DIABETES AND OBESITY AS INDEPENDENT RISK FACTORS FOR OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN: A POPULATION STUDY

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We aimed to analyze bone mineralization and the effect of different risk factors for osteoporosis in postmenopausal women. We studied 2,756 postmenopausal subjects out of ≥10,000 records from the ROIS registry in the frame of the PROF Project, a population study carried out in Salento (Taranto, Brindisi, Lecce) from 2009 to 2012. All subjects were assessed by phalangeal Quantitative Ultrasound (QUS) to evaluate their bone mineralization (assessed by Amplitude Dependent Speed of Sound, AD-SoS) and the association between demineralization and the presence of other conditions or risk factors. Mean age was 64±9.5 years and mean BMI was 28.7±3.5 Kg/m². Pearson correlation analyses revealed a negative association between bone mineralization (AD-SoS) and BMI (P<0.001). By using multivariate logistic regression analysis, we observed significant values of Odds Ratios of osteoporosis (adjusted for age, physical activity and the use of drugs known to increase the risk of fractures) in subjects with diabetes and obesity: 1.39 (CI: 1,05-1,83) and 1.46 (CI: 1.20-1.78), respectively. A statistically significant linear trend of higher Odds Ratios of osteoporosis was found for increasing values of BMI. The percent change in the odds of vertebral fractures per single SD decrease of AD-SoS was 47% (P<0.001). Diabetes and obesity in postmenopausal women are likely to represent independent risk factors for osteoporosis. Phalangeal QUS showed a good power of predictivity in identifying subjects with vertebral fractures.

Osteoporosis and fragility fractures represent a growing health problem in developed countries in terms of social costs and increased risk of death, especially in the elderly (1). Fracture incidence

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rates are closely related to the ageing of population, as older people present higher fracture rates than younger subjects with the same bone mineral density (2). This is due to a lower bone quality and a higher tendency to fall. It is estimated that 25% of women aged 80 years and over have already undergone at least one vertebral fracture (3).

According to the ESOPO study (Epidemiological Study On the Prevalence Osteoporosis in Italy), about 5 million Italians suffer from osteoporosis, with almost 1.5 million of these subjects being "at high risk" of femoral fracture because they have already experienced one or more vertebral fractures (4). Hospital costs of femoral fractures in the elderly Italian population account for 1 billion Euros per year (5). Prevention of osteoporosis is traditionally based on bone measurement tests, aimed to predict the risk of future fragility fractures. Diagnostic criteria for osteoporosis are based on Dual Energy X-ray Absorptiometry (DXA) measures, carried out at the hip or lumbar spine. DXA is considered the gold standard methodology for the diagnosis of bone demineralization. However, other kinds of diagnostic tests are available. Quantitative Ultrasounds (QUS) at calcaneal (heel) or phalangeal sites represent the most commonly used non-DXA methodologies. This kind of radiation-free test was shown to be user-friendly, cheap, non-invasive, and, most importantly, it is able to discriminate subjects at increased risk of fragility fracture (6). Quantitative Ultrasounds (QUS), developed by Langton et al. in 1984, have been decided for the evaluation of bone quality and skeletal disorders on the basis of various experiments which suggested that the ultrasonic parameters could provide information not only on bone density, but also on micro-architecture and elastic properties of bone tissue (6). The phalangeal QUS methodology was introduced in Europe in the years 1992-1993 and a series of studies were performed to validate the method in clinical settings (7). Bone resorption at the proximal phalanx is associated with significant changes in the speed of the ultrasonic signal that passes through the phalanx (8). Benitez et al. performed a comparison between phalangeal QUS and DXA (measured at total hip and lumbar spine), concluding that phalangeal QUS can be effectively used for the screening of osteoporosis in postmenopausal women (9). More recently, the assessment of clinical risk factors has become more and more important in the diagnosis of osteoporosis and to select patients for appropriate treatment.

