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Original Article

Utilizing nomograms to predict prevalent vertebral fracture risk: An analysis of dysmobility syndrome in a community-dwelling population

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ABSTRACT

Background: To determine a reliable method to predict prevalent vertebral fractures (VF) by assessing the association between dysmobility syndrome (DS) and VF in a community-dwelling population.

Methods: This cross-sectional study enrolled 518 participants from fracture-prevention educational activities held in multiple communities in Taiwan. Assessments included questionnaires, fracture risk assessment tool (FRAX), bone mineral density (BMD) and body composition using dual-energy x-ray absorptiometry (DXA), lateral thoracolumbar spine x-rays (specifically T8-S1), grip strength (GS), walking speed, and fall history.

Results: DS was noted in 257 participants (49.6%) and VF was identified in 196 participants (37.8%). A higher prevalence of VF was noted in those with DS. The prevalence of VF was significantly associated with age, gender, FRAX both with and without BMD, osteoporosis, low GS, and DS. In multivariate models accounting for age and sex, the c-index was greater in those with low GS plus osteoporosis as compared to DS alone. Low GS, osteoporosis, and pre-BMD FRAX all had similar c-indexes. Pre-BMD FRAX plus low GS and osteoporosis was superior in predicting VF compared to pre-BMD FRAX plus low GS or osteoporosis alone. Besides the inclusion of age and gender, the nomogram with pre-BMD FRAX major

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osteoporosis fracture probability (MOF) plus low GS had improved correlation between the estimated and actual VF probability than those with pre-BMD FRAX MOF plus osteoporosis. *Conclusions:* The constructed nomogram containing pre-BMD FRAX MOF plus low GS may be considered as a first-line prevalent VF screening method. Those with high-risk scores should subsequently undergo vertebral radiography and/or BMD.

At a glance commentary

Scientific background on the subject

Identification of prevalent vertebral fractures is a vital aspect of treating osteoporosis and preventing new fractures. Aside from bone loss, there are multiple factors contributing to vertebral fractures. To improve early identification of vertebral fractures, it is essential to ascertain and analyze independent variables.

What this study adds to the field

In dysmobility syndrome, only osteoporosis and low grip strength (GS) were associated with vertebral fractures (VF). The constructed nomogram containing pre-bone mineral density (BMD) FRAX plus GS may be considered as a first-line prevalent VF screening method, and as such, determine which patients should undergo spine radiography and/or BMD.

Fragility fractures often precede disability, loss of independence, and mortality in older adults [1,2]. Given the increasing prevalence of elderly individuals worldwide, it is imperative to not only prevent primary fractures but also subsequent fractures, especially those in the hip. Prevalent vertebral fractures (VF) are the most common fragility fractures and are also often preceded by hip fractures [3,4]. Previous studies have demonstrated that those with VF have a five-fold increased risk for subsequent hip fractures [3,5]. Thus, identification of prevalent VF is a vital aspect of treating osteoporosis and preventing new fractures.

It is reported that only about one-third of VF are actually diagnosed [6], as many prevalent or incident fractures are asymptomatic or present with minor symptoms such as mild back pain. Low bone mineral density (BMD) has been recognized to be highly associated with osteoporotic fracture [7–10], but almost half of VF occurred in patients with low bone mass rather than osteoporotic patients [11]. Furthermore, greater than 10% of "osteoporosis-related" fractures have been found in those with normal BMD [10,12]. Interestingly, fragility fractures increase dramatically with advancing age but bone mass does not have a comparable correlating decline [13]. Thus, identifying prevalent VF risk based solely on BMD is inaccurate.

Aside from bone loss, there are multiple factors contributing to fractures that need to be addressed. The fracture risk assessment tool (FRAX) is generally used to predict an individual's 10-year probability of major osteoporotic and hip fractures by evaluating the interaction of multiple risk factors both with and without BMD [14]. FRAX for major osteoporotic fracture has been shown to be predictive for incident VF in postmenopausal women with low BMD [15]. However, it also revealed that once femoral neck BMD and age are known, FRAX does not significantly improve the prediction of VF [15]. In addition, the value of FRAX in predicting prevalent VF in the general population has not been well investigated.

