


## CLINICAL ARTICLE

# Comprehensive Interventions Including Vitamin D Effectively Reduce the Risk of Falls in Elderly Osteoporotic Patients

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**Objective:** To evaluate the effects of different intervention measures to prevent falls in elderly osteoporotic patients.

**Methods:** A randomized controlled trial was conducted in our outpatient ward from August 2014 to September 2015. A total of 420 patients over 60 years of age were assigned to four groups. NA VitD group took 800 mg calcium and 800 IU non-active vitamin D. P-NA VitD group took 800 mg calcium, 800 IU non-active vitamin D, and received physical exercise. A VitD group took 800 mg calcium and 0.5 µg active vitamin D. P-A VitD took 800 mg calcium, 0.5 µg active vitamin D, and received physical exercise. Physical exercise includes guidance in improving muscle strength and balance ability. Short physical performance battery (SPPB), grip strength, modified falls efficacy scale (MFES), blood calcium, and 25-hydroxyl vitamin D were measured before interventions and at 3, 6, and 12 months after interventions. Bone mineral density (BMD) was detected before interventions and at 12 months after interventions. The incidence of falls and fractures, adverse events, and drug reactions were recorded for 12 months.

**Results:** A total of 420 patients were allocated in the four groups: 98 cases into the NA VitD group (11 males, 87 females), 97 cases into the P-NA VitD group (13 males, 84 females), 99 cases into the A VitD group (15 males, 84 females), and 98 cases into the P-A VitD group (11 males, 87 females). At 6 months after interventions, the SPPB of A VitD group significantly increased from  $6.9 \pm 1.9$  to  $8.0 \pm 2.4$  ( $P < 0.05$ ), and the SPPB of A VitD group significantly increased from  $7.2 \pm 2.1$  to  $8.6 \pm 1.7$  ( $P < 0.05$ ). At 6 months after interventions, MFES of P-NA VitD group  $7.0 \pm 1.6$  to  $7.6 \pm 1.6$  ( $P < 0.05$ ), and MFES of P-A VitD group significantly increased from  $6.7 \pm 1.6$  to  $7.5 \pm 1.6$  ( $P < 0.05$ ). At 12 months after interventions, SPPB of all groups, grip strength, and MFES of P-NA VitD group, A VitD group, P-A VitD group were significantly improved ( $P < 0.05$ ). The BMD of lumbar vertebrae of A VitD group significantly increased from  $0.742 \pm 0.042$  to  $0.776 \pm 0.039$ , and P-A VitD group significantly increased from  $0.743 \pm 0.048$  to  $0.783 \pm 0.042$  ( $P < 0.05$ ). No serious adverse events occurred during the 12 months of follow-up.

**Conclusion:** Active vitamin D is better than non-active vitamin D to improve physical ability and the BMD of lumbar vertebrae and reduce the risk of falls.

**Key words:** Aged; Bone density; Fracture; Osteoporosis; vitamin D

## Introduction

Lack of vitamin D in the elderly is one of the important causes of falls and fractures. Previous studies have shown that vitamin D and calcium supplementation may

reduce the risk of fractures in the elderly. In the United States, the National Institutes of Health (NIH) recommends those 51–70 years old take Vitamin D<sub>3</sub> 400 IU (International Units), and those over 70 years old take Vitamin D<sub>3</sub> 600 IU.

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Vitamin D<sub>3</sub> improve calcium absorption, and the calcium intake of adults over 50 years old should reach 1200 mg per day. However, two recent studies by British scientists show that supplementing vitamin D and calcium does not seem to prevent high-risk elderly fractures.

A large-scale clinical trial conducted by Dr. Adrian Grant, Director of the Health Care Research Center of the University of Aberdeen, UK, was completed in collaboration with 21 hospitals in the UK. A total of 5292 over 70-year-old elderly people (85% of whom were women) who had experienced one time fracture were included. They were randomly divided into four groups, vitamin D<sub>3</sub> (800 IU/d), calcium (1000 mg/d), vitamin D<sub>3</sub> plus calcium (same dose), and placebo. The results of following-up for 24 to 62 months showed that 698 (13%) subjects had new low-traumatic fractures, of which 183 (26%) were hip fractures. There was no significant difference in the incidence of fractures between the four groups. The fracture rate was 12.6% in the calcium group and 13.7% in the control group. The vitamin D<sub>3</sub> group had a fracture rate of 13.3% and the control group was 13.1%. The rate in vitamin D<sub>3</sub> plus calcium group was 12.6% while it was 13.4% in the control group. There were no significant differences in the incidence of all new fractures, fractures and hip fractures, the number of deaths, the number of falls, and the quality of life among the groups. This result does not support the traditional view that oral vitamin D and calcium supplementation can prevent fractures in the elderly<sup>1</sup>.

