A glimpse from the past: osteoporosis and osteoporotic fractures in a portuguese identified skeletal sample

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ABSTRACT

The diachronic variation of etiological factors, like longevity or diet, affected the prevalence of osteoporosis and the so-called osteoporotic fractures in the past. As such, it is important to understand the epidemiology of this disease in historical populations; with behaviors and customs that were unalike the modern westernized lifestyle.

Objectives: The main objective of this study is to characterize the epidemiological patterns of osteoporosis and related fractures in an identified Portuguese skeletal sample from the mid 19th - early 20th centuries.

Materials and methods: The sample studied comprised 196 skeletal individuals with known sex and age-at-death, housed at the University of Coimbra. Bone mineral density (BMD) was evaluated in the proximal femur through dual X-ray absorptiometry and osteoporotic fractures were recorded according to clinical and paleopathological protocols.

Results: BMD decreased significantly with age-at-death, both at the ROI «Total hip» and the ROI «Neck». At the «Total hip», peak bone mass (PBM) was achieved early (20-29 years age group) in both sexes. In the study-group as a whole, BMD was significantly higher in males when compared to females. As expected, the prevalence of osteoporosis in the proximal femur is higher in women and rises steeply with age. Comparisons with two modern Portuguese samples showed an equivalent pattern of BMD reduction. Nonetheless, BMD is usually lower in the skeletal sample. Women with osteoporosis had a much larger probability of showing a fragility fracture than women diagnosed with «normal» BMD or osteopenia.

Conclusions: In spite of enormous lifestyle differences, the epidemiological pattern of bone mass decrease in a Portuguese skeletal sample is strikingly similar to the ones observed in modern populations. This study adds further data to the recent notion that osteoporosis is a disease with deep roots in the past.

Keywords: Osteoporosis; Bone mineral density; Osteoporotic fractures; Paleopathology

RESUMO

A modificação diacrónica de factores etiológicos como a longevidade ou a alimentação afectou a prevalência da osteoporose (OP) e das fracturas que classicamente se lhe associam. Desse modo, a compreensão epidemiológica desta doença em populações históricas é extremamente importante.

Objectivos: O objectivo cardinal deste estudo passa pela caracterização dos padrões epidemiológicos da OP e das fracturas de fragilidade numa amostra osteológica identificada portuguesa de meados do séc. XIX – início do séc. XX.

Materiais e métodos: A amostra estudada incluía 196 indivíduos de sexo e idade à morte conhecidos, pertencentes à Colecção de Esqueletos Identificados da Universidade de Coimbra, cuja proveniência é o Cemitério da Conchada (Coimbra, Portugal). A densidade mineral óssea (DMO) foi avaliada no fémur proximal através de osteodensitometria e as fracturas osteoporóticas foram registadas de acordo com protocolos clínicos e paleopatológicos.

Resultados: A DMO declinou de forma significativa com o aumento da idade, tanto na ROI «anca total» como na ROI «colo». Na anca total, o pico de massa óssea foi atingido mais cedo (grupo etário 20-29 anos) em ambos os sexos. Os valores médios da DMO nos homens eram significativamente maiores que nas mulhe-

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res. A prevalência de osteoporose é mais elevada no grupo feminino e aumenta com a idade. A comparação com duas amostras modernas portuguesas evidenciou um padrão semelhante de redução da DMO. Não obstante, a DMO é, de um modo geral, menor na amostra osteológica. As mulheres com OP tinham uma maior probabilidade de ter uma fractura relativamente a mulheres diagnosticadas como «normais» ou com osteopenia.

Conclusões: Apesar das diferenças abissais no estilo de vida, o padrão de perda de massa óssea numa amostra osteológica portuguesa é idêntico àqueles observados em amostras portuguesas de referência. Este trabalho acrescenta novos dados à noção recente de que a OP se encontra profundamente ancorada no passado.

Palavras-chave: Osteoporose; Densidade mineral óssea; Fracturas osteoporóticas; Paleopatologia.

