Support Care Cancer (2016) 24:4229–4236
DOI 10.1007/s00520-016-3250-y

ORIGINAL ARTICLE

Change in bone mineral density during adjuvant chemotherapy for early-stage breast cancer

Carina Ørts Christensen[1,2] · **Deirdre Cronin-Fenton**[3] · **Trine Frøslev**[3] · **Anne Pernille Hermann**[2,4] · **Marianne Ewertz**[1,2]

Received: 14 March 2016 / Accepted: 25 April 2016 / Published online: 5 May 2016

Abstract
Purpose Adjuvant chemotherapy has been associated with loss of bone mineral density (BMD) either as a direct effect or due to glucocorticoids used as supportive care medication. A prospective cohort study was conducted to evaluate changes in BMD from baseline to right after completion of chemotherapy, i.e., 4 months.
Methods Dual-imaging X-ray absorptiometry (DXA) was performed at baseline and after completing anthracycline- and taxane-based chemotherapy to measure BMD in the spine, hip, and forearm in early-stage breast cancer patients. High-dose prednisolone was used at three weekly intervals to reduce nausea and vomiting. Patients were advised a daily calcium/vitamin D supplement. Linear regression was used to assess mean percentage change in BMD and 95 % confidence intervals (95 % CI) according to doses of prednisolone, menopausal status, smoking, and BMI.
Results Eight patients were excluded: seven because of initiation of bisphosphonate treatment due to osteoporosis at baseline, and one had non-interpretable DXA. The final cohort included 97 patients with a mean age of 53 years (range 34–72). Mean cumulative prednisolone dose was 1308 mg (95 % CI 1255; 1362). BMD increased 1.36 % (95 % CI 0.7; 2.0, $p<0.001$) in the spine and 1.27 % (95 % CI 0.9; 1.7, $p<0.001$) in the hip. Forearm BMD did not change. Postmenopausal women had increases in spine BMD of 2.35 % (95 % CI 1.1; 3.6, $p<0.001$) compared to premenopausal women. The spine BMD of current smokers decreased 1.67 % (95 % CI −3.3; −0.1, $p=0.04$) compared to never/former smokers.
Conclusions Adjuvant chemotherapy supplemented with prednisolone was not associated with loss of BMD. Postmenopausal women gained bone mass, whereas current smokers lost bone mass.

Keywords Breast cancer · Adjuvant chemotherapy · Osteoporosis · Bone mineral density · Glucocorticoids

Background

Breast cancer is the most frequent malignant disease among women worldwide with an estimated 1.67 million new cases diagnosed in 2012 (25 % of all cancers in women) and the fifth most common cause of death from cancer (522,000 deaths) [1]. Survival after breast cancer has improved substantially over the past 30–40 years [2] which is likely to be explained by earlier diagnosis via mammography screening and by advances in cancer-directed treatment [3]. Today, more than 90 % of patients with early-stage breast cancer are allocated to adjuvant medical treatment with chemotherapy, anti-HER2-treatment, and endocrine therapy depending on the biomarker profile of the primary tumor [4]. Since more than 80 % of breast cancer patients are expected to live for 10 years or longer, it is increasingly important to focus on potential harmful late-effects of the cancer treatment, such as osteoporosis.

✉ Carina Ørts Christensen
Carina.Oerts.Christensen@rsyd.dk

[1] Department of Oncology, Odense University Hospital, Sdr. Boulevard 29, DK-5000 Odense C, Denmark

[2] Institute of Clinical Research, University of Southern Denmark, Winsløwparken 19, 5000 Odense C, Denmark

[3] Department of Clinical Epidemiology, Aarhus University Hospital, Olof Palmes Allé 43-45, 8200 Aarhus N, Denmark

[4] Department of Endocrinology, Odense University Hospital, Sdr. Boulevard 29, 5000 Odense C, Denmark

Osteoporosis is characterized by reduced bone mass, deterioration of the bone micro-architecture, and an increased risk of fragility fractures. It affects millions of people worldwide, with the highest prevalence among postmenopausal women. The gold standard for evaluating osteoporosis is measuring bone mineral density (BMD) by dual energy X-ray absorptiometry (DXA), which measures the bone in two dimensions [5].

