

Predicting radiological vertebral fractures with a combined physical function and body composition scoring system

(一般住民の健診データを利用した運動機能を体組成による椎体骨折発生の予測スコアの開発)

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Abstract

Purpose: To investigate the incidence of vertebral fractures (VFX) and the value of physical function (PF) and body composition (BC) for predicting VFX in a Japanese population.

Methods: This study included 307 subjects (113 men, 194 women) at least 40 years of age who were assessed at community health check-ups in 2008 and 2016. PF was assessed by grip strength and by single-leg stance, timed up-and-go, and 30-second chair stand tests, each scored from 0 to 3 for a possible total of 12 points (higher scores reflect lower function). BC was scored on bioelectrical impedance measurements of trunk and appendage muscle volume, with 6 possible points. We diagnosed radiological VFX semiquantitatively on lateral views of the lumbar spine, and measured bone mineral status by quantitative ultrasound (QUS) of the calcaneus. We conducted logistic regression analysis with VFX as the dependent variable and age, sex, BMI, QUS, PF score, and BC score as independent variables.

Results: In 8 years, 36 participants (12%) sustained new VFX. After correcting for age, sex, BMI, and QUS, the odds of VFX increased with a PF score ≥ 8 (OR 5.6; 95% CI 1.21–25.90; $P = 0.028$) and increased further with a PF + BC score ≥ 9 (OR 8.1; 95% CI 1.80–36.00; $P < 0.01$).

Conclusions: Both PF and BC are important for predicting fragility fractures. The scoring system used here may reflect small differences better than categorical (single cut-off) definitions of poor function.

Introduction

Fragility fractures increase mortality, morbidity, and economic burden in the elderly (1) and these burdens will increase as the global population ages [2]. The cost of treating all postmenopausal women to prevent fractures may be nearly as great as the cost of treating the fractures, emphasizing the need to develop effective screening and prevention methods to identify and treat individuals at higher risk [1]. Although current screening methods based on medical comorbidities and bone mineral density (BMD) are somewhat successful, Crandall et al. [3] reported that these methods may not predict the majority of osteoporotic fractures in women aged 50–64. Furthermore, caution is needed when adapting these methods for use outside their native context [4]

Another issue with screening methods is that an endpoint of major osteoporotic fractures and self-reported fractures may overlook subclinical vertebral fractures (VFX), which also increase morbidity and the risk of future fractures and decrease quality of life (QOL) [5-7].

There is growing evidence that relationships between muscle, bone, and fat are involved in fragility fractures, and that these factors should be considered when predicting such fractures [8, 9]. Cross-sectional studies reported that patients with fragility fractures had lower muscle volumes [10, 11]. However, most studies measure body composition (BC) by whole-body DXA [12], which is difficult to translate to screening methods and to reproduce in epidemiological studies. Studies indicate that physical function (PF) tests may also be useful for predicting falls and fractures [13, 14]. Although PF measurements are important targets in exercise interventions and programs to prevent fractures [15], there is little information to indicate whether PF and BC measurements can be used to

predict radiographic fragility fractures. Thus, this study aimed to determine longitudinal relationships between PF and BC and the incidence of morphological VFx in a Japanese population, and to investigate whether BC and PF can predict radiographic VFx.

Methods

Study population

Study data were derived from a community-based public health project, introduced by our institution in 2005, that aims to prolong a healthy lifespan in the general population. The project provides annual health check-ups to approximately 1000 volunteers who live in a city in northern Japan and are at least 20 years old, and collects basic anthropometric data and lifestyle information, nutritional status, medical history, biomechanical test results, and biochemical blood and urine test results, as well as questionnaire and test findings related to examinations by various specialists.. In 2008, 886 people participated in this public health project. Previous studies of this population reported an association between lumbar spondylosis and mobility [16], and between neck pain and LDL cholesterol [17].

For the present study, we looked for subjects who participated in our public health project check-ups in both 2008 and 2016, were at least 40 years old at the 2008 checkup, and had the following data available: quantitative ultra sound (QUS) of the calcaneus, bioelectrical impedance analysis (BIA), lumbar spine x-rays, and PF tests at both the 2008 and 2016 examinations. Of 374 subjects, 307 met all of the criteria and participated in the study. There were 113 men and 194 women (average age when enrolling in this study: men 56.6 ± 10.2 years; women 58.2 ± 9.4 years). This study was approved by the Ethics

Committee of Hirosaki University Graduate School of Medicine, and all subjects provided written consent before participating in the study.