INTRODUCTION

Osteoporosis (OP) is a metabolic disease characterized by abnormalities in the amount and architectural arrangement of bone tissue, increasing the susceptibility to fracture[1,2]. The clinical impact of osteoporosis lies in the problems associated to it, namely the representative hip, Colles and vertebral fractures. Although described more than 250 years ago[3], osteoporosis only begun to be fully understood in the 1940's[4,5]. Contemporary knowledge about osteoporosis has been supported by the cooperative interaction of several scientific disciplines, including paleopathology – the study of disease in past populations[6].

Nowadays, OP is acknowledged as one of the major public health problems facing postmenopausal women and aging individuals from both sexes[2,7,8]. It is a multifactorial disease, influenced by a sizeable group of etiological factors, such as genetics, physical activity, parity status, nutrition, or alcohol and tobacco consumption[7-13].

Traditionally, osteoporosis has been recognized as a "modern disease" but osteoporosis has a history waiting for a posthumous redemption[14-17]. The diachronic modification of etiological factors, like longevity, physical activity or diet, affected the prevalence of osteoporosis and the so-called osteoporotic fractures in the past. As such, it is important to understand the epidemiology of this disease in historical populations, with habits and routines that were utterly different from the modern westernized lifestyle. Paleopathological studies focused on age-related bone involution go back at least to the 1960's[18]. Subsequently, a growing body of research conducted in the field of paleopathology has comprehensively documented bone loss, osteoporosis and fragility fractures in a wide range of skeletal past populations[15,16,19-23].

The key objective of this study is to identify and characterize the epidemiological patterns of osteoporosis and associated fractures in an identified Portuguese skeletal sample from the mid 19th – early 20th centuries, and compare them to modern (*in vivo*) Portuguese reference counterparts.

MATERIALS AND METHODS

The Coimbra Identified Skeletal Collection (CISC), curated at the Anthropological Museum in the University of Coimbra, was assembled between 1915 and 1942. This collection incorporates 505 skeletons; the majority of them exhumed from the major Coimbra cemetery, *Cemitério Municipal da Conchada*[24]. All these individuals died between 1904-1936, i.e., before the turning point article by Fuller Albright and colleagues and the massive introduction of medical therapies against osteoporosis[4]. Throughout the formative period of this skeletal collection a body of biographical information concerning the individuals was collected. Subsequently, these data were compiled in a *Registry Book*. Collected data include, for each individual, age--at-death, sex, cause-of-death, occupation, marital status, and ancestry, among others[24].

The sample studied comprised 196 individuals, evenly distributed from both sexes, with an age-at--death ranging from 20 to 96 years old. Sampling privileged the equivalence in sex and age classes' composition. The sample included individuals born between 1827 and 1914; and dead between 1910 and 1936. The majority of the sample comes from the Coimbra District (Central Portugal). Individuals were mostly manual workers with low socioeconomic status. Only individuals without post-depositional change and devoid of gross pathological modification were included in the sample.

Bone mineral density (BMD) was evaluated in the proximal femur through dual X-ray absorptiometry (DXA). The left femur from each individual was scanned using a Hologic QDR-4500A densitometer (Hologic, Inc., Bedford, MA) housed at the Nuclear Medicine Department, in the University of Coimbra Hospitals (Fi-

gure 1). Each femur was positioned anteroposteriorly, with the diaphysis parallel to the central axis of the scanner, in a low-density paper box containing dry rice (10 cm depth), which acted as a soft-tissue surrogate[25]. BMD at the ROI «Neck» was compared to modern *in vivo* reference samples[26,27]. The modern samples comprised women of Portuguese descent from the cities of Coimbra and Porto. The reference cross-sectional studies were accomplished between 1997 and 1998, and between 1999 and 2003, respectively.

The presence of the so-called osteoporotic fractures (proximal humerus, distal radius, proximal femur and vertebral fractures) was assessed macroscopically by the same observer (FC) in two different occasions using clinical and paleopathological protocols[28-32]. When necessary additional radiographic exams were performed at the Radiology Department (University of Coimbra Hospitals).

