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Anthropometric features and cutaneous melanoma risk: A prospective cohort study in French women

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ABSTRACT

Background: Epidemiological studies on anthropometric features and cutaneous melanoma risk in women yielded inconsistent results, with few analyses involving prospective cohort data. Our objective was to explore several anthropometric characteristics in relation to the risk of melanoma in women.
Methods: We prospectively analysed data from E3N, a French cohort involving 98,995 women born in 1925–1950. Participants completed self-administered questionnaires sent biennially over 1990–2008. Relative risks (RRs) and 95% confidence intervals (CIs) were computed using Cox proportional hazards regression models, adjusted for age, number of naevi, freckling, skin and hair colour, skin sensitivity to sun exposure, residential sun exposure, and physical activity.
Results: Height was positively associated with melanoma in age-adjusted models only (RR = 1.27, 95% CI = 1.05–1.55 for $\geq$164 cm vs. <160 cm; *P* for trend = 0.02). After full adjustment, there was a significantly positive relationship between sitting-to-standing height ratio and melanoma risk (RR = 1.40, 95% CI = 1.06–1.86 for $\geq$0.533 vs. <0.518; *P* for trend = 0.02). A large body shape at menarche was inversely associated with the risk of melanoma (RR = 0.78, 95% CI = 0.62–0.98; compared with lean). However, weight, body mass index, body surface area, waist or hip circumference, sitting height or leg length were not significantly associated with risk.
Conclusion: These results suggest that height, sitting-to-standing height ratio and body shape at menarche may be associated with melanoma risk. Further research is required to confirm these relationships and better understand the underlying mechanisms.

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1. Introduction

Cutaneous melanoma is a potentially lethal cancer for which incidence has risen considerably worldwide over recent decades [1]. Its main risk factors include sun exposure, pigmentary traits and familial history of the disease [2]. Associations with other factors are less clear, although evidence suggests a potential influence of sex hormones on melanoma risk [3–5]. Body size has been related to sex hormones [6–8], and some anthropometric characteristics were suggested to be risk factors for cancer in women, particularly breast [9,10], ovary [11], or endometrial [12] cancer. Several epidemiological studies examined the relationships between anthropometric factors and melanoma risk in women, but results have been inconsistent regarding measures of body fatness, and few analyses involved large prospective cohort data. Moreover, most studies generally included a narrow range of characteristics, such as height, weight, body mass index (BMI), and body surface area (BSA). However, other factors, such as components of height or body shapes throughout life, which were suggested to reflect pre-pubertal and pubertal growth [13,14], may

Abbreviations: BMI, body mass index; BSA, body surface area; CI, confidence interval; E3N, Etude Epidémiologique auprès de femmes de l'Education Nationale; IGF, insulin-like growth factor; MET, metabolism equivalent task; RR, relative risk; UVR, ultraviolet radiation; WHR, waist-to-hip ratio.

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also be of interest to better understand the associations between anthropometry and the risk of melanoma. Our objective was to assess the potential relationships between several anthropometric features and the risk of melanoma in women participating in the E3N cohort.

2. Methods

2.1. The E3N cohort

E3N (Etude Epidémiologique auprès de femmes de l'Education Nationale) is a prospective cohort study involving 98,995 French women born in 1925–1950 and insured by a national health scheme primarily covering teachers. Women were enrolled between 1989 and 1991 after returning a baseline self-administered questionnaire on their lifestyle and medical history along with an informed consent. Follow-up questionnaires were sent every 2–3 years thereafter and addressed medical events such as cancer, which were subsequently confirmed through pathology reports. The E3N cohort received ethical approval from the French National Commission for Computed Data and Individual Freedom (Commission Nationale Informatique et Libertés, CNIL).

2.2. Data collection

2.2.1. Anthropometric characteristics

Height was collected at baseline and in the 1994, 2000, 2002 and 2005 questionnaires, and self-reported weight was available in each questionnaire. Body mass index (BMI), calculated as weight in kilograms divided by height in metres squared, was computed at each follow-up cycle. We calculated body surface area (BSA) using the formula by Du Bois & Du Bois: BSA (m^2) = 0.007184 × weight $(kg)^{0.425}$ × height $(cm)^{0.725}$ [15]. Self-reported waist and hip circumferences were collected in the 1994, 2002 and 2005 questionnaires. Waist circumference was defined as the smallest circumference between the base of the ribs and the largest point of the iliac crest, while hip circumference was defined as the largest circumference below the umbilicus.