In addition to BMD and clinical risk factors, the falls-related risk factors for incident fractures have been identified [16,17]. Recently, the concept of "dysmobility syndrome (DS)" has been proposed to include osteoporosis, sarcopenia, obesity, and fall history, and as such, thought to improve the identification of those at risk for fractures [18]. The Osteoporotic Fractures in Men (MrOS) study revealed that men with DS are more likely than those without to sustain major osteoporotic fractures and hip fractures [19]. The Korean Urban-Rural Elderly (KURE) study also suggested that DS was associated with elevated odds of morphometric VF in community-dwelling older adults after modifying the DS criteria [20]. In contrast, the Hertfordshire Cohort study demonstrated that DS was associated with falls but not fractures [21]. As such, further studies are needed to evaluate the practicality of DS in clinical practice for predicting prevalent VF risk.

To improve early identification of prevalent VF, the main purpose of this study was to ascertain independent variables based on aforementioned existing knowledge that would enable a highly accurate prediction of VF. Then, according to the analytical results, nomograms aimed at effectively identifying prevalent VF risk were constructed for both the general population and those in a hospital setting.

Material and methods

All methods were carried out in accordance with the relevant guidelines and regulations. This study was approved by the Institutional Review Board of Chang Gung Medical Foundation (IRB: 201600772B0 and IRB: 201800841B0) and written informed consent was obtained from all subjects prior to participation in the trial.

Patient selection and study design

This cross-sectional study enrolled 543 men and women, aged 60 years or older, who participated in community fracture-prevention educational activities in Taiwan from January to December 2018. Enrollment criteria included patients capable of walking independently and those willing to undergo further assessment. The assessments included written questionnaires, FRAX, grip strength (GS), walking speed, fall history, and both BMD and body composition using dual-energy x-ray absorptiometry (DXA). Participants who were unable to respond independently, had a self-reported prior VF, had

Table 1 Characteristics of participants with and without dysmobility syndrome.

Characteristics	Total (N = 518) Mean ± SD	Dysmobility syndrome		p value
		No (N = 261) Mean ± SD	Yes (n = 257) Mean ± SD	
BMI (kg/m^2)	23.8 ± 3.5	24.2 ± 3.3	23.3 ± 3.6	0.002
Age (year)	72.1 ± 8.9	70.7 ± 8.3	73.5 ± 9.3	<0.001
Gender, n (%)				0.008
Female	352 (68.0)	192 (54.5)	160 (45.5)	
Male	166 (32.0)	69 (41.6)	97 (58.4)	
FRAX w/BMD[a]MOF[b]	13.4 ± 8.2	13.8 ± 8.4	12.9 ± 8.0	0.183
FRAX w/BMD[a] HF[c]	6.7 ± 6.3	6.6 ± 6.5	6.9 ± 6.2	0.549
Femoral neck BMD, g/cm^2	0.65 ± 0.12	0.68 ± 0.13	0.62 ± 0.11	<0.001
FRAX MOF[b]	16.6 ± 9.5	15.0 ± 8.7	18.2 ± 10.0	<0.001
FRAX HF[c]	7.6 ± 6.6	5.9 ± 5.8	9.2 ± 6.9	<0.001
Spine BMD, g/cm^2	0.92 ± 0.21	0.95 ± 0.20	0.90 ± 0.21	0.004
Osteoporosis, N (%)	324 (62.5)	113 (34.9)	211 (65.1)	<0.001
Low grip strength, N (%)	326 (62.9)	107 (32.8)	219 (67.2)	<0.001
Slow gait speed, N (%)	230 (44.4)	64 (27.8)	166 (72.2)	<0.001
Fall, N (%)	3 (0.6)	2 (66.7)	1 (33.3)	1.000
Low lean mass, N (%)	237 (43.4)	65 (27.4)	172 (72.6)	<0.001
Obesity, N (%)	195 (37.6)	65 (33.3)	130 (66.7)	<0.001
Vertebral fracture, N (%)	196 (37.8)	83 (42.3)	113 (57.7)	0.006

Abbreviations:
[a] FRAX w/BMD: FRAX without BMD.
[b] MOF: probability of major osteoporotic fracture.
[c] HF: probability of hip fracture.

received treatment for osteoporosis within the past year, or had significant cognitive impairment were excluded. As 25 subjects had incomplete assessments, 518 participants were included in the final analysis.

