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TITLE: Stage 1 breast cancer and bone mass in older women

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## Stage 1 breast cancer and bone mass in older women

### Abstract

The specific aims of the study are 1) to assess the bone mineral density of women 65 years of age and older with breast cancer in comparison with the bone mineral density of same aged women with normal mammograms; 2) to examine the risk factors associated with breast cancer and low bone mass in these two groups of women; 3) to develop a model based on the study population to determine the predictive value of low bone mass for risk of breast cancer.

During the three years of this study, a total of 300 women (cases with breast cancer and controls with a normal mammogram) aged 65 and older will be recruited from oncology and radiology offices to participate in a study consisting of one clinic visit. At the clinic visit, each subject will complete questionnaires detailing medical history, health habits, reproductive history, and medications. Height and weight will be measured. A blood sample will be drawn for storage. Bone mineral density will be measured at the forearm, hip, lumbar spine (L1-L4), and whole body using dual energy x-ray absorptiometry (DXA).

The results of this study can be used 1) to identify the likelihood of low bone mass in older women with breast cancer; 2) to identify the risk factors that are common to both low BMD and breast cancer; and 3) to determine the feasibility of discontinuing mammography after 65 in women with low bone mass.

### Subject Terms

- breast cancer
- bone mass
- older women
- mammogram
Table of Contents

Cover..................................................................................................................1
SF 298...........................................................................................................2
Table of Contents..........................................................................................3
Introduction.................................................................................................4
Body...............................................................................................................4
Key Research Accomplishments.................................................................7
Reportable Outcomes...................................................................................7
Conclusions...................................................................................................7
References....................................................................................................7
Appendices...................................................................................................8
Introduction:

Women with low bone mineral density (BMD) have a low risk for breast cancer.\(^1,^2\) Therefore, it has been suggested that mammography may not be worthwhile for older women with low bone density.\(^3\) Measuring BMD at age 65 and stopping mammography in women who have low BMD has been proposed as a cost-effective clinical practice. However, before implementation of this proposal, the question of what proportion of women with breast cancer have low BMD needs to be addressed. The specific aims of the proposed study are 1) to assess the bone mineral density of women 65 years of age and older with breast cancer in comparison with the bone mineral density of same aged women with normal mammograms; 2) to examine the risk factors associated with breast cancer and low bone mass in these two groups of women; 3) to develop a model based on the study population to determine the predictive value of low bone mass for risk of breast cancer. During the three years of this proposed case-control study, a total of 300 women (cases with breast cancer and controls with a normal mammogram) aged 65 and older will be recruited from oncology and radiology offices to participate in a study consisting of one clinic visit. At the clinic visit, each subject will complete questionnaires detailing medical history, health habits, reproductive history, and medications. Height and weight will be measured. A blood sample will be drawn for storage. Bone mineral density will be measured at the forearm, hip, lumbar spine (L1-L4), and whole body using dual energy x-ray absorptiometry (DXA).

Body:

Recruitment Phase

At the present time, end of Year 2 of 3, we are still in the recruitment phase for this case-control study. Our study goal was 150 cases of women with newly diagnosed breast cancer and 150 control subjects who have had a normal mammogram. However, we are re-evaluating 1:1 case control ratio and we would achieve greater statistical power using the current number of cases and increasing to 2-3 controls per case. Therefore, we are continuing recruitment of cases and opening up recruitment of additional controls. Cases are defined as women 65 years and older with newly diagnosed breast cancer (within 4 months of their definitive surgical procedure) and control subjects within 4 months of a normal mammogram.

