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L'influence de la cigarette sur la qualité osseuse chez les femmes lausannoises

Influence of tobacco on bone quality among women living in Lausanne

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Abstract

Cigarette smoking influences negatively bone health and is associated with a higher risk of osteoporotic fractures. Smokers have a lower bone mineral quantity measured by dual x-Ray absorptiometry (DXA), but the impact on the bone quality is less known. Few studies investigated this point in research and a poorer microarchitecture was found by high-resolution peripheral computed tomography (HR-pQCT). For the clinical practice, a new method has recently been developed to evaluate the fracture risk linked to the bone structure in osteoporotic women and men: the trabecular bone score (TBS). In this study, we investigated the bone texture by TBS in addition to the bone quantity by bone mineral density (BMD) in the population-based OstéoLaus cohort of 1'500 randomly selected Caucasian women aged 50 to 80 years living in Lausanne. 1'082 were non-smoker and 238 were smoker. After adjustments for age, BMI, calcium and vitamin D intake and menopausal hormone therapy (MHT) exposition, we found that smoker women had a lower BMD at the total hip and a lower TBS. The BMD difference at the other sites was not significant between groups. In conclusion, in our study, cigarette smoking had an impact on bone quality measured indirectly by TBS among the post-menopausal Caucasian women living in Lausanne. Regarding the density, we can recommend to measure the femur, which is a better site than the spine to show the effect of tobacco.

Keywords: osteoporosis, bone quality, trabecular bone score, tobacco, cigarette

Introduction

Osteoporosis is a chronic metabolic disease characterized by a progressive loss of bone mass and microarchitectural deterioration ultimately resulting in an increased risk of fragility fractures and a greater morbidity and mortality[1] [2,3]. Major osteoporotic fracture sites are the hip, the spine, the humerus and the wrist.

The risk factors for developing osteoporosis are nowadays well known. Some of them are pooled in an algorithm, called FRAX® [4-6], used to assess the 10-year probability of hip or major osteoporotic fractures. Cigarette smoking influences negatively bone health and is part of the FRAX algorithm [7].

It has been known for years that not only bone quantity but also bone quality plays a role in osteoporosis. Although many studies have shown that smokers have a lower BMD[7-10] and a higher risk of fractures [7,11-13], studies investigating the effect of smoking on bone quality are rare[14,15]. Most of them used HR-pQCT at the radius and the tibia, peripheral sites of the skeleton, to evaluate the bone microarchitecture. In a study conducted by Szulc et al., they found a greater loss of trabecular microarchitecture among the current smokers when compared to the former smokers and the non-smokers [15]. For the clinical practice, a new method has recently been developed to evaluate the fracture risk linked to the bone structure in osteoporotic women and men: the trabecular bone score (TBS) [16-18]. TBS is a gray-level measurement derived from the 2D DXA image, is known to strongly correlate to 3D microstructure parameters[19] and bone histomorphometry[20], and provides information which is independent from the BMD and the clinical risk factors[21] [22].

The aim of this study was to evaluate the impact of tobacco on bone quality as assessed indirectly by TBS in the women from the OstéoLaus cohort.

Materials and method

Participants

OstéoLaus is a population-based cohort of 1'500 randomly selected Caucasian women aged 50 to 80 years living in Lausanne, Switzerland, and followed every 2.5 years. Amongst other classical clinical factors for osteoporosis, those women were asked about their smoking habits (FRAX® questionnaire), and had both spine and femoral BMD measurements by DXA and a spine bone texture analysis by TBS. For this study, we used baseline data and excluded the women having hyperparathyroidism or malabsorption, being on corticosteroids or anticancer treatments, and being non-Caucasian.

After applying exclusion criteria, the participants were divided into smokers and non-smokers. All patients participating in this study gave their informed consent.