Measurements

FRAX score

FRAX scores were calculated with an online tool using the Taiwan algorithm [22]. Questions included age, sex, height, weight, history of previous fracture, history of parental hip fracture, current smoking status, glucocorticoids exposure, diagnosis of rheumatoid arthritis, secondary osteoporosis, and daily alcohol intake greater than three units. FRAX both with and without femoral neck BMD were calculated.

Assessment of body composition, BMD, and VF

Body composition and BMD of the lumbar spine and hip were measured using a DXA instrument (GE-Lunar, iDAX, Madision, WI, USA) installed at Keelung Chang Gung Memorial Hospital. Appendicular skeletal muscle mass index (ASMI) was calculated as the sum of the muscle mass of all four limbs divided by the height squared (kg/m^2). BMD was assessed according to the recommendations of the International Society for Clinical Densitometry (ISCD) [23]. Prevalent vertebral fracture was defined using the morphometry of lateral projection on spinal radiographs, following the visual semi-quantitative diagnosis [24]. Lateral thoracolumbar spine x-rays (specifically T8-S1) were examined. Diagnosis of vertebral fractures was based on the Genant scoring system [25].

Assessment of GS and physical performance

Grip strength was measured using a handgrip dynamometer (CAMRY, EH101, Zhongshan, China). Gait speed was determined using a timed 6-m walk and participants were instructed to walk at their usual pace with a static start and without deceleration down a 6-m straight line.

Definition of dysmobility syndrome (DS)

The definition of DS was modified from Binkley et al.'s original report. [18], aside from a modification of the fall history criterion. People with three or more of the following conditions were considered to have DS: obesity (total body fat percentage >40% for females, >30% for males), low lean mass (ASMI $\leq$5.45 kg/m^2 for females or $\leq$7.26 kg/m^2 for males), osteoporosis (T-score of ≤ -2.5 at the lumbar spine, femoral neck, or total hip), slow gait speed (<1.0 m/s), low GS (<30 kg for males or < 20 kg for females), and two or more self-reported falls in the preceding year (based on guidelines from the American Geriatrics Society and British Geriatrics Society (AGS/BGS) [26]). It has been demonstrated that a history of one fall without injury and without gait or balance problems does not warrant further assessment beyond continued annual fall risk screening [26]. Thus, the question regarding two or more falls is likely to be more valuable than the question asking about one or more falls as an equal-weighted risk factor of DS.

Statistical analysis

Baseline characteristics were described using means and standard deviations for continuous data and percentages for categorical data. Comparisons made between participants both with and without DS and with and without VF were carried out using independent sample t-tests for continuous data and Chi-square tests for categorical data. A logistic regression model was used to estimate odds ratios for

Table 2 Comparison of clinical characteristic between participants with and without vertebral fracture (VF).

