Impact of Age on the Management of Primary Melanoma Patients

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Key Words

Adjuvant therapy · Age · Disease management · Elderly · Melanoma

Abstract

Objectives: Age is an understudied factor when considering treatment options for melanoma. Here, we examine the impact of age on primary melanoma treatment in a prospective cohort of patients. **Methods:** We used logistic regression models to examine the associations between age and initial treatment, using recurrence and melanoma-specific survival as endpoints. **Results:** 444 primary melanoma patients were categorized into three groups by age at diagnosis: 19–45 years (24.3%), 46–70 (50.2%), and 71–95 (25.5%). In multivariate models, older patients experienced a higher risk of recurrence (hazard ratio 3.34, 95% confidence interval, CI, 1.53–7.25; $p < 0.01$). No significant differences were observed in positive biopsy margin rates or extent of surgical margins across age groups. Patients in the middle age group were more likely to receive adjuvant therapy than those in the older group (odds ratio 2.78, 95% CI 1.19–6.45; $p = 0.02$) and showed a trend to longer disease-free survival when receiving adjuvant therapy ($p = 0.09$). **Conclusion:** Our data support age as an independent negative prognostic factor in melanoma. Our data suggest that age does not affect pri-

mary surgical treatment but may affect decisions of whether or not patients receive postoperative treatment(s). Further work is needed to better understand the biological variables affecting treatment decisions and efficacy in older patients.

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Introduction

Melanoma clinicians routinely care for younger and older patients alike, making patient age an important factor when considering treatment options. Although age is not formally incorporated into melanoma treatment guidelines, several lines of evidence support a worse clinicopathological presentation of melanoma in older patients [1–5]. Nevertheless, there are currently no formal guidelines for clinical care of melanoma patients that incorporate patient age at diagnosis as a variable [6].

While the relationships between age, primary tumor characteristics, and prognosis have been studied, little attention has been given to the effect of age on melanoma treatment at the time of diagnosis. It is conceivable that the significantly worse prognosis of older patients is attributable, at least in part, to less aggressive treatment regimens for older patients. In this regard, there is some ev-

idence to suggest that older cancer patients in general are more likely to be undertreated (relative to the standard of care) than younger patients [7, 8]. To the best of our knowledge, though, no study to date has comprehensively examined the impact of age at the time of melanoma diagnosis on initial treatment decisions and effectiveness, including biopsy margin involvement, surgical excision, and the likelihood of receiving or responding to adjuvant therapy. Collectively, these factors represent crucial elements of the care and treatment of primary patients.

In this study, we examined the relationship between patient age at diagnosis and primary tumor characteristics, prognosis, biopsy and excisional margins, and adjuvant therapy in a cohort of melanoma patients prospectively enrolled in the New York University (NYU) Interdisciplinary Melanoma Cooperative Group. We considered the possibility that an improved understanding of the effects of age on melanoma progression and treatment decisions could help to better shape future guidelines for the treatment of patients.

Patients and Methods

The study cohort was comprised of patients who presented for treatment of primary invasive melanoma at NYU Langone Medical Center from September 2002 to February 2011 and were prospectively enrolled in the database of the Interdisciplinary Melanoma Cooperative Group. All patients underwent surgical treatment of the initial primary tumor. For nonrecurrent patients, a minimum of 5 years of continuous follow-up was required for survival analysis. The study was approved by the Institutional Research Board at NYU. All patients provided informed written consent at the time of enrollment.

Primary tumor characteristics were obtained from pathological reports. Slides were then reviewed by the pathologist of the Interdisciplinary Melanoma Cooperative Group, Dr. Farbod Darvishi-an, to confirm tumor characteristics and standardize all pathological information in the database. Variables assessed included Breslow thickness, ulceration, mitotic rate, histological subtype, anatomic site, regression, lymphatic vessel invasion, perineural invasion, solar elastosis, the presence of tumor-infiltrating lymphocytes, and biopsy margin involvement. BRAF and NRAS mutational status was determined directly from excised tumor specimens, when available. Surgical margin width and adjuvant therapy data were extracted from the patients' charts. Date of diagnosis was defined as the biopsy date of the primary tumor and was used to calculate age at diagnosis, follow-up time, and time to recurrence. Recurrence and survival information is collected by active prospective follow-up every 6 months for all patients enrolled in the database.

