Mammographic Changes Related to Different Types of Hormonal Therapies

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Objectives: *To determine the effects of different types of hormone therapies (HT) on mammographic breast density changes.*
Material and Method: *Between 1999 and 2002, mammograms obtained before and 12-18 months after different types of HT in 170 women were evaluated. Estrogen alone (n = 66), or estrogen in cyclic (n = 59) or continuous (n = 45) combination with progesterone were used. The baseline mammographic density was classified according to the Breast Imaging Reporting and Data Systems (BI-RADS). The serial changes observed mammographically were categorized as follows; no change, minimal change (10-25% increased density), moderate change (26-50% increased density), and marked change (> 50% increased density).*
Results: *Twelve (7%) of the women developed an increase in parenchymal density after HT. Mammographic changes were minimal change in five (2.9%) of the women, moderate change in four (2.3%), and marked change in three (1.8%). No mammographic change was observed in women receiving cyclic estrogen-progesterone. A greater percentage of women who had undergone continuous estrogen-progesterone therapy (22.2%, 10 of 45) demonstrated more change than those who had estrogen alone (3%, 2 of 66). The difference was statistically significant (p < 0.01).*
Conclusion: *Changes of increased density after HT was seen in only 7% of mammograms and depended on the selected hormone regimen.*

Keywords: *Mammographic changes, Hormone therapy*

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Hormonal therapy (HT) is frequently used to relieve menopausal symptoms and to prevent osteoporosis[1]. Many different therapeutic regimens are used. Hysterectomized women are commonly treated with estrogen alone, whereas in non-hysterectomized women, estrogen and progesterone either cyclic or continuous combination are used to prevent the development of estrogen-induced endometrial hyperplasia and carcinoma[2]. Although, HT provides several benefits, an increased risk of breast carcinoma has been reported with long-term HT[3,4]. The use of HT also induces breast pain and an increase in mammographic breast density[1,5-7]. Mammography is a valuable tool for the early detection of breast cancer [8], but the accuracy of screening mammography also depends on mammographic density[9]. HT may influence the performance characteristics of screening mammography through its effect on mammographic breast density. In the present study, the authors determined the effects of different types of HT on mammographic breast density changes.

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Material and Method

Between 1999 and 2002, mammograms obtained before and 12-18 months after different types of HT in 170 women were evaluated. 66 of 170 women were in surgical menopause because of benign gynecological disorders and were given conjugated equine estrogen (CEE) 0.625 mg/day. In this group, data has been

presented in a published paper[10]. 59 women were amenorrheic lasting less than 12 months and were given a cyclic combined regimen (Estradiol valerate 2mg/day on days 1-21 and Norgestrel 0.5 mg/day on days 12-21). The remaining45 of 170 women were amenorrheic lasting more than 12 months and were given a continuous combined regimen (CEE 0.625mg and medroxy-progesterone acetate 2.5 mg once daily). The baseline mammographic density was classified according to the Breast Imaging Reporting and Data Systems (BI-RADS) into four categories, namely; fatty, scattered fibro-glandular, heterogeneously dense, and homogeneously dense. The serial changes observed mammographically were categorized as follows: no change, minimal change (10-25% increased density), moderate change (26-50% increased density), and marked change (> 50% increased density). The pattern distribution of the density change was classified into two types, namely: focal, and diffuse. Differences within and between groups were assessed by Chi-square test or Fisher's exact test. A p-value of less than 0.05 was considered statistically significant.

Results

The mean age (± SD) of the patients was 47 (± 4.3) years, 48 (± 3) years, 52 (± 4) years, in patients receiving estrogen alone, cyclic combined regimen and continuous combined regimen respectively. The mean duration (± SD) of hormonal treatment was 14.3 (± 2.2) months. The baseline mammographic parenchymal density in each group is shown in Table 1. Twelve (7%) of the women developed increase in parenchymal density after HT. The distribution of serial mammographic changes is shown in Table 2. Two patients had focal increase in density and 10 patients had diffuse increase in density. No breast cancer or mammographic abnormality warranting biopsy was found in these patients.

