Correlation of Thicknesses of Superficial Spreading Malignant Melanomas and Ages of Patients

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In a prospective study of 455 consecutive patients with superficial spreading malignant melanomas entered into the data base of the Melanoma Cooperative Group of New York University Medical Center, it was found by linear-regression analysis that there is a statistically significant ($p = 0.005$) positive correlation between the ages of the patients and the thicknesses of their lesions. Although the reasons for the correlation between ages and thicknesses are not certain, several possible explanations were considered, namely: (1) the greater prevalence of superficial spreading malignant melanomas in the aged on the lower limbs where thicker lesions were present in our patients, (2) the altered skin of the elderly, which may favor deeper penetration by these neoplasms, (3) impaired immunologic responses in the aged, (4) the delay in diagnosis of malignant melanomas in the elderly because of obscuration of them by numerous benign pigmented lesions that frequently develop with aging, and (5) lesser concern of the elderly with their physical appearances in particular and medical problems in general.

INTRODUCTION

It has been previously reported that the thicker malignant melanomas are[1-13] and the later they occur in life[11-17] the poorer are prognoses in terms of recurrence, metastasis, and death. However, little has been written on the relationship, if any, between these two prognostic variables.

The purposes of this paper are to report that for superficial spreading melanomas there is a direct and highly significant correlation between thicknesses of lesions[1,2] and ages of patients and to discuss possible explanations for the finding.

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MATERIALS AND METHODS

Relevant facts were obtained from the computerized data base of the Melanoma Cooperative Group of New York University Medical Center from 1972 through 1979. The total number of records of patients with malignant melanomas of all sorts in this data base for that period was 846. Of these 846 records, 455 of superficial spreading malignant melanomas were used in this study because they had histologic confirmation of being superficial spreading malignant melanomas, measurements of thicknesses of lesions, and ages of the patients. Of the 455, 434 (95.5%) were Stage I lesions (local lesion only) and 21 (4.6%) were Stage II lesions (local lesion and metastases to regional nodes). Thicknesses of the melanomas were determined by the method of Breslow[1,2] in which an ocular micrometer is used to measure the extent of the lesion in millimeters between the top of the stratum granulosum of the epidermis to the deepest cells of the melanoma identifiable in the dermis or subcutis. The lesions were also classified according to Clark's levels.[18]

The computer used was a CDC 6600 located at the Courant Mathematics and Computing Laboratory of New York University. Analyses were performed with version No. 8.0 of Statistical Package for the Social Sciences. When a particular computer analysis was done, any record that lacked a value for a relevant variable was excluded. A finding was considered significant if by chi-square analysis (or linear-regression analysis where appropriate) $p \leq 0.05$, which revealed that there was at most a 5% probability that it was due to chance alone.

For some analyses, where appropriate, ages of patients and thicknesses of lesions were broken down into groups; i.e., ages were grouped by decades and thicknesses were grouped in ten ranges: 0–0.75 mm; 0.76–1.00; 1.01–1.50; 1.51–2.00; 2.01–2.50; 2.51–3.00; 3.01–3.50; 3.51–4.00; 4.01–4.50; more than 4.50 mm.

FINDINGS

Figure 1 shows the result of linear-regression analysis of the raw data of the ages of the patients and thicknesses of their superficial spreading malignant melanomas. There is a highly significant ($p = 0.005$) positive correlation between these two variables.

Table 1 displays the data of ages of patients by decades and grouped thicknesses of the superficial spreading malignant melanomas in ten ranges. Again, there was a significant and positive correlation between these variables ($p = 0.0009$). This computation was carried out because in some of the other studies recounted below the variable "ages-by-decades" was used rather than raw ages.

In order to study possible explanations for the positive correlation between thicknesses of the superficial spreading malignant melanomas and ages of the patients, additional computations were performed as follows.