Adjuvant therapy was defined as nonsurgical treatment given after the initial surgery and before the date of first recurrence, if any. Types of adjuvant therapy included interferon, other immunomodulators, and non-immunotherapies (including radiation and chemotherapy).

Statistical Methods

Age at diagnosis was categorized into three groups: younger (19–45 years), middle (46–70), and older (71–95). Fisher's exact test or the χ^2 test (for categorical variables) and analysis of variance (for continuous variables) were used to compare patients between the three groups with regard to clinicopathological characteristics, BRAF/NRAS mutation status, and adjuvant therapy received. In a subanalysis, stage IIB–IIIC (American Joint Committee on Cancer [9]) patients were categorized by whether adjuvant therapy was given or not. Fisher's exact test or the χ^2 test was used to compare patients between these two groups with regard to clinicopathological characteristics. In order to identify factors predictive of recurrence and of receiving adjuvant therapy, a logistic regression model was used. A univariate analysis was performed first, and only variables that were statistically significant in the univariate analysis were included in predictive models during subsequent multivariate analysis. We further assessed the relationship between age and recurrence, while adjusting for the initial stage, using a Cox proportional hazard regression model. The relationship between age and disease-specific survival was assessed via Fine and Gray's competing risk regression.

To analyze the effect of adjuvant therapy on recurrence, a Cox proportional hazard regression model was used and results were stratified by age group. As this is an observational study and the choice to give adjuvant therapy is dependent on a number of variables rather than being randomized, the analysis was adjusted for the propensity of patients to receive adjuvant therapy. This step minimizes confounding factors for comparisons between the treatment and nontreatment groups. Using the same covariates as the prior logistic regression model predicting the likelihood of receiving adjuvant therapy, a propensity score for each patient was determined and the analysis was adjusted for this score [10]. Specifically, by stratifying the propensity scores and matching each patient receiving therapy to one or more patients who did not receive therapy, the bias of nonrandomization is reduced. SPSS 18.0 was used for all analyses. A value of $p < 0.05$ (two-tailed analysis) was used as the metric for statistical significance.

Results

Table 1 illustrates the demographic and primary tumor characteristics of the cohort of 444 patients categorized into three groups by age at diagnosis: 19–45 (24.3%), 46–70 (50.2%), and 71–95 years (25.5%). Older patients were significantly more likely to have advanced initial stage ($p = 0.001$), greater Breslow thickness ($p = 0.010$), ulceration ($p < 0.001$), nodular histological subtype ($p = 0.002$), and BRAF wild-type tumors ($p = 0.043$), while no significant differences were observed in gender, mitotic index, sentinel lymph node (SLN) status, anatomic site, and NRAS status between the three age groups. Table 2 demonstrates the initial treatment received by the patient cohort. All 444 patients underwent surgical treatment of the primary melanoma. No significant differences were observed in biopsy margin involvement ($p = 0.715$) or

Table 1. Baseline characteristics of 444 NYU melanoma patients by age at diagnosis [n (%)]

Characteristics	Age groups			Total (n = 444)	p value
	19–45 years (n = 108)	46–70 years (n = 223)	71–95 years (n = 113)		
Gender					
Male	61 (56)	136 (61)	60 (53)	257 (58)	0.362
Female	47 (44)	87 (39)	53 (47)	187 (42)	
Initial pathological stage					
I	77 (71)	133 (60)	52 (46)	262 (59)	0.001 ^a
II	12 (11)	44 (20)	39 (35)	95 (21)	
III	19 (18)	45 (20)	22 (19)	86 (19)	
Breslow thickness					
Mean (SD), mm	1.40 (1.67)	2.35 (3.83)	2.90 (3.78)	2.26 (3.45)	0.004 ^a
≤1.0 mm	62 (57)	100 (45)	43 (38)	205 (46)	0.010 ^a
1.01–4.0 mm	39 (36)	96 (43)	48 (42)	183 (41)	
>4.0 mm	7 (7)	26 (12)	22 (20)	55 (12)	
Ulceration					
Present	13 (12)	58 (26)	39 (35)	110 (25)	<0.001
Absent	95 (88)	165 (74)	74 (65)	334 (75)	
Mitotic index					
<1/mm ²	35 (32)	76 (34)	29 (26)	140 (32)	0.292
≥1/mm ²	71 (66)	144 (65)	82 (73)	297 (67)	
Unclassified	2 (2)	3 (1)	2 (2)	7 (2)	
SLN positive					
Yes	17 (16)	41 (18)	18 (16)	76 (17)	0.775
No	91 (84)	182 (82)	95 (84)	368 (83)	
Anatomic site					
Axial	64 (59)	124 (55)	65 (58)	253 (57)	0.813
Extremity	44 (41)	99 (45)	48 (42)	191 (43)	
Histological subtype					
Superficial spreading	71 (66)	131 (59)	44 (39)	246 (55)	0.002
Nodular	27 (25)	63 (28)	46 (41)	136 (31)	
Other ^b	9 (8)	25 (11)	23 (20)	57 (13)	
Unclassified	1 (1)	4 (2)	0 (0)	5 (1)	
BRAF status					
Mutant	20 (19)	43 (19)	21 (19)	84 (19)	0.043
Wild type	11 (10)	58 (26)	35 (31)	104 (23)	
Unclassified	77 (71)	122 (55)	57 (50)	256 (58)	
NRAS status					
Mutant	8 (7)	24 (11)	18 (16)	50 (11)	0.753
Wild type	24 (22)	77 (35)	44 (39)	145 (33)	
Unclassified	76 (70)	122 (55)	51 (45)	249 (56)	

