HHS Public Access

Author manuscript

J Am Acad Dermatol. Author manuscript; available in PMC 2020 May 18.

Published in final edited form as:

J Am Acad Dermatol. 2019 June ; 80(6): 1640–1649. doi:10.1016/j.jaad.2019.01.009.

Poor prognosis for thin ulcerated melanomas and implications for a more aggressive approach to treatment

Makenzie L. Hawkins, MSPH[a], **Matthew J. Rioth, MD**[a,b], **Megan M. Eguchi, MPH**[a], **Myles Cockburn, PhD**[a,c,d,e]

[a]University of Colorado Cancer Center, University of Colorado, Aurora

[b]Department of Medicine-Biomedical Informatics and Personalized Medicine

[c]Department of Dermatology, School of Medicine, University of Colorado, Aurora

[d]Department of Preventive Medicine, Keck School of Medicine of the University of Southern California, Los Angeles

[e]Department of Dermatology, Keck School of Medicine of the University of Southern California, Los Angeles

Abstract

Background—Clinical guidelines for the treatment of melanoma are based largely on the behavior of thicker tumors. As a result, little is known about survival differences among patients with thinner tumors.

Objective—To investigate the variability in survival for American Joint Committee on Cancer stage T1 thin melanoma tumors, defined as tumors less than 1 mm thick at diagnosis.

Methods—This population-based series included 43,008 non-Hispanic whites in whom cutaneous melanoma was diagnosed between 2004 and 2013 from the California Cancer Registry. Survival outcomes were estimated using the Kaplan-Meier method. Cox proportional hazard models were used to estimate risk of death.

Results—Survival for patients with thin ulcerated tumors was comparable to that for patients with stage II tumors, who are currently treated more aggressively. At 12 months, patients with thin ulcerated tumors had approximately 6% lower survival (92.5% [95% confidence interval (CI), 90.6%−93.9%]) compared with patients with thin nonulcerated tumors (98.2% [95% CI, 98.0% −98.3%]). At 24 months, this survival difference increased (85.2% [95% CI, 82.8%−87.4%] vs 96.1% [95% CI, 95.8–96.3%] for those with thin ulcerated and thin nonulcerated tumors, respectively) and a greater than 15% survival difference was seen at 60 months.

Correspondence to: Myles Cockburn, PhD, 13001 E 17th Place, Campus Box F434, Aurora, CO 80045. myles.cockburn@ucdenver.edu.

Conflicts of interest: None disclosed.

The ideas and opinions expressed herein are those of the author(s) and do not necessarily reflect the opinions of the State of California, Department of Public Health, the National Cancer Institute, and the Centers for Disease Control and Prevention or their contractors and subcontractors.

Reprints not available from the authors.

Limitations—Previous reports of cancer registry data have noted some evidence of miscoding of thin tumors.

Conclusion—The poorer survival in patients with ulcerated tumors less than 1 mm thick implies the need for additional studies to determine potential benefits of more aggressive treatment.

Keywords

melanoma; staging; survival; tumor thickness

Melanoma prognosis is accurately predicted by Breslow depth (tumor thickness), nodal involvement, and ulceration, which together with clinical evidence of metastasis, form the basis of current staging and treatment practices. Guidelines for treatment of melanoma are largely based on the behavior of thicker tumors. Thin tumors comprise the largest proportion of melanomas (in most series more than 50% are <1 mm thick[1]), but little is known about survival differences among patients with thinner tumors, and little guidance is provided on treatment approaches for thinner tumors based on tumor characteristics such as ulceration.[2] We investigated the variability in survival for American Joint Committee on Cancer stage T1, thin tumors (<1 mm at diagnosis) in a population-based series and described survival patterns by ulceration and nodal involvement. Our objective was to identify tumor characteristics within thinner tumors to guide clinical decision making, particularly by identifying those tumors with the worst survival, which are more likely to warrant aggressive early or adjuvant treatment approaches. We are aware of no other data available that distinguishes survival outcomes within thin tumors in an unselected population (as opposed to specific clinical series possibly biased by selection) that could guide staging classification and clinical decision making.

DESIGN AND METHODS

Patient and tumor characteristics

A total of 43,008 non-Hispanic whites in whom cutaneous melanoma was diagnosed between January 1, 2004, and December 31, 2013, were identified from the California Cancer Registry, the population-based cancer registry for the State of California. The California Cancer Registry operates under the annual review of the State of California Committee for the Protection of Human Subjects, which provided approval for this analysis.

Tumors were categorized by Breslow thickness, in millimeters, and stage, in accordance with the primary tumor melanoma staging described by the American Joint Committee on Cancer.[3] Thin tumors were defined as those with a Breslow thickness less than 1 mm. Tumor ulceration was determined by using the Collaborative Stage version 02.05 Cancer Schema and categorized as ulcerated or nonulcerated. Nodal involvement was categorized as without nodal involvement, with nodal involvement, and unknown nodal involvement. Histologic subtype was accordingly coded to the *International Classification of Diseases for Oncology, Third Edition,* as nodular melanoma (8721), lentigo maligna melanoma (8742), superficial spreading melanoma (8743), acral lentiginous melanoma (8744), and malignant melanoma not otherwise specified (8720). Rare histologic subtypes (8722–8741 and 8745–8790) were classified as malignant melanoma not otherwise specified. Cancer treatment included

chemotherapy, immunotherapy, and sentinel lymph node biopsy (SLNB). Socioeconomic status (SES) of patients was determined by using an index measure developed by Yost et al.[4]