	Without VF (N = 322)	VF (N = 196)	*p* value
	Mean ± SD	Mean ± SD	
BMI (kg/m^2)	23.63 ± 3.59	24.00 ± 3.33	0.232
Age (year)	69.74 ± 8.62	76.05 ± 8.02	<0.001
Gender, n (%)			0.004
F	234 (66.5)	118 (33.5)	
M	88 (53.0)	78 (47.0)	
FRAX w/BMD[a]MOF[b]	12.40 ± 7.66	14.91 ± 8.86	0.001
FRAX w/BMD[a] HF[c]	5.98 ± 6.34	7.96 ± 6.15	<0.001
Femoral neck BMD, g/cm^2	0.66 ± 0.12	0.63 ± 0.14	0.002
FRAX MOF[b]	15.41 ± 8.33	18.44 ± 10.85	<0.001
FRAX HF[c]	6.53 ± 5.29	9.23 ± 7.97	<0.001
Spine BMD, T-score	−1.76 ± 1.59	−1.86 ± 1.72	0.532
Osteoporosis, n (%)			0.003
No	137 (70.6)	57 (29.4)	
Yes	185 (57.1)	139 (42.9)	
Low grip strength, n (%)			<0.001
No	148 (77.1)	44 (22.9)	
Yes	174 (53.4)	152 (46.6)	
Slow gait speed, n (%)			0.645
No	176 (61.1)	112 (38.9)	
Yes	146 (63.5)	84 (36.5)	
Fall, n (%)			1.000
No	320 (62.1)	195 (37.9)	
Yes	2 (66.7)	1 (33.3)	
Low lean mass, n (%)			0.564
No	171 (60.9)	110 (39.1)	
Yes	151 (63.7)	86 (36.3)	
Obesity, n (%)			0.669
No	198 (61.3)	125 (38.7)	
Yes	124 (63.6)	71 (36.4)	
Dysmobility syndrome, n (%)			0.006
No	178 (68.2)	83 (31.8)	
Yes	144 (56.0)	113 (44.0)	

[a] FRAX w/BMD: FRAX without BMD.
[b] MOF: probability of major osteoporotic fracture.
[c] HF: probability of hip fracture.

vertebral compression fracture. Univariate analysis was used to determine the association with clinical risk factors in participants both with and without VF. Then, significant factors were used to build a multivariate logistic model and to construct nomograms to predict VF. Concordance index (c-index) statistics were used to compare the differences between various models in discriminating VF. All statistical significance levels were using two sided tests with $p < 0.05$. All statistical analyses were performed using R 3.6.2 (copyright The R foundation for statistical computing).

Results

Characteristics of participants with or without DS

Table 1 summarizes the study participants' characteristics and examined differences based on whether they met the criteria for DS or not. DS was diagnosed in 257 participants (160 women and 97 men) (49.6%). There were significant differences in gender, body mass index (BMI), spine BMD, femoral neck BMD, and FRAX with BMD among those with and without DS. There was also a significant difference in DS components, except for fall history. In addition, higher incidence of prevalent VF was noted in those with DS ($p = 0.006$).

Table 3 Variables associated with vertebral fracture.

Univariate	Vertebral fracture			
	Odds Ratio	Lower	Upper	*p*-value
BMI	1.03	0.98	1.08	0.240
Age	1.10	1.07	1.13	<0.001
Gender				
Female	1.00			
Male	1.76	1.21	2.56	0.003
FRAX w/BMD[a]MOF[b]	1.04	1.02	1.06	0.001
FRAX w/BMD[a] HF[c]	1.05	1.02	1.08	0.001
Femoral neck BMD, g/cm^2	0.09	0.02	0.41	0.002
FRAX MOF[b]	1.03	1.01	1.05	0.001
FRAX HF[c]	1.07	1.04	1.10	<0.001
Osteoporosis	1.81	1.24	2.65	0.002
Low grip strength	2.94	1.98	4.42	<0.001
Slow gait speed	0.90	0.63	1.29	0.581
Fall	0.82	0.04	8.62	0.872
Low lean mass	0.89	0.62	1.26	0.504
Obesity	0.91	0.63	1.31	0.603
DS	1.68	1.18	2.41	0.004

[a] FRAX w/BMD: FRAX without BMD.
[b] MOF: probability of major osteoporotic fracture.
[c] HF: probability of hip fracture.

Characteristics of participants with or without prevalent VF

In this population at high risk for osteoporosis, prevalent VF was identified in 196 participants (37.8%). There were differences in baseline characteristics between participants with and without prevalent VF, which included age, sex, FRAX both with and without BMD, femoral neck BMD, osteoporosis, low GS, and DS diagnosis (Table 2).

Association between prevalent VF and various variables

We used univariable logistic regression to analyze the association between prevalent VF and variables, including basic characteristics, DS components, and FRAX (Table 3). Prevalent VF was significantly associated with age, gender, FRAX both with and without BMD, femoral neck BMD, and DS diagnosis. However, in terms of DS components, only osteoporosis and low GS were shown to have a positive association with prevalent VF.