^a Thickness, and therefore initial stage, could not be assessed for 1 patient with a fragmented primary tumor.

^b Other includes lentigo maligna, acral lentiginous, desmoplastic, nevoid, and spindle cell subtypes.

minimum surgical margin width ($p = 0.147$). However, a significant difference was observed in adjuvant therapy administration by age ($p = 0.010$).

Following initial surgery, 301 patients did not recur during the follow-up period (median 6.3 years), while 143 patients have recurred. We performed univariate analysis with the clinicopathological variables in table 1

to test the association with recurrence and entered only the significant predictors ($p < 0.05$) into a subsequent multivariate analysis (table 3). The variables included in multivariate analysis were age at diagnosis, gender, initial stage, and histological subtype. Although thickness, ulceration, mitotic rate, and SLN status were all significant predictors as well, we included only stage in the multi-

Table 2. Initial treatment characteristics of the patient cohort by age at diagnosis [n (%)]

Characteristics	Age group			Total (n = 444)	p value
	19–45 years (n = 108)	46–70 years (n = 223)	71–95 years (n = 113)		
Biopsy margin involvement					
Positive	71 (66)	140 (63)	75 (66)	286 (64)	0.715
Negative	33 (30)	67 (30)	30 (27)	130 (29)	
Unclassified	4 (4)	16 (7)	8 (7)	28 (7)	
Minimum surgical margin width					
1–1.5 cm	54 (50)	88 (39)	36 (32)	178 (40)	0.147
2–2.5 cm	42 (39)	103 (46)	55 (49)	200 (45)	
≥3 cm	2 (2)	8 (4)	7 (6)	17 (4)	
Unclassified	10 (9)	24 (11)	15 (13)	49 (11)	
Adjuvant therapy					
No adjuvant therapy	94 (87)	181 (82)	98 (87)	373 (84)	0.010 ^a
Interferon	4 (4)	4 (2)	1 (1)	9 (2)	
Other immunomodulators	4 (4)	21 (9)	1 (1)	26 (6)	
Chemo-/radiotherapy	5 (5)	16 (7)	13 (11)	34 (8)	

^a Excludes 2 patients who recurred before a planned course of adjuvant therapy could be started.

Table 3. Multivariate analysis of predictors of recurrence in melanoma patients

Variables	HR	95% CI	p value
Age at diagnosis			
71–95 vs. 19–45 years	3.34	1.53–7.25	0.002
46–70 vs. 19–45 years	2.14	1.05–4.34	0.036
71–95 vs. 46–70 years	1.41	0.78–2.56	0.252
Gender			
Male vs. female	1.74	1.03–2.94	0.040
Initial stage			
III vs. I	20.45	10.03–41.71	<0.001
II vs. I	4.71	2.53–8.78	<0.001
Histological subtype			
Nodular vs. all other histological subtypes	1.96	1.11–3.45	0.020
All other histological subtypes vs. superficial spreading	2.52	1.42–4.46	0.002

