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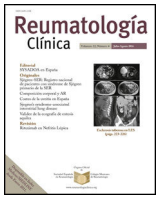

Original Article

Bone health and predictors of 15-year mortality in a physically active population☆

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ABSTRACT

Objective: To analyse determinants of mortality at 15 years in a population over 60 years of age and physically active.
Methods: This is a prospective longitudinal study. After 15 years of participating in an active ageing programme, participants were contacted by telephone to verify their state of health and to determine whether in that time they had had any fractures.
Results: 561 individuals over 60 years of age were included, 82% of whom were women. Only differences in densitometric data, FRAX values and history of previous fracture at baseline characteristics were found between the group that died at 15 years and the group that remained alive. The only variables that were related to mortality risk were the basal data of the densitometric t-score (OR = .50, $P < .001$) and history of fracture in any location (OR = 2.44, $P < .033$).
Conclusions: The value of bone mineral density could be considered as a useful biomarker to calculate the risk of mortality in people over 60 years old with a physically active lifestyle.

Salud ósea y predictores de mortalidad a 15 años en una población físicamente activa

Palabras clave:
Osteoporosis
Densidad mineral ósea
Mortalidad

RESUMEN

Objetivo: Analizar determinantes de mortalidad a 15 años en relación a la salud ósea en una población de mayores de 60 años y físicamente activos.
Métodos: Estudio longitudinal prospectivo. A los 15 años de participar en un programa de envejecimiento activo, y de los que se disponía de datos de salud ósea, se contactó telefónicamente con los participantes para constatar el estado vital y conocer si en ese intervalo de tiempo habían tenido alguna fractura; para ver la asociación entre la puntuación basal del FRAX, los datos denstométrios y la mortalidad al cabo del tiempo.

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Resultados: Se incluyeron 561 individuos mayores de 60 años, de los que el 82% eran mujeres. Solo se encontraron diferencias en las características basales entre el grupo que falleció a los 15 años y el grupo que siguió con vida en los datos densitométricos y en los valores del FRAX, así como en el antecedente de algún tipo de fractura. Las únicas variables que se relacionaron con el riesgo de mortalidad fueron los datos basales del t- score densitométricos (OR = 0,50; p < 0,001) y el antecedente de fractura en cualquier localización (OR = 2,44; p < 0,033).
Conclusiones: El valor de la densidad mineral ósea podría considerarse como un biomarcador útil para calcular el riesgo de mortalidad en mayores de 60 años con una vida físicamente activa.

Introduction

Osteoporosis is the most common metabolic bone disease, the prevalence of which increases with age. Osteoporotic fracture and subsequent fractures in the elderly are a rising public health problem,[1–4] with a high mortality rate.[5,6] Hip and vertebral fractures are associated with a significant, immediate and long-term risk of mortality.[7–10] In the case of a hip fracture, the mortality rate is higher during the first year,[11] but there appears to be a tendency for this to continue increasing over the following 10 years.[12] Osteoporotic fractures are also related to the risk of a further subsequent fracture,[13] and these later fractures are associated with an additional increase in risk of mortality for 5 years.

Several longitudinal studies have also linked osteoporosis with an increase in mortality (specifically excess mortality with hip fracture),[14–17] and it is known that the rate and prevalence of hip fractures vary from one geographical region to another.[18]

Several prospective studies have reported an association between low bone mineral density (BMD) and mortality in elderly women.[14] Patients with a drop in BMD in the proximal radius were reported to have an increase of 1.19 age-adjusted risk.[14]

The aim of this study was to analyse the history of the fracture, the role of the FRAX and the densitometry data as determinants of mortality in physically active people over 60 years of age after 15 years.

Material and methods

A prospective longitudinal study at 15 years. During the years 2003–2004 a sample of individuals who took part in the "Gent gran en marxa" programme was selected, promoted by the Consell Insular de Mallorca, the objective of which was to improve the health and quality of life of a group of elderly people through the development of a series of activities (including, among others, dance and gym) and also assess their health status and their physical possibilities (cardiovascular study, muscle strength, diagnosis of osteoporosis, among other studies). At that time everyone who attended the centres participating during the study period were invited to participate in the study and those who accepted were sent to a centre for interviews and densitometry. Data from this phase have already been published.[19] For this mortality study only individuals who were over 60 years of age at the baseline visit were included.