BC measurements

BC was measured with a BIA scanner (MC-190, Tanita, Japan), a method that has been validated in both young and older individuals and is correlated with DXA BC measurements [18, 19]. BIA has the advantage of being simple, fast, and relatively inexpensive, and it does not expose the subject to ionizing radiation. Its use and accuracy in epidemiological studies has been described [20]. BIA was used to measure the whole-body ratio of fat to body weight and to calculate the skeletal muscle index (SMI) for the trunk, legs, and appendages. The SMI, which is calculated as the muscle volume divided by height (meters) squared, is widely used as an index of corrected muscle mass [12]. SMI decrease (Δ SMI) was calculated as a percentage by dividing the difference between the SMI at baseline (2008) and follow-up (2016) by the baseline measurement. All measurements were taken in the morning after a night of fasting.

PF tests

PF tests were conducted on the same day as the health checkup. Participants were asked to wear lightweight clothing and flat-soled shoes appropriate for exercise, and physical tests were conducted in the afternoon after a light meal. The tests were supervised by experienced staff from our facility who were trained in the measurement criteria for each test. PF was assessed by the timed up-and-go (TUG) test, the single-leg stance test (SLST), the 30-second chair stand test (30SCST), and handgrip strength.

In the current study, subjects taking the TUG test were asked to stand up from a chair, walk briskly to a mark 3 meters away, walk back, and sit down. The chair had a seat height of 42 cm and did not have armrests. In accordance with the previous protocol [19], a cut-off of 12 seconds was used to differentiate between elderly individuals living in institutions and those living within the community [21].

The SLST is a reliable and reproducible test of balance [22] that predicts falls and self-reported fractures [23, 24]. For the SLST, we asked subjects to stand on one foot on a hard-surface floor. We then measured the time (seconds) from when the opposite foot left the floor to the time it touched the floor again. We used the best of three trials.

The 30SCST has been validated in a community-dwelling elderly population for measuring lower-extremity strength [25]. The test was designed to overcome the floor effect of the 5-repetition test, in which elderly participants may not be able to complete the task. Participants were asked to sit in a chair that had a 42-cm-high seat and no armrests, to cross their arms in front of their chest, and to stand and sit repeatedly for 30 seconds; we measured the number of full repetitions.

To measure handgrip strength, the subject used a handheld dynamometer while standing up. Two trials were performed for each hand, and the best value (in kilograms) was used.

PF and BC scoring system

We stratified results for the PF and BC tests using the original scoring system shown in Table 1. In this system, the TUG, 30SCST, and grip strength were scored (0–3 points each) according to cut-offs (mean minus 1, 2, or 3 SD) based on sex-specific T scores

calculated from younger volunteers (age 20–40 years) from the same health checkups. For feedback and educational purposes, the cut-off values were rounded to appropriate whole numbers. The SLST had a ceiling effect, since participants were stopped at 80 seconds even if they could remain standing longer, so the SLST was scored (0–3 points) using cut-off values of 10, 20, and 30 seconds as in previous studies [22, 23]. The total possible PF score was 12 points, with a higher score reflecting worse function. To explore the predictive value of adding BC values to this scoring system, limb and trunk SMI were scored (0–3 points each) according to cut-offs (young adult mean minus 1, 2, or 3 SD) calculated from younger volunteers given the same check-ups. The total possible score for PF + BC was 18 points.

Diagnosis of vertebral fractures and osteoporosis

VFx were evaluated on lateral-view x-rays of the lumbar spine using the semiquantitative method described by Genant et al. [26]. Two examiners, one with 13 years of experience as a spine surgeon (GK) and one with 7 years of experience as an orthopedic surgeon (OT), counted the grade 1 or greater fractures in the T12–L5 vertebrae. The examiners were blinded to the demographic data, such as age and sex, of the subjects. Cohen's κ for inter-rater reliability was 0.897 (95% CI, 0.76–1.04; $P < 0.001$), demonstrating very good agreement between the raters. We compared results between subjects who had sustained a new VFx (VFx group) and those with no new fractures (non-VFx group) at follow-up.

Bone QUS

Bone quality was assessed at baseline by QUS (AOS-100 scanner, Hitachi, Japan) of the left calcaneus (unless that region had been injured). At follow-up, we used the Osteo-Sono Index (OSI), calculated as $(\text{speed of sound})^2 \times \text{transmission index}$.

Statistical analysis

Baseline characteristics were compared using Fisher's exact test for categorical variables and the Mann–Whitney *U* test for non-categorical values. Comparison of age, PS and BC with single vs. multiple VFx was conducted using the Mann–Whitney *U* test. The association of age, PS and BC with the semi-quantitative grade of VFx was conducted using the Kruskal-Wallis test with post hoc Steel-Dwass analysis.

The relationship between VFx, PF, and BC was analyzed by logistic regression as in previous studies [27]. We used ROC curves to determine the optimal cut-off values for our proposed PF and BC scoring system. We used a stepwise method with VFx as the dependent variable and age, sex, BMI, OSI, and PF score as independent variables. The BC score was added as an independent variable to analyze the effect of body composition on VFx. A *P* value < 0.05 was considered statistically significant.

