2.2.23 Malignant melanoma

Malignant melanoma is the most lethal of the cancers of the skin. The incidence of melanoma varies between countries and is related to skin colour, with a higher risk for populations with lighter skin. Melanoma is known to be caused by exposure to ultraviolet radiation in people who are susceptible because of family history and/or who have a tendency to burn easily as a result of exposure to sunlight.

In 2001, the Working Group of the *IARC Handbook* on weight control and physical activity (<u>IARC</u>, 2002) concluded that the evidence of an association between avoidance of weight gain and malignant melanoma was *inadequate*.

(a) Cohort studies

The evidence published since 2000 includes eight cohort studies (excluding analyses that were later updated and analyses based on fewer than 100 incident cases) (Table 2.2.23a, web only, available at: http://publications.iarc.fr/570) and one meta-analysis (Table 2.2.23b, web only, available at: http://publications.iarc.fr/570).

In most studies, there was no association between BMI and risk of melanoma (Calle et al., 2003; Rapp et al., 2005; Dennis et al., 2008; Pothiawala et al., 2012; Bhaskaran et al., 2014). However, findings by sex have not been consistent. In two studies in men only, the estimated relative risk for BMI ≥ 30 kg/m² was 1.35 (95% CI, 1.06-1.73) in Swedish construction workers (Samanic et al., 2006) and 1.29 (95% CI, 1.14-1.46) in White men in the United States Veterans cohort (Samanic et al., 2004). In the Million Women Study (Reeves et al., 2007), the risk was also significantly increased (RR per 10 kg/m², 1.24; 95% CI, 1.03–1.48). In a meta-analysis of cohort studies (Sergentanis et al., 2013), the estimated relative risk of obesity was 1.30 (95% CI, 1.17-1.45) in men (based on 7 studies)

and 0.87 (95% CI, 0.70–1.08) in women (based on 6 studies).

Three cohorts have examined weight at earlier ages in relation to risk of melanoma. In both the Nurses' Health Study and the Male Health Professionals Follow-Up Study, BMI at 10 years before baseline was not related to risk (Pothiawala et al., 2012); in the study of agricultural workers in the USA (Dennis et al., 2008), recalled BMI at age 20 years was positively associated, with an estimated relative risk for BMI $\geq 25 \text{ kg/m}^2$ of 2.55 (95% CI, 1.52–4.30).

(b) Case-control studies

The meta-analysis by Sergentanis et al. (2013) included 10 published case-control studies that evaluated the association between BMI and risk of melanoma (Table 2.2.23b, web only, available at: http://publications.iarc.fr/570). The association between BMI and melanoma was significant both in overweight men and in obese men, although there was considerable between-study heterogeneity. No such association was observed in women. When the cohort and case-control studies were combined, the pooled effect estimate was 1.31 (95% CI, 1.18-1.45) in overweight men and 1.31 (95% CI, 1.19-1.44) in obese men. In women, no association was observed in either category (Sergentanis et al., 2013). [There was evidence for confounding by exposure to sunlight in women.]

The pooled analysis of case–control studies (Olsen et al., 2008) assessed BMI in early adulthood and weight change in relation to risk of melanoma in women. There was no association between BMI in early adulthood and melanoma risk, but an elevated risk was associated with a weight gain of 2 kg or more during adult life (pooled OR, 1.5, 95% CI, 1.1–2.0) (see Table 2.2.23b, web only, available at: http://publications.iarc.fr/570).

References

- Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L (2014). Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5.24 million UK adults. *Lancet*, 384(9945):755–65. doi:10.1016/S0140-6736(14)60892-8 PMID:25129328
- Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ (2003). Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med*, 348(17):1625–38. doi:10.1056/NEJMoa021423 PMID:12711737
- Dennis LK, Lowe JB, Lynch CF, Alavanja MC (2008). Cutaneous melanoma and obesity in the Agricultural Health Study. *Ann Epidemiol*, 18(3):214–21. doi:10.1016/j.annepidem.2007.09.003 PMID:18280921
- IARC (2002). Weight control and physical activity. Lyon, France: IARC Press (IARC Handbooks of Cancer Prevention, Vol. 6). Available from: http://publications.iarc.fr/376.
- Olsen CM, Green AC, Zens MS, Stukel TA, Bataille V, Berwick M, et al. (2008). Anthropometric factors and risk of melanoma in women: a pooled analysis. *Int J Cancer*, 122(5):1100–8. doi:10.1002/ijc.23214 PMID:17990316
- Pothiawala S, Qureshi AA, Li Y, Han J (2012). Obesity and the incidence of skin cancer in US Caucasians. *Cancer Causes Control*, 23(5):717–26. doi:10.1007/s10552-012-9941-x PMID:22450736
- Rapp K, Schroeder J, Klenk J, Stoehr S, Ulmer H, Concin H, et al. (2005). Obesity and incidence of cancer: a large cohort study of over 145,000 adults in Austria. *Br J Cancer*, 93(9):1062–7. doi:10.1038/sj.bjc.6602819 PMID:16234822
- Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D; Million Women Study Collaboration (2007). Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. *BMJ*, 335(7630):1134. doi:10.1136/bmj.39367.495995.AE PMID:17986716
- Samanic C, Chow WH, Gridley G, Jarvholm B, Fraumeni JF Jr (2006). Relation of body mass index to cancer risk in 362,552 Swedish men. *Cancer Causes Control*, 17(7):901–9. doi:10.1007/s10552-006-0023-9 PMID:16841257
- Samanic C, Gridley G, Chow WH, Lubin J, Hoover RN, Fraumeni JF Jr (2004). Obesity and cancer risk among white and black United States veterans. *Cancer Causes Control*, 15(1):35–43. doi:10.1023/B:-CACO.0000016573.79453.ba PMID:14970733
- Sergentanis TN, Antoniadis AG, Gogas HJ, Antonopoulos CN, Adami HO, Ekbom A, et al. (2013). Obesity and risk of malignant melanoma: a meta-analysis of cohort and case-control studies. *Eur J Cancer*, 49(3):642–57. doi:10.1016/j.ejca.2012.08.028 PMID:23200191