Another clinical study conducted by Dr. David Torgerson, director of the Yorkshire Trial Center at the University of York in the United Kingdom, was conducted on 3314 over 70-year-old women who were weak, in poor health, or had fractures before. The subjects were randomly divided into two groups, calcium (1000 mg/d) plus vitamin D<sub>3</sub> (800 IU/d) and the control group. After a follow-up of 18 to 42 months, the clinical fracture rates of the two groups of women were lower than expected, but women who received vitamin D<sub>3</sub> and calcium supplementation were not less likely to have fractures than those who did not. The study shows no evidence that calcium and vitamin D<sub>3</sub> supplementation can reduce the incidence of clinical fractures in women with one or more risk factors for hip fracture<sup>2</sup>.

Dr. Torgerson believes that their conclusions are the same as those published by *Lancet*, calcium and vitamin D supplementation cannot reduce the risk of hip fractures, and only calcium and vitamin D cannot treat osteoporosis. Other more effective treatments must be found; if medical imaging tests prove that there is a risk of hip fracture, calcium and vitamin D alone cannot reduce the risk of hip fracture. Therefore, whether supplementation of vitamin D<sub>3</sub> and calcium can prevent fractures in the elderly is still under debate<sup>3</sup>.

Thus, the aims of this study are: (i) to observe the effect of comprehensive intervention measures including vitamin D<sub>3</sub> on muscle strength, balance, physical functions; (ii) to observe whether the interventions are helpful to

improve BMD; (iii) to conclude whether the supplementation of vitamin D<sub>3</sub> and calcium may prevent elderly fracture. This study may provide a strategy for physicians to help the elderly prevent osteoporotic fractures.

A total of 420 patients over 60 years old were randomly divided into four groups. NA VitD group (800 mg calcium and 800 IU non-active vitamin D), P-NA VitD group (calcium 800 mg, non-active vitamin D 800 IU, and physical exercise), A VitD group (calcium 800 mg and active vitamin D 0.5 µg), P-A VitD group (calcium 800 mg and active vitamin D 0.5 µg, and physical exercise). Physical exercise includes guidance in improving muscle strength and balance ability. Short physical performance battery (SPPB), grip strength, modified falls efficacy scale (MFES), blood calcium and 25-hydroxyl vitamin D, and bone mineral density (BMD) were collected. The incidence of falls and fractures, adverse events and drug reactions were recorded for 12 months.

## Materials and Methods

### Inclusion and Exclusion Criteria

Each patient provided informed consent for participation in the study. This study was conducted in accordance with the Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects) and was approved by Beijing Friendship Hospital, Capital Medical University.

Inclusion criteria: (i) participants' bone mineral density (BMD) tested in lumbar vertebra or hip by dual energy X-ray absorptiometry (DXA) reached  $-2.5$  or less; (ii) participants regularly take calcium and active or non-active vitamin D, and could carry out physical exercise or not; (iii) participants could complete the follow-up, which consisted of SPPB, MFES, BMD, and blood calcium and 25-hydroxyl vitamin D test; (vi) participants presented with recurrent pain due to osteoporosis.

Exclusion criteria: (i) the patient suffered brain or neuromuscular disease, osteoarthopathy, eye disease, or other diseases that might affect their balance; (ii) those were diagnosed as secondary osteoporosis; (iii) those suffered two or more gallstones or kidney stones after taking calcium.

According to the inclusion and exclusion criteria, from August 2014 to December 2015, 420 patients in Older People-Community setting (FROP-Com) were selected and randomly divided into NA VitD group, P-NA VitD group, A VitD group, and P-A VitD group. A total of 392 patients were followed up by December 2015. The basic information of the four groups are presented in Table 1.