Results

VFx incidence and severity

At follow-up, 36 participants (12%; 12 men and 24 women) had sustained new VFx; of these, 10 had new VFx at multiple levels. The peak incidence of VFx was at T12, with most fractures occurring in the transitional zone from the thoracic to the lumbar vertebrae. By maximum fracture grade, 23 participants were classified as grade 1, nine as grade 2,

and four as grade 3 (Fig. 1). The VFx group was significantly older than the non-VFx group (65.8 ± 8.8 vs. 56.5 ± 9.3 ; $P < 0.001$), but the other demographic characteristics and the prevalence of medical comorbidities were statistically similar (Table 2). The self reported bodily pain category of the SF-36 did not differ between groups

Age, PF and BC scores among those with single and multiple VFx's did not differ significantly. Comparison of age, PF, PF+BC scores among the semiquantitative VFx grades showed no difference among groups. (table 3).

Longitudinal associations among VFx, PF, and BC

Baseline PF was worse in the VFx group than the non-VFx group in the SLST (52.0 ± 27.9 vs. 61.8 ± 22.0 , $P = 0.02$) and 30SCST (17.5 ± 5.6 vs. 19.5 ± 4.9 , $P = 0.03$). Although the baseline BC was similar in the two groups (Table 2), the rate of SMI decline (Δ SMI) was significantly higher in the VFx than the non-VFx group (Δ SMI trunk 3.4 ± 5.9 vs. 1.5 ± 4.5 , $P = 0.02$; Δ SMI appendicular 4.6 ± 5.0 vs. 2.5 ± 5.1 , $P = 0.01$).

As shown in Table 4, stepwise logistic regression showed that age and a PF score of 8 or more significantly increased the odds of VFx by 5.6 (95% CI 1.21–25.90, $P = 0.028$). For the combined PF + BC score, we determined a cut-off of 9 to be optimal, and the odds ratio rose to 8.1 (95% CI 1.80–36.00, $P < 0.01$).

Discussion

In this study, we examined the relationship between BC, PF, and radiographic VFx. Over an 8-year period, 36 participants (12%) sustained a new VFx. Baseline SLST and 30SCST values were worse in the VFx group than in the non-VFx group, but the baseline

SMI and body fat ratio were comparable in the two groups. We proposed a scoring system for PF and BC to help identify individuals with a high risk of VFx, as shown in Table 1.

Using this scoring system, we found that a PF score of 8 or more increased the odds of VFx by 5.6, and a combined PF + BC score of 9 or more increased the odds ratio to 8.1.

VFx is a hallmark of osteoporosis, and the presence of morphological VFx increases morbidity [5] and lowers QOL [6]. The cumulative incidence of radiological VFx in a Japanese rural population by decade of life (40s, 50s, 60s, and 70s) was reported to be 2.1%, 8.3%, 10.0%, and 12.2% for men and 2.1%, 6.1%, 18.0%, and 22.4% for women, respectively [28]. The incidence of VFx in our study population was 12%; when stratified by age, the incidence was 4.1%, 6.3%, 15.7%, and 33.3% for the entire population in their 40s, 50s, 60s, and 70s or above, respectively. The Incidence of fractures in women by age group was 2.4%, 4.2%, 20% and 33.3% in their 40s, 50s, 60s and 70 or above, respectively. This was comparable to previous studies conducted in Japan. Our study did not have an adequate number of male VFx to compare to previous studies of radiographic VFx[29-33].

Efforts to predict fragility fractures have focused on medical comorbidities and BMD, and have had some success. However, these screening methods must be calibrated for different populations [3, 34]. Moreover, after testing the performance of three predictive strategies (FRAX, fracture risk assessment tool; SCORE, simple calculated osteoporosis risk estimate; and OST, osteoporosis self-assessment tool), Crandall et al. [3] reported that these methods may not be able to predict the majority of osteoporotic fractures in women aged 50–64. After following women aged 70 or older over a 10-year period, Ensrud et al. [35] reported that the predictive strength of FRAX was similar to that

of simpler tools. Rubin et al. [36] reported that FRAX and even simpler tools were not superior to age alone in predicting fractures in women aged 45 to 90 over a 3-year period. These results suggest that risk factors for osteoporosis are of limited value for predicting fractures, and that the focus should be broadened to include risk factors for falls in both middle-aged and elderly women.

