ORIGINAL ARTICLE

Osteoporosis in women with breast cancer and its effect on quality of life: a pilot study

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Summary

Purpose: The primary aim of this study was to evaluate the risk of osteoporosis (OP) in patients who had received adjuvant chemotherapy for breast cancer. The secondary aim was to investigate the effect of OP on the quality of life of these patients.

Patients and methods: Twenty-six patients with breast cancer and 21 healthy controls were recruited into the study. All breast cancer patients were treated with 6 cycles of adjuvant chemotherapy. Bone mineral density (BMD) was measured by Dual-energy X-ray absorptiometry (DXA). Short Form-36 (SF-36) questionnaire was used to assess the quality of life.

Results: The mean lumbar area BMD value was sig-nificantly lower in patients with breast cancer than in healthy controls (p=0.017). There were no significant differences in the femoral area BMD measurements between the groups. OP was more pronounced after 24 months of the last chemotherapy course than in the first 12 months (p=0.04). The most affected domain of the SF-36 in patients with breast cancer was the physical role.

Conclusion: Adjuvant chemotherapy increases the risk of accelerated bone loss in the lumbar spine. OP should be investigated during follow-up in order to improve the quality of life of the surviving breast cancer patients.

Key words: breast cancer, chemotherapy, osteoporosis, quality of life

Introduction

Breast cancer is the most common type of cancer in women, both before and after menopause. Survival after breast cancer treatments is longer today due to improved early diagnosis and effective systemic and local therapies [1-3]. Hence, side effects of the treatments and their impact on quality of life in long-term survivors are becoming more important for the oncology community [4,5].

Adjuvant systemic chemotherapy is adminis-tered to the majority of patients after surgery in order to reduce the risk of recurrence [6,7]. However, the most common long-term side effect of adjuvant che-motherapy is premature ovarian failure (POF). POF affects more than half of the premenopausal women, particularly if a cyclophosphamide-containing che-motherapy regimen is administered. Early onset of OP caused by chemotherapy-induced POF may increase the risk of bone fractures which, in turn, may influence profoundly the patient's quality of life [8-12].

BMD measured by DXA is one of the most pre-dictive and widely used measurements in assessing the fracture risk of patients with OP [13]. DXA provides a direct measurement of bone density with a fast and accurate way [14].

The primary aim of the present study was to eval-uate the DXA measurements of breast cancer patients who had received adjuvant chemotherapy and compare the results with normal healthy controls. The secondary aim was to evaluate the quality of life of breast cancer patients with OP.

Patients and methods

Patient characteristics

Twenty-six women with breast cancer (study group) fulfilling the World Health Organization (WHO) criteria [13] for OP (lumbar spine or hip T-score -2.5 SD or less) and 21 women without OP (control group) were recruited into this study. Patients with a history of another cancer, metastatic breast cancer, and metabolic bone disease were excluded. Likewise, current or recent users of oral contraceptives, androgens, anabolic steroids, vitamin D, bisphosphonates, calcitonin and other antiosteoporotic drugs were excluded for the same reasons.

There were 2 stage I, 19 stage II and 5 stage III patients in the study group. The majority of them (21; 80.8%) had undergone mastectomy and 5 (19.2%) breast-conserving surgery plus adjuvant radiotherapy.

All patients in the study group had received 6 cycles of adjuvant chemotherapy and were under follow up for more than 6 months. Chemotherapy consisted of cyclophosphamide, epirubicin, and 5-fluorouracil. Ten (38.5%) patients had also received adjuvant hormonotherapy (tamoxifen). Median follow-up after chemotherapy was 29.5 months (range 6-52). Adjuvant radiotherapy was given to 22 (84.6%) patients. Radiation fields included chest wall-only in 4 (15.4%) patients, and chest wall, supraclavicular and axillary lymph nodes in 18 (69.2%). Median radiotherapy dose was 50 Gy (range 50-60).