### Methods

NA VitD group took 800 mg calcium and 800 IU non-active vitamin D per day. P-NA VitD group took 800 mg calcium and 800 IU non-active vitamin D per day and received guidance in improving muscle strength, balance ability, and health education for prevention of falls. A VitD group took 800 mg calcium and 0.5 µg active vitamin D per day. P-A

**TABLE 1 Basic characteristics of the four patient groups**

Items	NA VitD group (n = 98)	P-NA VitD group (n = 97)	A VitD group (n = 99)	P-A VitD group (n = 98)	P-value
Age (years)	70.7 ± 6.8	70.2 ± 5.8	71.3 ± 7.1	71.5 ± 6.8	0.460
Gender (n, %)					0.810
Males	11 (11.22)	13 (13.4)	15 (15.15)	11 (11.22)	
Females	87 (88.78)	84 (86.6)	84 (84.85)	87 (88.78)	
Height (cm)	159.83 ± 5.90	160.25 ± 6.06	159.76 ± 6.86	161.77 ± 6.83	0.100
Weight (kg)	60.79 ± 6.97	62.93 ± 10.73	61.37 ± 9.81	63.23 ± 9.79	0.200

VitD group took 800 mg calcium and 0.5 µg active vitamin D per day and received guidance in improving muscle strength, exercises to assist balance ability, and health education for prevention of falls. Each group received the interventions and was followed-up for 12 months.

Exercise: (i) Dynamic Flamingo (DF) exercise: standing on one leg for 1 min three times per day. Those subjects unable to complete DF independently were allowed to use tables, chairs, or other auxiliary props to perform single-leg standing until DF exercise reached 1 min without any assistance; (ii) tai chi for 10 min; (iii) walking for 30 min at a usual speed on flat ground.

### Parameters

#### Short Physical Performance Battery (SPPB)

The SPPB was calculated according to literature standards<sup>4</sup>. The patients were asked to perform three timed tasks: hierarchical assessment of standing balance, 4-m walking speed at usual pace, and standing five times from a seated position in a chair. The timed results of each sub-test were rescaled according to predefined cut-points for obtaining a score ranging from 0 (worst performance) to 4 (best performance). The total score of SPPB ranges from 0 to 12. For standing balance, participants were asked to remain standing with their feet as close together as possible, then in a semi-tandem position, and finally in a tandem position. Each position had to be held for 10 s. The presence of balance deficit is considered as the inability to maintain tandem position for at least 10 s.

#### Grip Strength

Hand-held dynamometer (HHD, J00105, Lafayette Instruments, UK) was performed according to the standard recommended by the American Hand Therapy Association<sup>5</sup>. The patients kept a standard posture with their upper limbs sagging on both sides of the body and the surface of the dynamometer orientating outwards. The subjects completed the formal measurement after practicing once. The grip strength was calculated by the average of both hands and recorded in kilograms.

#### Modified Falls Efficacy Scale (MFES)

This scale measures the degree of confidence that the subjects have that they will not fall when completing daily activities. The activities included nine indoor activities, changing clothes, preparing simple food, bathing, standing up from a

chair, going to/getting up from bed, answering the door/telephone, walking around the room, taking things from a box/drawer, doing light housework, and five outdoor activities—shopping, taking public transport, crossing the road, doing gardening/drying clothes, walking up and down stairs. The score per activity ranges from 0 (no confidence) to 10 (sufficient confidence) points. The average was recorded as the final score<sup>6</sup>.

SPPB, grip strength, and MFES were recorded before interventions and at 3, 6, and 12 months after interventions.

#### BMD

Dual-energy X-ray absorptive bone density detector (Hologic Discovery, USA) was used to detect the BMD of lumbar vertebra (L1-4), the femoral neck, and total hip bone in patients before interventions and at 12 months after interventions.

*Number of falls:* The number of falls or the fracture after a fall were recorded every month in outpatient service or by telephone every 3 months.

#### Blood Calcium and 25-Hydroxy Vitamin D(25(OH)D)

Serum calcium levels were measured before interventions and at 3, 6, and 12 months after interventions.

