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Stratifying SLN incidence in intermediate thickness melanoma patients

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Abstract

Background—Guidelines for melanoma recommend sentinel lymph node biopsy (SLNB) in patients with melanomas 1 mm thickness. Recent single institution studies have found tumors <1.5 mm a low-risk group for positive SLNB.

Methods—A retrospective review of the Sentinel Lymph Node Working Group multicenter database identified patients with intermediate thickness melanoma (1.01–4.00 mm) who had SLNB, and assessed predictors for positive SLNB.

Results—3460 patients were analyzed, 584 (17%) had a positive SLNB. Univariate factors associated with a positive SLNB included age <60 ($p < .001$), tumor on the trunk/lower extremity ($p < .001$), Breslow depth ≥ 2 mm ($p < .001$), ulceration ($p < .001$), mitotic rate $\geq 1/\text{mm}^2$ ($p = .01$), and microsatellitosis ($p < .001$). Multivariate analysis revealed age, location, and Breslow depth as significant predictors. Patients 75 with lesions 1.01–1.49 mm on the head/neck/upper extremity and 1.5–1.99 mm without high-risk features had <5% risk of SLN positivity.

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None.

Conclusions—Intermediate thickness melanoma has significant heterogeneity of SLNB positivity. Low-risk subgroups can be found among older patients in the absence of high-risk features.

1. Introduction

An estimated 76,380 new cases of melanoma will be diagnosed in the United States in 2016.¹ These patients will undergo a comprehensive assessment of their disease to determine their prognosis and potential treatment. The most important prognostic factor is the presence of lymph node metastases.^{2,3} Historically, elective lymph node dissection was used to determine whether the patient had lymph node metastases but subsequently lymphoscintigraphy had demonstrated that elective lymph node dissection may miss a significant amount of disease in the face of the morbidity of lymph node dissection. Lymphatic mapping of melanoma showed nodal metastases from cutaneous melanoma were not random but followed specific lymphatic pathway(s), and the histology of the sentinel node(s) removed accurately reflected the biology of the remaining lymphatic basin.⁴ A variety of studies embarked on proving the feasibility and efficacy of sentinel lymph node biopsy (SLNB) for identifying patients at high-risk of nodal metastases and targeting patients in whom completion lymphadenectomy may be warranted.⁵ SLNB has been found to have prognostic value and it has been shown to offer a survival benefit over observation alone.^{2,6,7}

Staging of melanoma using SLNB has revolutionized the field, improving patient selection for lymph node dissection. Lymph node metastasis is the single most important prognostic factor for patients with localized melanoma.^{2,8} In patients with thin melanomas (<1 mm), sentinel lymph node biopsy is considered for those with melanomas > 0.75 mm and/or those with high risk features.^{9–12} Prior studies have reported SLNB+ rates of around 15–25% in intermediate thickness melanoma.^{2,13–15} Overall, sentinel lymph node biopsy has been associated with low morbidity compared to elective lymphadenectomy.^{16,17}

National Comprehensive Cancer Network (NCCN) guidelines currently recommend SLNB for all patients with intermediate thickness melanomas (1.01–4.00 mm).¹⁸ Recently published work by Bartlett et al. has identified subgroups of patients (absent LVI, absent mitoses, and either absent regression or age of 60 and older) with intermediate thickness melanoma who may be at similarly low risk (<5%) for a positive sentinel lymph node biopsy as thin melanoma groups.¹³ Particularly in the older population of patients, the question arises as to who may be spared a SLNB. Similarly, prior papers have found the presence or absence of high-risk histopathologic features such as ulceration and lymphovascular invasion to be predictors of a positive sentinel lymph node biopsy.^{14,19,20} To answer these questions, our group queried a large, retrospective, multicenter database.

