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Lower skin cancer risk in women with higher body mass index: The Women's Health Initiative Observational Study

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Abstract

The unclear relationship of obesity to incident melanoma and nonmelanoma skin cancer (NMSC) risks was evaluated in the large, geographically diverse longitudinal, prospective Women's Health Initiative (WHI) Observational Study. Risks of melanoma and NMSC in normal weight women were compared to risks in overweight (BMI = 25 – 29.0 kg/m²) and obese (BMI ≥ 30 kg/m²) women, using Cox proportional hazards models for melanoma and logistic regression for NMSC. Over a mean 9.4 years of follow-up, there were 386 melanoma and 9,870 NMSC cases. Risk of melanoma did not differ across weight categories (p=0.86), whereas in fully adjusted models, NMSC risk was lower in overweight (OR 0.93, 95% CI: 0.89–0.99) and obese (OR 0.85, 95% CI: 0.80–0.91) women (p<0.001). Excess body weight was not associated with melanoma risk in postmenopausal women but was inversely associated with NMSC risk, possibly due to lower sun exposure in overweight and obese women. This supports previous work demonstrating the relationship between excess body weight and skin cancer risk.

Keywords

Excess body weight; fat; nonmelanoma skin cancer; melanoma

INTRODUCTION

Rates of skin cancer, the most common U.S. malignancy, affecting over 3.5 million Americans each year, are increasing for both melanoma and non-melanoma skin cancer (NMSC) (1). Whereas obesity is linked to increased risks of colon, breast, endometrial and ovarian cancers (2), its relationship to skin cancer is unclear. The Nurses' Health Study and Health Professionals Follow-up Study reported a lower NMSC risk in obese patients, but no association between BMI and melanoma (3). In a 2-year randomized low-fat diet trial,

subjects who reduced their BMI also reduced their risk of NMSC (4). The longitudinal, prospective Women's Health Initiative (WHI) Observational Study (OS) provided an opportunity to investigate relationships of body weight status to melanoma and NMSC risks, taking into account key sunlight exposure variables, the major etiologic factors in skin cancer development (1).

MATERIALS AND METHODS

Post-menopausal women, aged 50 to 79 years, enrolled in the WHI Observational Study at 40 U.S. clinical centers from 1994 to 1998 (N=93,676), completed baseline questionnaires on key demographic and lifestyle variables (5). Because the majority of skin cancers occur in Caucasians and other ethnic groups did not demonstrate significant numbers of cases (1), analyses were restricted to white women (N=78,016) who were not underweight (BMI not less than 18.5) (N=76,208) and had completed a sun exposure questionnaire at year 4 (N=75,842). Our final model utilized data from 61,657 subjects who had complete information on all variables included in the scientific model. Self-reported cases of melanoma and NMSC (representing both basal and squamous cell variants) were ascertained annually by questionnaire and melanoma cases were physician-adjudicated, using medical records. Risks of melanoma and NMSC in normal weight women (body mass index (BMI) = 18.5 to 24.9 kg/m²) were compared to risks in overweight (BMI = 25–29.0 kg/m²) and obese (BMI ≥ 30 kg/m²) women, using Cox proportional hazards models for melanoma and logistic regression for NMSC (odds ratios with 95%CI), with subsequent adjustments for known baseline risk factors, e.g. age, skin type (burn or tan), childhood summer sun exposure, baseline summer and ambient sun exposure (as Langley's at each clinical center across varying residential latitudes), smoking status, education, time walking outdoors per week, and self-reported history of skin or other cancer (see Table 1). Date of melanoma diagnosis was available from medical records thus allowing for time to event methods (Cox) for melanoma analysis. For NMSC, participants reported this outcome yearly and this was not medical record adjudicated, thus only logistic regression could be performed.

RESULTS

Small, but statistically significant, differences in baseline characteristics were found among the three BMI groups (Table 1), including prior skin cancer and sun exposure, the most important predictors of skin cancer risk (1). Compared to the normal weight group, overweight and obese women reported less sun exposure (Table 1), based on average time walking outside (p<0.001), current sun exposure (p<0.001), and likelihood of living in areas of high geographic UV exposure (p<0.0001).

