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ORIGINAL ARTICLE

Relationship between the FRAX index and physical and cognitive functioning in older people

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ABSTRACT

Objective: To assess the relationship between the FRAX index and the Barthel index/MiniMental State Examination in older people.

Patients and methods: Observational descriptive study. Demographic data, comorbidity, dependency and cognitive state, and risk of osteoporotic fracture were collected.

Results: A total of 375 patients were included (60% female) Patients with a low-risk FRAX for hip fractures had a higher Mini-mental (25, 95% CI = 24–27 vs. 22, 95% = 21 to 23, $p = .0001$), a higher Barthel index (88, 95% CI = 84–93 vs 72, 69 to 76, $p = .0001$) without differences in the Charlson index. Bivariate analysis showed an inverse association between FRAX and scales but logistic regression showed only female sex (OR 4.4, 95% CI = 2.6–7.6) and the non-dependent Barthel index (OR = 0.104, 95% CI = 0.014–0.792) remained significant and. Barthel index/Mini-mental constructed a significant model capable of predicting a risk of hip fracture of >3% measured by the FRAX index, with an area under the curve of 0.76 (95% CI = 0.7–0.81).

Conclusions: The FRAX index is related to other markers of geriatric assessment and the association between these variables can predict a risk of hip fracture of >3% measured by the FRAX index.

KEY MESSAGES

- Geriatric assessment indexes may be as important as the FRAX index, which is based on clinical risk factors, in predicting the fracture risk in older patient.

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Barthel Index; Charlson Index; FRAX; hip fracture; Mini-Mental State Examination

Introduction

Osteoporosis, a skeletal disorder that affects the bone microarchitecture, causes greater bone fragility and predisposes to fracture. Fragility fractures of osteoporotic origin appear spontaneously or after a low energy trauma (e.g. a fall from the persons own height) and mainly affect the humerus, hip, wrists and vertebrae [1–4], with hip fracture being the most serious in terms of high morbidity and mortality. At one year, 30% of patients die and only 30% regain the initial functional status. In 1984, the World Health Organization (WHO) defined osteoporosis according to double-beam radiological densitometry (DXA) bone mass measurement in the spine, femur and forearm in postmenopausal white women. Recent decades have shown that low bone mass density (BMD) alone does not explain 50% of fragility fractures, and that there are other contributing factors [3]. The FRAX index is an online algorithm designed by Kanis et al. of the University of Sheffield and sponsored by the WHO to calculate the absolute risk of global and hip osteoporotic fracture in the next 10 years in persons aged 40–90 years [5,6]. The population models were designed based on nine prospective population-based cohorts in Europe, North America, Asia and Australia. The FRAX index includes other factors, both dependent and independent of BMD, that contribute to fracture risk.

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However, some aspects, which influence the risk of fracture, above all hip fracture, are especially important in the elderly and are not evaluated by the FRAX index, including the risk of falls, the ability to perform the activities of daily living, the cognitive status and comorbidity.

Because the prevalence of osteoporotic fracture increases with age and is associated with increased morbidity and mortality, the FRAX index might be related to various aspects of the situation of the older people. The primary objective of this study was to assess the relationship between the FRAX index and the Barthel index (BI) and the Mini-Mental State Examination (MMSE) in older people. Secondary objectives were to study the population characteristics, physical, cognitive and comorbidity functional measures of older patients, and whether the origin of the patients (home-dwelling, residential and hospitalized) influenced the relationship between the FRAX scales and physical capacity, comorbidity and the mental situation.

Patients and methods

We made an observational, descriptive study of patients admitted to the Internal Medicine service of a 600-bed university hospital that serves a population of 260,000, residents of long-stay centres and home-dwelling patients. The sample size was calculated to demonstrate a correlation of 0.25 between qualitative variables, with a statistical power of 0.80 and a level of significance of 95%. It was calculated that 120 cases per group were needed, making 360 in total.

