
Upper extremity	1.00	(reference)	1.00	(reference)	1.00	(reference)
Lower extremity	1.16	(0.98–1.37)	1.03	(0.90–1.18)	1.06	(0.96–1.18)

*Overall test for site: Men: χ^2 (6) = 60.1, $P < 0.001$; women: χ^2 (6) = 66.7, $P < 0.001$; both sexes: χ^2 (6) = 110.6, $P < 0.001$.

Table 5. Estimation of expected length of life [yr (± S.E.)] and proportion of expected life lost (% lost) in male and female patients by tumor site

	Men			Women		
Anatomic site	yr	(±S.E.)	% lost	yr	(±S.E.)	% lost
Eyelid	17.7	(±3.8)	0.48	16.7	(±4.2)	0.79
External ear	13.0	(±1.4)	24.3	16.0	(±2.4)	17.3
Face	12.8	(±0.9)	13.8	15.6	(±0.8)	−2.1
Scalp–neck	8.8	(±1.2)	61.2	20.6	(±2.5)	18.8
Trunk	16.9	(±0.5)	27.8	19.9	(±0.8)	34.5
Upper extremity	18.3	(±1.4)	17.6	20.3	(±1.0)	19.7
Lower extremity	17.1	(±0.8)	28.3	23.2	(±0.5)	17.1

melanomas. The survival curve for patients with tumors at this anatomic site seemed to level off 6 years after diagnosis (Fig. 3; Table 3).

The risk of dying from the disease per year was highest during the first year after diagnosis for tumors located on the external ear (10.7%), and during the second year after diagnosis for those on the scalp–neck region (7.6%), followed by the trunk (7.5%), lower extremity (5.7%), upper extremity (5.6%) and face (4.6%).

The multivariate analysis for women showed a significantly different hazard by site ($P < 0.001$) in the overall test. The highest relative hazard in relation to the upper extremity was found for lesions of the trunk (1.40) and the lowest value for facial lesions (0.77) (Table 3). The results were only slightly affected by adjustment for year of diagnosis. Age had a confounding effect with regard to tumors of the eyelid, external ear and face, for which a better prognosis was noted in the multivariate than in the univariate analysis. In female trunk melanomas, age had the opposite effect, the relative hazard being higher following adjustment for age.

The expected length of life was most greatly

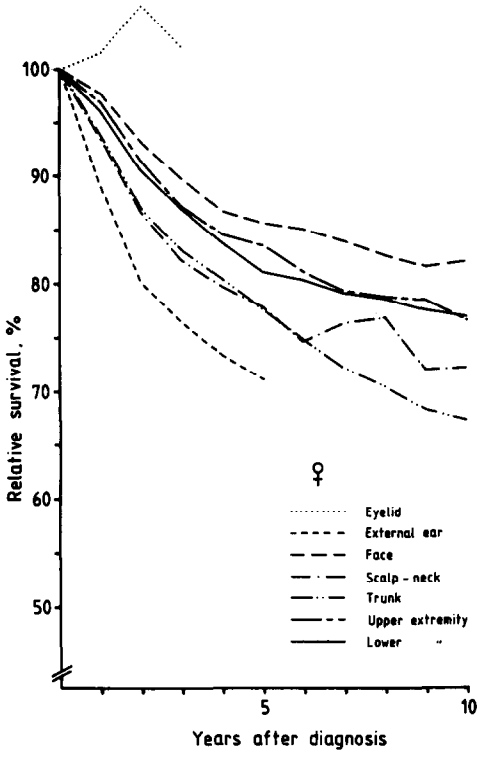

Fig. 3. Relative survival rates for women with malignant melanoma in Sweden 1960–1982, *by tumor site.*

influenced by melanomas located on the trunk, with a 34.5% reduction, followed by the upper extremity, scalp–neck region, external ear, and lower extremity (Table 5).

