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Geographic Variation in Utilization of Sentinel Lymph Node Biopsy for Intermediate Thickness Cutaneous Melanoma

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Abstract

Background and Objectives—Sentinel lymph node biopsy (SLNB) is the standard for evaluation of the draining lymphatic basin for intermediate thickness melanoma. Despite this, SLNB has not been uniformly adopted. We hypothesized that there are geographic areas of the United States where patients are less likely to receive SLNB.

Methods—The Surveillance, Epidemiology, and End Results database was queried for patients who underwent surgery for intermediate thickness cutaneous melanoma (Breslow thickness 1.00 to 4.00 mm) from 2004 through 2008. Patients were categorized according to geographic area based on the reporting registry. Multivariate logistic regression models predicted use of SLNB.

Results—Entry criteria were met by 8957 patients. On multivariate analysis, patients from the South were less likely (OR 0.54, CI 0.48–0.62; $p < 0.001$) to receive a SLNB. Additional factors associated with a decreased likelihood of receiving a SLNB included head and neck primary tumor site, high or unknown serum LDH, Asian, Hispanic, Native American or unknown race, and increasing age.

Conclusions—Patients from the South were less likely to receive a SLNB for an intermediate thickness cutaneous melanoma. This report of geographic disparities on a national level should be confirmed locally to better guide interventions aimed at eliminating these disparities.

Keywords

melanoma; sentinel lymph node biopsy; geography; variation; disparities

INTRODUCTION

Determining a patient's lymph node status is the single most important prognostic factor for cutaneous melanoma [1]. Of clinically node negative melanoma patients, approximately 20% will harbor lymph node metastases [2]. Accurately determining the presence of lymph node metastases is essential, because these patients should be offered completion lymphadenectomy and adjuvant therapy. Developed and popularized by Morton in 1992, SLNB represents the current standard for evaluation of the draining lymphatic basin for

intermediate thickness (1 mm but 4 mm) melanoma [1], supplanting the technique of elective lymph node dissection [2, 3].

The status of the sentinel lymph node (SLN) accurately predicts the status of the draining lymph node basin [2–4]. In a multicenter randomized clinical trial, patients who received a SLNB did not have significantly improved melanoma-specific survival relative to those who received wide excision of their melanoma and observation of the lymph node basin [3]. Patients who received a completion lymphadenectomy due to a positive SLNB had superior melanoma-specific survival compared to those patients whose lymphadenectomy was delayed until the onset of clinically palpable disease, however [3].

Given the value of the SLN status to melanoma prognosis and treatment, national consensus treatment guidelines have advocated its use for intermediate thickness melanomas since 1998 [5]. Current guidelines suggest the use of SLNB for all melanomas > 1 mm thick [6]. Cormier *et al* demonstrated significant regional differences in adherence to national melanoma treatment guidelines leading to either undertreatment or overtreatment in as many as 48.7% of cases from 1998 to 2001 [7]. We therefore hypothesized that there would be geographic disparities in the performance of SLNB for intermediate thickness melanoma in certain areas of the United States where patients would be less likely to receive SLNB.

MATERIALS AND METHODS

We queried the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute for patients who underwent surgery for intermediate thickness cutaneous melanoma (Breslow thickness 1.00 to 4.00 mm) from 2004 through 2008. SEER collects cancer incidence, prevalence, and survival data from 17 population-based cancer registries representing 28% of the U.S. population. SEER furthermore provides information on patient demographics, primary tumor site, tumor morphology, stage at diagnosis, and first course of treatment. Current SEER registries consist of the states of Connecticut, Hawaii, Iowa, Kentucky, Louisiana, New Jersey, New Mexico, and Utah; the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, Seattle-Puget Sound, and San Jose-Monterey; and the Alaska Native Tumor Registry, rural Georgia, Greater California, and Los Angeles County. Patients were categorized according to geographic area (Midwest, Northeast, South, West) based on the reporting SEER registry (Table 1). Patients with mucosal melanoma, those without a biopsy-proven diagnosis, or information on whether or not a SLNB was performed, and those diagnosed at autopsy were excluded. Patients were identified as having had a SLNB only if this was specifically coded.

Multivariate logistic regression evaluated the predictive value of geographic area and other tumor- and patient-related factors on the likelihood of undergoing SLNB. Additional covariates evaluated included patient age, sex, race/ethnicity (white, black, Asian, Hispanic, Native American, unknown), primary tumor site (head and neck, upper extremity, trunk, lower extremity, other), T stage (I, II, III), tumor ulceration (yes, no, unknown), serum LDH (elevated, not elevated, unknown), and histology (acral lentiginous, amelanotic, desmoplastic, lentigo maligna, nodular, regressing, superficial spreading, epidermoid, nevus-associated). Likelihood of undergoing SLNB was reported as odds ratios (OR) with 95% confidence intervals (CI); significance was set at $p = 0.05$. All statistical analyses were done using STAT 11 (College Station, TX). Since information in SEER contains de-identified patient data, this study was exempt from institutional review board approval.

