Cigarette Smoking, Alcohol Consumption, and Risk of Hip Fracture in Women

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Background: Previous studies regarding the impact of cigarette smoking on the risk of hip fracture in postmenopausal women have been inconsistent, suggesting different effects in different groups. The effect of alcohol intake on fracture risk is puzzling: moderate alcohol intake appears to increase bone density, and its association with hip fracture is not clear.

Methods: To assess the associations of cigarette smoking and alcohol consumption with hip fracture risk among postmenopausal women, we conducted an analysis of a population-based case-control study from Sweden. Cases were postmenopausal women, aged 50 to 81 years, who sustained a hip fracture after minor trauma between October 1, 1993, and February 28, 1995; controls were randomly selected from a population-based register during the same period. A mailed questionnaire requesting information on lifestyle habits and medical history was used 3 months after the hip fracture for cases and simultaneously for controls. Age-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were computed by means of logistic regression.

Results: Of those eligible, 1328 cases (82.5%) and 3312 controls (81.6%) responded. Compared with never smokers, current smokers had an increased risk of hip fracture (age-adjusted OR, 1.66; 95% CI, 1.41-1.95). Duration of smoking—particularly postmenopausal smoking—was more important than the amount smoked. Former smokers had a small increase in risk (age-adjusted OR, 1.15; 95% CI, 0.97-1.37) that decreased with the duration of cessation. The age-adjusted OR for women consuming alcohol was 0.80 (95% CI, 0.69-0.93).

Conclusions: Cigarette smoking is a risk factor for hip fracture among postmenopausal women; risk decreases after cessation. Alcohol consumption has a weak inverse association with risk.

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Cigarette smoking is often considered a risk factor for hip fracture, but several studies have found no association between cigarette smoking and hip fracture risk. Investigation of bone mass has similarly been conflicting; although many studies have found a negative association between smoking and bone mass, many have reported smoking to have at most a weak association with bone mass, particularly among younger women. These findings underscore uncertainties about the effect of smoking and, in particular, the effect of smoking in different populations or at different ages.

Less is known about the effect of consumption of alcoholic beverages on the risk of hip fracture. Although bone mineral density has been reported to be higher in persons with moderate alcohol intake than in those who abstain, epidemiologic studies have reported contradictory results regarding the association of alcohol intake and hip fracture risk.

To clarify the associations of cigarette smoking and alcohol intake with hip fracture risk, we analyzed data from a large, population-based, case-control study of hip fracture in Sweden.

RESULTS

The characteristics of the study participants are summarized in Table 1. The mean age (SD) was 72.5 (6.8) years in cases and 70.5 (7.7) years in controls. Most differences in risk factors reflected known epidemiologic associations.

More cases than controls were current smokers (26.1% vs 19.3%, respectively) (Table 1). Compared with never smokers, current smokers had a 66% increase in the age-adjusted risk of hip fracture (OR, 1.66; 95% CI, 1.41-1.95), and...
SUBJECTS AND METHODS

The study was conducted in the Swedish counties of Stockholm, Uppsala, Västmanland, Örebro, Göteborg, and Malmö, a largely urban area situated in the middle, west, and south of Sweden that includes nearly half (46%) of the country’s 8.6 million inhabitants. We aimed to ascertain all fractures of the cervical, pterochanteric, and subtrochanteric areas of the proximal femur among women residents in the study area who were born in 1914 or after, and who were treated between October 1, 1993, and February 28, 1995. All 24 hospitals in the study area used hospital discharge records or operation registers to identify cases, which were reported to the study center. We identified 2,997 possible incident female hip fracture cases and excluded those with a pathologic fracture (n = 26); high-energy trauma (mainly traffic accidents (n = 41); an incorrect diagnosis (n = 41); an old fracture (n = 10); a history of blindness (n = 5); place of birth outside Sweden (n = 202); a diagnosis of severe alcoholic abuse, psychosis, or senile dementia (n = 576); and death within 3 months of the fracture (n = 123). Hospital records for all potential cases were scrutinized to confirm eligibility, to ascertain type of hip fracture, and to identify patients with a previous hip fracture. There remained 1,610 cases eligible for the study, who were approached with a comprehensive questionnaire at a mean interval of 95 days (SD, 23 days) after the fracture. The Swedish Central Inpatient Register was used at the end of the study to identify any incident hip fracture cases overlooked; we found 34 additional eligible cases, who were also approached with a questionnaire.