In this frame, the Euro Mediterranean Biomedical Scientific Institute (ISBEM, Brindisi, Italy) has launched a pilot project for the disease management of osteoporosis, which is aimed at the prevention of fragility fractures through the early identification of people at higher risk through the use of phalangeal QUS and the collection of clinical risk factors in the R.O.I.S. registry (Ionian and Salento Osteoporosis Registry). The currently ongoing PR.O.F. project (Prevention of Osteoporosis and Fractures Project), started in 2009 thanks to a strong cooperation between ISBEM researchers and physicians from the Local Health Authorities ASL Brindisi, ASL Taranto and ASL Lecce (limited to the hospital of Gallipoli, Division of Orthopedics and Traumatology). This population study is of particular interest because it takes place in Salento, which represents the "oldest" area of Apulia and of the entire Southern Italy, as it is characterized by an "ageing index" (number of people aged ≥65 vs young people ≤14 years old) very closely reflecting the national average value (which has risen up to 143) (10). Therefore, this population could be considered representative of the whole Italian population and could be particularly useful both for case-control analyses and prospective cohort studies, thanks to the monitoring activities carried out within the ROIS registry integrated in the PR.O.F. project. In this work, we present the first results of the PR.O.F. project, focusing on the association between some major clinical conditions (i.e. obesity, dyslipidemias, diabetes, hypertension, cardiovascular diseases, rheumatic diseases and previous fractures) and bone demineralization.

MATERIALS AND METHODS

Subjects

The PR.O.F. study is a disease management project for the prevention of fragility fractures carried out at the ambulatorial and hospital centres for the diagnosis and treatment of osteoporosis of Local Health Authority of Brindisi, Taranto and Lecce (limited to the Hospital of Gallipoli, division of Orthopedics and Traumatology). Each subject was provided with adequate information regarding the privacy policy and each person was asked to sign her approval to the data processing for the purposes

of the study according to the current privacy. Before the kick-off of the project, ISBEM researchers had developed a questionnaire to record the main clinical information of each patient; the questionnaire incorporated all the mandatory fields and items of the electronic form developed by the Italian Society for Bone and Mineral Metabolic Diseases (SIOMMMS). During the enrollment visit, the weight of all patients was recorded, with a tolerance of 0.5 kg; standing height was measured on the balance stadiometer to the nearest centimeter. Body Mass Index (BMI) was calculated as weight/height^2 (Kg/m^2); obesity was defined as the presence of BMI ≥30. Each subject was interviewed about the frequency of alcohol consumption, cigarette smoking, calcium intake (by milk and dairy products), physical activity, previous fractures, parental history of osteoporotic fractures, age and cause of the menopause. In the interview, the presence of diseases known to be associated with osteoporosis and any other diseases was specifically recorded, as well as any previous or current use of anti-fracture drugs (including vitamin D and calcium supplementations), therapies influencing bone mineralization (i.e. corticosteroid, immunosuppressive, heparin, antiepileptic, antiestrogens and chemotherapies) or any other current treatment for other diseases. The use of drugs known to increase the risk of falls (i.e. benzodiazepines or hypnotics) was also recorded. Physical activity was assessed by a specific score (0=no physical activity; 1=moderate physical activity; 3=heavy physical activity).

All data were entered into the ROIS registry (Ionian and Salento Osteoporosis Registry). Between February 2009 and December 2012 approximately 10,000 consecutive patients undergoing bone densitometric examination by Quantitative Ultrasound (QUS) were enrolled in the PR.O.F. project and included in the R.O.I.S. registry. However, the number of enrolled subjects presenting a complete dataset of clinical variables and QUS measurements needed for the purpose of this study were 3,354 (311 men, 3,043 postmenopausal women, and 287 pre-menopausal patients). Premenopausal women, men, subjects with extreme BMI values (<18.5 and >50), and thalassemic patients examined at Taranto and Brindisi thalassemia centres were excluded from this study, so that the final sample analyzed consisted in 2,756 postmenopausal women.

