Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. 19, no. 2, 154−164, 2016

1094-6950/19:154−164/$36.00
http://dx.doi.org/10.1016/j.jocd.2015.03.005

BMD and Fractures

Combined Measures of Dynamic Bone Quality and Postural Balance—A Fracture Risk Assessment Approach in Osteoporosis

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Abstract

We evaluated functional measures of neuromuscular integrity and bone's resistance to fracture as a combined tool in discriminating osteoporosis patients with and without fractures. Functional aspects of neuromuscular integrity were quantified with a noninvasive measure of static and dynamic functional postural stability (FPS), and fracture resistance was obtained with bone shock absorption in patients with osteoporosis aged 65−85 and compared our measures with dual-energy X-ray absorptiometry and Fracture Risk Assessment Tool (FRAX [World Health Organization Collaborating Center for Metabolic Bone Diseases, Sheffield, UK]) in women with osteoporosis, some with and some without vertebral fractures. Patients with vertebral fracture showed larger static FPS (postural sway excursion) in the mediolateral and anterior-posterior directions, suggesting poorer balance. Most of the variables of dynamic FPS showed significant differences between fracture and no-fracture groups (e.g., the fracture group took significantly longer during turning, implying poorer dynamic balance control). Also, compared with healthy control subjects, all 4 dynamic FPS responses for osteoporosis patients with and without fracture were significantly poorer, suggesting potential risk for falls. In summary, patients with osteoporosis who have vertebral fractures (compared with patients with similarly low bone mineral density and other nonfracture risk fractures) have not only lower bone shock absorption damping (ζ) but also increased postural imbalance.

Key Words: Bone shock absorption; dynamic bone quality; fracture; functional postural balance; osteoporosis.

Introduction

Improved measures of fracture discrimination are needed as bone mineral density (BMD) alone is a crude predictor of fracture risk *(1−9)*. The Fracture Risk Assessment Tool (FRAX [World Health Organization Collaborating Center for Metabolic Bone Diseases, Sheffield, UK]) (including clinical risk factors) is better than BMD alone but does not include falling, a major contributing factor to fracture *(1,10−17)*. Bone shock absorption (BSA) and static and dynamic functional postural balance/stability (FPS) *(13,18−21)* encompass measures of structural bone health and neuromuscular integrity, which are both compromised in osteoporosis *(1,16,22−26)*. The purpose of this study was to evaluate functional measures of bone's resistance to fracture and neuromuscular integrity in discriminating osteoporosis patients with and without fractures.

The musculoskeletal system consists of natural shock absorbers (soft tissue, joints with cartilage and synovial fluids, and trabecular bone, including mineralized collagen fibrils, nonfibrillar organic matrix, and noncollagenous proteins in bone), which absorb external loads of activities of daily life, minimizing the potential for fractures *(27−33)*. Although each natural shock absorber provides different degrees of

Received 02/25/15; Accepted 03/27/15.
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absorption, ranging from 11% to 70% based on loading frequency, the collective absorption capacities help minimize the potential for fracture *(34)*. We developed BSA, a quantitative measure of combined bone and musculature (CBAM) system's resistance to fracture when exposed to dynamic loads such as heel strike *(35)*. Damping, the BSA metric, as a measure of fracture resistance in the musculoskeletal system, is supported by classical structural engineering studies quantifying composite materials' and structures' ability to absorb/dissipate external loads *(36–38)*. Bone, as a composite material, has mineralized collagen fibrils and nonfibrillar organic matrix, which can dissipate external loads to decrease fracture risk *(39–42)*. Resistance to fracture depends on the musculoskeletal systems' ability to absorb and/or dissipate externally applied loads but not necessarily the maximum strength of the structure *(42–44)*. In osteoporosis, both bone integrity and the neuromuscular system are compromised, as evidenced by higher prevalence of fractures and falls *(1,16,22–26)*. Although our previous publications showed that BSA discriminates between fracture and no-fracture groups, we have not looked at its association with postural instability, another risk factor for fracture *(35)*. One of our goals was to test the hypothesis that osteoporosis patients with decreased bone damping capacity (i.e., stiffer, more brittle bone) have increased postural sway as measured by FPS outcomes.

The objective of this study was to determine the fracture discriminating abilities of BSA and FPS in patients with osteoporosis, aged 65–85. Secondary objectives were to investigate contributions of static postural balance (postural sway), dynamic FPS outcomes, damping and age in modifying the FRAX scores and contributions of damping, BMD and age in modifying static postural balance outcomes and dynamic FPS outcomes.

Materials and Methods

Subjects

The University Institutional Review Board approved the protocol, and all subjects gave informed consent. We recruited postmenopausal women with osteoporosis from a convenience sample of patients who already had dual-energy X-ray absorptiometry and vertebral fracture assessment or lateral spine radiographs. One investigator (NBW) was aware of the subjects' fracture status but was blinded to the BSA test results; the other investigators were aware of the BSA test results but blinded about the fracture status.

Bone Densitometry, FRAX Scores, and Fracture Assessment

BMD results for spine, femoral neck (FN), and total hip (TH) were obtained using Hologic equipment performed within 12 mo of the study entry. FRAX scores were calculated using version 3.8 without BMD and with lowest ever FN (BMD_FN). Vertebral fractures were assessed from lateral spine images acquired using dual-energy X-ray absorptiometry or lateral spine X-rays; reduction in anterior, middle, and/or posterior vertebral height by ≥20% constituted a fracture *(45)*. Seven of the subjects had 1 or more vertebral fractures, whereas 22 had no vertebral fractures.