Potential controls were selected from a continuously updated Swedish population register that provides national registration number, name, address, and place of birth of all people resident in Sweden. More than half of the controls who took part in the study (n = 2,727, aged 70-81 years) were recruited from population samples that were frequency matched to the cases by 5-year age group and county of residence. The remainder of the controls (aged 50-74 years), also resident in the study area, were similarly selected, although in concert with an ongoing case-control study of breast cancer and so age-matched to breast cancer cases. Of those selected, 4,059 were eligible and 813 were excluded: 610 who were born outside Sweden, 157 who died before being approached, 44 with senility or psychosis, and 2 who were blind.

Data were collected through an extensive mailed questionnaire that included questions regarding reproductive history and use of exogenous sex hormones (oral contraceptives and hormone replacement therapy), current weight and height, dietary habits (food frequency questionnaire), comorbidity, lifelong exposure to active cigarette smoking, and patterns of alcohol consumption. Leisure physical activity was measured on a 4-grade scale (from never to more than 2 hours per week) at 3 time points: in childhood, between ages 18 and 30 years, and in recent years.

Approximately 50% of the participants were approached by telephone for completion of missing information. Some women refused participation with the postal questionnaire but accepted a less extensive telephone interview. Of those eligible, 1,328 cases (82.5%) and 3,312 controls (81.6%) provided questionnaire data; of these, 202 (15.2%) of the cases and 497 (15.0%) of the controls responded solely by telephone. Participants claiming natural menopause were classified as premenopausal (50 controls and 1 case) and were excluded from the analysis. The study design was approved by the Ethics Committee, Uppsala University.

former smokers had a 15% increase (OR, 1.15; 95% CI, 0.97-1.37). After additional adjustment for BMI and HRT use, the OR for former smokers remained essentially the same, but that for current smokers fell to 1.35 (95% CI, 1.12-1.64). The maximum number of cigarettes smoked was not closely related to hip fracture risk (Table 2), but duration of smoking had a marked effect: a 6% (95% CI, 0%-13%) increase in age-adjusted risk per 5 years smoked. With these trends, the risk of hip fracture was significantly increased only among women with a lifelong cumulative duration of cigarette smoking greater than 30 years.

Premenopausal and postmenopausal smoking had different associations with hip fracture risk. Women who smoked for more than 24 years before menopause had a significant increase in the risk of hip fractures, but only 11 or more years of postmenopausal smoking was required for a similar increase in risk (Table 3). With premenopausal and postmenopausal duration of smoking considered in the same model, the risk of hip fracture was more strongly elevated for postmenopausal smoking: the age-adjusted OR per 5 years’ postmenopausal smoking was 1.10 (95% CI, 1.04-1.17) vs 1.06 (95% CI, 1.00-1.12) for premenopausal smoking. After multivariate adjustment, these ORs were 1.05 (95% CI, 0.98-1.21) and 1.02 (95% CI, 0.96-1.09), respectively.

Among former smokers, the OR of hip fracture decreased with duration of cessation. The reduction in age-adjusted ORs among former smokers was 2% per 5 years’ cessation (OR, 0.98; 95% CI, 0.88-1.09). In comparison with current smokers, women who had stopped smoking within the past 14 years had a modest, nonsignificant decrement in risk (age-adjusted OR, 0.88; 95% CI, 0.66-1.17). Thereafter, the risk declined to levels similar to those of never smokers (Table 4).

To explore the possibility that recency and duration of smoking would confound each other’s effect, we included both variables in the same models, but the findings did not change substantially (data not shown). Among women currently smoking or who had stopped within 15 years of the index date, the age-adjusted OR per 5 years’ smoking was 1.08 (95% CI, 1.03-1.14). After 15 years’ cessation, however, there was no duration-dependent smoking effect (age-adjusted OR per 5 years’ smoking, 0.93; 95% CI, 0.83-1.04) (Table 4).