Statistical analysis

Differences in patient demographics were compared by using chi-square tests. Follow-up time was calculated from date of diagnosis to date of last known follow-up or death. Survival curves were generated by using the Kaplan-Meier method, and 95% confidence intervals (CIs) were generated by using the Hall-Wellner method.[5] A long-rank test was used to determine significance between the different Kaplan-Meier plots. Survival estimates and 95% CIs were reported at 12, 24, 36, and 60 months. Univariate and multivariate Cox proportional hazard models were used to estimate the risk of death (overall and melanoma-specific) after adjustment for sex, age at diagnosis, histology, year of diagnosis, SES, and cancer treatment. Proportionality of hazards of key covariates was examined, and proportional hazards assumptions were not violated. Within the thin ulcerated tumors, we examined differences between patients with more than 26 months of survival and patients with 26 or fewer months. This was the first point at which survival confidence limits of the thin ulcerated tumors did not overlap with the survival confidence limits of the stage IIB tumors. The analysis was conducted with SAS software (version 9.4, SAS Institute Inc, Cary, NC).

RESULTS

Patient characteristics

Patients with ulcerated tumors less than 1 mm thick (thin tumors) were older (53% were age ≥65 years) than patients in whom thin nonulcerated tumors had been diagnosed (42.6% were age ≥65 years) ($P < .001$; Table I). The majority of patients with both the thin ulcerated and thin nonulcerated tumors were classified as being of higher-middle or the highest SES (53.6% and 59.4%, respectively) ($P < .001$). However, a slightly higher proportion (22.0%) of patients with thin ulcerated tumors fell into the lower SES groups compared with the group with thin nonulcerated tumors (16.8%) ($P < .001$). Nearly 12% of patients with thin ulcerated tumors had nodular histology (11.9%) compared with 1.0% of those with thin nonulcerated tumors ($P < .001$). Conversely, patients with thin nonulcerated tumors had a higher proportion of superficial spreading melanoma (32.3%) than did patients with thin ulcerated tumors (25.2%) ($P < .001$). Compared with patients with thin nonulcerated tumors, patients with thin ulcerated tumors received slightly more chemotherapy (33.3%) ($P < .001$) or more immunotherapy (1.3%) ($P < .001$) and a higher proportion underwent SLNB (2.4%) ($P < .001$).

Survival

At 12 months, patients with thin ulcerated tumors had an approximately 6% lower survival rate (Table II) (92.5% [95% CI, 90.6%−93.9%]) than patients with thin nonulcerated tumors (98.2% [95% CI, 98.0%−98.3%]). At 24 months, this survival difference increased (85.2% [95% CI, 82.8%−87.4%)] vs 96.1% [95% CI, 95.8%−96.3%], respectively) and continued to increase more than 2-fold by 60 months (75.5% [95% CI, 72.1%−78.5%] vs 88.6% [95% CI, 88.2%−89.0%], respectively). The survival estimates of thin ulcerated melanomas with

unknown nodal involvement were between those with and without nodal invasion (not shown).

Survival of thin ulcerated tumors was significantly worse than survival of thin nonulcerated tumors and was comparable to survival in stage IIB (American Joint Committee on Cancer) tumors in the first 26 months after diagnosis (Fig 1). The survival rate at 24 months for thin ulcerated tumors was 85.2% (95% CI, 82.8%−87.4%) versus 81.8% (95% CI, 80.0% −83.4%) for stage IIB tumors at 24 months. After 26 months, survival of thin ulcerated tumors was still significantly worse than survival of thin nonulcerated tumors.

An investigation of a sentinel lymph node (SLN) is not standard in staging thin melanomas; populations with unknown and presumably unstaged SLNs are presented separately from those with known nodal status. Nodal involvement had a clear negative influence on survival rates in both ulcerated and nonulcerated thin tumors. Patients with thin ulcerated tumors with nodal involvement (stage III) had extremely poor survival; the survival rates were at least 10% lower than those for stage III tumors (Fig 2). At 36 months after diagnosis, the survival rate of patients with thin ulcerated tumors with nodal involvement (57.9% [95% CI, 46.8%−67.5%]) was more than 20% lower than the survival rate for patients with thin nonulcerated tumors with nodal involvement (73.7% [95% CI, 67.4%−79.0%]).

The overall risk of death in thin ulcerated tumors was as bad as that for stage IIA tumors (hazard ratio [HR] 2.2 [95% CI, 1.97–2.61] vs HR, 2.46 [95% CI, 2.262.66]; respectively) (Table II). The overall risk of death in thin ulcerated tumors with nodal invasion was double the risk seen in thin nonulcerated tumors with nodal invasion, even after adjustment for covariates (HR, 10.07 [95% CI, 7.33–13.83] vs HR, 4.55 [95% CI, 3.60–5.76], respectively). The risk of melanoma-specific death in patients with ulcerated tumors less than 1 mm thick (HR, 7.45 [95% CI, 5.849.51]) was 7-fold that in patients with nonulcerated tumors less than 1 mm thick (referent) and was also greater than the risk of stage IIA tumors (HR, 6.67 [95% CI, 5.64–7 .88]) The risk of melanoma-specific death in ulcerated tumors less than 1 mm thick with nodal invasion was significantly higher than that in nonulcerated tumors less than 1 mm thick with nodal invasion (HR, 45.64 [95% CI, 29.22–71.30] vs HR, 19.83 [95% CI, 14.24–27.60], respectively).