Image acquisition

The DXA used is a Hologic Discovery A (Hologic Inc., Bedford, MA, USA). We perform BMD of the lumbar spine (vertebrae L1-L4), the total hip and the femoral neck. TBS is analyzed by the means of DXA images of the lumbar spine. The software used for TBS calculation is TBS iNsight® Version 2.1 (Med-Imaps, Merignac, France). The TBS ranges updated according to the recent individual level meta-analysis[21] are: TBS ≥ 1.31: normal, 1.31 > TBS > 1.23: partially degraded, TBS ≤ 1.23: degraded.

Statistical analyses

We described our population as means and standard deviations for the quantitative variables, and as numbers and percentages for the qualitative variables. We collected and compared the BMD and TBS values for patients according to their tobacco consumption to look at significant differences in term of quantity and quality

of bone. Student's t test was used to compare quantitative parameters between the included and the excluded women, and chi-square test for the qualitative parameters. Oneway anova was used in order to compare the quantitative characteristics between our two groups, the smokers and the non-smokers, and chi-square test was used when comparing the qualitative characteristics.

The differences between the groups were assessed with adjustments for age, BMI, calcium and vitamin D intake and menopausal hormone therapy (MHT) exposition.

We considered a comparison as statistically significant when the p-value was < 0.05.

All statistical analyses were performed using the statistical software program STATA v14.1 (StataCorp).

Results

Description of our population

Our population involved 1'475 women. The mean age was 64.52 ± 7.59 years, and the mean BMI 25.91 ± 4.54 kg/m^2. 1'210 women were non-smoker, while 265 were smoker. We excluded 155 participants and included 1'320 women. The excluded women had a significantly higher BMI (27.3 ± 4.49 kg/m^2 vs. 25.75 ± 4.52 kg/m^2, $p < 0.01$), but no differences were found in mean age (63.61 ± 7.06 years vs. 64.63 ± 7.64 years, $p = 0.11$), alcohol intake (4.2 ± 5.7 units/week vs. 4.083 ± 5.12 units/week, $p = 0.79$), and percentage of smoker (17.42 % vs. 18.03 %, $p = 0.85$). Among the included women, 1'082 were non-smoker and 238 were smoker. The mean ages were 65.20 ± 7.66 years vs. 62.02 ± 7.02 years, $p < 0.01$ and the mean BMIs 26.00 ± 4.53 kg/m^2 vs. 24.62 ± 4.3 kg/m^2, $p < 0.01$, respectively for the non-smokers and the smokers. Alcohol intake (3.768 ± 4.73 units/week vs. 5.517 ± 6.44 units/week, $p < 0.01$, resp. non-smokers and smokers) and percentage of women exposed to MHT (56.38% vs. 44.12%, $p < 0.01$, resp. non-smokers and smokers) were also statistically different. However, no significant difference was found for the percentage of women taking calcium and vitamin D substitution (44.45% vs. 39.08%, $p = 0.130$). Table 1.

Bone health and smoking status

Without any adjustments, no significant differences between the non-smokers and the smokers were noted in spine BMD (0.926 ± 0.16 vs. 0.913 ± 0.16, $p = 0.26$), femoral neck BMD (0.729 ± 0.11 vs. 0.721 ± 0.12, $p = 0.29$), and TBS (1.366 ± 0.1 vs. 1.354 ± 0.09, $p = 0.09$). However, a significant difference was found between the groups for total hip BMD (0.857 ± 0.12 vs. 0.839 ± 0.12, $p = 0.04$). The smokers had lower values than the non-smokers. Table 2. After adjustments for age, BMI, MHT,

calcium and vitamin D substitution, no significant differences between the two groups were noted in spine BMD (0.926 vs. 0.913, $p^{adj} = 0.28$) and femoral neck BMD (0.729 vs. 0.721, $p^{adj} = 0.36$). However, significant differences were found for total hip BMD (0.857 vs. 0.839, $p^{adj} = 0.03$) and TBS (1.365 vs. 1.354, $p^{adj} < 0.01$). The smokers had lower values than the non-smokers. Table 2.

Discussion

In this study, we found a significant lower BMD at the total hip and a significant lower TBS among the Caucasian smoker women versus the non-smoker women from the OstéoLaus study. The BMD difference at the other sites was not significant between our groups even after adjustments for age, BMI, MHT, calcium and vitamin D substitution.

