Effects of vitamin D supplementation and exercise training on physical performance in Chilean vitamin D deficient elderly subjects ☆

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Abstract

The aim was to assess the effects of resistance training and vitamin D supplementation on physical performance of healthy elderly subjects. Ninety-six subjects, aged 70 years or more with 25 OH vitamin D levels of 16 ng/ml or less, were randomized to a resistance training or control group. Trained and control groups were further randomized to receive in a double blind fashion, vitamin D 400 IU plus 800 mg of calcium per day or calcium alone. Subjects were followed for nine months. Serum 25 OH vitamin D increased from 12.4 ± 2.2 to 25.8 ± 6.5 ng/ml among subjects supplemented with vitamin D. Trained subjects had significant improvements in quadriceps muscle strength, the short physical performance test and timed up and go. The latter improved more in trained subjects supplemented with vitamin D. At the end of the follow up, gait speed was higher among subjects supplemented with vitamin (whether trained or not) than in non-supplemented subjects (838 ± 147 and 768 ± 127 m/12 min, respectively, $p = 0.02$). Romberg ratio was lower among supplemented controls than non-supplemented trained subjects (128 ± 40% and 144 ± 37%, respectively, $p = 0.05$). In conclusion, vitamin D supplementation improved gait speed and body sway, and training improved muscle strength.

Keywords: Elderly; Training; Vitamin D; Muscle strength; Calcium

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1. Introduction

The elderly must face the risk of mental and physical disability. Both conditions are invalidating and limit the capacity to pursue an independent and productive life. Physical disability limits the capacity to walk and increases the risks of falls and injuries.

One of the main causes of physical impairment in the elderly is sarcopenia or the loss of muscle mass that occurs with aging (Bales and Ritchie, 2002). People over 70 years of age, lose approximately 300 g of muscle per year with the associated loss of strength and physical capacity (Visser et al., 2003b). The causes of sarcopenia are not well known but it is most probably due to skeletal muscle oxidative damage (Aiken et al., 2002). One of the few interventions that reverts the functional consequences of sarcopenia is physical training (Bunout et al., 2005).

Vitamin D deficiency is common in the elderly and may have a causal relationship with muscle weakness. Older people are prone to develop vitamin D deficiency, probably due to a lower dietary intake, sunlight exposure and impaired hydroxylation in liver and kidneys (Janssen et al., 2002). Studies in Europe reported that 42% of elderly people had low serum vitamin D levels (<30 nmol/L) (van der Wielen et al., 1995). Likewise, approximately 50% of African Americans and Hispanics in the Unites States are vitamin D deficient, figure that varies depending on the cut-off point that is used and the season when the measurements are performed (Nesby-O'Dell et al., 2002). Among Chilean elderly, this deficiency is also common, even

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considering that Santiago is located in the parallel 35 and we should receive enough solar radiation (Leiva L, unpublished results). Apart from its well-known effects on bone metabolism, vitamin D deficiency is associated with sarcopenia (Visser et al., 2003a; Iannuzzi-Sucich et al., 2002), loss of muscle strength and increased risk of falls (Dhesi et al., 2002). Muscle weakness due to vitamin D deficiency is predominantly of the proximal muscle groups and reduces the ability to walk, escalate stairs and rise from a chair (Pfeifer et al., 2002). However, the effects of vitamin D supplementation on muscle strength and the risk of falls are far from clear (Bischoff et al., 2003).

We postulated that training and vitamin D supplementation could have synergistic effects on muscle strength, among vitamin D deficient elderly subjects. Thus, this work assessed the effects of both interventions.

2. Materials and methods

Healthy elderly subjects living in the community were invited to participate in the study. After the signature of an informed consent, explaining the purposes and scope of the study, a morning blood sample was obtained to measure serum 25 OH vitamin D. Those subjects with a serum vitamin D of 16 ng/ml or less were scheduled for a medical baseline assessment, that included a history about previous diseases, an enquiry about their willingness to eventually participate in a exercise training program if they were randomized to training, assessment of Minimental state score (Folstein et al., 1975), Katz activities of daily living (McDowell and Newell, 1996), Yesavage depression score (McDowell and Newell, 1996) and a physical examination. Subjects were considered eligible if they did not have an evident physical limitation that would preclude the participation in an exercise training program (tested during the medical assessment), had a mini mental state score over of 20 or more and were not consuming calcium, vitamin D, estrogens, steroids or other drug that would eventually interfere with vitamin D metabolism.