BC is associated with bone strength and fractures [8]. Hida et al. [11] used whole-body DXA to measure muscle volume in 216 women with acute osteoporotic VFx diagnosed by MRI, and found that the appendicular SMI was lower and the prevalence of sarcopenia was higher in women with acute VFx compared to healthy control subjects. Walsh et al. [37] reported that a positive association between SMI and BMD disappeared when corrected for physical activity. The VFx and non-VFx groups in our study had a similar baseline SMI and prevalence of sarcopenia, but the rate of muscle decline was greater in the VFx group. This result is consistent with studies showing lower muscle volume in patients diagnosed with fragility fractures [11, 38, 39]. Because the baseline muscle volume was similar in the VFx and non-VFx groups, the loss of muscle volume may not be not a cause, but rather the result of a common confounding factor for bone strength and muscle volume, such as aging, a sedentary lifestyle, or comorbidities. Although a causal relationship between BC and fractures remains to be clarified, our study showed that muscle mass is unlikely to be an independent predictor, and thus a cause, of VFx. Sarcopenia, as defined by the Asia Working Group for Sarcopenia (AWGS), was less prevalent in our study population (12.5%) than that reported elsewhere (20%) [12], possibly because our population included younger individuals or because the study was

conducted in a region where the main industry is agriculture, and most workers are self-employed and continue to work into their later years.

In this study, we used a scoring system (PF score) to assess physical function based on the TUG test, SLST, 30SCST, and grip strength (Table 1). A PF score of 8 or more increased the odds of VFx by 5.6, which was significant after correcting for age, sex, BMI, and OSI. The relationship between poor PF and susceptibility to falls and subsequent fractures has been studied. Poor PF is hypothesized to increase the incidence of falls, which in turn increases the number of fractures. A cross-sectional study by Prato et al. [13] showed that a grip strength in the first quartile increased the odds ratio of self-reported falls by 2.3. Lee et al. [40] found that the incidence of VFx was higher in women with a lower jump strength, but was not associated with SMI. These reports are consistent with our current results, which showed that taken separately, poor PF but not BC increased the risk of VFx. Longitudinal studies have demonstrated associations between PF measurements and self-reported fractures in elderly individuals living in the general community [14, 24, 27, 41]. Although the method of diagnosing fractures differed, these studies concluded that a combination of PF tests, rather than a single measurement, is best for predicting osteoporotic fractures. These results agree with our findings that a combination of PF tests, rather than a single measurement, is required for predicting VFx. Different tests measure different abilities, and a decline in several areas may be necessary to increase the risk of fracture.

One advantage of our study is that our risk stratification includes both PF and BC. Previous studies have reported the risk of these factors independently, but few have considered both factors for predicting radiographic vertebral fractures. Our results showed

that the addition of BC to PF was cumulative in predicting fractures. The PF scoring system used in this study may reflect small differences better than a categorical definition of poor function (i.e., one cut-off value), and this may also be an advantage when tracking the value of interventions such as physical training and exercise. Our population was younger and more physically fit than populations in previous studies; for example, none of our subjects met the criteria for poor PF described by Chun et al. [24]. We believe that populations that are growing older but have a relatively low degree of functional decline, like our study population, can benefit the most from fracture prevention strategies. It is important to screen for and treat high-risk individuals before PF is severely impaired, when there is greater potential to conserve function and thereby conserve medical resources. Additional studies are warranted to confirm these results and determine whether targeted improvement of the physical measures used in our PF scoring system can prevent fractures.

Our study had several limitations. We excluded volunteers with incomplete data, which may have excluded volunteers whose condition was too poor to complete the PF tests. Thus, our data may be representative of a relatively fit population. Second, the study was conducted in a rural community with a relatively high percentage of elderly people compared to urban populations in Japan, and our results may not be representative for Japan as a whole.

Third, DXA measurements were not available in this study. DXA is widely used for the diagnosis and screening of osteoporosis and is a valuable factor for predicting fractures. However, there are screening tools that do not utilize DXA that have shown some success [3]. Because our physical function tests do not require any special

equipment, we believe our scoring system may be useful for screening purposes where DXA is unavailable.

The fourth limitation was the unavailability of thoracic X-rays. Incident vertebral fractures most frequently occur in the thoracolumbar region, but also occur in the upper thorax [29, 42]. Future studies should include the thoracic spine to validate our results.

Finally, our study did not consider symptoms such as knee or back pain. Knee pain is associated with falls in women [43], and knee pain and osteoarthritis are associated with osteoporotic fractures [44]. Pain is a possible feature and confounding factor in BC, PF, and VFx, and future studies should encompass all of these factors for a more complete understanding of the factors that increase the risk of VFx.

Our study also had several advantages. We used radiographic VFx as the outcome, in contrast to other studies based on self-reported fractures. Although the presence of subclinical radiographic VFx may seem insignificant, these fractures increase morbidity and decrease QOL [5, 6]. Second, our study included younger participants, who are ideal targets for preventative intervention.

Conclusions

The incidence of VFx over an 8-year period was 12% in our study population. Baseline SMI was not a factor in the risk of future VFx, but the rate of decline in muscle volume was greater in those who sustained VFx. In our proposed PF scoring system, which assigns a point value based on results from the TUG test, 30SCST, SLST, and grip strength, a cut-off of 8 points identified an increased risk of future VFx. The OR of this point system was increased by adding points for lower SMI in the trunk and limbs.

