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ARTICLE

Body Mass Index, Serum Sex Hormones, and Breast Cancer Risk in Postmenopausal Women

Endogenous Hormones Breast Cancer Collaborative Group

Correspondence to: Timothy J. Key, DPhil, Endogenous Hormones and Breast Cancer Collaborative Group, Cancer Research U.K. Epidemiology Unit, University of Oxford, Gibson Bldg., Radcliffe Infirmary, Oxford OX2 6HE, U.K. (e-mail: Tim.Key@cancer.org.uk).

Background: Obesity is associated with increased breast cancer risk among postmenopausal women. We examined whether this association could be explained by the relationship of body mass index (BMI) with serum sex hormone concentrations. **Methods:** We analyzed individual data from eight prospective studies of postmenopausal women. Data on BMI and prediagnostic estradiol levels were available for 624 case subjects and 1669 control subjects; data on the other sex hormones were available for fewer subjects. The relative risks (RRs) with 95% confidence intervals (CIs) of breast cancer associated with increasing BMI were estimated by conditional logistic regression on case-control sets, matched within each study for age and recruitment date, and adjusted for parity. All statistical tests were two-sided. **Results:** Breast cancer risk increased with increasing BMI ($P_{\text{trend}} = .002$), and this increase in RR was substantially reduced by adjustment for serum estrogen concentrations. Adjusting for free estradiol reduced the RR for breast cancer associated with a 5 kg/m² increase in BMI from 1.19 (95% CI = 1.05 to 1.34) to 1.02 (95% CI = 0.89 to 1.17). The increased risk was also substantially reduced after adjusting for other estrogens (total estradiol, non-sex hormone-binding globulin-bound estradiol, estrone, and estrone sulfate), and moderately reduced after adjusting for sex hormone-binding globulin, whereas adjustment for the androgens (androstenedione, dehydroepiandrosterone, dehydroepiandrosterone sulfate, and testosterone) had little effect on the

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excess risk. *Conclusion:* The results are compatible with the hypothesis that the increase in breast cancer risk with increasing BMI among postmenopausal women is largely the result of the associated increase in estrogens, particularly bioavailable estradiol.

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