There are several ways in which breast cancer chemotherapy can increase the risk of osteoporosis but in general, the evidence is sparse. It can induce premature menopause with menopause occurring on average 10 years earlier than normal [6]. We have identified a total of four studies, including 41 to 53 premenopausal breast cancer patients, who received chemotherapy with CMF (cyclophosphamide, methotrexate, fluorouracil) or anthracycline-cyclophosphamide regimens (AC) with measurements of BMD at baseline and 6 months later [7–10]. They demonstrated decreases in BMD in the lumbar spine of 1–4 %. It has been suggested that the bone loss may be associated with supportive care medication such as corticosteroids which are the most common cause of secondary osteoporosis with a 7–17-fold increased risk of fractures with daily doses of 10 mg for 3 months [11]. However, women undergoing chemotherapy receive much higher glucocorticoid doses albeit for short durations. Based on 16 patients with Graves' ophthalmopathy, increases in BMD of 3 % were found for treatment with high-dose glucocorticoids given as intravenous pulse-therapy, whereas BMD decreased 2.7 % in patients who received high-dose oral glucocorticoids continuously [12].

We conducted a prospective cohort study to evaluate the effect of adjuvant chemotherapy supplemented with high-dose glucocorticoids (prednisolone) on BMD among patients with early-stage breast cancer. We evaluated the combined effect of chemotherapy and prednisolone in the spine, hip, and forearm BMD from baseline to completion of adjuvant chemotherapy.

Material and methods

Patients

We recruited women aged 18 years or older diagnosed with histologically verified early-stage breast cancer who underwent surgery (mastectomy or lumpectomy) with axillary node excision (sentinel node or axillary dissection). Patients with inflammatory breast cancer, locally advanced or disseminated breast cancer, or primarily unresectable breast carcinoma were excluded. Patients were also excluded if diagnosed with any other malignancy within the past 5 years that required chemotherapy, had a pre-existing diagnosis of osteoporosis, or currently received systemic treatment with steroids. Women, who for various reasons, were deemed incapable of participating in the study due to psychiatric illness, difficulties understanding the Danish language, or physically unable to lie still when the DXA scan was performed were also excluded.

Patients were referred to the Department of Oncology, Odense University Hospital (OUH), Denmark, for adjuvant medical treatment from September 1, 2013 through August 31, 2014. They were offered a DXA scan at baseline before their first cycle of chemotherapy, and a second DXA scan approximately 3 weeks after their last cycle of chemotherapy. To be included in the final analyses, patients had to complete both DXA scans, receive at least five cycles of adjuvant chemotherapy, and not start bisphosphonate treatment for osteoporosis during chemotherapy.

Informed consent was obtained from all the participants. This study was approved by the Danish Data Protection Board (ID 2008-58-0035) and ethics committee in Region of Southern Denmark (Project ID S-20130065).

Chemotherapy

In the majority of the patients, adjuvant chemotherapy consisted of three cycles of epirubicin (90 mg/m^2) and cyclophosphamide (600 mg/m^2) (EC) followed by three cycles of docetaxel (100 mg/m^2) intravenously on day one at three weekly intervals, while some received two to six cycles of EC or docetaxel. There were no statistically significant differences in baseline characteristics between these two patient groups (data not shown). During EC chemotherapy, glucocorticoids were given as anti-emetic prophylaxis with a typical dose of 175 mg prednisolone for one cycle of EC, i.e., 525 mg in total for three cycles. During one cycle of docetaxel, patients received a standard dose of prednisolone 100 mg/day for 3 days, i.e., 300 mg/cycle, in total 900 mg for three cycles. Provided that patients did not need additional prednisolone beyond the amount given during chemotherapy, patients received in total 1425 mg prednisolone over an 18-week treatment period.

From March 2014, new guidelines were introduced at the Department of Oncology, OUH, regarding anti-emetic treatment in breast cancer patients. Thus, patients received 75 mg prednisolone instead of 175 mg prednisolone at each cycle of EC. This resulted in a reduction in the total prednisolone dose to 1125 mg prednisolone over the 18-week treatment period for the adjuvant regimen. All patients were advised to take a daily supplement of calcium (800 mg) and vitamin D (20 μg) while undergoing chemotherapy. No patients received concomitant endocrine treatment with their chemotherapy.

