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Obesity and risk of malignant melanoma: A meta-analysis of cohort and case–control studies

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Abstract Although obesity is an established risk factor for several cancer types, its possible role in the etiology of malignant melanoma remains unclear. This meta-analysis aims to examine the association between obesity and melanoma risk, exploring any tentative gender-specific associations. After the identification of eligible studies, we estimated pooled effect estimates (odds ratios and relative risks), undertook a meta-regression analysis and analyzed separately risk of malignant melanoma among males and females in relation to body mass index (BMI) and body surface area (BSA). Out of the 21 eligible articles, 11 used a case–control design encompassing 4460 cases/6342 controls; 10 used a cohort design whose total size comprised 7895 incident cases/6,368,671 subjects. Among males, the pooled effect estimate was 1.31 (95% confidence interval (CI): 1.18–1.45) for overweight and 1.31 (95% CI: 1.19–1.44) for obese. Meta-regression revealed no significant slope, most probably due to the underlying plateau in effect estimates. Among females, no significant association was documented; the pooled effect estimate for overweight and obese subjects was 0.98 (95% CI: 0.92–1.05) and 0.99 (95% CI: 0.83–1.18), respectively. Noticeably, there was evidence for confounding between sunlight exposure and obesity in females. All results were reproducible upon analyses on BSA. In conclusion, overweight and obesity is associated with increased risk of malignant melanoma among males. Meticulous assessment of sunlight exposure is needed especially in women, since self limited public sun exposure may be prevalent among overweight or obese females. Higher-order associations between BMI and melanoma risk should be addressed and examined by the future studies.

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1. Introduction

The epidemiology of malignant melanoma (hereafter called melanoma) has followed a long trajectory, starting with the *sunlight hypothesis* in the '50s[1]; the current palette of risk factors essentially encompasses exogenous parameters, among which sun exposure and its correlates represent the primary cornerstone,[1,2] as well as inherent features, such as skin-eye-hair color, family history,[3] presence of common or atypical naevi,[4] immunosuppression[5] or even novel genetic loci.[6] The attempts envisaging a link between melanoma and oral contraceptive use have not proven fruitful.[7]

Obesity is a well established risk factor for several cancer types[8]; noticeably, it has been postulated that obesity may account for approximately 20% of all cancer cases.[9] The spectrum of obesity-related cancer may span, among other types, colon,[10] endometrial,[11] postmenopausal breast,[9] renal,[8,9] esophageal,[8] thyroid,[8,9] prostate[12] and possibly some hematologic malignancies.[13]

Regarding melanoma, a possible association with obesity remains rather unclear at the meta-analytical level, whereas individual studies have yielded mutually conflicting results. So far, two pooling approaches have appeared in the literature. Renehan et al. performed a meta-analysis especially on prospective (cohort) studies and found elevated melanoma risk with increasing body mass index (BMI) among men.[8] On the other hand, Olsen et al. pooled eight case–control studies exclusively conducted on women; their results suggested a null association between BMI or body surface area (BSA) and melanoma risk.[14] To our knowledge, no effort has been undertaken till now, aiming to synthesize all published cohort and case–control studies, in order to evaluate the association between melanoma and obesity.

To this end, our aim was to comprehensively examine the association between obesity and melanoma risk, synthesizing all available evidence. Two indices have been assessed as markers of obesity, according to the individual studies i.e. BMI and BSA. Separate analyses were undertaken in males and females, so as to uncover sex-specific differences, if any.

2. Materials and methods

2.1. Search terms, eligibility and exclusion criteria

This meta-analysis was conducted in accordance with the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines.[15] Following a combined computerized and manual systematic database search of medical literature, potentially informative publications were retrieved from electronic search engines (Medline, Scopus, Google Scholar, Ovid and the Cochrane Library). Reference lists were thereafter systematically searched for relevant articles.

Eligible articles included case–control and cohort studies examining the association between melanoma and BMI and also between melanoma and BSA. Mesh terminology used for search purposes were ('melanoma' [All fields] OR 'cancer' [All fields] OR 'malignancy' [All fields]) AND ('obesity' [All fields] OR 'body mass index' [All fields] OR 'body surface area' OR 'overweight' [All fields] OR 'diet' [All fields] OR 'adiposity' [All fields] OR 'body size' [All fields]).

All scientific papers published through 31st October 2011 were examined and no restriction of publication language or participants' sex was applied. We excluded studies that did not refer to melanoma or studies that did not report BMI or BSA as an obesity index. When multiple publications on the same study population were identified or when study populations overlapped, only the study of larger size was included, unless the reported outcomes were mutually exclusive. The selection (inclusion or exclusion) of each study was independently made by two reviewers (T.N.S., A.A.) and final decision was reached by consensus.

Apart from the articles retrieved by the search strategy, an additional unpublished case–control dataset of our Department was included in the present meta-analysis (mentioned as 'Antoniadis, unpub.,' throughout the text). The details about patients and methods regarding this case–control study are presented in Supplemental Methods.

2.2. Data extraction

Data extracted from eligible studies included first author's name, study year, journal, type of study, follow up period, region of origin, age of participants, histological subtype of melanoma, sources of information for cases and controls (for case–control studies), number of cases and controls (case–control studies) or cohort size and recorded events (cohort studies), matching factors and factors adjusted for in multivariate analyses. If the required data for the meta-analysis were not readily available in the published article, the corresponding authors were contacted at least once. Data were independently extracted and analyzed by two reviewers (T.N.S., A.A.) and final decision was reached by consensus.

The maximally adjusted effect estimates i.e. odds ratios (ORs) for case–control studies or relative risks (RRs) for cohort studies, with corresponding confidence intervals (CIs) were extracted from each study and each category of the examined indices (BMI, BSA), separately for males and females. In case the above information was not available, crude effect estimates and 95% CIs were calculated on the basis of 2×2 tables presented in the articles.