Survival Differences Between Patients With Scalp or Neck Melanoma and Those With Melanoma of Other Sites in the Surveillance, Epidemiology, and End Results (SEER) Program

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Objective: To compare the prognosis of patients with scalp or neck (scalp/neck) melanomas with that of patients with melanomas at other sites in a large, population-based national data set controlling for known prognostic factors.

Design: Retrospective cohort study using US cancer registries that constitute the Surveillance, Epidemiology, and End Results 13 Registries (SEER-13) database.

Patients: A total of 51,704 non-Hispanic white adults in the United States with a first invasive cutaneous melanoma reported during the period 1992 to 2003.

Main Outcome Measures: Kaplan-Meier survival estimates were used to compare melanoma-specific survival by anatomic site at 5 and 10 years. Multivariate Cox models were used to examine the hazard ratio (HR) of melanoma-specific death associated with scalp/neck melanoma compared with melanoma of the extremities after controlling for other variables.

Results: The 5- and 10-year Kaplan-Meier survival probabilities for scalp/neck melanoma were 83.1% and 76.2%, respectively, compared with 92.1% and 88.7%, respectively, for melanoma of the other sites, including extremities, trunk, face, and ears (log-rank test; P < .001). In a multivariate Cox model, the patients with melanoma of the scalp/neck died of melanoma at 1.84 times (HR, 1.84; 95% confidence interval, 1.62-2.10) the rate of those with melanoma on the extremities, controlling for age, Breslow thickness, sex, and ulceration. Neither excluding cases of lentigo maligna and nodular melanoma nor controlling for lymph node involvement materially changed the HR for scalp/neck melanoma.

Conclusions: A notable survival difference remained between scalp/neck melanoma and melanoma of other sites even after adjustment for important prognostic factors. This finding has implications for screening and public health recommendations, and we urge physicians, physician assistants, nurses, and nurse practitioners to examine the scalp/neck carefully during routine skin examinations. Further studies are needed to understand the biological or environmental factors leading to survival differences by anatomic site.

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The American Cancer Society estimated that there would be 59,940 new invasive melanoma cases and 8110 deaths from melanoma in the United States in 2007.1 Melanoma incidence rates continue to increase, whereas rates for most other cancers have begun to decline.2 The American Joint Committee on Cancer has identified Breslow thickness, Clark level, ulceration, nodal and distant metastases, and serum lactate dehydrogenase as critical staging criteria.3 However, the prognostic significance of tumor location, especially the scalp or neck (scalp/neck) region, has been debated for decades.4-7 Understanding the role of anatomic site in melanoma survival is important for public health messages on skin awareness and sun protection. Moreover, because the role of screening in melanoma is considered important for early detection,8,9 it is useful to clarify those characteristics with prognostic significance.

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For editorial comment see page 538

Using the large-scale, population-based Surveillance, Epidemiology, and End Results (SEER) program, we give an update of SEER melanoma data and compare melanoma-specific survival of pa-
tients with melanomas of the scalp/neck vs that of patients with melanomas at other anatomic sites, controlling for important prognostic variables.

**METHODS**

Melanoma data were obtained from the National Cancer Institute’s SEER Program, Public-Use Data for the 1973-2003 period. This analysis was restricted to first invasive microscopically confirmed melanomas among white, non-Hispanic adults (≥20 years of age) collected by the SEER-13 Registries during the years 1992 to 2003 (Table 1). These 13 registries cover approximately 14% of the US population and include the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah; the metropolitan areas of San-Francisco–Oakland, San Jose–Monterey, and Los Angeles County, California; Atlanta, Georgia; Detroit, Michigan; Seattle–Puget Sound, Washington; 10 counties in rural Georgia; and the Alaska Native Tumor Registry. All cases from the Alaskan Native Tumor Registry were excluded because our analysis was restricted to white individuals (other ethnic groups have extremely low rates of melanoma).