Ultrasound measurements

Ultrasound measurements were performed for all subjects using DBM Sonic Bone Profiler 1200 (Igea®, Carpi, Italy). This device is based on the transmission of ultrasounds through proximal phalanges (II- V) of the fingers of the dominant or non-dominant hand; transmitting and receiving probes are applied to the lateral surface of each finger; the coupling of the probes with the skin is accomplished by using simple gel for ultrasound transmission. At each measurement session, the reference values of the patient's soft tissue were measured by applying the probes to the soft tissue of the hand ("anatomical snuff box"). The measurements were made by placing probes at the distal metaphysis of the first phalanges, in the proximity of the condyles. The measurement outcomes provided by the device were: Amplitude-dependent speed of sound (AD-SoS, m/s) and AD-SoS T- Score, where this latter parameter compares the measured AD-SoS value with the average value of young adults and it is expressed in standard deviations (SD). For this device, the specific T-score diagnostic threshold discriminating between healthy and osteoporotic people at increased risk of fractures was set up in a large study carried out on a population of 10,000 subjects and corresponds to -3.2 SD (11).

Statistical analysis

All statistical analyses were performed by using STATA/SE 11 software for Windows (STATA® 11.0, Texas, USA). Obesity, dyslipidemia, diabetes, hypertension, cardiovascular diseases, rheumatic diseases and previous fractures were used as dichotomous variables. Continuous data were presented as mean value ± SD; frequency and percentage of dichotomous variables were computed. Baseline characteristics of osteoporotic, osteopenic and normal postmenopausal subjects were compared by ANOVA for continuous variables and by chi-squared test for categorical variables.

Pearson correlation coefficients were calculated to assess the association between AD-SoS and BMI. Linear regression analysis was carried out to test the presence of linear trend among different classes of BMI for all the clinical variables.

Multivariate analysis was performed using a logistic regression model to assess the association between bone demineralization status and diabetes, hypertension, cardiovascular diseases and obesity. Models were adjusted to eliminate the effects of age, physical activity and that of previous or current use of any drug known to be associated to bone demineralization.

Mantel-Haenszel odds ratios of osteoporosis, crude and adjusted for age, physical activity and previous or current use of osteoporosis-inducing drugs, were calculated to assess the effect of the classes of BMI on the odds of being osteoporotic.

RESULTS

Table I summarizes baseline characteristics of

postmenopausal women stratified by their bone mineralization status (osteoporosis, osteopenia and normal). Mean age was higher in osteoporotic subjects (70.7±8.6) than in osteopenic (62.8± 8.3) and normal subjects (55.5±7.4). Osteoporotic subjects presented a higher mean BMI (29.84; SD 5.57) than osteopenic (28.64; SD 5.19) and normal people (26.72; SD 4.84). AD-SoS mean values were significantly higher (P<0.001) in normal subjects (2,086.8 m/s; SD 40.1) than in osteopenic (1973.5 m/s; SD 46.5) and osteoporotic patients (1,833.2 m/s; SD 65.7; P<0.0001).

The frequency of obesity, hypertension, type 1 and type 2 diabetes, dyslipidemia and cardiovascular diseases was significantly higher in osteoporotic subjects (P<0.001). No statistically significant differences were found among the three groups for the presence of rheumatic diseases and in case of previous or current use of drugs known to be associated to bone demineralization. Pearson correlation analysis between AD-SoS and BMI revealed a negative correlation: r = -0.2 (P<0.0001).

