G Model
JICC 442 No. of Pages 4
ARTICLE IN PRESS
Journal of Indian College of Cardiology xxx (2017) xxx–xxx
Contents lists available at ScienceDirect
Journal of Indian College of Cardiology
journal homepage: www.elsevier.com/locate/jicc

Relationship between impaired forearm endothelial function and osteoporosis in Tunisian postmenopausal women: Serum lipids or others factors?

K. Baccouche[a,*], H. Ben fraj[a], H. Debbabi[b], S. Belghali[a], N. Elamri[a], H. Zeglaoui[a], E. Bouajina[a]

[a] Department of Rheumatology, CHU Farhat Hached Hospital, Ibn Eljazzar University, Sousse, Tunisia
[b] Department of Physiology, CHU Farhat Hached Hospital, Ibn Eljazzar University, Sousse, Tunisia

ARTICLE INFO

Article history:
Received 21 November 2017
Accepted 12 December 2017
Available online xxx

Keywords:
Endothelial function
Menopause
Bone mineral density
Osteoporosis
Serum lipid

ABSTRACT

Aims: Recent research suggests that bone loss and vascular endothelial dysfunction are functionally interwoven in postmenopausal women. The aim of our study was to assess the relationship between forearm endothelial function and bone mineral density in postmenopausal women.
Methods: We studied the endothelial function of resistance arteries of the forearm in 113 Tunisians postmenopausal women, 75 with normal bone mineral density (BMD) and 38 with osteoporosis. Skin blood flow (SBF) was measured by laser Doppler during three cumulative doses of acetylcholine by iontophoresis (endothelium dependent vasodilatation: EDV) and after local heating (endothelium independent vasodilatation: EIV). Dual-energy X-ray absorptiometry was used to measure BMD of the hip and lumbar spine (L1–L4).
Results: women with normal BMD had a higher maximal EDV ($415,9 \pm 410\%$) than those with osteoporosis ($111 \pm 135\%$) ($P = .03$), even after adjusting for a variety of confounding factors (age, body mass index, years since the start of menopause, weekly exercise and cardiovascular diseases). For the EIV, no difference was detected between the two groups. In addition, we found no difference in serum lipid, lipoprotein and apolipoprotein concentrations, between the two groups. In multivariate regression analysis, the EDV was correlated only with lumbar spine BMD ($p = ,026$).
Conclusion: our study supports the hypothesis that postmenopausal women with osteoporosis have a weak forearm endothelial function.

1. Introduction

Many epidemiological studies have shown an association between osteoporosis and atherosclerotic diseases in the elderly or postmenopausal women.[1,2] Endothelial dysfunction is thought to be one of the initial stages in the development of atherosclerosis. The endothelium plays a major role in determining vascular tone through the production and release of vasodilators such as nitric oxide (NO), which helps to prevent atherosclerosis by maintaining vasodilation and inhibiting platelet aggregation, leukocyte adhesion, and the proliferation of smooth muscle cells.[3,4] Recent research suggests that bone loss and vascular endothelial dysfunction are functionally interwoven in postmenopausal women. It appears that cardiovascular disease and osteoporosis are linked to common inducing factors which act at the same time on both vascular and bone cells. Hormones and inflammatory mediators seem to be the most involved factors in this link.[5,6] Oxidized lipids, likewise, can be a common factor between these two diseases.[7] The aim of our study was to assess the relationship between forearm endothelial function and bone mineral density in postmenopausal women.

2. Methods

We have included 113 postmenopausal women who presented to our clinic between 2010 and 2011. We did not include any woman who has had a menopause for less than one year and any woman who has had a hormonal replacement therapy or any steroid hormones or medications known to affect lipid metabolism or bone metabolism. Consent for participation was obtained, prior to enrolment, from each subject.

* Corresponding author at: Department of Rheumatology, CHU Farhat Hached Hospital, Ibn Eljazzar medicine University, Sousse, Tunisia.
E-mail address: bac.khad@yahoo.fr (K. Baccouche).

https://doi.org/10.1016/j.jicc.2017.12.003
1561-8811/

Please cite this article in press as: K. Baccouche, et al., Relationship between impaired forearm endothelial function and osteoporosis in Tunisian postmenopausal women: Serum lipids or others factors?, J Indian Coll Cardiol. (2017), https://doi.org/10.1016/j.jicc.2017.12.003

Individuals were assigned to one of two groups according to BMD in the lumbar spine and/or the hip. A standardized score, called T-score, comparing BMD to average values for young healthy women is used to define the categories. We defined normal BMD group (T-score −1.0 and above, n = 38 women) and osteoporosis group (T-score −2.5 and below the mean value for young healthy women, n = 75 women). An expert panel of World Health Organization defined this classification system.[8] Each patient had a questionnaire about the following information: age, years since menopause, smoking habits, alcohol consumption, weekly exercise, history of diabetes, dyslipidemia and/or cardiovascular diseases. Body mass index (BMI) was calculated for all patients and defined as the body mass divided by the square of the body height, and expressed in units of kg/m. Dual-energy X-ray absorptiometry (DXA) was used to measure BMD in the hip and lumbar spine (L1–L4) for each woman. The same technician analyzed all of the scans.