Recruitment has been difficult despite having affirmation of recruitment assistance from multiple sources including hospitals, physicians offices and mailing to age-eligible women identified from voter registration lists. Over the past year we have concentrated on recruitment of cases. Additional resources for recruitment were requested from the sponsor and granted; so that those clinic or hospital staff screening for recruitment of women into the study are compensated for their time. The total number of subjects who have completed the study clinic visit is 106: 57 cases and 49 controls. The ethnicity is 82.1% White (not Hispanic), 10.4% Hispanic, 4.7% Asian or Pacific Islander, 2.8% Black or African American.
Study Clinic Visit

Subjects are seen at the General Clinical Research Center outpatient facility on the UCSD La Jolla campus for one clinic visit. Participants are asked to fast for 12 hours prior to their clinic appointment and to bring in all their medications, including over-the-counter preparations. The clinic visit has been averaging two hours in duration and the following procedures are being performed:

1. Description of the study and administering informed consent before starting any study procedures.
2. Self-administered questionnaires used to obtain information on medical history, family history, health habits detailing smoking history, alcohol consumption, caffeine use, physical activity (Pfaffenberger), and diet (Block Food Frequency).
3. Medications and over-the-counter preparations are validated and recorded detailing the name, dose, frequency, duration, and route of delivery.
4. Height, weight, waist and hip circumferences, and percent body fat from whole body DXA are measured.
5. A fasting sample of blood (30 cc) is drawn for frozen storage and urine sample is collected for frozen storage.
6. Bone mineral density is measured at the forearm, hip, lumbar spine (L1-L4), and whole body using dual energy x-ray absorptiometry (DXA).

Preliminary Results

For presentation at the annual Era of Hope meeting in September 2002, we analyzed the 57 cases and 49 controls who had completed their study visit. As shown in Table 1, the cases and controls were similar age, years postmenopausal and number of reproductive years. The cases had a higher mean BMI and waist circumference. Their use of current estrogen and other selected lifestyle factors were not significantly different (p>.10).

Table 1. Characteristics of selected covariates of breast cancer cases and age-matched controls, Breast and Bone Study, San Diego, CA, 2000-2002.

<table>
<thead>
<tr>
<th>Mean values (SD)</th>
<th>Cases (n= 57)</th>
<th>Controls (n=49)</th>
<th>t or x²</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>72.4 (5.8)</td>
<td>72.5 (5.3)</td>
<td>-.047</td>
<td>.963</td>
</tr>
<tr>
<td>BMI †</td>
<td>27.4 (4.7)</td>
<td>25.5 (5.2)</td>
<td>1.97</td>
<td>.051</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>89.7 (14.0)</td>
<td>82.8 (12.9)</td>
<td>2.53</td>
<td>.013</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>103.4 (9.7)</td>
<td>99.9 (10.3)</td>
<td>1.73</td>
<td>.087</td>
</tr>
<tr>
<td>Years postmenopausal</td>
<td>25.9 (10.7)</td>
<td>24.2 (9.8)</td>
<td>.857</td>
<td>.394</td>
</tr>
<tr>
<td>Number of reproductive years ‡</td>
<td>33.9 (9.0)</td>
<td>35.6 (7.1)</td>
<td>-1.02</td>
<td>.312</td>
</tr>
</tbody>
</table>

Percentages

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
<th>t or x²</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current estrogen use**</td>
<td>55.4</td>
<td>65.3</td>
<td>1.08</td>
<td>.324</td>
</tr>
<tr>
<td>Current smoking</td>
<td>7.0</td>
<td>4.1</td>
<td>.43</td>
<td>.684</td>
</tr>
<tr>
<td>Ever smoked</td>
<td>43.9</td>
<td>38.8</td>
<td>.28</td>
<td>.693</td>
</tr>
</tbody>
</table>
Alcohol use (at least 1-2 times/week) 43.9 32.7 1.40 .317
Calcium supplement use 64.2 68.9 .25 .672
Breast cancer staging
  Stage 0 14.6
  Stage I 43.9
  Stage II 41.5

* p value from t-test (continuous variables) or from χ² test (categorical variables)
† Weight (kg)/height (m)²
‡ Number of years between menarche and menopause
** using estrogen at time of breast cancer diagnosis or up to 1 year before diagnosis (cases)

As displayed in Table 2, there were no differences in the bone mineral density at the lumbar spine, hip, forearm, or total body between cases and controls.

Table 2. Bone mineral densities of breast cancer cases and age-matched controls, Breast and Bone Study, San Diego, CA, 2000-2002.