Table II presents the results of multivariate logistic regression analysis between osteoporotic

Table I. *Baseline characteristics of postmenopausal women stratified by bone mineralization status.*

	Osteoporotic	Osteopenic	Normal	p value
N	722	1,701	333	
Age, years	70.7± 8.6	62.8± 8.3	55.5± 7.4	<0.001
Weight, kg	71.3±13.7	70.3± 12.8	67.3 ±12.1	<0.001
Height, cm	1.55±0.07	1.57±0.07	1.59±0.06	<0.001
BMI (kg/cm^2)	29.84±5.56	28.64±5.19	26.71±4.87	<0.001
AD – SoS, (m/s)	1833.2±65.7	1973.5 ±46.5	2086.8±40.1	<0.001
Phalangeal T- Score	-4.20±0.92	-2.14±0.59	-0.50± 0.43	<0.001
Smoking, yes (%)	44 (6.09)	157 (9.23)	46 (13.81)	<0.001
Alcool, yes (%)	215 (29.78)	430 (25.28)	67 (20.12)	<0.01
Hip fractures, n (%)	25 (3.46)	19 (1.12)	1 (0.30)	<0.001
Vertebral fractures, n (%)	29 (4.02)	17 (1.0)	3 (0.90)	<0.01
Wrist fractures, n(%)	48 (6.65)	43 (2.53)	2 (0.60)	<0.001
Other fractures, n (%)	109 (15.10)	142 (8.35)	5 (1.5)	<0.001
Parental fractures, n (%)	88 (12.19)	277 (16.28)	60 (18.02)	<0.005
Obesity, n (%)	313 (43.35)	601 (35.33)	68 (20.42)	<0.001
Hypertension, n (%)	399 (55.26)	806 (47.38)	110 (33.03)	<0.001
Diabetes type 1 and 2	108 (14.96)	167 (9.82)	19 (5.71)	<0.001
Dislipidemia, n (%)	146 (20.22)	345 (20.28)	31 (9.31)	0.001
Cardiovascular diseases, n (%)	81 (11.22)	131 (7.70)	15 (4.50)	<0.001
Rheumatic diseases, n (%)	46 (6.37)	80 (4.70)	17 (5.11)	0.238
Previous or current use of inducing-osteoporosis drugs, n (%)	129 (17.87)	319 (18.75)	73 (21.92)	0.285
Previous or current use of antifracturative drugs , n (%)	299 (41.41)	460 (27.04)	54 (16.22)	<0.001
Moderate physical activity, yes(%)	220 (30.47)	709 (41.68)	142 (42.64)	<0.001
Regular physical activity, yes(%)	7 (0.97)	58 (3.43)	18 (5.41)	<0.001
Total physical activity, yes (%)	220 (30.5)	706 (41.6)	147 (43.11)	<0.001

status (AD-SoS T-score lower than -3.2 SD) and other conditions such as cardiovascular diseases, diabetes, hypertension and obesity (BMI ≥30). All these conditions presented odds ratios (ORs) > 1, thus resulting significantly associated to diagnosis of osteoporosis (P<0.001 and P<0.01). However, the association between osteoporosis and cardiovascular diseases and hypertension was revealed as not statistically significant after adjustment for age, physical activity and the use of drugs known to be associated to bone demineralization. At the opposite, obesity and diabetes were confirmed to be associated with osteoporosis even after adjustment for age, physical activity and use of osteoporosis-inducing drugs, with OR (CI 95%) of 1.39 (1.05-1.83) and 1.46 (1.20 -1.78), respectively.

All patients were divided into five groups corresponding to different BMI classes: subjects with optimal weight (BMI <25), overweight people (BMI ≥25 but < 30), grade 1 obesity (BMI ≥30 but < 35), grade 2 obesity (BMI ≥35 but <40) and grade 3 obesity (BMI ≥ 40). The average age, BMI, AD-SoS measurements and clinical characteristics for all the five groups are shown in Table III. A significant positive linear trend (P<0.0001) was found across categories of BMI in the frequency of diabetes, cardiovascular diseases, hypertension and dyslipidemia.

