Report

Premorbid body weight and its relations to primary tumour diameter in breast cancer patients; its dependence on estrogen and progesteron receptor status

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Summary

Hormonal mechanisms have been offered as an explanation for the higher frequency of large tumours, lymph node metastases and poorer prognosis in obese breast cancer patients than in lean ones. If hormonal mechanisms are important for these relations, they should probably act more strongly in patients with hormonal receptor positive tumours than in those with negative ones. We have examined if the relations between premorbid body weight or Quetelet’s index (weight/height²) and tumour diameter are modified by estrogen receptor alpha (ER) and progesteron receptor (PgR) status. The analyses were based on 1,241 women with unilateral disease treated with modified radical mastectomy living in the geographic area of Haukeland Hospital. Their body weight and height have been measured as a mean 12.5 years before presentation of the disease. Body weight and Quetelet’s index have been adjusted for age. The relations were studied using linear regression analyses adjusting the effect of body weight with height and mean nuclear area of the tumour cells and adjusting the effect of Quetelet’s index for mean nuclear area. The main findings showed that patients with high body weight or Quetelet’s index presented more often with PgR positive tumours than lean ones. Quetelet’s index was also positively related to ER. These relations were present in patients older than 50 years of age (older). Patients with large tumours (>2.0 cm) had significantly higher body weight and Quetelet’s index than those with small ones. These differences were significantly present in older patients and in patients with PgR negative and ER negative – PgR negative tumours. Linear regression analyses confirmed that tumour diameter increases with body weight and Quetelet’s index. These relations were present in both lymph node groups and in older patients. Stratification according to hormonal receptor status showed these relations to be significant in patients with ER negative, with PgR negative and those with ER negative – PgR negative tumours only. Taking age and hormonal receptor status into consideration simultaneously, both body weight and Quetelet’s index were significantly related to tumour diameter in older patients with hormone receptor negative tumours. In conclusion body size was positively related to hormone receptor status and to diameter of the primary tumour. The relation to tumour diameter was present in older patients with hormone receptor negative tumours. Although hormonal mechanisms able to act on the tumour can not be excluded, mechanisms acting independent of hormonal receptors must be considered. Different mechanisms related to body fat cytokines are discussed.

Introduction

Obese breast cancer patients present with larger primary tumours [1–6] and more often with lymph node metastases than lean ones [1–4, 6–10]. One study did not show a significant relation between body weight and tumour diameter [10] and another work showed no association between body weight and
lymph node status [11]. Obese postmenopausal women develop breast cancer more often than lean ones, while obesity seems to protect against breast cancer in premenopausal women [2, 12]. Obese breast cancer patients also have poorer prognosis than lean ones [1, 2, 4–6, 11, 13–17].

It has been claimed that a woman’s body exerts its influence on breast cancer by hormonal mechanisms [13]. Obese women have increased aromatization of androstendione to estrone in adipose tissue probably due to increased number of adipose cells and decreased sex hormone binding globulin compared to lean ones [18–20]. This theory is supported by the finding that the relation between body weight and lymph node status is strong in patients with estrogen receptor alpha (ER) positive tumours, while it is weak and inconsistent in the ER negative ones [4]. Others have, however, shown that body weight is associated with lymph node status and tumour size in premenopausal women, in whom the ovaries are the main estrogen source [2, 8]. In addition, the prognostic effect of obesity may be reversed in patients with estrogen receptor (PgR) negative tumours, lean patients having higher risk of dying than obese ones [21].

The associations between preclinical body weight, Quetelet’s index and primary tumour diameter appear not to have been examined according to hormonal receptor status of the tumour. If hormonal mechanisms are important for this relation, one should expect these mechanisms to act more strongly in patients with hormonal receptor positive tumours than in those with negative ones. To test this theory we have studied the relationships between body weight, Quetelet’s index and tumour diameter taking both ER and PgR of the primary tumour into consideration.

Materials and methods

Between 1963 and 1975 The National Mass Radiography Service measured height and weight of all participants in a nationwide tuberculosis screening program. The survey included all inhabitants over 15 years of age in 17 of 19 counties in Norway. A mean the height and weight measurements were recorded 12.5 years before presentation of the disease (range 1 year after to 26 years before). In the age-group between 26 and 69 years of age 567,333 women attended the screening. These women were followed until the end of 1981 through the population-based Norwegian Cancer Registry. Eight thousand four hundred twenty seven new cases of breast cancer were diagnosed and 97% were histologically verified [5, 12].

One thousand two hundred seventy one of these new cases were identified in our database of breast cancer patients living in the geographic area of Haukeland hospital with height and weight measurements from this survey. They presented with unilateral breast cancer and were treated by modified radical mastectomy with axillary dissection. Only patients with measurements taken before presentation of the disease were included. The specimens were received at this Department between January 1970 and January 1990 and the diagnosis of breast cancer histologically confirmed. Information on tumour diameter and lymph node status was present in all patients. Sections from the primary tumours had been fixed in 4% phosphate buffered formalin, embedded in paraffin and stained with haematoxylin and eosin. All histological types were included. The mean nuclear area (MNA) of the tumour cells was measured on sections from the primary tumour. The edge of the section was viewed in a Leitz microscope using a 40 x objective lens, projected onto a digitizer, and the data compiled on a Commodore computer. All measurements were taken without knowledge of tumour diameter [22, 23]. For patients with information on ER alpha (656 patients) and PgR (584 patients) status the specimens were received after 1974 and 1976, respectively. ER and PgR status were considered positive if the hormone receptor level was 15 fmol/mg or higher as measured by the modified charcoal method [24]. No patients had received Tamoxifen before operation.

Statistical methods

Two methods were used to create age-adjusted body weights. Using analysis of variance, we regressed the body weight data for patients younger than 45 years and those older than 55 years of age to the mean level of patients between 45 and 55 years of age, in this work called body weight. Quetelet’s index was also adjusted for age. Quintiles of Quetelet’s index were defined within each of the eight five-year age-groups at time of measurement in this series [5, 12]. Two categories were used for axillary lymph node status: without (715 patients, 57.6%) and with metastases (526 patients, 42.4%) independent of the number of positive nodes detected. Tumour diameter was divided