variate model as it incorporates all of these variables. Age was a significant independent factor in predicting recurrence, with older patients at greater risk than younger patients: the hazard ratio (HR) of the oldest age group to the youngest was 3.34 (95% confidence interval, CI, 1.53–7.25, $p = 0.002$), and the HR of the middle age group to the youngest was 2.14 (95% CI 1.05–4.34, $p = 0.036$). Additionally, the risk of recurrence was significantly higher for males (HR 1.74, 95% CI 1.03–2.94, $p = 0.040$) and for patients with a nodular subtype (HR 1.96, 95% CI 1.11–3.45, $p = 0.020$). As expected, initial clinical stage was a strong independent significant predictor of recur-

rence, with HRs of 20.45 (95% CI 10.03–41.71, $p < 0.001$) when comparing stage III versus stage I, and 4.71 (95% CI 2.53–8.78, $p < 0.001$) when comparing stage II versus stage I.

Using a Cox hazard regression model, we compared recurrence risk and survival time between the three age groups. Figure 1a illustrates an increasing risk of recurrence at older ages, while adjusting for initial stage ($p = 0.016$). Figure 1b demonstrates decreasing disease-specific survival at older ages, again adjusting for initial stage ($p < 0.001$). This confirms that older age at diagnosis is an independent negative prognostic factor in melanoma.

Fig. 1. Recurrence risk and disease-specific survival by age at diagnosis. **a** Cox hazards regression of recurrence of melanoma patients by age at diagnosis. **b** Disease-specific survival of melanoma patients by age at diagnosis.

To further examine the effect of age on treatment, we assessed the likelihood and effectiveness of receiving adjuvant therapy by age. As adjuvant therapy is generally not considered for patients presenting with clinical stage <IIB, stage I and IIA patients were excluded from the adjuvant therapy analysis. Additionally, 2 patients were excluded from the analysis because a planned course of adjuvant treatment was given after the patients recurred. Overall, 126 stage IIB–IIIC patients were included. Specific treatments given are detailed in online supplementary table S1 (for all online suppl. material, see www.karger.com/doi/10.1159/000351499). Sixty-seven patients received some form of adjuvant therapy: 8 patients were treated with interferon, 26 patients with other immunomodulators (including recombinant colony-stimulating factors), and 33 patients with radiation and/or chemotherapy. In the oldest age group, of 15 patients receiving adjuvant therapy, only 2 (13%) received immunotherapy, while in the younger age groups, immunotherapies accounted for 32 of 52 patients (62%) receiving adjuvant therapy. Of note, 23 patients participated in clinical trials to receive adjuvant therapy, of which only 1 was in the oldest age group despite the fact that old age was not an exclusion criterion for any of the trials. A list of clinical trials enrolling patients in the study cohort can be found in online supplementary table S2.

Table 4 demonstrates the baseline characteristics of the 126 patients eligible for adjuvant therapy, categorized

by whether therapy was received (53%) or not (47%). Patients receiving adjuvant therapy were significantly more likely to have younger age, advanced initial stage, and positive SLN ($p = 0.007$, <0.001 , and <0.001 , respectively), while no significant differences were observed in gender, Breslow thickness, ulceration, mitotic index, anatomic site, histological subtype, and BRAF and NRAS status between the two groups. To identify factors predictive of receiving adjuvant therapy in the 126 patients, we performed a univariate analysis and included only those variables which were significant in subsequent multivariate analysis (table 5). The variables included in the multivariate analysis were age at diagnosis and initial stage (SLN status was excluded from the multivariate analysis as it is already accounted for in the clinical stage). Patients in the middle age group were the most likely to receive adjuvant therapy (odds ratio 2.78, 95% CI 1.19–6.45, $p = 0.018$ for middle vs. oldest age group). Clinical stage was the major predictor of adjuvant therapy use, with stage III patients more likely to receive adjuvant therapy than stage II patients (odds ratio 3.38, 95% CI 1.47–7.76, $p = 0.004$).