Dynamic Bone Quality Measure

CBAM capacity outcome, damping (ζ), was quantified from acceleration measurements at 3 anatomical sites *(3,35)* (Fig. 1): (1) below the knee at the tibial tuberosity ($\zeta_{BELOWKNEE\text{-}R}$ and $\zeta_{BELOWKNEE\text{-}L}$; R for right heel strike and L for left heel strike), (2) above knee at the lateral femoral condyle ($\zeta_{ABOVEKNEE\text{-}R}$ and $\zeta_{ABOVEKNEE\text{-}L}$) for each leg, and (3) upper back (T-7) ($\zeta_{UPPERBACK\text{-}R}$ and $\zeta_{UPPERBACK\text{-}L}$). Low mass skin-mounted accelerometers were attached to bony prominences, and signals obtained as per our previous publication *(35)*. Each subject performed 5 stationary tasks, lifting the bare foot and placing it down with the heel striking the force platform with a force equivalent (or slightly higher) than used for during natural walking. Our custom BSA software (BSA software 2009-15; University of Cincinnati, Cincinnati, OH) was used to collect data and calculate shock absorption response variables. An average of 5 heel strikes was used for statistical analysis. Reproducibility of BSA test trials was demonstrated in our previous study *(46)*. CBAM damping (ζ) and resonance/dominant frequencies at anatomical sites were calculated as described previously *(3,35,46)*.

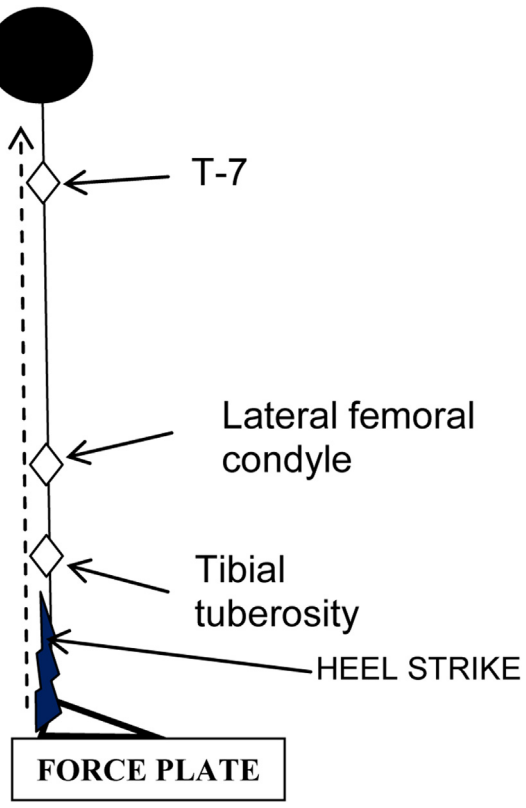

Fig. 1. Schematic of accelerometer-placement sites for bone shock absorption test.

Measures of Static and Dynamic FPS

Each subject underwent 2 tests: (1) static postural balance standing on a force platform system (this quantifies movement of center of pressure [CP] as a measure of static postural balance) *(47)* and (2) dynamic FPS test with instrumented timed up and go (iTUG) protocol as described herein:

1. *Static postural balance test*: Each subject performed tests addressing vision, proprioception, and the vestibular system in maintaining upright balance using our published protocol *(47)*. Tests were performed with subjects standing on a force platform (1) with eyes open (EO) and eyes closed (EC) standing directly on the platform and (2) with eyes open (FO) and eyes closed (FC) on a 4 inch thick foam pad placed on the platform. Outcome variables of postural balance tests are sway area (SA; cm^2), sway length (SL; cm), excursion in mediolateral direction (Excur-ML; cm), and excursion in anterior-posterior direction (Excur-AP; cm), which are significant discriminators of faller status *(26)*. The SA is encompassed by movement patterns of *X-Y* coordinates of CP movements during postural balance tests. SL is the total distance traveled by the subjects' CP during postural balance tests. The Excur-ML and Excur-AP are maximum displacements of subject's CP in the ML and AP directions, respectively, during postural balance tests.
2. *Dynamic FPS iTUG test*: The FPS iTUG test is performed using an inertial link 6D sensor system (3-dimensional accelerometers and 3-dimensional gyroscopes) for quantifying dynamic FPS *(48,49)*. The wireless sensor is attached to the chest and 2 wrists, as per the protocol of Zampieri et al and others *(48,49)* (Fig. 2). The TUG test is designed to assess balance control status during the dynamic task of getting up from a chair, walking, and turning *(50–54)*. The outcomes of TUG test are (1) peak turn velocity (PTV, deg/s) of torso, (2) peak swing velocity of right arm (PSVr, deg/s), (3) peak swing velocity of left arm (PSVl, deg/s), (4) turn duration (TD, s), (5) average turning velocity of torso (degrees/s), and (6) range of motion (ROM left and right arms) about the shoulder joint (in the sagittal plane), spanned by each arm swing during walking (degrees). The receiver operating characteristic (ROC) analysis of data from TUG test revealed that these variables have high discrimination for postural mobility between healthy and diseased patients' values with area under the curve (AUC) ranging between 0.76 and 0.87 *(55–58)*.

