Effect of Alcohol Intake on Bone Mineral Density in Elderly Women

The EPIDOS Study

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To study potential associations between alcohol consumption and bone mineral density in women aged 75 years or older, the authors analyzed 7,598 ambulatory women (mean age, 79.9 years; standard deviation, 3.8 years) recruited at five centers in France between 1992 and 1994. The current alcohol intake was assessed using a self-questionnaire. Bone mineral density was measured by dual-photon X-ray absorptiometry of the proximal femur and total body and adjusted for age, weight, and height (Z score). Compared with nonusers, women who drank 11–29 g of alcohol per day (g/day) had higher bone mineral density values at the trochanteric site (p = 0.0017). Neither 1–10 g/day nor ≥30 g/day users had increased bone mineral density levels. These results were unrelated to estrogen replacement therapy use, dietary calcium intake, current smoking status, usual physical activity, educational attainment, household monthly income, and general health status. Alcohol intake was not associated with bone mineral density at the femoral neck. Total body bone mineral density was lower in subjects with alcohol intakes ≥30 g/day (p = 0.047). Our data suggest that moderate drinking (e.g., 1–3 glasses of wine per day) is associated with an increase in trochanteric bone mineral density in elderly ambulatory women. However, higher intakes may have detrimental effects on bone mass. Am J Epidemiol 2000; 151:773–80.

Heavy drinking is well known to be associated with osteoporosis and osteoporotic fractures in chronic alcoholics (1, 2). Epidemiologic studies (3–5) have shown that long-term heavy drinkers have multiple risk factors for bone loss, including low dietary calcium and other nutritional deficiencies, low body weight, smoking, and a high caffeine intake (6, 7). Although the detrimental effects of alcohol on bone metabolism have been confirmed by animal studies (8, 9), most of these involved administration of large amounts of alcohol. Several recently published epidemiologic studies have suggested that moderate drinking in social settings may be associated with higher bone mineral density values (10–14). The results were somewhat conflicting, however, and definitions of alcohol intake categories lacked accuracy and varied across studies. Also variable were the accuracy of the alcohol intake questionnaires used and the length of the study period. In most studies, the sample size was small (6, 14–17), a fact that required use of a limited number of alcohol intake categories. Few studies specified the type of alcoholic beverage used (wine, beer, or liquor), a potentially important parameter since an estrogen-like compound has recently been identified in some bourbon whiskies (18). Few studies included a large sample of women (19, 20). As a rule, the statistical analysis did not involve adjustment for the effects of potentially important confounding variables, such as smoking, dietary calcium intake, estrogen replacement therapy, or physical activity. The rationale underlying the choice of covariates for adjusting the crude data was unclear (21). Finally, the anatomic sites of bone mineral density measurement varied across studies.

Because postmenopausal women are the population at highest risk for osteoporosis, we evaluated potential associations between alcohol intake and bone mineral density measured at the proximal femur and total body in 7,598 women aged 75 years or older. These women were participants in a prospective French study of risk factors for hip fractures (Épidémiologie de l'Ostéoporose (EPIDOS) Study). Our analysis took into account the main potential confounding factors reported in the literature, namely, estrogen replacement therapy, smoking history, calcium intake, physi-
cal activity, social status (educational attainment and family income), and general health status (6, 14, 15).

MATERIALS AND METHODS

Recruitment

The recruitment procedure has been described previously (22, 23). In brief, between January 1992 and January 1994, women aged 75 years or older from five cities throughout France (Amiens, Paris, Lyon, Toulouse, Montpellier) were randomly selected from registries such as voting or healthcare lists. Each woman was sent a letter inviting her to participate in a study conducted at a university hospital in her city. Based on findings from a history and physical examination, women with a history of hip fracture or bilateral hip replacement, Paget’s disease, renal failure, hyperthyroidism, or treatment for hypothyroidism were excluded. Further letters were sent until 1,500 women had been included at each center. The final study population consisted of 7,598 ambulatory women, evenly distributed over the five centers. The baseline evaluation was done at the center clinics by trained nurses and included administration of a structured questionnaire, a physical examination, and a functional assessment. The study subjects completed the questionnaire at the hospital, during the recruitment visit, with the help of a trained interviewer if necessary. The study was approved by an ethics committee, and all women gave their written informed consent.