Differences in patients with thin ulcerated tumors surviving < 26 months compared to those surviving longer

Of those surviving 26 months or less and those surviving more than 26 months, the majority were male (Table III). Patients with shorter survival time were also significantly older than patients surviving past 26 months. More patients surviving 26 months or less had their disease diagnosed as nodular melanoma (20.5%) than did patients surviving longer, who had a higher proportion of superficial spreading melanoma (29.8%). Of the patients surviving more than 26 months, more underwent SLNB (33.4%) ($P < .001$), but they received less chemotherapy (0.2%) ($P < .001$) or immunotherapy (1.3%) ($P < .001$) treatment than did those with shorter survival time. There were no significant differences in year of diagnosis or SES for those surviving past 26 months compared with for those not surviving to 26 months.

DISCUSSION

These population-based data demonstrate a substantial survival disadvantage for patients who present with thin melanomas with evidence of ulceration versus for those who present with thin melanomas with no ulceration. Survival for patients with thin ulcerated tumors is as poor as that experienced by patients with thicker lesions (greater than stage II), who are currently treated more aggressively. Patients with lesions thicker than 1 mm are generally surgically staged with SLNB, in addition to which wider margins are used for excision of their primary tumor.[6] Moreover, among the patients with thin ulcerated tumors, those with evidence of both ulceration and nodal involvement have still worse survival.

Although ulcerated tumors represent a small proportion of all thin tumors (2.5% in this data set), they represent a substantial number of patients (>1000 in this data set). Therefore, patients with thin ulcerated tumors represent an important subset of patients with melanoma who would potentially benefit from more aggressive management, routine SLN evaluation, and potentially adjuvant treatment, given their 10.1% rate of nodal positivity and generally poorer outcomes (Table II). Indeed, this approach has recently been under investigation in NCT03405155, which is a study of adjuvant immunotherapy versus placebo in stage IIB and IIC melanoma. Our findings also support the current National Comprehensive Cancer Network guidelines, which recommend consideration of SLNB for thin melanomas in the presence of risk factors such as ulceration.[7]

Thin ulcerated melanomas with SLN involvement have previously been shown to have significantly poorer survival than those without SLN involvement,[8] and they appear to have survival comparable to that of thicker (2-to 4-mm) tumors with nodal involvement.[2] Although it is understandable that lymph node involvement and metastasis would affect melanoma survival regardless of tumor thickness, the role of ulceration in substantially reducing survival among the thinnest tumors has been less clear, but it has been hypothesized that the biology of ulcerated tumors gives rise to a more aggressive phenotype.[9] Ulceration has been linked to increased expression of matrix proteins that reduce melanocyte adhesion and would promote dissemination and metastasis.[10] Indeed, Table II demonstrates a much higher incidence of node positivity in ulcerated tumors than in nonulcerated tumors (8.9% vs 0.9% [$P < .001$]). In the context of thin melanomas, ulceration may represent a population of tumors that constitute biologically aggressive tumors with a poor prognosis even if they are clinically detected early with shallow invasion.

This study represents the largest population of thin melanomas reported to date, allowing for the investigation of detailed tumor and patient characteristics and representing data that are not available from existing clinical trials or series of selected patients. This population-based data source represents all melanomas diagnosed in California over the 10-year period considered and avoids biases often inherent in clinic-based series, such as selection bias. These data also reflect standardized methods of evaluating tumor characteristics (ulceration, Breslow depth) and patient characteristics across all tumors. Previous smaller studies of patients selected to undergo SLNB have been conflicting in their conclusions regarding the prognostic role of ulceration.[11,12] Our data represent more direct evidence as to the clinical implication of ulceration in thin primary melanoma. Ulceration had a higher rate of SLNB,

potentially reflecting a difference in practice for patients with ulcerated primary tumors and therefore providing a greater chance for detection of stage III disease; however, even in patients with a negative SLNB result, survival was worse for patients with ulcerated primary tumors across all time points.

There are some limitations to this analysis. Although approaches to coding tumor characteristics are standardized and manually reviewed by certified tumor registrars in California's population-based Surveillance, Epidemiology, and End Results (SEER) registry, previous reports have noted some evidence of miscoding of thin tumors, specifically, in the Detroit SEER registry.[13] However, the 3 central tumor registries of California have taken steps to address the issue. Each melanoma incident case report is reviewed for more detailed information on anatomic site beyond what is required for *International Classification of Diseases for Oncology* coding, providing the opportunity for more in-depth consideration of potential coding inaccuracies. California central tumor registries routinely review and audit tumor thickness coding for melanomas, and the current data set is unlikely to contain the errors in coding thickness that have been reported in the Detroit SEER registry, in which 88% of all thin melanomas (<1 mm) and 71% of ultrathin (<.25mm) melanomas were in fact actually coded correctly. Gimotty et al[13] also noted that some SEER registries had survival rates for thin melanomas outside the range observed in data from other countries, shedding doubt on the accuracy of some SEER thickness data. However, the 5-year and 10-year cumulative melanoma-related death rates for ultrathin melanomas in Los Angeles and San Francisco—Oakland (the data included in this study) overlap with the confidence bands of the international cumulative melanoma-related death rates for these time periods reported in Gimotty et al,[13] which further supports our contention that California SEER data are unlikely to be subject to coding errors.

