Türk Kadın Sağlığı ve Neonatoloji Dergisi

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Orijinal Makale

The Influence of Hyperlipidemia on the Results of Mammography in Postmenopausal Women

Postmenopozal Kadınlarda Hiperlipideminin Mamografi Sonuçları Üzerindeki Etkisi

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Abstract

Aim: To determine whether hyperlipidemia causes specific or nonspecific changes that can be detected by mammography in postmenopausal women.

Materials and Method: This study was conducted retrospectively and designed as a case-control study in the gynecology clinics of Etlik Zubeyde Hanim Women's Health Education and Training Hospital between January 2017 and January 2020. Healthy postmenopausal women with a total cholesterol (TC) level of 200 mg/dL and above 200 mg/dL, who were examined in our outpatient clinics and whose mammographic controls were performed in our hospital, were included in the study group (Group I). Healthy postmenopausal women with a TC level below 200 mg/dL who were followed up at the same clinic and whose mammographic controls were performed at our clinic were included in the control group (Group II). We analyzed TC, low-density lipoprotein cholesterol, very-low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides with mammography findings.

Results: There were no significant differences between the groups in terms of age and body mass index. There were no significant differences between smoking status and family history of breast cancer. The BAC and BI-RADS scoring category scores differed significantly (p=0.006 and p=0.042, respectively).

Conclusion: Postmenopausal women with hyperlipidemia have mammographic findings that can lead to breast cancer. Considering that hyperlipidemia may also have other causes of morbidity and mortality, such as hypertension, diabetes mellitus and cardiovascular disease, it is necessary to treat it with lifestyle changes and / or medications. As this was a retrospective study with a limited number of patients, it is clear that future randomized controlled trials could provide more reliable data on this topic.

Keywords: breast cancer; hyperlipidemia; mammography; post-menopause

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Öz

Amaç: Postmenopozal kadınlarda hiperlipideminin mamografi ile saptanabilen spesifik veya nonspesifik değişikliklere neden olup olmadığını belirlemek.

Gereç ve Yöntem: Bu çalışma Ocak 2017-Ocak 2020 tarihleri arasında Etlik Zübeyde Hanım Kadın Sağlığı Eğitim ve Araştırma Hastanesi jinekoloji kliniklerinde retrospektif olarak yürütülmüş ve vaka-kontrol çalışması olarak tasarlanmıştır. Polikliniklerimizde muayene olan ve mamografik kontrolleri hastanemizde gerçekleşen, total kolesterol (TC) düzeyi 200 mg/dL ve 200 mg/dL'nin üzerinde olan sağlıklı postmenopozal kadınlar çalışma grubuna (Grup I) dahil edildi. Aynı klinikte takip edilen ve mamografik kontrolleri kliniğimizde yapılan sağlıklı postmenopozal kadınlardan TC düzeyi 200 mg/dL'nin altında olanlar kontrol grubuna (Grup II) dahil edildi. Mamografi bulguları ile TC, düşük yoğunluklu lipoprotein kolesterol, çok düşük yoğunluklu lipoprotein kolesterol, yüksek yoğunluklu lipoprotein kolesterol ve trigliseridler analiz edildi.

Bulgular: Gruplar arasında yaş ve vücut kitle indeksi açısından anlamlı bir fark yoktu. Sigara içme durumu ve ailede meme kanseri öyküsü arasında anlamlı bir fark bulunmamıştır. BAC ve BI-RADS skorlama kategorileri değerleri arasında anlamlı fark vardı (sırasıyla p=0.006 vs p=0.042)

Sonuç: Hiperlipidemisi olan postmenopozal kadınlar meme kanserine yol açabilecek mamografik bulgulara sahiptir. Hiperlipideminin hipertansiyon, diabetes mellitus ve kardiyovasküler hastalık gibi başka morbidite ve mortalite nedenleri de olabileceği düşünüldüğünde, yaşam tarzı değişiklikleri ve/veya ilaç tedavisi ile tedavi edilmesi gerekmektedir. Bu çalışma sınırlı sayıda hastayı içeren retrospektif bir çalışma olduğundan, gelecekte yapılacak randomize kontrollü çalışmaların bu konuda daha güvenilir veriler sağlayabileceği açıktır.

Anahtar Kelimeler: meme kanseri; hiperlipidemi; mamografi; post-menopoz

1. Introduction

Breast cancer is one of the most commonly diagnosed malignancies worldwide and the leading cause of cancer-related death in the female population (1-4). Although it is more common in Western Europe and North America, more than 2 million new cases were detected in 2018 (2). Today, the prevalence is increasing in the older population and is more common in postmenopausal women (2,3). According to the American Cancer Society, the five-year survival rate has increased from 63% in 1960 to 90,8% today (5). This is thanks to early detection and improved treatment options through mammography screening, which has now become a routine examination in cancer prevention centers (2). The mortality rate has also fallen rapidly and was 6.6% in 2018 (2,5).