Our study had two aims: first, could we stratify patients with intermediate thickness melanoma based upon prognostic factors to determine sentinel lymph node positivity to identify clinically significant subgroups which may be groups of patients in clinical practice who may be spared a sentinel lymph node biopsy based on a low pre-test probability of a positive sentinel node. Second, certain patients (75) are burdened with significant co-

morbidities, can we identify subgroups that may be at low risk for a positive SLNB and therefore have the opportunity to decrease their surgical morbidity. The age of 75 was a group consensus regarding the age at which co-morbidities were more likely to influence clinical decision making.²¹

2. Materials and methods

The Sentinel Lymph Node Working Group (SLN WG) consists of 7 member institutions. All members obtained approval from their respective institutional review boards before submitting patients for this retrospective study. Informed consent was obtained from all patients except where waiver of informed consent was granted by the institutional review board for retrospective data collection. The SLN WG database is maintained at the Mayo Clinic in Phoenix, Arizona. Patient data are submitted by each member institution through a password-protected Web site into this standardized database.

SLN biopsy was performed as previously described using blue dye, radioactive colloid, or both. Indications for SLN biopsy and specific operative techniques were determined by individual investigators. In general, the investigators in this multicenter study used a combination of radioactive colloid and blue dye with preoperative lymphoscintigraphy.

Patients from 1993 to 2015 were identified with intermediate thickness melanoma (1.01–4.0 mm) and their demographic information and tumor characteristics were analyzed for factors predictive of sentinel lymph node positivity. A positive sentinel lymph node was defined as any malignant cells identified in the specimen.

2.1. Statistical analysis

Descriptive statistics were used to summarize results by negative or positive sentinel lymph node biopsy. Patient demographics and tumor characteristics were compared between categories by analysis of variance (ANOVA) for continuous variables or chi-square tests for categorical variables. Statistical analysis to assess the predictive variables included univariate logistic regression and multivariable forward selection logistic regression models. Variables in which $p < .20$ in univariate analysis were considered for inclusion in the multivariable model. This included age group, location, thickness, Clark level, ulceration, lymphovascular invasion and mitotic rate. Adjusted odds ratios (OR) and 95% confidence intervals were calculated. A second multivariate analysis was performed using age of 75 to determine predictive factors in this population. Two-sided p -value $< .05$ were considered statistically significant.

3. Results

3.1. Patient and tumor characteristics (Table 1)

A total of 3460 patients were identified and included in the analysis. Overall positive sentinel lymph node biopsy (SLNB) rate was 17%. The median age was 57.8 (mean 57.1). 59% ($n = 2027$) were male, and 99% ($n = 3177$) patients were Caucasian. Patients with positive SLNB were more likely to be younger ($p < .0001$). No difference was seen in positive SLNB rates regarding gender ($p = .47$) or race ($p = .92$). Patients with tumors

located on the head or neck (HN), or upper extremity (UE) were significantly less likely to have a positive SLNB than patients with lesions located on the trunk (TK) or lower extremity (LE) ($p < .0001$). Thicker lesions were more likely to have a positive SLNB ($p < .0001$). In the subgroup of patients with melanoma between 1.01 and 1.99 mm, a statistical difference was found between patients from 1.01 to 1.49 mm and 1.5–1.99 mm ($p < .0001$). Melanomas with a Clark's level of IV/V were more likely to be associated with a positive SLNB ($p = .0034$). Ulceration ($p < .0001$), lymphovascular invasion ($p < .0001$), mitotic rate ($p = .011$), and microsatellitosis ($p < .0001$). Tumor regression ($p = .35$) and tumor infiltrating lymphocytes ($p = .30$) were not found to have an association with SLN status, however information regarding tumor regression was available in 50% of patients ($n = 1723$), and 38% of patients had tumor infiltrating lymphocyte information available ($n = 1322$).