Data sources

Baseline data were abstracted from the patient records on date and type of surgery, co-morbidity, prior cancers, regular

medication, menopause, tobacco consumption, adjuvant cancer-directed treatments, number of treatment cycles, and anti-emetic treatment with glucocorticoids. Data were abstracted from the pathology report on tumor size, histological type and grade, estrogen receptor (ER) status (% positivity), human epidermal growth factor receptor 2 (HER-2) status, and nodal status. Data were derived directly from the DXA scanner at the Osteoporosis Clinic, Department of Endocrinology, OUH, and included dates of baseline and follow-up scans, height, weight, T- and Z-scores, area (g), bone mineral content (cm^2), and BMD (g/cm^2) in the spine, hip, and forearm.

Bone densitometry

BMD measurements of the lumbar spine (L1–L4), left hip, and left forearm were obtained using Hologic Discovery QDR, Scanner ID: 82245. All scans were performed by specially trained personnel, and quality standards of the scanner were tested daily with a "Hologic Spine Phantom" ID: 13520 with a median BMD value of 0.974 (0.9594–0.9887). Coefficients of variation (CV) of the BMD measurements were 1.025 and 0.875 % for the lumbar spine and hip, respectively.

Osteoporosis was defined by the World Health Organization (WHO) as a BMD below a certain value, i.e., a T-score for BMD less than 2.5 standard deviations (SDs) below the mean value expected for a young healthy female adult either in the spine and/or the hip. The relative BMD value, the Z-score, describes the number of SDs by which the BMD in an individual differs from the mean value expected for age and sex [5]. Spine T- and Z-scores were calculated with the Hologic manufacturer's reference ranges, and for the hip region, the National Health and Nutrition Examination Survey (NHANES) III reference ranges were used [13].

Exposure variables

The cumulative dose of prednisolone was calculated as follows: the total dose of prednisolone received during chemotherapy was calculated as the sum of each prednisolone dose administered during each cycle of chemotherapy. In case of an allergic reaction to chemotherapy, the patient received additional methylprednisolone in the acute phase. The dose of methylprednisolone was converted to prednisolone equivalent doses, i.e., multiplying the dose of methylprednisolone by the conversion factor 1.25. The cumulative dose of prednisolone also included any additional prednisolone administered to patients in the 3-week periods between each cycle of chemotherapy. Women who at diagnosis had a menstrual period within the last 12 months were categorized as premenopausal. The others were categorized postmenopausal. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. BMI was categorized according to World Health Organization (WHO) criteria as normal (less than 25), overweight (25–30), or obese (30 or more). Patients were categorized into two categories of smoking: current or never/former smokers.

Statistical analyses

Baseline BMD at each of the three anatomic sites was checked for normality by use of Shapiro-Wilks test and found to be normally distributed. Percentage change in BMD was calculated as (BMD at follow-up − BMD at baseline) / BMD at baseline × 100 % in the spine, hip, and forearm, respectively. Categorical data were described using frequencies and percentages. Continuous data were described using means ± standard deviations. We used uni- and multivariate linear regression to test the association between percentage change in BMD of the spine, hip, and forearm by different factors hypothesized to impact BMD either in a positive (e.g., BMI) or negative (e.g., cumulative dose of prednisolone, menopausal status, and smoking) direction. In the full model, we adjusted for all the factors. We used linear regression to compute the mean percentage change in BMD, and 95 % confidence intervals (95 % CI) for the spine, hip, and forearm BMD. All statistical analyses were carried out using STATA/IC 14.0.

Results

The study consort diagram is shown in Fig. 1. Among 168 potentially eligible breast cancer patients, 36 did not meet the inclusion criteria. A further 21 patients with a mean age of 51 (range 31–73) years withdrew informed consent or had no baseline DXA scan. One hundred and five out of 111 patients (95 %) completed both the baseline and the second DXA scan at completion of chemotherapy. The entire study population had mean Z-scores of 0.3, 0.2, and 0.2 in the lumbar spine, hip and forearm, respectively (Table 1). Ten patients (9 %) were diagnosed with osteoporosis at baseline with a mean T-score of −2.8 (95 % CI −3.1; −2.5) in the spine and −1.9 (95 % CI −2.2; −1.7) in the hip. Seven patients with a mean age of 56 (range 35–65) years were excluded from further analyses due to bisphosphonate treatment during chemotherapy, and one patient due to an unreadable baseline DXA. For all characteristics, these patients were similar to the other patients.

