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8

Obesity and female malignancies

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Obesity increases the risk of endometrial and ovarian cancer, and oestrogen receptor (ER)–progesterone receptor (PR)-positive postmenopausal breast cancer. A modest positive association between body mass index (BMI) and cervical cancer has also been found. By contrast, an inverse correlation between BMI and premenopausal breast cancer exists.

Endogenous sex hormones, insulin resistance/hyperinsulinaemia, adipokines, cytokines and chronic inflammation, among other factors, may be involved in the promotion of cancer in obese patients. Obesity is also associated with an increased risk of cancer recurrence and mortality most likely due to suboptimal treatment and/or co-morbidities.

It is recommended that chemotherapy doses be calculated on the actual body weight and that radical surgery be performed as in non-obese patients. The high risk of peri-operative complications may be reduced by optimizing preoperative clinical conditions.

As part of cancer prevention, obese women should be encouraged to adopt healthy lifestyles leading to weight loss and to undergo regular cancer screening.

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Introduction

Overweight and obesity are defined as abnormal or excessive fat accumulation as measured by the body mass index (BMI). In 2014, >1.9 billion adults were overweight worldwide. Of these, >600 million were obese [1].

Obesity represents a major under-recognized preventable risk factor for cancer development and mortality [2]. It is estimated that approximately 20% of cancer cases are related to obesity [3]. On the other hand, 15–30% of weight loss in women is associated with a reduced risk of cancer [4]. Obesity is also predictive of increased cancer mortality [5]. Clinicians should be aware that preventing/treating obesity should be considered part of cancer prevention. Increased trunk-abdominal fat, as measured by either the waist-to-hip ratio (WHR) or the waist circumference (WC), is also associated with an increased risk of several types of cancer, independently from BMI [6]. However, most studies on cancer and body weight limit their investigations to BMI, which is more commonly used in clinical practice. Postmenopausal breast cancer, endometrial cancer and, to a lesser extent, ovarian cancer are among the malignancies most commonly associated with obesity [7]. In the following, we address the impact of obesity on the epidemiology, biology and clinical management of female malignancies.

Impact of obesity on the epidemiology and prognosis

Breast cancer

Epidemiology

Breast cancer is the most prevalent cancer in women, with >1.7 million new cases worldwide in 2012, and the fifth cause of death from cancer overall [8].

The impact of obesity on the incidence and the evolution of breast cancer is not fully elucidated, due to several confounding factors, such as the use of hormone replacement therapy (HRT), ethnicity and the biology of different cancer subtypes.

Oestrogen receptor (ER)-negative and aggressive tumour subtypes are found more frequently in premenopause, whereas ER-positive subtypes occur more often among postmenopausal women. Obesity is considered a risk factor for postmenopausal breast cancer, whereas it seems to be neutral or even inversely related to the incidence of breast cancer in premenopausal women [9].

Postmenopausal breast cancer

The association between obesity and the increased overall risk of breast cancer is consistent for postmenopausal women. Large meta-analyses and one very large cohort study confirmed a direct association between BMI and the risk of developing the disease [10,11]. General adiposity appears to be more strongly related to the risk of breast cancer than measures of abdominal adiposity [12].

A recent meta-analysis [13] investigated ER and progesterone receptor (PR) status. A correlation between BMI $\geq$30 kg/m^2 and the incidence of postmenopausal breast cancer was found for ER-positive/PR-positive cancer (relative risk (RR) 1.39, 95% confidence interval (CI): 1.14- 1.70), but not for ER-negative/PR-negative cancer. This finding suggests that the effect of obesity in postmenopausal women may be mediated by endogenous sex hormones. Furthermore, the obesity-dependent risk was lower for women under postmenopausal oestrogen–progestin therapy, suggesting that hormonal therapy is a confounding factor in the obesity–cancer relationship.

Premenopausal breast cancer

There is still controversy on the impact of obesity on the risk of premenopausal breast cancer. Body fatness is considered as possibly protective against premenopausal breast cancer [14]. This notion is supported by several cohort studies and meta-analyses. In the most recent study, BMI and the incidence of breast cancer show a linear inverse correlation, with a peak at BMI 22 kg/m [2], and a decrease as BMI increases further (hazard ratio (HR) 0.89, 99% CI 0.86–0.92) [10]. A large meta-analysis showed that obesity (BMI $\geq$30 kg/m^2) is associated with a significantly reduced risk of premenopausal breast cancer (RR 0.83; 95% CI: 0.75–0.91), compared to the risk for normal-weight women. This association

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