Comparison of Fracture Risk Assessment Tool Score to Bone Mineral Density for Estimating Fracture Risk in Patients With Advanced Prostate Cancer on Androgen Deprivation Therapy

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OBJECTIVE To estimate the risk of fracture (Fracture Risk Assessment Tool [FRAX] algorithm) because of the development of osteoporosis in prostate cancer patients undergoing androgen deprivation therapy (ADT) for patients who would otherwise not have been identified for treatment by the T score.

METHODS This study includes men undergoing ADT for prostate cancer at our urology group. Clinical data were collected via chart review. Subjects were evaluated for fracture risk using country specific (for the United States of America) World Health Organization's FRAX. The FRAX calculations were then compared to fracture risk as determined by T score, for a subset of our cohort that received dual-energy X-ray absorptiometry.

RESULTS Our cohort consisted of 613 patients on ADT, 94 of which had a dual-energy X-ray absorptiometry scan. The FRAX algorithm identified 61.6% patients requiring therapy without bone mass density (BMD), 46.8% with BMD, and 19.14% with T score alone. In addition, positive correlation was found between FRAX with and without BMD as well as T score and FRAX with BMD and without BMD.

CONCLUSION Our data indicate that many patients who were not found at significant risk for fracture with T score were in fact found to be at risk with the FRAX calculation. The largest proportion of patients was found to be at risk through the FRAX calculation without BMD, followed by FRAX with BMD, followed by T score alone. The utility of FRAX is beneficial in identifying patients that may benefit from effective bone-tropic treatment modalities. UROLOGY 84: 164–168, 2014.

Androgen deprivation therapy (ADT), a common treatment option for patients with prostate cancer (PCa) that reduces circulating testosterone levels, has a detrimental effect on bone mass density (BMD), leading to a substantial increase in fracture risk.[1,2] In fact, men undergoing ADT are 4 times more likely to develop significant bone deficiency.[2] Furthermore, it has been well established that fractures are associated with significant morbidity and mortality. Although many modalities for bone-tropic therapy exist,[3] it remains an underdiagnosed and undertreated condition, especially in men.[4] Failure to properly screen patients is detrimental to both quality and quantity of life, especially for those with PCa, given the continuing increase in life expectancy.

The conventional method used to identify patients who require treatment for osteoporosis is with a BMD measurement obtained through dual-energy X-ray absorptiometry (DXA) scan. Standardization exists by using a T score, which is derived by comparing an individual's femoral neck BMD with that of young-adult population of the same sex. Osteoporosis is diagnosed in patients with $\geq$2.5 standard deviations below the comparison BMD, whereas low bone mass (osteopenia) is considered in -1 to -2.5 standard deviations and greater than -1 are considered normal.[5] However, studies have illustrated that fractures are not uncommon in men whose T score does not suggest the need to treat osteoporosis, especially

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in low bone mass individuals.[6] Therefore, the Fracture Risk Assessment Tool (FRAX) algorithm was created to improve fracture risk assessment by accounting for additional patient characteristics to better detect patients with high probability of fracture,[7] with or without the use of BMD.[21] These factors include age, sex, race, body mass index, alcohol use, tobacco use, glucocorticoid use, rheumatoid arthritis, previous fragility fracture, family history of hip fracture, and secondary osteoporosis.[8-16] However, it has been postulated that the FRAX model should not be considered as the gold standard; rather, it should be used as a platform to build on as we move forward with novel approaches for targeted bone-tropic therapy.[17]

The FRAX tool calculates the probability of risk for hip fracture and major osteoporotic fracture (MOF) for the next 10 years. Cost-effectiveness has been illustrated for initiating treatment with risk thresholds of 3.0% for hip fracture and 20% for MOF, and it has been modified accordingly by region.[18] According to recent guidelines by the National Osteoporosis Foundation (NOF) in adaptation of the World Health Organization (WHO) guidelines, hypogonadism is considered secondary osteoporosis.[19] Therefore, secondary osteoporosis may be considered in patients undergoing ADT.[20] However, studies incorporating FRAX score as an indication for bone-tropic therapy in patients on ADT have demonstrated some inconsistencies that need further investigation. The use of FRAX score solely on the previously mentioned clinical parameters, without BMD, has been shown to provide useful insight on which to make treatment decisions.[21] The purpose of our study was to evaluate and compare osteoporosis risk by using the FRAX algorithm with and without BMD, as well as with T score for a cohort of patients on ADT.