Discussion

The type of HT does not depend only on the physician's choice but also depends on the patient's preference and conditions such as previous hysterectomy, menstrual history, allergy to transdermal preparations or gastrointestinal intolerance to oral preparations. Previous studies have shown that women undergoing HT may have an increase in breast density on mammograms[1,5-7], and that the combination HT regimen has a greater effect on the breast density than the estrogen alone regimen[1,7,11-13]. The breast epithelial proliferation has also been found to be higher during

Table 1. Distribution of baseline mammographic parenchymal density

Types of HT	Fatty	Scattered fibroglandular	Heterogeneously dense	Homogeneously dense
Estrogen alone (n = 66)	3	15	46	2
Cyclic combined regimen (n = 59)	1	7	46	5
Continuous combined regimen (n = 45)	2	14	28	1

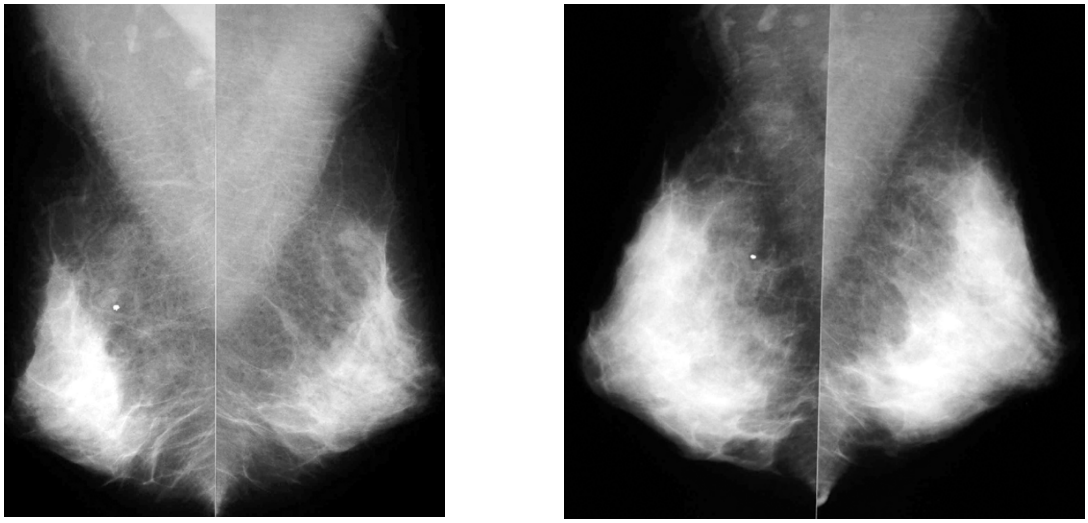
$X^2 = 9.12$, $p = 0.167$

Table 2. Distribution of serial mammographic density changes

Types of HT	Density Change			
	No change	Mild	Moderate	Marked
Estrogen alone (n = 66)	64	-	1	1
Cyclic combined regimen (n = 59)	59	-	-	-
Continuous combined regimen (n = 45)	35	5	3	2