FIGURE 1. Osteodensitometry of the left femur at the Nuclear Medicine Department (University of Coimbra Hospitals)

RESULTS

BMD AND OSTEOPOROSIS

Regression analysis showed that BMD decreased significantly with age-at-death, both at the ROI «Total hip» (*Pearson r*=-0.591; p=0.000) and the ROI «Neck» (*Pearson r*=-0.675; p=0.000). At the «Total hip», peak bone mass was achieved early (20-29 years age group) in both sexes (♀:0.930; SD=0.11; 95% CI: 0.858--0.987/♂: 1.045; SD=0.09; 95% CI: 0.992-1.097). At the ROI «Neck», PBM was attained earlier (20-29 years age group) in men (0.954; SD=0.07; 95%CI: 0.912--0.996) and somewhat later (30-39 years age group) in women (0.836; SD=0.11; 95% CI: 0.772-0.900). Age--related BMD decline was more pronounced in women («Total hip»: *Pearson r*=-0.694; p=0.000/«Neck»: *Pearson r*=-0.744; p=0.000) when compared to men («Total hip»: *Pearson r*=-0.533; p=0.000/«Neck»: *Pearson r*=-0.641; p=0.000). In the study-group as a whole, BMD was greater in males («Total hip»: 0.882; SD=0.16; 95%CI: 0.849-0.915/«Neck»: 0.757; SD=0.16; 95%CI: 0.725-0.789) than in females («Total hip»: 0.780; SD=0.16; 95%CI: 0.747-0.813/ /«Neck»: 0.679; SD=0.16; 95%CI: 0.647-0.710). This trend was observed in all age categories, but the differences become more pronounced in older age-at--death groups (Table I).

Osteoporosis diagnosis by age category is depicted in Figure 2 and Figure 3, for females and males, respectively. As expected, the prevalence of OP increased significantly with age-at-death in both sexes (*Kruskal--Wallis H*=93.759; d.f.=6; p=0.000). Also, osteoporosis was more prevalent in the female group (♀: 29.6%; 95%CI 21.5-39.3 [29/98] /♂: 13.3%; 95%CI 7.9-21.1 [13/98]). The difference is significant (*Mann-Whitney U*=4032.5; p=0.037). The discrepancy between sexes was greater amongst individuals that died with more than 50 years (♀: 50.0%; 95%CI 37.3-62.7 [28/56]/♂: 21.4%; 95%CI 12.7-33.8 [12/56]; *Mann--Whitney U*=1104.0; p=0.003).

As previously mentioned, BMD_{neck} values obtained in the CISC female study base were compared to modern *in vivo* reference samples from Coimbra and Porto[26,27]. The general pattern of BMD decrease is equivalent in the three samples. Bone mineral density at the ROI «Neck» was very similar in younger age-classes – suggesting an identical peak bone mass – but, in older individuals, it was significantly reduced in the skeletal sample (Tables I and II, Figure 4). In men from the CISC and Coimbra (modern *in vivo*) samples, the pattern of BMD_{neck} decline was also very similar, with a comparable PBM and a stronger BMD decay in the older age groups of the osteological assemblage (Tables I and II).

OSTEOPOROTIC FRACTURES AND BMD

The frequency of the so-called osteoporotic fractures increased with age at death in both sexes (Table III). The prevalence in older individuals (age at death >= 50 years) was 22.3% (95%CI 15.6-30.9 [25/112]). In the sample as a whole, females exhibited a higher, but non--significant, frequency of fragility fractures (♀: 16.3%; 95%CI 10.3-24.9 [16/98] / ♂: 14.3% 95%CI 8.7-22.6

TABLE I. AGE AND SEX-SPECIFIC BMD VALUES (G/CM²) AT THE ROI «NECK» AND ROI «TOTAL HIP» IN THE CISC SAMPLE. DATA PROVIDED WITH STANDARD DEVIATION (SD) AND 95% CONFIDENCE INTERVALS (95%CI)