Data Analysis

Data are described using mean, standard deviation, or standard error. Because of the small sample size, outcomes were compared between fracture and no-fracture groups using Wilcoxon rank sum test. As a pilot study with expected directions of all outcomes' responses, a 1-sided $p < 0.10$ was used for statistical significance. The ROC curve analysis was carried out for damping, static postural balance outcomes (postural sway variables), dynamic FPS (or balance [FPS]; iTUG outcomes), and BMD measures for differentiating facture from no-fracture groups. The results of ROC analysis are summarized with AUC. Spearman rank correlations (r) were obtained among static and dynamic FPS outcomes with damping outcomes, BMD outcomes, and FRAX outcomes. Similarly, Spearman rank correlations were also computed between outcomes for damping BMD and FRAX. Because of smaller sample size for the fracture group (n = 7), correlations among outcome variables were carried out for the no-fracture group (N = 22) only. In addition, exploratory multivariable regression analysis was also done. Two regression models were developed: for model 1, the dependent variable was FRAX score (based on lowest ever BMD) and independent variables were static postural balance outcomes for FO and FC, dynamic FPS, damping, and age. We first assessed the univariate association of cofactors using ordinary linear regression; significant cofactors at 20% level of significance in the univariate regression analyses with known expected directions were included in the multivariable linear regression analysis. Backward elimination was used, starting from the full model, including all independent effects, then deleting effects 1 by 1 until a stopping condition ($p = 0.10$; 1 sided) was satisfied. Similarly, for model 2,

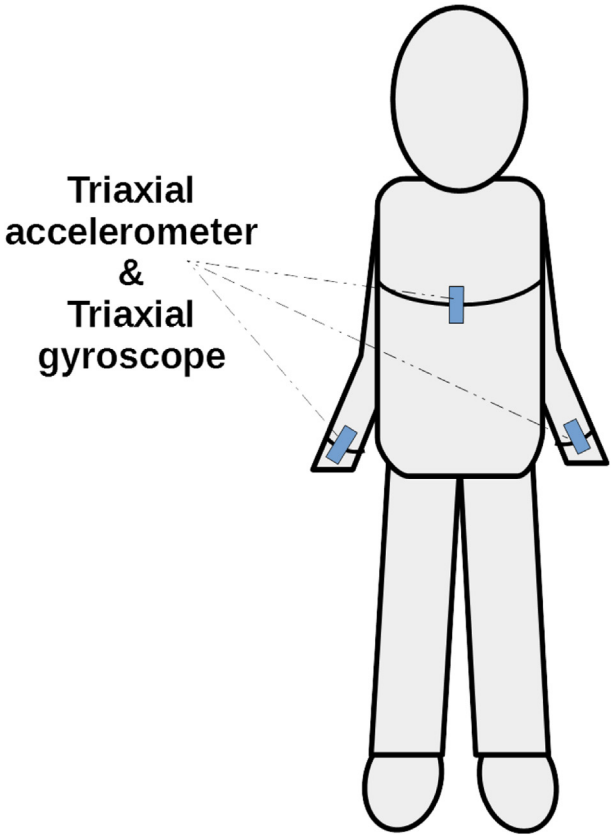

Fig. 2. Schematic of triaxial accelerometers and gyroscopes—placement sites for the functional postural stability instrumented timed up and go test.

individual regression models were developed for each of the dependent variables of static postural balance and dynamic FPS outcomes. The results of regression model are reported using regression coefficient, standard error of regression coefficient, 1-tailed p value along with model-adjusted coefficient of determination (R^2). Statistical software used was SAS, version 9.3 (SAS Institute, Inc., Cary, NC).

Results

Table 1 provides demographic data, fracture status, BMD scores, and FRAX scores for the study groups. There were no significant differences in body weight, height, BMI, and BMD between groups except that on the average the fracture group was 6 yr older than the no-fracture group and FRAX scores were higher for the fracture group (Table 1). Except for fractures, which increase the FRAX scores, the 2 groups had similar risk based on other risk factors.

Comparison of Static and Dynamic FPS Responses Between Fracture and No-Fracture Groups

Five of 6 variables of dynamic FPS showed statistically significant differences (p values ranged between 0.0488 and 0.088) between fracture and no-fracture groups (Fig. 3A−F). For example, the fracture group took significantly longer (+12%) than the no-fracture group during turning (TD). ROM responses were higher for the fracture group, an unexpected finding. Static postural balance responses to all 4 test conditions were not statistically different between the groups.

We also tested the diagnostic performance of static postural balance and dynamic FPS responses in differentiating fracture and no-fracture groups. Maximum AUC was for PTV (0.71, 95% confidence interval [CI]: 0.51−0.92, $p = 0.045$) followed by TD (0.70, 95% CI: 0.47−0.94, $p = 0.057$), left PSV (0.68, 95% CI: 0.41−0.95, $p = 0.077$), and right PSV (0.68, 95% CI: 0.42−0.93, $p = 0.085$). In the static postural balance responses, the AUC was statistically significant for Excur-ML (0.66, 95% CI: 0.41−0.91, $p = 0.10$) in FC test and SL (0.71, 95% CI: 0.53−0.89, $p = 0.05$) in EC test.