In 2019, 15 years after the survey, the people over 60 were contacted by phone to check on their status and if they were still living, to ask them about possible fractures during the time interval (any location). If a person could not be contacted the medical history was consulted to obtain both the date of death and the history of fractures (the Balearic Islands health service has a centralised information service). Medical histories were in electronic format, since an electronic history has been available since 2011 (with digitalisation of previous data).

Osteoporosis was defined according to the densitometry criteria of the WHO, i.e. osteoporosis was present when the result from the BMD showed a T score < 2.5 SD in the spinal column or the femoral neck. Osteopenia was defined as a T score between –2.5 and –1 SD. A previously calibrated DXA Norland® unit, model XR-46 was used to perform BMD of the lumbar spine and femoral neck. The unit had been appropriately maintained in keeping with the supplier's calibrations. The densitometry was performed by a qualified technician who had been previously trained in the densitometry unit, patient positioning and software support. The reference values of NHANES III were used. The reference population, both for men and women, came from the Third National Health and Nutrition Examination Survey (NHANES III).[20]

In the baseline survey all the participants had been for a medical check-up which collected data on: age, sex, morphotype, height and weight, history of maternal hip fracture (no paternal hip fracture history was available), history of Colles fracture, hip fracture or any other previous osteoporotic fracture, hyperthyroidism, diabetes mellitus, Parkinson's disease, history of cerebrovascular disease. Other collected variables were: tobacco consumption (non-active vs. active) and alcohol consumption (some vs. none), exposure to the sun (avoidance vs. any exposure), physical activity (no exercise/planned activity vs. any planned physical activity), number of hours standing, history of ingestion of corticosteroids or benzodiazepines. In women gynaecological variables were also collected, such as a history of breast cancer, pregnancy, breast-feeding, early menopause (before 42 years of age), previous oophorectory, ingestion of oral contraceptives and duration of menstruation in years.

Statistical analysis

The analysis sample was described and possible differences in the baseline characteristics between subjects who had died and those who had not were studied. To do this, mean differences and proportion tests were performed (Mann–Whitney and chi square) depending on the nature and distribution of the variables.

The association between the FRAX score, the densitometry data and mortality, collected over time, was analysed using bi and multivariate logistic regression models. The dependent variable of these models was death (yes/no), and T-score data were introduced as independent variables as well as the baseline characteristics and the possible confusion variables. In the multivariate models clinically meaningful variables were introduced or those with a *P* value in the bivariate <.25. Based on a saturated model, models were created with successive elimination of the variables with the lowest contribution, and a stepwise regression procedure was also used. The most parsimonious model was chosen as the final one (lowest number of variables), with highest clinical meaningfulness and lowest information criteria (AIC and BIC) values.

Results

During phase one of the project data were obtained from 731 individuals, whilst in phase two data were obtained from 561 individuals (amounting to 76.7% response at 15 years; these were

Table 1
Baseline factors associated with mortality at 15 years.