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Ethical approval

This study was approved by the Ethics Committee of Hirosaki University Graduate School of Medicine and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Each individual participant gave informed consent before participating.

Conflict of Interest

The authors have no conflicts of interests to declare.

References

1. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. *Lancet*. 2002;359(9319):1761-7.
2. Hernlund E, Svedbom A, Ivergård M, Compston J, Cooper C, Stenmark J, et al. Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). *Arch Osteoporos*. 2013;8:136.
3. Crandall CJ, Larson JC, Watts NB, Gourlay ML, Donaldson MG, LaCroix A, et al. Comparison of fracture risk prediction by the US Preventive Services Task Force strategy and two alternative strategies in women 50-64 years old in the Women's Health Initiative. *J Clin Endocrinol Metab*. 2014;99(12):4514-22.
4. Sandhu SK, Nguyen ND, Center JR, Pocock NA, Eisman JA, Nguyen TV. Prognosis of fracture: evaluation of predictive accuracy of the FRAX algorithm and Garvan nomogram. *Osteoporos Int*. 2010;21(5):863-71.
5. Kanis JA, Johnell O, Oden A, Borgstrom F, Zethraeus N, De Laet C, et al. The risk and burden of vertebral fractures in Sweden. *Osteoporos Int*. 2004;15(1):20-6.
6. Cockerill W, Lunt M, Silman AJ, Cooper C, Lips P, Bhalla AK, et al. Health-related quality of life and radiographic vertebral fracture. *Osteoporos Int*. 2004;15(2):113-9.

7. Lindsay R, Silverman SL, Cooper C, Hanley DA, Barton I, Broy SB, et al. Risk of new vertebral fracture in the year following a fracture. *JAMA*. 2001;285(3):320-3.
8. Rolland Y, Abellan van Kan G, Bénéto A, Blain H, Bonnefoy M, Chassagne P, et al. Frailty, osteoporosis and hip fracture: causes, consequences and therapeutic perspectives. *J Nutr Health Aging*. 2008;12(5):335-46.
9. Scott D, Seibel M, Cumming R, Naganathan V, Blyth F, Le Couteur DG, et al. Sarcopenic Obesity and Its Temporal Associations With Changes in Bone Mineral Density, Incident Falls, and Fractures in Older Men: The Concord Health and Ageing in Men Project. *J Bone Miner Res*. 2017;32(3):575-83.
10. Mokhtarzadeh H, Anderson DE. The Role of Trunk Musculature in Osteoporotic Vertebral Fractures: Implications for Prediction, Prevention, and Management. *Curr Osteoporos Rep*. 2016;14(3):67-76.
11. Hida T, Shimokata H, Sakai Y, Ito S, Matsui Y, Takemura M, et al. Sarcopenia and sarcopenic leg as potential risk factors for acute osteoporotic vertebral fracture among older women. *Eur Spine J*. 2016;25(11):3424-31.
12. Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. *J Am Med Dir Assoc*. 2014;15(2):95-101.
13. Prato SCF, Andrade SM, Cabrera MAS, Dip RM, Santos HGD, Dellaroza MSG, et al. Frequency and factors associated with falls in adults aged 55 years or more. *Rev Saude Publica*. 2017;51(0):37.

14. Stel VS, Pluijm SM, Deeg DJ, Smit JH, Bouter LM, Lips P. Functional limitations and poor physical performance as independent risk factors for self-reported fractures in older persons. *Osteoporos Int.* 2004;15(9):742-50.
15. Watson SL, Weeks BK, Weis LJ, Harding AT, Horan SA, Beck BR. High-Intensity Resistance and Impact Training Improves Bone Mineral Density and Physical Function in Postmenopausal Women With Osteopenia and Osteoporosis: The LIFTMOR Randomized Controlled Trial. *J Bone Miner Res.* 2017.
16. Chiba D, Tsuda E, Wada K, Kumagai G, Sasaki E, Nawata A, et al. Lumbar spondylosis, lumbar spinal stenosis, knee pain, back muscle strength are associated with the locomotive syndrome: Rural population study in Japan. *J Orthop Sci.* 2016;21(3):366-72.
17. Kumagai G, Wada K, Tanaka T, Kudo H, Asari T, Chiba D, et al. Associations between neck symptoms and LDL cholesterol in a cross-sectional population-based study. *J Orthop Sci.* 2018;23(2):277-81.
18. Shafer KJ, Siders WA, Johnson LK, Lukaski HC. Validity of segmental multiple-frequency bioelectrical impedance analysis to estimate body composition of adults across a range of body mass indexes. *Nutrition.* 2009;25(1):25-32.
19. Bosy-Westphal A, Later W, Hitze B, Sato T, Kossel E, Gluer CC, et al. Accuracy of bioelectrical impedance consumer devices for measurement of body composition in comparison to whole body magnetic resonance imaging and dual X-ray absorptiometry. *Obes Facts.* 2008;1(6):319-24.