Using the same multivariable model (i.e., using age and stage as covariates), we calculated a ‘propensity score’ that reflects the likelihood of each patient of receiving adjuvant therapy. Using a Cox hazard regression model and adjusting for the propensity score in order to reduce bias from the selection factors, we found no difference in recurrence hazard between treatment and nontreatment groups (fig. 2a, $p = 0.697$). Figure 2b–d il-

Table 4. Baseline characteristics of 126 stage IIB–IIIC melanoma patients by adjuvant therapy status [n (%)]

Characteristics	Adjuvant therapy		p value
	yes (n = 67)	no (n = 59)	
Age at diagnosis			
19–45 years	13 (19)	7 (12)	0.007
46–70 years	39 (59)	23 (39)	
71–95 years	15 (22)	29 (49)	
Gender			
Male	44 (66)	35 (59)	0.462
Female	23 (34)	24 (41)	
Initial pathological stage			
IIB/IIIC	13 (19)	29 (49)	<0.001
IIIA–C	54 (81)	30 (51)	
Breslow thickness			
≤1.0 mm	3 (4)	1 (2)	0.612
1.01–4.0 mm	35 (52)	34 (58)	
>4.0 mm	29 (43)	24 (40)	
Ulceration			
Present	42 (63)	43 (73)	0.223
Absent	25 (37)	16 (27)	
Mitotic index			
<1/mm ²	6 (9)	4 (7)	0.618
≥1/mm ²	58 (91)	54 (92)	
Unclassified	0 (0)	1 (2)	
SLN positive			
Yes	51 (76)	23 (39)	<0.001
No	16 (24)	36 (61)	
Anatomic site			
Axial	39 (58)	30 (51)	0.407
Extremity	28 (42)	29 (49)	
Histological subtype			
Superficial spreading	10 (15)	9 (15)	0.163
Nodular	40 (60)	43 (73)	
Other ^a	15 (22)	6 (10)	
Unclassified	2 (3)	1 (2)	
BRAF status			
Mutant	19 (28)	17 (29)	0.301
Wild type	20 (30)	26 (44)	
Unclassified	28 (42)	16 (27)	
NRAS status			
Mutant	8 (12)	13 (22)	0.343
Wild type	33 (49)	31 (53)	
Unclassified	26 (39)	15 (25)	

^a Other includes lentigo maligna, acral lentiginous, desmoplastic, nevoid, and spindle cell subtypes.

illustrates the analysis separately in each age group. Notably, in the middle age group only, patients receiving adjuvant therapy had a lower recurrence risk than patients not receiving therapy, a difference that trended towards significance ($p = 0.09$). There was no significant difference in the recurrence risk from adjuvant therapy use in

Table 5. Multivariate analysis of factors influencing likelihood of receiving adjuvant therapy in 126 patients of stage IIB–IIIC

Variables	Odds ratio	95% CI	p value
Age at diagnosis			
46–70 vs. 19–45 years	1.17	0.39–3.50	0.775
46–70 vs. 71–95 years	2.78	1.19–6.45	0.018
Initial stage			
IIIA–C vs. IIB–C	3.38	1.47–7.76	0.004

the youngest and oldest age groups; indeed, patients receiving adjuvant therapy had a slightly higher risk of recurrence in these groups ($p = 0.480$ and 0.581 , respectively).

Discussion

Our data suggest that patient age at the time of primary melanoma diagnosis is an independent prognostic variable of recurrence and death, consistent with previous studies in independent cohorts of patients [1–5, 11]. More importantly, our data demonstrate that age has effects on the initial treatment strategy of primary melanoma. Patients aged over 70 at diagnosis were significantly less likely to receive any form of adjuvant therapy (including participation in clinical trials) than patients aged 46–70 years. We did not, however, observe any significant differences in terms of biopsy or surgical margins. Our study addresses the limited published research on the effect of patient age on initial treatment for melanoma, both in terms of selection and effectiveness of therapies.

While the efficacy of adjuvant therapy for melanoma has been questioned due to the limited effect of interferon on overall survival [12], adjuvant therapy remains a relevant strategy for primary melanoma patients at high risk of recurrence. Although interferon α -2b is currently the only systemic adjuvant therapy approved by the Food and Drug Administration for melanoma, several other immunotherapies are currently being evaluated in clinical trial settings, some of which have shown promise [13]. In this regard, our group has previously reported that for metastatic patients, enrollment in clinical trials correlates with improved survival [14]. Of note, of 23 patients in our cohort receiving adjuvant therapy through clinical trials, only 1 of these patients was in the older age group, despite the fact that none of the protocols had an upper age limit

Fig. 2. Effect of adjuvant therapy on the risk of recurrence in stage IIB–IIIC melanoma patients stratified by age groups. **a** All stage IIB–IIIC patients. **b** Patients 19–45 years old at diagnosis. **c** Patients 46–70 years old at diagnosis. **d** Patients ≥ 71 years at diagnosis.

for enrollment. Finally, radiation therapy has been shown to provide strong local control over melanoma recurrence [15].

