Bone 62 (2014) 43–50

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Original Full Length Article

Impact of changes in mortality on FRAX-derived fracture probabilities

Omar I. Kreidieh, Ghada El-Hajj Fuleihan *

Calcium Metabolism and Osteoporosis Program, WHO Collaborating Center for Metabolic Bone Disorders, Division of Endocrinology, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon

ARTICLE INFO

Article history:
Received 14 May 2013
Revised 6 January 2014
Accepted 20 January 2014
Available online 27 January 2014

Edited by: Felicia Cosman

Keywords:
Mortality
FRAX
Major osteoporotic fracture
Hip fracture
Case finding strategy
Fracture prediction

ABSTRACT

Background: Accurate hip fracture incidence and mortality rates are two essential requirements for FRAX calculators.
Purpose: To investigate the effects of change in mortality on FRAX-derived fracture estimates.
Methods: Lebanese FRAX calculator was updated in 2012 from version 3.00 utilizing WHO mortality data from year 1999, and hip fracture incidence rates from 2007, to version 3.05 utilizing mortality data from 2009, but with identical hip fracture data. FRAX-derived estimates from 679 patients were computed using both FRAX versions and compared. Numbers presented as median [25th–75th] percentiles.
Results: The 10-year FRAX-derived probability of major osteoporotic fracture and hip fracture increased substantially. Changes were most pronounced in high risk sub-groups. The relative increase in probability of major osteoporotic fracture in individuals with a baseline risk of 10–20% was 79% [19%–127%], and in individuals with a baseline risk >20% it was 125% ($N = 3$). The numbers for relative increase in hip fracture probability were 98% [33%–135%], and 129%, respectively. Similarly, individuals older than 70 years had a 125% [89%–150%] relative increase in probability of major osteoporotic fracture and a 122% [95%–145%] relative increase in hip fracture probability. Using the FRAX-based Lebanese guidelines, FRAX 3.05 led to an additional increase in treatment qualification of 3.8 patients per 100 patients, or a relative increase of 24%.
Conclusions: Updates in mortality values increased FRAX-derived estimates, most substantially in older patients, and those at high risk for fracture. The update results in altering individuals' treatment decisions and modifying country wide osteoporosis management. Our results are relevant to the development and update of FRAX models for countries worldwide, and more importantly those with increasing longevity and possible increase in fracture rates.

Introduction

As longevity continues to increase, fractures will contribute to a substantial and greater proportion of morbidity and mortality in our societies. Until recently, bone mineral density (BMD) was the single best test to assess fracture risk, but this single measure is limited by low sensitivity, specificity, variability between measurement tools and site, and its association with relative rather than absolute fracture risk estimates [1–3]. FRAX, a web-based fracture probability calculation tool introduced in 2008, allows the calculation of absolute fracture risk probabilities, based on risk factors, with or without BMD, and facilitates risk stratification and patient tailored therapy. It has since created a paradigm shift in care pathway models and has become the cornerstone for the development of national osteoporosis guidelines [4–6]. Today, there are over 58 FRAX calculators developed in 52 countries accessible online http://www.shef.ac.uk/FRAX/index.aspx?lang=En (accessed December 17, 2013).

The unique features that render the FRAX calculator country specific are the FRAX requirements of availability of country specific hip fracture incidence rates, major osteoporotic fracture incidence rates whenever available, and longevity data. These are all dynamically changing variables that are affected by changes in healthcare and socioeconomic factors [6,7]. Indeed, secular trends in hip fractures have been recently described, with a decline in the West, and a continued rise in the East, with the exception of Hong Kong and Taiwan [8–12]. Concomitantly, while global life expectancy at 60 years of age has only increased by one year from 18 to 19 years in Middle East countries between 2000 and 2011, http://apps.who.int/gho/data/view.main.690?lang, changes in certain countries have been more pronounced and exceeded 20% in certain instances [13].

The possible effects of such changes in epidemiologic data are best exemplified by the recent changes observed in the US population. Age-adjusted fracture incidence and mortality rate have both been on the decline in the US since 1995 [14–16], and revision of the US FRAX version to include an updated data source, the Health Cost and Utilization Project Nationwide Inpatient Sample, as well as a statistical discount in reported fracture rates to accommodate for multiple fractures in the same individuals culminated in lower fracture estimates. Indeed, median probability estimates were lowered by 19% and 24%, for ages 60 and 80 years respectively [17]. The exclusive effect of changes in life expectancy on FRAX derived fracture probabilities have not been

* Corresponding author. Fax: +961 1 745321, +961 1 744464.
E-mail address: gf01@aub.edu.lb (G. El-Hajj Fuleihan).

8756-3282/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.bone.2014.01.014

elucidated. While maintaining the same hip fracture rates, Lebanon's FRAX calculator was updated in early 2012 from the original model that used WHO life expectancy Tables from 1999, to updated WHO 2009 data reflecting improved life expectancy (Table 1).

This study therefore aims at investigating the effects of increasing longevity on FRAX fracture predictions and treatment algorithms, using actual patient information.

Methods

BMD and T-scores

BMD was measured using a Hologic 4500A densitometer, and the NHANES III database was used to derive femoral T-scores. At our institution, same day duplicate scans are usually performed after obtaining permission on different patients, one for each skeletal site, including the femoral neck. The mean ± SD is then calculated monthly. Precision has been stable over the years and is below the International Society of Clinical Densitometry's recommended quality assurance cut-offs, averaging 1.4 ± 0.27% at the femoral neck during the scan acquisition period.