Eligible subjects were randomly allocated to a control and training group, balancing for gender, age and body mass index. Then, subjects in each of these two groups were randomly assigned, using random numbers generated by a computer, to receive 800 mg/day of calcium or the same amount of calcium plus vitamin D_3(cholecalciferol) 400 IU/day in a double blind design. Capsules containing calcium alone or calcium plus vitamin D were indistinguishable and were identified with a numeric code that was unique for each subject. They were instructed to take one capsule per day in the evening. Thus, four groups were formed: training plus calcium (training–calcium), training plus calcium and vitamin D (training–vitD), no training plus calcium (no training–calcium) and no training plus calcium and vitamin D (no training–vitD).

At baseline and after nine months of follow up, the following assessments were done:

1. Body composition and bone mineral density using a Lunar Prodigy bone double beam densitometer (Lunar Corporation, Madison, Wisconsin, USA). The equipment was calibrated daily with an anthropometric phantom and all scans were read by the same trained operator to reduce the coefficient of variation.
2. Hand grip strength using a hand grip dynamometer (Therapeutic Instruments, Clifton, NJ, USA) in the dominant hand and expressed in kg.
3. Isometric quadriceps maximum voluntary strength in both legs, using a quadriceps table and expressed as 1RM in kg.
4. Endurance was measured as the distance that subjects could walk at a constant pace in a flat surface during 12 min (McGavin et al., 1967).
5. General physical fitness, measuring the timed up and go (TUG), expressed in seconds and fraction (better performance at lower time required) (Rockwood et al., 2000) and the short physical performance battery (SPPB), expressed as a score (better performance at higher scores) (Guralnik et al., 2000).
6. Body sway was assessed using a computerized posturograph that analyzes the tract of the center of gravity and measures track length, track density and track area, while a subject stands erect. All results are expressed as the percentage of the ratio between results obtained with closed and open eyes (Romberg ratio) (Fujita et al., 2005).
7. A fasting blood sample was obtained to measure routine blood chemistry, serum insulin, serum thyroid stimulating hormone (TSH), parathyroid hormone (PTH) and 25 hydroxy vitamin D.

Subjects ascribed to exercise training were instructed to attend biweekly sessions lasting approximately 1.5 h of strength, balance and aerobic workout. We used the same training protocol, used previously, that resulted in a significant improvement in muscle strength (Bunout et al., 2001, 2005). Strength training consisted in a period of warming up and three levels of chair stands (five sets of 10 repetitions; levels included sitting and fake sitting with and without the use of arm supports), three levels of modified squats (five sets of 10 repetitions; levels included squats with or without Thera-bands (Thera-Bands, The Hygienic Corporation, Akron, OH, USA) to increase gravitational force), three levels of step ups in a stair (10 sets of 10 repetitions; levels included one step, two steps and two steps without using the hand rails) and six sets of 15 repetitions of arm pull-ups using Thera-bands. The bands are color coded to confer progressive resistance. Quality of exercise was visually determined by the range of movements and the absence of substitution by other muscles. To determine which color of rubber band should be used initially, 12–15 repetitions of good quality exercise, until fatigue, were carried out. In each exercise, subjects made three series of 10 repetitions with the rubber bands. Balance training included tandem walking with different degrees of difficulty (leaning on a wall, without leaning and using soft weights to increase instability) and standing on soft foam surfaces in 1 or 2 ft (Balance trainers, Thera-Band). As aerobic exercise, subjects were also engaged in walking periods before and after resistance training. Subjects were encouraged to walk without stopping for 15 min, at the faster pace they could, without becoming extenuated (not becoming short of breath). Exercise was supervised by a specialized coach according to the progression of each subject and based on the Borg scale (McArdle et al., 1996). After every exercise session, subjects indicated, using the Borg scale, their subjective feeling about the exercises. Once the subject considered that specific exercises were light or very light (a score of four or less in the Borg scale), a higher level of difficulty was indicated. This was achieved by increasing the number of steps to climb or avoiding the use of arm supports to the chairs or changing the color of the rubber band used. Attendance to each training session was recorded to assess compliance with the exercise program. The percentage of programmed sessions that the subject attended was calculated.