The inclusion criteria were willingness to participate and age $\geq$65 years. Exclusion criteria were the rejection of participation and an expected life expectancy of $<$6 months.

Patients and/or their legal representatives were informed of the characteristics of the study in writing. Patients were recruited between March 2016 and December 2016. All participants gave signed informed consent. Patients who declined to participate had similar characteristics to participants.

In the initial visit, a patient questionnaire was administered that included demographic data and comorbidities. Data were also extracted from the medical record.

The main study variables were: Demographic data: age, sex, source (home-dwelling, residential, hospitalized). Dependence was measured using the BI, which has a score of 100 points categorized as independent; 91–99 points, mild dependence; 61–90 points, moderate dependence; 21–60: severe dependence $\leq$20 points, and total dependence. Cognitive assessment was made using the MMSE, categorized as 0–8 points, dementia; serious cognitive impairment, 9–12; moderate cognitive impairment, 13–18 points; mild cognitive impairment, 19–24; borderline impairment, 24–26 and $\geq$27: normal. Comorbidity was measure using the Charlson Comorbidity Index, categorized as 0–1; no comorbidity, 2 points; low comorbidity, $\geq$3 points; high comorbidity.

The risk of osteoporotic fracture was calculated using the FRAX index, without including densitometry. This algorithm includes 11 items: age (40–90 years), sex, weight (kg), height (cm), prior fracture, parental hip fracture, active smoker, current corticosteroid intake (or corticosteroid use for $>$3 months at an equivalent dose of 5 mg of prednisolone/day), rheumatoid arthritis, secondary osteoporosis (type-I diabetes, osteogenesis imperfecta, hyperthyroidism without long-term treatment, hypogonadism, early menopause, malnutrition or chronic malabsorption or liver disease), alcohol consumption ($>$3 units/day) and, optionally, bone mineral density (BMD) of the femoral neck if available. Patients were stratified for the risk of major osteoporotic fracture: low ($<$10%), moderate (10–20%) and high risk ($\geq$20%). For hip fracture, they were stratified as high risk, $>$3% or not high risk $<$3%.

A descriptive univariate analysis was made and expressed as means and standard deviation (SD). Continuous variables were compared using the Student *t*-test. Subjects in different risk situations were compared using ANOVA. Pearson's correlation between FRAX for hip fracture and geriatric assessement was conducted. An enter multivariate regression analysis analysed the adjusted factors. A multivariate logistic regression analysis was carried out to construct a model that determined the effect of the BI/MMSE on a risk of hip fracture $>$3% measured by the FRAX® index, identifying the independent factors and constructing a ROC curve. The covariates introduced were sex and the Charlson index. The statistical analysis was made using the SPSS version 22.0 statistical program. Statistical significance was established as $p < .05$.

Patient anonymity was guaranteed at all times. The Organic Law on Data Protection (15/1999) was complied with. The study was approved by the Ethics Committee of the Río Hortega University Hospital of Valladolid (CEIC 53/16).

Results

We included 375 patients (mean age: 81.4 (80.6–83.8) years, 225 [60%] female). Females predominated in all

Table 1. Baseline characteristics of the study sample.

	Mean difference (95 % CI)				
	Home-dwelling $N = 125$ (33.3 %)	Residential $N = 121$ (32.2 %)	Hospitalizaed $N = 129$ (34.4 %)	Total $N = 375$	p*
Age	76.5 (75.4–77.7)	85.5 (82.8–84.8)	82.3 (80.6–82.2)	81.4 (80.6–83.8)	
Female/male	72/53	87/34	66/63	225/150	
BMI	28 (27.2–28.8)	27.5 (26.3–28)	25.2 (24.3–26.1)	26.8 (26.3–27.4)	.0001
MMSE	27.8 (27.4–28.2)	22.7 (21.6–23.8)	17.9 (15.9–19.8)	22.8 (21.9–23.6)	.0001
Barthel	97.9(96.9–98.7)	71.4 (66.7–75.9)	60.3 (54.1–66.5)	76.4 (73.4–79.4)	.0001
Charlson	1.25 (1.01–1.5)	2.32 (1.9–2.7)	2.32 (2.03–2.6)	1.96 (1.8–2.1)	.0001
FRAX major fracture	10.2 (8.8–11.6)	15.2 (13.6–16.8)	13.7 (11.8–15.6)	13.02 (12.04–13.9)	.0001
FRAX hip fracture	5.8 (4.4–6.4)	8.4 (7.3–9.5)	8.4 (6.7–10.1)	7.4 (6.6–8.1)	.001

