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Prognostic factors in young women with cutaneous melanoma

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Abstract

BACKGROUND: Gender is an established prognostic factor in cutaneous melanoma; women as a group have a better overall prognosis than men. However, the investigators hypothesized that melanoma in young women may have distinct clinicopathologic features and biologic behavior compared with melanoma in older women, possibly related to tanning bed use and excessive acute episodes of sun exposure.

METHODS: A retrospective analysis was performed of a large multicenter study that accrued patients between 1996 and 2003 and included patients aged 18 to 70 years with cutaneous melanoma $\geq$1 mm Breslow thickness and no evidence of regional or distant metastatic disease. All women with follow-up data were included. Univariate and multivariate analyses as well as Kaplan-Meier (KM) analysis were performed to test for differences in clinicopathologic variables, disease-free survival (DFS), and overall survival (OS) between female patients $\leq$40 and >40 years of age.

RESULTS: A total of 1,056 female patients were divided into 2 groups: those >40 years of age (n = 757 [71.7%]) and those $\leq$40 years of age (n = 299 [28.3%]). Overall, there were no differences in Breslow thickness, ulceration, or sentinel lymph node status between groups. Compared with older women, younger women were more likely to have truncal melanomas (39.5% vs 29.5%, P = .0017) and less likely to have regression of the primary tumor (6.4% vs 11.5%, P = .0208). The mean number of sentinel lymph nodes removed was 2.82 for younger women and 2.29 for older women (P < .0001). Multivariate analysis revealed that Breslow thickness, ulceration, and tumor-positive sentinel lymph node were associated with worse DFS in both the younger and older groups; truncal location was associated with worse DFS in the younger group only. The same factors were predictive of OS in both groups, except that ulceration was not significant in the younger

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patient group. In the younger patient group, the 5-year KM DFS rates were 78.1% for truncal melanomas and 92.5% for nontruncal melanoma locations ($P = .0009$); the corresponding 5-year KM OS rates were 76.6% and 93.9% ($P = .0003$). In the older patient group, the 5-year KM DFS rates were 84.1% for truncal and 82.8% for nontruncal melanomas (P = NS), and the corresponding 5-year KM OS rates were 81.6% and 87.5% ($P = .0049$).

CONCLUSIONS: Although women with cutaneous melanoma tend to have a better prognosis than men, women $\leq$40 years of age with primary melanoma of the trunk may represent a subgroup at higher risk for disease recurrence and metastasis.

Melanoma has become an epidemic among the Caucasian population in the United States, with an increasing number of patients diagnosed each year.[1] Gender is an established prognostic indicator in cutaneous melanoma. Although women are at higher risk for being diagnosed with the disease, as a whole, they have a better prognosis than men.[2–4] It remains unclear why women experience a survival benefit despite having an increased risk for developing the disease. To further investigate the role of gender in melanoma, the purpose of this study was to evaluate the differences between older and younger women with melanoma.

Several theories have been proposed to explain the potential differences in the etiology of melanoma in younger versus older women. Demko et al[5] emphasized the role of acute sun exposure through sunbathing and indoor tanning by adolescents and young women. This has been further corroborated by studies showing behavioral differences in the proportion of skin that is covered by clothing or sunscreen in younger versus older women.[6] Others have cited decreases in immune system function and regulation, or immunosenescence, with aging.[7] Additionally, hormones and menopausal status may play a role in melanoma risk and prognosis.[8–11]

Regardless of the cause, we hypothesized that melanoma in young women may have distinct clinicopathologic features and biologic behavior compared with melanoma in older women.

Methods

The Sunbelt Melanoma Trial (SMT) is a multi-institutional randomized controlled trial with 79 centers throughout North America. Institutional review board approval was obtained at each participating institution. From 1996 to 2003, the trial accrued 3,600 patients between the ages of 18 and 70 years with cutaneous melanomas $\geq$1 mm and no evidence of metastatic disease. All patients underwent sentinel lymph node (SLN) biopsy; those patients with tumor-positive SLNs underwent completion lymph node dissection. The technical aspects of the SMT have previously been described elsewhere.[12]

This study represents a post hoc analysis performed on data from the SMT. All patients who were women and had follow-up data available were included. Clinicopathologic, recurrence, and survival data were prospectively collected for the SMT. Categorical variables were analyzed using chi-square analysis. Univariate and multivariate analyses as well as Kaplan-Meier (KM) analysis were performed to test for differences in clinicopathologic variables, disease-free

Table 1 Clinicopathologic factors associated with female patients by age

Variable	Age $\leq$ 40 y	Age $>$ 40 y	*P*
Number of patients	299 (28.3%)	757 (71.7%)	
Mean Breslow thickness (mm)	1.98	2.09	.3127
Clark level IV or V	220 (75.6%)	545 (74.9%)	.8055
LVI present	14 (5.3%)	50 (7.6%)	.2102
Superficial spreading histology	146 (48.8%)	363 (48.0%)	.7972
Truncal site	118 (39.5%)	223 (29.5%)	.0017
Regression present	17 (6.4%)	77 (11.5%)	.0208
Ulceration present	58 (19.7%)	181 (24.4%)	.1004
SLN positive	61 (20.4%)	132 (17.4%)	.2615
Mean number of SLNs removed	2.82	2.29	$<$.0001
Mean number of positive SLNs (in SLN-positive patients)	1.39	1.25	.2264
Mean number of positive lymph nodes (SLN + NSN, in SLN-positive patients)	1.57	1.45	.6040

LVI = lymphovascular invasion; NSN = nonsentinel lymph node; SLN = sentinel lymph node.