3.2. Predictive factors for a positive sentinel lymph node biopsy (Table 2)

Age, location, Breslow thickness, Clark level, and high-risk features such as ulceration, lymphovascular invasion, mitotic rate and microsatellitosis were all significant in univariate logistic regression analysis. Significant factors included: age 60–74 and age ≥ 75 , location on the lower extremity and trunk, Clark level IV/V, ulceration, lymphovascular invasion, mitotic rate $\geq 1/\text{mm}^2$, and microsatellitosis, Breslow thickness 2–2.99 mm vs 3–4.00 mm. Breslow thickness was also found to be predictive of a positive SNLB.

The factors that remained predictive of sentinel lymph node positivity in multivariate analysis were: age 60–74, age ≥ 75 , location on the lower extremity or trunk, Breslow thickness >2 , and microsatellitosis.

We then evaluated a model focusing on the effect of a poor prognostic features (ulceration, lymphovascular invasion, mitotic rate ≥ 1 , and/or microsatellitosis) as determined by the univariate analysis. We divided patients by age ≥ 60 or <60 , Breslow thickness, tumor location, and presence or absence of high-risk features (Table 4). Only patients younger than 60, with tumors 1.5–1.99 mm, located on the head/neck/upper extremity, without high risk features had a positive sentinel lymph node biopsy rate of less than 5% ($n = 65$, 95% confidence interval 0.9–12.9%). Interestingly, the impact of poor prognostic features appeared to lose significance in patients ≥ 60 years, with minimal increase in positive sentinel lymph node rate dependent on the presence or absence of high-risk features.

3.3. Older patients (Table 4)

Patients ≥ 75 were examined separately as a group. This group had an overall positive SLNB rate of 12.1%. Of note, the rate of SLNB positivity decreased with age ≥ 60 , but did not reach significance when comparing age groups 60–69 vs 70–79 vs 80+ years old ($p = .60$).

Patients ≥ 75 years were more likely to have thicker tumors ($p = .037$), lymphovascular invasion present ($p = .0001$), and microsatellitosis ($p = .01$). Multivariate logistic regression revealed only the presence of lymphovascular invasion as being significant. A similar model was performed on the ≥ 75 year old patient group dividing patients by age ≥ 75 or <75 , Breslow thickness, tumor location, and presence or absence of high-risk features (Table 3). This analysis identified a small group of patients who had a low incidence of SLN positivity of

<5% who were 75 years of age with a head and neck/upper extremity melanoma of 1.0–1.49 mm with or without poor prognostic features (n = 66) or a thickness of 1.5–1.99 mm without high-risk features (n = 37).

4. Discussion

Our study of 3460 patients with intermediate thickness melanoma from centers across the United States had an overall positive sentinel lymph node biopsy rate of 17%, congruent with the 15% rate from the SEER database as reported by Kachare et al.⁶ Other large studies reported similar rates, though these were not confined to intermediate thickness lesions; 17% positive SLNB rate from the Melanoma Institute of Australia, 17% from the M.D. Anderson Cancer Center, and 17% from the Italian Multicenter Study.^{15,22,23} We identified age <60, location on the trunk or lower extremity, Breslow thickness 2 mm, and microsatellitosis as being independent predictors of having a positive SLNB in multivariate analysis. Age 60 was found to be protective of a positive SLNB. These findings are consistent with prior studies.^{14,24–27}

Lesions located on the trunk or lower extremity were noted to be predictive of a positive SLNB. Callender et al. found an inverse relationship between melanoma thickness and risk for a positive SLNB based on the lesion location on the body.²⁸ For instance, lesions on the head and neck had thicker melanomas, but a lower incidence of positive SLNB (5.1%) as compared to the thinner melanomas on the trunk but higher rate of positive SLNB. Further, Fadaki et al. have found that head and neck melanoma had the lowest SLN-positive rate at 10.8% (16.8% for extremity and 19.3% for trunk; p = .002) but had the worst 5-year DFS (p < .0001) and 5-year OS (p < .0001) as compared with other sites.²⁹ Balch et al. similarly found trunk and lower extremity melanomas to be more likely associated with a positive SLNB compared to other sites.^{27,28} Our results showed similar variance of positive SLNB rates by lesion location to Balch et al. and Callender et al.

