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DISTRIBUTION OF MAMMOGRAPHIC DENSITIES IN 5052 WOMEN AT THE PERIMENOPAUSAL AND POSTMENOPAUSAL STAGE

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Aims: To establish the frequency and age distribution of breast tissue density, mammographic masses and benign calcifications and to study the effect of hormone replacement therapy (HRT), which has been suggested to affect parenchymal density on mammograms.

Methods: The mammograms of all patients attending the Zekai Tahir Burak Women Health Education and Research Hospital menopause clinic between January 2001 and January 2004 were evaluated. We reviewed 5052 women. The density for each breast was classified into one of four groups as defined by the BI-RADS system. For each patient, benign or probably benign calcifications were also recorded. The use of HRT was recorded systematically for every patient. Chi-square and Spearman correlation tests were performed. The statistical significance of observed differences was set at $p<0.05$.

Results: In the evaluation of mammographic densities, 2246 (44.4%) of the 5052 patients had heterogeneously dense or extremely dense breasts. It is shown in this study that as age increases mammographic density progressively decreases. Mammographic masses thought to be malign are mostly seen in the upper external zone and central zone. HRT use increases parenchymal density and decreases mammographic sensitivity.

Conclusion: Mammography is the basic imaging modality for the evaluation of patients with breast abnormalities. The sensitivity of screening mammography decreases as parenchymal density increases. Benign calcifications can be seen in any age group. There is no need for any further diagnostic approach for calcifications thought to be benign.

Key Words: Mammographic density, Benign calcifications, Mass lesions.

PERİMENOPOZAL VE POSTMENOPOZAL DÖNEMDEKİ 5052 HASTANIN MAMOGRAFİK DANSİTELERİNİN DAĞILIMI

Amaç: Mamografide saptanan kitlelerin, meme dansitesinin ve benign özellikteki kalsifikasyonların yaşlara göre dağılımını ve sıklıklarını saptamak ve HRT'nin meme dansitesi üzerindeki etkisini değerlendirmek.

Metod: Ocak 2001 ve Ocak 2004 tarihleri arasında Dr. Zekai Tahir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi menapoz polikliniğine başvuran 5052 hastanın mamografileri değerlendirildi. Her meme dansitesi BI-RADS sistemine göre dört gruptan birinde olacak şekilde değerlendirildi. Hastalarda saptanan mamografik kitleleler ve benign özellikteki kalsifikasyonlar not edildi. Hastaların HRT kullanma durumları değerlendirildi. İstatistiksel incelemeler için ki-kare ve Spearman korelasyon testleri kullanıldı ve $p<0.05$ değeri istatistiksel anlamlılık olarak kabul edildi.

Sonuçlar: Mamografik dansitelerin değerlendirilmesinde 5052 hastanın 2246 tanesi (44,4%) heterojen dens veya dens memeye sahipti. Yaş ilerledikçe meme dansitesi azalmaktadır. Malign olduğu düşünülen mamografik kitleler en sık üst dış kadran ve santral bölgede yer almaktadır. HRT kullanımı dansiteyi artırırken mamografik sensitiviteyi azaltır.

Tartışma: Mamografi, meme rahatsızlığı olan hastaların değerlendirilmesinde en temel yöntemdir. Mamografinin sensitivitesi parankimal dansite arttıkça azalmaktadır. Benign kalsifikasyonlar her yaş grubunda görülebilmektedir, bunlar için daha ileri inceleme yapılmasına gerek yoktur.

Anahtar Sözcükler: Mamografik dansite, benign kalsifikasyon, kitle lezyonu.

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INTRODUCTION

Mammography is the mainstay of the early diagnosis of breast cancer. Although this screening contributes to the reduction in breast cancer mortality, it also increases the detection of non-palpable breast lesions (1). Nonpalpable breast cancers may present radiographically as masses, calcifications, or masses with calcifications.

In clinical trials, screening mammography has been shown to reduce mortality from breast cancer 20% to 39% among women aged 50 years or older (2-7). Among women aged 40 to 49 years, the evidence to support the efficacy of screening mammography is less convincing. Six randomized controlled trials have reported no statistically significant reduction in breast cancer mortality in women aged 40 to 49 years after 7 to 10 years of follow up (3-8).

Although there has been some controversy over the past 20 years, most studies indicate that dense mammographic parenchymal patterns are related to an increased risk of breast cancer (9-11). Increased parenchymal density is, however, of greater clinical significance as a cause of false-negative mammograms (12). Further, it has been reported that hormone replacement therapy (HRT) makes the breast denser (13, 14).