Data abstracted from SEER included age at diagnosis, sex, anatomic site, Breslow thickness, Clark level, ulceration, lymph node involvement, and histologic subtype. Age at diagnosis and sex were available for all 51,704 cases. Melanomas with anatomic site coded in SEER as “overlapping lesion of skin” or “skin, not otherwise specified” (n = 2,097 [4%]) were considered to have an unknown anatomic site. Occult tumors (n = 248 [<1%]),...
Death from melanoma was the survival outcome of interest, and all remaining cases were treated as censored. Bivariate analyses were performed to examine the associations between death from melanoma and all the other study variables: the t test was used for normal continuous variables, the Wilcoxon rank sum test for nonnormal continuous variables, and the chi-square test for categorical variables. For survival analyses, cases diagnosed by death certificate or autopsy only (n=5) were excluded so that all cases had the potential to contribute survival time. Likewise, cases in which the patient was classified as dead at follow-up but with survival time recorded in SEER as 0 months (n=107) were recorded as having survival time of 0.5 months so that these cases could contribute survival time. The Kaplan-Meier product-limit method was used to estimate 5- and 10-year survival of melanoma-specific death for patients with scalp/neck melanomas vs those with melanomas of other sites, including extremities, trunk, face, and ears. Survival curves were compared with the 2-sided log-rank test.

A multivariate Cox proportional hazards model was created to examine the relative effects of tumor characteristics on melanoma survival in the absence of other causes of death. Adjusted hazard ratios (HRs) were calculated from a full model that included age (continuous), sex (male or female), thickness (continuous), ulceration (absent or present), and site (extremities, trunk, face or ears [face/ears], and scalp/neck). Clark level was not included in the model because it was highly correlated with Breslow thickness. No variables used in modeling violated the proportional hazards assumption, and no notable interactions were detected between site and sex. Patients with melanomas of unknown anatomic site, thickness, or ulceration status (n=8846), as well as those patients alive at follow-up but with survival time recorded in SEER as 0 months (n=621), were excluded from the multivariable model. Because Garbe et al. suggested that patients with melanomas of the thorax, upper arm, neck, and scalp (TANS) sites have a worse prognosis than those with melanomas at other sites, a second model was created dichotomizing anatomic location into modified TANS sites as allowed by SEER coding, including trunk, arms, and scalp/neck, and other sites (ears, face, and legs).

Several additional multivariate Cox models were created during further analyses. The sample was stratified by age (<60 years and ≥60 years), and 2 models were created to examine the effect of site on survival in younger and older age groups. A third model included cases with known lymph node status (negative or positive) and controlled for this variable as well. Finally, models excluding cases known to be lentigo maligna melanoma (LMM), nodular melanoma (NM), or both LMM and NM were created. Histologic subtype and lymph node status variables were not included in our primary model because 41% of cases had histologic subtype recorded as “not otherwise specified,” and 37% of cases had unknown lymph node status. In addition, the literature suggests that patients with head/neck melanomas are less likely to undergo sentinel lymph node biopsy procedures than those with melanomas at other sites, which may result in a misclassification of lymph node status.

All P values were 2-sided, and P<.05 was considered statistically significant. Stata statistical software (release 9.0; StataCorp LP, College Station, Texas) was used for all analyses.

**RESULTS**

From 1992 to 2003, the SEER-13 Registry collected 51,704 cases of first invasivecutaneous melanomas among non-Hispanic, white adults (Table 2). The mean age at diagnosis was 55.5 years, and 56% of the patients were male. After excluding tumors with occult or unknown thickness, the median Breslow thickness was 0.64 mm (interquartile range, 0.38-1.25 mm). Forty-three percent of melanomas were located on the extremities, 34% on the trunk, 12% on the face/ears, 6% on the scalp or neck, and 4% had an unspecified site. Ulceration was absent in 87% of cases. Lymph nodes were negative in 57% of cases; however, 37% of cases were missing data on lymph node involvement. Although 41% of melanomas were recorded as “melanoma, not otherwise specified,” 40% were classified as superficial spreading melanoma, 8% as NM, and 6% as LMM.

When characteristics were compared between melanomas of the scalp/neck and melanomas of the extremities, trunk, face, or ears (“other sites”), several significant differences were identified (P<.001 for all comparisons). Patients with scalp/neck melanomas were older (mean age at diagnosis, 55.1 years vs 58.8 years), presented with thicker tumors (median thickness, 0.80 mm vs 0.63 mm), and were more likely to be male (74% vs 54%). In addition, melanomas of the scalp/neck were more likely to be ulcerated (7% vs 5%), to have positive lymph nodes (7% vs 4%), and to be classified as NM (10% vs 8%) or LMM (12% vs 6%).