#### Adverse Reactions and Compliance

Patients were asked, via telephone and at outpatient follow-ups, whether they experienced symptoms of lack of hunger, headache, vomiting, constipation, and biliary and urinary system stones after taking calcium and vitamin D.

#### Quality Control

This study was registered at the China Clinical Trial Center (ChiCTR—IOR—16008564).

One orthopaedic professor selects the patients in the outpatient ward after informing them of the specific content of the subject and signs the informed consent. Two orthopaedic doctors and four postgraduate students record the general information of the patient. A simple physical ability test, a grip test, and a fall energy scale score were performed on the patients in the rest room of the orthopaedic clinic. Besides, bone mineral density and bone metabolism indexes were tested. Once gaining the test results, the postgraduates will call the patients according to the results and arrange an outpatient review. In the outpatient ward, the patients will be issued a fall prevention education manual to popularize fall-

**TABLE 2 Measured parameters in the four groups of patients**

Variables	NA VitD group (n = 98)	P-NA VitD group (n = 97)	A VitD group (n = 99)	P-A VitD group (n = 98)
SPPB (Before intervention)	7.1 ± 2.3	7.4 ± 2.1	6.9 ± 1.9	7.2 ± 2.1
SPPB (3 months)	7.2 ± 2.3	7.4 ± 2.1	7.3 ± 2.4	7.3 ± 2.3
SPPB (6 months)	7.4 ± 2.2	7.5 ± 2.3	8.0 ± 2.4*	8.6 ± 1.7*
SPPB (12 months)	8.0 ± 2.0*	8.6 ± 2.2*	9.2 ± 1.8*	9.3 ± 1.4*
Grip strength (kg, before intervention)	21.5 ± 5.2	21.7 ± 5.5	20.8 ± 5.1	22.1 ± 5.3
Grip strength (kg, 3 months)	21.5 ± 6.1	21.9 ± 6.0	21.7 ± 5.2	22.2 ± 6.1
Grip strength (kg, 6 months)	21.6 ± 6.5	22.0 ± 6.6	22.3 ± 6.9	22.7 ± 7.2
Grip strength (kg, 12 months)	21.9 ± 7.1	24.0 ± 6.7*	24.3 ± 6.7*	25.3 ± 6.9*
MFES (before intervention)	6.8 ± 1.7	7.0 ± 1.6	7.0 ± 1.5	6.7 ± 1.6
MFES (3 months)	7.2 ± 1.8	7.3 ± 1.8	7.0 ± 1.5	7.0 ± 1.8
MFES (6 months)	7.2 ± 1.6	7.6 ± 1.6*	7.1 ± 1.4	7.5 ± 1.6*
MFES (12 months)	7.2 ± 1.6	7.9 ± 1.6*	7.6 ± 1.4*	8.5 ± 1.4*

Paired t-test was used to analyze potential differences between each observation index and the baseline values in each group. Compared with the baseline values, \* $P < 0.05$ .

**TABLE 3 Falls and fractures in the four groups**

Fall(time/s)	NA VitD group (n = 98)	P-NA VitD group (n = 97)	A VitD group (n = 99)	P-A VitD group (n = 98)	P-value
1	18 (18.37%)	15 (15.46%)	15 (15.15%)	13 (13.27%)	0.645
2	5 (5.10%)	4 (4.12%)	2 (2.02%)	4 (4.08%)	0.860
3	2 (2.04%)	3 (3.09%)	3 (3.03%)	1 (1.02%)	0.741
Fractures	4 (11.11%)	3 (8.57%)	3 (9.67%)	2 (8.00%)	0.876

A chi-squared test was used to analyze the number of patients who fell and the fractures and times of falls but there were no statistical differences between the four groups.