RESULTS

Entry criteria were met by 8,957 patients. Characteristics of the study population are summarized in Table 2. Briefly, the majority of patients were white (94%) males (61.3%) living in the Western geographic area (60.8%). The majority (77.2%) of patients had either superficial spreading or nodular melanomas; truncal (29.9%), head and neck (23.9%) and upper extremity (26.3%) sites were most common and nearly equally represented. Most patients had no associated tumor ulceration (71.5%). Only 60.2% of patients received a SLNB. The highest percentage of patients receiving a SLNB was from the Western geographic area (63.1%), while the lowest percentage was from the Southern geographic area (48%). On univariate analysis, the differences in rates of SLNB among various geographic areas were significantly different ($p<0.001$). The multivariate logistic regression model is summarized in Table 3. On multivariate analysis, patients from the South were less likely (OR 0.54, CI 0.48–0.62; $p<0.001$) to receive a SLNB. Additional factors associated with a decreased likelihood of receiving a SLNB included head and neck primary tumor site (OR 0.52, CI 0.46–0.59; $p<0.001$), high (OR 0.49, CI 0.33–0.73; $p<0.001$) or unknown (OR 0.38, CI 0.33–0.44; $p<0.001$) serum LDH, Asian (OR 0.28, CI 0.16–0.50; $p<0.001$), Hispanic (OR 0.58, CI 0.43–0.79; $p<0.001$), Native American (OR 0.19, CI 0.05–0.76; $p=0.019$) or unknown (OR 0.39, CI 0.27–0.55; $p<0.001$) race, and increasing age (OR 0.97, CI 0.97–0.98; $p<0.001$).

Factors associated with an increased likelihood of receiving a SLNB included: T stage II (OR 1.41, CI 1.17–1.70; $p<0.001$) and T stage III tumors (OR 1.35, CI 1.11–1.64; $p=0.003$), and those occurring on the lower extremity (OR 1.24, CI 1.07–1.43; $p=0.004$).

DISCUSSION

We identified geographic disparities in the use of SLNB for intermediate thickness cutaneous melanoma consistent with our hypothesis. Relative to patients in western areas of the United States, those in the south have a 46% decreased odds of receiving a SLNB. These data are consistent with those from Bilimoria et al who looked at use of SLNB among AJCC stage Ia and Ib/II melanoma according to health system and socioeconomic factors [8]. This analysis incorporated data from the National Cancer Data Base for 2004 and 2005. Rather than dividing the patients into geographic regions, the authors categorized cases by census tracts. Nevertheless, the authors found a decreased likelihood of patients in the south, with an odds ratio identical to our analysis. There were some differences between studies, however. Most of our patients came from Western regions of the United States, so we opted to use these patients as the referent population for analysis. Bilimoria et al used the Atlantic census tract as their referent population. Finally, while both of our studies demonstrated a decreased likelihood of patients from the south undergoing SLNB, Bilimoria found that patients in the Southeastern census tract did not. Bilimoria found that patients in the Pacific census tract were the most likely to receive a SLNB for stage Ib/II melanoma. Another study by Lane et al similarly utilized the SEER database to assess regional differences in the use of SLNB [9]. Although the authors only analyzed 1 year of data (2004), and did not perform a multivariate analysis, they similarly concluded that patients from the South received lower rates of SLNB compared to the West (83.6% vs. 60.2%). Unfortunately, these authors only provided descriptive statistics and did not perform a multivariate analysis to assess the impact of known patient and tumor-specific variables that may influence the use of SLNB. None of these studies, including our own, were designed to determine the reasons for these geographic disparities, but we believe them to be multifactorial.

While the population reporting to SEER is comparable to the general population with respect to measures of poverty and education, it is more urban than the general United States

population. Patients living in rural areas are less likely to receive standard care and more likely to have poorer survival than those living in urban areas [10–12]. It is possible that patients reporting to Southern SEER registries represented a more rural cohort and had less access to surgeons skilled at using this technique. These areas may be less likely to have academic institutions or National Cancer Institute-designated cancer centers that are more likely to utilize SLNB for lymph node staging. Garreau et al studied the adoption of the SLNB technique among surgeons in Oregon via mailed questionnaire and found that surgeons in smaller hospitals and rural areas were less likely to incorporate SLNB into their practice [13]. Some researchers have documented that minority populations are more distrustful of their healthcare providers [14, 15]. It is possible, then, that patients from the South are more likely to be racial/ethnic minorities that do not desire a SLNB, although it is suggested to them. We think this is unlikely. The majority of patients in the current study were white, regardless of geographic area, with a range of 93.1% in the Midwest to 94.5% in the South, so there seems to be relatively equal distribution of non-white, racial/ethnic minority populations. Our study did demonstrate that Asian, Hispanic, and Native American (but not black) patients had a lower likelihood of receiving a SLNB, despite small numbers of individuals in these groups.