Every month, all subjects attended the clinic for evaluation. The leftover pills were counted and a new supply of medication was delivered for the next month. Subjects were specifically interrogated about falls occurring the previous month and about possible adverse events. There was also a hot line were subjects could request an appointment with a physician, if they experienced an adverse event (related or not related to the study protocol).

Researchers who measured muscle strength and balance were not involved in training and were not aware of the intervention group. For data analysis, one investigator separated intervention groups and coded them with a number from 1 to 4. The investigators who performed the data analysis used these number codes, but were unaware of the specific intervention that each group received.

Statistical analysis was done using Stata for Windows (Stata Corporation, Texas USA). All results are expressed as means ± standard deviation, unless otherwise stated. Changes in parameters, after the nine months of follow up, were expressed as percentage of the initial value ((final value − initial value)/initial value) * 100. When comparing more than two groups, one way ANOVA was used. Student's "*t*" test was used to compare two groups. Proportions were compared using χ^2 test. Fall free survival was calculated using life tables, considering the date of the first episode of fall, if there was one. The study was approved by INTAs Ethics Committee.

3. Results

Ninety-six subjects aged 76 ± 4 years, 86 females, were randomized for the study. Subject flow is shown in Fig. 1. Baseline demographic and anthropometric data is shown in Table 1.

Trained subjects attended 53 ± 26% of programmed training sessions. The main reasons to miss a training session were lack of motivation, too cold or too warm weather and lack of time due to work or house chores. Compliance with the medication, according to the count of leftover tablets was 92 ± 3%, both in subjects receiving calcium alone or calcium plus vitamin D. During the follow up, there were four adverse events that required hospital admission (three in the training–vitD group, due to a retrosternal pain, a non-ST elevation myocardial infarction and a transient ischemic attack of the carotideal territory and one in the no training-calcium group, due to an acute cholecystitis). None of these events occurred during a training session. A total of 81 minor adverse events were reported by study participants (11 in the no training–calcium group, 30 in the training–calcium group, four in the no training–vitD group and 32 in the training–vitD group, $p < 0.001$). Ninety four of these events (96%) of these events were considered unrelated to the intervention. Fall free survival was not different among groups (Fig. 2).

Among supplemented subjects, serum 25 OH vitamin D increased from 12.4 ± 2.2 to 25.8 ± 6.5 ng/ml ($p < 0.001$). Among non supplemented subjects, no changes in these levels were observed (13.1 ± 2.7 and 14.5 4.6 ng/ml at baseline and 9 months, respectively).

Gait speed, muscle strength, functional measures and Romberg ratio are shown in Tables 2 and 3. Trained subjects had a significant increase in quadriceps strength, SPPB and TUG. However TUG improved more in trained subjects supplemented with vitamin D. At 9 months, Romberg ratio was significantly lower among supplemented controls than non-supplemented trained subjects, and subjects supplemented with vitamin D (whether trained or not) had a higher gait speed than non-supplemented subjects (838 ± 147 and 768 ± 127 m, respectively, $p = 0.02$). The effect of training in these last two parameters did not reach statistical significance.

No significant changes in weight, circumferences or body composition measured by DEXA, were observed in any of the four groups. Femoral neck bone mineral density increased 1.14 ± 0.56% in supplemented subjects and decreased 1.08 ± 0.55% in non-supplemented individuals ($p = 0.006$). No changes in spine bone mineral density were observed (1.61 ± 0.6 and 1.17 ± 0.6 in supplemented and non supplemented individuals, respectively, NS). Training had non-influence on these results.

No significant changes in routine laboratory, serum insulin, serum TSH or serum PTH were observed in any of the studied groups. The correlation of serum vitamin D and serum PTH was $r = 0.85$, $p = 0.43$ and $r = -0.27$ $p < 0.01$ and the start and end of follow up, respectively.

A secondary analysis, incorporating the variable compliance with training sessions as a covariate, did not change substantially the results.

