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Nomograms for determining the probability of axillary node involvement in women with breast cancer

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Abstract We have previously reported that a history of pregnancy is independently associated with axillary node involvement in breast cancer patients. We have now studied additional women with breast cancer and have used our data and the logistic model to produce nomograms for determining the risk of axillary node involvement, based on tumor size, age, and number of pregnancies. There was an increase in the incidence of axillary node involvement in women with a history of pregnancy. To exclude the confounding effect that tumor size or age might have on node involvement, logistic regression was performed. Pregnancy, tumor size, and age were the three independent variables. History of pregnancy had a significant effect on node involvement (P = 0.036) that was independent of tumor size and age. Nomograms were constructed from these data. Surgeons do not perform an axillary dissection in every breast cancer patient. If the axilla is clinically negative and the tumor small, the surgeon, medical oncologist, and radiation oncologist may decide that a dissection need not be done. The nomograms in this article may allow for a more methodical choice of patients for axillary dissection. Moreover, a radiation oncologist might use the nomograms to help decide whether to irradiate an undissected axilla.

Introduction

In women with invasive breast carcinoma, the presence or absence of metastases in axillary nodes is of paramount prognostic importance (Spratt et al. 1988). If there is no node involvement, the average 10-year survival is 74%. If there is node involvement, the 10-year survival drops to 30%.

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There is a direct relationship between tumor size and the probability of axillary node involvement (Haagensen 1986; Chadha et al. 1994). The larger the tumor, the greater the probability of axillary node involvement.

Age is also related to axillary node involvement (Daniell 1988; Haagensen 1986; Chadha et al. 1994). Older women have fewer axillary node metastases.

We have reported that a history of pregnancy, whether full-term or interrupted, is independently associated with axillary node involvement (Lehrer et al. 1992). Our finding has recently been corroborated twice (Orr and Fraher 1993; Lehrer 1993), and once it was not confirmed (Fossati et al. 1993). Moreover, others have found an increased incidence of node involvement in pregnant women with breast cancer (Ishida et al. 1992), as well as poor prognosis (Guinee et al. 1994). We have now studied additional women with breast cancer and have used our data to produce nomograms for calculating the risk of axillary node involvement, based on tumor size, age, and number of pregnancies. Other parameters, such as hormone receptor status and histological grade are not known to affect probability of node involvement (Daniell 1988; Haagensen 1986; Chadha et al. 1994).

Materials and Methods

We evaluated 350 women receiving radiation therapy for breast cancer between 1984 and 1994. Patients were selected for study if information on their age, number of pregnancies, and node involvement was available. Information on age and number of pregnancies was obtained from the patient's chart. The average age of women studied was 55 ± 13 years (mean $\pm$ SD); the youngest woman was 25 and the oldest was 85. The average number of pregnancies was 2.6 ± 2.2; the minimum number of pregnancies was zero and the maximum was 13. Tumor size and axillary node status were determined from the surgical pathology report. The smallest tumor was 0.2 cm, while the largest was 10 cm.

Information on axillary node involvement was obtained from the pathology report. The patient was considered to have no axillary node involvement if histological examination showed no node involvement after axillary dissection. The axillary nodes were considered to be involved only if demonstrated by histopathological examination. In patients who had node involvement, the average number of involved