The effect of smoking did not differ materially between women with BMI or height above or below the (control) median, between women who ever or never took HRT, or among women of various ages (<70, 70-75, and
The questions regarding cigarette smoking addressed lifelong exposure (usual number of cigarettes smoked per day at different specified ages), and smoking status 1 year before the interview. We considered as smokers those women who smoked continuously for at least for 1 year or who smoked 100 or more cigarettes in their lifetime. We created categories of lifelong duration of cigarette smoking in approximate quartiles among controls who smoked (ie, 1-14, 15-30, 31-45, and >45 years). The same principle was applied to create groups of duration of exposure in premenopausal and postmenopausal periods. Information on alcoholic beverage consumption was collected as the usual pattern 1 year before interview. Quantities were recorded in glasses per week or month of specified products: wine, fortified wine, weak beer (2.8% alcohol), strong beer (4.5% alcohol), and spirits. These amounts were then converted to grams of alcohol per day.

Current use of hormone replacement therapy (HRT) was determined with reference to an index date: the time of the fracture for cases, or 95 days before the mailing of the questionnaire for controls (ie, the mean interval between hip fracture and response to the questionnaire for cases). Former HRT use was defined as cessation of therapy before the index date. The 3 responses regarding exercise at different periods of life were summed and dichotomized as above or below the control median. Body mass index (BMI) was calculated as weight (in kilograms) 1 year before answering the questionnaire divided by the square of height (in meters) and then categorized into quartiles (according to the distribution in the control population).

Age at menopause was defined as the age at last menstrual period or age at bilateral oophorectomy, if these occurred 1 year or more before the data collection. (If later, women were considered premenopausal and excluded from analysis.) Women with unknown menopausal age because of hysterectomy or menses resulting from use of HRT, or with missing information, were considered postmenopausal if they had reached the age when natural menopause had occurred in 90% of the subjects (53 years in current smokers and 55 years in nonsmokers, independent of case-control status), or otherwise unknown. Menopausal age was then used as a 3-level variable (<45, 46-54, and >54 years). Climacteric symptoms (eg, hot flashes) were categorized as present or absent. Education was classified as primary school only vs higher educational level.

Odds ratios (ORs) and 95% confidence intervals (CIs) computed by unconditional logistic regression were used as measures of association. In the final logistic regression models, the following covariates were considered: age (<60, 60-64, 65-69, 70-74, and >74 years), HRT use (never, former, and current), and BMI (<22, 22-23, 24-25, 26-27, and >27). Adjustment for other covariates did not change the results more than marginally, and these estimates are not presented herein. For the smoking analyses, we also adjusted for alcohol consumption (0, 1-2, 3-6, and >6 g/d), and in analyses of alcoholic beverage consumption, we adjusted for smoking (never, current, and former). Because the relationship between exposures (maximum number of cigarettes smoked per day in any period of life, overall duration of cigarette smoking, and duration of premenopausal and postmenopausal smoking) and hip fracture risk were not clearly linear, we created categorical variables based on the frequency distribution of controls. Because of the possibility that smoking might affect peak bone mass and postmenopausal bone loss differently, we considered premenopausal and postmenopausal smoking separately. Interactions were considered through inclusion of product terms in the analysis, using likelihood ratio tests for the assessment of significance.

In this large, population-based, case-control study, there was a strong association between the risk of hip fracture and duration of smoking, but no clear relationship between the numbers of cigarettes smoked and fracture risk. Smoking after menopause had a more deleterious effect than smoking before menopause. The impact of smoking appeared to be reversible: after 15 years of cessation, there was no association with hip fracture risk. Moderate alcohol consumption conferred a slightly reduced risk, although without a regular trend of decreasing risk with increasing amount drunk.

In some previous studies, current smokers have had approximately a 50% increased risk of hip fracture, as compared with never smokers. In contrast to our findings, some studies have reported higher hip fracture risks among heavier smokers than among lighter smokers. One investigation considered duration of smoking and showed no suggestion of an increased risk of hip fracture with increasing number of years of smoking. As in our study, most previous investigations have found former

>75 years) (data not shown). However, smoking was more strongly associated with hip fracture risk among women who drank some alcohol (age-adjusted OR per 5 years' smoking, 1.15; 95% CI, 1.08-1.23) than among women who abstained from alcohol (OR per 5 years' smoking, 1.04; 95% CI, 0.98-1.09) (P for interaction, .03).