4. Discussion

In this prospective study in vitamin D deficient elderly subjects, training resulted in enhancement of muscle

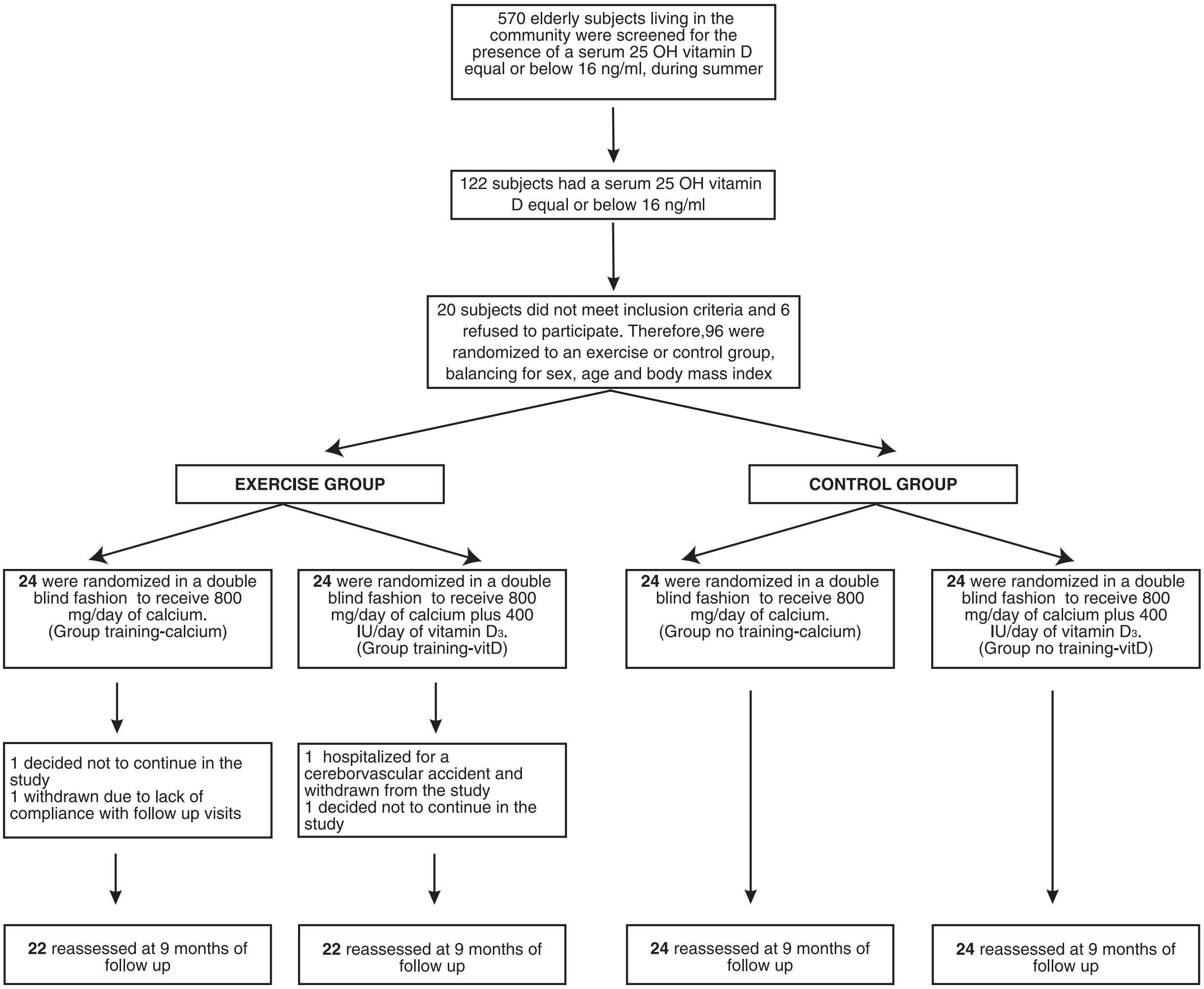

Fig. 1. Subject flow during the study.

strength, as expected, while vitamin D plus calcium supplementation resulted in improvements in bone mass, and tests that reflect a complex association between strength, aerobic capacity and balance, such as timed up and go, gait speed and body sway. The latter are critically relevant to overall functionality and risk of falls in the elderly population.