CONCLUSION

Substantial variation in survival exists for patients with thin (<1 mm at diagnosis) melanomas: some of those thin tumors, especially those with evidence of ulceration, have worse survival than much thicker lesions do, implying that they should be upstaged and potentially treated more aggressively to improve outcomes. Ulceration among thinner (<1 mm) lesions appears to be the biggest driver of compromised survival for patients with thin lesions. Although TNM staging classifies these tumors separately (T1b), there have to date been no data available that distinguish survival or treatment approach compared with those with other stage I tumor types. The close overlap of survival curves and similar rate of SLN involvement imply that T1b tumors should be treated in a manner similar to that used with stage IIA and higher-stage tumors. Although the most recent staging system put forth by the American Joint Committee on Cancer incorporates only ulceration and not mitoses as with previous systems, ulceration in the absence of nodal involvement does not currently predicate a change in management, such as routine SLN evaluation. However, given the poor prognosis of ulceration, further iterations of staging systems for melanoma staging should be conducted to more heavily weigh the survival outcomes of ulceration regardless of depth. Changes in the staging of thin high-risk melanoma are especially relevant in consideration of recent adjuvant clinical trials that demonstrate efficacious and well-tolerated adjuvant treatments for high-risk melanomas.[14–16] In the BRIM-8 study, patients with high-risk

primary melanomas (>4 mm with ulceration) but without nodal involvement seemed to demonstrate benefit from adjuvant treatment, which is a first for this patient population.[16]

Among patients with thin ulcerated tumors, those with nodal involvement have still worse survival; however, survival was also worse in the first 2 years after diagnosis of thin ulcerated melanomas for males, older patients, and those with nodular melanomas, which could represent additional stratifying indicators for the treatment of thin ulcerated lesions. These characteristics could also represent a difference in underlying tumor biology, raising the possibility of future research in identification of biomarkers of aggressive phenotype. The same conclusion might be drawn for thin ulcerated melanomas in general: in effect, a thin ulcerated tumor represents a tumor in which ulceration has occurred very early in the development of the tumor. Thin melanomas already showing evidence of ulceration could represent a particularly aggressive phenotype that is destined to progress rapidly, especially if we consider tumor thickness to be a proxy for how long the tumor has been developing.

Acknowledgments

Funding sources: Supported by grant R01CA158407 from the National Cancer Institute and the National Institute of Child Health and Human Development. The collection of cancer incidence data used in this study was supported by the California Department of Public Health pursuant to California Health and Safety Code Section 103885; the Centers for Disease Control and Prevention's National Program of Cancer Registries, under cooperative agreement 5NU58DP003862–04/DP003862; and the National Cancer Institute's Surveillance, Epidemiology and End Results Program under contract HHSN2 61201000140C awarded to the Cancer Prevention Institute of California, contract HHSN261201000035C awarded to the University of Southern California, and contract HHSN261201000034C awarded to the Public Health Institute. Supported in part by the Population Health Shared Resource of the University of Colorado Cancer Center (P30CA046934).

Abbreviations used

CI	confidence interval
SEER	Surveillance, Epidemiology, and End Results
SES	socioeconomic status
SLN	sentinel lymph node
SLNB	sentinel lymph node biopsy

REFERENCES

1. Landow SM, Gjelsvik A, Weinstock MA. Mortality burden and prognosis of thin melanomas overall and by subcategory of thickness, SEER registry data, 1992–2013. J Am Acad Dermatol. 2017;76(2):258–263. [PubMed: 27887797]
2. Bagaria SP, Ray PS, Joseph RW, et al. Ultrathin primary is a marker for worse prognosis in lymph node-positive cutaneous melanoma. Cancer. 2013;119(10):1860–1867. [PubMed: 23408288]
3. Amin MB, Edge S, Greene F, et al., eds. AJCC Cancer Staging Manual. 8th ed. New York, NY: Spring International Publishing; 2017.
4. Yost K, Perkins C, Cohen R, Morris C, Wright W. Socioeco nomic status and breast cancer incidence in California for different race/ethnic groups. Cancer Causes Control. 2001; 12(8):703–711. [PubMed: 11562110]
5. Hall W, Wellner J. Confidence bands for a survival curve from censored data. Biometrika. 1980;67:133–143.