1. *Correlation of Locations of Superficial Spreading Malignant Melanomas and Ages of Patients (Table 2).* Overall, there was no statistically significant relationship between anatomical sites of lesions and ages of the patients ($p = 0.2016$). However, the percentage of lesions on the lower limbs was progressively greater from the fourth through the seventh decade, and analysis then showed the relationship in these years to be statistically significant ($p = 0.05$).

2. *Correlation of Locations of Superficial Spreading Malignant Melanomas and Their Thicknesses (Table 3).* A highly significant relationship was found between these two variables ($p = 0.009$), especially because there was a greater percentage (47.0%) of lesions that were more than 1.5 mm thick on the lower extremities, whereas only about 30% were more than 1.5 mm thick on the head and neck, upper extremities, and trunk.

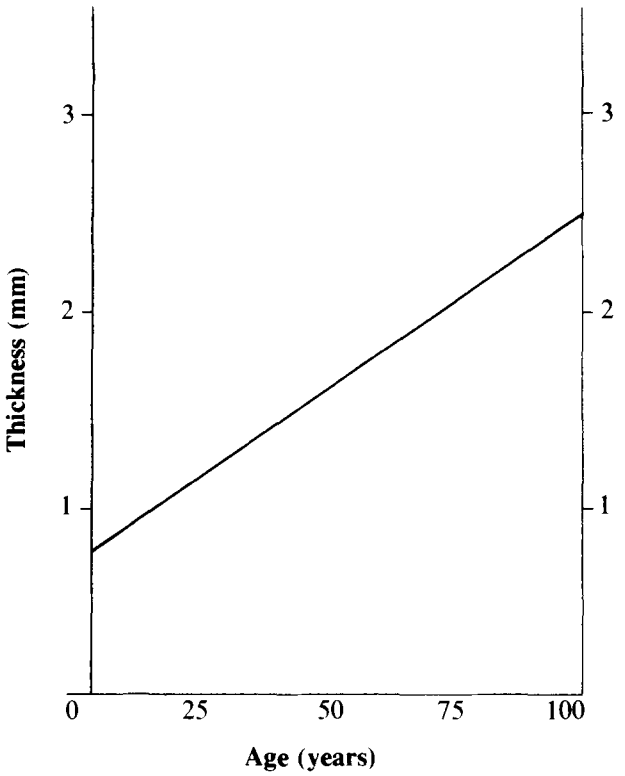

FIGURE 1. *Linear-regression analysis of ages of patients and thicknesses of their superficial spreading malignant melanomas. Number of lesions, 434; p = 0.005.*

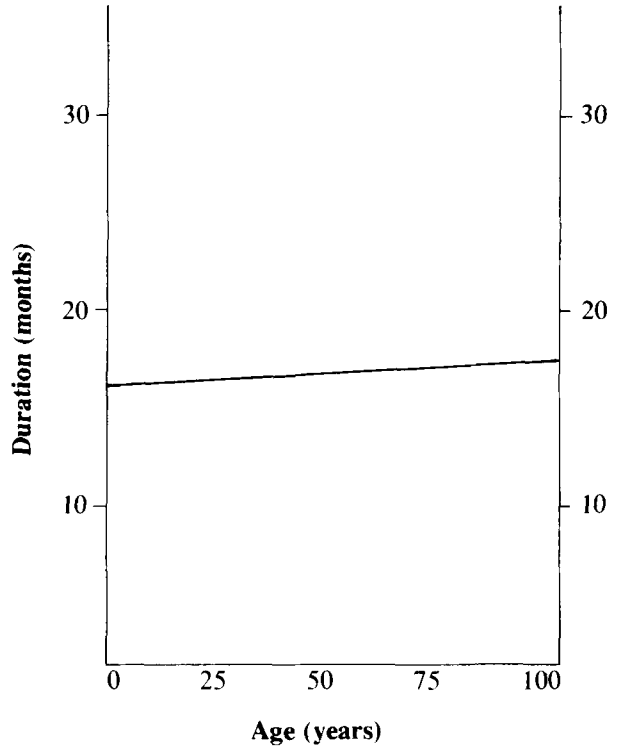

FIGURE 2. *Linear-regression analysis of stated durations of superficial spreading malignant melanomas and ages of patients. Number of lesions, 425; p = 0.394.*