Comparison of Damping and BMD Values Between Fracture and No-Fracture Groups

Regarding BSA outcomes, the left heel strike-associated mean damping (ζ) values for the fracture group were 55%, 42%, and 71% lower than for the no-fracture group for sites above knee, below knee, and upper back, respectively (Fig. 4). The right heel strike mean damping values for the fracture group were 50%, 38%, and 61% lower than values for no-fracture group for sites above knee, below knee, and upper back, respectively (Fig. 5). The AUC for damping upper back ($\zeta_{UPPERBACK}$) was 0.72 (95% CI: 0.52−0.92, $p = 0.043$), followed by above knee ($\zeta_{ABOVEKNEE}$ [0.65, 95% CI: 0.42−0.87]) and below knee ($\zeta_{BELOWKNEE}$ [0.62, 95% CI: 0.39−0.85]). Although the mean damping values for the fracture group were lower than the no-fracture group for all sites, the AUC of $\zeta_{UPPERBACK}$ was the only site reaching significance, possibly because of small sample size. AUCs of BMD measures were between 0.50 and 0.58. None of the BMD measures had significant AUC for differentiating fracture from no-fracture groups.

Associations Between Static Postural Balance and Damping

Three of 4 postural balance outcomes (SA, SL, and Excur-ML) for the FC test showed significant negative association with damping of the upper back or torso. Damping upper back ($\zeta_{UPPERBACK}$) was correlated with SA ($r = -0.046$, $p = 0.018$), SL ($r = -0.39$, $p = 0.039$), and Excur-ML ($r = -0.52$, $p = 0.007$). On the other hand, although the Excur-AP was in the expected direction (i.e., negatively associated with damping), the differences between groups was not

Table 1
Demographics and Patient Characteristics of Fracture and No-Fracture Groups

	Fracture (N = 7)		No fracture (N = 22)		
Variables	Mean	SD	Mean	SD	p (1 tailed)
Age (yr)	76.20	5.94	70.6	3.97	0.0233[a]
Height (cm)	158.7	10.15	161.3	6.34	0.6463[a]
Weight (kg)	62.9	5.96	61.5	10.57	0.6464[a]
BMI (kg/m^2)	25	2.29	23.6	3.97	0.1768[a]
BMD-femoral neck (g/cm^2)	0.586	0.087	0.597	0.052	0.3606
BMD-total hip (g/cm^2)	0.699	0.074	0.724	0.062	0.2457
FRAX-lowest BMD	26.71	9.76	17.33	6.68	0.0053
FRAX-lowest hip fracture	9.91	7.82	5.98	5.09	0.0487

Abbr: BMD, bone mineral density; BMI, body mass index; FRAX, Fracture Risk Assessment Tool; SD, standard deviation.
[a]Two tailed p value obtained from Wilcoxon rank sum test.

