Short Communication

Mammographic Density Changes During the Menstrual Cycle

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Abstract

The ability to detect small tumors is impaired in dense mammograms. It has been suggested that the sensitivity of mammograms could be lower in mammograms obtained during the luteal phase of the menstrual cycle. We examined the change in mammographic density from the follicular to the luteal phase of the menstrual cycle in 11 women. Although the average increase in densities was quite small (1.2%; $P = 0.08$), six women had clinically significant increases (1.4–7.8%), suggesting that premenopausal women should undergo mammographic examinations in the follicular part of the menstrual cycle

Introduction

A number of studies have suggested that the ability of mammograms to detect small tumors (sensitivity) is lower in women with mammographically dense breasts (1–3). One report suggested that mammograms obtained from women in the luteal phase of the menstrual cycle were more likely to be classified as "extremely dense" and would therefore have lower sensitivity than mammograms obtained from women in the follicular phase (4). Another report suggested that screening mammograms obtained from women in the luteal phase were more likely to be false negative than those obtained from women in the follicular phase (5). However, the study subjects in both of these studies had a single mammographic examination; the quoted results were a comparison of groups of women examined either in the follicular or luteal phase. We decided to address the question of whether mammographic density changes during the menstrual cycle in a pilot study in which we asked women to undergo two mammograms during the course of a single menstrual cycle.

Materials and Methods

We recruited 11 healthy volunteers of ages 30 to 45 years (median, 35 years; SD, 5.0), who had had regular menstrual cycles over the previous 6 months (length, 26–30 days) and who were not currently using exogenous hormones. The first mammogram was obtained on days 7–10, and the second on days 24–27 of the menstrual cycle. These time points were selected to maximize the possibility that each mammogram reflected the hormone levels in that phase and not the preceding phase. Mammograms were digitized using a Cobrascan CX312T scanner (Radiographic Digital Imaging, Compton, CA). Density assessments were made by one of us (G. U.) as described previously (6) using a validated computer-assisted method to outline densities on the craniocaudal images. This has been found to be a highly reproducible method that correlates very highly with assessment of densities through subjective classification (6).

In short, on a digitized mammographic image displayed on the screen, the reader outlines the breast and then uses a tinting tool to apply a yellow tint to gray levels above some threshold X where all pixels $\geq X$ are considered to represent mammographic densities. The software counts the number of pixels within the defined breast area and the number of tinted pixels. The fraction (%) of the breast area with densities is taken as the ratio of the tinted area:total area of the breast. After estimating the percentage of the breast with densities separately for the left and the right breasts, the average percentage densities for the two breasts is calculated.

Results

There was on average an absolute increase of 1.2% in percentage density of the breast (Fig. 1; two-sided P for paired comparison t test = 0.08). Six of the 11 women had 1.4–7.8% increase in percentage densities, four women experienced essentially no (<1%) change, and one woman had a 13.4% reduction. The latter woman had a follicular phase density of 97%.

Discussion

This finding confirms the suggestion by White *et al.* (4) that women should have their mammograms in the follicular phase of the cycle. This also suggests that in comparative studies of mammographic densities in premenopausal women, mammograms for comparison should be obtained at approximately the same day in the menstrual cycle. Furthermore, this would imply that studies examining changes in densities over time should take into account recent exogenous hormone exposures, and that intervention studies aimed at reducing mammographic densities should expect to begin seeing changes after a short period of time. This is consistent with results from the study by Harvey *et al.* (7), where among 47 women who had a new mass or density increase while on postmenopausal hormonal replacement therapy, 35 (74.5%) experienced a reduction in density or resolution of the new mass after short-term (10–30 days) cessation of hormone replacement therapy.

Studies of breast cell proliferate activity have shown that most proliferative activity takes place during the luteal phase of the menstrual cycle (8). In [^{3}H]thymidine labeling index studies, the percentage of cells incorporating thymidine is 2–2.5-fold higher in the luteal phase than in the follicular phase, and epithelial cell mitotic counts behave similarly. We have argued previously that mammographic density represents a marker for

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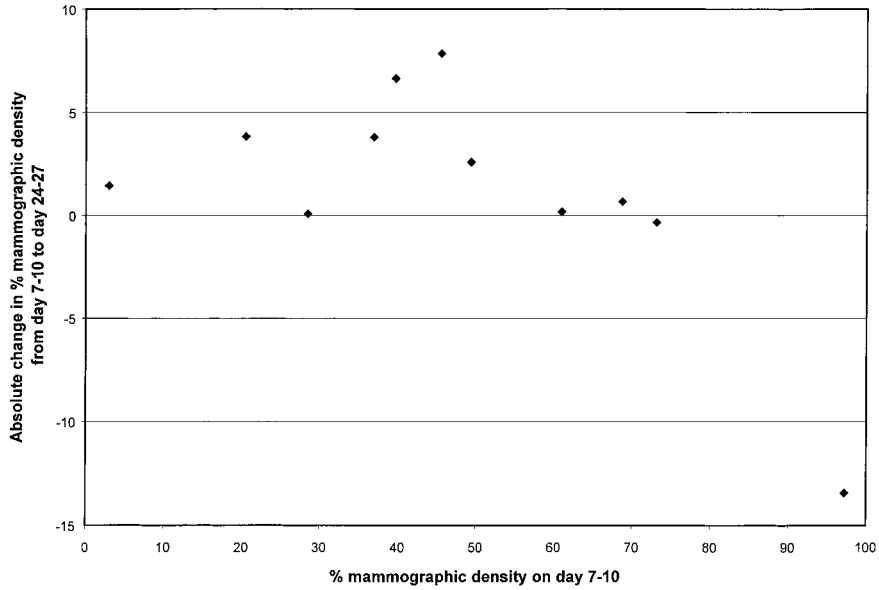

Fig. 1. Absolute change in percentage of mammographic density from days 7–10 to days 24–27 in the menstrual cycle in 11 women of ages 30–45 years.

breast cell proliferative activity (9). The mammographic density results above are compatible with the reported change in breast cell proliferative activity (8) and fibroglandular tissue (10) over the menstrual cycle. If, as we hypothesize, mammograms "mirror" current and recent breast cell proliferative activity, then having increased mammographic densities over a long time period should reflect increased mitotic activity over a long period of time and, therefore, be associated with increased risk; the longer the duration of increased densities, the higher the risk.

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