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Original Article

Combining Computed Tomography-Based Bone Density Assessment with FRAX Screening in Men with Prostate Cancer

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Abstract

To investigate the addition of a computed tomography (CT)-based method of osteoporosis screening to FRAX without bone mineral density (BMD) fracture risk assessment in men undergoing radiotherapy for prostate cancer, we reviewed the records of all patients with localized prostate cancer treated with external beam radiotherapy at our institution between 2001 and 2012. The 10-yr probability of hip fracture was calculated using the FRAX algorithm without BMD. The CT attenuation of the L5 trabecular bone ($L5_{CT}$) was assessed by contouring the trabecular bone on a single CT slice at the level of the midvertebral body and by averaging the Hounsfield units (HU) of all included voxels. $L5_{CT}$ values of 105 and 130 HU were used as screening thresholds. The clinical characteristics of additional patients identified by each $L5_{CT}$ screening threshold value were compared to patients whose estimated 10-yr risk of hip fracture was 3% or greater by FRAX without BMD. A total of 609 patients treated between 2001 and 2012 had CT scans available for review and complete clinical information allowing for FRAX without BMD risk calculation. Seventy-four (12.2%) patients had an estimated 10-yr risk of hip fracture of 3% or greater. An additional 22 (3.6%) and 71 (11.6%) patients were identified by CT screening when thresholds $L5_{CT}$ = 105 HU and $L5_{CT}$ = 130 HU were used, respectively. Compared to the group of patients identified by FRAX without BMD, the additional patients identified by CT screening at each $L5_{CT}$ threshold level tended to be younger and heavier, and were more likely to be African–American or treated without androgen deprivation therapy. These results suggest that the addition of CT-based screening to FRAX without BMD risk assessment identifies additional men with different underlying clinical characteristics who may be at risk for osteoporosis and may benefit from pharmacological therapy to increase BMD and reduce fracture risk.

Key Words: Androgen deprivation therapy; bone density screening; FRAX; prostate cancer.

Introduction

Hip fracture is an uncommon, but potentially devastating, outcome in men with localized prostate cancer who have received radiotherapy (RT). The incidence is estimated at 0.8–1.0 per 100 person-years *(1)*. Men with intermediate or high-risk prostate cancer are commonly prescribed androgen deprivation therapy (ADT), which has been shown to decrease bone mineral density (BMD) and increase fracture risk *(2–7)*. Current guidelines published by the National Osteoporosis Foundation (NOF) *(8)* and the National Comprehensive Cancer Network (NCCN) *(9)* recommend screening all men undergoing prostate cancer treatment by calculating their 10-yr fracture risk using the FRAX *(10)* algorithm. For men at increased risk of fracture,

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dual-energy X-ray absorptiometry (DXA) is recommended and treatment to increase BMD and reduce fracture risk should be considered.

The FRAX algorithm is a useful screening tool for men with prostate cancer because it can be used to estimate fracture risk in the absence of BMD measurement, based on body habitus and historical information *(10)*. An alternative method of osteoporosis screening has recently been described, performed by calculating the computed tomography (CT) attenuation values of trabecular bone within the vertebral bodies of the lumbar spine *(11)*. When using DXA measurements as the reference standard, various CT-attenuation threshold levels yielded sensitivities and specificities greater than 90% for predicting osteoporosis *(11)*. Because CT scans are obtained as part of the external beam RT planning process for men with prostate cancer, this alternative method of osteoporosis screening could be utilized efficiently without the need to obtain additional testing. We retrospectively applied both screening methods to patients treated at our institution to determine if additional patients at high risk for fractures could be identified with the addition of CT-based screening.

