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Original Article

Comparison of bone mineral density in young patients with breast cancer and healthy women

Sousan Kolahi[1], Hamid Noshad*[2], Jamal Eivazi-Ziaei[3], Alireza Nikanfar[4], Parvin Shakori-Partovi[5], Iraj Asvadi-Kermani[3], Farid Panahi[6], Nassim Mahmoudzade[7]

[1] *Associate Professor, Hematology and Oncology Research Center AND Connective Tissue Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran*
[2] *Associate Professor, Chronic Kidney Disease Research Center, Connective Tissue Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran*
[3] *Professor, Hematology and Oncology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran*
[4] *Associate Professor, Hematology and Oncology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran*
[5] *Associate Professor, Department of Radiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran*
[6] *Student of Medicine, Head of Student Division of Research Development and Coordination Center (RDCC), School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran*
[7] *Student of Medicine, School of Medicine, Islamic Azad University, Tabriz Branch, Tabriz, Iran*

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Abstract

Introduction: Almost 1 in 8 women will have breast cancer during their lifetime. Several risk factors were identified; however, 70% of females with breast cancer have no risk factors. Many risk factors are associated with sex steroid hormones. Some studies have been focused on identification of the indices of cumulative exposures to estrogen during the patients' life. One of these indicators is bone mineral density (BMD). Our aim was the comparison of BMD in young patients with and without breast cancer, and finding a relationship between breast cancer and bone density.

Methods: In this case-control study, 120 people were enrolled; 40 patients with breast cancer and 80 normal healthy persons as control group. Measurement of BMD was performed in both groups and compared.

Results: Both groups were matched in age, weight, age at menarche, age at first marriage and first pregnancy, number of pregnancies over 32 weeks and lactation period, and taking supplemental calcium and vitamin D. However, there was a significant difference between the two groups in terms of estrogen intake, family history of breast cancer, and history of breast masses ($P = 0.03$, $P = 0.03$, $P \leq 0.01$, respectively). A significant difference was found between BMD, bone mineral content (BMC), and t-scores of lumbar spine of the two groups; they were higher in the control group ($P = 0.08$, $P \leq 0.01$, $P = 0.06$, respectively).

Conclusion: This study shows that BMD of young patients with breast cancer is not higher than normal similar age females; thus, BMD is not directly a risk factor for breast cancer.

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Introduction

Breast cancer is one of the most common cancers in females (near to 1 out of 8 females). Several risk factors have been identified for breast cancer including lack of delivery, age at first marriage, early menarche, late menopause,

*** Corresponding Author:** Hamid Noshad, Email: hamidnoshad1@yahoo.com

history of breast cancer in immediate family, familial history of benign breast diseases, hormone replacement therapy, completed pregnancy until more than 30 weeks, obesity after menopause, high socioeconomic status, personal history of ovarian and endometrium cancers, specific radiation to chest wall, and many other risk factors. However, 70% of females who develop breast cancer have no known risk factor for cancer development.[1,2]

Sex steroid hormones and prolactin originated from the ovary are among the most important factors. Estrogen is biologically active in breast tissue and causes breast epithelium proliferation.[3]

A single measurement of blood or urine to evaluate serum estrogen cannot indicate prolonged contact with estrogen.[4] Some studies have identified that prolonged exposure to estrogen or elevated level of hormones in circulation can affect bone mineral density (BMD) (for this reason estrogen therapy was previously a recommended method for osteoporosis prevention in post-menopausal women); therefore, BMD may be a marker for prolonged exposure to estrogen and may be an indirect risk factor for breast cancer. Measurement of serum or urine level of estrogen due to fluctuation of this hormone during the women's menstrual cycle is difficult and cannot reveal prolonged exposure to this hormone.[4]