Self-reported sitting height was recorded in 1994, where women were asked to sit upright on a hard seat, buttocks and scapulas against the wall, to measure their height using a tape measure with an angle bracket placed on their heads, and then to subtract the seat height. This allowed to derive a sitting-to-standing height ratio and calculate leg length (as standing height minus sitting height). All anthropometric factors were analysed in tertiles. Body shapes were estimated at inclusion using the figure drawings proposed by Sörensen et al. [16]: women were asked to report the drawing that best reflected their body shape at different ages, with drawings ranking from 1 to 8 corresponding to increasing body size, from the leanest to the largest. The baseline questionnaire recorded body shape at age 8 years, at menarche, at ages 20–25 years, 35–40 years, and at current age. For each of these variables, we created three categories (lean, medium, and large) using a different classification according to the period of life (Table 1).

A validation study of most of these measures was undertaken in 2002 and involved 152 women from the Paris centre of the cohort, who had been clinically examined while providing a blood sample [17]. Correlation coefficients between self-reported and technician-measured anthropometric factors were 0.89 for height, 0.56 for sitting height, 0.94 for weight, 0.92 for BMI, and 0.85 for body shape.

2.2.2. Non-anthropometric factors

Pigmentary characteristics were collected at baseline and include hair colour (red, blond, chestnut, brown, or black), skin complexion (very fair, fair, medium, dark, or very dark), number of naevi and of freckles (none, few, many, or very many), and skin sensitivity to sun exposure (none, moderate, high). Education was collected at baseline, profession of the father was collected in 1992, and age at menarche was available in the 1990 and 1992 questionnaires. Smoking status was available at each questionnaire but was considered at baseline for the description of the study population. Alcohol consumption and total energy intake were derived from the dietary history questionnaire sent to participants in 1993. Counties of birth and of residence were collected at baseline. Childhood and adult residential sun exposure were estimated by linking these data with a database containing mean daily ultraviolet radiation (UVR) in French counties [18]. Physical activity was assessed in Metabolic Equivalent of Task per hour (MET/h) and was recorded at inclusion and in the 1993, 1997 and 2002 questionnaires, where women were asked to report their time spent walking, biking, swimming, playing tennis, or fitness exercising in a typical week over the past year. To check if socioeconomic status had an impact on our findings, as described in detail elsewhere [19], we computed an index for the income of the participants' father determined by data from income according to professional categories provided by the French National Institute for Statistics and Economic Studies and by using the median category "employee (public service)" as the reference (value of 100) [20].

Table 1
Classification of body shapes at different ages throughout life, E3N cohort.

Body shape	Lean	Medium	Large
At age 8 years	1	2	≥3
At puberty	≤2	3	≥4
At ages 20–25 years	≤2	3	≥4
At ages 35–40 years	≤2	3	≥4
As reported at baseline[a]			
Premenopausal	≤2	3	≥4
Postmenopausal	≤3	4	≥5

Body shape drawings as first proposed by Sörensen et al. [16].
[a] Since changes in body shape often occur after menopause, the definition of body shapes was increased by unity in postmenopausal women.

2.3. Population for analysis

Participants who reported a history of cancer other than basal-cell carcinoma at baseline (n = 4788), those who were lost to follow-up from baseline (n = 2207), or who reported to have never menstruated (n = 28) were excluded. Woman-years were computed from the date the first questionnaire was returned to the date of diagnosis of melanoma, date of diagnosis of any other cancer, date of last questionnaire returned, or date of end of follow-up (July 2008), whichever occurred first. For anthropometric variables available from inclusion (and thus involving maximal length of follow-up), the final sample included 91,972 women. For factors available from the 1994 questionnaire only (components of height, waist and hip circumferences), follow-up started on the date the 1994 questionnaire was returned and involved 63,763 women.

2.4. Statistical analysis

Statistical analyses were performed using the SAS statistical software package (version 9.2). We estimated relative risks (RRs) and 95% confidence intervals (CIs) using Cox proportional hazards regression models with age as the time scale. The association between anthropometric factors and melanoma risk was assessed in age-adjusted models, and we then additionally adjusted for pigmentary characteristics, residential sun exposure in childhood

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