Alcohol Intake

Each woman completed a food consumption self-questionnaire including 58 items of which the last five were on alcohol consumption. One item (translated to English) was “Do you drink wine, beer, or liquor?” and was to be answered by “yes” or “no”; subjects who answered “yes” completed an item asking how many glasses of each alcoholic beverage they drank on average per day, during or outside meals. To obtain the total daily alcohol intake, these answers were converted to grams as follows (24, 25): one glass of wine (4 oz or 120 ml) = 10 g of alcohol; one glass of beer (4 oz or 120 ml) = 4 g of alcohol; and one standard shot of liquor = 10 g of alcohol.

Bone mineral density measurement

Bone mineral content was measured by dual-photon X-ray absorptiometry using a Lunar DPX unit (Lunar Corporation, Madison, Wisconsin) and Lunar version 3.61 software. The measurement sites were the total body and the trochanter, femoral neck, and Ward’s tri-angle of the right femur. Lumbar spine bone mineral density was not measured. The results were expressed as bone mineral density in grams per square centimeter obtained by dividing the bone mineral content by the projected area of the region scanned. Bone mineral densities in the EPIDOS Study women had a normal distribution, consistent with data from other populations (26).

Covariates

Estrogen replacement therapy. Questionnaire items on estrogen replacement therapy asked whether estrogens had ever been used to relieve menopausal symptoms, the brand(s) used, the age at which use was initiated, and the total number of years of use. The use of hormones other than estrogens to alleviate menopausal symptoms was not evaluated. Categories for duration of estrogen replacement therapy use were never used, <5 years, and ≥5 years.

Smoking status. Based on current smoking status, patients were categorized as nonsmokers or smokers, with the latter being defined as subjects who smoked at least one cigarette per day. Because only 2 percent of the study subjects smoked more than 20 cigarettes per day, this category was not studied separately. No information was collected on cigars and pipes, which are rarely used by women in France.

Calcium intake. The current dietary calcium intake was assessed using a food frequency questionnaire. Dietary calcium intake was calculated from the calcium content of each food, typical portion sizes, and the frequency of consumption per week. In a previous study (27), we found that the calcium intake estimates obtained using this questionnaire were closely correlated with those derived from food frequency methods. Calcium was analyzed as a quantitative variable.

Physical activity. Usual physical activity was estimated by items on three types of activity, namely, shopping or walking outdoors to satisfy daily needs, exercise (walking, working out, cycling, gardening, swimming), and heavy housework (e.g., vacuum cleaning or mopping floors). These items were answered by “yes” or “no.” The women were categorized into four groups based on whether they engaged in none, one, two, or three of these activities.

Education. Educational attainment was categorized in four groups as follows: 5 years of formal education, more than 5 but less than 12 years, high school graduate, and college education.

Family income. Monthly family incomes were evaluated in three groups (<6,000 French francs (FF)/month, 6,000–8,500 FF/month, and >8,500 FF/month; equivalent approximately from 920 to 1,300 US dollars, with 1 dollar = 6.50 FF).
Health status. Self-rated health was classified in three categories based on whether the response to the question “Compared with women of your age, how do you rate your health status?” was “better,” “similar,” or “worse.”

Estrogen replacement therapy use, current smoking status, and usual physical activity were determined during a face-to-face interview. Dietary calcium intake, educational attainment, monthly household income, and general health status were assessed from the self-administered questionnaire. Height and weight were measured while the women were dressed in light clothes with shoes removed.

