Editorial article

Spanish FRAX®: Pathing the way through walking

FRAX® español: se hace camino al andar

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Due to a greater life expectancy in developed countries such as Spain, the incidence of osteoporotic fracture is increasing, which has a direct effect on a higher health expense. In the case of hip fracture, which encompasses more severity, the incidence varies up to 7 times among different European countries, being Spain among the countries with lower incidence (711 cases per 100,000 women and year). Norway is considered to be of high incidence (1665 cases per 100,000 women and year) together with other countries from the north of Europe and America.

These differences for hip fracture in both sexes are also observed among Spanish regions, being Catalonia the one of highest incidence and Galicia the lowest one (623 and 317 cases per 100,000 inhabitants and year, respectively).

Opposite to a hip fracture incident, which occurs at an average age of 80 years, is prevention. In this context, age, sex and the most frequent risk factors such as early menopause, personal and family history of fracture and intake of corticosteroids are taken into account. The grater the number of present factors, the bigger the future risk of fracture. Sometimes bone densitometry is not available, or the patient’s risk is so high that the test is not necessary to start a treatment. Besides, we would have patients without risk factors whose probability of osteoporosis and fracture is low. But, certainly, there are many cases in which defining a high or low risk with a simple medical history is not easy.

The FRAX® tool was developed by WHO to assess the risk of fracture. It is based on models which combine clinical risk factors with or without bone mineral density (BMD) of the femoral neck. The models were built using information obtained from data of population cohorts from all 5 continents (FRAX® version 3.8). The algorithms of FRAX® calculate the probability of having hip fracture and main osteoporotic fracture (clinical vertebral fracture, forearm, hip or shoulder) in the next 10 years in men and women (http://www.shef.ac.uk/FRAX/index.aspx?lang=sp). The probability of fracture varies significantly in different regions; therefore, the thresholds of FRAX® have to be measured for every country. The main application of FRAX® is to identify those people who would be eligible for a densitometry or pharmacological intervention among the subjects with greatest risk.

The FRAX® tool establishes the risk of fracture regardless of the BMD measurement, even though using this improves the calculation. But it also has its weaknesses, such as just including the BMD of the femoral neck or not analysing the cases with several fractures, the dose of glucocorticoids and the intensity of smoking or alcohol consumption. An item regarding falls is not included in the formula either. In this way, when there is densitometric osteoporosis only in the spine, or several fractures or high doses of glucocorticoids, the result of FRAX® has to be individually assessed. Due to the characteristics of the cohorts included in the FRAX® tool, its application is, strictly speaking, for patients not being treated for osteoporosis. Despite these limitations, FRAX® is an invaluable help for the decision making in the treatment of patients with risk of osteoporosis and fracture. For the Spanish population we have an adjustment of FRAX®, which proved to have a good ability to detect densitometric osteoporosis of hip in women.

The study of Azagra et al. published in this edition of MEDICINA CLÍNICA proposes thresholds of FRAX® for main fracture in a cohort from Barcelona. The authors observe that the relation among fractures observed when analysing its cohort and fractures expected by the FRAX® tool, without carrying out a densitometry, was of 1.72. Consequently, according to this study, the FRAX® currently available for the Spanish population underestimates the risks of main fracture that will happen in the next 10 years. Based on its data, Azagra et al. stratified the main fracture risk in the Spanish population at <5% for low risk, ≥5% and <7.5% for medium risk, and ≥7.5% for high risk. In addition, the authors performed a cost analysis, and concluded that the most cost-effective option is to perform a densitometry with a FRAX® ≥5% (medium and high risk). Afterwards, they suggested to reclassify the cases through FRAX® with densitometry in high/low risk, and prescribe pharmaceutical treatment in those patients with risk ≥7.5%, and suggest general measures to patients with low risk. By applying this algorithm to its cohort of 816 women between 40 and 90 years, the percentage of women eligible for a densitometry reduces to 17.5%, compared to the common practice in Spain. The common practice is defined as the selection for densitometry through clinical criteria and isolated risk factors.

The study of Azagra et al. is interesting because we lack of sufficient analysis in the Spanish population to establish the threshold level that identifies subjects with risk of developing osteoporotic
fractures through FRAX®. It is focused on a relatively young population where there are probably more doubts at the moment to request a densitometry and start a treatment. It is a relevant study because it provides results of the real incidence of fractures for the next 10 years in our environment. The study has some weaknesses, such as the average age of 56 years and the absence of a uniform inclusion criterion in the cohort (criterion to request the densitometry), which would affect mainly its extrapolation to clinical practice.