A total of 97 patients were included in the final analyses. Their mean age was 53 (range 34–72) years, and 8 of the patients were younger than 40 years. Most tumors (91 %) were invasive ductal carcinomas, with 81 % estrogen receptor positive, 17 % HER-2 positive, and 39 % lymph node positive. About 24 % of patients had a BMI above 30, and 18 % were current smokers (Table 1). At baseline, no patients were treated with systemic glucocorticoids but 13 % were using

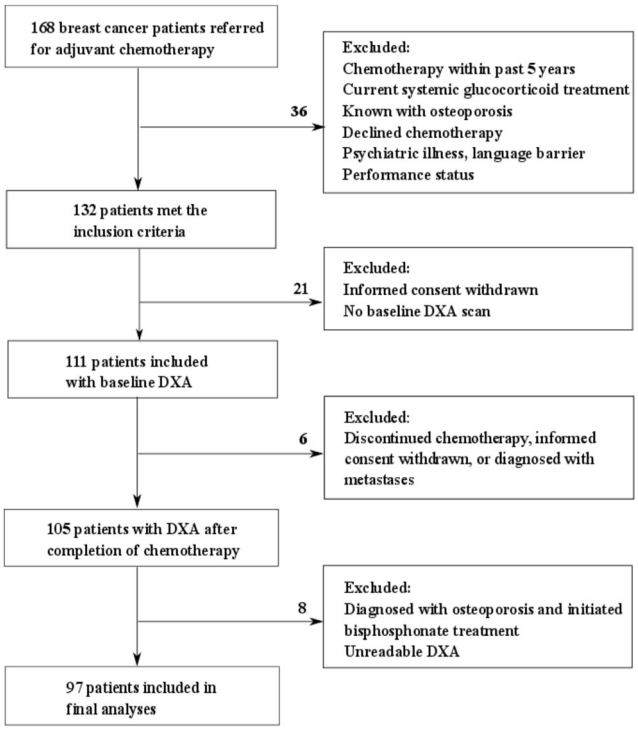

Fig. 1 Consort diagram of the study population

inhaled corticosteroids, nose sprays, crème, or suppositories with corticosteroids either on a regular basis or as required. Four patients had an allergic reaction related to docetaxel and received additional methylprednisolone in the acute phase.

During chemotherapy, patients received a median total cumulative prednisolone dose of 1325 mg with 90 % of patients receiving at least 1125 mg (range 475–2046 mg). Mean prednisolone dose was 1308 mg (95 % CI 1255; 1362). In uni- and multivariate analyses, no statistically significant associations were found between cumulative dose of prednisolone and percentage change in BMD at all three anatomic sites.

At baseline, 55 % had a normal BMD, 42 % had osteopenia, and 3 % were osteoporotic. Mean BMD at baseline was 0.98 g/cm^2 (95 % CI 0.96; 1.01) for the spine, 0.90 g/cm^2 (95 % CI 0.87; 0.92) for the hip, and 0.65 g/cm^2 (95 % CI 0.64; 0.67) for the forearm. Mean time interval from baseline to the second DXA scan was 4.4 (range 3.6–6.3) months. Increases were observed in spine BMD of 1.36 % (95 % CI 0.7; 2.0, $p<0.001$) and hip BMD of 1.27 % (95 % CI 0.9; 1.7, $p<0.001$) while forearm BMD did not change (−0.19 %, 95 % CI −0.7; 0.3, $p=0.5$) (Fig. 2).

Table 2 shows that no change in spine BMD was observed in premenopausal women whereas there was a significant increase of 2.42 % among postmenopausal women. Adjusting for the effects of other variables in multivariate analyses, the significant increase in spine BMD of 2.35 % (95 % CI 1.1; 3.6, $p<0.001$) persisted in postmenopausal women compared with premenopausal women. Among current smokers BMD decreased 1.67 % (95 % CI −3.3; −0.1, $p=0.04$) compared with never/former smokers. The multivariate analyses did not reveal any significant association between BMI and BMD. No significant associations were detected between hip and forearm BMD and the investigated characteristics (data not shown).

Discussion

The literature indicates that continuous use of glucocorticoids is associated with loss of bone mass. However, contrary to expectation, we observed no significant changes in BMD associated with prednisolone dose. A bone loss of 10 % corresponds to a reduction of 1 SD, which is expected to increase the risk of fractures by a factor two to three [14]. Glucocorticoids have shown to increase bone resorption and decrease bone formation [15]. This effect seems to persist throughout the duration of glucocorticoid treatment. Moreover, continuous use of glucocorticoid therapy is associated with increased risk of fracture with increasing dose and duration of treatment, particularly, within the first 3 to 6 months. A few months after cessation of the treatment, a corresponding rapid decrease is seen in fracture risk [16]. Based on 191,752 patients from the UK General Practice Database who were followed for 10 years, De Vries et al. reported a strong association between continuous daily doses of oral glucocorticoids (cumulative exposure >1 g of prednisolone) and risk of fracture, whereas patients who received intermittent high-dose oral glucocorticoids were associated with a substantial lower risk of fractures [17].