**TABLE 4 Relative incidence rate (95% CI) of the incidence rate of falls**

Incidence of falls	Active VD/non-active VD	With/without anti-fall intervention	Vitamin D types (active vs non-active)	Anti-fall education and exercise (with vs without)	Interaction among vitamin D types and with/without anti-fall education and exercise
Baseline to 48 weeks	0.815 (0.522, 1.272)	0.807 (0.517, 1.260)	$P = 0.367$	$P = 0.345$	$P = 0.714$
Baseline to 12 weeks	0.808 (0.350, 1.864)	0.825 (0.358, 1.903)	$P = 0.617$	$P = 0.651$	$P = 0.962$
12 to 24 weeks	0.808 (0.356, 1.836)	0.742 (0.327, 1.686)	$P = 0.610$	$P = 0.476$	$P = 0.627$
24 to 48 weeks	0.821 (0.432, 1.560)	0.838 (0.441, 1.592)	$P = 0.546$	$P = 0.588$	$P = 0.869$

For each patient, the incidence of falls was calculated separately for each time period, i.e. the number of falls per patient at each time period divided by the time that the patient experienced the fall during that time period (standardized for 100 patients per year).; The correlations between the incidence of falls in each intervention time period and variables of vitamin D types or with/without anti-fall education and exercise were analyzed by a negative binomial regression model, and the interaction among vitamin D types with/without anti-fall education and exercise were also analyzed by a negative binomial regression model.

related knowledge, and the hazards of falls and how to effectively prevent falls will be explained<sup>7</sup>.

Four postgraduates will follow up the patients by telephone once a month. The items include asking them if they have any adverse reactions after taking calcium and vitamin D preparations, teaching the patients to exercise in due time

and appropriately according to their physical conditions, reminding the patients to return to the outpatient clinic separately for reexamination at 3, 6, and 12 months. After each follow-up is completed, strictly control the acquisition and entry of various data. The determination of blood calcium, bone metabolism indicators, and bone density shall be

**TABLE 5 Analysis of BMD, the level of calcium and 25(OH)D<sub>3</sub>**

Variables	NA VitD group (n = 98)	P-NA VitD group (n = 97)	A VitD group (n = 99)	P-A VitD group (n = 98)
BMD(g/cm <sup>2</sup> )				
Lumbar				
Before intervention	0.741 ± 0.038	0.743 ± 0.034	0.742 ± 0.042	0.743 ± 0.048
12 months	0.742 ± 0.038	0.749 ± 0.038	0.776 ± 0.039*	0.783 ± 0.042*
Hip				
Before the intervention	0.569 ± 0.037	0.575 ± 0.040	0.572 ± 0.036	0.571 ± 0.037
12 months	0.573 ± 0.043	0.579 ± 0.040	0.576 ± 0.043	0.574 ± 0.046
Femoral neck				
Before the intervention	0.566 ± 0.054	0.561 ± 0.035	0.566 ± 0.036	0.564 ± 0.035
12 months	0.569 ± 0.046	0.564 ± 0.035	0.572 ± 0.036	0.576 ± 0.045
Blood calcium(mmol/L)				
Before the intervention	2.22 ± 0.13	2.23 ± 0.15	2.22 ± 0.14	2.25 ± 0.13
3 months	2.23 ± 0.13	2.23 ± 0.14	2.25 ± 0.14*	2.25 ± 0.13
6 months	2.31 ± 0.12*	2.32 ± 0.14*	2.28 ± 0.14*	2.31 ± 0.15*
12 months	2.36 ± 0.12*	2.36 ± 0.12*	2.43 ± 0.13*	2.43 ± 0.14*
25(OH)D <sub>3</sub>				
Before the intervention	18.92 ± 7.43	17.40 ± 6.35	17.69 ± 7.16	18.99 ± 7.90
3 months	19.39 ± 7.96	18.39 ± 7.68	18.09 ± 8.27	18.18 ± 7.79
6 months	20.16 ± 7.60	19.52 ± 7.14*	17.13 ± 7.28	17.01 ± 6.52
12 months	24.14 ± 10.96*	23.56 ± 10.21*	17.49 ± 7.63	17.54 ± 6.13

\*P &lt; 0.05

unified in personnel, reagents, and instrument. The study members record the number of people lost to follow-up and regularly report the process to the professor in charge of coordinating the study.

### Statistical Analysis

In this study, the data was analyzed by SAS version 9.2 statistical software (SAS INSTITUTE Inc., USA). The measurement data was presented as the mean ± standard deviation. The difference in baseline between the groups was tested by variance analysis or chi-squared test, while the difference between the patients in the same group at different times were compared by using paired *t*-test. The covariance model was applied to measure whether the interaction existed between the SPPB scores, muscle strength, and MFES scores after 12 months for the different interventions. The interaction between the incidence of falls at different times and for different interventions was also analyzed by a negative binomial regression model. *P*-value of <0.05 was considered to be statistically significant.