6. Hayes AJ, Maynard L, Coombes G, et al. Wide versus narrow excision margins for high-risk, primary cutaneous melanomas: long-term follow-up of survival in a randomised trial. Lancet Oncol. 2016;17(2):184–192. [PubMed: 26790922]
7. National Comprehensive Cancer Network. NCCN guidelines: cutaneous melanoma (version 1.2019). Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed November 12, 2018.
8. Karakousis G, Gimotty PA, Bartlett EK, et al. Thin melanoma with nodal involvement: analysis of demographic, pathologic, and treatment factors with regard to prognosis. Ann Surg Oncol. 2017;24(4):952–959. [PubMed: 27807729]
9. Spatz A, Stock N, Batist G, van Kempen LC. The biology of melanoma prognostic factors. Discov Med. 2010;10(50): 87–93. [PubMed: 20670603]
10. Rakosy Z, Ecsedi S, Toth R, et al. Integrative genomics identifies gene signature associated with melanoma ulcera tion. PLoS One. 2013;8(1):e54958. [PubMed: 23383013]
11. Han D, Zager JS, Shyr Y, et al. Clinicopathologic predictors of sentinel lymph node metastasis in thin melanoma. J Clin Oncol. 2013;31(35):4387–4393. [PubMed: 24190111]
12. Mitteldorf C, Bertsch HP, Jung K, et al. Sentinel node biopsy improves prognostic stratification in patients with thin (pT1) melanomas and an additional risk factor. Ann Surg Oncol. 2014;21(7):2252–2258. [PubMed: 24652352]
13. Gimotty PA, Shore R, Lozon NL, et al. Miscoding of melanoma thickness in SEER: research and clinical implications. J Invest Dermatol. 2016;136(11):2168–2172. [PubMed: 27354265]
14. Weber J, Mandala M, Del Vecchio M, et al. Adjuvant nivolumab versus ipilimumab in resected stage III or IV melanoma. N Engl J Med. 2017;377:1824–1835. [PubMed: 28891423]
15. Long GV, Hauschild A, Santinami M, et al. Adjuvant dabrafenib plus trametinib in stage III BRAF-mutated melanoma. N Engl J Med. 2017;377:1813–1823. [PubMed: 28891408]
16. Lewis K, Maio M, Demidov L, et al. LBA7_PR BRIM8: a randomized, double-blind, placebo-controlled study of adjuvant vemurafenib in patients (pts) with completely resected, BRAFV600 + melanoma at high risk for recurrence. Ann Oncol. 2017;28(suppl 5):v605–v649.

CAPSULE SUMMARY

- Survival differences among patients with thin melanoma tumors are unclear. This population-based study found that survival of patients with thin ulcerated melanoma was similar to that of patients with thicker lesions.
- The poorer survival of patients with thin ulcerated tumors implies the need for additional studies to determine the benefits of aggressive or targeted treatment.

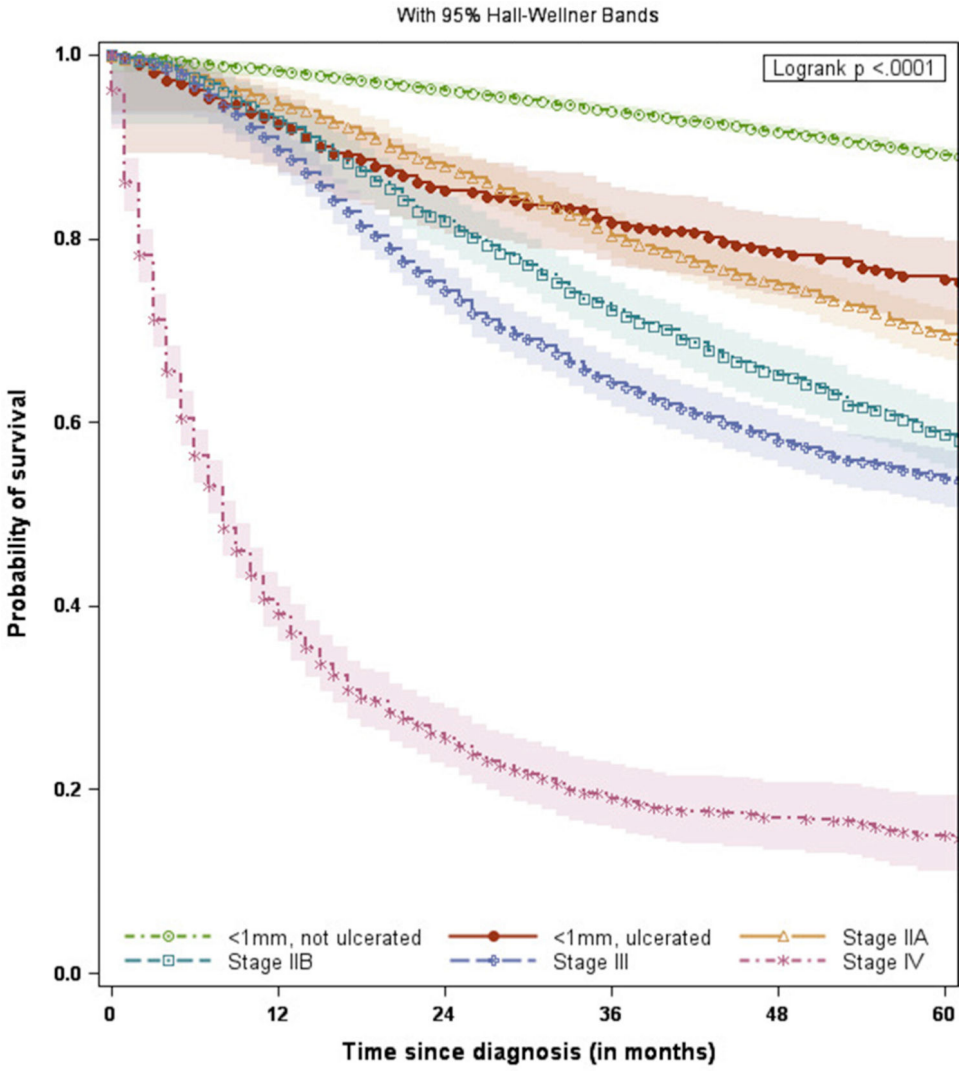

Fig 1.

Melanoma. Survival in non-Hispanic white patients by tumor thickness, ulceration, and stage from the California Cancer Registry (2004–2013).