The impact of duration of follow-up after diagnosis by site

The association between tumor site and survival (relative hazard) was largely confined to the first 4-year period of follow-up. A significant relationship was found for the subsequent 4-year interval, however, in the overall test and for patients whose malignant melanoma was located on the trunk (Table 6).

DISCUSSION

The present study took advantage of a nationwide Cancer Registry, of long-term observation with complete follow-up through computerized linkage of registries, and of reliable figures for expected mortality in the general population. The extent of skin cancer notification to the Cancer Registry—99.3% of all cases [14]—and the low proportion of patients with no follow-up indicate that the results are representative of the entire Swedish population. Histopathologic reviews of malignant melanoma with application of uniform diagnostic criteria revealed that the proportion of benign lesions misclassified as malignant was only 3.7% in Sweden [23]. We conclude that the results obtained in this study cannot be attributable to biases in the notification, diagnosis or follow-up of malignant melanoma at different anatomic sites.

During the time period 1960–1982 the age-standardized incidence rate of malignant melanoma in Sweden increased among males from 3.0 (per 10^5) to 11.8 and among females from 3.7 to 11.2 [13]. There is no information on the stage of the disease in the Cancer Register, but we assume that more than 95% of the patients would have had localized disease (stage I) at the time of diagnosis. This assumption is based on figures from the Stockholm melanoma database, where it is found that out of 1674 consecutive patients recorded for the years from 1976 through 1986, 98% were in stage I at diagnosis (Ringborg U., unpublished).

The distribution by primary site in our material was similar to that reported by other investigators [1, 8, 24] and showed a predominance of lesions of the trunk among male patients and of lower extremity lesions in females. The sex difference in the distribution of skin melanomas may be due to differences in exposure to u.v. light. This idea is in accord with the finding that the distribution of primary melanomas does not seem to be proportional to the skin area but rather to the sun-exposed skin area [25]. The number of head–neck melanomas increased with increasing age, especially among females. One reason for this might be the relatively high proportion of lentigo maligna melanomas found in the face [26]. Lentigo maligna melanomas, which develop in lentigo maligna spots, are located on skin areas which have received the highest solar irradiation, and appear in the skin of elderly patients [27].

Several studies have shown an association between the anatomic site of the primary cutaneous melanoma and survival [28–34]. Extremity lesions have generally entailed a more favorable prognosis than trunk and head–neck lesions [1, 7, 28, 32–34], even when the tumor type and thickness have been taken into account [8, 35–38]. The importance of anatomic site of the primary lesion was further demonstrated by Day *et al.*, who showed by multivariate analyses that patients with melanoma located on the forearm and anterior upper arm have a significantly better prognosis compared to patients with melanoma located on the hand and posterior upper arm [39]. In a recent analysis of more than 500 patients, trunk and head–neck melanomas were found to be associated with a poorer prognosis than limb melanomas, even when consideration was paid to known prognostic factors such as sex, age, level of invasion, thickness of the vertical growth phase, ulceration, and the mitotic index (Clark W.H., personal communication). In consistency with these results we found in women a higher relative survival for lesions of the extremities than for trunk and head–neck lesions. In women, upper extremity lesions have been shown

Table 6. Multivariate analysis for completed 4-year periods after diagnosis of malignant melanoma, taking into account year of diagnosis and age of patient, by tumor site. Relative hazards (RH) with 95% confidence intervals (CI) for both sexes. The upper extremity location is used as reference