We also found other predictors for the use of SLNB. Primary tumors originating from the head or neck had a 48% decreased odds of undergoing a SLNB. There are several potential reasons for this. It is possible that because lymphatic mapping and the SLNB procedure itself may be more challenging in the head and neck region compared to other lymph node basins, fewer providers overall may offer it [16–18]. Another possibility is that more of these procedures are performed by otolaryngologists who are less familiar with SLNB than their surgical oncology or general surgery colleagues. By comparison, a primary melanoma site on the lower extremity, with its relatively straightforward mapping to the inguinal nodes, was found to be a predictor of an increased likelihood of receiving a SLNB. An elevated serum LDH was also associated with a decreased likelihood of undergoing SLNB. An elevated LDH is a non-specific indicator, but may be a surrogate marker of melanoma or non-melanoma-related systemic disease. LDH may be elevated in other cancers, such as lymphoma, liver disease, or in cases of HIV infection [19–22]. Such comorbidities may influence a physician not to offer, or a patient not to accept, a SLNB. Consistent with a body of literature indicating that older patients often do not receive optimal or standard care [23–25], we found that increasing age was associated with a decreased likelihood of receiving a SLNB. For each increasing year in our model, a patient would have a 3% decreased odds of receiving a SLNB.

Our study has limitations to be expected from a data source such as SEER. Most notably, SEER does not provide information on individual patient comorbidities, patient preference, or history of prior wide excision that may influence the recommendation to perform a surgical procedure, such as SLNB. Although our sample size was fairly robust, we only included patients diagnosed with intermediate thickness melanoma from 2004 through 2008. We chose to restrict our analysis to these years for the following reasons: 1) To give enough time from the publication of national consensus guidelines in 1998 and the American Joint Committee on Cancer 6th edition cancer staging manual in 2002 (both advocating the use of SLNB) for the use of SLNB to permeate into clinical practice; 2) To provide an up-to-date assessment of geographic and regional disparities in the use of SLNB; and 3) To take advantage of more complete data fields in SEER regarding documentation of SLNB. Additionally, our data may be subject to selection bias, since we only included patients for whom data was complete regarding whether or not SLNB was performed. Such a decision provided us with a more homogeneous population and allowed us to exclude patients that underwent a full lymphadenectomy, likely because of clinically palpable nodal disease. Nevertheless, we may have excluded patients that would have otherwise altered our

measured outcomes. Finally, SEER does not provide information on patient-level socioeconomic status such as monthly/yearly income or surrogates of socioeconomic status like education level or insurance status. Such factors may influence access to optimal cancer care. The status of the SLN represents the most important prognostic factor for melanoma. SLNB is also associated with decreased rates of morbidity relative to complete lymphadenectomy and may be used to stratify patients for subsequent treatment and surveillance. It is essential that the patients with appropriate indications for SLNB have access to this procedure and that it is performed by a surgeon well-versed in its technique.

CONCLUSIONS

We have identified a geographic area of the United States with low rates of SLNB for intermediate thickness melanoma. These geographic disparities on a national level should be confirmed locally to better guide interventions aimed at eliminating these inequalities.

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Synopsis

Sentinel lymph node biopsy (SLNB) is standard for evaluation of the draining lymphatic basin for intermediate thickness melanoma. We have identified factors associated with use and avoidance of this procedure, including geographic region.

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Table 1

Geographic areas of the reporting Surveillance Epidemiology and End Results registries.

West	Midwest	Northeast	South
Hawia <i>i</i>	Detroit	Connecticut	Atlanta
New Mexico	Iowa	New Jersey	Rural Georgia
San Francisco-Oakland			Kentucky
Seattle-Puget Sound			Louisiana
Utah			
Los Angeles			
San Jose-Monterey			
Alaska Native Registry			
Greater California			

Table 2

Patient, tumor and treatment-related factors of the study population (N=8957) with intermediate thickness cutaneous melanoma.