In Table 4, we further analyzed the relationship between prevalent VF and risk factors using multivariable logistic regression and calculated the power for predicting prevalent VF in these various models. In all models adjusted for age and sex, there was a significant association between prevalent VF and increased age. In multivariate model 1, DS was not significant in predicting prevalent VF. Contrastingly, low GS in patients both with and without osteoporosis was shown to be significantly associated with prevalent VF in models 2, 3, and

Table 4 Multivariable logistic regression of predictors and Concordance index (c-index) statistics for vertebral fracture in eight models.

Model	Model 1		Model 2		Model 3		Model 4	
c-index	0.716		0.732		0.726		0.726	
	OR[a] (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age	1.09 (1.07, 1.12)	<0.001	1.08 (1.05, 1.11)	<0.001	1.08 (1.06, 1.11)	<0.001	1.09 (1.06, 1.12)	<0.001
Sex								
Female	1.00		1.00		1.00		1.00	
Male	1.45 (0.97, 2.17)	0.072	1.58 (1.04, 2.40)	0.032	1.43 (0.95, 2.14)	0.086	1.68 (1.11, 2.54)	0.014
Osteoporosis			1.63 (1.07, 2.49)	0.024			1.74 (1.15, 2.65)	0.009
Low grip strength			1.87 (1.21, 2.89)	0.005	1.98 (1.29, 3.05)	0.002		
DS[b]	1.33 (0.90, 1.95)	0.150						

Model	Model 5		Model 6		Model 7		Model 8	
c-index	0.724		0.738		0.735		0.745	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age	1.09 (1.06, 1.11)	<0.001	1.07 (1.05, 1.10)	<0.001	1.08 (1.06, 1.11)	<0.001	1.07 (1.04, 1.10)	<0.001
Sex								
Female	1.00		1.00		1.00		1.00	
Male	2.00 (1.26, 3.18)	0.003	1.96 (1.23, 3.13)	0.005	2.29 (1.42, 3.72)	0.001	2.21 (1.36, 3.59)	0.001
Osteoporosis					1.78 (1.17, 2.74)	0.007	1.66 (1.09, 2.56)	0.020
Low grip strength			2.07 (1.35, 3.22)	0.001			1.95 (1.26, 3.05)	0.003
Pre-BMD FRAX[c] MOF[d]	1.05 (1.00, 1.09)	0.034	1.05 (1.01, 1.10)	0.017	1.05 (1.01, 1.10)	0.024	1.06 (1.01, 1.11)	0.014
Pre-BMD FRAX HF[e]	0.98 (0.93, 1.03)	0.479	0.97 (0.92, 1.02)	0.327	0.97 (0.92, 1.02)	0.346	0.97 (0.91, 1.02)	0.247

Model 1: age + sex + DS; Model 2: age + sex + osteoporosis + low grip strength; Model 3: age + sex + low grip strength; Model 4: age + sex + osteoporosis; Model 5: age + sex + Pre-BMD FRAX; Model 6: age + sex + low grip strength + Pre-BMD FRAX; Model 7: age + sex + osteoporosis + Pre-BMD FRAX; Model 8: age + sex + osteoporosis + low grip strength + Pre-BMD FRAX.

[a] OR: Odds Ratio.

[b] DS: dysmobility syndrome.

[c] Pre-BMD FRAX: FRAX without bone mineral density of femoral neck.

[d] MOF: probability of major osteoporotic fracture.

[e] HF: probability of hip fracture.

4. In addition, c-index in model 2 (which incorporated low GS and osteoporosis) was higher than that of model 1 (which incorporated DS), model 3 (which incorporated low GS), and model 4 (which incorporated osteoporosis). This revealed that of the numerous DS components, the utilization of both osteoporosis and low GS potentially provides the highest predictive power for prevalent VF. Upon further analysis of the association between prevalent VF and pre-BMD FRAX in model 5, only the major osteoporosis fracture probability (MOF) of pre-BMD FRAX was significant in predicting VF. C-index in model 5 with pre-BMD FRAX was also higher than that of model 1 (which incorporated DS) but was lower than that of model 2 (which incorporated low GS and osteoporosis). It demonstrated that although pre-BMD FRAX is significant and has a higher predictive power for prevalent VF than DS, the utilization of two DS components, specifically osteoporosis and low GS, may provide even higher predictive capability. The addition of low GS, osteoporosis, and both low GS and osteoporosis to pre-BMD FRAX in models 6, 7, and 8 respectively showed that low GS, osteoporosis, and MOF of pre-BMD FRAX were also significantly associated with prevalent VF. The c-index for predicting prevalent VF was 0.738, 0.735, and 0.745 respectively.