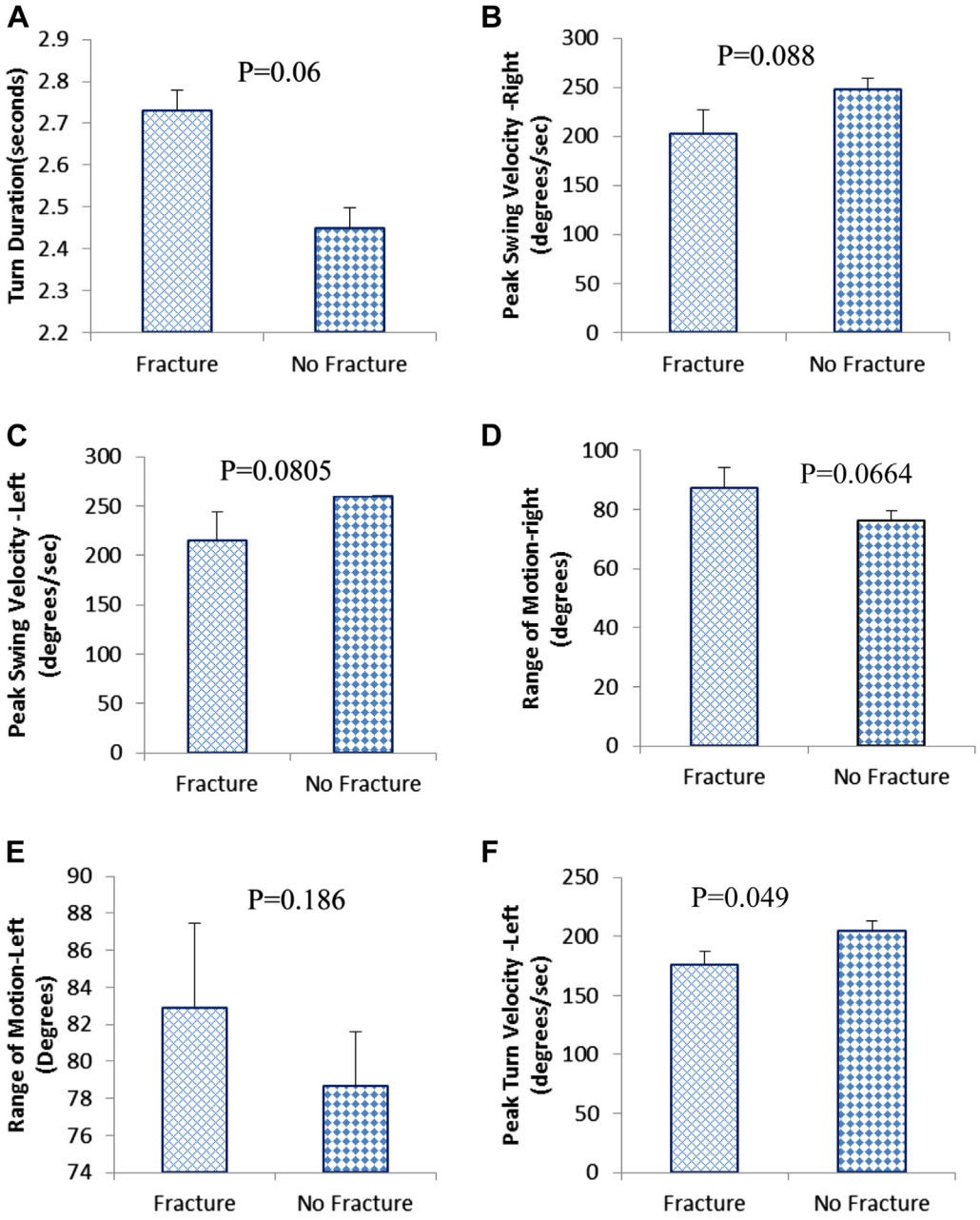

Fig. 3. Dynamic functional postural stability responses to timed up and go test. (**A**) Turn duration. (**B**) Peak swing velocity—right arm. (**C**) Peak swing velocity—left arm, (**D**) Range of motion—right arm. (**E**) Range of motion—left arm. (**F**) Peak turn velocity.

significant (Excur-AP [$r = -0.27$, $p = 0.12$]). Two of 4 postural sway outcomes (SL and Excur-ML) for the EC test showed significant negative association with $\zeta_{\text{UPPERBACK}}$ (r: −0.30 to −0.31; p: 0.085−0.09).

Associations Between Dynamic FPS and Damping

There were no consistent association among dynamic FPS outcomes and damping variables.

Associations Between Static Postural Balance and BMD

Higher BMD_TH was significantly associated with decrease in postural sway outcomes in all conditions, suggesting better postural balance. For 3 of 4 test conditions, EO, EC, and FO, all 4 postural sway outcomes (SA, SL, Excur-ML, and Excur-AP) were significantly negatively correlated with BMD_TH. The correlation coefficient ranged from −0.28 to −0.48. For the FC test condition, only 1 of 4 sway outcomes

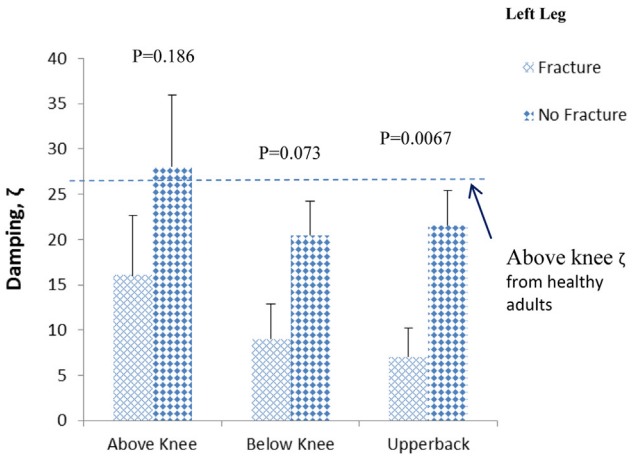

Fig. 4. Mean ± standard error of the mean damping values at various anatomical sites of patients with osteoporosis for left leg.

(Excur-AP, $r = -0.31$, $p = 0.08$) was significantly negatively associated with BMD_TH. BMD_FN showed significantly negative correlations with 3 of 4 postural sway outcomes (SA, SL, and Excur-ML) for the EC test condition. The correlation coefficient ranged from −0.36 to −0.52.

Associations Between Dynamic FPS and BMD

Higher BMD_TH ($r = 0.57$, $p = 0.003$) was significantly associated with an increase in PSVr, an increase in PTV ($r = 0.32$, $p = 0.075$), and a decrease in TD ($r = -0.28$; $p = 0.10$).

Associations Between Dynamic FPS and FRAX Scores

The FPS outcomes correlated negatively with FRAX scores—patients with higher FRAX scores had reduced dynamic functional balance, poorer balance, and increased potential of falling during walking. Of 6 FPS outcomes, 4 (mean PTV, mean PSV right arm, mean ROM right arm, and mean ROM left arm) showed significant negative

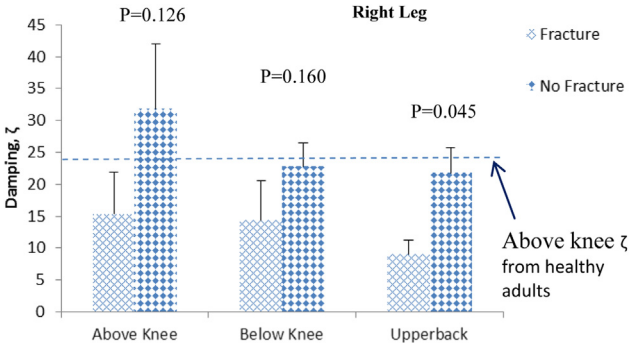

Fig. 5. Mean ± standard error of the mean damping values at various anatomical sites of patients with osteoporosis for right leg.

associations with FRAX scores for major fracture risk (based on lowest BMD) ($r = -0.53$ to -0.40; $p = 0.006$–0.031) and hip fracture risk ($r = -0.56$ to -0.40; $p = 0.0036$–0.018). Similar correlations with FRAX scores without BMD were found.