Next, bivariate analyses were used to examine potential risk factors for melanoma-related death (Table 2).
mean age at diagnosis and median Breslow thickness were significantly greater among those who died from melanoma than among those who did not die from melanoma (60.0 years vs 55.0 years and 2.17 mm vs 0.60 mm, respectively; \( P < .001 \) for both comparisons). Fourteen percent of those with scalp/neck melanoma and 41% of those with melanomas at unknown sites died compared with only 6% of those with extremity melanoma, 8% with trunk melanomas, and 6% with face/ear melanomas. Male sex, presence of ulceration, and positive lymph nodes also seemed to be risk factors for melanoma-related death. The association of melanoma-related death in relationship to potential ambient UV radiation at residence of diagnosis was explored but found to be inconclusive.

More than 42% of patients were followed for at least 5 years. Kaplan-Meier melanoma-specific survival curves were significantly different between scalp/neck melanomas and those at other sites (log-rank test; \( P < .001 \) (Figure 1). The 5-year and 10-year Kaplan-Meier survival probabilities for patients with scalp/neck melanoma were 83.1% and 76.2%, respectively, compared with 92.1% and 88.7%, respectively, for those with melanomas at other sites.

Overall, 42,437 cases (81%) were included in our final multivariate Cox model. Patients excluded owing to missing data were older (57.6 vs 55.0 years; \( P < .001 \), more likely to be male (59% vs 55%; \( P < .001 \), and had a poorer chance of 5-year survival (74.4% vs 93.1%; \( P < .001 \)) than included patients. A significant difference in melanoma-specific survival by anatomic site persisted after controlling for age, thickness, sex, and ulceration in a multivariate Cox model (see Table 3 for \( P \) values). Patients with scalp/neck melanoma died from melanoma at 1.84 times (HR, 1.84; 95% CI, 1.62-2.10) the rate of patients with extremity melanomas, adjusted for other variables. Patients with melanomas located on the trunk (HR, 1.27; 95% CI, 1.16-1.40), but not those with melanomas of the face/ears (HR, 0.95; 95% CI, 0.83-1.09), also died from melanoma at faster rates than those with extremity melanoma. Older age, increasing Breslow thickness, male sex, and the presence of ulceration also independently predicted faster rates of melanoma-related death. Predicted melanoma-specific survival curves after adjusting for other variables are shown by anatomic site in Figure 2. Harrell’s C concordance statistic for this model was 0.82, thus demonstrating good predictive ability for melanoma survival. When location was dichotomized into modified TANS sites vs other sites, patients with melanoma at modified TANS sites died from melanoma at 1.14 times (HR, 1.14; 95% CI, 1.05-1.24) the rate of patients with melanomas at other sites, adjusted for age, thickness, sex, and ulceration.

After stratifying the cohort by age 60 years, the HR for scalp/neck melanoma compared with extremity melanoma adjusted for other variables was significant for both age groups but higher for those younger than 60 years compared with those 60 years or older (HR, 1.93; 95% CI, 1.62-2.34; and HR, 1.75; 95% CI, 1.47-2.08, respectively) (Table 4). Neither excluding known cases of LMM, NM,
or LMM and NM nor controlling for lymph node status materially changed the HR for scalp/neck melanoma compared with extremity melanoma (Table 4). Among those with known lymph node status, patients with positive lymph nodes died from melanoma at 4.81 times (HR, 4.81; 95% CI, 4.29-5.40) the rate of patients with negative lymph nodes. Excluding cases known to be LMM or NM; and to have positive lymph nodes than melanomas at other sites. Nevertheless, scalp/neck melanomas were classified as NM and LMM and persisted after controlling for Breslow thickness, ulceration, and lymph node status in our multivariate analysis. In addition, we noted that a higher percentage of scalp/neck melanomas were classified as NM and LMM histologic subtypes, so biological differences between melanomas at distinct sites may lead to variations in survival. However, excluding cases known to be LMM or NM from our Cox model did not change the HR for scalp/neck melanoma.