Several risk factors for breast cancer have been identified, which are referred to as modifiable and non-modifiable risk factors (6,7). Modifiable risk factors are important because they are preventable (8). These factors include dietary habits and obesity (8-10). Obesity in particular is associated with poor survival rates and increased mortality from breast cancer in postmenopausal women (9). Obesity is one of the biggest health problems in the world (11). The fact that most women in Turkiye are housewives, traditionally do not exercise and eat a diet high in carbohydrates and fat suggests that this could pave the way for obesity usually in the postmenopausal period and also pose a risk for breast cancer at this time (12). Some studies have also shown that a diet rich in foods containing fat and carbohydrates increases the risk of breast cancer (13). This increased risk explains why obesity in the postmenopausal period increases the risk of breast cancer (14).

Breast arterial calcification (BAC) is a radiologic finding on mammography that is not associated with cancer and usually occurs in postmenopausal women. BAC is classified as medial arterial calcification or Mönckeberg calcification, which is distinct from intimal calcification (15). Some studies suggest that BAC is associated with cardiovascular disease, diabetes or hypertension and can be used as a marker for arterial disease or cardiovascular disease (15,16). Arterial disease is associated with established risk factors for cardiovascular disease, including body mass index (BMI), elevated total cholesterol (TC) (≥ 200 mg/dL) (hyperlipidemia) or low-density lipoprotein cholesterol (LDL-C) levels, hypertension, and diabetes mellitus. BAC can be an indicator of arterial disease, cardiovascular disease and abnormal cardiovascular risk factors (16-18).

In light of this information, the aim of our study was to determine whether hyperlipidemia causes specific or nonspecific changes that can be detected by mammography in postmenopausal women.

2. Materials and method

This study was conducted retrospectively and designed as a case-control study in the gynecology clinics of Etlik Zubeyde Hanim Women's Health Education and Training Hospital between January 2017 and January 2020. This study was

conducted in accordance with the principles of the Declaration of Helsinki and was approved by the local ethics committee (with number: 01/08; January 2022).

Inclusion and exclusion criteria

Healthy postmenopausal women without underlying metabolic or systemic diseases (type 2 diabetes, high blood pressure, etc.) were included in the study.

Postmenopausal women were excluded from the study if they had any of the following risk factors or conditions: Hyperlipidemia due to secondary causes (including congenital adrenal hyperplasia, Cushing's syndrome, hyperprolactinemia, thyroid dysfunction, and adrenal disease); pre-existing systemic disease (hypertension, chronic renal failure, familial hypertriglyceridemia etc.); taking medication that affects carbohydrate or lipid metabolism (contraceptive pills, metformin, anti-epileptic drugs, antipsychotics, statins, and fish oil); women with known breast cancer or mammography changes; if BMI ≥ 40 kg/m2

Data

The sample size was calculated using a manual power analysis program. The analysis was calculated with an effect size of 0.20, an error of 0.05, and a power of 0.80. A total of 180 participants were identified. A sample of 90 cases (postmenopausal women with hyperlipidemia) and 90 controls (healthy postmenopausal women) was required for the study.

Data were extracted from patient records or hospital records of both groups, including demographic information (age, smoking status, family history of breast cancer), anthropometric parameters of the participants (height and weight to calculate body mass index), results of biochemical laboratory tests and mammography findings.

Study design

Healthy postmenopausal women with a TC level of 200 mg/dL and above 200 mg/dL, who were examined in our outpatient clinics and whose mammographic controls took place in our hospital, were included in the study group (Group I). Healthy postmenopausal women with a TC level below 200 mg/dL who were followed up in the same clinic and whose mammographic controls were performed in our clinic were included in the control group (Group II). We plan to form our control group by randomization from postmenopausal women who meet the inclusion criteria. We plan to perform the randomization in chronological order by including in the control group the postmenopausal women who were admitted to the outpatient clinic immediately after the women from the study group. We analyzed TC, LDL-C, very-low-density lipoprotein cholesterol (VLDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) with mammography findings.

Laboratory analysis of biological samples

We analyzed blood TC levels and other cholesterol components (LDL-C, HDL-C, TG and VLDL-C) using the ADVIA® 1800 Chemistry System (Siemens Healthcare Diagnostics Inc., Tarrytown, NY, USA).

