European Journal of Cancer 67 (2016) 99–105

Available online at www.sciencedirect.com

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journal homepage: www.ejcancer.com

Original Research

Associations between childhood height and morphologically different variants of melanoma in adulthood

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Received 19 May 2016; received in revised form 27 July 2016; accepted 2 August 2016

KEYWORDS
Body height;
Child;
Cohort studies;
Melanoma;
Neoplasms by histologic type

Abstract ***Aim of the study:*** Melanoma subtypes have different aetiological characteristics. Child height is positively associated with adult melanoma; however, a clarification of associations with specific melanoma variants is necessary for an improved understanding of risk factors underlying the histologic entities. This study investigated associations between childhood height and future development of cutaneous melanoma variants.
Method: A cohort study of 316,193 individuals from the Copenhagen School Health Records Register, with measured heights at ages 7–13 years who were born from 1930 to 1989. Melanoma cases were identified via linkage to the national Danish Cancer Registry and subdivided into subtypes. Cox proportional hazards regressions were performed.
Results: A total of 2223 cases of melanoma distributed as 60% superficial spreading melanoma (SSM), 27.5% melanoma not otherwise specified (NOS), 8.5% nodular melanoma (NM), and 2% lentigo maligna melanoma (LMM). The remaining rare melanoma forms were not analysed. Childhood height was positively and significantly associated with SSM, melanoma NOS, and NM, but not LMM, in adulthood. Per height z-score at age 13 years, the hazard ratios were 1.20 (95% confidence intervals [CI]: 1.13–1.27) for SSM, 1.19 (95% CI: 1.09–1.29) for melanoma NOS, and 1.21 (95% CI: 1.04–1.41) for NM. Further, growth patterns were linked to the melanoma variants with persistently tall children having an increased risk of developing SSM, melanoma NOS, or NM.

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http://dx.doi.org/10.1016/j.ejca.2016.08.002

Conclusion: Childhood height is positively associated with the majority of the melanoma variants. These results suggest that the underlying processes contributing to childhood height and growth patterns interconnect early-life events with the predisposition to melanomagenesis in adulthood.

1. Introduction

Melanoma is one of the most rapidly increasing human malignancies in populations of Caucasian descent [1]. Since both young and old individuals are affected by this cancer form, it places a substantial economic burden on societies [2].

Melanoma is subdivided into histopathological subtypes, with the most common being superficial spreading melanoma (SSM), nodular melanoma (NM), lentigo maligna melanoma (LMM), and acral lentiginous melanoma (ALM) [3]. Histologic subdivisions are based on differences in cytological and architectural features, growth patterns and, to some extent, the site on the body [4]. The subtypes are important for aetiological and diagnostic purposes, but not necessarily for prognosis as this often depends on the lesion thickness [5]. Genetic vulnerability is known to prime certain individuals for melanomagenesis [6]. Moreover, sun exposure, nevi count, and a fair pigmentation phenotype can increase susceptibility to melanoma; however, their significance differs among the subtypes [7].

Previously, we found that children who were one height z-score taller than their peers had approximately a 20% higher risk of developing adult melanoma in a population of Danish schoolchildren [8]. This suggests that mechanisms regulating childhood height may also contribute to melanoma development in adulthood. Nonetheless, it remains unknown if the future risk of specific melanoma variants is related to height in childhood. Therefore, this study investigated whether childhood height was associated with the risk of morphologically different cutaneous melanoma variants in adulthood by analysing data from the same Danish cohort of children.

2. Methods

2.1. Study population

In the Copenhagen municipality, physicians and nurses annually measured the height and weight of Danish children who attended public and private schools. These measurements are contained in the electronic Copenhagen School Health Records Register, including information on body size on 372,636 Danish children, born from 1930 to 1989 [9]. Information exists for each child from the ages of 7–13 years until 1983 as subsequently the children were only measured at school entry and exit. Using the Lamda Mu Sigma method [10], height was converted into z-scores according to age-, sex- and birth cohort-specific (5-year interval) references.

Since April 2, 1968, all Danish citizens have been assigned a personal identification number [11], enabling record linkages to national health registers. One is the national Danish Cancer Registry which was established in 1942 and contains information on malignancies [12]. Until 1994, the Danish Cancer Registry classified cancers using the International Classification of Diseases (ICD) version 7 and thereafter according to ICD-10. In the period of 1978–2004, the first version of the International Classification of Diseases for Oncology (ICD-O-1) was used followed by the third version (ICD-O-3) to describe cancer morphology. In 2004, the Danish Cancer Registry was modernised and cancers diagnosed from 1978 to 2004 were converted into ICD-10 and ICD-O-3 [12].

In this study, the identification numbers were used to identify melanoma cases according to ICD-10 (C43) and they were subdivided into histological categories in agreement with ICD-O-3: SSM (8743), NM (8721), ALM (8744), LMM (8742), and melanoma not otherwise specified (NOS) (8720). The variants were analysed separately, and individuals with other forms of melanoma were censored. Vital status for each individual was obtained from the Danish Civil Registration System [11].

Follow-up began on January 1, 1978, or age 15 years, whichever came later. From an initial population of 372,636 individuals, we excluded individuals who did not have an identification number (N = 42,668), who were deceased, emigrated, or lost to follow-up prior to January 1, 1978, or before age 15 years (N = 7628), who were diagnosed with melanoma prior to 1978 (N = 96) or before age 15 years (N = 5), who were missing the date at melanoma diagnosis (N = 4) or missing height or weight values at all ages (N = 6033) or who had outlying measures of height or body mass index (kg/m^2) (z-score <-4.5 or >4.5) at all ages (N = 9), resulting in an eligible cohort of 316,193 individuals (160,013 men, 156,180 women) (Supplementary Fig. 1).

In analyses investigating associations between change in height and the melanoma variants, we only included