Associations Between Static Postural Balance and FRAX Scores

Static postural sway was positively correlated with FRAX scores—patients with higher FRAX scores demonstrated higher postural sway, poorer balance, and increased potential of falling, even during static conditions. For the FO test, all sway outcomes demonstrated significant positive associations with FRAX scores ($r = 0.55$–0.28; $p = 0.0041$–0.11). For the EO test, except for SL (not significant), Excur-ML, Excur-AP, and SA were significantly associated with higher FRAX scores ($r = 0.50$–0.34; $p = 0.009$–0.062). For the FC test, only Excur-AP and SA were significantly associated with FRAX scores ($r = 0.36$–0.30; $p = 0.048$–0.085). For the EC test, only Excur-ML showed significant association with FRAX scores ($r = 0.30$; $p = 0.089$).

Associations Between Damping and FRAX Scores

There were no correlations between FRAX scores and damping values, but each was an independent discriminator of fracture groups (Figs. 4 and 5; Table 1).

Regression Models Relating Static and Dynamic FPS Outcomes to FRAX Scores

After covariate adjustment within the regression analysis for static postural sway outcomes, only Excur-ML sway for the FO test reached significance with FRAX score (based on lowest BMD) for major hip fracture risk (Table 2). Age was the only covariate significant with both FRAX scores. After covariate adjustment within the regression analysis for dynamic FPS outcomes, none of the variables reached significance with FRAX scores.

Regression Models Relating Damping to Dynamic FPS Outcomes

After covariate adjustment within the regression analysis, only $\zeta_{\text{ABOVEKNEE}}$ reached significance with only 2 of the dynamic FPS variables, TD and PTV, respectively (Table 3). Table 3 provides 1-tailed p values. BMD_TH was the only covariate that was significant with both TD and PTV. Age was significant in the PTV regression model only.

Regression Models Relating Damping to Static Postural Balance Outcomes

The regression models were developed only for FC and FO tests as they showed more consistent bivariate associations for multiple postural balance outcomes with damping. After covariate adjustment within the regression analysis, $\zeta_{\text{UPPERBACK-R}}$ reached significance with static postural balance variables SL and Excur-ML for FO and FC tests and

Table 2
Regression Models Relating FRAX Scores to Static Postural Balance outcomes

Dependent variable	Independent variable	Regression coefficient	Standard error	p (1 tailed)	Model R^2 (adjusted)
FRAX based on lowest BMD major fracture risk	Intercept	−43.17	18.63	0.014	0.42
	Age	0.75	0.29	0.008	
	Excur-ML (FO)	3.31	1.82	0.040	
FRAX based on lowest BMD hip fracture risk	Intercept	−32.28	14.58	0.018	0.30
	Age	0.47	0.23	0.025	
	Excur-ML (FO)	1.96	1.42	0.090	

Abbr: BMD, bone mineral density; Excur-ML, excursion in mediolateral direction; FO, eyes open standing on a 4 inch thick foam pad placed on the platform; FRAX, Fracture Risk Assessment Tool.

with SA and Excur-AP for FC test. Table 4 provides 1-tailed p values. In addition, $\zeta_{\text{ABOVEKNEE-R}}$ also reached significance with Excur-ML for FO and FC tests, whereas $\zeta_{\text{ABOVEKNEE-L}}$ was significantly associated with Excur-AP for the FC test only. Only 1 of 4 damping outcomes, $\zeta_{\text{BELOWKNEE-R}}$, showed an unexpected positive relationship with postural balance outcomes; this may be because of chance and/or small sample size. Covariate of age, as expected, showed significant positive relationships with all postural balance outcomes for all test conditions, consistent with previous studies *(55−58)*.

Discussion

We noninvasively quantitated static and dynamic FPS as well as dynamic bone quality (damping [ζ]) among patients with osteoporosis with and without vertebral fractures. As before, damping values were significantly lower in the fracture group compared with patients without fracture (Figs. 4 and 5) and normal healthy younger groups *(3,35,46)*. Although area under the ROC curve analysis (0.72) for $\zeta_{\text{UPPERBACK}}$ showed significant fracture discrimination, none of the BMD measures had significant AUC (0.50−0.58) for differentiating fracture status. This further supports the literature that BMD alone is not sufficient to discriminate between fracture and no-fracture groups.

In addition to BMD, bone quality, postural balance, and age-related decreases in muscle strength contribute independently to fracture risk *(1,5,13,19,22,25,59−61)*. Our dual approach of combining impaired bone quality with poor postural balance risk factors or fracture is consistent with the concept of *sarco-osteoporosis (18)*. With aging, muscle mass decreases and muscle strength is reduced even more, and, with the additional effects of osteoporosis, detrimentally impacts FPS, thereby increasing the risk of falls/fracture *(62,63)*.