BMI: body mass index; MMSE: mini mental state examination
*ANOVA.

Table 2. Risk of major osteoporotic fracture, impaired mental and physical capacity and comorbidity Mean difference (95% CI).

	Risk <10% $n = 179$ (48.4%)	Risk 10–20% $n = 117$ (31.6%)	Risk >20% $n = 74$ (20%)	p*
Age	78 (77–79)	84 (83–85)	85 (83–86)	
BMI	28 (27–28.4)	27 (26–28)	24 (23–26)	.0001
MMSE	25(24–26)	22 (20–23)	19(17–22)	.0001
Barthel Index	84 (80–88)	73 (68 to79)	63 (55–71)	.0001
Charlson Index 95% CI	1.9 (1.7–2.2)	2.03 (1.7–2.4)	1.9 (1.5–2.2)	$p = .78$

BMI: body mass index; MMSE: mini mental state examination.
*ANOVA.

groups. The mean body mass index (BMI) was 26.8 (26.3–27.4) kg/m^2, and was higher in home-dwelling patients than in hospitalized patients (28 (27.2–28.8) vs. 25.2 (24.3–26.1), respectively, $p < .0001$) (Table 1).

Table 1 also compares the means of the scales according to the origin. MMSE scores were lower in home-dwelling and residential patients than in hospitalized patients (27.8 (27.4–28.2) and 22.7 (21.6–23.8) vs. 17.9 (15.9–19.8), $p < .0001$). There was less dependence in home-dwelling and residential patients than in hospitalized patients (97.9 (96.9–98.7) and 71.4 (66.7–75.9) vs. 60.3 (54.1–66.5), $p < .0001$). The Charlson index was higher in residential and hospitalized patients than in home-dwelling patients (2.32 (1.9–2.7) and 2.32 (2.03–2.6) vs. 1.25 (1.02–1.5), $p < .0001$). The FRAX index scores for the risk of osteoporotic major fracture and the risk of hip fracture were higher in residential and hospitalized patients than in home-dwelling patients (15.2 (13.6–16.8) and 13.7 (11.8–15.6) vs. 10.2 (8.8–11.6); $p < .0001$) and (8.4 (7.3–9.5) and 8.4 (6.7–10.1) vs. 5.8 (4.4–6.4), $p = .001$).

Table 2 compares the risk of major osteoporotic fracture in the study groups. FRAX index scores were obtained in 370 patients (the BMI and, therefore, the FRAX index could not be calculated in five residential patients): 179 (48.38%) had a low risk (<10%) compared with patients with a medium risk (10–20%) and a high risk (>20%). Patients with a low risk were significantly younger and had significantly higher BMI, and higher MMSE and Barthel index scores. However, the Charlson index was non-significantly similar in all three groups.

Table 3. Risk of hip fracture, impaired mental and physical capacity and comorbidity Mean difference (95% CI).

	Risk <3% N: 94	Risk> 3% N: 276	p**
Age	76 (74 to78)	83 (82–84)	
BMI	29 (5)	26 (5)	.0001
	29 (28–30)	26 (25–27)	
MMSE	25 (24–27)	22 (21–23)	.0001
Barthel Index	88 (84–93)	72 (69–76)	.0001
Charlson Index	1. 71 (1.4–2.1)	2.02 (1.8–2.2)	.92

BMI: body mass index; MMSE: mini mental state examination.
**Student *t*.