Statistical analyses

All statistical analyzes were performed using SPSS software (version 27.0, for Windows) was used to analyze the data (19). The variables were investigated using visual (histogram, probability plots) and analytic methods (Kolmogrov-Simirnov/ Shapiro-Wilk's test) to determine whether or not they are normally distributed. Relationships between categorical variables were analyzed with the Chi-square test and relationships between non-categorical variables were analyzed with t-test. A p-value of less than 0.05 was considered to show a statistically significant result.

3. Results

After the data search, 238 postmenopausal women were found who had been admitted to our tertiary care hospital (Figure 1). After exclusion based on the criteria described in the Material and Methods section, 90 postmenopausal women who were admitted to our hospital between 2017 and 2020 with a high TC value for mammography control formed the study group (Group I) and 90 postmenopausal women who were included in the study according to the randomization system formed the control group (Group II).

A comparison of age, BMI and lipid profile is shown in Table I. There were no significant differences between the groups in terms of age and BMI (Table 1).

A comparison of BAC, Breast Imaging-Reporting and Data Systems (BI-RADS) scoring categories, smoking status and family history of breast cancer is shown in Table II. There were no significant differences between smoking status and family history of breast cancer. The BAC and BI-RADS scoring category scores differed significantly (p=0.006 and p=0.042, respectively) (Table 2).

4. Discussion

To our knowledge, there are few data that shed light on the effect of hyperlipidemia on mammography results in postmenopausal women. In this study, it was found that BAC and BI-RADS scoring categories were higher in postmenopausal patients with hyperlipidemia.

Table 1. Comparison of the groups in terms of age, BMI and blood lipid profiles

	Group I (n=90)					Group II (n=90)						
	Min.	Max.	X	SD	Median	Min.	Max.	X	SD	Median	t	p
Age (years)	45	78	60,61	6,90	60,00	48	76	58,64	6,93	57,00	1,908	0,058
BMI (kg/m^2)	19	40	28,67	4,15	29,00	22	36	27,74	2,69	28,00	1,768	0,079
TC	200	390	250,89	38,21	243,00	117	199	173,38	18,30	178,00	17,358	**0,000***
LDL-C	30	296	158,04	34,73	153,00	57	160	101,23	17,98	102,00	13,783	**0,000***
VLDL-C	10	75	29,58	13,96	26,00	9	32	19,36	5,33	19,00	6,489	**0,000***
HDL-C	36	107	60,98	13,63	62,00	33	160	52,83	13,71	54,00	3,997	**0,000***
TG	50	655	155,31	87,73	133,00	45	150	99,47	26,44	97,00	5,782	**0,000***

BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; n: numbers; SD: standart deviation; t: t-test; TC: total cholesterol; TG: triglycerides; VLDL-C: very-low-density lipoprotein cholesterol.
A p value of <0.05 indicates a significant difference. Statistically significant p-values are in bold.

Table 2. Comparison of the groups with regard to BI-RADS, calcification, smoking status and family history of breast cancer

		Group I (n=90)		Grup II (n=90)			
		n	%	n	%	X2	p
BI-RADS	0	4	4,4	0	0,0	8,226	**0,042***
	1	46	51,1	61	67,8		
	2	34	37,8	23	25,6		
	3-4	6	6,7	6	6,7		
BAC	No	44	48,9	62	68,9	7,435	**0,006***
	Yes	46	51,1	28	31,1		
Smoking status	No	74	82,2	82	91,1	3,077	0,079
	Yes	16	17,8	8	8,9		
Familial history of breast cancer	No	84	93,3	86	95,6	0,424	0,515
	Yes	6	6,7	4	4,4		

BAC: breast arterial calcification; BI-RADS: Breast Imaging-Reporting and Data Systems; n: numbers; X^2: chi square test.
A p value of <0.05 indicates a significant difference. Statistically significant p-values are in bold.

