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Letters to the Editor

Association of Increased Body Mass Index With Diminished Tumor Estrogen Receptor (ER) Level in Breast Cancer Patients Younger Than 50 Years of Age With ER-Positive Tumors: Schapira and colleagues have recently reported on their studies of obesity, body fat distribution, and prognosis of women with breast cancer.[1] They noticed that increased abdomen/thigh skinfold ratio, a mark of male-pattern obesity, was associated with higher tumor estrogen receptor (ER) levels. Male-pattern obesity was also associated with smaller tumors and less lymph nodal involvement. But weight and body mass index (BMI), that is weight/height,[2] were not related to ER level.[1]

Our data confirm the finding that there is no overall relationship between BMI and ER level. We have found, however, that there is a relationship between these two factors in a subgroup of breast cancer cases, *i.e.*, women younger than 50 years of age whose tumors contain ER (ER greater than or equal to 2 fmol/mg). In these women, ER level declines significantly as BMI increases (Fig. 1). There are two reasons to look at this subgrouping. First, the relationship of age to breast cancer incidence. Second, the relationship of ER expression and spontaneous abortion in breast cancer.

In countries where breast cancer is common, there is a continued increase in the incidence of breast cancer with age. In countries where breast cancer is uncommon, the rate of development of breast cancer diminishes after menopause. These variations, documented in many studies, produce a distinctive "hook" at 50 years of age in the incidence curves, suggesting that premenopausal and postmenopausal breast cancer may be distinct entities.[2]

ER expression in breast tumors behaves differently with respect to spontaneous abortion, a risk factor,[3] depending on whether the tumor is ER positive or ER negative. Although multiple spontaneous abortions are associated with diminished ER/PR ratio in ER-positive tumors, there is no relationship when ER-negative tumors are included in the analysis.[4] This finding suggests that the mechanism that causes a tumor to be ER positive or ER negative is different from that which regulates the amount of tumor ER. In other words, with regard to tumor ER, the off–on switch is separate from the volume control. Thus, it is reasonable to analyze, as a group, only those tumors that are ER positive because we are only concerned with tumor ER level and not with whether ER is present or absent. Analyzed in this way, the results presented suggest why BMI and obesity influence outcome.

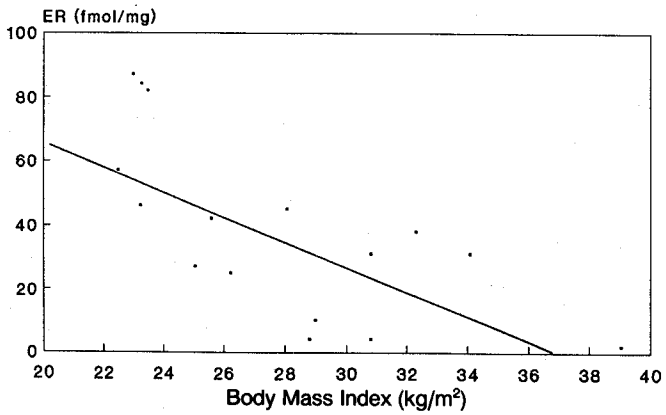

FIG. 1. Notice that in women younger than 50 years of age with ER-positive tumors, there is a significant inverse relationship between BMI and ER (n = 16, r = 0.69, $P = 0.0030$).

Obese women may have a worse prognosis because aromatization of androstenedione to estrone in their adipose tissue could produce increased estrogen levels.[5] Also, there is decreased sex hormone binding globulin in obese women and increased circulating estrogen.[6] Increased estrogen stimulates the growth of tumor cells and might be responsible for the poor outlook documented in clinical studies.[5,7]

Our data suggest an additional reason why obesity may be linked to a worse prognosis in the younger subgroup of ER-positive women presented here. Because the number of objective remissions in patients with breast cancer who are given hormone therapy increases with tumor ER level,[8] increased BMI and diminished ER would be associated with more aggressive disease.

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