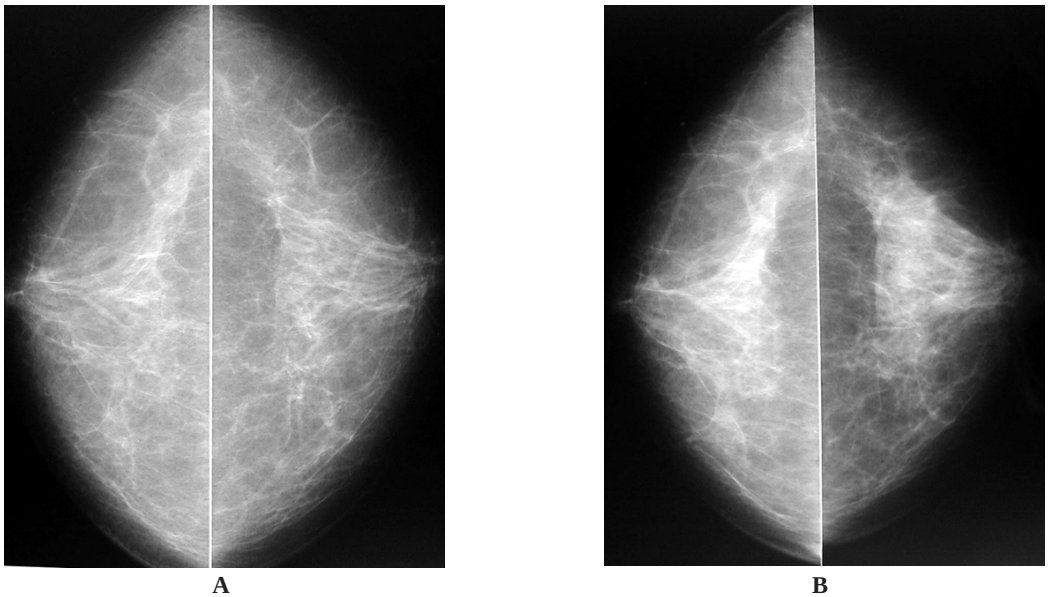
$X^2 = 23.47$, $p < 0.001$

the luteal phase of the menstrual cycle than during the follicular phase, suggesting that progesterone and estrogen together induce more mitoses than estrogen alone[12,14]. However, the continuous combined regimen induces more effects than the cyclic combined regimen because cyclic withdrawal of progesterone may stimulate spontaneous apoptosis. Therefore, the effects of progesterone may differ according to dosage and dura-tion of exposure. Moreover, the baseline characteristics of the patients especially age and duration of amenorrhea were not similar between the groups. The older women with the longer duration of amenorrhea



A B

Fig. 1 (A) Mediolateral oblique mammograms of both breasts in a 58-year-old woman before commencing CEE
(B) 14 months after therapy show marked diffuse increase in density in both breasts



A B

Fig. 2 (A) Craniocaudal mammograms of both breasts in a 49-year-old woman before commencing continuous combined CEE and progesterone therapy
(B) 13 months after therapy show mild diffuse increase density in both breasts

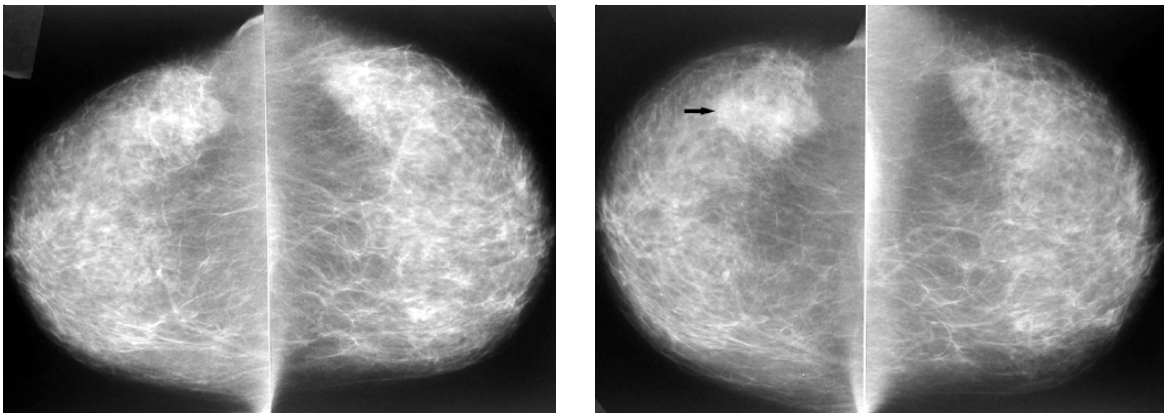


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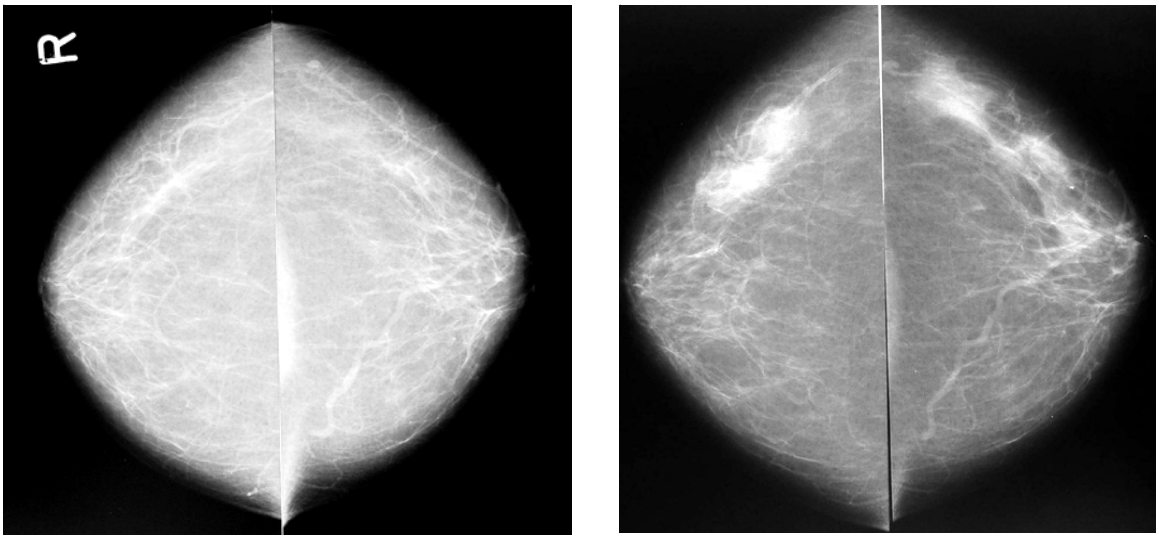
Fig. 3 (A) Craniocaudal mammograms of both breasts in a 51-year-old woman before commencing continuous combined CEE and progesterone therapy
(B) 16 months after therapy show focal increase density in the right outer quadrant (arrow)