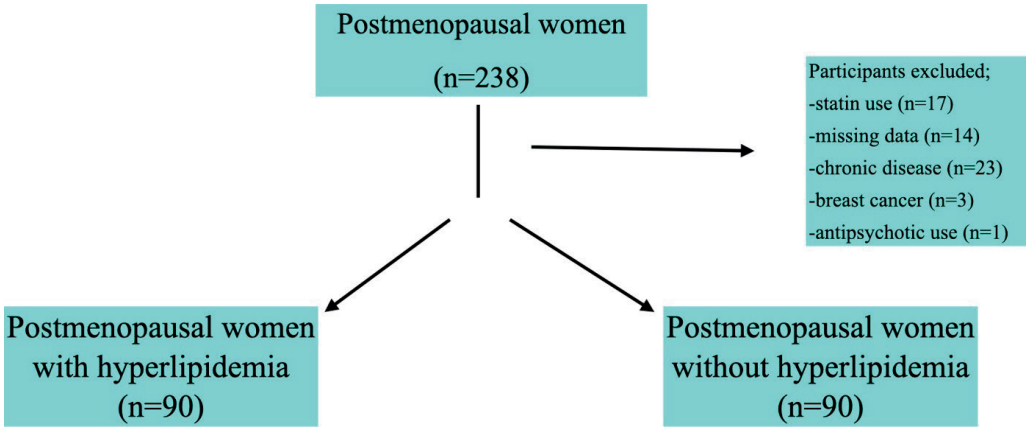

Figure 1. Flowchart of the participants

Hyperlipidemia is a term used to describe TC levels above the current threshold (TC ≥ 200 mg/dL) (20). Hyperlipidemia is a chronic and progressive but controllable disease whose treatment requires lifestyle and dietary changes and sometimes additional lipid-lowering medications (20). If hyperlipidemia remains uncontrolled, the disease progresses and can not only lead to severe arterial and cardiovascular disease, which is often fatal, but can also affect other tissues or organs (20,21). In a cross-sectional study by Torgutalp et al. (22), they concluded that patients with hyperlipidemia had significantly higher shear wave velocities in the patellar tendon and that hyperlipidemia had a direct effect on patellar tendon stiffness, independent of BMI. There is also a study showing that Achilles tendon damage occurs in patients with familial hypercholesterolemia due to cholesterol accumulation (23).

In Turkiye, women aged 40-69 years undergo mammography screening every two years in accordance with the National Standards of the Breast Cancer Screening Program for the early detection of breast cancer (24). In 1993, the American College of Radiology defined a scoring system for radiologists called BI-RADS to describe mammography findings (25). For each BI-RADS category, there is a corresponding follow-up plan to help physicians manage their patients appropriately (25). BI-RADS also contains four categories for breast density that can be specified so that the physician reading the mammogram can select the category that best describes the degree of breast density on the mammography (25). This is because dense breasts not only make mammograms difficult to read, but are also a risk factor for breast cancer (25). BAC is an identical finding in mammography that was first described by Sickles et al. in 1985 (26). It was later described by Cetin et al. (27) as calcium deposition in the medial layer of peripheral arterioles and termed Mönckeberg medial calcified sclerosis or medial arterial calcification on the mammogram. Studies have been published showing an association between BAC and cardiovascular disease, hypertension and diabetes mellitus (28).

In this study, we also attempted to demonstrate the association between mammography findings and hyperlipidemia. In a study conducted by Caglayan et al. (29) comparing breast density and hyperlipidemia in 215 postmenopausal women, no statistically significant difference was found between the groups of 40 women with dense breast tissue and 175 women with non-dense breast tissue. Kim et al. (30) identified age, height, weight, BMI, hematocrit, mean corpuscular hemoglobin, red blood cell distribution width, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, uric acid, gamma-glutamyl transferase, TG, TC, HDL-C and LDL-C as factors that may influence breast density. In our study, postmenopausal women with hyperlipidemia were found to have significant differences in BAC and BI-RADS scoring categories on mammography, independent of age, smoking, BMI and family history of breast cancer. From our results it can be concluded that BAC and BI-RADS are increased in postmenopausal women with hyperlipidemia, which in turn increases the risk of breast cancer.

In conclusion, postmenopausal women with hyperlipidemia have mammographic findings that can lead to breast cancer. Considering that hyperlipidemia may also have other causes of morbidity and mortality, such as hypertension, diabetes mellitus and cardiovascular disease, it is necessary to treat it with lifestyle changes and / or medications. As this was a retrospective study with a limited number of patients, it is clear that future randomized controlled trials could provide more reliable data on this topic.

The strengths and limitations

The study was conducted as a retrospective case-control study, so it has some limitations due to its design. This is because we lacked some data/information from the participants and the number of participants was small. The strength of the study depends in the fact that it was conducted in a large tertiary referral center, where the same algorithms were used to follow up the patients and the groups were conducted with G-power analyzes.

Author contribution

Study conception and design: FBF, BSÜ, and YAR; data collection: FBF, BSÜ, and YAR; analysis and interpretation of results: ES; draft manuscript preparation: FBF, ES, and YEÜ. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The study was approved by the Etlik Zubeyde Hanim Women's Health Education and Research Hospital (Protocol no. 01/11.01.2022).

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Conflict of interest

The authors declare that there is no conflict of interest.

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Araştırma fikri ve tasarımı: FBF, BSÜ ve YAR; veri toplama: FBF, BSÜ ve YAR; sonuçların analizi ve yorumlanması: ES; araştırma

metnini hazırlama: FBF, ES ve YEÜ. Tüm yazarlar araştırma sonuçlarını gözden geçirdi ve araştırmanın son halini onayladı.

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