Table 1
Ages of Patients by Decades and Ranges of Thicknesses in Millimeters of Their Superficial Spreading Malignant Melanomas*

Age (decade)	Number of Patients	Percentage in Each Thickness Group									
		0.00 to 0.75	0.76 to 1.00	1.01 to 1.50	1.51 to 2.00	2.01 to 2.50	2.51 to 3.00	3.01 to 3.50	3.51 to 4.00	4.01 to 4.50	4.51 and over
2	3	0	33.3	33.3	0	0	0	0	33.3	0	0
3	37	35.1	21.6	18.9	10.8	5.4	2.7	2.7	2.7	0	0
4	62	43.5	11.3	19.4	12.9	1.6	1.6	4.8	3.2	0	1.6
5	97	29.9	22.7	15.5	9.3	8.2	4.1	1.0	0	2.1	7.2
6	101	34.7	13.9	13.9	11.9	7.9	6.9	5.9	2.0	3.0	0
7	93	30.1	12.9	15.1	10.8	8.6	5.4	5.4	3.2	5.4	3.2
8	35	34.3	11.4	8.6	5.7	11.4	11.4	2.9	2.9	2.9	8.6
9	5	20.0	0	0	20.0	20.0	0	0	0	0	40.0
10	1	100	0	0	0	0	0	0	0	0	0
Total	434	33.6	15.7	15.2	10.6	7.4	5.1	3.9	2.3	2.5	3.7

* $p = 0.0009$ (using Pearson's correlative factor).

Table 2
Percentage of Superficial Spreading Malignant Melanomas on Upper and Lower Extremities in Patients in the Fourth through Seventh Decades of Life*

Age (decade)	Number of Patients	Extremities			
		Upper		Lower	
		No./Total	Percentage	No./Total	Percentage
4	67	21/67	31.3	15/67	22.4
5	106	22/106	20.8	29/106	27.4
6	103	21/103	20.4	29/103	28.2
7	96	17/96	17.7	31/96	32.3

* $p = 0.05$.

Table 3
Thicknesses of Superficial Spreading Malignant Melanomas on Different Anatomic Sites*

Site	Number of Patients	Thicknesses of Lesions	
		≤1.5 mm	>1.5 mm
Head and neck	46	71.7%	28.3%
Upper limbs	92	68.5%	31.5%
Trunk	176	69.9%	30.1%
Lower limbs	115	53.0%	47.0%
Total	429	65.3%	34.7%

* $p = 0.009$.

3. *Correlation of Durations of Superficial Spreading Malignant Melanomas (as Stated by Patients) and Ages of the Patients (Fig. 2)*. There was no significant correlation ($p = 0.394$) between these two variables.

4. *Correlation of Thicknesses of Superficial Spreading Malignant Melanomas of Less than Two Years' Stated Duration and Ages of Patients (Table 4)*. Two years was chosen as a cutoff point for this correlation because it was thought that the accuracy of patients to recall the durations of their lesions would be greater for shorter durations. For lesions up to two years in stated duration, the percentage of them thicker than 1.5 mm tended to increase with age ($p = 0.002$).

Table 4
Comparison of Thicknesses of Superficial Spreading Malignant Melanomas of Less than Two Years' Duration in Ages-by-Decades*

Age (decade)	Number of Patients	Thicknesses of Lesions	
		≤1.5 mm	>1.5 mm
2	3	66.6%	33.3%
3	33	72.8%	27.2%
4	51	72.5%	27.5%
5	76	69.8%	30.2%
6	78	57.7%	42.3%
7	71	64.8%	35.2%
8	25	40.0%	60.0%
9	5	20.0%	80.0%
10	1	100.0%	0.0%
Total	343	63.6%	36.4%

* $p = 0.002$.