Melanoma

386 incident melanoma cases were reported (Table 2), 175 cases (0.66%) occurring in the normal weight group, 137 (0.65%) in the overweight group, and 74 (0.53%) in the obese group. Melanoma risk did not vary by weight category in either unadjusted or fully adjusted models (p=0.86). Relative to normal weight, hazard ratios for overweight and obese women were 0.98 (95% CI: 0.74–1.29) and 1.10 (95% CI: 0.95–1.28), respectively (Table 2). Excluding women with prior history of skin cancer (N=7,000) did not change the result (P=0.8).

Nonmelanoma skin cancer (NMSC)

A total of 9,870 NMSC cases were reported (Table 2) as follows: normal weight, 1,874 cases (17.6%); overweight, 3,358 (15.8%); obese, 4,638 (13.3%), with a significant difference in risk among weight groups in both unadjusted and fully adjusted models,

($p < 0.0001$). Relative to normal weight, odds ratios for overweight and obese women were 0.93 (95% CI: 0.86–0.99) and 0.86 (95% CI: 0.80–0.91), respectively (Table 2). This relationship persisted even when participants with a history of skin cancer were excluded.

DISCUSSION

Excess body weight was not associated with melanoma risk in white postmenopausal women in the WHI cohort over 9 years of follow-up, whereas it was significantly associated with NMSC risk. Specifically, overweight and obese women had a lower risk of NMSC compared to normal weight women. Overweight and obese women also reported less baseline sun exposure and it is conceivable that the lower NMSC risk was due to less sun exposure. Obese individuals have been shown to be less physically active and have less sun exposure at least in part because of being outdoors less frequently (3, 6). Pothiwala et al. demonstrated risk of NMSC, for which UV radiation has been shown to be most important, to be reduced to a greater extent in obese individuals. This supports the notion of diminished sun exposure for obese individuals, and could explain the decreased risk of NMSC seen in the WHI cohort. In contrast, melanoma risk is less well correlated to sun exposure (1). Of interest, this is in contrast to work demonstrating obese mice to have an increased (not decreased) susceptibility to skin cancer (7).

One of the strengths of the current analysis is the ability to adjust for sun exposure across a large, geographically diverse cohort over 9.4 years of follow up. Despite adjustment for the major risk factor for skin cancer, i.e. sun exposure, it is possible that residual confounding arising from error in the self-reporting of this measure (8) may underlie the difference in NMSC risk by weight status.

Although there is a biological mechanism between excess fat and skin cancer via oxidative DNA damage and intake of fatty foods (2), we did not observe a relationship between obesity and skin cancer risk in post-menopausal women. This confirms the prior work of Pothiwala et al (3), and supports their finding that obesity may be a surrogate for lifetime sun exposure resulting in lower rates of NMSC in overweight and obese women who receive less sun exposure.

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Table 1

Baseline Demographics among BMI groups of white women in the Women's Health Initiative Observational Study

Covariate	Normal 18.5 – 24.9 kg/m ²	Overweight 25–29.9kg/m ²	Obese 30+ kg/m ²	Total
BMI (No., %)	26,396 42.8	21,208 34.4	14,053 22.8	61,657 100
<i>Age group at baseline (No., %)</i>				P<0.0001
50–59	8845 33.5	6150 29.0	4471 31.8	19,466
60–69	11477 43.5	9724 45.9	6625 47.1	27,826
70–79+	6074 23.0	5334 25.1	2957 21.1	14,365
<i>Education (No., %)</i>				P<0.0001
Less than high school diploma or GED	6141 23.2	6145 29.0	5072 36.1	17,358
Some school after high school diploma	6807 25.8	5936 28.0	4089 29.1	16,832
College degree or higher	13448 51.0	9127 43.0	4892 34.8	27,467
<i>Times walked outside</i>				P<0.0001
Never	2884 10.9	2858 13.5	3009 21.4	8751
1–3x/month	3137 11.9	2969 14.0	2535 18.0	8641
1–3x/week	10082 38.2	8452 39.8	5404 38.5	23,938
4–7+/week	10293 39.0	6929 32.7	3105 22.1	20,327
<i>Geographic sun exposure (Langleys)</i>				P<0.0001
300 – 325	7887 29.9	7007 33.0	4944 35.2	19,838
350	5154 19.5	4612 21.7	3313 23.6	13,079
375 – 380	3399 12.9	2203 10.4	1333 9.5	6935
400 – 430	4427 16.7	3344 15.8	2037 14.5	9808
475 – 500	5529 21.0	4042 19.1	2426 17.2	11,997
<i>NMSC at baseline</i>				P<0.0001
No	23,665 89.7	19,333 91.2	12,979 92.4	55,977
Yes	2731 10.3	1875 8.8	1074 7.6	5680
<i>Melanoma at baseline</i>				P=0.021
No	26,120 99.0	20,934 98.7	13,872 98.7	60,926