	BMDneck				BMDtotal hip			
Age category	Mean	SD	95%CI	N	Mean	SD	95%CI	N
Females								
20-29	0.821	0.12	0.751-0.891	14	0.923	0.11	0.858-0.987	14
30-39	0.836	0.11	0.772-0.900	14	0.913	0.10	0.853-0.974	14
40-49	0.732	0.13	0.658-0.806	14	0.834	0.13	0.760-0.907	14
50-59	0.674	0.10	0.615-0.733	14	0.781	0.14	0.702-0.861	14
60-69	0.611	0.11	0.549-0.672	14	0.746	0.12	0.675-0.817	14
70+	0.539	0.08	0.498-0.579	28	0.632	0.13	0.582-0.683	28
Males								
20-29	0.954	0.07	0.912-0.996	14	1.045	0.09	0.992-1.097	14
30-39	0.862	0.12	0.795-0.929	14	0.958	0.14	0.877-1.040	14
40-49	0.757	0.16	0.665-0.848	14	0.892	0.17	0.792-0.991	14
50-59	0.756	0.17	0.657-0.855	14	0.895	0.17	0.797-0993	14
60-69	0.695	0.10	0.637-0.753	14	0.834	0.10	0.774-0.894	14
70+	0.638	0.09	0.600-0.676	28	0.774	0.14	0.720-0.823	28

[14/98]; *Yates corrected* 2=0.039; d.f.=1; p=0.843).

BMD measured at the ROI «Total hip» ($BMD_{with\ fracture}$: 0.738; SD=0.20; 95% CI 0.663-0.813/$BMD_{without\ fracture}$: 0.848; SD=0.16; 95% CI 0.823-0.873; *Student's t*=3.331, d.f.=194; p=0.001) and ROI «Neck» ($BMD_{with\ fracture}$: 0.631; SD=0.19; 95% CI 0.560-0.702/$BMD_{without\ fracture}$: 0.734; SD=0.15; 95% CI 0.709-0.759; *Student's t*=3.229, d.f.=194; p=0.001) was significantly lower in fractured individuals. Logistic regression showed that BMD at the ROI «Total hip» significantly influenced the probability of displaying a fragility fracture in the female sample ($B\_{BMDtotal}$=-19.569; *Wald*=9.718; p=0.002). In the men's group, only age-at-death seems to have influenced the presence of an osteoporotic fracture (B_{idade}=0.039; *Wald*=4.220; p=0.040). As for that, an overwhelmingly majority of women with fragility fractures was diagnosed with osteoporosis (75%; 12/16), while fractured men were mainly diagnosed with osteopenia (50%; 7/14). A woman with osteoporosis had a much greater probability of having a fragility fracture than a woman diagnosed with «normal» BMD or osteopenia (OR=11.5; 95% CI 3.3-40.1).

DISCUSSION

BMD AND OSTEOPOROSIS

The prevalence of chronic diseases (such as osteoporosis) tends to increase with age, fitting a «Gompertzian» pattern[33]. Theoretical expectations – supported by epidemiological models – are in agreement with the results of this study: the frequency of OP increased significantly in older age classes in both sexes. Also, BMD was significantly lower in older individuals. Age is an acknowledged risk factor for osteoporosis and BMD decrease[7,8,34-37]. Osteoblastic activity declines during ageing, hampering bone formation; and intestinal calcium absorption diminishes, resulting in secondary hyperparathyroidism and, indirectly, in the escalation of bone resorption[38,39].

Osteoporosis prevalence was higher in the female group, especially in the older age-at-death categories. Also, BMD at both the ROI «Total hip» and «Neck» was significantly lower in women when compared to men. Sexual differences in OP frequency and BMD values at the proximal femur were epidemiologically expected[31,40,41]. Male bones are usually stronger because men attain a higher BMD during growth. Men tend to experience a less pronounced loss of bone during ageing, reduced endocortical resorption and intracortical porosity, and higher periosteal expansion[42]. Also, menopause is a physiological event restricted to women. Estrogen depletion after menopause thwarts bone health, both directly and indirectly[37,43].

The general pattern of BMD decline in the proximal femur is comparable in three Portuguese female sam-

ples (one skeletal sample, two modern *in vivo* reference samples) with utterly dissimilar lifestyles. BMD_{neck} values reached a maximum in the younger age classes (20-29 and 30-39 years) of all samples, and started to decay afterwards. In the skeletal and Porto samples peak bone mass (PBM) was attained in the 30-39 years age class, later than in the modern *in vivo* study base from Coimbra. Somewhat strikingly, PBM was very similar in all three samples. PBM is influenced by genetic and environmental factors[44]. Of the latter, physical activity and nutritional status are, perhaps, the most relevant. Physical activity is positively correlated with BMD in young adults and historical data suggest that the levels of strain and effort in the past were more strenuous[14,45]. The majority of the women from CISC were "housekeepers", a physically demanding type of work during the 19th and early 20th centuries[46]. Malnutrition during childhood can hinder peak bone mass and BMD later in life[47]. In the 19th – early 20th centuries Coimbra, the dietary makeup of the economically deprived classes generally included bread (maize, corn or rye), vegetables (soups and broths) and some fish (sardine and codfish). Calcium deficiency was not probable: the city was still very "rural", physically surrounded by crop fields, fruit orchards and animal farms. As such, most underprivileged individuals had a fairly good nutritional status[48,49].