METHODS

Our study included men undergoing ADT for PCa at our urology group. Patient evaluation and subsequent treatment for osteoporosis risk was conducted according to current guidelines. Patient information was collected on height, weight, age, race, use of systemic steroids, tobacco and alcohol, as well as relevant medical history including any kind of inflammatory or degenerative arthritis. Treatment information collected included the duration and type of ADT administered, as well as all bone-targeted therapy. Subjects were evaluated for risk of fracture using the WHO/FRAX calculator. All subjects within our bone clinic database were considered to have secondary osteoporosis because of ADT. Managing physicians determined the necessity of obtaining DXA. Therefore, femoral neck BMD was available for 94 of the 613 patients.

We describe the presence of osteoporotic fracture risk and subsequent therapy recommendation, both according to the NOF T score guidelines and FRAX calculation parameters. All subjects on ADT with a history of PCa were included in the analysis.

To analyze the strength of the relation between our measurements, a Pearson bivariate correlation was performed. The correlation coefficient "r" is stronger when close to 1 or −1, for a positive or negative correlation, respectively. An "r" ranging from 0 to 0.3 was considered weak, whereas 0.3-0.7 was counted as moderate, and strong if >0.7, respectively. A P value ≤.05 was considered statistically significant in this study.

Table 1. Calculated fracture risks

FRAX Score	Pts, n	% (Range)
Without BMD (n = 613)		
Pts with ≥3% 10-yr hip FRAX	378	61.6
Median % hip FRAX	—	4.1 (0.1-19.0)
Pts with ≥20% 10-yr MOF FRAX	12	2
Median % MOF FRAX	—	10.0 (1.7-24.0)
With BMD (n = 94)		
Pts with ≥3% 10-yr hip FRAX	44	46.8
Median % hip FRAX	—	2.8 (0.2-8.0)
Pts with ≥3% 10-yr hip FRAX without BMD	65	69.1
Median % hip FRAX without BMD	—	6 (0.2-14.0)
Pts with 20% ≥10-yr MOF FRAX	4	4.3
Median % MOF FRAX	—	7.7 (2.0-27.0)
Pts with T score ≤−2.5	18	19.1

BMD, bone mass density; FRAX, World Health Organization Fracture Risk Assessment Tool; MOF, major osteoporotic fracture; Pts, patients.

RESULTS

The age of the 613 men in our study ranged from 49 to 90 years, with a median age of 75 years. The median ADT duration was 13 months (range, 1-72). Standard indication for administering ADT was used after failure of primary definitive treatment. ADT in our cohort included simple orchiectomy, gonadotropin releasing hormone agonists and antagonists, androgen antagonists, and a CYP17 inhibitor. The median body mass index was 28.5 kg/m^2 (range, 15-49). Of the total number of patients, 581 patients (94.8%) were white, 22 patients (3.6%) were African American, 2 patients (0.3%) were of Asian descent, whereas the remaining 8 (1.3%) self-reported as "other". In addition, 45 patients (7.3%) used oral glucocorticoids and 98 patients (16.3%) self-reported as current smokers, whereas 14 (2.6%) declined to respond on smoking status.

FRAX was calculated for all 613 patients without the use of BMD. In this cohort, 378 (61.6%) patients met or exceeded the established treatment threshold of 3% for hip fracture without the use of BMD, with a median 4.0% (range, 0.2%-22.8%). A total of 12 patients (2.0%) exceeded the treatment threshold set for 20% 10-year MOF risk, with a median of 10.0% (range, 1.7%-24.0%; Table 1).

Measurement of BMD was available for 94 patients, who had a median T score of −1.6 (range, −4.7 to −0.3). By using the T score alone, 18 patients (19.14%) qualified for bone-tropic therapy. Of the same patients, the FRAX algorithm identified 44 patients (46.8%) with the use of BMD and 65 patients (69.1%) without the use of BMD who qualified for treatment.