Table 5
Comparison of Lymphocytic and Melanophagic Responses to Vertical-Growth Components of Superficial Spreading Malignant Melanomas in Ages-by-Decades

Age (decade)	Lymphocytic Response		Melanophagic Response	
	Present	Absent	Present	Absent
2	2(100.0%)	0(0.0%)	1(50.0%)	1(50.0%)
3	24(80.0%)	6(20.0%)	21(72.7%)	8(27.6%)
4	39(76.5%)	12(23.5%)	37(72.5%)	14(27.5%)
5	75(93.8%)	5(6.2%)	61(76.2%)	19(23.8%)
6	66(82.5%)	14(17.5%)	61(76.2%)	19(23.8%)
7	62(79.5%)	16(20.5%)	52(67.5%)	25(32.5%)
8	22(78.6%)	6(21.4%)	22(78.6%)	6(21.4%)
9	4(80.0%)	1(20.0%)	4(80.0%)	1(20.0%)
Total	294(83.1%)*	60(16.9%)*	259(73.6%)†	93(26.4%)†

*† p = not significant.

5. *Correlation of Lymphocytic and Melanophagic Responses to Superficial Spreading Malignant Melanomas in Ages-by-Decades* (*Table 5*). There was no statistically significant difference in these responses that could be related to ages.

6. *Correlation of Clark's Levels of Superficial Spreading Malignant Melanomas and Ages-by-Decades* (*Table 6*). There was a statistically significant ($p = 0.0026$) correlation between the ages-by-decades and levels of their lesions.

DISCUSSION

This study demonstrated that there is a direct and highly statistically significant correlation between the ages of patients and the thicknesses of their superficial spreading malignant melanomas. In an attempt to explain this observation we considered a number of possible reasons.

Is anatomical location of superficial spreading melanomas a factor influencing the thicknesses of lesions as age advances? There was a statistically significant correlation between the locations of superficial spreading malignant melanomas and their thicknesses (Table 3). Only about 30% of the lesions on the trunk, head and neck, and upper limbs were 1.5 mm or greater in thicknesses, whereas 47% of the lesions on the lower limbs were of these thicknesses.

While there was no statistically significant correlation between locations of superficial spreading malignant melanomas overall and the ages of patients, the

Table 6
Comparison of Clark's Levels of Superficial Spreading Malignant Melanomas and Ages of Patients*

Age (decade)	Number of Patients	Level				
		I	II	III	IV	V
2	3	0	33.3%	33.0%	33.3%	0
3	38	5.3%	34.2%	42.1%	15.8%	2.6%
4	66	1.5%	40.9%	21.2%	33.3%	3.0%
5	103	3.9%	31.1%	33.0%	27.2%	4.9%
6	104	2.9%	28.8%	31.7%	35.6%	1.0%
7	95	3.2%	27.4%	22.1%	44.2%	3.2%
8	35	0	34.3%	11.4%	48.6%	5.7%
9	5	0	20.0%	0	60.0%	20.0%
10	1	0	100%	0	0	0
Total	450	2.9%	31.8%	27.3%	34.7%	3.3%

* $p = 0.0026$.

percentage of lesions situated on the lower extremities increased significantly with age (Table 2). Thus, whereas only 22.4% of patients in the fourth decade of life had superficial spreading malignant melanomas on the lower extremities, 32.3% of patients in the seventh decade had such lesions on the lower extremities. The progressively greater percentage of women in the older decades (due to their greater longevity in general) could account for the larger percentage of lesions on the lower extremities because women tend to develop superficial spreading malignant melanomas on the legs more often.[19–21] Perhaps one of the reasons that the elderly had thicker lesions is because they had a larger percentage of lesions on their lower limbs (Table 2) and because this anatomical site had thicker lesions (Table 3).