We investigated the ORs of osteoporosis for all the five BMI groups, calculating both the crude and the adjusted ORs for age, physical activity and use of osteoporosis-inducing drugs, using the

Table II. *Odds Ratios (ORs) and 95% CIs of osteoporosis (AD SoS T score lower than -3.2 SD) in presence of diabetes, cardiovascular diseases, hypertension and obesity.*

Variables	OR (95 % CI)	p value	Adjusted OR[1] (95 % CI)	p value
Diabetes	1.75 (1.35-2.25)	<0.001	1.39 (1.05-1.83)	<0.05
Cardiovascular diseases	1.63 (1.23-2.17)	<0.01	0.93 (0.67-1.28)	0.645
Hypertension	1.51 (1.27-1.79)	<0.001	0.95 (0.78-1.15)	0.596
Obesity	1.56 (1.31-1.86)	<0.001	1.46 (1.20 -1.78)	<0.001

[1]*ORs were adjusted for age, physical activity and use of osteoporosis-inducing drugs*

Table III. *Baseline characteristics of study population stratified by classes of BMI.*

Variable	Healthy weight (BMI < 25)	Overweight 25 ≤ BMI < 30	Grade 1 obesity 30 ≤ BMI < 35	Grade 2 obesity 35 ≤ BMI < 40	Grade 3 obesity BMI ≥ 40
N	697	1077	652	232	98
Age (years) [1]	62.0 ± 9.8	64.3 ± 9.8	65.0 ± 8.8	65.0 ± 9.0	64.3 ± 8.2
Weight (kg) [1]	57.05 ± 6.21	67.75 ± 6.50	77.56 ± 7.29	86.71 ± 8.03	102.50 ± 12.50
Height (m) [1]	1.58 ± 0.06	1.57 ± 0.06	1.55 ± 0.07	1.53 ±0.06	1.53 ± 0.06
BMI (kg/m^2) [1]	22.75 ±1.75	27.46 ± 1.44	32.03 ± 1.39	36.89 ± 1.42	43.62 ± 3.54
AD SoS (m/s) [1]	1980.9± 93.2	1947.3± 92.8	1939.3± 88.0	1916.6± 97.0	1921.3 ±86.1
Hypertension [n (%)][1]	205 (29.4)	506 (47.0)	376 (57.7)	153 (65.9)	75 (76.5)
Diabetes type 1 and 2 [n (%)][1]	39(5.6)	92 (8.5)	89 (13.6)	50 (21.5)	24 (24.5)
Dislipidemia, [n (%)][1]	98 (14.1)	211 (19.6)	138 (21.2)	51 (22.0)	24 (24.5)
Cardiovascular diseases [n (%)][1]	39 (5.6)	81 (7.5)	66 (10.1)	26 (11.2)	15 (15.3)
Rheumatic diseases [n (%)][2]	43 (6.2)	52 (4.83)	31 (4.8)	11 (4.7)	6(6.1)

[1]*p<0.0001*
[2]*p value no statistically significant*

Table IV. *Crude and adjusted Odds Ratios and 95% CIs of osteoporosis for different BMI categories (optimal weight was chosen as reference group, thus being assigned value=1).*

	OR[2]	p value	Adjusted OR[1,2]	p value
Optimal weight	1		1	
Overweight	1.52 (1.2 - 1.93)	<0.001	1.22 (0.93 - 1.6)	0.151
Grade 1 obesity	1.85 (1.43 - 2.39)	<0.0001	1.4 (1.05 - 1.87)	<0.05
Grade 2 obesity	2.34 (1.67 - 3.27)	<0.0001	1.94 (1.27 - 2.97)	<0.01
Grade 3 obesity	2.76 (1.75 - 4.35)	<0.0001	2.51 (1.38 - 4.56)	<0.01

[1]*ORs adjusted for age, physical activity and use of drugs causing osteoporosis*
[2]*Significant linear trend with increasing BMI category , resultant p value of the score test for trend was <0.0001*

Table V. *Characteristics of study population stratified by presence or absence of vertebral fractures.*

	Vertebral fracture	Without vertebral fracture	p value
N	49	2,707	
Mean Age, years	71.8±6.2	63.8±9.5	<0.0001
AD SoS, m/s	1,951.6 ± 93.7	1,883 ±89.0	<0.0001
BMI, kg/m^2	29.37 ± 5.42	28.71 ± 5.33	0.386
Years since menopause	25.3±8.4	15.4±10.7	<0.0001
AD SoS Tscore under -3.2 SD	29 (59.18)	693 (25.60)	<0.0001
Early menopause,n (%)	20 (40.82)	666 (24.60)	<0.01
Diabetes n (%)	9 (18.37)	285 (10.53)	0.078
Obesity, n (%)	22 (44.90)	960 (35.46)	0.172

class of optimal weight as reference group, thus being assigned value=1 (Table IV). Considering the adjusted ORs, we found a significant linear trend over BMI categories, with a significant score test for trend (P<0.001).