Consumption of alcoholic beverages during the year preceding the interview was reported by 40% of cases and 48% of controls (Table 1). Thus, alcohol consumption was inversely associated with hip fracture risk; those who reported drinking alcohol had an age-adjusted OR of 0.80 (95% CI, 0.69-0.93) vs nondrinkers (Table 5). There was no material trend of risk with the amount of alcohol consumed per day. The BMI and HRT use did not substantially modify the effect of alcohol intake on fracture risk (data not shown), but height may have modified this effect. Among women no taller than 163 cm, there was no trend in fracture risk with increasing amounts of alcohol consumed. However, among taller women, there was a trend of decreasing risk with increasing amounts drunk (P for trend, <.001); in these women, the age-adjusted OR for alcohol intake of 7 g/d or more (vs none) was 0.58 (95% CI, 0.41-0.81) (P for interaction, .03). After adjustment for BMI and cigarette smoking, each type of alcoholic beverage studied was inversely associated with risk (Table 5), although strong beer and wine conferred lower risks than other types of alcoholic beverages.
smokers to have hip fracture risks between those of current and never smokers,6,8,11 although there has been little research regarding the duration of cessation required for a return to never-smoking levels of risk.

The waning of the effect of smoking after cessation and the relatively weak effect of premenopausal smoking in postmenopausal women clearly are related phenomena. Among women currently smoking as well as among those who have stopped, it is relatively recent smoking experience that most affects hip fracture risk.

Adjustment for body weight has generally been observed to remove some, but not all, of the effect of smoking. Since smoking is probably causally associated with a lower body weight,12 adjustment for body weight removes some of the biological effect of smoking. Thus age-adjusted estimates may provide the best assessment of the overall effect of smoking. In our data there was no increase with age in the smoking-related risk, in contrast to a pattern postulated in a recent meta-analysis.3

There are several mechanisms through which cigarette smoking could affect fracture risk. The lower body weight in smokers could lead to decreased estrogen production, decreased padding during falls, and decreased physical loading of weight-bearing bones (with consequent reduction in the stimulus for growth). Even after consideration of body weight, the “antiestrogenic” effect of cigarette smoking could also have an effect on bone in women.13 Our finding that postmenopausal smoking had more impact than premenopausal smoking is consistent with this mechanism, since the antiestrogenic effect of smoking is most prominent among postmenopausal women.13

Smokers also may have lower levels of parathyroid hormone, 25-hydroxyvitamin D, and 1,25-dihydroxyvitamin D,14-17 all of which could reflect increased bone resorption. Perhaps because of these hormonal characteristics, cigarette smoking (or nicotine) seems to lead to decreased calcium absorption or retention in the gut.18-21 Smoking also probably leads to a modest long-term

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**Table 1. Characteristics of the Study Population**

<table>
<thead>
<tr>
<th>Age, mean ± SD, y</th>
<th>Cases (n = 1327)</th>
<th>Controls (n = 3262)</th>
</tr>
</thead>
<tbody>
<tr>
<td>72.5 ± 6.8</td>
<td>70.5 ± 7.7</td>
<td></td>
</tr>
</tbody>
</table>

**Body mass index, mean ± SD, kg/m²**

<table>
<thead>
<tr>
<th>Smoking status, No. (%)</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>719 (54.3)</td>
<td>1872 (60.7)</td>
</tr>
<tr>
<td>Former</td>
<td>260 (19.6)</td>
<td>619 (20.0)</td>
</tr>
<tr>
<td>Current</td>
<td>345 (26.1)</td>
<td>595 (19.3)</td>
</tr>
</tbody>
</table>

**Mean duration of smoking, mean ± SE, y‡**

<table>
<thead>
<tr>
<th>Type of beverage reported</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>665 (59.6)</td>
<td>1427 (52.4)</td>
</tr>
<tr>
<td>Yes</td>
<td>451 (40.4)</td>
<td>1297 (47.6)</td>
</tr>
</tbody>
</table>

