

Original Article

Assessment of the antiosteoporotic treatment initiation: A retrospective observational study in Greece

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Abstract

Objective: A study to retrospectively assess the decision to implement treatment for osteoporosis based on Greek version of FRAX tool. **Methods:** The study population was 1000 postmenopausal women aged 45 or above, excluding those with medical conditions demanding specific osteoporosis management. Data were collected regarding their medical history and additionally, risk factors incorporated in FRAX questionnaire. FRAX score was estimated at the time of the anti-osteoporotic treatment initiation. **Results:** The mean age of the study sample was 58.5±8.79 years. 46.8% of the participating osteopenic women had initiated treatment for osteoporosis at their first consultation while the 80.6% met the current national intervention threshold of FRAX tool. **Conclusion:** Stemming from our results there is an indication that women who are borderline eligible for treatment and seek consultation for osteoporosis are likely to be given treatment regardless of the potential benefit. One cannot ignore the fact that a clinician's good clinical judgment is of the utmost importance and under no circumstances can be replaced by any prognostic assessment tool.

Keywords: FRAX, Osteoporosis, Postmenopausal women, Fracture risk

Introduction

Osteoporosis not only constitutes a major health problem but also a social and economic burden. The only clinical consequence of osteoporosis is fragility fractures, which occur at a relatively advanced stage of the disease. They have severe effects on patients such as persistent pain, limited function and disability resulting in low life quality. Osteoporotic fractures have also been associated with higher morbidity and mortality rates in the elderly^{1,2}. Based on the overall incidence rate of osteoporosis-related fractures, Greece is among the high risk countries³. According to the International Osteoporosis Foundation (IOF) report, it was estimated that for 2010 the total cost stemming from the osteoporotic fractures for Greece was €680 million, and it is forecast that this burden will increase dramatically as the population ages^{4,5}.

The primary aim of the therapeutic management of osteoporosis is to minimize the fracture risk. A comprehensive strategy should include both prevention and pharmacological interventions. The main concern initially of any therapeutic approach to osteoporosis is

the estimation of absolute fracture risk. Following that and depending on the patient's individual needs treatment must be administered accordingly. Currently, the definitive goal of any antiosteoporotic treatment is to decrease the possibility of fracture. This is due to the fact that not only osteoporotic patients (T-scores≤-2.5) are likely to incur a fracture but also those who are within the osteopenic range (-2.5<T-score<-1). Specifically, almost half of vertebral fractures in postmenopausal women appear in those with a BMD measurement consistent with osteopenia^{6,7}.

The authors have no conflict of interest.

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	Age (Years)			
	Total (n= 1000)	45-54 (n=382)	55-64 (n=396)	≥65 (n=222)
Weight (Kg)	65.02±10.45	64.45±10.27	65.68±10.6	64.83±10.44
Height (cm)	158.5±6.16	160.1±5.58	157.9±6.32	156.9±6.27
Previous Fracture [n(%)]	263 (26.3%)	64 (16.7%)	97 (24.5%)	102 (45.9%)
Parent Fractured Hip [n(%)]	212 (21.2%)	92 (24.1%)	93 (23.5%)	27 (12.2%)
Current Smoking [n (%)]	248 (24.8%)	151 (39.5%)	74 (18.7%)	23 (10.4%)
Rheumatoid arthritis [n (%)]	70 (7%)	23 (6%)	43 (10.8%)	4 (1.8%)
Secondary osteoporosis [n (%)]	326 (32.6%)	114 (29.8%)	129 (32.6%)	83 (37.4%)
Alcohol 3 or more units/day [n (%)]	14 (1.4%)	6 (1.6%)	7 (1.8%)	1 (0.4%)
FRAX-Major osteoporotic	9.3 (9.1)	5.65 (4.4)	10 (7.8)	17 (11.2)
FRAX-Hip Fracture	2.8 (3.8)	1.4 (1.9)	3.1 (3)	6.25 (7.4)

Table 1. Main clinical characteristics on the study sample based on FRAX. Values are expressed as mean ± Standard Deviation, N are the number of subject, percentage (%) or median (interquartile range).

Each patient's fracture risk profile should be taken into account before determining the initiation of an osteoporosis treatment along with BMD measurements. Numerous clinical risk factors have been identified to associate with an increase in fracture risk. FRAX is a ubiquitous fracture risk assessment tool⁸. The FRAX model has been available for Greece since 2012 and is included in the national diagnostic and therapeutic guidelines⁹. Moreover, cost-effective intervention thresholds have also been determined for Greece. Namely, these are set at 2.5% and 10% for the 10-year probability of hip and major osteoporotic fractures respectively, for individuals up to age of 75. For older subjects the intervention thresholds are raised to 5% and 15%¹⁰. Nonetheless, these thresholds are not yet in implementation in our national guidelines where the US-adapted intervention cut-off points (probability for major osteoporotic fracture ≥20 or hip fracture ≥3) are in place.