The prevalence of vertebral fractures in our study population of postmenopausal women was 1.78%. The characteristics of the study population stratified by presence or absence of vertebral fractures are shown in Table V.

Among subjects with prevalent vertebral fractures, 59.2% presented AD SoS T-Score under the threshold of -3.2 SD (diagnosis of osteoporosis), whereas among subjects without prevalent vertebral fractures only 25.6% had AD SoS T-score under this threshold. Mean age and AD-SoS values of subjects with prevalent vertebral fractures were significantly lower than age and AD-SoS of non-fractured people (P<0.0001). The prevalence of subjects with early menopause was 40.8% in the fractured group and 24.6 % in the non-fractured group. Statistically significant differences between these fractured and non-fractured people were found also in terms of years elapsed since menopause. There were no statistically significant differences concerning BMI and frequency of subjects affected by diabetes or obesity between fractured and non-fractured people.

By multivariate logistic regression we computed the percent change in odds of vertebral fractures per single SD decrease of AD-SoS in postmenopausal women, showing a value of 47% (P<0.001). Calculating the percent change in odds of vertebral fracture per single SD increase of BMI, a statistically non-significant value of 12.6% was obtained (P= 0.386).

DISCUSSION

This study took place in Salento, a sub-region of Southern Apulia characterized by the same ageing

index of the entire Italian population, therefore being representative of the general population and particularly useful for further analyses as soon as the registry enlargens. The value of this cross sectional study, carried out on 2,756 postmenopausal women, consists in having demonstrated an independent association between obesity or diabetes and osteoporosis as diagnosed by using a radiation-free, non-invasive methodology such as Quantitative Ultrasounds (QUS). This kind of technology has showed no significant difference when compared to DXA in terms of ability to predict hip fractures in large cohorts of patients or discriminate fractured patients (12).

Correlation analysis between BMI and AD-SoS revealed a negative correlation coefficient, demonstrating a negative impact of BMI increase on bone ultrasound velocity at proximal phalanges. This findings seems to confirm the results of a cross-sectional study which found an association between fat mass and osteoporotic fractures (13).

The relationship between osteoporosis and obesity is currently controversial. Considerable evidence, including that from the NORA study, reported that an increasing BMI is associated to a BMD increase (14). These observations could be explained taking into account the mechanical load exerted by the increased body weight, which results in an increase of bone mass (15). Moreover, adipocytes in postmenopausal women represent the main source of estrogens, that are known for their inhibitory activity of osteoclast-mediated bone resorption (16). Finally, obesity is often related to high plasma insulin levels, a fact which contributes to overproduction of sex hormones - estrogens and androgens - responsible for increased osteoblast activity and reduced osteoclast activity (17).

On the contrary, other evidence suggests that obesity might negatively influence bone health (18, 19). This complex relationship between obesity and bone mass could be explained by the effect on bone of a series of adipokines and cytokines secreted by adipose tissue, such as leptin, resistin, adiponectin, interleukin 6, and tumor necrosis factor-alpha (20). A study involving obese patients found a lower lumbar spine BMD than was expected for age and BMI (21). In several studies carried out by using QUS, soft tissues were proved to reduce the speed of sound (SOS) transmitted across bones (22); on the basis of these studies, some authors have proposed that the negative impact of BMI on QUS parameters can be ascribed to the interference of soft tissues (23). In their paper, Biino et al., found a negative correlation between AD-SoS and BMI, with AD–SoS showing the highest correlation coefficient with BMI among all among QUS parameters (23). However, in the same study, the bioimpedance analysis proved that an increase in fat mass results in a negative impact on bone health.

