Definition of Italian Specific DXA References for Diagnosis of Osteoporosis: Preliminary Data from the Osteoporosis Registry of Magenta Rheumatology School (OSTEOREMA)

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Abstract: *Background*: Osteoporosis is the most common metabolic bone disease and dual energy X ray absorptiometry (DXA) scans is the gold standard to evaluate individuals at risk of osteoporosis. Up to date, studies focused on population specific DXA values among general population are lacking. Primary aim of this study was to obtain lumbar and femoral DXA values of Italy adult females based on a nationally representative sample aged 20 years and older, attempting to obtain a national specific normative bone mineral density (BMD) levels curve.

Methods: demographic and anthropometric data of females aged 20 years and older that performed their first DXA (QDR 9000 Hologic, Waltham, Mass.) in our Hospital between 2006 and 2015 were extracted from our local registry using a random sampling technique. Criteria for patient choice were: absence of known risk factors of Osteoporosis (e.g. smoke, alcohol), metabolic disease that affects bone (e.g. diabetes), a normal BMI between 18.5 to 24.5, previous fractures, any medication for treatment of osteoporosis or corticosteroids, spondylosis radiologically relevant. Our database was compared to Caucasian normal values incorporated into Hologic's scan analysis software, that we proven were comparable in terms of BMI, gender and age.

Results: DXA scan of 15335 women were extracted and analysed. Mean age was 64.2 ± 12.8 years (range 20.8 to 90). Mean BMI was 22.4± 5.1 (range 20.1 to 24.3). Mean menopause age was 41.3±5 (range 31-54). Mean menarche age was 16.3±5 (range 11-17). The lumbar and femoral BMD were substantially constant between 25 and 35 years (test for trend using ANOVA: P =0.31); these data collected in premenopausal women (mean 1.043± 0.12 g/cm^2 for lumbar spine and 0.97± 0.136 g/cm^2 for femoral neck) were thus defined as the reference peak bone mass values, significantly lower compared to the Hologic reference values (mean 1.079±0.11 g/cm^2, $p<0.05$). The frequency of osteopenia and osteoporosis were so significantly different depending on whether you use the manufacturer criteria rather than those derived from collected data (X square p=0,01).

Conclusions: our data suggest that the reference curves for the lumbar spine and femoral neck are significantly different from the current normative data reported by the manufacturer for the Italian population.

Keywords: Reference data, Osteopenia, Osteoporosis, prevalence.

INTRODUCTION

Osteoporosis is a metabolic skeletal disease characterized by reduced bone mineral density, which may lead to an increased risk of bone fractures, especially in the wrist, hip, and spine [1,2]. Osteoporosis represents a major public health problem because of increased susceptibility to fractures that increase patient's morbidity and mortality. Patients with proximal hip fracture present a mortality of 15-30% within one year from data fracture [3,4]. In osteoporotic patients, the bone mineral density (BMD) is ≥2.5 standard deviation below the average mineral density of young adults as stated by WHO criteria, and so expressed as T Score. Previous studies indicated that peak BMD is different among ethnicities and between men and women [5-8]. Therefore, the diagnosis of osteoporosis should ideally be based on sex and ethnicity-specific reference range [3-7]. Up-to-date it is not clear whether the reference database used in the derivation of T-scores in densitometers are appropriate for a local population as the Italian one. Our study attempted primarily to determine reference range of peak bone density for an Italian population, and then to compare the concordance between a population and DXA-based T-scores in the diagnosis of osteoporosis [8-12]. The Osteoporosis Registry of Magenta's Rheumatology School (OsteoReMa) is an ongoing single center study that aims to establish reference values for bone DXA in female Italian population. Preliminary data are available for bone mineral density of the lumbar vertebrae (L2-L4) and proximal femur (neck and total), which will be presented in this paper.