Covariate	Normal 18.5 – 24.9 kg/m ²	Overweight 25–29.9kg/m ²	Obese 30+ kg/m ²	Total
Yes	276 1.0	274 1.3	181 1.3	731
<i>Smoking status</i>				P<0.0001
Never Smoked	13,326 50.5	10,520 49.6	6996 49.8	30,842
Past Smoker	11,431 43.3	9605 45.3	6451 45.9	27,487
Current Smoker	1639 6.2	1083 5.1	606 4.3	3328
<i>Hormone therapy use</i>				P<0.0001
Never used	8769 33.2	8020 37.8	6329 45.1	23,118
Past user	3713 14.1	3205 15.1	2126 15.1	9044
Current user	13,914 52.7	9983 47.1	5598 39.8	29,495
<i>Skin reaction to the sun</i>				P<0.0001
Doesn't burn	9601 36.4	7654 36.1	4753 33.8	22008
Burns and then tans	14212 53.8	11004 51.9	7310 52.0	32526
Burns and does not tan	2583 9.8	2550 12.0	1990 14.2	7123
<i>Time spent outdoors in summer as a child</i>				P<0.0001
Less than 30 minutes	609 2.3	440 2.1	322 2.3	1371
30 minutes to 2 hours	7282 27.6	5419 25.6	3194 22.7	15895
More than 2 hours	18505 70.2	15349 72.4	10537 75.0	44,391
<i>Time spent outdoors in summer now</i>				P<0.0001
Less than 30 minutes	7063 26.7	6359 30.0	5336 38.0	18,758
30 minutes to 2 hours	13705 51.9	10705 50.5	6532 46.5	30,942
More than 2 hours	5628 21.4	4144 19.5	2185 15.5	11957
<i>Usually use sunscreen outside</i>				P<0.0001
No	10841 41.1	9953 46.9	7765 55.3	28,559
Yes	15555 58.9	11255 53.1	6288 44.7	33,098

Description: Only those participants who were in the WHI Observational Study of the WHI, reported their ethnicity as White, and were not missing any variables in the scientific model were included (there were 78,016 White women who were eligible). Outcomes are recorded from the start of the study period and participants are censored at death, last study visit, or 10 years from the start of the study period, whichever came first. Outcome events are recorded through August 2006.

Table 2

Age-adjusted and multivariate models for melanoma and non-melanoma skin cancer (NMSC).

Melanoma		NMSC	
HR (95% CI)		OR (95% CI)	
Cases (N, %)	Age adjusted model	Cases (N, %)	Adjusted model*
Normal N=26,396	1.0 (ref)	4683 17.6%	1.0 (ref)
Overweight N=21,208	0.98 (0.78–1.22)	3358 15.8%	0.87 (0.83–0.91)
Obese N=14,053	0.80 (0.61–1.05)	1874 13.3%	0.73 (0.69–0.78)
			0.93 (0.89–0.99)
			0.86 (0.80–0.91)

* Adjusted for age, education, smoking, skin type, sun exposure, previous history of skin cancer, hormone therapy use, and sunscreen use.