The primary aim of the present study was to gain experience by using a tertiary health care center's records to establish the frequency and age distribution of breast tissue density, mammographic masses and benign calcifications, and to study the effect of HRT, which has been suggested to affect parenchymal density on mammograms.

METHODS

The mammograms of all patients attending the Zekai Tahir Burak Women Health Education and Research Hospital menopause clinic between January 2001 and January 2004 were evaluated, without considering them premenopausal or postmenopausal. Before the study started, hospital ethics committee approval was obtained. We reviewed 5052 women: 1557 of them under 50 years of age and 3495 of them above 50 years of age.

All mammographies were performed with the same device (GE Medical Systems, Senographe DMR+, 2001). The mammographies were interpreted by the same radiologist throughout the study. The density for each breast was classified into one of four groups as defined by the BI-RADS system: 1) almost entirely fat, 2) scattered fibroglandular tissue, 3) heterogeneously dense, and 4) extremely dense (15).

Breast density, features of mass lesions and calcifications were assessed visually on both craniocaudal and mediolateral oblique views. The presence of palpable lesions was an indication for ultrasonography. Other indications were patient age <35 years and

dense breast tissue on mammography. For each patient, benign or probably benign calcifications were also recorded. Routine or short-term mammographic follow-up was recommended for these findings.

A diffuse distribution of calcifications throughout the breast (scattered), five or less calcifications per cluster, annular calcifications, and macrocalcifications were the signs of benign calcifications (17). The use of HRT was recorded systematically for every patient. Patients who had breast cancer in their past history were excluded from the study.

The BI-RADS system was used to assess the masses seen on the mammograms. Location of the mass (right or left breast), location in the breast, shape, margins, and density of each mass were assessed with parenchymal density. Mass margins are described as circumscribed, microlobulated, obscured, indistinct and spiculated. Mass shape can be described as round, oval, lobular or irregular. Mass density can be described as high, equal, low or fat containing. The features with the highest positive predictive value for masses for malignancy were spiculated borders and irregular shape (15).

In this study, the breast is classified in seven zones, with vertical lines passing from the areola, anterior axillar line and lateral sternum, and with a horizontal line passing from the areola. The distribution of masses and calcifications within these zones was determined. Chi-square and Spearman correlation tests were performed. The statistical significance of observed differences was set at $p<0.05$.

RESULTS

The patients in the study group ranged in age from 36 to 71 years, with a median age of 53 years.

In the evaluation of mammographic densities, 2246 (44.4%) of the 5052 patients had heterogeneously dense or extremely dense breasts, and 273 (5.4%) of them had extremely dense breasts. The distribution of mammographic densities in the two groups of patients is seen in Table 1.

It is clear from the table that as age increases mammographic density progressively decreases. In the group 50 years and younger, only 6.7% of them had entirely fat mammographic density, but this proportion was 13.6% in the 50 years and older group ($p<0.05$).

The distribution of mammographic masses seen in the mammograms in patients 50 years old or younger is shown in Table 2. In this group, lesions thought to be malign were mostly seen in the central zone (n=16, 0.31%) and less frequently in the upper external zone (n=15, 0.29%).

The distribution of mammographic masses seen in the mammograms in women 50 years old or older is shown in Table 3. In contrast to the first group, in this group, masses thought to be malign were mostly seen in the upper external zone (n=30, 0.59%) and less frequently in the central zone (n=18, 0.35%). Mammographic masses thought to be malign were mostly seen in the upper external zone and central zone in both groups, and for such lesions ultrasonography was also performed. Both mammographic and ultrasonographic examinations guided the selection of patients for biopsy. All malignancies were confirmed by pathological examination.

According to the BI-RADS system, which is used to assess the masses seen from the mammograms, the malignancy rate for the group of patients 50 years or younger was 0.27%, for the group of patients 50 years or older it was 0.64% and for the general population it was 0.45%, and this was concordant with previous studies (15, 16).

When we evaluated the patients according to their HRT use, 837 (23.9%) of the 3495 patients in the 50 years and older group were using HRT; this proportion was 19.6% (n=305) for the group 50 years and younger. Mean duration of HRT use was 4.1±2.9 years for both groups. Standard HRT was given, consisting of concurrent estrogen and progestin, to all patients with an intact uterus. Estrogen only medications were given to women who had had hysterectomies. In the group not using HRT, 75.1% of them had entirely fat density compared with

Table 1: Distribution of patients' mammographic breast densities according to age groups.

	Almost entirely fat		Scattered fibroglandular tissue		Heterogeneously dense		Extremely dense	
	n	%	n	%	n	%	n	%
50 Years and younger	120	6.7	679	38.4	848	47.9	121	6.8
Older than 50 Years	448	13.6	1559	47.4	1125	34.2	152	4.6

Table 2: Distribution of mammographic masses determined in the 50 years and younger group.