Statistical analysis

Bone mineral density measurements were adjusted for the age, height, and weight of non-alcohol users according to a three-stage procedure previously used by several authors (28). First, within the non-alcohol user subgroup, we estimated the specific parameters of the multiple linear regression of bone mineral density according to age, height, and weight. Second, for each woman, irrespective of alcohol use, we calculated the difference between measured bone mineral density values and bone mineral density values predicted by multiple linear regression. Third, we derived a standardized value, the Z score, by dividing all these differences by the standard deviation of the differences in the non-alcohol user subgroup. Consequently, the Z score in the non-alcohol user subgroup was on a scale with zero mean and unit standard deviation. The Z score measures the deviation of a woman’s bone mineral density above or below the expected value for a non-alcohol user of the same age, height, and weight.

The univariate analysis of the effect of alcohol use alone on the Z score was evaluated using one-way analysis of variance and multivariate analysis, using multiple linear regression. In this last analysis, the statistical assessment of the alcohol effect was based on the lack-of-fit test. If this test was significant, we partitioned the alcohol effect, first using cubic polynomial contrast to check for a nonlinear distribution of the Z score over alcohol intake and then using Dunnett’s post hoc test to check for a nonlinear distribution of the Z score. The level of significance was set at 0.05. All probability values were two-tailed.

RESULTS

Alcohol intake

Table 1 shows the distribution of alcohol intakes. The range was 0–80 g/day, 60 percent of the women reported no alcohol intake, and 3 percent drank more than 30 g/day. Among the 3,062 alcohol users, 2,932 (96 percent) gave answers clustered on three values (10 g/day, 20 g/day, and >30 g/day). The remaining 130 patients reported the following alcohol intakes: 1:9 g/day (n = 8), 11–19 g/day (n = 25), 21–29 g/day (n = 28), and >30 g/day (n = 69). We consequently created four categories: 1) no alcohol use (0 g/day); 2) light drinking (1–10 g/day); 3) moderate drinking (11–29 g/day); 4) heavy drinking (30 g/day). Table 1 also displays links between the amount and type of alcohol consumed. Wine was the most frequently consumed alcoholic beverage: consumption of wine alone was reported by 96.8 percent, 91.1 percent, and 65.7 percent of light, moderate, and heavy alcohol users, respectively. Increases in alcohol intake from one category to the next were due primarily to consumption of

<table>
<thead>
<tr>
<th>Alcohol Intake</th>
<th>Type of alcohol (%)</th>
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<tbody>
<tr>
<td>Light (1–10 g/day)</td>
<td>Wine : 97.2, Beer : 5.0, Aperitif and/or hard liquor : 0.3</td>
</tr>
<tr>
<td>Moderate (11–29 g/day)</td>
<td>Wine : 97.4, Beer : 5.0, Aperitif and/or hard liquor : 3.7</td>
</tr>
<tr>
<td>High (≥30 g/day)</td>
<td>Wine : 98.9, Beer : 7.3, Aperitif and/or hard liquor : 27.5</td>
</tr>
</tbody>
</table>

Table 1. Type and quantity of alcohol consumed by EPIDOS* Study women,† France, 1992–1994

* EPIDOS, Épidémiologie de l’Osteoporose.
† In response to questions about alcohol consumption, 4,536 women did not drink alcohol, and only 23 women failed to answer.
§ The consumption of wine in glasses per day was 1 = 1,867 women, 2 = 996 women, 3 = 82 women, 4 = 41 women, 5 = 5 women, and 6 = 1 woman.
$ In France, aperitif drinks are commonly taken before meals, supposedly to stimulate the appetite, and hard liquor after meals, supposedly to aid digestion.
* The distributions display all values as they were collected, without gathering.
other alcoholic beverages in addition to wine (0.4 percent, 6.6 percent, and 33.1 percent of light, moderate, and heavy users, respectively). Heavy users drank wine and strong liquor (25.8 percent) or beer (5.6 percent). Among alcohol users who did not drink wine, light users drank only alcoholic beverages traditionally taken before or after meals (2.3 percent), whereas moderate users drank only beer (1.7 percent).