According to the results of our study, the ORs of being osteoporotic for obese subjects as well as for diabetic ones indicate that being obese or diabetic increases the probability of belonging to the osteoporotic group by 46% and 39%, respectively.

When our study population was stratified by class of BMI, the ORs of being osteoporotic confirmed that an increase in the BMI value affects negatively the bone mineralization. As shown in Table IV, considering optimal weight (BMI <25 kg/m^2) as reference group, we found a two-fold probability of being osteoporotic in subjects with grade 2 and grade 3 obesity (ORs=1.94, CI: 1.27 - 2.97, and OR=2.51, CI: 1.38 - 4.56, respectively).

Our findings are consistent with other evidence also concerning the association between diabetes and bone demineralization, where type 1 diabetes has already been associated to a BMD reduction; in people with type 2 diabetes, a higher BMD at the hip has been documented only at baseline, with a rapid bone loss having been observed over time in a longitudinal study (24). Leslie et al. observed that type 2 diabetes is associated with high BMD values, but also to an increased risk of fragility fractures, thus urging for new markers and new preventive approaches to evaluate the risk of fractures in these patients (25); these authors have also suggested to include type 2 diabetes in the questionnaire of the FRAX international algorithm for the fracture risk assessment. A recent study carried out on Canadian women affected by type 2 diabetes confirmed the existence of a "bone fragility paradox": although patients with type 2 diabetes had a normal femoral neck BMD compared to controls, they showed a weaker response to mechanical loading on the neck of the femur when entering a simulated mechanical model depicting forces acting on the femoral bone

(25). As hyperglycemia itself is an important factor in the regulation of osteoclast-mediated bone degradation, several studies have investigated the effect of hyperglycemia in fostering bone quality reduction and microarchitecture impairment in diabetic patients (26). Moreover, non-enzymatic glycation (NEG), which consists of spontaneous reactions between extra-cellular sugars and free amino groups of several matrix proteins including collagen type I, leads to formation of molecular crosslinks which are known as advanced glycation end-products (AGEs). The elevated concentrations of AGEs are known to increase bone fragility (27).

Phalangeal QUS was found to be comparable to DXA in discriminating people at a higher risk of fracture, with QUS being also able to provide additional information for the skeletal assessment in type 2 diabetic patients (28). Considering this ability of QUS to provide the physician with additional information on bone micro-architecture, this technology could be tested for specific use in clinical practice in combination with Spinal Deformity Index (SDI), an index of bone quality used for the diagnosis of osteoporosis in subjects affected by type 2 diabetes. In a recent controlled study involving subjects with type 2 diabetes, the Spinal Deformity Index revealed its ability to identify subjects with vertebral fractures in a more specific way than the simple use of BMD for the diagnosis of osteoporosis (29). Moreover, phalangeal AD-SoS showed the same diagnostic power of lumbar spine BMD in identifying women with or without vertebral fractures (30). Also in our study, the percentage change in odds of vertebral fractures for single SD decrease of AD–SoS was statistically significant and confirmed the ability of phalangeal QUS in identifying fractured people. When analyzing the two groups of subjects with and without vertebral fractures, AD-SoS was significantly lower in the fractured group. However, no statistically significant differences were found between fractured and non-fractured patients in terms of BMI, diagnosis of diabetes and obesity. Therefore, in our postmenopausal sample, it was not possible to associate the increased bone demineralization found in obese or diabetic subjects with an increased risk of vertebral fractures. A possible explanation for that could be found in the lack of data on the value of BMI at the time when the vertebral fracture occurred, so that further research might clarify the role of BMI in determining vertebral fractures.

Diabetes and obesity in postmenopausal women are likely to represent independent risk factors for osteoporosis. Phalangeal QUS showed a good power of predictivity in identifying subjects with vertebral fractures.

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