Several studies have shown a positive correlation between BMD and breast cancer especially when increasing of estrogen level is 2.7-3.5 times more than standard level.[4-7] In contrast, there are other studies that do not confirm this association.[8,9] There are other evidences which illustrate that females with no ovarian function and without any estrogen therapy have not developed breast cancer, and females with high estrogen level or those who receive estrogen therapy have shown a risk factor for developing breast cancer.[10] In addition, some other studies did not reveal similar effects.[6]

These differences are probably due to disturbing factors such as contact with exogenous estrogen In contrast to endogenous estrogen; for example, females at the age of menopause who were treated with estrogen and also routes of administration of estrogen.[11] This information reveals that those with higher BMD have higher risk of breast cancer and those who are suffering from osteoporosis are less likely to develop breast cancer.[6]

The aim of this study is to determine the relationship between BMD and breast cancer among 30 to 40 year old patients referred to Hematology and Oncology Research Center of Tabriz University of Medical Sciences, Iran. Predicted findings will be used as a non-invasive determination method for breast cancer probability or susceptibility to breast cancer in high risk females at earlier stages. In addition, it may clarify doubts in the treatment of osteoporosis with estrogen, especially in postmenopausal females who are at increased risk of both osteoporosis and breast cancer.

Methods

In this case–control study, referred patients have been selected and evaluated using stratified random sampling method. Then, 40 patients with breast cancer as case and 80 healthy persons were enrolled in this study. These numbers are based on the prevalence of high bone density; 1% in healthy persons and 20% in cancer patients, which is calculated with confidence interval of 95% and 80% power.

The case group included cancer patients who were referred to the bone densitometry center of Sina Teaching Hospital of Tabriz University of Medical Sciences, Iran, following biopsy or surgery and pathological diagnosis of breast cancer, and determination of receptor type by oncologist. Their breast cancer is diagnosed and referred to the hospital during June 2011-April 2013. The control group consisted of healthy individuals without breast cancer that were matched with the case group in terms of demographic features following history taking and physical examination, they were chosen regarding to inclusion and exclusion criteria.

Females between the ages of 30-40 years

with breast cancer who did not received any medical treatment, radiotherapy, and chemotherapy were enrolled as case group. These patients had no previous history of problems affecting bone density including hyperthyroidism, chronic liver disease, chronic renal failure, Cushing's syndrome, the risk of osteoporosis (including irregular menstrual periods, ovarian surgery, inability to walk, history of fracture in the femur and spine, and history of phenytoin and levothyroxine medications), and history of corticosteroid therapy with a dose of higher than 7.5 mg per day.

BMD evaluation was performed using a Hologic device (QDR-4500 elite, Hologic Inc., Waltham, USA) with dual-energy X-ray absorptiometry technique. In this method, the value of T-score (compared to the ideal or peak BMD of a healthy 30-year-old adult) and Z-score (compared to that of a typical individual to the participants of the present study), BMD (grams per cm^2), and bone mineral content (BMC) (grams) were calculated. In addition, T-scores above +1 standard deviation were defined as high, between +1 and -1 as normal, between -1 and -2.5 as osteopenia, and more than -2.5 as osteoporosis.[12] The International Society for Clinical Densitometry (ISCD) recommends that instead of T-scores, ethnic or race adjusted Z-scores be used; Z-score of -2.0 or lower is defined as low, and above -2.0 is defined as normal for expected age.

Technical points were observed carefully for densitometry equipment's validity, especially in terms of patient positioning and selecting the zone of densitometry. During the research, quality control was performed daily for the device and for phantom spine. The local ethical committee of Tabriz University of Medical Sciences approved this study. On the other hand, the study was explained to them and signed a written consent. There was no intervention, and the patients were only followed and questionnaires were filled.

Data were expressed as Mean ± SD, frequency, and percentage. The data were analyzed by SPSS for Windows (version 17; SPSS Inc., Chicago, IL, USA). The uniform distribution of data was evaluated by the Kolmogorov-Smirnov test. Means were compared using Student's independent t-test, and in values of non-uniform distribution, Mann-Whitney and chi-square tests were used. Values of $P \leq 0.05$ were considered statistically significant.