The effects of training on muscle strength are not surprising and only confirm previous studies done by our group (Bunout et al., 2001, 2005). The compliance with training sessions was also very similar to that reported by us previously. The dose of exercise in this intervention was enough to increase muscle strength, but had no effect of muscle mass. The likelihood to gain muscle mass is low, if resistance exercise is done at an intensity lower than 65% of one repetition maximum (RM) as in our study (McDonagh et al., 1983). However, the beneficial effects of a higher intensity exercise must be counterbalanced with a higher incidence of adverse effects and a lower compliance of subjects. The influence of vitamin D on muscle performance is not as clear as the effect of exercise. Cross sectional studies have reported that vitamin D deficiency is associated with lower muscle strength, gait speed, higher body sway and performance in functional tests (Gerdhem et al., 2005), but when elderly subjects are supplemented with vitamin D, most studies show that these parameters do not improve significantly (Latham et al., 2003; Kenny et al., 2003). However, Verhaar et al. (2000) demonstrated that 6 months of treatment with 0.5 μg α-calcidiol/day improved knee extension strength and walking distance only in vitamin D deficiency elderly women. As recommended by most authors, vitamin D was given along with calcium in this trial, since a low calcium intake can limit the effects of the vitamin (Lips, 2001). To isolate the effect of the vitamin, controls for supplementation received calcium also. The dose of vitamin D chosen was low, to avoid possible adverse effects on a long term intervention. The same dose was used in a large randomized trial during 7 years and was associated with a reduction in the rate of fractures among women over 60 years old, and a slight increase in the incidence of kidney stones (Jackson et al., 2006). Therefore, even this low dose may be associated with side effects. We hypothesized that training could add to vitamin D supplementation and enhance its effects on muscle function. This was the case for TUG that improved more in trained and supplemented subjects, compared with the other

Table 1
Basal demographic and anthropometric data of studied subjects

	No training plus calcium	Training plus calcium	No training plus calcium and vitamin D	Training plus calcium and vitamin D	ANOVA
Gender (females/males)	21/3	21/3	22/2	22/2	
Age (years)	77 ± 4	76 ± 4	77 ± 5	78 ± 4	
Anthropometric parameters					
Height (cm)	149.04 ± 5.03	151.92 ± 9.36	151.79 ± 6.61	151.63 ± 6.42	0.44
Weight (kg)	65.51 ± 11.07	64.91 ± 11.88	64.44 ± 11.57	67.60 ± 9.44	0.77
Body mass index (kg m^2)	29.58 ± 5.21	28.14 ± 4.51	27.98 ± 4.85	29.48 ± 4.09	0.50
Arm circumference (cm)	31.13 ± 3.73	30.38 ± 3.33	30.60 ± 3.89	30.08 ± 3.15	0.77
Waist circumference (cm)	98.42 ± 10.80	97.13 ± 12.28	134.67 ± 184.38	98.31 ± 9.55	0.42
Hip circumference (cm)	103.31 ± 10.92	102.21 ± 9.63	102.81 ± 10.12	106.00 ± 8.85	0.56
Body composition and bone mineral density by DEXA					
Fat mass (g)	26525.36 ± 9364.69	25850.53 ± 8623.49	25836.97 ± 8413.69	27664.95 ± 7105.91	0.86
Lean mass (g)	36701.98 ± 5832.02	36646.92 ± 6195.59	36439.71 ± 6005.32	37901.72 ± 4875.78	0.81
Spine bone mineral density (g/cm^2)	1.000 ± 0.186	1.048 ± 0.179	1.021 ± 0.179	0.994 ± 0.214	0.750
Spine bone mineral density (T score)	−1.71 ± 1.5	−1.31 ± 1.51	−1.51 ± 1.48	−1.75 ± 1.73	0.75
Number with spine osteoporosis[a]	9	7	4	9	
Femoral neck bone mineral density (g/cm^2)	0.794 ± 0.165	0.820 ± 0.136	0.792 ± 0.083	0.791 ± 0.132	0.850
Femoral neck bone mineral density (T score)	−1.63 ± 1.21	−1.39 ± 1.18	−1.62 ± 0.68	−1.63 ± 1.04	0.83
Number with femoral osteoporosis[a]	4	2	2	6	
Geriatric scores					
Mini mental state score	26.17 ± 2.63	25.63 ± 3.16	25.83 ± 3.50	27.13 ± 2.51	0.32
Activities of daily living	5.88 ± 0.34	5.79 ± 0.41	5.79 ± 0.41	5.92 ± 0.28	0.56
Yessavage depression score	5.58 ± 3.88	4.21 ± 2.70	5.13 ± 3.78	4.17 ± 3.61	0.42

[a] Osteoporosis was defined according to WHO as a T score below −2.5.