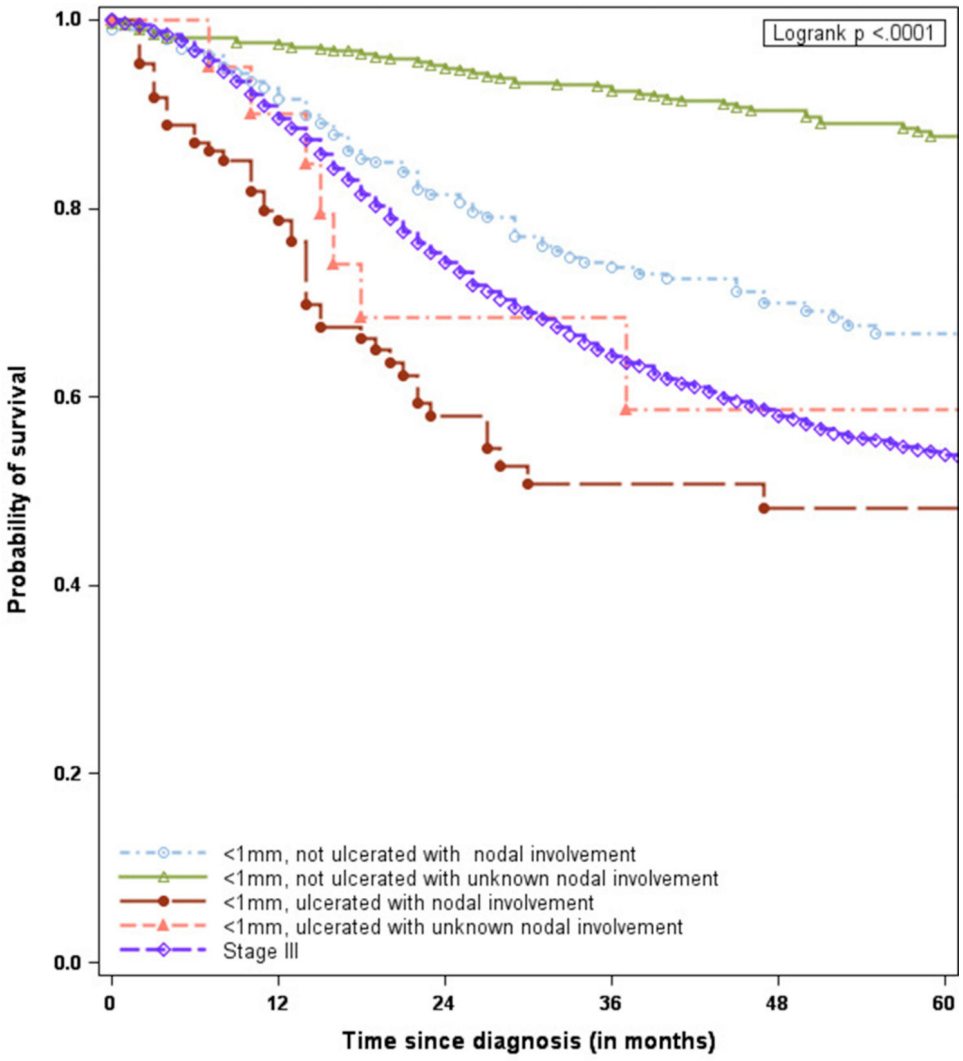

Fig 2.

Thin Melanoma. Survival in non-Hispanic white patients by ulceration and nodal involvement from the California Cancer Registry (2004–2013).

J Am Acad Dermatol. Author manuscript; available in PMC 2020 May 18.

Table I.

Patient demographics, cancer characteristics, and cancer treatment in non-Hispanic white patients with melanoma by tumor thickness and stage from the California Cancer Registry (2004-2013)

	<1 mm not ulcerated (n = 30,873 [71.6%])		<1 mm not ulcerated (n = 1092 [2.5%])		Stage IIA (n = 3447 [8.0%])		Stage IIB (n = 2350 [5.5%])		Stage III (n = 3137 [7.3%])		Stage IV (n = 2209 [5.1%])		
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	***P* value**
Sex													
Male	17,964	58.2%	698	63.9%	2242	65.0%	1593	67.8%	2124	67.7%	1575	713%	
Female	12,909	41.8%	394	36.1%	1205	35.0%	757	322%	1013	323%	634	28.7%	<.001
Age at diagnosis, y													
<5	1970	6.4%	48	4.4%	133	3.9%	59	25%	224	7.1%	78	35%	
35–44	3023	9.8%	76	7.0%	175	5.1%	103	4.4%	291	93%	116	53%	
45–54	5710	185%	154	14.1%	459	133%	248	10.6%	581	185%	317	14.4%	
55 64	7033	22.8%	233	213%	647	18.8%	444	18.9%	719	22.9%	540	24.4%	
65–74	6288	20.4%	226	20.7%	712	20.7%	503	21.4%	579	185%	498	225%	
>75+	6849	22.2%	355	325%	1321	383%	993	423%	743	23.7%	660	29.9%	<.001
SES													
Lowest SES	1772	5.7%	78	7.1%	244	7.1%	191	8.1%	259	83%	204	92%	
Lower-middle SES	3439	11.1%	163	14.9%	490	142%	345	14.7%	447	142%	341	15.4%	
Middle SES	5341	173%	192	17.6%	666	193%	446	19.0%	633	202%	447	202%	
Higher-middle SES	7473	242%	259	23.7%	795	23.1%	546	232%	718	22.9%	527	23.9%	
Highest SES	10,874	352%	326	29.9%	1011	293%	676	28.8%	880	28.1%	549	24.9%	
Missing	1974	6.4%	74	6.8%	241	7.0%	146	62%	200	6.4%	141	6.4%	<0.001
Year of diagnosis													
2004–2006	9683	31.4%	332	30.4%	1056	30.6%	704	30.0%	942	30.0%	670	303%	
2007–2009	10,791	35.0%	334	30.6%	1060	30.8%	747	31.8%	1002	31.9%	728	33.0%	
2010–2013	10,399	33.7%	426	39.0%	1331	38.6%	899	383%	1193	38.0%	811	36.7%	<.001
Histology													
Malignant melanoma, NOS	CO	605%	646	592%	2052	595%	1368	582%	1871	59.6%	1985	89.9%	
Nodular melanoma	299	1.0%	130	11.9%	660	19.1%	609	25.9%	690	22.0%	158	72%	