Results

In 80 healthy females (30–40 years old) mammography was performed in order to enroll them in this study as control group. Of these healthy women, 6 had suspicious mammogram results; therefore, sonography and macrograph were repeated three months later. Accordingly, breast cancer was not detected in control group during study period.

Breast cancer (case) and control group (without disease) participants had no significant differences in terms of age, weight, age at menarche, age at first marriage and first pregnancy, number of pregnancies over 32 weeks and lactation period, and taking supplemental calcium and vitamin D (Table 1).

Table 1 shows that BMD, BMC, and T-score of lumbar spines were lower in the case group ($P = 0.08$, $P = 0.01$, $P = 0.06$, respectively).On the other hand, BMD, BMC, and T-score of hip were not statistically different between the 2 groups ($P = 0.58$, $P = 0.92$, $P = 0.64$, respectively).

However, there was a significant difference between the 2 groups in terms of estrogen use, family history of breast cancer, and history of benign breast masses ($P = 0.03$, $P = 0.03$, $P \leq 0.01$, respectively). None of the case and control group participants were smokers.

In patients with breast cancer, cancer staging was done and patients were categorized into three stages; 1, 2, and 3 (consisting of 7, 13, and 20 cases, respectively). Further evaluation revealed that 20 patients (50%) had estrogen-receptor-positive breast cancer. A significant difference was found between BMD of lumbar spine of the two groups, which was higher in the control group (Figure 1).

Table 1. Demographic data of the two study groups

Variable	Group		P
	Control	Case	
Age (year)	35.43 ± 3	36.20 ± 3	0.30
Height (cm)	160.00 ± 4	160.10 ± 3	0.87
BMI	27.48 ± 3	27.22 ± 4	0.74
Weight (kg)	70.30 ± 10	69.93 ± 11	0.83
Age of menarche	13.17 ± 1.6	13.26 ± 1.0	0.80
Aga of first marriage	18.45 ± 6	19.63 ± 4	0.80
Age of first pregnancy	20.89 ± 4	21.31 ± 4	0.69
Number of pregnancy	2.13 ± 1	2.23 ± 1	0.53
Breastfeeding (month)	38.25 ± 25	38.90 ± 23	0.72
Use of any Ca supplement (number)	21	4	0.12
Use of any Vitamin D supplement (number)	14	4	0.21
Estrogen user	12	15	0.03*
Cancer history in family	5	1	0.03
History of benign tumor	0	6	0.01*
BMD Spine	1.02 ± 0.10	0.95 ± 0.09	0.08*
BMC Spine	61.01 ± 10	56.39 ± 8	0.01*
T-score of Spine	-0.16 ± 1.2	-0.78 ± 0.8	0.06*
Z-score of Spine	-0.08 ± 1.26	-0.07 ± 0.86	0.02
BMD Hip	0.91 ± 0.1	0.93 ± 0.1	0.58
BMC Hip	29.30 ± 5	29.40 ± 5	0.92
T-score of hip	-0.19 ± 1.0	-0.1 ± 0.9	0.64
Z-score of hip	0.21 ± 0.91	-0.18 ± 0.87	0.14

Data are presented as Mean ± SD and Frequency; *Values of P ≤ 0.05 were significant
BMI: Body mass index; BMD: Bone mineral density; BMC: Bone mineral content; Ca: Calcium