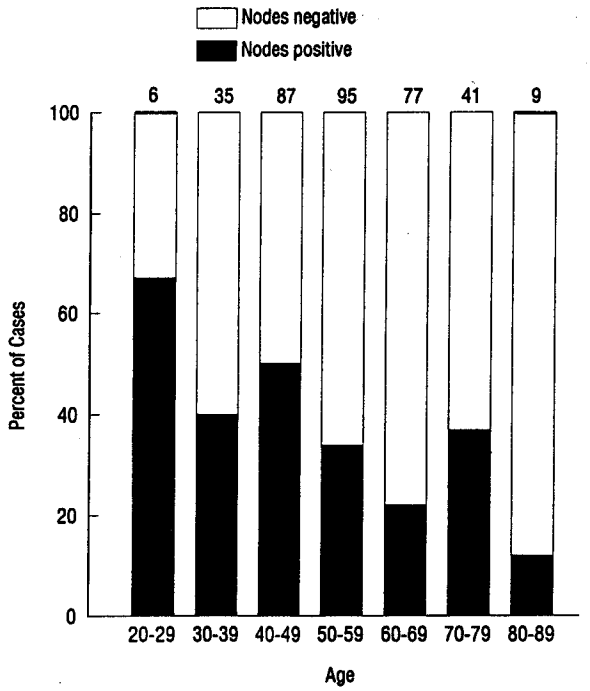

Fig. 1 Axillary node involvement in 350 breast cancer patients as a function of age. There is a significant effect of age ($\chi^2 = 18.6$, $P = 0.005$) and a significant downward trend (Mantel Haenszel $\chi^2 = 9.8$, $P = 0.0017$). Number of cases in each age group is indicated above the corresponding bar

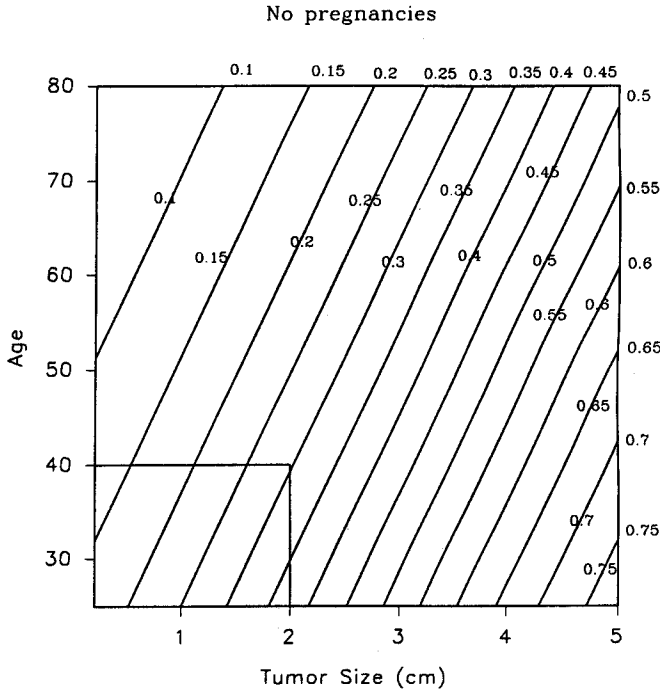

Fig. 2 Nomogram for calculating risk of axillary node involvement in women without a history of pregnancy. The diagonal lines are isorisk lines and the numbers printed on them are risk estimates. Thus 0.4 represents a 40% risk, while 0.45 represents a 45% risk. Example of use of the nomogram: in this hypothetical example, probability of axillary node involvement is assessed for a woman with no history of pregnancy, age 40, with a tumor size of 2.0 cm. Note that the perpendicular lines intersect at the 0.30 isorisk line on the nomogram. Therefore, the hypothetical patient has a 30% risk of axillary node involvement

Table 1 Maximum-likelihood fit of a binary logistic regression model to node involvement in 350 women with breast cancer. Note that the effect of pregnancy was significant ($P = 0.036$) and independent of the effects of tumor size and age

Factor	Odds ratio	95% CI	P
Pregnancy[a]	2.01	1.04 –3.86	0.0362
Tumor size	1.80	1.45 –2.24	<0.0001
Age[b]	0.98	0.958–0.995	0.012

[a] Never pregnant compared to pregnant once or more
[b] Risk per year

nodes was 5.4±5.8; the minimum number of involved nodes was 1 and the maximum number was 30. We were not able to evaluate the extent of axillary dissection in the women studied because this information was not included in patient records or the pathology report.

Only data from patients with infiltrating tumors were included. Statistical analyses were performed with the SPSS system (Norusis 1992).

Results

There was an increase in the incidence of axillary node involvement in women with a history of pregnancy. Of the 350 women studied, 126 had node involvement. Of the 64 women who had never been pregnant, 16 had node involvement (25%). Of the 286 women who had been pregnant at least once, 110 had node involvement (38%). This difference was significant ($\chi^2 = 4.11$, $P = 0.04$, odds ratio for node involvement 1.9, 95% CI = 1.01–3.46).