Methods and Materials

We retrospectively reviewed the records of all patients undergoing external beam RT for prostate cancer in our department between 2001 and 2012. Demographic, disease, and treatment characteristics were abstracted from each patient's medical record, and the 10-yr probabilities of major osteoporotic and hip fracture were calculated using the FRAX algorithm without BMD *(10)*. All patients who had adequate past medical history documented within 3 mo of RT and who had CT imaging for RT planning inclusive of the L4–L5 vertebral interspace available for review were included in this analysis. When calculating fracture risk using FRAX, patients who were prescribed ADT were considered to have secondary osteoporosis (one of the key inputs) as recommended in the NCCN Guidelines *(9)*. Screening using FRAX without BMD was considered positive if the 10-yr hip fracture risk was 3% or if the 10-yr major osteoporotic fracture risk was 20% *(9)*.

The CT attenuation of the L5 trabecular bone ($L5_{CT}$) was assessed as follows: first, Eclipse software (Varian Medical Systems, Palo Alto, CA) was used to contour only the cancellous bone at the midvertebral level of L5 (Fig. 1). Care was taken so as to exclude the cortical bone, vascular channels, and any bony abnormalities. The CT attenuation of the contour was then calculated using a custom script we developed within the Eclipse Scripting Application Programmer Interface. The script functions by averaging the Hounsfield units across all voxels within the contour (source available at https://github.com/rexcardan/AverageHU_ESAPI).

$L5_{CT}$ values of 105 and 130 HU were chosen as possible screening thresholds based on the work of Pickhardt et al, who utilized DXA as a gold standard and found

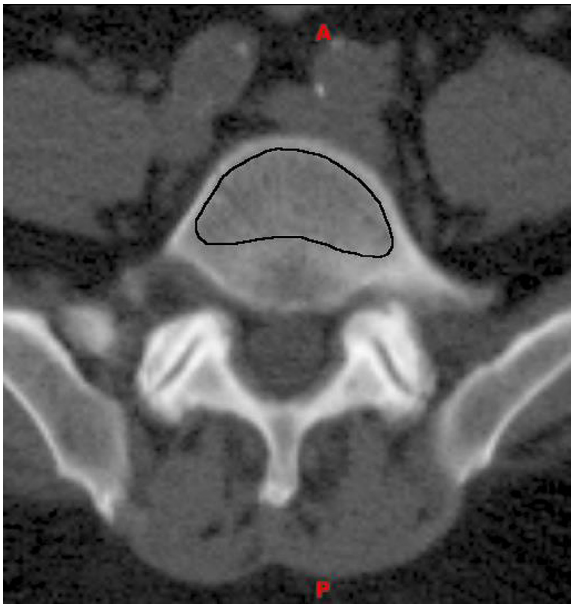

Fig. 1. Delineation of trabecular bone of L5 vertebral body. A, anterior; P, posterior.

$L5_{CT} < 105$ HU to be 89.4% specific for predicting osteoporosis and $L5_{CT} < 130$ HU to be balanced with a sensitivity of 73.3% and a specificity of 74.1% *(11)*. The cohorts of additional patients whose FRAX-assessed risk was <3% but were identified by each screening $L5_{CT}$ threshold value were compared to the group of patients whose estimated 10-yr risk of hip fracture was 3% or greater based on the FRAX algorithm. This threshold is the current NCCN-recommended cut point for obtaining a DXA scan and considering treatment to increase BMD.

Categorical data were compared between groups using the Pearson χ^2 test and means were compared using the independent samples *t*-test. For all patients who had undergone DXA within 6 mo of the start of RT, spine BMD (in gram per square centimeter) was recorded and assessed for correlation with $L5_{CT}$ using Pearson's *r*. All analyses were performed using SPSS Statistics version 22.0 (IBM, Armonk, NY).

Results

Of the 756 patients who underwent definitive RT in our department between 2001 and 2012, 609 met the inclusion criteria for this analysis. The reasons for excluding patients were as follows: 40 patients' CT scans were unavailable for review or did not extend up to L5, patient height was missing from the medical record in 46 cases, and the FRAX score could not be accurately calculated in 61 cases because of missing historical information (typically tobacco or alcohol use). A description of the demographic, disease, and treatment characteristics of the cohort is given in Table 1. All patients received external beam RT, 17 (2.8%) underwent low dose-rate brachytherapy boost, and 391 (64.2%) received a course of ADT.