Characteristics	Total (n = 561)	No death (n = 529)	Death (n = 32)
Age (years)[a]	68 (65–72)	69 (65–72)	68 (65,5–72)
Female sex	462 (82,3)	433 (81,8)	29 (90,6)
Weight[a]	65 (58–72)	65 (58–71)	65.5 (59.5–72.5)
Physical activity			
No/slight, moderate	358 (63.8)	340 (64.3)	18 (56.2)
Intense	203 (36.2)	189 (35.7)	14 (43.7)
BMI[a]	26.1 (23.8–28.6)	26.1 (23.9–28.6)	26.2 (24.0–28.9)
Alcohol consumption	71 (12.7)	69 (13.0)	2 (6.2)
HBP	29 (5.17)	28 (5.3)	1 (3.1)
Diabetes	66 (11.8)	62 (11.7)	4 (12.5)
Dyslipidaemia	155 (27.9)	146 (27.8)	9 (30.0)
Previous stroke	10 (1.8)	9 (1.7)	1 (3.1)
Corticosteroids	24 (4.3)	23 (4.7)	1 (3.1)
Tobacco habit	37 (6.9)	37 (6.6)	0
T-score (neck)[a]	−1.3 (−1.9 a −.5)	−1.2 (−1.9 a −.5)	−2.1 (−2.4[a] −1.9)[b]
BMD (neck)[a]	.7 (.6–.8)	.7 (.6–.8)	.6 (.6–.7)[b]
Femoral neck FRAX (without BMD)[a]	1.3 (.6–3.2)	1.2 (.5–3.1)	3.2 (1.4–9.9)[b]
Total FRAX (without BMD)[a]	5.1 (3–9.1)	4.8 (2.8–8.8)	8.55 (4.85–17[b])
Total FRAX (with BMD)[a]	4.9 (3–8.7)	4.9 (2.9–8.3)	9.6 (4.5–18.5)[b]
Total FRAX (with T-score)[a]	−1.9 (−2.4 a −1.3)	−1.9 (−2.4 a −1.3)	−2.5 (−2.85 a −1.7)[b]
DXA spine[a]	.8 (.7–.9)	.8 (.7–.9)	.8 (.7–.9)
Hip (maternal) Fx	77 (13.7)	69 (13.0)	8 (25.0)
Hip Fx	46 (8.2)	41 (7.7)	5 (15.6)
Vertebral Fx	4 (.7)	3 (.6)	1 (3.1)
Humeral Fx	7 (1.2)	5 (.9)	2 (6.2)[b]
Colles Fx	9 (1.6)	8 (1.5)	1 (3.1)
Other fractures	39 (6.9)	32 (6.0)	7 (21.9)[b]
History of fx[c]	87 (15.5)	77 (14.6)	10 (31.2)[b]

BMD: bone mineral density; BMI: body mass index; DXA: densitometry; Fx: fracture; HBP: high blood pressure.
All variables express n(%), unless indicated.
[a] Indicates median (p25–p75).
[b] p < .05.
[c] Having had a fracture in any location is grouped within this variable.

mainly women (82%) and the median age at that time was 68 years of age.

The main baseline differences observed between individuals who had died and those who had not died after the period of 15 years were observed in the densitometry data and FRAX values, together with any history of fractures (Table 1). Regarding comorbidities, such as cardiovascular risk factors, no differences were found between the two groups.

Table 2 shows the measurements of association of all the variables studied with mortality. The only parameters associated with death were the T-score data and a previous fracture in any location (OR = .50; *P* < .0001 and 2.44; *P* = .033) (Table 2).

Table 2
Bivariate and multivariate analysis of mortality risk factors in a sample of active people over 60 years of age after 15 years follow-up.

Variable	Bivariate OR [IC 95%] (*P*)	Multivariate OR [IC 95%] (*P*)
Age	1.00 [0,94; 1,06] (.969)	.99 [0,92; 1,06] (.851)
Female sex	2.14 [0,63; 7,18] (.217)	
BMI	1.00 [0,91; 1,12] (.853)	
Intense physical activity[a]	1.40 [0,68-2,88] (.361)	
Alcohol consumption	.44 [010; 1,90] (.274)	
HBP	.59 [0,08; 4,38] (.595)	
Diabetes	1.07 [0,36; 3,16] (.897)	
Dyslipidaemia	1.11 [0,50; 2,49] (.790)	
Previous stroke	1.87 [0,23; 15,18] (.561)	
Corticosteroids	.71 [0,09; 5,14] (.740)	
T-score (neck)	.53 [0,38; 0,74] (<.0001)	.50 [0,36; 0,72] (<.0001)
BMD (neck)	.002 [0,00; 0,05] (<.0001)	
Total FRAX (without BMD)	1.10 [1,05; 1,14] (<.0001)	
FRAX neck (without BMD)	1.18 [1,10; 1,26] (<.0001)	
Total FRAX (with BMD)	1.12 [1,07; 1,17] (<.0001)	
FRAX (with T-score)	.54 [0,36; 0,82] (.004)	
Hip (maternal) Fx	2.22 [0,96; 5,14] (.062)	2.06 [0,85; 5,03] (.110)
Hip Fx	2.20 [0,80; 6,02] (.124)	
Vertebral Fx	5.65 [057; 55,96] (.138)	
Humeral Fx	6.98 [1,30; 37,50] (.023)	
Colles Fx	2.10 [0,25; 17,33] (.491)	
Other fractures	4.34 [1,75; 10,81] (.002)	
History of fx (any location)	2.66 [1,21; 5,85] (.014)	2.44 [1,07; 5,57] (.033)
Constant		.02 [0,00; 3,49] (.142)

BMD: bone mineral density; BMI: body mass index; Fx: fracture; HBP: high blood pressure; Fx: fracture.
[a] Compared with no/moderate.