MATERIALS AND METHODS

Demographic (age, age at menarche and menopause) and anthropometric (weight, height, BMI) data of females aged 20 years and older that performed their first DXA in our Hospital between 2006 and 2014 were extracted from our local registry using a random sampling technique. Bone mineral density (BMD) was determined using dual-energy X-ray absorptiometry (DXA) on a Hologic bone densitometer

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(QDR 9000 Hologic, Waltham, Mass.). Criteria for patient's data extraction were: solar exposure at least 15 minutes per day, dietary intake of at least 800 mg of calcium daily, absence of known risk factors of osteoporosis (e.g. smoke, alcohol), metabolic disease that affects bone, fractures, any medication for treatment of osteoporosis or corticosteroids, radiological spondylosis. Their doctors referred subjects to our centre as part of screening for osteoporosis. The absolute measures of bone mineral density (BMD) expressed in g/(100 mm^2) of the femoral neck and lumbar spine L2-L4 were used in further analysis. Menopausal status was defined according to the absence of menses within the last 1 year without other biological or physiological causes. The results are expressed as means and SD. The distribution of variables was evaluated with the Shapiro-Wilks and Kolmogorov Smirnov test, to confirm the normal distribution of variables values. R Pearson's correlation index was calculated between all variables collected. X square test was assessed between the frequencies of osteopenia and osteoporosis estimated using manufacturer reference data and local registry.

RESULTS

DXA scan of 15335 patients were extracted from our data registry and analysed. Mean age was 64.2 ± 12.8 years (range 20.8 to 90). Patients in menopause were 11138. Mean BMI was 22.4± 5.1 (range 20.1 to 24.3). Mean menopause age was 41.3±5 years (range 31-54). Mean menarche age was 16.3±5 years (range 11-17).

Data about Lumbar Spine

The lumbar BMD was constant between 25 and 35 years (test for trend using ANOVA: P =0.31); the BMD mean value between 25–35 in premenopausal women (mean 1.043± 0.12 g/cm^2) was thus defined as the reference peak bone mass value, significantly lower compared to the Hologic reference value (mean 1.079±0.11 g/cm^2, p<0.05) (Figure **1**). The cutoff values (g/cm^2) for the definition of osteopenia (T-score: <1) and osteoporosis (T-score <2.5) using our reference values were, respectively, 0.856 and 0.714 (SD 0.065). The prevalence of osteoporosis according to the WHO criteria using Hologic values in post-menopausal women was 51,7%, osteopenia 26,6%. When the diagnosis was based using our reference values, the prevalence of osteoporosis and osteopenia were 34,3% and 43,9% respectively (X square test p=0.01). Between 35 to 45 years we observed a linear rapid lowering of BMD of 0.8% per year (Figure **1**, green box). This linear decrease was more gradual between 45 and 79 years (0.4% per year) (Figure **1**, blue box).

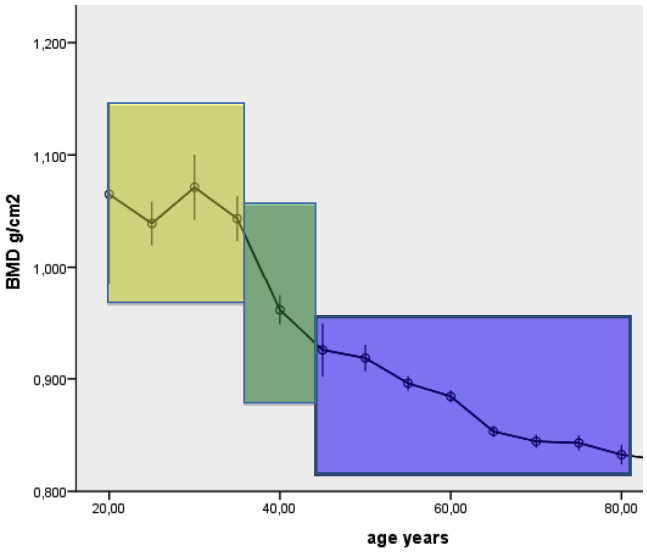

Figure 1: Lumbar BMD values in g/cm^2. Yellow box values of peak bone mass, green box rapid post menopausal decrease, blue box linear slow decrease of BMD values.