Many studies have previously investigated the impact of smoking on bone quantity and found significant BMD differences between smokers and non-smokers at different sites of the skeleton[8,14]. The smoking status is included in the FRAX® calculator[7], but this is not clear if it has an impact in term of BMD at all sites of osteoporosis.

Hollenbach et al.[8] analyzed prospectively the effect of cigarette smoking on bone density among the participants of the Rancho Bernado Heart and Chronic Disease Study. This cohort included 1'258 Caucasian men and women aged 60 years or older. The BMD measurements were taken at the spine, the hip, the midradius and the distal radius. As our study, the results were statistically significant only at the hip in both men and women.

Law et al.[23] published a meta-analysis of 29 cross-sectional studies investigating the BMD values among smoker women and non-smoker women. The BMD measurements were taken at the femoral neck, the radius or the calcaneus bone, and were combined. Among the postmenopausal women, the current smokers had an additional 0.2% reduction of bone quantity per year at all sites compared to the non-smokers. The effect on BMD was independent from body weight and physical activity. They did not examine the effect on the spine.

In another meta-analysis, Ward et al.[9] reviewed 86 prospective and cross-sectional

studies in which men (26%) and women (74%) had a BMD measurement at the hip, the forearm, the lumbar spine or the calcaneus. Among the post-menopausal women, the BMD was lower at all sites among the current smokers compared to the non-smokers. The impact on the BMD was independent from body weight and age.

Nguyen TV et al. [24] analyzed the impact of lifestyle factors, including smoking, on bone mass in people older than 60 years of age. This longitudinal, community-based study, named The Dubbo Osteoporosis Epidemiologic Study (DOES), found that the smokers, both the men and the women, had a lower BMD value at the spine and at the femoral neck compared to the non-smokers. The results were independent from calcium intake and weight.

Jutberger et al.[12] published a prospective study investigating the risk factors of fractures in a Swedish cohort comprising men aged 69 to 80 years. This was a part of the international Mr. OS study. 3'003 men had a BMD measurement at the spine and the femur. The men who were smoker had a lower BMD value at both sites compared to the non-smokers, even after adjustments for age, height, weight, physical activity and calcium intake. Osteoarthritis was not a criterion of exclusion.

Finally in a cross-sectional study, Lee JH et al. [25] investigated the effect of the amount of smoking on BMD in Korean men aged 50 to 64 years. The data came from the Korean National Health and Nutrition Examination Survey hold between 2008 and 2011. The smokers were divided into three groups depending on their number of pack-years of smoking. After many adjustments (age, weight, forced expiratory volume in one second, alcohol consumption, physical activity and vitamin D levels), the heavier smokers had a significant lower total hip BMD, but no significant differences between groups were found at the lumbar spine or at the femoral neck. The men having rheumatoid arthritis were excluded.

Some discrepancies about which sites of the skeleton have a bone quantity impaired by smoking are noticed between our study and previous studies. Many factors might explain them: 1) the size of the populations studied, 2) the exclusion criteria: for example we did not exclude the women having degenerative disorders (as osteoarthritis, sclerosis,…) which influence DXA images and lead to a higher BMD value, 3) the assessment of smoking status: some studies categorized the participants into current smokers, former smokers and never smoked whereas we divided our population into smokers and non-smokers.

Regarding the bone quality, few studies have previously examined the effect of smoking on the bone quality at the radius and the tibia in men using peripheral quantitative computed tomography (pQCT) and high-resolution peripheral computed tomography (HR-pQCT).

Szulc et al. [15] evaluated the skeletal effects of smoking in the cross-sectional STRAMBO study. 810 French men aged 60 to 87 years had a BMD measurement by DXA and a bone microarchitecture investigation by HR-pQCT. The current smokers had a greater loss of trabecular microarchitecture at the tibia and the radius compared to the former smokers and the non-smokers after adjustments for weight, height, age, alcohol and calcium consumption, and physical activity.