## Results

### SPPB, Grip Strength, and MFES

At 6 months after the interventions, SPPB in A VitD group and P-A VitD group are significantly higher than before the intervention ( $9.2 \pm 1.8$  vs  $6.9 \pm 1.9$  and  $8.6 \pm 1.7$  vs  $7.2 \pm 2.1$ ,  $P < 0.05$ ). At 12 months after the interventions, all four groups are significantly higher than before the intervention ( $P < 0.05$ ).

At 12 months after the interventions, grip strength in P-NA VitD group, A VitD group, and P-A VitD group were significantly higher than before the intervention ( $24.0 \pm 6.7$  vs  $21.7 \pm 5.5$ ,  $24.3 \pm 6.7$  vs  $20.8 \pm 5.1$ , and  $25.3 \pm 6.9$  vs  $22.1 \pm 5.3$ ,  $P < 0.05$ ).

At 6 months after the interventions, MFES in A VitD group and P-A VitD group were significantly higher than before the intervention ( $7.6 \pm 1.6$  vs  $7.0 \pm 1.6$  and  $7.5 \pm 1.6$  vs  $6.7 \pm 1.6$ ,  $P < 0.05$ ). At 12 months after the interventions, MFES in P-NA VitD group, A VitD group, and P-A VitD group are significantly higher than before the intervention ( $P < 0.05$ ). The details of the follow-up are shown in Table 2.

### Incidence of Falls

During the follow-up, the incidence of falls, thus fractures, are four in NA VitD group, three in P-NA VitD group, three in A VitD group, and two in P-A VitD group. There were no statistical differences between the four groups ( $P > 0.05$ , Table 3).

### Analysis Results of Negative Binomial Regression Model

After 48 weeks, the 95% CI of active VD/non-active VD is 0.522 to 1.272. The result did not show a significant difference. After 48 weeks, the 95% CI of with/without anti-fall intervention is 0.517 to 1.260 ( $P > 0.05$ ). The results of anti-fall education and exercise (with vs without) also did not show a significant effect on the incidence of falls or the fractures ( $P > 0.05$ , Table 4).

### BMD, Blood Calcium, and 25(OH)D<sub>3</sub>

At 12 months after the interventions, the lumbar BMD of A VitD group increased from  $0.742 \pm 0.042$  to  $0.776 \pm 0.039$



( $P < 0.05$ ), P-A VitD group increased from  $0.743 \pm 0.048$  to  $0.783 \pm 0.042$  ( $P < 0.05$ ), while the BMD in hip and femoral neck of all groups did not show a significant increase. At 6 and 12 months after the interventions, the level of blood calcium in all groups increased significantly. Notably, A VitD group increased significantly from  $2.22 \pm 0.14$  to  $2.25 \pm 0.14$  at early 3 months after the interventions. In terms of 25(OH)D<sub>3</sub>, only NA VitD group and P-NA VitD group increased significantly at 12 months after the interventions ( $P < 0.05$ , Table 5).

#### Adverse Events

During the follow-up, one case in the NA VitD group, one case in the P-NA VitD group, two cases in the A VitD group, and two cases in the P-A VitD group experienced gastric discomfort when taking calcium and vitamin D. The symptoms disappeared after the timing of calcium and vitamin D administration was altered with food at the same time. Two cases in the NA VitD group, one case in the P-NA VitD group, one case in the A VitD group, and one case in the P-A VitD group suffered constipation. After adjusting their diet and taking appropriate purgative drugs, the constipation improved.

#### Quality Control

Due to the limited funds, this study cannot solve the transportation cost of each the subjects, resulting in the withdrawal or loss of follow-up of 28 patients, seven in the NA VitD group, eight in the P-NA VitD group, six in the A VitD group, and seven in the P-A VitD group.