Control group characteristics

All healthy volunteers had a recent mammogram done, confirming that there was no detectable breast cancer and all had no personal history of any other type of cancer. All healthy volunteers were postmenopausal. Women with psychiatric disorders and chronic sys-temic diseases were excluded from the control group. Baseline body mass index (BMI), age, as well as lifestyle and living conditions of the controls matched with those of women with breast cancer (Table 1).

BMD measurements

BMD was measured at the lumbar spine (L2-4) and femoral area (neck, trochanter and Ward's triangle) by DXA using a LUNAR DPX densitometer (GE Lunar Corporation, Madison, WI, USA). The diagnosis of OP was based on the WHO criteria [13]. OP was defined as a T score of -2.5 or less, indicating a BMD that was at least 2.5 standard deviation (SD) scores less than the mean for young adults.

Thoracic and lumbar spine radiographs which were chosen to investigate the presence of compression fractures were studied.

Quality of life questionnaire

The SF-36 questionnaire was used to assess the quality of life. Considering the latest 4 weeks, the SF-36 distinguishes 8 areas to measure physical and mental health. These include physical health problems, physical function, physical role difficulties, pain in the body, and general health perception. Mental health area consists of vitality, emotional role difficulties, social function, and mental health problems. Subscales measure the health conditions between 0 and 100 points. 0 point indicates the worst health condition, while 100 indicates the best health condition [15]. The Turkish version of the SF-36 index has been validated [16].

Statistical analyses

The software statistical package Sciences for Windows (v. 11.0) was used for all calculations. For discrepancies among the groups, Mann-Whitney U test

Table 1. Demographic and behavioral characteristics of both groups

Characteristic	Patients (n= 26)		Controls (n=21)		p-value
Age (years, median)	49		53.5		0.061
BMI [kg/m², mean (SD)]	28.1	(5.6)	28.5 (5.4)		0.776
Age at menarche [years, mean (SD)]	13.8	(1.5)	13.3 (1.1)		0.188
Menopause duration [months, mean (SD)]	62.6	(94.6)	109.3 (101.7)		0.013*
Mastectomy, n (%)	21	(80.8)	0		
Sedentary life, n (%)	3	(11.5)	4	(19)	
Consumption of alcohol, n (%)	0	0			
Cigarette smoking, n (%)	0	0			

*statistically significant by Mann-Whitney U test
BMI: body mass index, SD: standard deviation

was employed. Chi-square test was used to compare categorical variables. Those with a p-value below 0.05 were considered as statistically significant.

Results

Median age and range were 49 years (range 26-75) and 53.5 years (range 45-71) in the study and control groups, respectively. In the study group, there were 9 (34.6%) premenopausal, 6 (23.1%) perimenopausal and 11 (42.3%) postmenopausal women. In the control group, all of the patients were postmenopausal. All premenopausal patients in the study group became amenorrheic during chemotherapy. The demographics of patients and controls are shown in Table 1.

The time between menopause and the DXA measurement was longer (i.g. increased OP risk) in the control group than in the study group (109.3 [SD: 101.7] vs. 62.6 [SD: 94.6] months). This difference was significant (p=0.013). The mean lumbar BMD was lower in patients with breast cancer (mean 0.9381; SD: 0.1503) than in control women (mean 1.0660; SD: 0.1920). This difference was significant (p=0.01). However, femoral neck, trochanter and Ward's triangle BMD measurements were not significantly different (Table 2). OP was significantly higher in patients younger than 50 during chemotherapy (p=0.008). Menopausal status influenced OP in the study group; postmenopausal patients were more osteoporotic than pre- or perimenopausal ones (p=0.006).

OP was significantly higher in patients who were under follow up longer than 24 months after the last chemotherapy (p=0.04).

No compression deformities were encountered in the thoracic and lumbar areas of breast cancer patients.