Calibrations of the FRAX® were done in other populations, observing that in some countries, such as Sweden, the tool overestimates the risk of fracture almost two times, while in other countries, such as China, it underestimates it.6

It has also been observed in other 2 studies of cohorts carried out in the Spanish population that the FRAX® tool underestimates the risk of main fracture.11,12 One of the possible explanations is that the relation main fracture/hip fracture in Spain is not the same as the reference relation in the FRAX® tool in general. In this way, when comparing the incidence of fracture of the ECOSAP cohort with the reference cohort from Malmö, it is observed that the incidence is similar for main fracture, whereas in our population is the half for hip fracture.12 It has to be considered that non-hip fractures are more difficult for their coding. Another aspect to be considered is that the FRAX® tool has worse prediction ability in patients with extreme fracture risk, as the ECOSAP study shows, in which FRAX® made worse predictions in women with the lowest risk.12 In fact, as the authors indicate, this flaw of FRAX® would not be so significant since those patients with low fracture risk rarely require treatment. However, the FRAX® for hip fracture in the Spanish population seems to be well-adjusted, according to the results obtained in 3 published studies of cohorts.11-13

Therefore, the study of Azagra et al.10 shows that fracture thresholds can be adjusted to our population and build support on the diagnosis and treatment of osteoporosis, especially for those professionals with less experience in bone metabolism treatment, that so far were based in the conventional method of the combination of clinical risk factors and densitometry. In addition, it might be the first step to perform similar studies in different Spanish cohorts, to build FRAX® models of national use with greater sample sizes and representative sizes from our country.

We would like to give a warning regarding the systematic application of the recommendations from Azagra et al.10 for using FRAX® as screening to request a densitometry. The FRIDEX cohort has an average age of 56 years (only 18% of women are over 65); therefore, the results would be applicable especially to women between 50 and 60 years. Nevertheless, in our opinion, in this decade there is a great number of patients that request a densitometry. Besides, patients come from a geographic area where the incidence of hip fracture is one of the highest in Spain, so its applicability to areas with lower fracture incidence is questionable.

The consequences to apply the fracture thresholds determined by the FRAX®, according to Azagra et al., are that the threshold levels used in other populations (main fracture <10% low risk, >20% high risk);14 which have been used in our country due to the lack of own data, are not adequate. Regarding this, we have revised the data published by our group, corresponding to a sample of 339 women referred to a densitometry with an average age of 63 years and an average FRAX® for main fracture of 5.7%. If the 5% threshold proposed by Azagra et al. had been used, it would have been necessary to perform a densitometry to 40% of the patients (4.6% of women between 50 and 60 years). However, using the 10% threshold, 16% would have been eligible (none of the women between 50 and 60 years), and 22% would have been eligible if the 3% FRAX® threshold for hip had been used.15 Other Spanish authors have chosen as threshold for the request of a densitometry in women <65 years a FRAX® of 3.6% for main fracture, equivalent to a 65-year-old woman without risk factors.16

The criteria used to request a densitometry widely vary at national and international level. The National Osteoporosis Foundation (NOF), the International Society for Clinical Densitometry (ISCD) and the Spanish Society of Rheumatology (Sociedad Española de Reumatología, SER)17-19 recommend to perform the study to women over 65 and men over 70. The rest of the indications are variable. In this way, the NOF recommends the densitometry to younger people if there are risk factors of fracture, to those over 50 who have had a fracture and to those cases in which there is a disease or medication associated to bone loss.17 The ISCD has similar proposals for younger people,18 while the SER recommends the densitometry to women with early menopause with any higher risk factor, postmenopausal women of any age and men over 50 with at least one higher risk factor, people over 50 with fracture history due to fragility or with a disease or medication associated to bone loss, and for the assessment of pharmacological treatment. For those cases where FRAX® is used, the SER also recommends to perform a densitometry to women under 65 with risk of main fracture equivalent to the one of a 65-year-old woman without risk factors (Spanish FRAX® 3.6%).17 The National Osteoporosis Guideline Group (NOGG) establishes some FRAX® thresholds to select patients eligible for densitometry.20

In general, women under 60 have a low risk of fracture and it would be necessary to be more restrictive in this group at the moment of requesting a densitometry. In this way, some guidelines do not consider the densitometry in the management of primary prevention in women under 60 years old.21 Some authors state that the right strategy would be the search of cases instead of the systematic screening through densitometry. This way, the risk of fracture would be the most important thing and, based on it, it would be decided to quantify the BMD and to start treatment.21

Other issues remain to be clarified as regards the usefulness of the FRAX® tool in the Spanish population. One of them would be giving more significance to the risk of hip fracture because it is adjusted to our population. Thereby, in some guidelines, such as the NOF, it is considered of high risk a FRAX® for main fracture ≥20% or for hip fracture ≥3%.17

Likewise, it is necessary to reach consensus among different medical societies from our country related to osteoporosis to be on the same page about when a patient is considered to have high risk of fracture. Another aspect that should also be discussed is if a progressive increase of the FRAX® thresholds in relation to age should be applied in our population, as the NOGG establishes, in such way that it increases the threshold for the initial decision making from 4% at 50 years old up to 20% at 80 years old.20

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References