Study patient characteristics are shown in table 2. No significant relation was found between alcohol intake and age, age at menopause, estrogen replacement therapy use, or physical activity. The percentages of smoking and low calcium intake increased with the alcohol intake. The heaviest drinkers were taller and heavier than the other study subjects. The proportion of women who felt their health status was better than that of women of the same age and the proportion of women at the higher end of the socioeconomic spectrum (based on educational attainment and family income) increased with alcohol intake.

**Bone mineral density**

The unadjusted analysis found no significant effect of alcohol consumption on bone mineral density measured at the proximal femur (table 3). After stratification for age and weight conducted by dividing patients into two subgroups based on whether these two parameters were above or below the median value, the alcohol effect was statistically significant at the trochanteric site ($p = 0.032$). A more powerful adjustment on age, weight, and height was then performed using the $Z$ score. This showed a highly significant effect of alcohol intake at the trochanteric site ($p = ...
When the covariates were taken into account, the effect of alcohol intake on the Z score at the trochanteric site remained highly significant ($p = 0.0004$).

To determine whether the relation between the Z score and the alcohol intake was linear, we fit a polynomial regression of degree 3. We found a significant quadratic term (linear $p = 0.54$, quadratic $p = 0.032$, cubic $p = 0.054$), suggesting a nonlinear relation. The multiple comparison test of each of the three alcohol user groups with the non-alcohol user group showed that this effect existed only for the moderate drinkers (11–29 g/day), who had the highest Z scores (table 3; figure 1).

Neither femoral neck and Ward’s triangle bone mineral densities nor their Z scores were significantly linked to alcohol intake.

For total body bone mineral density, the difference among alcohol intake groups was highly significant before adjustment ($p = 0.007$), but it became less so after adjustment on age and weight using the rough adjustment procedure described above ($p = 0.046$) or the Z score ($p = 0.047$). The multiple comparisons tests showed that this difference was entirely ascribable to lower Z-score values in the heavy users (≥30 g/day). After adjustment on the covariates, the difference remained close to the level of significance.

Neither femoral neck and Ward’s triangle bone mineral densities nor their Z scores were significantly linked to alcohol intake.

DISCUSSION

We found that moderate alcohol use (11–29 g/day) was associated with a significant increase in trochanteric bone mineral density in elderly women. This increase corresponded to one tenth of the standard deviation, which was similar to the increase seen in estrogen replacement therapy used under the same study conditions (figure 1). Compared with nonusers, light and heavy users showed no increase in bone mineral density. The results suggest that the beneficial effect on bone mineral density occurred only with the moderate alcohol intake provided by three glasses of wine, three drinks of hard liquor, or almost eight beers per day.

Table 4 shows previously published results on the link between moderate alcohol consumption and bone mineral density among postmenopausal women. All these studies measured bone mineral density at the proximal femur, although one (11) did not measure the trochanteric site. In three of these studies (11, 12, 14), there was no significant relation between alcohol intake and trochanteric bone mineral density. However, the numbers of patients were small, so that only two alcohol intake categories could be studied (nonusers and users); furthermore, the statistical tests used in these studies were not adjusted on covariates. Finally, our results are very similar to those of the Framingham Study (10), which included a large sample of women with approximately the same age distribution as in our sample. Thus, both the Framingham and EPI DOS studies support a beneficial effect on bone mass of moderate alcohol use.

As in the Framingham Study (10), we found that age, weight, and height were significant covariates in the analysis of the link between alcohol intake and bone mineral density. Because this type of adjustment may produce spurious positive associations, we strengthened our conclusions by using two different adjustment methods: the adjusted Z score, which is a powerful tool but requires stringent statistical conditions of application, and a bone mineral density analysis with two age and two weight categories, which is a less powerful but more robust test. The two methods yielded similar results.

An important issue was to determine the threshold or range of alcohol consumption likely to be beneficial or detrimental for bone mass. In the Framingham Study, bone mineral density was higher at the upper end of the range of alcohol intake studied (207–414 ml/week). The broader alcohol intake range in our study allowed us to show that the beneficial effect of alcohol intake on bone mass was no longer present above three glasses of wine per day.