The advances in the diagnostic techniques give the opportunity to detect osteoporosis before fracture occurs and to identify those at high risk. The therapeutic strategy should be planned individually for each patient depending on their needs, medical history and other patient related circumstances. This is due to the fact that the treating physician should account for osteoporosis being a chronic condition requiring chronic management. Suitable treatment for osteoporosis should reflect medical history, fracture risk and previously received antiosteoporotic treatment. Furthermore, the balance between potential risks and benefits is an issue that should always be addressed in the therapeutic decisions^{9,11}.

In determining patients' treatment initiation, it is important to assess the fracture risk. FRAX offers the ability to clinicians to distinguish between patients at elevated fracture risk and those who are not and consequently offer treatment to those most likely to benefit from it. The purpose of this study

was to assess the initiation of antiosteoporotic treatment retrospectively based on Greek version of FRAX score.

Methods

This is a cross-sectional, observational, retrospective study of 1000 postmenopausal women from the age of 45 and over who have had a consultation for osteoporosis evaluation. Patients were selected by osteoporosis experts (primarily orthopedics the specialty which mainly treat osteoporosis in Greece, but also rheumatologist, endocrinologist and general practitioners). The accumulated data covered a 15-year period (1999-2014). There were five participating centres in Greece: two large Public Hospitals in Athens, one health centre serving in rural area and two private osteoporosis practices, one in Athens and one in Thessaloniki, the second largest city in Greece.

The inclusion criteria encompassed sex (female), age (45 to 90) and postmenopausal state. Whereas, the exclusion criteria were: malignancy, transplantation, chronic kidney disease and bone disease other than osteoporosis such as osteomalacia, since these patients require specific management.

The study was conducted in accordance with the World Medical Association Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects and the ethical approval for the study was granted by the Ethics Committee of Aretaieion Hospital, University of Athens. Based on the protocol we retrieved the following data for each participant: age, year of first osteoporosis diagnosis, height and weight, current smoking, alcohol consumption, first degree relatives with hip fracture, personal history, rheumatoid arthritis, secondary osteoporosis, previous osteoporotic fracture, T-score values of hip femur neck or/and lumbar spine (L2-L4), wherever available. We calculated FRAX retrospectively at the time of the anti-osteoporotic treatment initiation so

as to evaluate the percentage of patients that did or did not receive treatment because of the doctors' overestimation or underestimation of actual fracture risk.

Statistical Analysis

Descriptive statistics are presented as mean \pm standard deviation (SD) and range, median and interquartile range (IQR, in case of violation of normality) for quantitative parameters, and as percentage for qualitative parameters. All analyses were performed using the statistical package SPSS v.17.00 (Statistical Package for the Social Sciences, SPSS Inc., Chicago, Ill., USA).

Results

The mean age of the study sample was 58.5 ± 8.79 years. According to diagnostic criteria based on the T-score for BMD, the study sample was 50.2% osteoporotic, 48.8% osteopenic and only 1% had normal BMD. The baseline characteristics of the participants are summarized in the Table 1.

A total of 26.3% had suffered at least one osteoporotic fracture before the initiation of any treatment and 21.2% had family history of osteoporotic fracture. The median risk of major osteoporotic fracture (%) was 5.65 (4.4) in women younger than 55 years, 10 (7.8) in women aged between 55 and 64 and 17 (11.2) in women older than 65 years; the median risk of hip fracture (%) was 1.4 (1.9), 3.1 (3) and 6.25 (7.24) respectively (Table 1).

In our study, all the women (50.2%) with T-score equal or above -2.5 SD received antiosteoporotic treatment. From the 48.8% of osteopenic participants, the 95.9% (N=468) had already initiated treatment for osteoporosis at their first consultation. The 19.9% of those participants had a vertebral or/and hip fracture. According to the US-adapted therapeutic intervention thresholds, since Greek ones are even today not incorporated in our clinical guidelines, the 80.6% of those osteopenic patients should have initiated treatment. Thus, the remaining 19.4% are not well indicated cases. If we were to take into consideration the Greek thresholds, only 9.3% did not meet the criteria for treatment.