In the SEER program, scalp/neck melanomas represented 6% of melanomas but accounted for 10% of all deaths from melanoma (470 of 4634). Scalp/neck melanomas were more likely to be found on older male patients; to be thicker, ulcerated, and classified as LMM or NM; and to have positive lymph nodes than melanomas at other sites. Nevertheless, scalp/neck melanomas had nearly 2 times the rate of melanoma-specific death than extremity melanomas even after adjustment for age, sex, Breslow thickness, and ulceration. This survival difference was retained after controlling for lymph node status and excluding cases known to be LMM or NM. Patients with melanomas on the trunk had an intermediate survival rate between those with scalp/neck melanomas and those with extremity melanomas.

The reason for worse survival among patients with scalp/neck melanomas is unclear. The lymphatic drainage and vascular supply of the head/neck are rich and complex, which may facilitate the entry of melanoma cells into lymphatic and systemic circulation. Lymphatic drainage patterns of the head/neck can be unpredictable, leading to false-negative findings for sentinel lymph node biopsies and local recurrence. In addition, patients with head/neck melanomas have a markedly higher incidence of brain metastases than do those with extremity and trunk melanomas. Kienstra and Padhya suggested that melanomas of the head/neck may not receive adequate margin resection owing to cosmetic or functional concerns.

Scalp/neck melanomas, often hidden by hair, may have poorer prognosis as a result of late diagnosis. We noted that scalp/neck melanomas are thicker and more frequently have ulceration and positive lymph nodes at presentation; however, this cannot completely explain variations by anatomic site because survival differences persisted after controlling for Breslow thickness, ulceration, and lymph node status in our multivariate analysis. In addition, we noted that a higher percentage of scalp/neck melanomas were classified as NM and LMM histologic subtypes, so biological differences between melanomas at distinct sites may lead to variations in survival. However, excluding cases known to be LMM or NM from our Cox model did not change the HR for scalp/neck melanoma.

To our knowledge, this is the first article examining the role of anatomic site on melanoma prognosis in a large, population-based US cohort, such as the SEER program. Nonetheless, we are able to discuss our findings in the context of several published studies of more than 1000 patients using multivariate Cox modeling to elucidate the influence of scalp, neck, or head/neck location on melanoma prognosis. Three European population-based studies reached mixed conclusions. Thorn et al found that among 12 353 Swedish patients with melanoma, the highest relative hazards for death were for scalp/neck tumors in males and trunk lesions in females after controlling for age and year of diagnosis. Levi et al used data from 1229 patients in the Swiss canton of Vaud and
found that those with trunk lesions had notably worse prognosis compared with those with melanomas of the limbs. Patients with head/neck lesions had worse survival as well, but the difference was not statistically significant. The lack of significance may be because their sample contained fewer head/neck lesions \( (n=240) \) or because scalp/neck lesions were combined with other head lesions. Gillgren et al.\(^7\) used a computerized method to compare the prognosis of 1891 patients with melanomas in 24 anatomic sites without evidence of metastasis from the Stockholm-Gotland database of the National Swedish Cancer Registry. They found that patients with melanomas of the middle and lower back and supra-mammary and mammary areas to be at significantly higher risk for death; however, their study included only 50 patients with scalp/neck melanomas, of whom 15 died.

Several hospital-based studies have examined this association as well. Weinstock et al.\(^7\) performed a meta-analysis pooling more than 1400 patients from 6 studies that implicated the BANS (upper back, posterior arm, posterior neck, and posterior scalp) regions as higher-risk melanoma sites for intermediate-thickness melanomas (0.76-1.69 mm). A study\(^8\) of 1082 patients at 2 Italian centers corroborated this hypothesis. Law and Wong\(^9\) examined the BANS sites individually and noted that among those patients with melanomas without nodal metastases \( (n=2576) \), only those with melanomas of the scalp had a notably lower 5-year survival rate. Among patients with melanomas with nodal metastases \( (n=852) \), those with both scalp and neck melanomas had strikingly poorer prognoses than those with melanomas at other sites. Garbe et al.\(^10\), who investigated 5093 patients in 4 German centers, suggested that the TANS (thorax, upper arm, scalp, and neck) regions were actually the higher-risk melanoma sites compared with other anatomic locations. Our multivariate model comparing modified TANS sites (trunk, arms, neck, and scalp) with other sites also demonstrated a notable difference in survival. However, the difference in survival was not nearly as striking as that seen when scalp/neck melanomas were separated from other sites, including the trunk and arms.