A statistical breakpoint for risk of SLNB positivity appears around age 60 and this has been reported previously in the Intergroup Melanoma Trial as well as the Sunbelt Melanoma Trial.^{30,31} Our study, as well as the Intergroup Melanoma Trial and Sunbelt Melanoma Trial have shown that older patients have a lower incidence of SLN positivity. Our study did not evaluate survival but it has been previously demonstrated that age is an independent poor prognostic factor for survival in melanoma.^{32–34} Some authors have theorized this difference may result from the association of older patients with a higher incidence of acral lentiginous melanoma, desmoplastic melanoma, and head and neck melanomas associated with a lower incidence of nodal metastases.^{12,26,29} Despite this lower incidence of positive SLNB, older patients have worse prognosis for unclear reasons.³⁴ This paradoxical relationship may be attributed to a tendency of melanoma in older patients for hematogenous rather than lymphatic spread.

There has been little debate regarding the recommendation for all patients with melanoma thicker than 1 mm to undergo a sentinel lymph node biopsy in the absence of clinically positive lymph nodes. Attempts to find low risk subgroups that may be spared SLNB in this intermediate subgroup have been pursued. Balch et al. performed a review of the AJCC

database finding significant variance in rates of positive SLNB, inversely related regarding increasing age and decreasing rates of positive SLNB.

Bartlett et al. recently published subgroups of intermediate thickness melanoma that are at high risk for a positive sentinel node such as younger age, greater thickness, absent TIL, and present lymphovascular invasion or microsatellitosis. Additionally, they also described low risk groups with melanoma >1 mm in Breslow thickness. The authors identified 30% of their population (absent LVI, absent mitoses, and either absent regression or age of 60 and older) who may have a risk of a positive SLNB of less than 5%, suggesting that sentinel node biopsy could be omitted. Bartlett et al. identified two groups: patients with melanoma <1.5 mm Breslow thickness with absent mitoses, or with TIL present with absent regression (positive SLNB rate 2.6% and 4.3% respectively), or age of 60 and older without high risk features (no regression, present TIL, no ulceration, no LVI and no satellitosis), and tumors 1.5 mm Breslow thickness absent LVI, absent mitoses, absent regression or age of 60 and older (positive SLNB rate <5%). In our cohort, patients with melanoma <1.5 mm without stratification had a positive SLNB rate of 8.8% compared to 6.6% as published by Bartlett et al. Unfortunately in stratifying this group similarly (melanoma <1.5 mm thickness without high risk features) we found a higher positive SLNB rate of 7.1% (n = 224) compared to 2.6% (n = 38). In our patients with tumors 1.5 mm thickness in the absence of high risk features we found a positive SLNB rate of 16.0% (n = 748). Further stratifying these to patients older than 60 we still found a positive SLNB rate of 12.3% (n = 325), and were unable to reproduce the SLN positivity rate of <5% by Bartlett et al.

We were only able to find a small group of patients who fall into that less than 5% risk category such as demonstrated by the work by Bartlett et al.¹³ We found a number of subgroups with rates of positive SLNB less than 10%, however, only patients <60, with a Breslow thickness of 1.50–1.99, located on the head/neck/upper extremity and without any high-risk features had a positive SLNB rate of less than 5%, representing 1.9% of our study population (n = 65). 27.6% of patients (n = 936) had rates <10%; all low risk patients had a Breslow thickness of 1.01–1.99 mm. Searching for a larger group of patients at low risk for a positive SLNB, we then turned to our 75 year old cohort.