Older age and certain diseases (e.g., osteoporosis, Parkinson disease) bring about gradual changes in posture, spinal flexibility, mobility, and decreased sensory capacity, which collectively affect postural balance and contribute to fall-related injuries *(1,13,16,22,23,64−66)*. Greig et al *(22)* reported that vertebral fracture interferes with the vertical alignment of skeleton, shifting the body's center of gravity, thereby impairing postural balance. Recent studies *(1,12)* show that falls are stronger predictor of fractures than BMD.

It is hypothesized that structural integrity of CBAM system will be an equally important fall/fracture risk factors in osteoporosis. Postural control associated with upright balance depends on interactions between neural and musculoskeletal systems (i.e., CBAM system). Age-associated declines in both musculoskeletal system and neural system play a significant role in jeopardizing postural balance. In particular, age-associated decreasing capacity of somatosensory systems

Table 3
Regression Models Relating Damping to Dynamic Functional Postural Balance/Stability Outcomes

Dependent variable	Independent variable	Regression coefficient	Standard error	p (1 tailed)	Model R^2 (adjusted)
TD	Intercept	4.60	0.94	<.0001	0.14
	$\zeta_{\text{ABOVEKNEE-R}}$	0.00	0.00	0.018	
	BMD_TH	−2.72	1.26	0.021	
PTV	Intercept	156.62	166.13	0.178	0.26
	Age	−2.06	1.45	0.083	
	$\zeta_{\text{ABOVEKNEE-R}}$	0.31	0.19	0.052	
	BMD_TH	250.09	122.38	0.026	

Abbr: $\zeta_{\text{ABOVEKNEE-R}}$, above knee at the lateral femoral condyle; BMD_TH, total hip bone mineral density; PTV, peak turn velocity; R for right heel strike; TD, turn duration.

Table 4
Regression Models Relating Damping to Static Postural Balance Outcomes

Test	Dependent variable	Independent variable	Regression coefficient	Standard error	p (1 tailed)	Model R^2 (adjusted)
FO	SA	Intercept	−0.46	6.47	0.472	0.50
		Age	0.23	0.06	0.001	
		BMD_TH	−15.38	4.94	0.002	
FO	SL	Intercept	44.54	78.21	0.287	0.10
		Age	1.10	0.78	0.085	
		BMD_TH	−82.06	59.71	0.091	
FO	Excur-ML	Intercept	4.79	2.59	0.039	0.60
		Age	0.05	0.02	0.013	
		$\zeta_{\text{ABOVEKNEE-R}}$	0.00	0.00	0.079	
		$\zeta_{\text{UPPERBACK-R}}$	−0.01	0.01	0.041	
FO	Excur-AP	BMD_TH	−7.71	1.94	0.000	
		Intercept	2.35	2.64	0.191	0.38
		Age	0.07	0.03	0.009	
		BMD_TH	−5.57	2.02	0.005	
FC	SA	Intercept	−13.87	13.17	0.151	0.44
		Age	0.48	0.13	0.001	
		$\zeta_{\text{UPPERBACK-R}}$	−0.07	0.04	0.045	
		BMD_TH	−15.38	10.07	0.070	
FC	SL	Intercept	−53.66	128.14	0.340	0.08
		Age	2.40	1.76	0.092	
		$\zeta_{\text{UPPERBACK-R}}$	−0.77	0.52	0.078	
FC	Excur-ML	Intercept	2.05	4.31	0.319	0.39
		Age	0.08	0.04	0.019	
		$\zeta_{\text{ABOVEKNEE-R}}$	−0.01	0.00	0.086	
		$\zeta_{\text{UPPERBACK-R}}$	−0.02	0.01	0.045	
		BMD_TH	−5.33	3.22	0.056	
FC	Excur-AP	Intercept	3.93	4.00	0.168	0.29
		Age	0.08	0.04	0.022	
		$\zeta_{\text{ABOVEKNEE-L}}$	−0.01	0.01	0.086	
		BMD_Troch	−7.37	3.09	0.013	

Abbr: $\zeta_{\text{ABOVEKNEE-R}}$, above knee at the lateral femoral condyle; BMD_TH, total hip bone mineral density; BMD_Troch, Trochanter bone mineral density; Excur-AP, excursion in anterior-posterior direction; Excur-ML, excursion in mediolateral direction; FC, eyes open standing on a 4 inch thick foam pad placed on the platform; FO, eyes open standing on a 4 inch thick foam pad placed on the platform; L, left heel strike; R, right heel strike; SA, sway area; SL, sway length; $\zeta_{\text{UPPERBACK-R}}$, upper back (T-7).

has serious consequences in perceiving the degree of slipperiness of a wet and/or uneven surface, which will impact the ability to negotiate a threatening environment and may increase susceptibility to falling *(67,68)*.