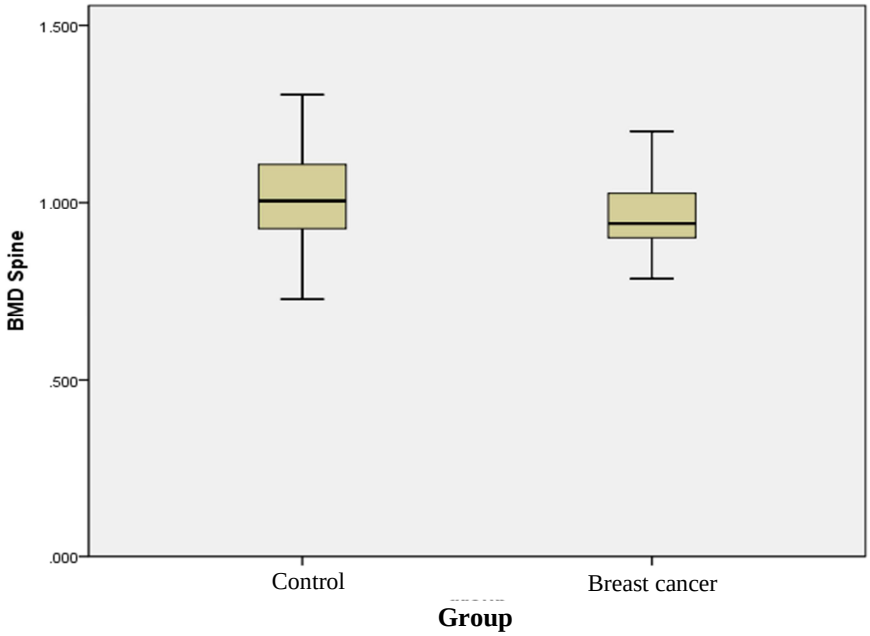

Figure 1. BMD (Bone mineral density) in breast cancer and control groups
BMD: Bone mineral density

Discussion

In our study, BMD, BMC, and t-score of spine were significantly lower in the case group than the control group (P = 0.08, P ≤ 0.01, P = 0.06, respectively). However, BMD, BMC, and t-score of hip in the case group were higher than the control group; however, this difference was not statistically significant

(P = 0.58, P = 0.92, P = 0.64, respectively). Qu et al. showed that higher BMD is a potent risk factor for breast cancer.[4] This was not in accordance with our results, but their studied population consisted of postmenopausal patients not young individuals with breast cancer. Zmuda et al. also reported that breast cancer, especially advanced forms, are more frequent in older patients with higher BMD.[5]

Cauley et al. also reported similar results and presented higher BMD as a risk factor for breast cancer.[7] Hadji et al. also showed that breast cancer is more frequent in women with higher quartiles of BMD.[13]

Ganry et al. reported that BMD is a potent risk factor for breast cancer in elderly women and lower BMD values have preventive effects.[14] In one study, 46% of females with a history of forearm fractures, and in other study, 16% of females who had a history of hip fracture, had low breast cancer risk.[15,16]

Our results are similar to the findings of Newcomb et al, and Tremollieres et al., which showed there were no differences between BMD of patients with breast cancer and control group particioants.[16-18]

There are several possible explanations for this discrepancy. Our study was carried out in young women; however, all other studied were performed in premenopausal and postmenopausal women. In addition, the age and duration of exposure to estrogen was lower in our study compared to other studies. Our study has some positive points. In addition to studying young women, most of the important variables affecting BMD were excluded. All patients were diagnosed and referred by only one oncologist. Moreover, we found that estrogen intake in the cancer group was significantly higher than the control group; this fact is also reported in most of the above-mentioned studies.

In general, it seems that high bone density is a risk factor for breast cancer in elderly women compared with young women. In addition, females with high BMD may have a longer lifetime, but are more likely to develop breast cancer.[6,19]

Limitations

This type of study must be done with greater sample sizes for generalizing of results. There were some other minor confounding factors which we could not consider, but we tried to match the most important and known factors in case and control groups.

Conclusion

BMD of young patients with breast cancer is not higher than normal females; therefore, BMD is not directly a risk factor for breast cancer in this group. BMD, BMC, and t-score evaluation cannot help us in early breast cancer detection and clarifying of previous estrogen exposure.

Conflict of Interests

Authors have no conflict of interest.