Characteristic	<1 mm not ulcerated (n = 30,873 [71.6%])		<1 mm not ulcerated (n = 1092 [2.5%])		Stage IIA (n = 3447 [8.0%])		Stage IIB (n = 2350 [5.5%])		Stage III (n = 3137 [7.3%])		Stage IV (n = 2209 [5.1%])		*P* value
	n	%	n	%	n	%	n	%	n	%	n	%	
Lentigo maligna melanoma	1800	5.8%	37	3.4%	66	1.9%	30	13%	20	0.6%	2	0.1%	
Superficial spreading melanoma	9977	323%	275	252%	629	182%	313	133%	497	15.8%	57	2.6%	
Acral lentiginous melanoma	120	0.4%	4	0.4%	40	12%	30	13%	59	1.9%	7	03%	<.001
Lymph node biopsy													
No	26,494	853%	725	66.4%	1454	422%	1096	46.6%	1742	555%	2021	915%	
Yes	4332	14.0%	364	333%	1988	57.7%	1252	533%	1385	442%	98	4.4%	
Unknown	47	02%	3	0.4%	5	0.1%	2	0.1%	10	03%	90	4.1%	<.0001
Chemotherapy													
No	30,738	99.6%	1075	98.4%	3415	99.1%	2308	982%	2824	90.0%	1525	69.0%	
Yes	72	02%	14	13%	28	0.8%	36	15%	275	83%	647	293%	
Unknown	63	02%	3	03%	4	0.1%	6	03%	38	12%	37	1.7%	<.0001
Immunotherapy													
No	30,726	995%	1060	97.1%	3394	985%	2262	962%	2439	773%	1972	893%	
Yes	96	03%	26	2.4%	46	13%	79	3.4%	640	20.4%	224	10.1%	
Unknown	51	02%	6	0.6%	7	02%	9	0.4%	58	13%	13	0.6%	<.0001

NOS. Not otherwise specified; *SES,* socioeconomic status.

J Am Acad Dermatol. Author manuscript; available in PMC 2020 May 18.

Table II.

Survival estimates and risk of death by tumor thickness, ulceration, nodal involvement, and stage of non-Hispanic white patients with melanoma from the California Cancer Registry (2004–2013)

Survival estimate														
Tumor classification			12 mo			24 mo			36 mo			60 mo		
Characteristic	n	%	Survival estimate	95% CI		Survival estimate	95% CI		Survival estimate	95% CI		Survival estimate	95% CI	
<0.8 mm	28,110	87.9	98.1%	97.9%	98.2%	95.9%	95.6%	96.1%	93.7%	93.4%	94.0%	89.0%	88.5%	89.4%
0.8-1.0 mm	3855	12.1	97.5%	96.9%	98.0%	94.6%	93.8%	95.3%	91.6%	90.6%	92.5%	86.3%	84.9%	87.6%
≤1.0	31,965	74.3	98.0%	97.8%	98.1%	95.7%	95.4%	95.9%	93.4%	93.1%	93.7%	88.6%	88.2%	89.0%
Nonulcerated	30,873	71.8	98.2%	98.0%	98.3%	96.1%	95.8%	96.3%	93.9%	93.6%	94.2%	89.1%	88.6%	89.5%
Without nodal involvement	29,877	69.5	98.3%	98.1%	98.4%	96.2%	96.0%	96.5%	94.1%	93.8%	94.4%	89.3%	88.9%	89.8%
With nodal involvement	297	0.7	91.5%	87.5%	94.3%	80.6%	75.0%	85.0%	73.7%	67.4%	79.0%	66.7%	59.6%	72.9%
With unknown nodal involvement	699	1.6	97.4%	95.9%	98.4%	94.9%	92.9%	96.4%	92.4%	89.9%	94.3%	87.6%	83.9%	90.5%
Ulcerated	1092	2.5	92.5%	90.6%	93.9%	85.2%	82.8%	87.4%	81.7%	78.9%	84.1%	75.5%	72.1%	78.5%
Without nodal involvement	960	2.2	94.1%	92.3%	95.5%	88.7%	86.3%	90.7%	85.3%	82.6%	87.7%	78.8%	75.4%	81.8%
With nodal involvement	111	0.3	79.8%	70.6%	86.3%	57.9%	46.8%	67.5%	50.8%	39.1%	61.3%	—	—	—
Staged tumors														
Stage IIA	3347	7.8	94.5%	93.7%	95.3%	87.8%	86.5%	88.9%	80.3%	78.8%	81.8%	69.5%	67.5%	71.4%
Stage IIB	2350	5.5	92.7%	91.5%	93.7%	81.8%	80.0%	83.4%	72.2%	70.0%	74.2%	58.6%	56.0%	61.1%
Stage III	3137	7.3	89.6%	88.4%	90.6%	74.3%	72.6%	76.0%	64.3%	62.4%	66.2%	53.9%	51.7%	56.0%
Stage IV	2209	5.1	39.1%	37.0%	41.2%	25.5%	23.5%	27.5%	19.1%	17.3%	21.0%	14.9%	13.1%	16.8%