20. Dehghan M, Merchant AT. Is bioelectrical impedance accurate for use in large epidemiological studies? *Nutr J*. 2008;7:26.
21. Bischoff HA, Stähelin HB, Monsch AU, Iversen MD, Weyh A, von Dechend M, et al. Identifying a cut-off point for normal mobility: a comparison of the timed 'up and go' test in community-dwelling and institutionalised elderly women. *Age Ageing*. 2003;32(3):315-20.
22. Giorgetti MM, Harris BA, Jette A. Reliability of clinical balance outcome measures in the elderly. *Physiother Res Int*. 1998;3(4):274-83.
23. Chomiak T, Pereira FV, Hu B. The single-leg-stance test in Parkinson's disease. *J Clin Med Res*. 2015;7(3):182-5.
24. Chun SH, Cho B, Yang HK, Ahn E, Han MK, Oh B, et al. Performance on physical function tests and the risk of fractures and admissions: Findings from a national health screening of 557,648 community-dwelling older adults. *Arch Gerontol Geriatr*. 2017;68:174-80.
25. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Res Q Exerc Sport*. 1999;70(2):113-9.
26. Genant HK, Wu CY, van Kuijk C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. *J Bone Miner Res*. 1993;8(9):1137-48.
27. Cawthon PM, Blackwell TL, Marshall LM, Fink HA, Kado DM, Ensrud KE, et al. Physical performance and radiographic and clinical vertebral fractures in older men. *J Bone Miner Res*. 2014;29(9):2101-8.

28. Yoshimura N, Kinoshita H, Takijiri T, Oka H, Muraki S, Mabuchi A, et al. Association between height loss and bone loss, cumulative incidence of vertebral fractures and future quality of life: the Miyama study. *Osteoporos Int.* 2008;19(1):21-8.
29. Ross PD, Fujiwara S, Huang C, Davis JW, Epstein RS, Wasnich RD, et al. Vertebral fracture prevalence in women in Hiroshima compared to Caucasians or Japanese in the US. *Int J Epidemiol.* 1995;24(6):1171-7.
30. Fujiwara S, Kasagi F, Masunari N, Naito K, Suzuki G, Fukunaga M. Fracture prediction from bone mineral density in Japanese men and women. *J Bone Miner Res.* 2003;18(8):1547-53.
31. Lopes JB, Danilevicius CF, Takayama L, Caparbo VF, Menezes PR, Scazufca M, et al. Prevalence and risk factors of radiographic vertebral fracture in Brazilian community-dwelling elderly. *Osteoporos Int.* 2011;22(2):711-9.
32. Baddoura R, Arabi A, Haddad-Zebouni S, Khoury N, Salamoun M, Ayoub G, et al. Vertebral fracture risk and impact of database selection on identifying elderly Lebanese with osteoporosis. *Bone.* 2007;40(4):1066-72.
33. Ballane G, Cauley JA, Luckey MM, El-Hajj Fuleihan G. Worldwide prevalence and incidence of osteoporotic vertebral fractures. *Osteoporos Int.* 2017;28(5):1531-42.
34. Fraser LA, Langsetmo L, Berger C, Ioannidis G, Goltzman D, Adachi JD, et al. Fracture prediction and calibration of a Canadian FRAX® tool: a population-based report from CaMos. *Osteoporos Int.* 2011;22(3):829-37.

35. Ensrud KE, Lui LY, Taylor BC, Schousboe JT, Donaldson MG, Fink HA, et al. A comparison of prediction models for fractures in older women: is more better? *Arch Intern Med.* 2009;169(22):2087-94.
36. Rubin KH, Abrahamsen B, Friis-Holmberg T, Hjelmborg JV, Bech M, Hermann AP, et al. Comparison of different screening tools (FRAX®, OST, ORAI, OSIRIS, SCORE and age alone) to identify women with increased risk of fracture. A population-based prospective study. *Bone.* 2013;56(1):16-22.
37. Walsh MC, Hunter GR, Livingstone MB. Sarcopenia in premenopausal and postmenopausal women with osteopenia, osteoporosis and normal bone mineral density. *Osteoporos Int.* 2006;17(1):61-7.
38. Blain H, Vuillemin A, Teissier A, Hanesse B, Guillemin F, Jeandel C. Influence of muscle strength and body weight and composition on regional bone mineral density in healthy women aged 60 years and over. *Gerontology.* 2001;47(4):207-12.
39. Segal NA, Torner JC, Yang M, Curtis JR, Felson DT, Nevitt MC, et al. Muscle mass is more strongly related to hip bone mineral density than is quadriceps strength or lower activity level in adults over age 50 year. *J Clin Densitom.* 2008;11(4):503-10.
40. Lee EY, Lee SJ, Kim KM, Seo DH, Lee SW, Choi HS, et al. Lower Jump Power Rather Than Muscle Mass Itself is Associated with Vertebral Fracture in Community-Dwelling Elderly Korean Women. *Calcif Tissue Int.* 2017;100(6):585-94.