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References

1. Hulka BS, Moorman PG. Breast cancer: hormones and other risk factors. Maturitas 2008; 61(1-2): 203-13.
2. Trehan AS, Arora MK, Seth S, Chauhan A. Endogenous hormones in postmenopausal females with breast cancer-before and after treatment. Clin Lab 2012; 58(7-8): 771-7.
3. Ceber E, Mermer G, Okcin F, Sari D, Demireloz M, Eksioglu A, et al. Breast cancer risk and early diagnosis applications in Turkish women aged 50 and over. Asian Pac J Cancer Prev 2013; 14(10): 5877-82.
4. Qu X, Zhang X, Qin A, Liu G, Zhai Z, Hao Y, et al. Bone mineral density and risk of breast cancer in postmenopausal women. Breast Cancer Res Treat 2013; 138(1): 261-71.
5. Zmuda JM, Cauley JA, Ljung BM, Bauer DC, Cummings SR, Kuller LH. Bone mass and breast cancer risk in older women: differences by stage at diagnosis. J Natl Cancer Inst 2001; 93(12): 930-6.
6. Nguyen TV, Center JR, Eisman JA. Association between breast cancer and bone mineral density: the Dubbo

Osteoporosis Epidemiology Study. Maturitas 2000; 36(1): 27-34.
7. Cauley JA, Lucas FL, Kuller LH, Vogt MT, Browner WS, Cummings SR. Bone mineral density and risk of breast cancer in older women: the study of osteoporotic fractures. Study of Osteoporotic Fractures Research Group. JAMA 1996; 276(17): 1404-8.
8. Atkins CD. Bone mass and the risk of breast cancer. N Engl J Med 1997; 337(3): 199.
9. Ballesteros M, Nash D, Fix A, Bush T. Bone mass and the risk of breast cancer. N Engl J Med 1997; 337(3): 200.
10. Clemons M, Goss P. Estrogen and the risk of breast cancer. N Engl J Med 2001; 344(4): 276-85.
11. Peppone LJ, Mustian KM, Rosier RN, Carroll JK, Purnell JQ, Janelsins MC, et al. Bone health issues in breast cancer survivors: a Medicare Current Beneficiary Survey (MCBS) study. Support Care Cancer 2014; 22(1): 245-51.
12. Kanis JA, Melton LJ, III, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. J Bone Miner Res 1994; 9(8): 1137-41.
13. Hadji P, Gottschalk M, Ziller V, Kalder M, Jackisch C, Wagner U. Bone mass and the risk of breast cancer: the influence of cumulative exposure to oestrogen and reproductive correlates. Results of the Marburg breast cancer and osteoporosis trial (MABOT). Maturitas 2007; 56(3): 312-21.
14. Ganry O, Tramier B, Fardellone P, Raverdy N, Dubreuil A. High bone-mass density as a marker for breast cancer in post-menopausal women. Breast 2001; 10(4): 313-7.
15. Rennert G, Pinchev M, Rennert HS. Use of bisphosphonates and risk of postmenopausal breast cancer. J Clin Oncol 2010; 28(22): 3577-81.
16. Newcomb PA, Trentham-Dietz A, Hampton JM. Bisphosphonates for osteoporosis treatment are associated with reduced breast cancer risk. Br J Cancer 2010; 102(5): 799-802.
17. Lin J, Manson JE, Lee IM, Cook NR, Buring JE, Zhang SM. Intakes of calcium and vitamin D and breast cancer risk in women. Arch Intern Med 2007; 167(10): 1050-9.
18. Tremollieres FA, Pouilles JM, Drewniak N, Laparra J, Ribot CA, Dargent-Molina P. Fracture risk prediction using BMD and clinical risk factors in early postmenopausal women: sensitivity of the WHO FRAX tool. J Bone Miner Res 2010; 25(5): 1002-9.
19. Chung M, Lee J, Terasawa T, Lau J, Trikalinos TA. Vitamin D with or without calcium supplementation for prevention of cancer and fractures: an updated meta-analysis for the U.S. Preventive Services Task Force. Ann Intern Med 2011; 155(12): 827-38.