Our area under the ROC analyses results show that dynamic FPS responses (i.e., PTV, TD, and left PSV) during performance of tasks of daily living were able to discriminate fracture from no-fracture groups (Fig. 3). In comparison to the no-fracture group, osteoporosis patients with fracture had lower PTV and PSV and took longer to make the turn during the TUG test. In addition, static postural balance outcomes for FC and EC test conditions allowed discrimination between fracture groups for Excur-ML and Excur-SL, respectively. In comparison to the no-fracture group, osteoporosis patients with fracture demonstrated larger postural sway excursion in the ML direction and increased movement of body's CP (SL outcome) in both ML and AP directions, suggesting poorer balance. Our findings suggest that both static and dynamic FPS outcomes can discriminate between fracture and no-fracture groups. Interestingly, the mean TD value of the osteoporosis patients with fracture (standard error of the mean [SEM]: 2.73 [0.15 s]) was similar to the values (SEM: 2.67 [0.13 s]) obtained in Parkinson disease patients with history of falls in another study in our laboratory *(69)*, suggesting potential high risk for falling in our osteoporosis patients. Also, in comparison to healthy control subjects (mean age [SEM]: 64.2 [2.86]; n = 10) in another of our studies, all 4 dynamic FPS responses for osteoporosis patients with and without fracture were significantly poorer, suggesting potential risk for falls *(69)*.

FRAX scores were not associated with dynamic FPS outcomes, and only 1 static postural sway outcome (Excur-ML) showed significant association with FRAX (Table 2). Therefore, FRAX does not quantify fall-related fracture risk associated with reduced dynamic postural balance as determined by the TUG test. Although FRAX and BSA were not correlated, individually each was an independent discriminator of fracture status as shown in Figs. 4 and 5 and Table 1. Although both BMD and FRAX provide a measure of fracture risk because of skeletal fragility, they do not assess risks associated with falling, a common outcome in osteoporosis *(1,16,22,23)*. On the other hand, our findings provide encouraging results supporting the abilities of BSA-FPS for discriminating fracture groups with measures of dynamic bone quality (damping, ζ) and dynamic FPS outcomes.

We hypothesized that reduced damping capacity of CBAM is detrimental to the static postural sway or balance and the dynamic FPS in osteoporosis patients, increasing the risk of falling and fracturing. To evaluate potential interplay between damping and static postural balance outcomes and dynamic FPS outcomes, we used regression modeling (Tables 3 and 4). Within the regression analysis between damping and dynamic FPS outcomes, the negative relationship between TD and $\zeta_{\text{ABOVEKNEE-R}}$ suggests that a higher damping is associated with shorter TD (i.e., the subject is turning quicker during the TUG test), an indication of better dynamic motor control. Similarly, a positive relationship between PTV and $\zeta_{\text{ABOVEKNEE-R}}$ suggests that increased damping is associated with increased PTV during TUG, also an indication of better dynamic motor control. Regression models relating damping to static postural balance outcomes were also carried out (Table 4). A negative relationship between postural sway outcomes and $\zeta_{\text{UPPERBACK-R}}$ suggests that higher damping is associated with lower SL and Excur-ML for FO and FC tests and lower SA and Excur-AP for FC test, implying better static balance/stability. Both $\zeta_{\text{ABOVEKNEE-R}}$ and $\zeta_{\text{ABOVEKNEE-L}}$ were negatively associated with Excur-ML and Excur-AP, respectively—higher damping was associated with better balance in ML and AP directions, less postural sway, implying better balance. This is consistent with the hypothesis that higher damping capacity of CBAM would effectively absorb the perturbing energy associated with movement of body segments trying to maintain upright balance and thereby would reduce postural sway or movement of CP. It is reasonable that both dynamic and static balances are influenced by the damping capacity of the CBAM system. Although static postural balance is primarily impacted by neuromuscular properties of large body mass segments such as torso, dynamic functional balance as measured by TUG has multiple contributing factors provided by all moving body segments, such as torso, head, legs, and swinging arms. Under dynamic conditions, such as getting up from chair and walking, interactions among damping properties of the various body segments of the musculoskeletal system affecting dynamic FPS outcomes would be complex. Further study with larger numbers and mechanistic biomechanical modeling will be needed to better understand intrinsic mechanisms of interplay between damping capacity of the CBAM system and postural balance influencing fall-related fracture risk.

In summary, this study provides an approach for identification of patients at risk of fracture using the dual approach noninvasive BSA-FPS tool to quantify the status of structural integrity of subjects' CBAM system and their FPS. Poor structural integrity is characterized by reduced damping capacity of the CBAM system tested under realistic in vivo loading of simple heel strike *(35)*. Reduced damping capacity of CBAM is likely detrimental to the FPS, increasing the risk of falling and fracturing. Further larger studies are warranted to confirm these findings, but results from this study provide support for potential new diagnostic approach, which could have positive impact (lower cost, fewer patients exposed to radiation) compared with testing with BMD alone and FRAX *(70,71)* and also to better target therapy to those in need. Our study is based on a small sample size; therefore, findings should be interpreted with caution.

Acknowledgments

The authors thank the patients and their families for their participation and cooperation. Thanks are due Cyndy Cox, Kelley James, Ramya Raghavan, for bone vibration, postural balance, and iTUG data collection and analyses. Thanks are also due Zhouyang Weng for her assistance in SAS programming and analysis. This study was supported by a grant from University of Cincinnati Provost Pilot Research Project Program, College of Medicine's Discovery Acceleration Initiative. The BSA technology used in this study is a patented device under the names of the first two authors, A. Bhattacharya and Nelson B Watts (Patent approved 2014-Serial No. 12/402,586).

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