Discussion

The decision to initiate antiosteoporotic treatment, especially for patients who are borderline eligible for treatment, to a certain extent remains an ambiguous topic. Undeniably, there are clear benefits to osteoporotic treatment for patients at high risk for fracture. It is obvious that clinical guidelines contribute to better patient care. Each country releases its recommendations providing more precise clinical guidance for physicians treating patients who are at risk for fractures^{9,12-14}. Through these, clinicians are assisted to treat high-risk patients for an appropriate duration and not treat low risk patients unless absolutely necessary. Having said that, ambivalent cases remain present.

A specific cut-off point of fracture risk below which fracture will occur or above which it will not, is difficult to establish, thus the diagnostic thresholds could be considered to some level arbitrary. Therefore, the necessity for better communication on the controversial nature of certain disease thresholds exists¹⁵. Each country bases its cost-effective cut-off points for intervention on epidemiological studies and they are subject to ongoing observation and fluctuation. The cut-off points are only indicative and should be only used supplementary in the clinicians' decision based on the specific clinical characteristics of the patient.

Where fracture risk estimations regarding eligible for treatment patients is reached with uncertainty, therapeutic management of osteoporosis has extended variability, as a result, high fracture risk patients may be undertreated while low fracture risk patients may be overtreated¹⁶.

The results of our study show that approximately 20% of the treatments were not clearly indicated. The same pattern has been reported in a study carried out in Spain which concluded that 48% of patients prescribed antiosteoporotic treatment did not meet the criteria for treatment¹⁷. Another study conducted in a Spanish regional health care system revealed that two-thirds of new prescriptions in the population were inappropriate¹⁸. Sanf elix-Gimeno G. et al. (2015) concluded that the medicinal management of osteoporosis in women aged 50 and above embodies to a notable extent overuse and to a secondary extent, underuse, nonetheless the degree of ineligibility is contingent upon which clinical guidelines were used. combines significant overuse and to a lesser grade, underuse, although the level of inappropriateness differentiate depending on the clinical guidelines used¹⁹. The unnecessary management of overdiagnosed diseases seems to be an increasingly significant issue in clinical practice especially in developed countries^{20,21}, with financial and personal effects^{22,23}.

Research has shown that excessive use of osteoporosis screening in women at low fracture risk may be a pivotal reason that leads to overdiagnosis²⁴. Moreover, inadequate patient perception in regards to the benefits and harms of pharmacological intervention can affect decision making and play a contributory factor to increased treatment intake²⁵. In addition, there is a possibility for clinicians to over or underestimate harms and benefits, resulting in substandard clinical decisions. Taking into account the above factors, effective interventions may be underused and low value interventions overused²⁶ as also shown by our results.

Patient factors, including patient preferences, physician's clinical judgment, doctor-patient relationship, communication and agreement on the severity of the case are factors of important relevance that it should be taken into consideration when discussing the issue of treatment initiation^{16,27}.

Another factor to consider regarding the less well indicated cases based on FRAX thresholds, is throughout the years the various criteria for the initiation of osteoporosis

treatment undergo changes. Specifically, up to 2011 the therapeutic intervention in osteoporosis in Greece was mainly based on the T-score of individuals, preceding that rapid bone loss was a main reason to initiate treatment.

Despite indications of overtreatment, the existence of treatment gap remains undisputed. According to IOF, the treatment gap in Greece was estimated at 25 % and 31 % for women and men respectively²⁸. Furthermore, various studies have shown that of the patients who have had a low trauma fracture just about 20% receive treatment for osteoporosis^{29,30}. Patients being unaware and having limited knowledge regarding osteoporosis, its consequences and the benefit of treatment is a significant reason for osteoporosis undertreatment^{31,32}.

A limitation of this study is that the main source of data was clinical files but since at the time in Greece public hospitals and medical centres held no electronic records and faced lack of staff, there is a possibility that the patients' medical history was not fully recorded. That is to say, that significant data, which would have explained the decision for treatment, were possibly not included thus our results should be interpreted with caution. Another issue we had to take into consideration is that the attending physicians alternated. Thus, years of experience, training, specialty and time working in current position affect the approach taken and the evaluation of each patient case especially in ambiguous ones.

Conclusion

Focusing solely on the results there is an indication that women who consult a clinician for osteoporosis but are not well defined cases will receive treatment regardless of whether or not there is an absolute necessity for it. In juxtaposition to those in actual need of treatment but who fail to seek consultation and are, therefore, undertreated. All treatment decisions require clinical judgment and consideration of individual patient factors, including risk factors not captured in the FRAX model. We have to underline that any prognostic assessment tool does not replace good clinical judgment. Decisions to treat must be made on a case-by-case basis.

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