	0–3 years		4–7 years		8–11 years		≥12 years	
Site*	RH	95% CI	RH	95% CI	RH	95% CI	RH	95% CI
Eyelid	0.50	(0.30–0.86)	0.79	(0.34–1.80)				
External ear	0.99	(0.78–1.26)	0.80	(0.50–1.29)	0.67	(0.30–1.51)	1.15	(0.56–2.34)
Face	0.76	(0.66–0.88)	0.83	(0.64–1.08)	1.02	(0.68–1.53)	0.70	(0.43–1.14)
Scalp–neck	1.53	(1.26–1.86)	1.18	(0.78–1.80)	1.45	(0.74–2.83)	1.26	(0.60–2.63)
Trunk	1.27	(1.12–1.44)	1.37	(1.09–1.71)	1.09	(0.75–1.59)	0.81	(0.52–1.26)
Upper extremity	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
Lower extremity	1.10	(0.97–1.25)	1.04	(0.82–1.32)	0.96	(0.66–1.41)	0.83	(0.54–1.26)

*Overall test for site. 0–3 years: χ^2 (6) = 98.3, $P < 0.001$; 4–7 years: χ^2 (6) = 26.6, $P < 0.001$; 8–11 years: χ^2 (5) = 3.3, NS; ≥12 years: χ^2 (5) = 4.3, NS.

to have a better prognosis than those of the lower extremity [40]. In the present study no difference in survival was found, however, between women with upper and lower extremity lesions, either in the univariate or in the multivariate analysis when the relative hazards were adjusted for age and year of diagnosis. The estimated length of life was longer for female patients with lower extremity than for those with upper extremity lesions. When the malignant melanomas of the head and neck were subgrouped into those of the eyelid, external ear, face, and scalp–neck region, it was noted for women that tumors of the external ear and scalp–neck region implied a poor prognosis, similar to that in trunk melanomas. In contrast, tumors of the eyelid and face showed the best prognosis when compared with all other sites.

Contrary to the findings in the women, scalp–neck melanomas in the male group of patients showed the poorest prognosis, with a survival curve well separated from that of all other specified locations. The prognosis in men with lower extremity lesions was also poor and up to 10 years after diagnosis it was only slightly better than that in trunk lesions. Upper extremity lesions in men showed a relatively good prognosis, similar to that for lesions of the face. In men the findings for different melanomas of the head and neck region were similar to those in women, with a good prognosis for eyelid and facial tumors and a poor prognosis for those of the external ear and scalp–neck region.

The tumor thickness and level of invasion have been shown to be strongly related to survival [3–5]. Although these variables might differ between the sites and thus confound the analysis of survival, in the present nationwide study it was not possible to take them into account. One reason, however, for not adjusting for tumor characteristics is that the location itself could affect the biology of the disease and thus influence the aggressiveness of the tumors. The histologic characteristics of the tumors would in that case be regarded as intervening rather than confounding variables.

It has been reported that melanomas located on the hands and feet are associated with a worse prognosis than those of the rest of the upper and lower extremities [32, 39–41]. If these sites had been excluded from our material, the prognosis for extremity melanomas would probably have been somewhat better. It has also been reported that melanomas at specific subsites, such as the upper part of the back, the postero-lateral region of the arm, the posterior and lateral parts of the neck and the posterior region of the scalp have a worse prognosis than the rest of the trunk, upper extremity and head–neck region [39, 42–44]. Except for the scalp melanomas these results could not be reproduced when the malignant melanoma cases in the combined databases of Sydney and Alabama were analyzed [40, 45].

Our finding of a poor prognosis for malignant melanomas of the scalp–neck and external ear offer further support to the previous observations of differences in prognosis between subsites. The reasons for these differences are not known. One explanation for a poor prognosis in melanomas of the external ear might be that some of these tumors are located in the auricular canal and are thus difficult to discover, as a result of which these patients come late for treatment. It has been suggested that regional differences in lymphatic drainage and microcirculation could imply differences in host defense and in the development of micrometastases [46]. Additional explanations are required, however, for the finding, for example, that a scalp–neck location is a much more unfavorable characteristic in males than in females.

The results of the multivariate analysis showed that the association between various locations and

relative hazard was largely confined to the first 4 years of observation. This finding suggests that the relative excess associated with certain locations in the proportion of patients with systemic (and thus incurable) disease is fully manifested in terms of clinical presentation and death within this period of time.

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