This cohort of older patients was stratified by thickness, tumor location, and presence or absence of high risk features (ulceration, lymphovascular invasion, mitotic rate 1, microsatellitosis). Patients older than or 75 years old with tumors 1.01–1.49 mm thickness on the head/neck/upper extremity with 1 high risk feature had a positive SLNB rate of 4.5% (n = 66). In this same 75 year old cohort patients with tumors 1.5–1.99 mm in thickness without high risk features regardless of location had a SLNB positivity rate of 2.7% (n = 37). If we use the acceptable threshold of 5% positive SLNB rate, then approximately 20% of patients (n = 103) in this population 75 years old (n = 517) could potentially be spared a sentinel lymph node biopsy. If we raise this threshold to a 10% positive SLNB rate, then 35.8% (n = 185) would fall beneath this positivity rate, again potentially sparing them an operation. However, overall we were unable to reproduce the low risk groups of positive SLNB as reported by Bartlett et al., and we did not find tumor infiltrating lymphocytes and absent tumor regression to be protective in our analysis.^{13,26}

Our study was limited by factors inherent to retrospective, multi-institutional reports. All pathology was performed by institutional pathologists. Assessment of sentinel nodes was similar in performing multiple level sections and stained with hematoxylin and eosin, reflexing to immunohistochemistry if negative for metastases. One of the major limitations of the study is subgroup analysis and small numbers of patients in each subgroup, exemplified by the relatively broad confidence intervals associated with SLN positivity rates in our subgroups of patients ≥ 75 years of age. To verify this data or the data presented by Bartlett et al., a larger dataset needs to be analyzed to validate the findings.

5. Conclusions

Intermediate thickness melanoma is a heterogeneous group with varying risk of a positive sentinel lymph node biopsy. While the overall rate of a positive sentinel lymph node was 17%, various subgroups had substantially lower rates of positive SLNB. In particular, patients over the age of 60 had minimal increase in SLNB positivity from previously acknowledged high risk features (ulceration, lymphovascular invasion, mitotic rate ≥ 1 , and/or microsatellitosis) and a lower overall sentinel lymph node biopsy positivity rate. An age cut off of 75 found groups of patients did have positive SLNB rates of less than 5% (19.9% of patients ≥ 75 years old) and who may avoid a sentinel lymph node biopsy. This may prove to be a clinically relevant subgroup for further clinical trials. In the ≥ 75 population, the likely low-risk for a positive sentinel lymph node must be weighed against the morbidity of the procedure and potential information to be gained. The decision to pursue a sentinel lymph node biopsy must be a decision between patient and provider based on the individual's clinical situation and tumor characteristics which are more complex than just Breslow thickness and presence of mitosis or ulceration.

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Table 1Patient and tumor characteristics.^d

	SLNB- ^c (N = 2876)	SLNB+ ^c (N = 584)	Total (N = 3460)	p value
Age				<.0001 ^a
Mean (SD)	57.8 (16.3)	53.8 (16.8)	57.1 (16.4)	
Interquartile Range	(46.0–70.9)	(41.7–66.4)	(45.2–70.0)	
Age Group				<.0001 ^b
<60	1486 (53%)	364 (63%)	1850 (55%)	
60–74	879 (31%)	143 (25%)	1022 (30%)	
75+	447 (16%)	70 (12%)	517 (15%)	
Gender				.4682 ^b
Male	1677 (58%)	350 (60%)	2027 (59%)	
Race				.9177 ^b
Caucasian	2640 (99%)	537 (99%)	3177 (99%)	
African American	5 (0.2%)	1 (0.2%)	6 (0.2%)	
Hispanic	11 (0.4%)	2 (0.4%)	13 (0.4%)	
Asian	10 (0.4%)	3 (0.6%)	13 (0.4%)	
Native American/Alaskan	2 (0.1%)	1 (0.2%)	3 (0.1%)	
Lesion Site				<.0001 ^b
Head/Neck	567 (20%)	76 (13%)	643 (19%)	
Upper Extremity	645 (22%)	91 (16%)	736 (21%)	
Lower Extremity	682 (24%)	169 (29%)	851 (25%)	
Trunk	980 (34%)	247 (42%)	1227 (36%)	
Breslow Thickness				<.0001 ^a
N	2876	584	3460	
Mean (SD)	1.9 (0.8)	2.3 (0.8)	2.0 (0.8)	
Range	(1.0–4.0)	(1.0–4.0)	(1.0–4.0)	
Breslow Thickness Group				<.0001 ^b
1.01–1.49	1071 (37%)	126 (22%)	1197 (35%)	
1.50–1.99	655 (23%)	115 (20%)	770 (22%)	
2.0–2.99	760 (26%)	209 (36%)	969 (28%)	
3.0–4.0	390 (14%)	134 (23%)	524 (15%)	
Breslow Thickness Group				<.00012
1.01–1.99	1726 (60%)	241 (41%)	1967 (57%)	
2.0–2.99	760 (26%)	209 (36%)	969 (28%)	
3.0–4.0	390 (14%)	134 (23%)	524 (15%)	
Clark Level Group				.0034 ^b
II/III	612 (29%)	98 (22%)	710 (27%)	
IV/V	1532 (72%)	352 (78%)	1884 (73%)	
Ulceration				<.0001 ^b