To exclude the confounding effect that tumor size or age (Fig. 1) might have on node involvement, logistic regression was performed (Norusis 1992). Pregnancy, tumor size, and age were the three independent variables, and the results are shown in Table 1. Note that a history of pregnancy had a significant effect on node involvement ($P = 0.036$), which was independent of tumor size and age.

The logistic model can be used for calculating the probability of node involvement $P(n)$ with the following equations (Norusis 1992):

$$P(n) = 1/(1 + e^{-z})$$

where

$$z = (-1.0851 + 0.694 \times \text{pregnancy} + 0.59 \times \text{tumor size} - 0.024 \times \text{age}),$$

the value of the pregnancy variable being either 0 or 1, 1 signifying 1 or more pregnancies.

The equations are employed to produce the nomograms (contour plots) of Figs. 2 and 3. Figure 2 is used to determine the probability of axillary node involvement in women with no history of pregnancy, while Fig. 3 is used to determine the probability of node involvement in women

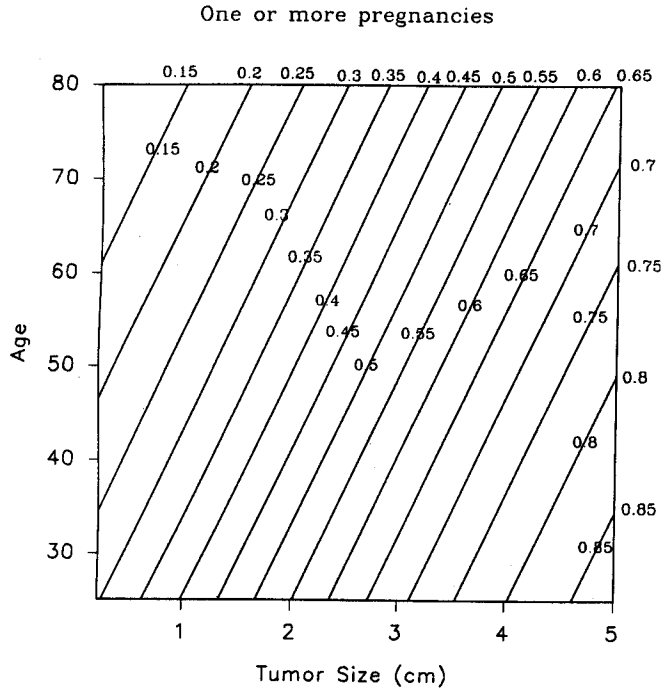

Fig. 3 Nomogram for calculating risk of axillary node involvement in women with a history of one or more pregnancies

with a history of one or more pregnancies. Figure 2 also gives an example of use of the nomograms.

Discussion

Pregnancy causes changes in the breast which might predispose a woman to tumors of increased malignancy. At the beginning of pregnancy, there is heightened vascularity, as well as rapid growth and branching of mammary tissue (Haagensen 1986). Moreover, the mammary tissue is exposed to high levels of many hormones during pregnancy, among them prolactin, which may have a role in the genesis of breast cancer (Haagensen 1986).

Although a history of pregnancy increases the risk of node involvement, and a history of full-term pregnancy diminishes the risk of breast cancer (Berkowitz and Kelsey 1988), at least one study indicates that a history of pregnancy does not affect survival (Ewertz et al. 1991). This would seem paradoxical, because of the well-known effect of node involvement on survival, noted above (Spratt et al. 1988). But another study found that young women diagnosed as having breast cancer during pregnancy or within a few years of pregnancy have a higher risk of death than those who have not been pregnant (Evans 1994).

Surgeons do not perform an axillary dissection in every breast cancer patient. If the axilla is clinically negative and the tumor small, or the patient unwilling, the surgeon, the medical oncologist, and the radiation oncologist may decide that a dissection need not be done. The nomograms in this article may allow for a more methodical choice of patients for axillary dissection. Moreover, a radiation oncologist might use the nomograms to help decide whether to irradiate an undissected axilla.

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