Table 3 compares the risk of hip fracture according to the FRAX index. We calculated 370 indices, with 74.6% identified as having the highest risk (>3). Compared with subjects with a low risk (<3), patients with a high risk had significantly higher age, lower BMI, lower MMSE and lower BI. The Charlson index was non-significantly similar in both groups.

Table 4 shows the relationship between prior osteoporotic fracture and alterations in mental and physical capacity and comorbidity. The 269 (72.7%) individuals without a prior fracture, were younger and has a significantly higher MMSE and BI. There were no significant variations in the BMI or Charlson index.

Table 5 shows the bivariate relationships between the FRAX index for hip fracture and the other variables in the total population, which were significant for all variables (age, BMI, MMSE, Charlson index and BI).

Table 4. Patients with prior osteoporotic fracture and their relationship with impaired mental and physical capacity and comorbidity Mean difference (95% CI).

	No prior fracture $n = 269$ (73.7%)	Prior fracture $n = 106$ (28.3%)	p^{**}
Age	81 (70–82)	83 (82–84)	
BMI	27 (26–28)	27 (25–28)	.45
MMSE	23 (22–24)	21 (19–23)	.018
Barthel Index	80 (77–84)	67 (61–73)	.0001
Charlson Index	1.91 (1.7–2.1)	2.10 (1.8–2.4)	.93

BMI: body mass index; MMSE: mini mental state examination.
**Student *t*.

Table 5. Pearson's correlation and multivariate regression analysis of FRAX for hip fracture.

	Pearson's correlation		Multivariante regression analysis	
	r	*p*	β	*p*
Age	−0.302	.0001	0.182	.001
BMI	−0.336	.0001	−0.272	.0001
MMSE	−0.275	.0001	0	.996
Barthel Index	−0.342	.0001	−0.193	.005
Charlson Index	−0.101	.052	0.043	.879

BMI: body mass index; MMSE: mini mental state examination.

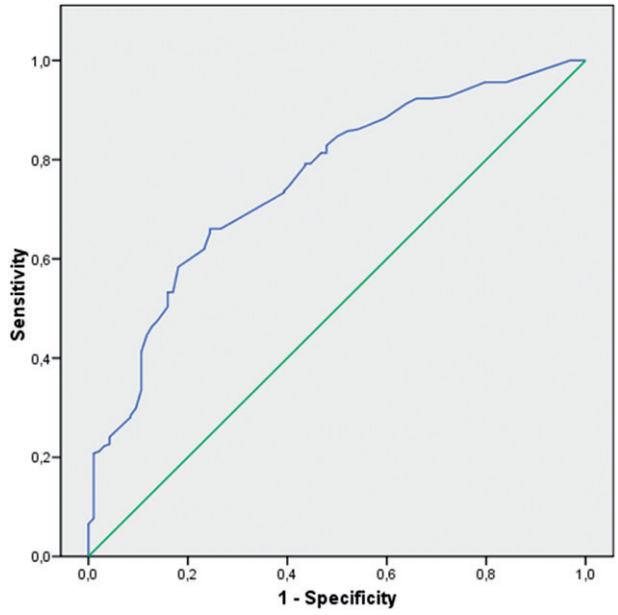

Figure 1. ROC curve. Relationship between the BI/MMSE and hip fracture risk >3.

The multiple regression analysis showed significant for age, BMI and BI.

The logistic regression analysis constructed a model that included sex, the MMSE, BI, and the Charlson index, with a risk of hip fracture of >3 as the dependent variable. The model was significant ($p < .0001$) although only female sex (4.4 95% CI = 2.6–7.6, $p < .0001$) and a high BI (0.104, 95% CI = 0.014–0.792, $p = .043$) were independently significant. Figure 1 shows the ROC curve that established the relationship between BI/MMSE and hip fracture risk >3 measured by FRAX. The area under the curve was 0.76 (95% CI = 0.7–0.81).