	SLNB- ^c (N = 2876)	SLNB+ ^c (N = 584)	Total (N = 3460)	p value
Present	656 (27%)	186 (37%)	842 (29%)	
Lymphovascular Invasion				<.0001 ^b
Present	123 (8%)	58 (17%)	181 (10%)	
Mitotic rate (per mm²)				.0108 ^b
<1	182 (12%)	24 (7%)	206 (11%)	
1	1352 (88%)	315 (93%)	1667 (89%)	
Tumor regression				.3502 ^b
Present	253 (18%)	45 (15%)	298 (17%)	
Microsatellitosis				<.0001 ^b
Present	42 (3%)	32 (9%)	74 (4%)	
Tumor-infiltrating Lymphocytes				.2978 ^b
Present	844 (77%)	164 (74%)	1008 (76%)	

^aANOVA F-Test.

^bChi-Square.

^cSLNB-Sentinel Lymph Node Biopsy.

^dNot all patients had full complement of data points.

Table 2

Predictive factors for a positive sentinel lymph node biopsy.

Prognostic Factor	Univariate Analysis			Multivariate Analysis		
	n (%)	Odds ratio	95% Confidence Interval	p-value	Odds ratio	95% Confidence Interval
Age Group						
<60	1850 (55%)	Ref				
60–74	1022 (30%)	0.66	0.54–0.82	<.001	0.45	0.30–0.67
75+	517 (15%)	0.64	0.48–0.84	.002	0.48	0.28–0.82
Gender						
Female	1427 (41%)	Ref				
Male	2027 (59%)	1.07	0.89–1.28	.468		
Location						
Head/Neck	643 (19%)	Ref				
Lower Extremity	851 (25%)	1.85	1.38–2.48	<.001	2.15	1.20–3.86
Upper Extremity	736 (21%)	1.05	0.76–1.46	.757	1.65	0.86–3.16
Trunk	1227 (36%)	1.88	1.43–2.48	<.001	2.12	1.21–3.71
Breslow Thickness (mm)						
1.01–1.49	1197 (35%)	Ref				
1.50–1.99	770 (22%)	1.49	1.14–1.96	.004	1.43	0.86–2.36
2.00–2.99	969 (28%)	2.34	1.84–2.97	<.001	2.73	1.72–4.34
3.00–4.00	524 (15%)	2.92	2.23–3.82	<.001	3.60	2.14–6.05
Breslow Thickness (mm)						