#### Discussion

Decreased muscle strength and physical balance and mobility may be the factors that result in the increased risk of falling in elderly osteoporotic individuals<sup>8</sup>. After the age of 50 years, muscle strength decreased at a rate of about 12% to 15% every 10 years<sup>9</sup>. Especially for lower limb strength, it may increase the relative risk of falling by up to 4.4 times<sup>10,11</sup>. Strengthening muscle strength and improving balance ability may prevent falls and fractures in the elderly<sup>12</sup>.

In this study, the muscle strength of patients was assessed quantitatively by measurement of grip strength. The physical balance and mobility of the patients was measured by SPPB, formulated by the US National Institute of Health with a total score of 12 points<sup>4</sup>. MFES, a relatively mature international assessment tool developed by the Australian National Institute on Aging, was selected to evaluate the confidence level of the elderly who completed daily activities including nine indoor activities and five outdoor activities with each item scoring 11 points<sup>6</sup>.

#### Active Vitamin D is Better to Decrease the Risk of Falling

Our results have shown that after 6 months of vitamin D, no matter if non-active or active, the muscle strength and

physical balance and mobility of all patients were improved, and the risk of falling decreased. After 12 months of vitamin D, the results were further improved. A VitD group who took active vitamin D presented better effects that significantly improved their physical ability and reduced their risk of falling compared with NA VitD group and P-NA VitD group. Thus, we conclude vitamin D is helpful to decrease the risk of falling and active vitamins are better than non-active vitamins (>12 months). Relevant research has suggested that about 20% of falls could be reduced by appropriate interventions<sup>13</sup>. Vitamin D was considered as an effective intervention measure to prevent falls of the elderly in both the clinical guidelines of the American and British Geriatric Societies and in reports of the International Osteoporosis Foundation<sup>14–16</sup>. Basic research has found that Vitamin D<sub>3</sub> exists in muscle tissues and its activation promotes the synthesis of nascent muscle proteins and directly act on muscles to strengthen them<sup>17,18</sup>.

In addition, vitamin D induces the synthesis of nerve growth factor thereby enhancing the coordination of neuromuscular system, improving balance and physical ability, and thus reducing the risk of a fall<sup>19,20</sup>. A meta-analysis indicated that vitamin D supplementation could reduce the incidence of falls in the elderly over the age of 70 years by up to 49%<sup>21</sup>.

#### Active Vitamin D Was More Effective in Preventing Bone Loss

Active vitamin D effectively increases BMD of the lumbar vertebra in this study. It may improve bone quality by changing the microstructure of trabecular bone and the formation of collagen<sup>23,24</sup>. Non-active vitamin D is converted by the liver and kidney into active vitamin D. However, aging will lead to a decreased renal function, which will affect the conversion of vitamin D to active vitamin D. In addition, the effect of vitamin D supplementation on calcium absorption in the intestine is undermined due to impaired renal function<sup>25</sup>. In our study, active vitamin D was more effective in reducing the fall risk, preventing bone loss, and reducing the fracture rate, consistent with previous reports<sup>26,27</sup>. Therefore, active vitamin D is more suitable for the elderly.

The study did not implement a placebo group as control was guided by strengthening muscle strength and balancing exercise without vitamin D. The reason is that it was not ethically acceptable to withhold anti-osteoporosis drug treatment for patients with osteoporosis enrolled in our study. For elderly patients with osteoporosis, the prevention of falls and anti-osteoporosis treatment should be carried out simultaneously<sup>22</sup>.

#### Limitations

Clinically, the bone metabolism markers detect non-active 25-(OH)-VD, not the active 25-(OH)-VD<sub>3</sub>. Therefore, this method may not be able to identify if people actually lack

25-(OH)-VD<sub>3</sub>. In the future, there is an urgent need to develop a direct method to detect active 25-(OH)-VD<sub>3</sub>.

### Conclusion

Vitamin D effectively and safely improves the muscle strength and physical ability of elderly patients with osteoporosis, reducing the risk of falls. Compared with non-active vitamin D, active vitamin D is better to improve physical ability and the BMD of lumbar vertebrae, while reducing the risk of falls.

### Declarations

#### Ethics Approval

Ethics approval was obtained from the ethics committee of Capital Medical University, Beijing Friendship Hospital (BJFH-EC/2014-029).

#### Consent for Publication

All authors provided consent for this article to be published.

#### Availability of Data and Material

All data and material is available.

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