Predictive accuracy of nomograms for VF

Nomograms to estimate the probability of prevalent VF risk and calibrating plots based on multivariable models 6, 7, and 8 were constructed and are shown in Fig. 1A–C. Each variable is listed on the nomogram, with assigned points that correspond to specific degrees of the variable. An upward vertical line should be drawn to the "points" bar to assign points for each individual variable. Then, all points from the various variables should be calculated and based on the cumulative point score, a vertical line from the "total points" bar should be drawn downwards to the "VF risk" bar and that will determine personalized prevalent VF risk. All nomograms included age, sex, and MOF of pre-BMD FRAX. The c-index for the nomogram with low GS and osteoporosis (Fig. 1C) was higher than that of low GS alone (Fig. 1A) or osteoporosis alone (Fig. 1B). The mean absolute error for the nomogram that included low GS and MOF of pre-BMD FRAX was 0.014 (Fig. 1A) and 0.022 (Fig. 1C) for the nomogram that included low GS, osteoporosis, and MOF of pre-BMD FRAX. These two nomograms were found to have superior correlation between the estimated and actual prevalent VF probability than the nomogram that included osteoporosis and MOF of pre-BMD FRAX (Fig. 1B).

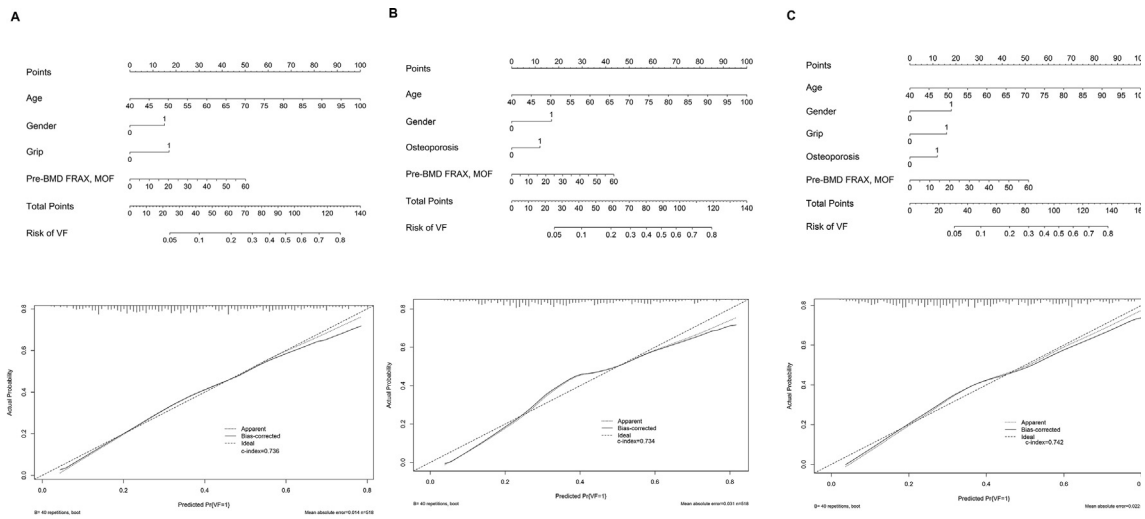

Fig. 1 Predictive nomograms and calibration plots for vertebral fractures (VF). These predictive nomograms were constructed based on multivariable models. Points for each variable are assigned by drawing an upwards line to the "points" bar. The sum of the points for all the various variables are then calculated. A vertical line from the "total points" bar should be drawn downwards to the "VF risk" bar to vertebral fracture probability. The calibration curve shows concordance between actual and predicted probability of vertebral fractures. Besides age and gender, variables of the three nomograms include (A) low grip strength and probability of major osteoporosis fracture using FRAX without bone mineral density (Pre-BMD FRAX MOF), (B) osteoporosis diagnosis and pre-BMD FRAX MOF, and (C) low grip strength, osteoporosis diagnosis, and pre-BMD FRAX MOF.