41. Wihlborg A, Englund M, Åkesson K, Gerdhem P. Fracture predictive ability of physical performance tests and history of falls in elderly women: a 10-year prospective study. *Osteoporos Int.* 2015;26(8):2101-9.
42. van der Klift M, Pols HA, Hak AE, Witteman JC, Hofman A, de Laet CE. Bone mineral density and the risk of peripheral arterial disease: the Rotterdam Study. *Calcif Tissue Int.* 2002;70(6):443-9.
43. Muraki S, Akune T, Ishimoto Y, Nagata K, Yoshida M, Tanaka S, et al. Risk factors for falls in a longitudinal population-based cohort study of Japanese men and women: the ROAD Study. *Bone.* 2013;52(1):516-23.
44. Arden NK, Crozier S, Smith H, Anderson F, Edwards C, Raphael H, et al. Knee pain, knee osteoarthritis, and the risk of fracture. *Arthritis Rheum.* 2006;55(4):610-5.

Tables

Table 1. Combined PF and BC scoring system for predicting fragility fractures^a

Men						
Points	PF tests				BC values	
	Grip strength ^b (kg)	TUG ^b (sec)	30SCST ^b	SLST ^c (sec)	SMI limbs	SMI trunk
0	≥40	≤6	≥20	≥30	≥8.2	≥9.6
1	<40	>6	<20	<30	<8.2	<9.6
2	<30	>7	<13	<20	<7.2	<8.8
3	<20	>8	<8	<10	<6.2	<8.1
Women						
Points	Grip strength ^b (kg)	TUG ^b (sec)	30SCST ^b	SLST ^c (sec)	SMI limbs	SMI trunk
	Grip strength ^b (kg)	TUG ^b (sec)	30SCST ^b	SLST ^c (sec)	SMI limbs	SMI trunk
0	≥25	≥6	≥20	≥30	≥6.4	≥8.2
1	<25	>6	<20	<30	<6.4	<8.2
2	<20	>7	<13	<20	<5.7	<7.6
3	<15	>8	<8	<10	<5.1	<7

Abbreviations: 30SCST, 30-second chair stand test; BC, body condition; PF, physical function; SLST, single leg stand test; SMI, skeletal muscle index; TUG, timed up-and-go test.

^a In this scoring system, each test or measurement is assigned 0–3 points, with more points assigned for worse function. The sum of the PF tests scores is the PF score (0–12 points). The PF + BC score (0–18 points) is the sum of the PF score plus the scores for trunk and limb SMI.

^b Cut-off values for grip strength, TUG, and 30SCT were calculated as the mean minus 1, 2, and 3 SD, calculated from gender-specific T scores for healthy volunteers (age 20–40 years) from the same community program. Cut-off values were rounded to the appropriate whole number.

^c Cut-off values of 20, 15, and 10 seconds were used for the SLST.

Table 2. Background data for VFx and non-VFx subjects^a

	Non-VFx (n = 271)	VFx (n = 36)	<i>P</i>
Age, y	56.5±9.3	65.8±8.8	<0.001*
Women, no. (%)	170 (63)	24 (67)	0.72
Height, cm	158.6±8.5	156.8±8.6	0.29
Weight, kg	58.6±10.2	57.8±10.1	0.64
BMI, kg/m ²	23.2±3.1	23.4±2.7	0.79
OSI	2.64±0.37	2.60±0.57	0.19
Existing VFx, no. (%)	12 (4.4)	2 (5.6)	0.67
Osteoporosis treatment (%)	6 (2.2)	3 (8.3)	0.08
Trunk SMI, kg/m ²	9.0±0.9	9.0±0.8	0.53
Leg SMI, kg/m ²	5.5±0.8	5.3±0.7	0.13
Appendicular SMI, kg/m ²	7.2±1.1	6.9±0.9	0.24
Body fat, %	25.6±8.0	27.3±6.5	0.16
ΔSMI trunk	−1.5±4.5	−3.4±5.9	0.02*
ΔSMI legs	−2.1±5.6	−4.0±5.6	0.06
ΔSMI appendicular	−2.5±5.1	−4.8±5.0	0.01*
Grip Strength, kg	35.9±11.2	32.5±10.7	0.08
TUG, sec	7.0 ±1.6	7.2±1.7	0.56
SLST, sec	61.8±22.0	52.0±27.9	0.02*
30CST	19.5±4.9	17.5±5.6	0.03*
PF score	2.5±1.9	3.5±2.8	0.14
PF + BC score	4.7±2.3	6.1±3.4	0.10

Abbreviations: 30CST, 30-second chair stand test; BC, body composition; BMI, body mass index; PF, physical function; OSI, osteo-sono index; SLST, single-leg stance test; SMI, skeletal muscle index; TUG, timed up-and-go test; VFx, vertebral fracture.