All-cause and melanoma-specific risk of death														
Tumor characteristics			All-cause risk of death						Melanoma-specific risk of death					
	n	%	HRc	95% CI		HRa	95% CI		HRc	95% CI		HRa	95% CI	
<1 mm, not ulcerated	30,872	71.6	1.00			1.00			1.00			1.00		
<1 mm, ulcerated	1092	2.5	2.54	2.22	2.92	2.27	1.97	2.61	7.89	6.23	10.0	7.45	5.84	9.51
Stage IIA	3446	8.0	3.00	2.78	3.24	2.46	2.26	2.66	7.06	6.00	8.31	6.67	5.64	7.88
Stage IIB	2350	5.5	4.38	4.05	4.75	3.31	3.04	3.60	13.14	11.25	15.34	11.56	9.83	13.59
Stage III	3137	7.3	5.17	4.82	5.54	5.31	4.93	5.72	27.23	24.00	30.90	26.52	23.23	30.29
Stage IV	2207	5.1	25.43	23.89	27.06	22.36	20.89	23.94	127.07	112.50	143.52	113.53	99.65	129.34

Thin melanomas													
	n	%	HRc	95% CI		HRa	95% CI		HRc	95% CI		HRa	95% CI	
<1 mm, not ulcerated														
Without nodal invasion	29,876	93.5	1.00			1.00			1.00			1.00		
With nodal invasion	297	0.9	3.67	2.92	4.62	4.55	3.60	5.76	20.33	14.90	27.75	19.83	14.24	27.60
With unknown nodal invasion	699	2.2	1.25	0.98	1.59	1.14	0.89	1.46	1.79	0.98	3.26	1.72	0.91	3.24
<1 mm, ulcerated														
Without nodal invasion	960	3.0	2.19	1.87	2.56	1.88	1.60	2.20	6.82	5.13	9.06	6.14	4.58	8.23
With nodal invasion	111	0.3	9.04	6.71	12.19	10.07	7.33	13.83	43.62	28.72	66.25	45.64	29.22	71.30
With unknown nodal invasion	21	0.1	5.32	2.53	11.17	6.76	3.22	14.23	27.92	10.41	74.91	32.07	11.90	86.39

Cl, Confidence interval; *HRa*,fully adjusted hazard ratio (adjusted for sex. age at diagnosis, socioeconomic status, histology, chemotherapy, immunotherapy, sentinel lymph node biopsy,and year of diagnosis; *HRc*, crude hazard ratio

J Am Acad Dermatol. Author manuscript; available in PMC 2020 May 18.

Table III.

Patient demographics, cancer characteristics, and cancer treatment of non-Hispanic white patients with melanoma diagnosed as less than 1-mm-thick ulcerated tumors by survival before or after 26 months

	Survival ≤26 mo		Survival >26 mo		
	112		554		
Characterktic	**n**	**%**	**n**	**%**	***P* value**
Sex					
Male	78	69.6%	341	61.6%	
Female	34	30.4%	213	38.4%	.1059
Age at diagnosis, y					
<35	1	0.9%	34	6.1%	
35–44	4	3.6%	41	7.4%	
45–54	14	125%	92	16.6%	
55–64	13	11.6%	130	235%	
65–74	15	13.4%	117	21.1%	
>75	65	58.0%	140	253%	<.0001
Socioeconomic status					
Lowest SES	10	8.9%	24	43%	
Lower-middle SES	19	17.0%	79	143%	
Middle SES	17	15.2%	97	175%	
Higher-middle SES	32	28.6%	129	233%	
Highest SES	25	223%	194	35.0%	
Missing	9	8.0%	31	5.6%	.0479
Histology					
Malignant melanoma, NOS	67	59.8%	314	56.7%	
Nodular melanoma	23	20.5%	54	9.7%	
Lentigo maligna melanoma	5	4.5%	19	3.4%	
Superficial spreading melanoma	15	13.4%	165	29.8%	
Acral lentiginous melanoma	2	1.8%	2	0.4%	.0002
Year of diagnosis *					
2004–2006	56	50.0%	276	49.8%	

	Survival ≤26 mo		Survival >26 mo		
	112		554		
Characterktic	n	%	n	%	*P* value
2007–2009	56	50.0%	278	50.2%	.9722
Lymph node biopsy					
No	87	77.7%	369	66.6%	
Yes	24	21.4%	185	33.4%	
Unknown	1	0.9%	0	0.0%	<.0001
Chemotherapy					
No	104	92.9%	552	99.6%	
Yes	8	7.1%	1	0.2%	
Unknown	0	0.0%	1	0.2%	<.0001
Immunotherapy					
No	105	93.8%	545	98.4%	
Yes	6	5.4%	7	13%	
Unknown	1	0.9%	2	0.4%	.0124

NOS, Not otherwise specified; *SES*, socioeconomic status.

*Limited to diagnosis between 2004 and 2009 to account for difference in amount of follow-up time available.