Discussion

This study demonstrated a high prevalence (49.6%) of DS in a population at high risk for osteoporosis and fractures. Although those with DS had higher FRAX scores and higher frequency of prevalent VF, prevalent VF was found to be significantly associated with only certain components of DS, such as osteoporosis and low GS, after adjustment for age and gender. When comparing the predictive ability of prevalent VF in the various models, models that combined pre-BMD FRAX with low GS, regardless of osteoporosis diagnosis, were superior to those with DS, FRAX, BMD, or low GS alone. Our nomograms that included low GS and MOF of pre-BMD FRAX (regardless of osteoporosis diagnosis) demonstrated the highest correlation in predicting prevalent VF. Since BMD measurement is not universally available in all practice settings, pre-BMD FRAX combined with low GS should be considered as a first-line primary screening method for prevalent VF in the general population. As such, it would also be cost-saving with easier accessibility.

The prevalence of DS in this study was higher, ranging up to 49.6%, when compared with previous reports with ranges from 22% [27] to 34% [18]. This may be associated with the implementation of prior screening programs that lead to a high-risk population participating in our community fracture-prevention educational activities, seeing as up to 65% of our participants had high-risk pre-BMD FRAX. It has been demonstrated that the risk of DS is significantly higher in postmenopausal women with a fragility fracture [28]. We also found a significant association not only between DS and FRAX (including HF and MOF) but also between DS and prevalent VF. This is compatible with results from the MrOS prospective cohort study [19] and the KURE study [20]. Upon analysis of the association between DS components and prevalent VF, we found that the only significant predictors were osteoporosis and GS. However, it should be taken into account that the MrOS study only enrolled male participants and examined the association between DS and both future hip and/or major osteoporotic fractures over a median of 14 years [19]. The KURE study only focused on Genant grade 2 or higher (moderate or severe) VF and utilized a modified DS definition (with <7.0 kg/m^2 in men and <5.7 kg/m^2 in women cutoff for low lean mass using bioimpedance analysis and physical performance tests with timed get-up-and-go) [20]. These factors could potentially impact the association between DS components and VF.

By utilizing multivariable models to identify prevalent VF risk, this study revealed that the use of DS does not enhance prediction, compared to using a simple model that incorporates osteoporosis and low GS. Many studies have demonstrated the association between GS and BMD [29–32] but there are relatively limited and conflicting reports regarding the relationship between GS and VF [33]. Impaired and low GS in both women [34,35] and men [36] have been reported to be associated with a significant increase in incident or clinical VF risk but with no statistically significant association with prevalent VF [34]. In contrast, Kärkkäinen et al. found that clinical VF was not associated with GS in postmenopausal women [37]. The predictive value of physical performance markers, such as chair stand time, walking speed, and GS, for fracture has been demonstrated in a series of US MrOS cohort studies using different analytic methodologies [16,17,38–41]. Although these MrOS studies are limited to the male population, one of these studies that focused on VF revealed results similar to this study, in which poorer GS performance was associated with an increased risk of incident radiographic VF [17]. Associations between appendicular lean mass and fracture are still controversial. No association

between ASMI and hip fracture was found in the US MrOS cohort [42] or in women in the Framingham study [43], while a study with Swiss retirees showed that low lean mass was a predictor of incident fracture [44]. In addition, Iolascon et al. reported a 66.6% prevalence of low ASMI in 67 women with VF and an increased risk of sarcopenia (OR 2.63) when more than two VFs were present [45]. However, the relationships between ASMI and incident fracture are attenuated when BMD is factored in Refs. [41,46]. Since the majority of enrolled participants in this study had low bone mass, we found that ASMI was also not significantly associated with prevalent VF.