Prognostic Factor	Univariate Analysis			Multivariate Analysis		
	n (%)	Odds ratio	95% Confidence Interval		Odds ratio	95% Confidence Interval
1.01–1.99	1967 (57%)	Ref				
2.00–2.99	969 (28%)	1.97	1.61–2.42	<.001	2.31	1.57–3.41
3.00–4.00	524 (15%)	2.46	1.94–3.12	<.001	3.04	1.93–4.79
Clark Level						
II/III	710 (27%)					<.001
IV/V	1884 (73%)	1.43	1.12–1.83	.004		
Ulceration						
Absent	2073 (71%)	Ref				
Present	842 (29%)	1.56	1.27–1.91	<.001		
Lymphovascular Invasion						
Absent	1705 (90%)	Ref				
Present	181 (10%)	2.43	1.73–3.41	<.001		
Tumor Mitotic Rate (per mm ²)						
<1	206 (11%)	Ref				
1	1667 (89%)	1.77	1.16–2.82	.012		
Regression						
Absent	1425 (83%)	Ref				
Present	298 (17%)	0.85	0.60–1.20	.351		
Microsatellitosis						
Absent	1917 (96%)	Ref				
Present	74 (4%)	3.85	2.39–6.19	<.001	2.31	1.09–4.89
						0.029

Prognostic Factor	Univariate Analysis	p-value	Multivariate Analysis	p-value	
	n (%)	Odds ratio	95% Confidence Interval	Odds ratio	95% Confidence Interval
Tumor Lymphocytes					
Absent	314 (24%)	Ref			
Present	1008 (76%)	0.84	0.60, 1.17	.298	

Table 3

Patients stratified by age, thickness, location, and presence/absence of high risk features.

Age	Thickness(mm)	Location	High-risk features ^a	SLNB+ (%)	n
<60	1.01–1.49	Head/neck/upper extremity	None	6.5	123
		Trunk/lower extremity	At least one	11.9	118
			None	9.4	233
	1.50–1.99	Head/neck/upper extremity	At least one	16.4	232
			None	4.6	65
		Trunk/lower extremity	At least one	9.8	61
			None	21.8	124
	2.0–2.99	Head/neck/upper extremity	At least one	26.0	177
			None	10.3	58
		Trunk/lower extremity	At least one	21.4	103
			None	27.1	107
60	3.0–4.0	Head/neck/upper extremity	At least one	30.1	206
			None	17.9	28
		Trunk/lower extremity	At least one	26.2	61
			None	24.4	41
	1.01–1.49	Head/neck/upper extremity	At least one	43.8	112
			None	7.9	101
		Trunk/lower extremity	At least one	6.9	131
			None	10.8	111
	1.50–1.99	Head/neck/upper extremity	At least one	11.4	123
			None	7.5	53
		Trunk/lower extremity	At least one	9.8	102
			None	7.5	67
2.0–2.99	Head/neck/upper extremity	None	At least one	12.1	107
			None	12.3	65
	Trunk/lower extremity	None	At least one	14.6	158
			None	17.3	75
		At least one	23.7	177	

Age	Thickness(mm)	Location	High-risk features ^a	SLNB+ (%)	n
<75	3.0–4.0	Head/neck/upper extremity	None	10.0	30
		At least one		19.0	100
		Trunk/lower extremity	None	20.0	35
		At least one		22.1	104
	1.01–1.49	Head/neck/upper extremity	None	7.5	199
		At least one		10.1	208
		Trunk/lower extremity	None	10.0	321
		At least one		14.6	321
	1.50–1.99	Head/neck/upper extremity	None	6.1	99
		At least one		8.7	127
		Trunk/lower extremity	None	18.5	173
		At least one		21.7	253
	2.0–2.99	Head/neck/upper extremity	None	9.5	95
		Trunk/lower extremity			
		At least one		16.4	195
		None		24.4	156
		At least one		28.4	331
		None		17.1	41
	3.0–4.0	Head/neck/upper extremity			
		Trunk/lower extremity			
75		At least one		22.4	116
		None		21.0	62
		At least one		39.1	174
		None		4.0	25
	1.01–1.49	Head/neck/upper extremity			
		Trunk/lower extremity			
		At least one		4.9	41
		None		8.7	23
		At least one		14.7	34
		None		5.3	19
	1.50–1.99	Head/neck/upper extremity			
		Trunk/lower extremity			
		At least one		13.9	36
		None		0.0	18

Age	Thickness(mm)	Location	High-risk features ^a	SLNB+ (%)	n
2.0–2.99		Head/neck/upper extremity	At least one	12.9	31
		None		17.9	28
	Trunk/lower extremity	At least one		19.7	66
		None		15.4	26
3.0–4.0		At least one		19.2	52
		None		5.9	17
	Head/neck/upper extremity	At least one		20.0	45
		None		28.6	14
	Trunk/lower extremity	At least one		9.5	42

^aUlceration, lymphovascular invasion, mitotic rate 1, and/or microsatellitosis. Missing values for high-risk features were considered to be indicative of absence of the given high-risk feature.