In the SF-36 subgroup analysis, the most affected area in the breast cancer patients was physical role (mean: 17.3, SD: 37.3). Higher scores (i.e. good health condition) were observed in the domains of bodily pain (mean: 70.8, SD: 32.7) (Table 3). Comparison

Table 3. Distribution of SF-36 subgroups in patients with breast cancer

Subgroup	Mean (SD)
Physical function	62.1 (24.2)
Physical role	17.3 (37.3)
Bodily pain	70.8 (32.7)
General health	56.7 (26.5)
Vitality	51.2 (25.0)
Social function	70.2 (29.5)
Emotional role	30.8 (45.1)
Mental health	54.2 (23.9)

SD: standard deviation

between the SF-36 patient subgroups with and without OP showed significant correlation only in the physical role functioning subgroup (p=0.05).

Discussion

OP in women with breast cancer has been attributed to premature ovarian failure, direct effect of chemotherapy, antiestrogen hormonal agents and direct effect of breast cancer itself [5,17-19]. In the present study, the lumbar BMD score of breast cancer patients was significantly lower compared to the control group (p=0.01). However, no differences were observed for the femoral areas between the study and control group. Vehmanen et al. compared the lumbar and femoral neck BMD measurements in the 3rd and 5th year of follow-up of patients with breast cancer who received adjuvant chemotherapy and reported a significant decrease in the lumbar BMD but no difference in the femoral neck [10].

In our study the mean time between menopause and the DXA measurements was longer in the control group. In fact, one could expect to see worse DXA measurements in the control group due to the longer menopause duration. However, DXA measurements of the lumbar area were worse in breast cancer patients

Table 2. Correlation between lumbar and femoral DXA score in both groups

	Patients Mean (SD)	Controls Mean (SD)	p-value
Lumbar BMD	0.9381 (0.1503)	1.0660 (0.1920)	0.017*
Femoral neck BMD	0.8135 (0.1544)	0.8418 (0.1383)	0.511
Femoral trochanter BMD	0.6389 (0.1204)	0.6688 (0.1155)	0.392
Femoral wards BMD	0.6004 (0.1265)	0.6384 (0.1455)	0.351

* statistically significant by Mann-Whitney U test
BMD: bone mineral density, SD: standard deviation

despite shorter menopause duration. Six cycles of cyclophosphamide, epirubicin, and 5-fluorouracil chemotherapy as adjuvant treatment for breast cancer was a significant risk factor for lumbar OP in the present study. In the study of Vehmanen et al., chemotherapy-induced bone mineral loss was reported in the lumbar spine of the premenopausal breast cancer women [10]. Rodrigues et al. recorded a significant reduction in BMD of lumbar and femoral areas of non-metastatic breast cancer patients receiving chemotherapy [20]. In a study by Shapiro et al. conducted on early-stage breast cancer patients, chemotherapy-induced ovarian failure caused rapid and highly significant bone loss in the lumbar spine [11].

In several studies, the time elapsed after chemotherapy was significantly related to the decline of lumbar and femoral scores [11,21-23]. Lumbar BMD became significantly lower 2 years after chemotherapy in the present study as well.

The most affected SF-36 parameter in the breast cancer patients was physical role. Physical role includes the problems at work or in daily life activities due to deterioration of physical health [15]. We compared the physical role of the patients with and without OP in the study group and found a significant difference in the role functioning scale (physical) of the SF-36 (p=0.05). Physical role was more adversely affected by OP in patients with breast cancer. Mental parameters of SF-36 were not affected in the study group. Our findings are consistent with the recent study reported by Aranha et al. They found that the most affected parameters of SF-36 in patients with OP were physical dimensions [24].

Bodily pain domains of SF-36 assess limitations due to the pain. The reason why we observed higher scores in this domain might be related to the absence of compression fractures of any breast cancer patients. Patients experience high level of pain only if compression fractures develop [25].

It is well known that diminished physical activity causes OP and fractures [26]. Therefore, clinical oncologists who follow breast cancer patients should not only investigate the cancer status itself but also evaluate the risk factors for OP. Clinicians should make recommendations concerning OP, screen bone density and encourage regular physical activity in order to improve the quality of life of breast cancer survivors.

In conclusion, this study suggests that women who receive chemotherapy for breast cancer are at increased risk of bone loss and may be at risk for development of lumbar OP. Providing early medical treatment and high calcium diet may protect these patients from more serious problems.

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