In the older age classes, BMD_{neck} was always lower

TABLE II. AGE AND SEX-SPECIFIC BMD VALUES (G/CM²) AT THE ROI «NECK» IN THE MODERN IN VIVO PORTO AND COIMBRA SAMPLES[26,27]. DATA PROVIDED WITH STANDARD DEVIATION (SD) AND 95% CONFIDENCE INTERVALS (95%CI)

	Porto (modern)[27]				Coimbra (modern)[26]			
Age category	Mean	SD	95%CI	N	Mean	SD	95%CI	N
Females								
20-29	0.814	0.13	0.764-0.864	28	0.826	0.11	0.809-0.843	159
30-39	0.819	0.12	0.783-0.855	45	0.793	0.10	0.776-0.811	125
40-49	0.766	0.10	0.749-0.783	141	0.772	0.10	0.756-0.788	144
50-59	0.724	0.12	0.705-0.743	155	0.734	0.10	0.713-0.755	90
60-69	0.657	0.10	0.640-0.674	133	0.701	0.11	0.678-0.724	84
70+	0.632	0.10	0.608-0.656	71	0.654	0.09	0.630-0.678	52
Males								
20-29	–	–	–	–	0.960	0.14	0.933-0.987	101
30-39	–	–	–	–	0.872	0.13	0.843-0.901	79
40-49	–	–	–	–	0.870	0.14	0.836-0.904	66
50-59	–	–	–	–	0.830	0.12	0.801-0.859	66
60-69	–	–	–	–	0.800	0.11	0.771-0.829	56
70+	–	–	–	–	0.730	0.11	0.696-0.765	39

TABLE III. AGE AND SEX-SPECIFIC PREVALENCE OF FRAGILITY FRACTURES (PROXIMAL FEMUR, DISTAL RADIUS, PROXIMAL HUMERUS, AND VERTEBRAE) IN THE CISC SAMPLE.

	♀			♂		
Age category	%	n	N	%	n	N
20-29	0.0	0	14	0.0	0	14
30-39	7.1	1	14	14.3	2	14
40-49	0.0	0	14	7.1	1	14
50-59	14.3	2	14	14.3	2	14
60-69	7.1	1	14	14.3	2	14
70+	42.8	12	28	25.0	7	28
Total	16.3	16	98	14.3	14	98

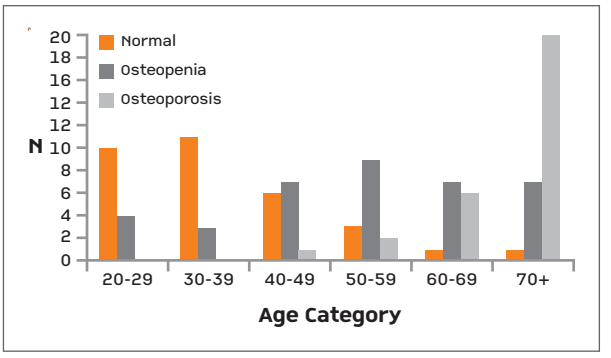

FIGURE 2. Osteoporosis diagnosis in each age category (CISC sample, females)