There are a number of limitations to our study. The EPI DOS Study population is composed of women who...
attainment and those who reported the best general health status have a higher bone mass, which in turn has been shown to be associated with benefits on bone mass.

The link between alcohol intake and bone mass identified in our study may be questionable, however. Subjects who lead an active life and have a good health status have a higher bone mass, which in turn has been shown to be associated with a longer life span (31).

Volunteered for participation in the study and may, therefore, not be representative of the population at large. Because we recruited only ambulatory elderly women, the ranges of alcohol intakes and bone mineral density values in our study sample may not reflect those in the general population. Our study patients were probably higher up in the socioeconomic spectrum and healthier than most women of the same age. Recruitment bias may have occurred because the goal of our study explained in the letter sent to potential participants was perhaps unlikely to hold appeal for alcoholic women. Nevertheless, the alcohol intakes in our population were similar to those in earlier studies of the elderly (10, 30).

The link between alcohol intake and bone mass identified in our study may be questionable, however. Subjects who lead an active life and have a good health status have a higher bone mass, which in turn has been shown to be associated with a longer life span (31).

The authors of the Framingham Study pointed out that the bone mineral density increase in heavier drinkers in their study may have been due to either alcohol intake or the longer survival of women who were both alcohol users and had high bone densities. As in earlier studies (10, 32, 33), moderate or heavy users were more likely than nonusers to rate their health as good or excellent, to report exercising regularly, to have higher incomes, and to have a better socioeconomic status. In our study, however, the women with the highest socioeconomic status and/or educational attainment and those who reported the best general health status had alcohol intakes above the range associated with benefits on bone mass.

Although our sample size was sufficient to allow comparisons of nonusers, light users, and moderate users, the statistical power of our study was limited for the heavy user group. To study our alcohol users, we compared only three alcohol intake categories, corresponding approximately to one, two, and three glasses of wine per day. This categorization corresponded exactly to the answers given by 96 percent of alcohol users. We do not know whether the very small proportion of answers indicating intake of intermediate quantities was due to the form of our questions (we asked how many glasses the respondents took per day) or reflected drinking habits, particularly the custom of drinking wine by the glass. If the first hypothesis is true, our questionnaire probably resulted in a number of random misclassifications between two adjacent intake categories, which would not affect our conclusions. Reported alcohol intakes may have been lower than actual alcohol intakes, particularly in the heaviest drinkers. This would produce a systematic misclassification, either toward the lowest alcohol intake categories or toward a virtual dose of alcohol intake categories or toward a virtual dose.

Another source of attenuation of the effect of intake

### Table 4: Epidemiologic studies of associations between alcohol intake and bone mineral density in women

<table>
<thead>
<tr>
<th>Setting</th>
<th>Year of study</th>
<th>Mean age (years)</th>
<th>Alcohol use (%)</th>
<th>Bone mineral density (significance)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Nonusers</td>
<td>Users</td>
<td>Trochanter</td>
</tr>
<tr>
<td>Sydney, Australia</td>
<td>1988‡</td>
<td>59 (1)</td>
<td>35¶</td>
<td>36</td>
</tr>
<tr>
<td>Rancho Bernardo, CA</td>
<td>1988–1991</td>
<td>60 (8)</td>
<td>71</td>
<td>190‡‡</td>
</tr>
<tr>
<td>Framingham Study, MA</td>
<td>1988–1989</td>
<td>76 (5)</td>
<td>384</td>
<td>355‡†</td>
</tr>
<tr>
<td>Copenhagen, Denmark</td>
<td>1989</td>
<td>63 (2)</td>
<td>71</td>
<td>506‡§§</td>
</tr>
<tr>
<td>Helsinki, Finland</td>
<td>1991‡</td>
<td>59 (6)</td>
<td>37###</td>
<td>22</td>
</tr>
<tr>
<td>EPIDOS‡‡ Study, France</td>
<td>1998</td>
<td>80 (4)</td>
<td>4,536</td>
<td>3,062</td>
</tr>
</tbody>
</table>