A B

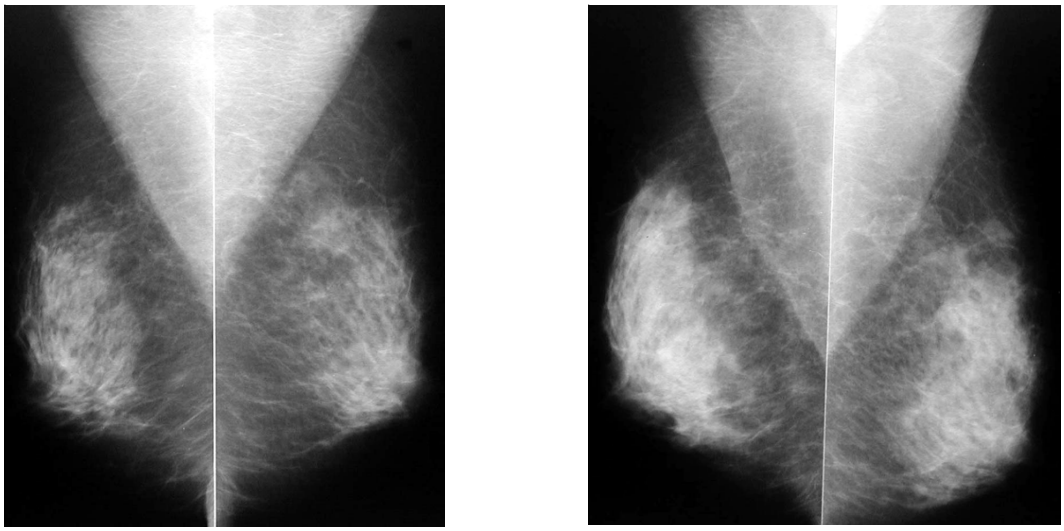
Fig. 4 (A) Craniocaudal mammograms of both breasts in a 64-year-old woman before commencing continuous combined CEE and progesterone therapy
(B) 14 months after therapy show focal increase in density in the outer quadrants of both breasts

were using the continuous combined regimen of estrogen plus progesterone, while the younger hysterectomized women were using the estrogen only regimen. So, the different baseline characteristic might significantly affect the mammographic density change. So age of the patient and duration of amenorrhea may be the additional independent risk factors of mammographic changes.

In the present study, an increase in mammographic breast density was much more common among women receiving continuous combined regimen than among those receiving estrogen therapy alone. These mammographic changes can be either focal or diffuse increase in breast density. The cyclic combination group showed no change at all.