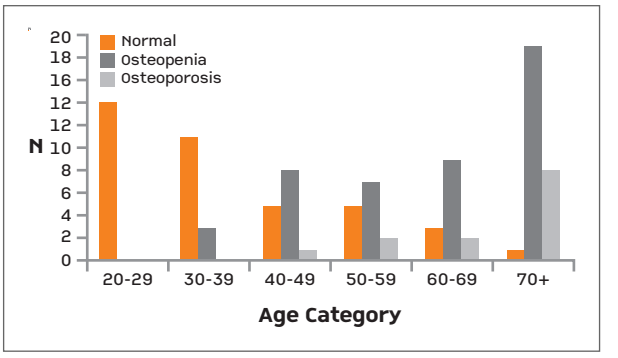

FIGURE 3. Osteoporosis diagnosis in each age category (CISC sample, males)

in the CISC sample – with a higher rate of bone loss in the skeletal women after the 30-39 years age class, and a significant difference in the 70+ years age class. It is possible that, for most of the women, menopause occurred earlier in the CISC study base; nonetheless, some studies suggest that the mean age of menopause has been stable since at least Classical Greece and Rome[50]. Weight is correlated with a BMD increase and it is very likely that the mean weight in the modern *in vivo* reference samples was considerably larger than the weight of the 19th-early 20th centuries' women[51]. On the other hand, as we have seen before, physical activity levels were probably higher in the skeletal sample. Also, fecundity rates were higher during the 19th and the beginning of the 20th centuries, and parity status is most likely connected to a better bone health later in life[52,53]. BMD_{neck} differences between the skeletal and the modern *in vivo* reference samples in the older age classes are probably related to a multitude of factors, including genetics, age of menopause, weight, diet, physical activity, and reproductive history. Unfortunately, available historical data is sparse and somewhat paradoxical – as such, it is impossible to ascertain the exact causes of these differences. Also, it is important to note that the lack of soft tissues and bone marrow in historical skeletal remains hampers any comparison with living individuals[22].

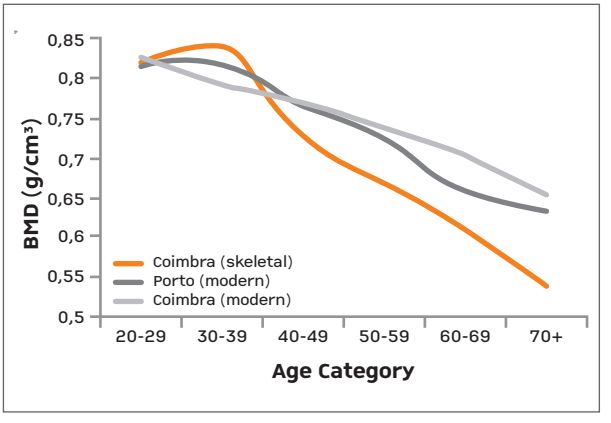

FIGURE 4. BMDneck decline with age in three Portuguese female samples

OSTEOPOROTIC FRACTURES AND BMD

As expected, the frequency of osteoporotic fractures (proximal humerus, distal radius, vertebrae and proximal femur) increased with age in both sexes[54,55]. Nonetheless, no significant difference in fracture prevalence between sexes was found. Small sample size, or the effects of other factors influencing fractures beyond BMD (e.g., falling patterns, trabecular microarchitecture, occupational hazards), may explain this finding.

The etiology of osteoporotic fractures is intricate, but bone fragility is a major risk factor, perhaps the greatest[56,57]. Just in the beginning of the 18th century, the French physician Jean-Louis Petit observed that frail bones were more prone to fractures, an idea echoed later by the Portuguese surgeon António Gomes Lourenço or the English surgeon and anatomist Sir Astley Paston Cooper[58-60]. BMD succeeds as a fitting proxy of bone strength, and large prospective reports have acknowledged a strong relationship between BMD and the likelihood of suffering a fragility fracture[55,57]. The results of our study are consistent with the epidemiological data, especially in the females' group, where BMD measured in the ROI «total hip» conspicuously influenced the probability of fracture presence. Also, any woman diagnosed with osteoporosis had a much greater prospect of displaying an osteoporotic fracture than «normal» or osteopenic women.

CONCLUSIONS

As a privileged space of origin and distribution of disease, the human skeleton provides concrete scientific knowledge about a substantial group of nosological entities – OP included – that affected the bones of individuals in past populations. In spite of huge lifestyle disparities, the epidemiological pattern of bone mass decrease in a Portuguese skeletal sample from the 19th century is interestingly alike the ones observed in modern populations. This study adds further data to the contemporary perception that osteoporosis is a disease with deep roots in the past.

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