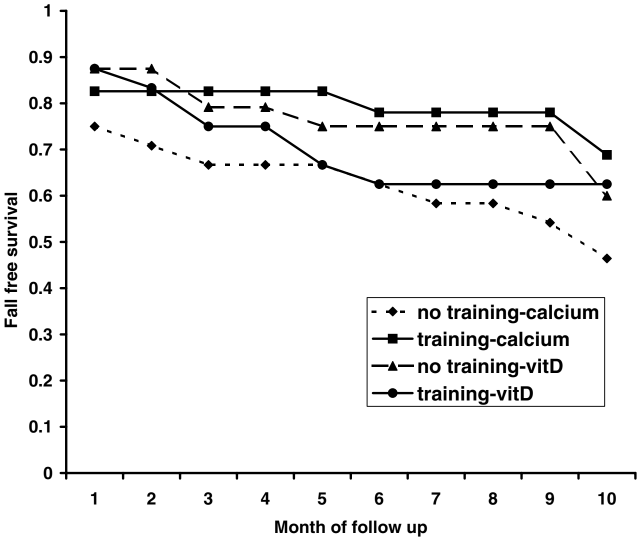

Fig. 2. Fall free survival of studied subjects. Study groups are: training plus calcium (training–calcium), training plus calcium and vitamin D (training–vitD), no training plus calcium (no training–calcium) and no training plus calcium and vitamin D (no training–vitD). No significant difference between groups was detected.

groups. However, gait speed and Romberg index were modified by supplementation and training did not significantly influence the results. The notorious improvement if quadriceps strength with training, probably concealed an eventual effect of supplementation.

The effect of vitamin D on body sway has been reported previously (Dhesi et al., 2004). This study was not powered to detect changes in fall incidence. However, we observed effects on parameters that most probably have an influence on falls, such as body sway, which is known to decrease through correction of vitamin D deficit in elderly (Dhesi et al., 2004). In accordance to these results, a recent meta analysis, confirmed that vitamin D supplementation reduced falls by 20% (Bischoff-Ferrari et al., 2005). As another intervention influencing the risk of falls (Haines et al., 2004), we also included balance exercises for subjects that were randomized to training. Whether the latter contributed more to the synergistic effects of training plus vitamin D supplementation is still speculative. Thus, it is probably worth attempting a large trial including vitamin D supplementation plus balance training, to reduce the incidence of falls and their consequences in the elderly.

The beneficial effect of vitamin D supplementation on femoral bone mineral density has also been reported previously (Dawson-Hughes et al., 1997). The 1% improvement in 9 months is comparable with the 1.9% increase over 2 years, achieved with alendronate (Hosking et al., 1998) and similar to the improvement observed by Jackson et al. (2006). Despite this marked effect on bone mineral density, vitamin D supplementation does not have an undisputed effect on fractures. Indeed, two recent large trials do no show a reduction in the incidence of fractures with vitamin D (The RECORD Trial Group, 2005; Porthouse et al., 2005) alone, but the synergy of training and