Other studies have examined the effect of site on prognosis for large cohorts of patients with cutaneous melanoma of the head and neck. O’Brien et al.\(^11\) examined 998 patients receiving care at the Sydney (Australia) Melanoma Unit and noted that those with scalp melanomas had a substantially worse chance of survival than those with ear/face/neck melanomas, adjusting for patient and tumor characteristics, presence of positive lymph nodes and distant metastases, and treatment by elective lymph node dissection. Ringborg et al.\(^12\) examining 581 melanomas registered in the population-based Sweden National Cancer Registry for the 1959-1974 period, found that patients with melanomas of the scalp/near and auricle/external ear canal had notably worse prognosis than those with melanomas on the face, adjusting for other variables. However, Gillgren et al.\(^13\) found that, among 496 patients entered into that same registry from 1976 to 1994, anatomic site was no longer an independent predictor of survival after adjustment for other factors. Leong et al.\(^14\) noted that, among 614 patients receiving selective sentinel lymph node biopsy at multiple tertiary care medical centers, those with melanomas located on the scalp had more than 3-fold greater mortality than those with melanomas on the face. Most recently, Golger et al.\(^15\), analyzing 2218 head and neck melanomas from the provincial Cancer Registry of Ontario, Canada, found that patients with scalp/neck lesions were 53% more likely to die than patients with melanomas on the face. Although much of the literature is in accord with our conclusions, disagreement among studies may result from differences in sample sizes, in study populations, or in variables used in multivariate modeling.

This study has multiple strengths. The SEER program is a population-based registry that gathers data from multiple sources and performs continual quality control activities to ensure the collection of high-quality data.\(^16\) The SEER-13 program represents approximately 14% of the US population from several geographic regions.\(^17\) Our recent data, collected from 1992 to 2003, includes more than 50,000 cases of microscopically confirmed, invasive cutaneous melanoma, and over 80% of cases had pathology data, including Breslow thickness and ulceration.

This study also has several caveats. Our population was limited to non-Hispanic white adults with first invasive melanomas, excluding ocular and mucosal melanomas, and was geographically restricted to areas with primarily medium melanoma incidence. Therefore, although the characteristics of our study population are comparable with those of most patients diagnosed as having melanoma in the United States, these results may not be generalizable to other racial or ethnic groups, pediatric populations, or those living outside the United States. Also, because the scalp and neck are coded as 1 site in SEER, we were unable to examine these sites individually. Although some studies suggest that scalp melanomas have somewhat worse prognosis than neck melanomas,\(^18,20-24\) others have found similar survival rates for these sites\(^25\) or have grouped them together for analysis.\(^6,22,25\)

Overall, the prognosis for both scalp and neck melanomas seems to be poorer than for melanomas arising elsewhere.

In addition, our study is susceptible to selection bias, misclassification bias, and confounding. The SEER program meticulously collects data from a variety of sources, conducts extensive quality control activities, and releases data on a 2-year time delay to maximize ascertainment and to minimize misclassification and missing data.\(^26\) Even so, 2 sources of selection bias still remain: (1) thin melanomas are potentially underreported and (2) cases excluded from our multivariate model owing to missing data had poorer survival. However, because scalp/neck melanomas were thicker and more likely to have missing data than melanomas of other sites, we would expect the direction of these biases to be toward the null. Finally, although we controlled for a variety of factors to limit confounding, it is possible that treatment may differ by anatomic site affecting prognosis.

The recognition that scalp/neck location is associated with poorer melanoma survival has implications for screening and public health recommendations. We suggest that all full-skin examinations and future screening studies include a careful inspection of the scalp/neck. Perhaps hairdressers could be targeted with education about...
Acquisition of data: Ms Lachiewicz had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Lachiewicz, Wiggins, and Thomas. Acquisition of data: Lachiewicz, Wiggins, and Thomas. Analysis and interpretation of data: Lachiewicz, Berwick, Wiggins, and Thomas. Drafting of the manuscript: Lachiewicz, Berwick, and Thomas. Critical revision of the manuscript for important intellectual content: Berwick, Wiggins, and Thomas. Statistical analysis: Lachiewicz. Obtained funding: Lachiewicz. Administrative, technical, and material support: Lachiewicz, Wiggins, and Thomas. Study supervision: Thomas.

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