	Central		Axillary tail		Upper external		Upper internal		Lower internal	
	B	M	B	M	B	M	B	M	B	M
SHAPE	24	5	12	0	93	3	6	0	10	2
MARGIN	13	6	14	0	51	5	2	0	9	0
DENSITY	27	5	14	2	103	7	4	2	12	1

B = Benign, M = Malign

Table 3: Distribution of mammographic masses determined in the 50 years and older group.

	Central		Axillary tail		Upper external		Upper internal		Lower internal	
	B	M	B	M	B	M	B	M	B	M
SHAPE	65	4	32	8	206	5	4	1	30	1
MARGIN	35	10	22	2	112	11	3	0	19	2
DENSITY	80	4	36	1	259	14	7	0	27	1

B = Benign, M = Malign

50.7% in the group using HRT ($p<0.01$). The clinical significance of this is that increasing parenchymal density decreases mammographic sensitivity.

When we looked at the calcifications thought to be benign (Figure 1) seen on the mammograms, in the group of 50 years and younger, we found 255 calcifications in the left breast and 153 (60%) of them were in the upper external zone and 34 (13.3%) of them were in the central zone. In the same group, there were 263 calcifications in the right breast and 160 (60.1%) of them were in the upper external zone and 35 (13.1%) of them were in the central zone.

For the group of patients 50 years and older, there were 596 calcifications in the left breast thought to be benign, and 330 (55.3%) of them were in the upper external zone and 135 (22.6%) of them were in the central zone. In the same group, there were 608 calcifications in the right breast and 413 (67.9%) of them were in the upper external zone and 70 (11.5%) of them were in the central zone. This distribution shows that in both groups of patients calcifications were mostly seen in the upper external zone, followed by the central zone.

DISCUSSION

Mammography is the basic imaging modality for the evaluation of patients with breast abnormalities (16). Screening mammography significantly reduces breast cancer mortality in women aged 50 to 74 years, regardless of the screening interval or the number of mammographic views per screen. There is no reduction in breast cancer mortality in women aged 40 to 49 years (1). Women aged 40 to 49 years have a lower breast cancer incidence, faster breast cancer growth rates, and a tendency to have denser, more fibroglandular breast tissue in which mammography is less sensitive, and when compared with postmenopausal group much more false negative mammograms are seen (18, 19).

Kerlikowske et al. reported that clinical breast examination in addition to mammography did not decrease breast cancer mortality beyond the reduction achieved by mammography alone for women aged 50 to 74 years or for women aged 40 to 49 years (1).

In agreement with Stomper et al., we also found that density on mammograms decreases progressively from younger ages to older ages (18).

Mandelson et al. evaluated breast density as a predictor of mammographic detection. Mammographic sensitivity was 80% among women with predominantly fatty breasts but 30% in women with extremely dense breasts (20).

Like Salminen et al., we also found HRT to be a factor that makes the mammographic parenchymal patterns denser. HRT can also make the detection of breast cancer more difficult by reducing the sensitivity of mammography to detect small tumors and by reducing the quality of mammography by increasing breast tenderness and making adequate compression of the breast difficult (21, 22). Today specific guidelines and protocols to optimize the screening of neoplastic breast pathology in HRT users do not exist and it is unknown if short-term suspension of therapy improves mammographic sensitivity. The genes that determine breast density might also be associated with a risk of breast cancer, and their identification is likely to provide insights into the biology of the breast and identify potential targets for preventive strategies. Maybe the best way to apply HRT is to use hormones for short periods around the menopause.

Benign calcifications can be seen in any age group. There is no need for any further diagnostic approach for calcifications thought to be benign (20).

The time between screenings can affect the benefits. If the interval between screenings is too long, many rapidly growing tumors will surface clinically between screenings or will be detected by screening only shortly before they would have become clinically apparent, thereby reducing the benefit of screening. Mandelson et al. reported that, by reducing the screening interval from 24 months to 12 months, 85% success rates can be achieved (20), but there are some groups advocating a conflicting opinion, like Kerlikowske et al. (1). In our hospital, we think that annual screening is more effective than screening offered every 1 to 2 years.

In conclusion, we determined that younger age and for the postmenopausal group the use of HRT are associated with increased parenchymal density. Screening mammography can substantially reduce death rates from breast cancer among women aged 40 years and older. Mammography cannot detect all breast cancers and may result in some unnecessary diagnostic imaging work-up and biopsies; however, it is the best available screening test for breast cancer and will remain so for the foreseeable future.

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