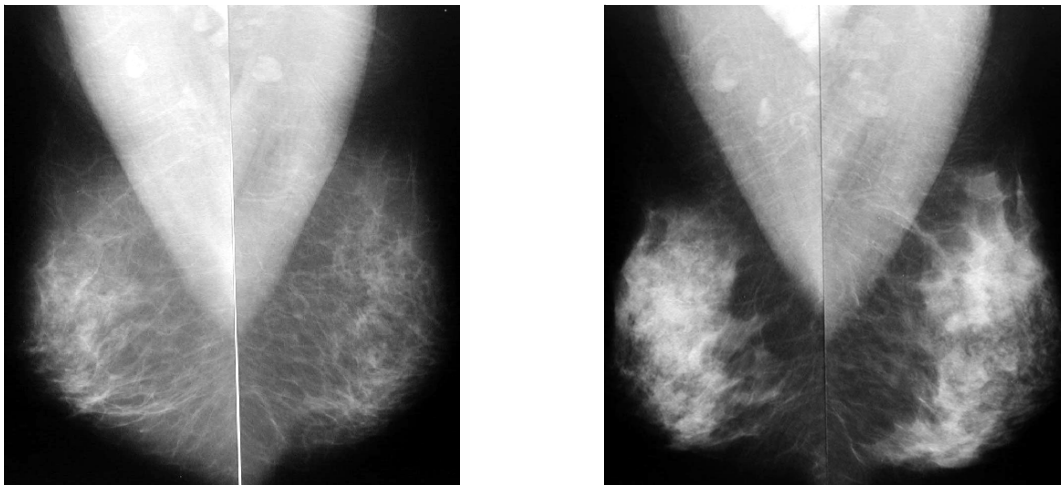
Conclusion

Changes of increased density after HT were seen in only 7% of mammograms and depended on the selected hormone regimen. The continuous combined



A B

Fig. 5 (A) Mediolateral oblique mammograms of both breasts in a 52-year-old woman before commencing continuous combined CEE and progesterone therapy
(B) 14 months after therapy show moderate diffuse increase in density in both breasts



A B

Fig. 6 (A) Mediolateral oblique mammograms of both breasts in a 59-year-old woman before commencing continuous combined CEE and progesterone therapy
(B) 17 months after therapy show marked diffuse increase in density in both breasts

regimen affects the breast density most. However, age of the patient and duration of amenorrhea may be the additional independent risk factors for mammographic changes.

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การเปลี่ยนแปลงลักษณะภาพแมมโมแกรมในสตรีที่ใช้ฮอร์โมนชนิดต่าง ๆ

สายพิณ พงษธา, มาลัย มุตตารักษ์, สมศักดิ์ เชาว์วิศิษฐ์เสรี, สุชยา ลือวรรณ, อรรถพร พันธ์พานิช

วัตถุประสงค์: *เพื่อศึกษาผลของฮอร์โมนชนิดต่างๆต่อการเปลี่ยนแปลงลักษณะภาพแมมโมแกรม*

วัสดุและวิธีการ: *ในช่วงระยะเวลาปี พ.ศ. 2542-2546 มีสตรีที่ได้รับการตรวจแมมโมแกรมก่อนใช้ฮอร์โมน และหลังใช้ฮอร์โมน 12-18 เดือนจำนวน 170 คน โดยใช้ฮอร์โมนเอสโตรเจนอย่างเดียว 66 คน, ฮอร์โมนเอสโตรเจน และโปรเจสโตโรนแบบเป็นรอบ 59 คน, ฮอร์โมนเอสโตรเจนและโปรเจสโตโรนแบบต่อเนื่อง 45 คน โดยประเมินความเข้มของภาพแมมโมแกรมก่อนใช้ฮอร์โมนตามเกณฑ์ของ Breast Imaging Reporting and Data System (BI-RADS) การเปลี่ยนแปลงของภาพแมมโมแกรมหลังการใช้ฮอร์โมนดังนี้*

ไม่เปลี่ยนแปลง, เปลี่ยนแปลงเล็กน้อย (ความเข้มเพิ่มขึ้น 10-25%), เปลี่ยนแปลงปานกลาง (ความเข้มเพิ่มขึ้น 26-50%) และเปลี่ยนแปลงมาก (ความเข้มเพิ่มขึ้น > 50%)

ผลการศึกษา: *ร้อยละ 7 ของสตรีที่ใช้ฮอร์โมนมีความเข้มของภาพแมมโมแกรมเพิ่มขึ้นโดยมีความเข้มเพิ่มขึ้นเล็กน้อยร้อยละ 2.9, ปานกลางร้อยละ 2.3, มากร้อยละ1.8 ไม่พบสตรีรายใดเลยมีการเปลี่ยนแปลงหลังได้ฮอร์โมนเอสโตรเจนและโปรเจสโตโรนแบบเป็นรอบแต่พบการเปลี่ยนแปลงมากในกลุ่มที่ได้ฮอร์โมนเอสโตรเจนและโปรเจสโตโรนแบบต่อเนื่องคือร้อยละ 22.5 (10 ใน 45) ในกลุ่มที่ได้ฮอร์โมนเอสโตรเจนอย่างเดียวพบร้อยละ 3 (2 ใน 66) โดยมีความแตกต่างอย่างมีนัยสำคัญทางสถิติ*

สรุป: *การเปลี่ยนแปลงลักษณะภาพแมมโมแกรมหลังได้รับฮอร์โมนพบประมาณร้อยละ 7 จากการศึกษานี้ โดยขึ้นกับชนิดของฮอร์โมนที่ใช้*