Discussion

Our results show that the BI and MMSE, which are included in various frailty indexes, can predict a risk of hip fracture of >3% measured by the FRAX index in the older patients. Geriatric patients are increasingly complex and usually have comorbidities, forcing health professionals to have a more global vision [7–9]. Comorbidity indexes, such as the Charlson index [7], should not be interpreted in isolation, but should form part of an integral assessment in which functional, mental and psychosocial aspects are taken into account [9–11].

González et al [12] estimated the 10-year risk of osteoporotic fracture using the QFracture tool, based on population data from the 2006 Spanish National Health Survey 2006. They found that the risk of osteoporotic fracture increases with age. After a hip fracture, the elderly present greater morbidity and mortality, and although mortality is important and has been widely studied, morbidity may have implications such as loss of independence and the need for social support [13–16]. High FRAX index scores [5,6] were assessed as a predictor of mortality in Japanese haemodialysis patients [17], and the study concluded that the FRAX index seems to be useful in predicting mortality in these patients, especially men, after adjusting for confounding variables. We have found no studies of the relationship between the FRAX index and the BI/MMSE.

Current comorbidity evaluation indexes [7,18–20] do not include physical and cognitive functional measures, which have suggested as predictors of hospital admission in the older people [18], with some authors finding them to be the best predictor of hospital mortality in this age group [19].

The variables evaluated from part of the frailty syndrome which has been described as a dynamic condition affecting the individual experiencing losses in one or more domains of human functioning (physical, psychological, social) and which is caused by different variables and increases the risk of adverse events [21]. These models are associated with age and could reflect the natural history of aging [22]. Unfortunately, there is no single validated index to assess frailty in clinical practice [23]. Some indices used have been associated with an increased risk of fractures [24] and falls [25]. The Glow cohort and the CaMos cohort used

different indices to assess the relationship between frailty and fractures, but both include many of the parameters assessed in our study. The Glow fragility fractures index variables included 15 items on comorbidity, 12 on basic activities of daily life (similar to BI), 6 items on signs and symptoms (fullness of life, energy, exhaustion, tiredness, self-evaluated pain/discomfort, unintentional weight loss). The frailty index used in the CaMos cohort included 30 items, 13 referring to pathology, 5 on functional aspects (vision, hearing, walking, manual dexterity/use of tools and cognition) and 12 on general health and daily activities. Some authors have proposed adding frailty to the FRAX index to improve its predictive value [26].

In our sample, the FRAX index was negatively correlated with the BI and the MMSE. That is to say, the lower the cognitive deterioration (higher MMSE score), the lower the likelihood of major osteoporotic fracture at ten years (lower FRAX) and the higher the dependency (lower BI), the greater the likelihood of osteoporotic fracture (higher FRAX index score). However, the Charlson index was not associated with the fracture risk, although some studies, such as the SIDIAP registry, which included 186,171 males, found a Charlson index $\geq$3 was associated with an increased risk of hip fracture [27].

Our study had some limitations. First, it was difficult to measure height due to physiological kyphosis, and in some cases (heel-knee) had to be used. Secondly, there were difficulties in comprehension among some patients, which made it difficult to obtain informed consent and may thus have resulted in selection bias, especially in long-stay residents of geriatric centres and hospitalized patients without relatives or legal guardians. Thirdly, observational studies cannot draw etiological conclusions, but may generate hypotheses and associations between the variables studied.

In conclusion, our results suggest that the use of the BI and MMSE, which form part of geriatric and frailty assessments, are associated with the ability of the FRAX index to predict a high risk of hip fracture (>3%) which are an indication criterion for the treatment of osteoporosis [28]. This joint evaluation could increase the number of patients with a high risk of hip fracture treated, with the consequent associated benefits. Frailty indexes may be as important as the FRAX index, which is based on clinical risk factors, in predicting the fracture risk in older patients.

Disclosure statement

The authors report no conflict of interest.

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