Patients in our study received a mean prednisolone dose of 1304 mg administered at intervals with chemotherapy. Since no bone loss was observed, our data demonstrate that such a chemotherapy regimen seems safe. This is reassuring because glucocorticoids are essential in preventing chemotherapy-induced nausea and vomiting [18]. We investigated a limited period of 4 months. During this time, no fractures were reported. However, we cannot rule out the possibility that patients, due to exposure of glucocorticoids, may be at increased risk of fractures, since other studies have reported increased fracture risk caused by deterioration of bone quality, which is not captured by BMD [19, 20].

Interestingly, we found increases in both spine and hip BMD from baseline to completion of adjuvant chemotherapy. In spine BMD, the increase was statistically significant among postmenopausal women whereas current smokers had a significant decrease compared to never/former smokers.

Animal studies have shown that cytotoxic agents such as doxorubicin and methotrexate reduce bone formation by reducing osteoblastic activity in rats [21, 22]. Four studies reported changes in spine and hip BMD in breast cancer patients during a 6-month period after start of chemotherapy

Table 1 Characteristics of the study population

	Patients in total $N = 111$ (%)	Patients in final analyses $N = 97$ (%)
Age at diagnosis		
50	32 (29)	30 (31)
50–59	53 (48)	47 (48)
≥60	26 (23)	20 (21)
Menopausal status		
Premenopausal	45 (41)	43 (44)
Postmenopausal	66 (59)	54 (56)
Type of surgery		
Lumpectomy	63 (57)	56 (58)
Mastectomy	48 (43)	41 (42)
Type of carcinoma		
Ductal	101 (91)	88 (91)
Lobular	4 (4)	4 (4)
Others	6 (5)	5 (5)
Tumorsize		
0–9 mm	6 (5)	4 (4)
10–19 mm	51 (46)	43 (44)
20+ mm	54 (49)	50 (52)
Histological grade		
Low (I)	15 (14)	11 (11)
Moderate (II)	36 (32)	30 (31)
High (III)	54 (49)	51 (53)
(Unknown)	6 (5)	5 (5)
Estrogen status		
ER negative 0 %	19 (17)	18 (19)
ER poor 1–10 %	6 (5)	6 (6)
ER positive 10 %	86 (78)	73 (75)
HER2 status		
HER2 negative	92 (83)	81 (83)
HER2 positive	19 (17)	16 (17)
Nodal status		
Node negative	67 (60)	59 (61)
Node positive	44 (40)	38 (39)
Body mass index (kg/m^2)		
25 normal	43 (39)	38 (39)
25–30 overweight	38 (34)	36 (37)
30 obese	30 (27)	23 (24)
Smoking status		
Never/former smokers	91 (82)	80 (82)
Current smokers	20 (18)	17 (18)
Baseline T-score		
Spine	-0.7 ± 1.3^{bc}	-0.5 ± 1.2^{b}
Hip	-0.5 ± 1.1^{a}	-0.4 ± 1.0^{a}
Forearm	-0.8 ± 1.0^{a}	-0.7 ± 1.0^{a}
Baseline Z-score		
Spine	0.3 ± 1.3^{ab}	0.4 ± 1.2^{a}
Hip	0.2 ± 1.1^{a}	0.3 ± 1.1^{a}
Forearm	0.2 ± 1.0^{a}	0.3 ± 0.9^{a}

[a] Mean ± standard deviation (SD)

[b] $N = 110$ patients

[7–10]. Based on 41 to 53 premenopausal patients who received CMF- or AC-based chemotherapy, decreases were reported in BMD of 1–4 % in the spine and −0.7 to 2.6 % in the hip. Cameron et al. reported on 41 premenopausal women with decreases in BMD of 4 % in the spine and 2 % in the hip [10]. Nine patients received chemotherapy with docetaxel. All patients received glucocorticoids (dexamethasone) as antiemetic treatment. However, the dose and regimen of glucocorticoids was not stated. Nor was it mentioned whether the patients received supplements of calcium and vitamin D.