Discussion

The results obtained revealed that a previous fracture doubled the risk of death after 15 years compared to patients without fractures. This data was obtained from a potentially healthy population, since they went to a day centre where they performed physical activities. The result from the T-score suggested the same, where a poorer result in BMD was also associated with increased mortality.

In the results obtained neither cardiovascular risk factors nor other comorbidities mentioned in the questionnaire were related to mortality, but an increased risk was detected with the previous any-location fracture variable, that was directly related to bone quality.

Traditionally osteoporosis has been considered a minor phenomenon associated with ageing. However, in recent years this idea has changed and it is now recognised as being one of the main risk factors leading to fractures. Morbidity is high, as is its social and health impact, which is in keeping with what our results on mortality reaffirm.

Hip and vertebral fractures are associated with a significant, immediate and long-term risk of mortality.[7–10] In the case of hip fracture, the mortality rate is higher in the first year,[21] and it has already been published that this could continue increasing up to 10 years.[12] In one case and control study it was found that mortality after vertebral fracture increased up to 10 years in women and 3 years in men.[22] Osteoporotic fractures are also linked to the risk of a posterior fracture.[13] In our case, after 15 years we found that a past fracture in any location would also significantly increase the risk of mortality (OR = 2.44 [1.07; 5.57]; $P = .033$).

Notwithstanding, other authors also note that osteoporosis without fracture would be associated with mortality. Recently, Cai et al.[23] presented a study in the American population where the presence of femoral osteoporosis was related to a higher risk of mortality by all causes. The protective role of a good BMD in the femur was also found to reduce the risk of mortality by cancer in men and cardiac diseases in women. These authors found no association between the BMD of the spinal column and the risk of mortality. In women of an advanced age it was established that a low BMD in the femoral neck could be a possible predictor of increased mortality.[24] In one study which included patients aged 65 years or above[25] they found that patients who had BMD outcomes in the lowest quartile in the hip demonstrated a 110% increase in mortality by all causes, compared with the highest quartile.

What is striking in our study is that BMD is surpasses other factors in association with mortality, such as cardiovascular risk factors. A low BMD is related to multiple factors, such as, for example, nutrition,[26] the metabolism of calcium,[27] oestrogen levels[28] and environmental xeno-oestrogens,[29] and genetic factors,[30] which could in turn be related to mortality and which were not directly collected. Another explanation could come from the selected population itself, with greater physical activity than expected because the sample source was a place where programmed physical activity took place, and there could have theoretically been high control of other factors relating to increased mortality.

This study was not exempt from limitations. One of them was the quality of the data, since it was collected by means of a questionnaire, and there could have been a measurement bias or error in collection due to patient interpretation errors (in this respect the higher number of hip fractures than in other locations is of note, possibly because they are more limiting for the patients and they remember them more). Although the questionnaires collected the most relevant variables, for performing FRAX we lacked data about paternal hip fracture histories. Also, the cause of death of the individuals included in this study was unable to be determined. It was also unknown as to what treatment was received for osteoporosis throughout the study and there was no general validated test, such as the Charlson index. It is of note that, because there was no follow-up of 23% of patients at 15 years, we were unaware of the mortality of this group, and it could have constituted a major bias in results.

The essential strength of this study comes from the BMD being able to be considered a new mortality biomarker, at least in a physically active population over 65 years of age. Also of note is that follow-up of all patients with no losses was completed, which has helped to endorse the outcome consistency.

Bearing in mind these results, the BMD value appears to be necessary in order to calculate the risk of mortality long-term (15 years), where it could then be used as an accessible and valid biomarker in certain population groups.

Conflict of interests

The authors have no conflict of interests to declare with this study.

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