Table 4Elderly patient (≥ 75) characteristics and prognostic factors.

	SLNB– (n = 447)	SLNB+ (n = 70)	Total (n = 517)	p value
Age				.5608 ^a
Mean (SD)	80.7 (4.3)	80.3 (6.4)	80.6 (4.6)	
Range	(75.0–97.2)	(75.0–125.5)	(75.0–125.5)	
Gender				.6888 ^b
Male	289 (65%)	43 (62%)	332 (65%)	
Race				.7504 ^b
Caucasian	415 (98%)	67 (99%)	482 (98%)	
African American	2 (0.5%)	0 (0.0%)	2 (0.4%)	
Hispanic	3 (0.7%)	0 (0.0%)	3 (0.6%)	
Asian	2 (0.5%)	1 (1.5%)	3 (0.6%)	
Native American/Alaskan	1 (0.2%)	0 (0.0%)	1 (0.2%)	
Lesion Site				.5015 ^b
Head/Neck	130 (29%)	17 (24%)	147 (28%)	
Upper Extremity	110 (25%)	20 (29%)	130 (25%)	
Lower Extremity	105 (24%)	13 (19%)	118 (23%)	
Trunk	102 (23%)	20 (29%)	122 (24%)	
Breslow Thickness				.0305 ^a
N	447	70	517	
Mean (SD)	2.2 (0.8)	2.4 (0.7)	2.2 (0.8)	
Range	(1.0–4.0)	(1.1–4.0)	(1.0–4.0)	
Breslow Thickness Group				.0366 ^b
1.01–1.49	113 (25%)	10 (14%)	123 (24%)	
1.50–1.99	94 (21%)	10 (14%)	104 (20%)	
2.0–2.99	140 (31%)	32 (46%)	172 (33%)	
3.0–4.0	100 (22%)	18 (26%)	118 (23%)	
Breslow Thickness Group				.0150 ^b
1.01–1.99	207 (46%)	20 (29%)	227 (44%)	
2.0–2.99	140 (31%)	32 (46%)	172 (33%)	
3.0–4.0	100 (22%)	18 (26%)	118 (23%)	
Clark Level Group				.0728 ^b
II/III	56 (17%)	4 (7%)	60 (16%)	
IV/V	274 (83%)	50 (93%)	324 (84%)	
Ulceration				.0887 ^b
Present	134 (34%)	27 (46%)	161 (36%)	
Lymphovascular invasion				.0001 ^b
Present	16 (7%)	10 (27%)	26 (9%)	
Mitotic rate (per mm²)				.4771 ^b

	SLNB– (n = 447)	SLNB+ (n = 70)	Total (n = 517)	p value
<1	28 (11%)	3 (7%)	31 (11%)	
1	227 (89%)	38 (93%)	265 (89%)	
Tumor regression				.5090 ^b
Present	40 (18%)	5 (14%)	45 (18%)	
Microsatellitosis				.0101 ^b
Present	10 (4%)	6 (13%)	16 (5%)	
Tumor-infiltrating lymphocytes				.2784 ^b
Present	121 (70%)	24 (80%)	145 (72%)	
Prognostic Factor	Multivariate Analysis			
	Odds ratio	95% CI	p value	
Vascular invasion				
Yes	4.43	1.68–11.69	.003	

Multivariate Forward Logistic Regression Analysis.

^aANOVA F-Test.

^bChi-Square.