2.1. Measurement of forearm endothelial function

Endothelium-dependent and −independent vasodilation of the forearm skin microcirculation was evaluated by iontophoresis and skin heating in combination with laser Doppler flowmetry (LDF). The validity of this method has been demonstrated in previous studies.[9–11] According to the data, after the subjects had rested in supine position for 10 min, imaging of the forearm arteries and measurement of vasodilator responses were elicited using a laser Doppler flowmetry (LDF). It is a technique studying the microcirculation and can thus visualize the phenomena of subcutaneous blood flow variation by noninvasive probe.

These variations depend on the rate and number of red blood cells, hematocrit, tissue optic properties, and vascular network geometry.

2.1.1. Measuring equipment

- A laser probe to receive and emit the laser spindle.
- A PERIMED PF 383 electrode (positive),
- A few drops of acetylcholine at 2% (Ach).
- A measuring device for the laser signal (PF 5010 Doppler Laser Monitor) and the skin temperature (PF 5020 thermal module).
- A battery PERIMED PF 382b Power Supply for the delivery of the current,
- Computer software (PSW2) and a computer.
- A PERIMED PF 384 gel electrode (negative).

2.1.2. Procedure

Patients were studied between 8 and 12 a.m. after an overnight fast. The measures were performed in a temperature-controlled quiet room (24–25 °C) after the subjects had 10 min of semisupine rest. For each patient we followed the following steps:

- Fix the electrode on the laser probe.
- Pour a few drops of Ach to deceive the little rag of the electrode.
- Fix the electrode on the smooth skin (sensitive to the transcutaneous injection of the Ach) of the forearm of the patient in question, while avoiding the veins.
- At 10 cm from the first, a second gel electrode (negative) is coupled, both coupled to the battery delivering the current for 10 s and at 10 mA,
- For each subject, the basic state is measured for 2 min.
- After 4 min, the injection of the first dose of Ach is started for 2 min.
- Two minutes later, the second dose is injected.
- Two minutes later, we inject the third dose and we take the maximum vasodilator response of the 3 injections (Response endothelium dependent),
- Two minutes later, there will be a follow-up of the action of the increase of the temperature at 44 °C for 5 min and a recording of the maximal response to local skin heating, i.e. the maximal vasodilatation (non-endothelium dependent Response).[11]

The responses are calculated as a percentage (%) increase in arterial diameter during Ach injections (endothelium-dependent) and temperature increase (non-endothelial dependent response).

2.2. Serum lipids samples

Blood samples of the serum lipids were collected in the morning after fasting overnight (12 h). We used enzymatic assay based on a Vitros-250 (Johnson & Johnson) to dose serum total cholesterol, triglyceride, and high-density lipoprotein (HDL) cholesterol. LDL cholesterol was calculated by Friedewald formula ($LDL-C = TC-HDL-C-0.45 \times TG$).[11] Lipoprotein (a), ApoA1, and ApoB were measured by the Cobas Mira (Hoffman-La Roche) automatic blood analyzer.

2.3. Statistical analysis

Student's *t*-test was used to compare the clinical characteristics among the 2 groups. Univariate correlation analysis was used to determine the Confounding factors between BMD and endothelial function (EF). The laboratory data for the 2 groups were compared by using Mann-Whitney u test, after adjusting for confounders. Pearson's correlation coefficient analyses were used to examine the relationships between the values of EF and the values of BMD and other clinical variables. Furthermore, multiple regression analysis was performed among the values of EF and the values of BMD and other clinical variables. The p values .05 were considered to denote statistical significance. Data are expressed as mean ± SD. The statistical analyses used the SPSS 11.0.

3. Results

Table 1 summarizes the characteristics of the groups. Age and years since the onset of menopause were significantly greater in the osteoporotic group (P .001 for). Body mass index and Weekly exercise were significantly lower in the osteoporotic group (p respectively .001 and .038). Endothelium dependent vasodilatation (EDV) and endothelium independent vasodilatation (EIV) were significantly lower in the osteoporotic group (p respectively .01 and .04). There were no significant differences in serum lipid level between the 2 groups; likewise, no difference was detected in other characteristics among the 2 groups. In a further analysis using Mann-Whitney u test (Table 2), adjusted for confounding factors (defined as age, body mass index, years since the onset of menopause, weekly exercise and cardiovascular diseases), postmenopausal osteoporotic women had a lower EDV than those of normal BMD group (p = .03). However, the significant difference of the EIV between the two groups has disappeared. Multivariate regression analysis (Table 3) revealed that the EDV was positively correlated with only lumbar spine BMD (p = ,026), but showed no significant association with hip BMD nor with other variables

4. Discussion

The present study showed an impaired response of skin blood flow of the forearm to the iontophoresis of acetylcholine in postmenopausal women with osteoporosis than in those with normal bone mass. It was positively correlated with lumbar spine BMD. The association between forearm endothelial function and lumbar spine BMD has been shown in several Studies. Sanada et al[12] reported that postmenopausal women with a lower lumbar

Please cite this article in press as: K. Baccouche, et al., Relationship between impaired forearm endothelial function and osteoporosis in Tunisian postmenopausal women: Serum lipids or others factors?, J Indian Coll Cardiol. (2017), https://doi.org/10.1016/j.jicc.2017.12.003