Schousboe et al. reported that a model with age, femoral neck BMD, historical height loss (HHL), prior non-spine fracture, BMI, back pain, and GS was only minimally better in identifying prevalent VF than that of a more parsimonious model with age, BMD, and HHL in older women [47] and men [48]. As such, these studies did not focus on or emphasize the role of GS in detecting prevalent VF. Therefore, this study is the first, to our knowledge, to demonstrate that low GS is so highly correlated with prevalent VF. This finding echoes the recent revision to the sarcopenia definition by the European Working Group on Sarcopenia in Older People (EWGSOP) [49], which highlights low GS as a key characteristic of sarcopenia.

VF diagnosis is dependent upon spine x-ray. Clinical indications for spine radiographs, in the absence of trauma or malignancy, include acute back pain, focal tenderness, loss of height, and known or suspected cases of osteoporosis [50]. In addition, the 2013 Position Development Conference of ISCD has adopted age, historical height loss, use of systemic glucocorticoid therapy, and self-reported but undocumented prior vertebral fracture as indications for vertebral fracture assessment [51]. However, it has been shown that up to 70% of VF remain undiagnosed [6]. Therefore, a cost-effective nomogram capable of identifying those at risk for VF is vital, especially for preliminary screening. Compared with BMD and the Osteoporosis Self-Assessment Tool for Asians (OSTA), FRAX without BMD has been reported as having the best discriminative ability to predict new vertebral fractures in men aged 50 years or above with pain [52]. Ensrud et al. found that FRAX does not improve fracture prediction in older women beyond a simple model based on age and BMD [53]. In this study, which enrolled both men and women, the c-index of models 3, 4, and 5, were identical. Low GS plus osteoporosis was superior to pre-BMD FRAX in predicting prevalent VF (c-index: 0.732 vs 0.724). Although osteoporosis, GS, and FRAX were independent predictors of prevalent VF in this study, each alone was of limited value for identifying prevalent VF. Therefore, focus should be broadened to include clinical factors, body performance, and BMD. As such, the nomograms developed in this study only included those significant predictors in our multivariable analysis, such as age, gender, low GS, osteoporosis, and MOF of pre-BMD FRAX.

Previous reports regarding prediction models for prevalent VF [20,47,48], all included BMD testing. According to our constructed nomograms, the MOF of pre-BMD FRAX plus low GS, regardless of osteoporosis diagnosis, has increased correlation between the estimated and actual probability of VF than the MOF of pre-BMD FRAX plus osteoporosis. The high cost and availability of DXA for osteoporosis evaluation and the ignored high prevalence of VF in subjects with low bone mass is prohibitive for early VF identification in local hospitals and communities. Thus, MOF of pre-BMD FRAX plus low GS should be considered as a simple and cost-saving method for primary screening in the general population.

This study has a number of strengths. In this cross-section study, enrolled participants were not recruited from a single hospital or single community. All participants underwent assessments that included all current recognized predictive methods for the categorization of DS and FRAX. This study confirmed that our screening program, which included pre-BMD FRAX, GS, and walking speed, could accurately identify those with DS who may be at risk for future fractures and frailty. It should be noted that this study is, to our knowledge, the first to propose a cost-saving primary screening tool without using expensive instruments for early VF detection, especially in local hospitals or community health service centers. This study is not without limitations. By enrolling participants capable of independent walking, these results may not be extrapolated to other populations, including those institutionalized and those unable to independently walk. Furthermore, as a cross-sectional study, additional studies are needed regarding this tool's ability to predict future fragile fractures and incident VF.

In conclusion, we found that aside from age, gender, and clinical factors, GS and BMD are also significantly associated with prevalent VF. Compared with DS or FRAX, low GS combined with pre-BMD FRAX MOF can serve as a more effective and cost-saving primary screening tool in determining those at high risk for prevalent VF, and as such, determine which patients should undergo spine radiography and/or DXA evaluation. FRAX combined with low GS and confirmed diagnosis of osteoporosis provided the best discriminative ability to predict VF.

Conflicts of interest

None.

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