Rudäng et al. [14] published a study about the impact of smoking on bone mass development in young adult men from the Gothenburg Osteoporosis and Obesity Determinants (GOOD) study. 833 men aged 23 to 25 years had a bone quality examination by HR-pQCT at 5 years follow-up. The smokers had a lower trabecular thickness and a lower trabecular bone volume fraction at the tibia compared to the non-smokers even after adjustments for age, weight, height, calcium and alcohol consumption and physical activity.

Those studies have shown an impact of smoking on bone quality in men, but have not investigated women. Moreover, pQCT and HR-pQCT are used at the radius and the tibia, peripheral parts of the skeleton, and cannot be used at the spine and in clinical routine. The impact of smoking on the bone quality at the spine in women had never been investigated.

TBS is a new tool allowing the evaluation of bone quality at the spine by analyzing its texture[19]. TBS analysis can be used as a clinical parameter to predict the risk of fracture among men and postmenopausal women[18,22]. It adds important information in the evaluation of bone health and improves the prediction of fractures when combined with BMD measurements.

By using TBS, our study is the first one demonstrating the impact of smoking on the bone quality of the axial skeleton among postmenopausal women.

Our significant results are not of a strong magnitude and our study has limitations that should be kept in mind. First, our cohort involved only post-menopausal Caucasian women. Second, smoking status is hard to evaluate and might be biased. Indeed, some people deny smoking. In addition, we did not take into account the number of cigarettes smoked per day, for how long they have been smoking, nor the amount of smoke inhaled. Those parameters may vary significantly between people. The decline of bone mass is associated with the dose of cigarette exposure and the smokers should have been stratified in many groups depending on the number of cigarettes smoked per day. Moreover, our population was divided into current smokers and non-smokers. Some non-smoker women may have smoked in their past, as well as some smokers may have just started. As smoking cessation influences bone density and quality, another group should have contained the former smokers. Third, many other confounding factors that the ones tested (age, BMI,

alcohol consumption, calcium and vitamin D intake, and MHT) have an impact on bone health and were not taken into account. We can mention mechanical stress, physical activity, diet, pharmaceuticals, early menopause and some diseases. Fourth, we had too few data on prevalent osteoporotic fractures and we were not able to evaluate the prediction of them by the BMD and/or the TBS.

On the other hand, the strengths of our study are the size of the OstéoLaus cohort, which involves a large sample of women, and the high quality of the radiological techniques that allows precise measurements of BMD and TBS.

In the near future, we will be able to compare the TBS values gathered at baseline with those gathered at the follow-up in order to analyze the evolution of bone quality among those women.

In conclusion, in our study, cigarette smoking has an impact on bone quality, measured indirectly by TBS, among the post-menopausal Caucasian women living in Lausanne. Regarding the density, we can recommend to measure the femur, which is a better site than the spine to show the effect of tobacco.

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Tables

Variables	Non-smoker (1082 women)	Smoker (238 women)	p
Age (years)	65.20	62.02	*< 0.01*
BMI (kg/m2)	26.00	24.62	*< 0.01*
Alcohol (units/week)	3.768	5.517	*< 0.01*
MHT	610 (56.38%)	105 (44.12%)	*< 0.01*
Calcium	481 (44.45%)	93 (39.08%)	0.130

Table 1: Characteristics of the included population. BMI: body mass index, MHT: menopausal hormone therapy.

Variables	Non-smoker (1'082 women)	Smoker (238 women)	p	p^{adj}
Age	65.20	62.02	**< 0.01**	
Spine BMD g/cm2	0.926	0.913	0.26	0.8962
Femoral neck BMD g/cm2	0.729	0.721	0.297	0.3622
Total hip BMD g/cm2	0.857	0.839	**0.0403**	**0.0363**
TBS	1.365	1.354	0.09	**< 0.01**

Table 2: Bone health and smoking status. p: p-value without adjustments; p^{adj}: p-value adjusted for age, BMI (body mass index), MHT (menopausal hormone therapy), calcium and vitamin D substitution.

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