In our study, the time interval between baseline and follow-up DXA was 4.4 months, and patients represented a mix of both pre- and postmenopausal women. Since our finding is not in line with previous findings, we cannot rule out that the rather short time of follow-up may be a possible explanation. However, our findings may be explained by the calcium and vitamin D given in our study, which is known to affect bone turnover rate in persons with low calcium intake or low calcium absorption, e.g., postmenopausal women [23].

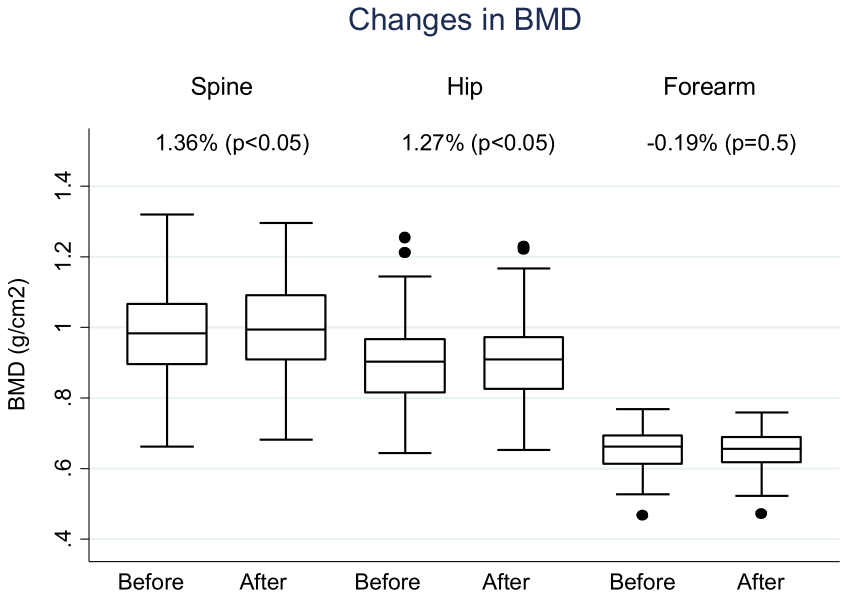

Fig. 2 Changes in median BMD and interquartile ranges for DXA scans before and after chemotherapy in 97 Danish patients with early-stage breast cancer

Physiologically, premenopausal women have a low bone turnover compared to postmenopausal women who have a higher bone turnover. Moreover, the spine has the largest bone surface, and it consists primarily of cancellous bone. Thus, the spine is the location where changes in bone turnover are first seen [24]. This correlates well with our results detected in the spine. Moreover, the significant increases in spine BMD seen in older women are compatible with normal physiology of the bones. When women enter menopause, they undergo two phases of bone loss. An initial accelerated phase of predominantly cancellous bone loss that declines rapidly over 4–8 years which subsequently merges with a slow phase that continues indefinitely [25]. The majority of premenopausal women who receive chemotherapy experience chemotherapy-induced ovarian failure (CIOF) with rapid decreases in estrogen levels and a shift in bone turnover from a low to a high state [26]. This is seen as a decrease in BMD measured by DXA. Thus, bone turnover is driven by the withdrawal of estrogen [27]. In contrast, postmenopausal women are in the slow phase of bone loss. Instead, they experience an age-related insufficient calcium absorption from the intestines, which causes an increase in parathyroid hormone (PTH) with resorption of calcium from the bones to maintain a systemic steady state of calcium in the blood. Thus, PTH is the dominating mechanism associated to bone turnover in postmenopausal women [27]. When postmenopausal women receive calcium and vitamin D supplements, bone turnover decreases due to closing of the gaps of remodeling. This is seen as an increase in BMD [27].

At follow-up, the majority (72 %) of patients had received a daily calcium and vitamin D supplement during chemotherapy,

Table 2 Absolute (ΔBMD) and relative (Coef.) changes in spine BMD from baseline to completion of adjuvant chemotherapy in 97 Danish patients with early-stage breast cancer