<table>
<thead>
<tr>
<th>Mean values (SD)</th>
<th>Cases (n= 57)</th>
<th>Controls (n=49)</th>
<th>t</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar spine</td>
<td>.973 (.173)</td>
<td>.962 (.178)</td>
<td>.295</td>
<td>.768</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>.700 (.116)</td>
<td>.678 (.109)</td>
<td>1.02</td>
<td>.313</td>
</tr>
<tr>
<td>Total hip</td>
<td>.835 (.134)</td>
<td>.791 (.130)</td>
<td>1.69</td>
<td>.093</td>
</tr>
<tr>
<td>Forearm</td>
<td>.510 (.066)</td>
<td>.505 (.071)</td>
<td>.349</td>
<td>.728</td>
</tr>
<tr>
<td>Total body</td>
<td>1.014 (.125)</td>
<td>.988 (.099)</td>
<td>1.18</td>
<td>.241</td>
</tr>
</tbody>
</table>

As shown in Table 3, adjusted odds ratios for breast cancer were did not differ significantly by tertile of bone mineral density at the hip or lumbar spine.


<table>
<thead>
<tr>
<th>Breast cancer BMD tertile</th>
<th>Breast cancer OR</th>
<th>95 % CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip BMD tertile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 † (.453 - .743)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>2 (.744 - .869)</td>
<td>1.62</td>
<td>0.50 – 5.28</td>
</tr>
<tr>
<td>3 (.870 – 1.317)</td>
<td>1.26</td>
<td>0.38 – 4.21</td>
</tr>
<tr>
<td>Lumbar spine BMD tertile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 † (.561 - .891)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>2 (.892 – 1.016)</td>
<td>1.35</td>
<td>0.42 – 4.38</td>
</tr>
</tbody>
</table>
In summary, the preliminary results do not shown any differences in bone mineral density at multiple sites between newly diagnosed women with breast cancer in comparison with age-matched women with normal mammograms. Therefore, our preliminary data suggests that bone mineral density would not be useful as prescreening for mammography in older women.

Future plans are continued recruitment of cases and controls. In order to increase the power of this case-control study, we are planning to increase the recruitment of controls with 2-3 controls per case rather than the current 1:1 ratio.

Key Research Accomplishments:
Not applicable at this time.

Reportable Outcomes:
Abstract and poster presentation (refer to appendices) were submitted and presented at the 2002 Era of Hope Meeting in Orlando, Florida.

Conclusions:
Not applicable at this time.

References:
Appendices:

Abstract
Poster
ABSTRACT:
Recent studies have shown that women with low bone mineral density (BMD) have a low risk for breast cancer. Therefore, it has been suggested that mammography may not be worthwhile for older women with low bone density. Measuring BMD at age 65 and stopping mammography in women who have low BMD has been proposed as a cost-effective clinical practice. However, women with newly diagnosed breast cancer have not been evaluated to determine what their BMD levels are at the time of diagnosis. The purpose of our study is to assess the BMD of women 65 years of age and older with newly diagnosed breast cancer in comparison with the bone mineral density of same aged women with normal mammograms and to examine the risk factors associated with breast cancer and low bone mass in these two groups of women; and to develop a model based on the study population to determine the predictive value of low bone mass for risk of breast cancer.

We are in the process of recruiting women 65 years and older for 150 cases, women within 4 months of their definitive surgical procedure for breast cancer, and 150 controls, women within 4 months of a normal mammogram. At one clinic visit, subjects complete a health questionnaire. Height, weight, waist and hip girth are measured. Bone mineral density is measured at the hip, spine, forearm, and total body by dual energy x-ray absorptiometry (Hologic QDR 2000).

Preliminary results from 24 cases and 42 controls were evaluated. The mean age for both groups is 72 years. Bone mass index is higher in cases than controls, 27.1 (±4.1 SD) versus 26.2 (±6.0 SD). Bone mineral density at the total hip was lower in the cases in comparison with the controls, 0.785 g/cm² (±0.108 SD) and 0.795 (±0.127 SD), respectively. At the lumbar spine, the mean BMD was also lower in the cases, 0.933 (±0.126 SD), than controls, 0.978 (±0.182 SD).