Data about Femoral BMD

The femoral neck BMD was constant between 25 to 39 years (test for trend using ANOVA P=0.22); the BMD mean value was 0.97g/cm^2 ± 0.136. Osteopenia and osteoporosis cut off were 0.854 and 0.77 (SD 0.05). Between 39 to 80 years we observed a slow linear decrease of 0.3% per year without the rapid postmenopausal decline observed in lumbar BMD data (Figure **2**). The prevalence of osteoporosis with the manufacturer using Hologic values in post-menopausal women was 43.3%, osteopenia 36.6%. When the

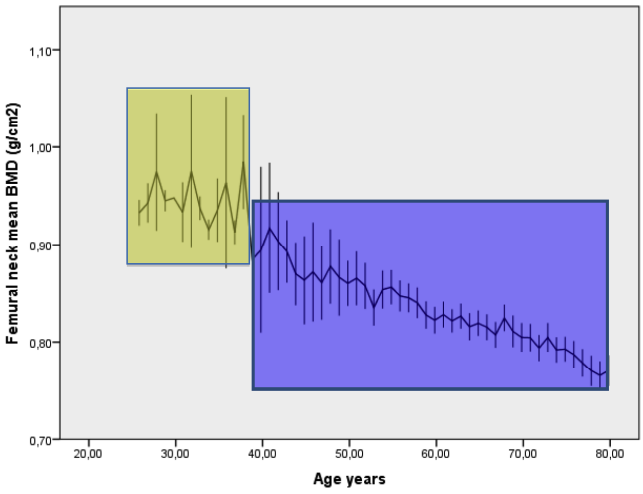

Figure 2: Femural neck BMD values in g/cm^2. Yellow box values of peak bone mass, blu box linear slow decrease of BMD values.

diagnosis was based using our reference values, the prevalence of osteoporosis and osteopenia were 33.1% and 42.2% respectively (X square test p=0.03).

DISCUSSION

The aim of DXA is to identify a patient with osteoporosis, to predict the risk of fracture and to detect small changes of bone densities resulting from treatment. The realisation of these targets requires accuracy and precision in measuring the BMD and that suitable references ranges is used. Normal reference range plays a crucial role because T-scores' calculations are based on it [13-18]. The normal values provided by manufacturers may not be fully representative of specific local populations. So far, there are no normative data in the Italian population using Hologic densitometers. DXA values are determined even in healthy people by various factors such as weight, BMI, nutritional status, making it difficult to create reliable Datum curves [19-25]. In our study we extracted data from a sample of adequate size that have allowed us to create reference curves for lumbar and femoral DXA in Italian females. In our study the BMD of the lumbar vertebrae was virtually constant between 25 to 35 years, confirming other reports with Hologic densitometers. The peak bone mass values were lower than those provided by the manufacturer based on a generic Caucasian ethnicity reference curve, but are close to those observed in other reports, in particular in a similar study in Spanish women. The similarity to the Spanish population values is also consistent with similar genetic, nutritional and lifestyle factors or body size [26,27]. This raises the question of the reliability of the manufacturer's curve because of differences in the selection and the number of the subjects and the mode of calculation of the peak value. Using our data, established on a sample of adequate size, we found important differences in T-score and so in classification according to the WHO criteria. A large proportion of women classified as osteoporotic using manufacturers data were categorised instead as osteopenic using our data curve. This difference not only affects the mere classification of patients but also have an impact on the clinical assessment and the therapeutic approach according to the current guidelines. In conclusion our data suggest Italian BMD reference curves (femoral and lumbar) for women based on a sample of adequate size, significantly different from the current normative data reported by the manufacturer, with a noteworthy impact on management of subjects with osteoporosis.

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