Our data revealed a particularly large difference in the administration of adjuvant immunotherapies between age groups, possibly because patient age may have significant effects on the efficacy of interferon therapy. Response to interferon therapy has been correlated with general immune response following treatment, suggesting that healthy patients with a strong immune system are more likely to respond to the drug [16, 17]. Younger age

is also a significant predictor of response for dendritic cell vaccines, another immunotherapy that was administered to several patients in our cohort [18]. The lower likelihood of successful response may affect the choice to administer interferon and other immunotherapies: in our cohort, patients in the oldest age group rarely received immunotherapies, whereas patients in the younger age groups received immunotherapies more frequently than nonimmunotherapies.

There are other possible explanations for the less aggressive treatment of older patients, a phenomenon that

has previously been reported with regard to surgical treatment such as performing SLN biopsies, complete nodal dissections, and achieving adequate excisional margins [8, 19, 20]. There may be concerns about administering costly and aggressive treatments to elderly patients who already have a limited life expectancy. One recent study performed a cost-effectiveness analysis of interferon treatment of high-risk melanoma patients and concluded that interferon treatment in most patients older than 63 demands an inordinately high cost for each quality-adjusted year of life gained [21]. Logistical difficulties can be a factor for elderly patients as well: at least 6 older patients in our cohort refused adjuvant treatment due to the difficulty of making frequent visits to the clinic.

Another potential factor in the lower rates of treatment in elderly patients is higher frequencies of comorbidities that may make treatment inadvisable or impractical. To account for the effects of comorbidities on choice and effectiveness of adjuvant therapies, information was extracted from medical records when available. Of the patients in the older age group, 20/20 (100%) patients who did not receive adjuvant treatment and 12/13 (92%) who did receive treatment had notable comorbidities. When focusing only on cardiovascular conditions, including hypertension and coronary artery disease, 17/20 (85%) who did not and 10/13 (77%) who did receive therapy had such conditions. Therefore, comorbidity rates in the older age group were very high among treated patients as well as nontreated ones, suggesting that the presence of comorbidities is not a major determining factor of whether or not a patient will receive adjuvant treatment.

In terms of benefiting from adjuvant therapy, we observed a nonsignificant trend to longer disease-free survival among patients receiving any adjuvant therapy compared to observation in the middle age group only ($p = 0.09$). Notably, there was no reduction in the recurrence risk from adjuvant therapy use in the oldest age group, showing that, in our cohort, adjuvant therapy options for older patients were ineffective. One possibility is that this trend reflects the difference in therapy type received: patients in the middle age group received more immunotherapies and participated in more clinical trials, whereas older patients were more likely to receive only radiation or chemotherapy. Another possibility, which remains untested, is that the trend reflects biological differences in response to treatment by age. Recent research in the divergent pathway model of cutaneous melanoma suggests that the melanoma that affects the younger population may be biologically distinct from the melanoma

affecting older individuals [5, 22]. For instance, in our study, older patients were more likely to have a nodular histological subtype and less likely to have BRAF-mutated tumors, consistent with previously published studies [5, 23, 24]. This difference in cancer biology by age may be reflected in the trend observed in our study towards a relationship between adjuvant therapy effectiveness and age. Indeed, studies of the Wnt signaling pathway have drawn a link between older age and an aggressive, treatment-resistant phenotype of melanoma, although clinical data are lacking [25]. As such, one important future direction of research should be an examination of clinical data on response to specific forms of adjuvant therapy in expanded sample sizes of patients, with higher statistical power.

Our study suffered limitations that must be considered in interpreting the data. This was a hospital-based study, making its applicability to a larger population uncertain. However, this also allowed for strict standardization of patient clinical data and standard of care treatments across all patients, substantially limiting outside confounding factors such as differential access to clinical trials. We also recognize that independent validation in a different set of patients is needed before firm conclusions can be made. Nevertheless, our results highlight some pronounced differences between older and younger melanoma patients and identify key areas to be followed up on in future research.

Conclusion

Our data support age as an independent negative prognostic factor in melanoma and suggest that age does not affect primary surgical treatment but may affect decisions of whether or not patients receive postoperative treatment(s). Further work is needed to better understand the biological variables affecting treatment decisions and efficacy in older patients.

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