In the first group of women evaluated for this study, the BMD of women with newly diagnosed breast cancer is lower than controls. However, the results of this study are preliminary and cannot be yet be used to make any conclusions.

The U.S. Army Medical Research Materiel Command under DAMD17-00-1-0185 supported this work.
BREAST CANCER AND BONE MINERAL DENSITY
Diane L Schneider, Donna Kritz-Silverstein, Julie Sandwell.
University of California San Diego

ABSTRACT
Recent studies have shown that women with low bone mineral density (BMD) have a low risk for breast cancer. However, it has been suggested that mammography may not be worthwhile for older women with low BMD. Measuring BMD at age 65 and applying screening mammography to women who have already been selected to be cost-effective may not be worthwhile for older women with low BMD. The purpose of our study is to assess the BMD of women 65 years of age and older with newly diagnosed breast cancers compared with the bone mineral density of very aged women with no breast cancer and nonsmokers in these two groups of women. We also report the mean and median values of bone mineral density for the BMD of breast cancer and nonsmokers in two age groups of women, as well as a mean and median based on the study population. The study population is a cross-sectional study of the prevalence of low bone mass among different age groups of breast cancer and nonsmokers in these two age groups of women.

BACKGROUND
Recent studies have shown that women with low bone mineral density (BMD) have a low risk for breast cancer.

It has been suggested that mammography may not be worthwhile for older women with low BMD.

Measuring BMD at age 65 and applying screening mammography to women who have already been selected to be cost-effective may not be worthwhile for older women with low BMD.

Women with newly diagnosed breast cancer have not been studied to determine what their BMD levels are at the time of diagnosis.

AIM
The purpose of our study is to assess the BMD of women 65 years of age and older with newly diagnosed breast cancer in comparison with the bone mineral density of very aged women with no breast cancer and low bone mass in these two groups of women.

METHODS
STUDY POPULATION
• 136 postmenopausal women
• Age 65 to 85 years; mean age 72.0 years
• 17 cases with newly diagnosed breast cancer
• 16 controls of matched controls (66.5 years old)
• 48 matched controls (mean age 66 years)
• Age 65 to 85 years; mean age 72.0 years

• BMD measured with Hologic QDR 4500A or Hologic QDR 4500B
• Data collection site: United States

RESULTS
TABLE 1
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD)</th>
<th>Cases (n=57)</th>
<th>Controls (n=56)</th>
<th>t</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>72.5 (5.4)</td>
<td>72.5 (5.6)</td>
<td>72.5 (5.4)</td>
<td>0.49</td>
<td>0.62</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.7 (3.5)</td>
<td>24.7 (3.5)</td>
<td>24.7 (3.5)</td>
<td>0.05</td>
<td>0.95</td>
</tr>
<tr>
<td>Body fat mass (%)</td>
<td>42.5 (3.5)</td>
<td>42.5 (3.5)</td>
<td>42.5 (3.5)</td>
<td>0.02</td>
<td>0.90</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>93.5 (14.8)</td>
<td>93.5 (14.8)</td>
<td>93.5 (14.8)</td>
<td>0.42</td>
<td>0.67</td>
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<tr>
<td>Total hip circumference (cm)</td>
<td>93.5 (14.8)</td>
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<td>93.5 (14.8)</td>
<td>0.42</td>
<td>0.67</td>
</tr>
<tr>
<td>Hip bone density (g/cm²)</td>
<td>0.96 (0.05)</td>
<td>0.96 (0.05)</td>
<td>0.96 (0.05)</td>
<td>0.02</td>
<td>0.90</td>
</tr>
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<td>Total hip bone density (g/cm²)</td>
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<td>0.96 (0.05)</td>
<td>0.02</td>
<td>0.90</td>
</tr>
</tbody>
</table>

LIMITATIONS
• These are preliminary results.
• Limited subject numbers thus far, therefore results may not reflect truth.
• Unable to determine which participants stopped hormone use based on abnormal mammogram.

CONCLUSION
In this small case-control study, there were no differences in bone mineral density between the women with new diagnosed breast cancer and controls.

Therefore, bone mineral density would not be useful as prescreening for mammography in older women.