* p < 0.05; ** p < 0.01; *** p < 0.001.
† Sydney, Australia (Felson et al., Am J Epidemiol 1995;142:485–92); Rancho Bernardo, CA (Holbrook et al., BMJ 1993;306:1506–9); Framingham Study, MA (Angus et al., Bone Miner 1988;4:265–77); Copenhagen, Denmark (Hansen et al., Osteoporos Int 1991;1:35–102); Helsinki, Finland (Laatinen et al., Calcif Tissue Int 1991;48:224–31).
‡ Year of publication.
§ Numbers in parentheses, standard deviation (SD).
¶ Nonusers and users, not defined. Mean consumption: 12 (SD, 6) g/day; range: 1–43 g/day.
†† The analysis was not adjusted.
‡‡ The analysis was based on the correlation coefficient (Pearson's or Spearman's).
### Adjusted for age, estrogen replacement therapy, body mass index, smoking, and exercise.
### Nonusers, <1 oz (29.57 ml/week); users (three classes), ≤1–3 oz (88.71 ml/week); >3–7 oz (206.99 ml/week); >7–14 oz (414 ml/week). There were no women who consumed over 14 oz.
** Adjusted for age, estrogen replacement therapy, body mass index, smoking, and exercise.
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### Adjusted for age, menopause, number of years of estrogen replacement therapy use, weight, height, and mean number of cigarettes smoked.
### Regular intake registered as weekly consumption of one or more units of alcohol for at least 1 year. None of the participants abused alcohol.
###‡‡‡ A statistically significant difference (p < 0.01) in bone mineral content (in percentage) was found between the first measurement performed in 1979 and the second measurement in 1986. This difference was highest in nonusers.
## Nonusers and users, not defined. Mean consumption: 36 g/week (95% confidence interval: 11, 77); 26% consumed ≥20 g/week.

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on bone mineral density may be the absence, in our study, of data on past alcohol consumption, which did not allow us to differentiate exusers from never users in our nonuser category. Several studies have shown that moderate users, particularly women, keep their alcohol intake constant, whereas heavy users older than 65 years of age tend to decrease their intake over time (33). It has been shown that even a single administration of questionnaires similar to ours provides useful estimates of alcohol intake over an extended period of time (25).

The potential causal link between moderate alcohol consumption and increased bone mineral density deserves discussion. As seen in table 4, bone measurement sites varied across studies. The skeleton is composed of trabecular and cortical bone. Trabecular bone predominates at some sites (spine, 66 percent; ultradistal radius, 66 percent; trochanteric region, 50 percent) and cortical bone at others (femoral neck, 75 percent; total body, 80 percent; distal radius, 80 percent; midradius, 99 percent) (34). In most studies, moderate alcohol intakes were associated with increased bone mass at the trochanter and spine, which are predominantly trabecular. No studies found any significant effect at the femoral neck. Effects on midradius and total body bone mineral density were less consistent. Taken in aggregate, these findings suggest a protective effect of moderate drinking against loss of trabecular bone. Because trabecular bone has a higher rate of bone turnover and a faster metabolic rate than cortical bone, the magnitude of any effect on bone mass tends to be greatest at heavily trabecular sites. The bone mass-protecting effect of moderate drinking may involve estrogen-like effects on bone stimulation. Estrogen has well-known effects on bone formation and remodeling. In experimental studies (35) and clinical studies in postmenopausal women (36, 37), moderate alcohol consumption increased estradiol levels. In addition, alcohol may affect osteoblasts directly (38) and/or indirectly via other factors such as hormones (39).

In conclusion, our data suggesting that social drinking in elderly ambulatory women may have a positive effect on bone mass at heavily trabecular sites such as the trochanter are reassuring. The detrimental effect of alcohol consumption on bone may occur only above three glasses of wine per day. Multiple factors are probably involved in the beneficial effects of moderate alcohol consumption on bone metabolism. Alcohol in modest amounts may have estrogen-like effects on bone. However, daily alcohol intake is influenced by many factors, including nutritional and physical activity habits, which may have their own effects on bone mass.

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