Table 2
Muscle strength

	No training plus calcium	Training plus calcium	No training plus calcium and vitamin D	Training plus calcium and vitamin D	ANOVA
Right quadriceps strength basal (kg)	20.1 ± 6.4	20.9 ± 6.0	21.2 ± 6.7	21.7 ± 5.9	0.83
Right quadriceps strength final (kg)[b]	19.7 ± 6.4	24.6 ± 6.3	19.6 ± 6.8	25.0 ± 5.9	0.003
% change right quadriceps strength[b]	−1.0 ± 19.1	21.1 ± 27.0	−7.3 ± 14.7	16.7 ± 19.0	<0.001
Left quadriceps strength basal (kg)	21.7 ± 6.3	21.5 ± 5.8	19.6 ± 4.9	21.8 ± 6.9	0.54
Left quadriceps strength final (kg)[b]	20.0 ± 5.7	24.3 ± 6.4	17.4 ± 5.3	23.7 ± 5.9	<0.001
% change left quadriceps strength[b]	−6.3 ± 12.5	16.4 ± 31.6	−9.1 ± 16.4	10.8 ± 14.4	<0.001
Right hand grip strength basal (kg)	21.5 ± 4.7	21.6 ± 6.3	21.7 ± 6.8	22.1 ± 7.4	0.98
Right hand grip strength final (kg)	19.5 ± 4.5	21.1 ± 5.0	20.6 ± 5.3	21.1 ± 6.7	0.72
% change right hand grip strength	−8.5 ± 15.0	0.0 ± 16.8	3.2 ± 53.0	−4.3 ± 16.3	0.58
Left hand grip strength basal (kg)	20.4 ± 6.6	20.7 ± 6.3	20.3 ± 6.5	21.0 ± 7.9	0.98
Left hand grip strength final (kg)	17.0 ± 3.2	19.0 ± 5.2	18.2 ± 5.3	19.5 ± 6.4	0.39
% change left hand grip strength	−13.3 ± 18.3	−7.0 ± 16.9	−7.4 ± 22.6	−9.2 ± 14.1	0.64

Bonferroni post hoc: [b]trained significantly different from control subjects.

Table 3
Physical performance tests

	No training plus calcium	Training plus calcium	No training plus calcium and vitamin D	Training plus calcium and vitamin D	ANOVA
Twelve minutes walk basal (m)	694.5 ± 153.0	739.7 ± 184.0	739.3 ± 159.8	749.2 ± 119.3	0.61
Twelve minutes walk final (m)[a]	747.4 ± 157.1	790.7 ± 135.5	859.7 ± 110.1	814.6 ± 142.6	0.045
% change twelve minutes walk	9.2 ± 18.4	9.3 ± 25.7	20.9 ± 27.7	8.8 ± 17.6	0.2
Short physical performance battery basal	8.8 ± 1.5	8.8 ± 1.9	9.0 ± 1.5	9.2 ± 2.3	0.85
Short physical performance battery final[b]	7.9 ± 2.1	9.5 ± 2.1	8.9 ± 1.9	10.2 ± 1.9	0.002
% change short physical performance battery[b]	−9.6 ± 20.5	10.5 ± 23.5	−0.3 ± 17.9	14.7 ± 28.3	0.002
Timed up and go basal (s)	12.9 ± 3.5	12.0 ± 3.2	11.4 ± 2.0	11.8 ± 2.4	0.31
Timed up and go final (s)[c]	15.2 ± 4.7	12.6 ± 4.3	13.8 ± 2.5	12.0 ± 2.2	0.02
% change timed up and go[d]	19.7 ± 29.2	6.3 ± 15.8	22.3 ± 20.8	2.4 ± 16.0	0.004
Romberg ratio basal (%)	143.9 ± 39.1	139.5 ± 47.4	124.3 ± 21.8	140.2 ± 38.6	0.29
Romberg ratio final (%)[e]	134.7 ± 31.9	153.9 ± 45.2	119.8 ± 38.3	137.2 ± 34.9	0.03
% change Romberg ratio	2.1 ± 43.1	17.4 ± 39.9	−0.6 ± 35.8	2.8 ± 33.8	0.39

Bonferroni post hoc: [a]no training plus calcium different from no training plus calcium and vitD, [b]trained significantly different from control subjects, [c]training plus calcium and vitamin D significantly different from no training plus calcium, [d]supplemented significantly different from non-supplemented subjects, [e]no training plus calcium and vitamin D significantly different from training plus calcium.

vitamin D on the incidence of fractures, aiming to sum the effects of two eventually useful interventions, can be supported by a recent Cochrane Systematic Review (Gillespie et al., 2003).

There was a higher report of minor adverse events among subjects randomized to exercise training. Most of these events were considered unrelated to the intervention by the professionals in charge. This is probably a bias caused by a closer contact of trained individuals with the research team. Although every study subject was evaluated monthly, trained subjects had twice weekly contacts with the research team and requested more consultations, that were not denied. Safety of resistance training in the elderly has been demonstrated by several authors. Although there is a higher incidence of musculoskeletal injuries among individuals that exercise regularly (Latham et al., 2004; Nelson et al., 2004), these are outweighed by the benefits of physical activity.

In conclusion, vitamin D plus calcium supplementation with or without physical training improved femoral bone density and functional capacity.

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