**Alcohol consumption, No. (%)**

<table>
<thead>
<tr>
<th>Type of beverage reported</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>665 (59.6)</td>
<td>1427 (52.4)</td>
</tr>
<tr>
<td>Yes</td>
<td>451 (40.4)</td>
<td>1297 (47.6)</td>
</tr>
</tbody>
</table>

**Table 2. Adjusted Odds Ratios (ORs) and 95% Confidence Intervals (CIs) Regarding Smoking History and the Risk of Hip Fracture**

<table>
<thead>
<tr>
<th>No. of Cases/Controls</th>
<th>Age-Adjusted OR (95% CI)</th>
<th>Multivariate OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never smoker</td>
<td>719/1872</td>
<td>1.00</td>
</tr>
<tr>
<td>Current smoker</td>
<td>345/695</td>
<td>1.08 (0.97-1.22)</td>
</tr>
<tr>
<td>Former smokers</td>
<td>260/819</td>
<td>1.18 (1.06-1.30)</td>
</tr>
<tr>
<td>Cessation before menopause</td>
<td>134/359</td>
<td>1.03 (0.88-1.20)</td>
</tr>
<tr>
<td>Cessation after menopause</td>
<td>126/260</td>
<td>1.23 (1.01-1.51)</td>
</tr>
</tbody>
</table>

**Table 3. Odds Ratios (ORs) and 95% Confidence Intervals (CIs) Regarding Premenopausal and Postmenopausal Smoking and Risk of Hip Fracture**

<table>
<thead>
<tr>
<th>No. of Cases/Controls</th>
<th>Age-Adjusted OR (95% CI)</th>
<th>Multivariate OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No smoking</td>
<td>719/1872</td>
<td>1.00</td>
</tr>
<tr>
<td>0-10</td>
<td>231/612</td>
<td>1.19 (0.97-1.47)</td>
</tr>
<tr>
<td>11-20</td>
<td>171/285</td>
<td>1.33 (1.04-1.73)</td>
</tr>
<tr>
<td>&gt;20</td>
<td>173/251</td>
<td>1.44 (1.11-1.85)</td>
</tr>
</tbody>
</table>

**Adjusted for age, use of hormone replacement therapy, body mass index, and alcohol consumption (grams per day).**

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*R* n = 1294.

† n = 3216.

‡ Among ever smokers.

§ Expressed as the number who drank that beverage/the number who responded to the question about that beverage, with percentage in parentheses.

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*Adjusted for age, use of hormone replacement therapy, body mass index, and alcoholic beverage consumption (grams per day).*
crease the incidence of hip fracture and may modestly contrast, moderate alcohol intake does not appear to in-
cessation offers the prospect of normalization of risk. In with regard to postmenopausal hip fracture; sustained epidemiologic studies.
itory findings between in vitro studies and the incon-
testrogenic" effect that could explain the contradic-
tion and risk of hip fracture have been conflicting,
proposed.
Direct effects of nicotine on osteoblasts also have been pro-
posed.25
Previous studies of moderate alcohol consump-
tion and risk of hip fracture have been conflicting,
showing no substantial or statistically significant associa-
tion,2,4-6,9,10,24-27 a decreased risk,28 or an increased risk.2,26,29-34 However, heavier alcohol intake (variably
defined) has been associated with an increased risk.3,26
One study found that a preference for beer over other alco-
holic beverages was associated with an increased risk.6,26

Although data are not entirely consistent, most studies show that moderate alcohol intake appears to in-
crease bone density among postmenopausal women.31-35 although perhaps not in premenopausal
women.36,37 Alcoholism, however, is associated with fracture risk31,38 and an increased risk of osteopo-
rosis.31,39,40 Alcohol consumption has been associated with increases in estrone sulfate concentra-
tions, an "estrogenic" effect that could explain the contradic-
tory findings between in vitro studies and the incon-
sistent epidemiologic studies.

These findings point to the complexity of the relation-
ship between lifestyle and osteoporosis. Cigarette smoking—especially late in life—is harmful to women with regard to postmenopausal hip fracture; sustained cessation offers the prospect of normalization of risk. In contrast, moderate alcohol intake does not appear to in-
crease the incidence of hip fracture and may modestly de-
te it.

elevation of cortisol levels, which might affect bone.22

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