^a Non-categorical variables are shown as mean±SD.

* *P* < 0.05. Non-categorical variables were tested by Mann–Whitney *U* test and categorical variables by Fisher’s exact test.

Table 3. Difference of age, PF, and BC between single or multiple VFX and VFX grade.

	Single VFX (n=26)	Multiple VFX (n = 10)		<i>P</i>
Age, y	65.5±9.3	68.5±7.8		0.62
PF score	2.5	3.0		0.53
PF + BC score	3.0±3.1	4.0±3.4		0.52
VFX grade	1	2	3	<i>P</i>
Age, y	64.7±9.0	66.2±9.8	71.5±3.5	0.22
PF score	3.2±2.7	3.4±2.6	5.3±3.9	0.41
PF + BC score	4.3±3.1	4.1±2.9	6.5±3.7	0.40

Mann-Whitney U test, Kruskal-Wallis test with post hoc Steel-Dwass analysis

Table 4. Relationship between PF, BC, and VFx^a

		OR	95% CI			P
Model 1 ^b	Intercept	4.7×10 ⁻⁴	0.00	-	0.01	<0.01
	Age	1.1	1.1	-	1.2	<0.01
	PF score ≥8	5.6	1.2	-	25.9	0.028
Model 2 ^c	Intercept	4.7×10 ⁻⁴	2.9×10 ⁻⁵	-	7.7×10 ⁻²	<0.01
	Age	1.1	1.1	-	1.1	<0.01
	PF + BC score ≥9	8.1	1.8	-	36.0	<0.01

Abbreviations: BC, body composition; PF, physical function; VFx, vertebral fractures.

^aResults of stepwise logistic regression with VFx as a dependent variable and age, sex, BMI, OSI, and PF score (model 1) or PF + BC score (model 2) as independent variables.

^bModel 1: Higher age and a PF score of 8 or more significantly increased the risk of vertebral fractures.

^cModel 2: A PF + BC score of 9 or more significantly increased the risk of vertebral fractures.

Figure Legends

Figure 1.

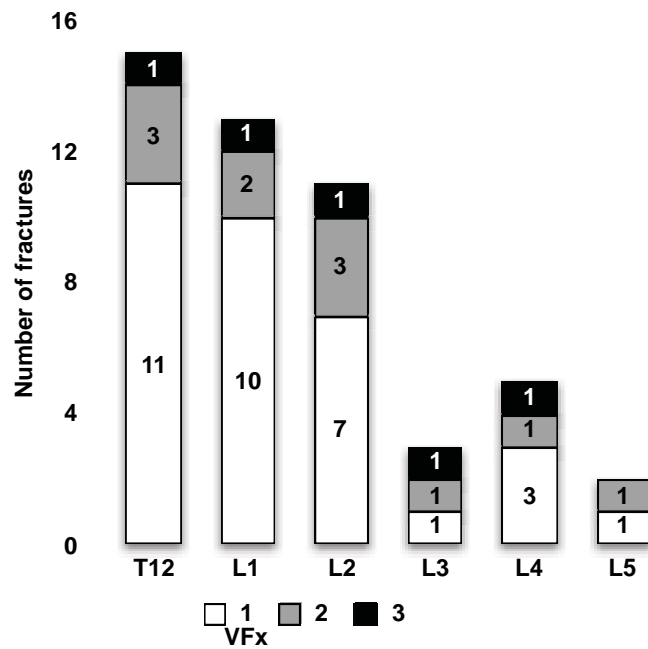


Figure 1. Incidence and grade of fractures per vertebral level.

Supplementary table. Comparison of SF-36 between VFx and non-VFx groups.

SF-36	VFx	Non-VFx	P
Physical Function	44.1 ± 15.8	49.6 ± 10.9	0.017*
Role Physical	49.5 ± 11.4	52.5 ± 8.1	0.017*
Bodily Pain	49.1 ± 10.6	50.1 ± 9.4	0.83
General Health	49.4 ± 9.0	48.4 ± 8.9	0.54
Vitality	54.7 ± 9.6	51.1 ± 9.0	0.015*
Social Function	51.5 ± 11.9	53.3 ± 7.7	0.83
Role Emotion	53.2 ± 9.4	53.6 ± 7.3	0.56
Mental Health	55.5 ± 9.1	52.8 ± 8.2	0.05*
Physical Component Summary	46.1 ± 12.1	51.6 ± 8.9	0.001*
Mental Component Summary	60.6 ± 0.8	60.1 ± 0.9	0.008*

*statistically significant.