Variable		N (%)
Age (median = 63 yr)	<i>1 to 39</i>	950 (10.6)
	<i>40 to 49</i>	1195 (13.3)
	<i>50 to 59</i>	1703 (19)
	<i>60 to 69</i>	1789 (20)
	<i>70 to 79</i>	1785 (19.9)
	<i>80 or more</i>	1535 (17.1)
Sex	<i>Female</i>	3470 (38.7)
	<i>Male</i>	5487 (61.3)
Race/Ethnicity	<i>Asian</i>	55 (0.6)
	<i>Black</i>	41 (0.5)
	<i>Hispanic</i>	255 (2.9)
	<i>Native American</i>	9 (0.1)
	<i>Unknown</i>	182 (2)
	<i>White</i>	8415 (94)
T stage	<i>T1</i>	575 (6.4)
	<i>T2</i>	5116 (57.1)
	<i>T3</i>	3266 (36.5)
Tumor Histology	<i>Acral Lentiginous</i>	292 (3.3)
	<i>Amelanotic</i>	137 (1.5)
	<i>Desmoplastic</i>	784 (8.8)
	<i>Epidermoid</i>	137 (1.5)
	<i>Lentigo Maligna</i>	466 (5.2)
	<i>Nevus-associated</i>	147 (1.6)
	<i>Nodular</i>	2594 (29)
	<i>Regressing</i>	81 (0.9)
	<i>Superficial Spreading</i>	4319 (48.2)
	<i>Unknown</i>	137 (1.5)
Tumor Location	<i>Arm</i>	2358 (26.3)
	<i>Head/Neck</i>	2143 (23.9)
	<i>Leg</i>	1761 (19.7)
	<i>Trunk</i>	2674 (29.9)
	<i>Overlapping/Other</i>	22 (0.2)
Tumor Ulceration	<i>No</i>	6407 (71.5)
	<i>Yes</i>	2320 (25.9)
	<i>Unknown</i>	230 (2.6)
Serum LDH	<i>High</i>	127 (1.4)
	<i>Normal</i>	1361 (15.2)

Variable		N (%)
	<i>Unknown</i>	7469 (83.4)
Geographic Area	<i>West</i>	5447 (60.8)
	<i>Midwest</i>	1134 (12.7)
	<i>Northeast</i>	1024 (11.4)
	<i>South</i>	1352 (15.1)
SLNB	<i>Yes</i>	5390 (60.2)
	<i>No</i>	3567 (39.8)

Table 3

Multivariate logistic regression model predicting the use of sentinel lymph node biopsy (SLNB).

<i>Variable</i>		Odds Ratio (95% CI)	P value
Age		0.97 (0.97–0.98)	<0.001
Sex	<i>Female</i>	Referent	Referent
	<i>Male</i>	1.09 (0.99–1.20)	=0.089
Race/Ethnicity	<i>White</i>	Referent	Referent
	<i>Asian</i>	0.28 (0.16–0.50)	<0.001
	<i>Black</i>	0.64 (0.31–1.32)	=0.227
	<i>Hispanic</i>	0.58 (0.43–0.79)	<0.001
	<i>Native American</i>	0.19 (0.46–0.76)	=0.019
	<i>Unknown</i>	0.39 (0.27–0.55)	<0.001
T stage	<i>T1</i>	Referent	Referent
	<i>T2</i>	1.41 (1.17–1.70)	<0.001
	<i>T3</i>	1.35 (1.11–1.64)	=0.003
Tumor Histology	<i>Superficial Spreading</i>	Referent	Referent
	<i>Acral Lentiginous</i>	0.94 (0.72–1.23)	=0.673
	<i>Amelanotic</i>	1.09 (0.75–1.57)	=0.650
	<i>Desmoplastic</i>	1.11 (0.94–1.32)	=0.228
	<i>Epidermoid</i>	0.83 (0.67–1.02)	=0.078
	<i>Lentigo Maligna</i>	1.11 (0.99–1.24)	=0.078
	<i>Nevus-associated</i>	0.99 (0.62–1.60)	=0.983
	<i>Nodular</i>	1.34 (0.91–1.97)	=0.140
	<i>Regressing</i>	0.81 (0.56–1.16)	=0.242
	<i>Unknown</i>	0.99 (0.62–1.60)	=0.983
Tumor Location	<i>Trunk</i>	Referent	Referent
	<i>Arm</i>	1.12 (1.00–1.27)	=0.06
	<i>Head/Neck</i>	0.52 (0.46–0.59)	<0.001
	<i>Leg</i>	1.24 (1.07–1.43)	=0.004
	<i>Overlapping/Other</i>	0.48 (0.19–1.21)	=0.121
Tumor Ulceration	<i>No</i>	Referent	Referent
	<i>Unknown</i>	0.91 (0.68–1.20)	=0.496
	<i>Yes</i>	1.03 (0.92–1.14)	=0.638
Serum LDH	<i>Normal</i>	Referent	Referent
	<i>High</i>	0.49 (0.33–0.73)	<0.001
	<i>Unknown</i>	0.38 (0.33–0.44)	<0.001
Geographic Area	<i>West</i>	Referent	Referent
	<i>Midwest</i>	1.03 (0.89–1.18)	=0.72
	<i>Northeast</i>	0.89 (0.77–1.02)	=0.099
	<i>South</i>	0.54 (0.48–0.62)	<0.001