Does the altered skin of the aged predispose them to thicker lesions? In addition to thickness, there is a significant correlation between ages of the patients and Clark's[18] levels of invasion (Table 6). Black[22] reported that the skins of persons who are over 65 years of age are thinner than those who are under 65. If the thickness of skin diminishes with age, then of younger and older patients with lesions of the same thickness, the older ones may be expected to have deeper levels of invasion. This may have practical implications since superficial spreading malignant melanomas are more likely to metastasize the deeper they penetrate (i.e., the greater their levels of invasion).

Is the delay in diagnosis greater in older patients who have superficial spreading malignant melanomas? It is well known that as persons age they tend to develop numerous pigmented cutaneous lesions like seborrheic keratoses and solar lentigines. This is especially true for those who have had excessive exposure to sunlight. Data are accumulating that implicate prolonged exposure to the sun as an important role in the causation of cutaneous malignant melanomas.[23] Thus, it has been reported that, compared to a control population, patients who have malignant melanomas had spent considerably more time outdoors even though they had light complexions, blond or red hair, light-colored eyes, and a tendency to sunburn easily.[24] Patients who have superficial spreading malignant melanomas are likely to have more sun-induced pigmented cutaneous lesions (e.g., solar lentigines) than those who do not. In our experience, it is not unusual to encounter patients in whom it is difficult to identify very early malignant melanomas when they also have numerous pigmented lesions on sun-damaged skin. Thus, the detection of malignant melanomas may be delayed and their thicknesses may be enhanced in the elderly because the malignant lesions were obscured by other pigmented lesions.

Finally, one may speculate that the older patients are, the more they procrastinate before seeking treatment for pigmented lesions. We did not find in our data base support for this speculation, but it is probable that the reliability of statements of durations of the neoplasms is questionable and, therefore, the speculation may still be true.

Are thicknesses of superficial spreading malignant melanomas related to immunologic deficits as age progresses? Aging, no doubt, has a deleterious effect on immunologic competence. Burnet[25] suggested that the immune system tends to progressive malfunction with aging, which results in increased liability to malignant disease. Diminished immunologic responsiveness could explain why older patients have thicker lesions than younger ones for superficial spreading malignant melanomas that have been present for the same length of time. To obtain data to support or negate this concept, we examined 343 patients who stated that their lesions appeared less than two years before consultation (Table 4). We found that the percentage of lesions thicker than 1.5 mm generally increased with age. Thus, for lesions of comparable stated durations, elderly people have thicker lesions, which would be consistent with the concept that superficial spreading malignant melanomas grow faster in older patients and with the hypothesis that this could be due to deficient host-response mechanisms. Although both humoral and cellular immune reactivities are generally preserved or only slightly reduced in malignant melanomas of Stages I and II,[26] no one, to our knowledge, has compared the immune status of younger and older patients with superficial spreading malignant melanomas of similar thicknesses. We also examined the data base for the presence or absence of lymphocytes and melanophages in histologic sections in order to try to judge host responses to thicknesses of superficial spreading malignant melanomas, but could find no convincing differences between younger and older groups of patients (Table 5).

In conclusion, we report here a direct and statistically significant correlation between the thicknesses of superficial spreading melanomas and the ages of patients who developed them. Possible factors responsible for this observation were a preponderance of superficial spreading malignant melanomas on the lower limbs of older patients and the greater thicknesses of such lesions on lower extremities in our patients as compared to thicknesses on other anatomic locations; difficulty and delay in detecting superficial spreading malignant melanomas in the elderly because of the large number of pigmented lesions on them, which obscures superficial spreading malignant melanomas; reduced immunologic responsiveness in the aged, which allows more rapid growth of superficial spreading malignant melanomas in older patients; less concern of the el-

derly with physical appearance, which makes for longer intervals between onset and consultation; and diminution of thickness of skin in the aged, which may permit deeper penetration by malignant cells.

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