Lebanon FRAX Model

Lebanon FRAX Model was originally launched in 2009, as FRAX version 3.0, based on national hip fracture incidence rates derived from a hip fracture registry maintained by the Lebanese Ministry of Health [18], and WHO life expectancy tables that were available at the time for year 1999. It was since revised and updated to FRAX version 3.05, using WHO life expectancy tables for the country for year 2009. We calculated 1-year survival probability from 1-year mortality data for years 1999 and 2009, as used in FRAX by FRAX Sheffield team, and provided by Dr. Kanis (Table 1).

Study group

We reviewed 805 de-identified bone density hip scans of patients presenting to the bone densitometry unit at the American University of Beirut between February and September 2012; and an additional 202 hip scans of subjects enrolled in a vitamin D supplementation trial in 2011–2012 (http://clinicaltrials.gov/ct2/show/NCT01315366). Scans of non-Lebanese patients, those less than 60 years in age, or those with missing information on risk factors entered into FRAX data were also excluded. Therefore, a total of 679 out of 1007 screened scans were included in the study. Appendix 1 shows patient demographics by source of entry into the study. Risk was estimated for each patient using femoral neck BMD and FRAX 3.0 and FRAX 3.05 software versions.

We classified patients into 3 risk subgroups based on baseline FRAX probability of major osteoporotic fracture, where a probability of fracture <10% was considered to be mild risk, a probability of fracture between 10% and 20% was moderate risk, while a probability ≥20% was considered high risk.

Table 1
1-year survival data and crude hip fracture rates used in original and revised FRAX models.

		Survival 2009[a]	Survival 1999[a]	Absolute increase in survival probability[b]	Relative increase in survival probability (%) [c]	Hip fracture incidence rates[d]
Male	60–64	97.99	97.00	0.99	1	38.7
	65–69	96.84	94.04	2.80	3	78.7
	70–74	95.01	88.18	6.83	8	103.8
	75–79	92.12	79.17	12.95	16	250.2
	80–84	87.39	69.32	18.07	26	838.1[e]
	85–89	80.60	54.8	25.80	47	838.1[e]
Female	60–64	99	97.29	1.71	2	40.4
	65–69	98.36	94.07	4.29	5	113.8
	70–74	97.13	86.99	10.14	12	284.2
	75–79	94.91	76.35	18.56	24	530.8
	80–84	90.79	67.52	23.27	34	1446.7[e]
	85–89	84.33	55.41	28.92	52	1446.7[e]

*Data was provided by Dr. John Kanis (2013).
[a]Probability of 1-year survival derived from data provided by Dr. John Kanis (as used when FRAX Lebanon calculator was revised).
[b]Absolute increase in 1-year survival probability between years 1999 (FRAX 3.00) and 2009 (FRAX 3.05). Calculated as survival probability 2009 − survival probability 1999.
[c]Relative increase in 1-year survival probability between years 1999 (FRAX 3.00) and 2009 (FRAX 3.05). Calculated as (survival probability 2009 − survival probability 1999)/survival probability 1999, rounded to include no decimals
[d]Fracture incidence rates per age group in the entire Lebanese population, expressed as hip fractures/10,0000/year.
[e]Fracture incidence rates for all individuals above 80 years of age.

Treatment allocation by guidelines

Treatment allocation using FRAX was determined for each patient twice by using the most recent Lebanese guidelines in conjunction with FRAX probability estimates obtained from each FRAX version, as detailed below. The Lebanese guidelines recommend the administration of pharmacologic therapy to patients who had a previous fragility fracture of the spine, hip, or two or more other fragility fractures. In the absence of fractures, treatment is recommended in patients with FRAX derived 10 year risk of major osteoporotic fracture ≥10% for patients with age up to 70 years, and according to a moving 10 year FRAX derived moving threshold for major osteoporotic fracture in patients older than 70 years (see Appendix 2). The moving threshold was determined according to the same criteria used in the National Osteoporosis Guidelines Group in the UK, that is the FRAX derived probability of a female patient with the same age, a history of fragility fracture, and a nation specific body mass index (BMI) (30 kg/m^2 in the elderly Lebanese)[19].

Statistical analyses

Analysis of the data was carried out using SPSS for Windows version 20.0 (IBM Corp. Armonk, NY) [20]. For all statistical analysis, we set a-priori a p-value ≤ 0.05 as significant. Because of an obtained skewed distribution of the data, all values are presented as median [25th–75th] percentiles. Independent t-test and ANOVA were used to compare mean values between continuous variables of normally distributed data, while comparisons of non-normally distributed data was done through Wilcoxon signed-rank test for paired distributions, and Mann–Whitney U test for unpaired distributions. Chi-squared analysis was used to assess the differences in the proportions of subjects between two groups, including differences between the proportions of subjects to be treated between the two FRAX versions. Absolute changes in fracture probabilities were calculated as the differences in FRAX derived probabilities FRAX 3.05 − FRAX 3.00.

Results

Patient characteristics

Six hundred seventy nine patients were included in the study. Their median age was 69 [65–74] years, and BMI 28.1 [25.1–31.6] kg/m^2. The median femoral neck BMD T-score was −1.85 [−2.4– −1.2], and less than one in five of the study subjects had a FRAX risk factor other than female gender (personal history of fracture, parent fracture, smoking history, glucocorticoid use, rheumatoid arthritis, secondary osteoporosis, and daily alcohol use) (Table 2). The average number of FRAX risk factors, including female gender, was therefore 1.47 ± 0.9 risk factors per patient, while the median was 1 [1,2] risk factor, thus representing a low risk group overall. Patient characteristics by sub-study group are shown in Appendix 1.