Lumbar spine				Univariate analyses			Multivariate analyses[c]		
Co-variates	Number	ΔBMD[a] (%)	95 % CI	Coef.[b] (%)	*P* value	95 % CI	Coef.[b] (%)	*P* value	95 % CI
Prednisolone pr. 1 g	97	0.97	−1.5;3.4	0.97	0.43	−1.5;3.4	1.57	0.17	−0.7;3.8
Premenopausal at diagnosis	43	0.03	−0.8;0.8	0 (ref.)			0 (ref.)		
Postmenopausal at diagnosis	54	2.42	1.6;3.3	2.39	<0.001	1.2;3.6	2.35	<0.001	1.1;3.6
Never/former smoker	80	1.70	1.0;2.4	0 (ref.)			0 (ref.)		
Current smoker	17	0.22	−1.5;1.1	−1.92	0.02	−3.6;−0.3	−1.67	0.04	−3.3;−0.1
BMI (<25)	38	1.03	0.1;1.9	0 (ref.)			0 (ref.)		
BMI (25–30)	36	1.70	0.7;2.7	0.67	0.37	−0.8;2.1	0.19	0.78	−1.2;1.6
BMI (>30)	23	1.39	−0.3;3.1	0.36	0.67	−1.3;2.0	−0.40	0.61	−2.0;1.2

[a] ΔBMD = mean percent change

[b] *Coef.* coefficient = (BMD at follow-up − BMD at baseline) / BMD at baseline × 100 % = mean percent change in BMD (%)

[c] Multivariate analyses adjusted for prednisolone, menopausal status, smoking, and BMI

which most likely has contributed to the increased BMD observed in our study. We examined whether there was a difference in BMD between patients who received calcium and vitamin D supplements and those who did not and noted an increase in spine and hip BMD in both the groups. However, the analyses were based on too few patients to give a meaningful result. The reduction in BMD observed in current smokers fits well with the explanation since one of the deleterious effects of smoking on bone is to reduce intestinal calcium absorption [28].

At baseline, 9 % of patients (10/111 patients) were diagnosed with osteoporosis. In 2010, the prevalence of osteoporosis was estimated to be 21 % in Danish women aged 50 years or more and 5 % in the general population when measuring hip BMD [5]. In another study of 9933 Danish women, the prevalence of osteoporosis was reported to be 14 % when BMD was measured at the spine, hip, or both [29]. Our patients had mean baseline Z-scores greater than zero for all the anatomic sites, which translates into higher BMD values at baseline compared to the female background population of the same age. However, the mean Z-scores may represent an overestimation of BMD, due to possible selection bias of the patients included in the study.

The main strength of our study is the prospective data collection. All eligible patients were enrolled consecutively in the study and had a baseline DXA performed before onset of the first cycle of chemotherapy. Each patient was her own control, and the second DXA was performed on the same DXA scanner approximately 3 weeks after completion of chemotherapy. Only four patients started endocrine treatment before the second DXA was performed.

However, there are some limitations to our study, one of them being that it is a single institution experience limiting the generalizability. We had no reliable information on alcohol consumption, physical activity, or prior hormone replacement therapy which are known to affect bone density in a positive way mostly among postmenopausal women [30–32]. We did not check the compliance to prednisolone prescribed as an anti-emetic treatment, and we were also unable to account for glucocorticoids, prescribed for underlying medical indications. Also, it would have been preferable to include a control group without steroids but it was considered unethical to withhold steroids as anti-emetic treatment from these patients. Finally, unfortunately, we had no measurements of vitamin D or biochemical markers of bone turnover.

Conclusion

In summary, contrary to expectation, we found that adjuvant anthracycline- and taxane-based chemotherapy supplemented with supportive therapy (prednisolone) for early-stage breast cancer was not associated with bone loss when supplemented with calcium and vitamin D. Postmenopausal women gained significantly bone mass in the spine, whereas current smokers had a significant bone loss in the spine. It was reassuring, that no significant association was detected between prednisolone dose and changes in BMD. Furthermore, guidelines have changed, and lower total doses are now recommended as anti-emetic prophylaxis allowing the use of corticosteroids to continue in anti-emetic treatment. Our data suggest that in patients who receive chemotherapy, it may not be necessary to perform a DXA before start of chemotherapy, but that it will be safe to postpone it until later.

Acknowledgments Funding for this study was provided by the Region of Southern Denmark; the Department of Oncology, Odense University Hospital; the Department of Endocrinology, Odense University Hospital; the Danish Cancer Society; and the University of Southern Denmark.

A special thanks to all the patients who participated in the study and to the doctors, nurses, and secretaries at the Department of Oncology, Odense University Hospital, Denmark, for each of their contribution to make this project possible.

Also a special thanks to the staff, and in particularly, to Jane Nielsen at the Osteoporosis Clinic, Department of Endocrinology, Odense University Hospital, Denmark.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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