22 Vitamin D, Exercise, and Health

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Abstract

Targeted exercise training and sufficient vitamin D intake may significantly improve muscle performance and balance and thus reduce the risk of falling among older people.

A 2-year randomized controlled vitamin D and exercise trial of 409 home-dwelling women aged 70–80 years included four study arms: (1) exercise + vitamin D (800 IU/day), (2) exercise + placebo, (3) no exercise + vitamin D (800 IU/day), (4) no exercise + placebo. Primary outcomes were falls. Injurious falls, bone health, physical functioning, quality of life and fear of falling were also assessed.

Neither vitamin D nor exercise reduced falls. However, exercise more than halved injurious falls with and without vitamin D. Vitamin D maintained femur BMC and increased tibial trabecular density slightly, while only exercise improved physical functioning, but neither treatment improved quality of life, nor reduced fear of falling. Participants were largely well-functioning and vitamin D replete.

Future research is needed to elaborate the effects of interventions on people with varying baseline levels of vitamin D and physical functioning.

Keywords

Falls • Injurious falls • Vitamin D • Exercise • Physical function • Older women

Falls in older adults are a major health concern in ageing societies. They often result in severe injuries, functional limitations, long-term care and reduced quality of life. Although it is important to prevent falls in general, it is particularly important to prevent injurious falls; the most serious

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consequences of falls being fractures and head injuries. Moreover, if ageing is combined with extended years of healthy life it could also produce desirable social, economic and health benefits. Health maintenance for people throughout life, via actions such as exercise and proper nutrition, contribute to lifelong wellbeing [1].

Sustaining a fracture depends on the force of impact of the fall event and the strength of bone. Osteoporosis is a multifactorial disease in older adults characterized by low bone mineral density (BMD) and decreased bone strength, which predisposes to fractures. However, a majority of all fractures occur as the result of a fall. Older persons are often susceptible to falls, which are the leading cause of unintentional injuries and death among this population. Approximately 30 % of community living people aged 65 years or older fall each year, the number being even higher in institutions. Although only 5–10 % of falls result in serious injuries [2, 3], fall prevention is widely seen as the most essential element in the planning of effective injury and fracture prevention among any elderly population.

In addition to physical injuries, falls may increase fear of falling, which further may lead to a loss of confidence in the ability to ambulate safely, and mobility restrictions and functional decline, depression, social isolation and reduced quality of life (QoL) [4]. Although cross-sectional and prospective studies in the general population have found positive associations between physical activity and QoL, evidence from randomized trials is limited [5]. A recent Cochrane review showed positive, but temporary effects of exercise interventions on fear of falling [6].

Preventing falls and injuries among older adults is challenging, even promoting physical activity is a major challenge because our lifestyle is designed to reduce, or even eliminate physical activity at every opportunity [7]. However, there is strong evidence from randomized controlled trials and subsequent systematic reviews and meta-analyses that regular strength and balance training among community-living older adults can reduce the risk of both noninjurious and injurious falls by 15–50 % [8, 9]. Randomized controlled trials indicate that not only individually tailored training but also more untargeted group exercise programs are effective in preventing falls [10, 11]. However, all exercise is not equally effective. The most effective exercise approach for the prevention of falls and fractures in community-dwelling older adults is a combination of balance and strength training. To be effective, multifactorial preventive programs should include an exercise component accompanied by individually tailored measures focused on high-risk populations [12].

Vitamin D is known to be vital for bone metabolism and health; insufficient serum 25-hydroxivitamin D levels [25(OH)D] are associated with increased bone loss and risk of fractures, and even with increased fall rates. Furthermore, people with low 25(OH)D levels have been suggested to have lower physical functioning [13, 14]. However, systematic reviews and meta-analyses of clinical trials exploring the role of vitamin D in reducing falls and fractures and improving physical functioning in community dwelling older people, are inconclusive [15–19]. In addition, vitamin D supplementation is suggested to be related with improved psychosocial functions, including quality of life, self-rated health, and mood [20, 21].

In randomized controlled trials the incidence of falls was almost halved and musculoskeletal function improved among older people with a combination of vitamin D and calcium compared with calcium supplement alone [22, 23]. Falling may, at least partly, be a consequence of impaired neuromuscular function associated with vitamin D deficiency, since abnormal motor performance, increased body sway, and quadriceps weakness have been reported in those with low vitamin D status [13]. The dose of vitamin D in falls prevention efficacy is probably more important than the type of vitamin D, duration of therapy, and sex. Participants receiving 20 μg/day (800 IU) seem to have lower risk of falls, while 10 μg (400 IU) was insufficient for reducing falls [24].

Although a recently published meta-analysis found insufficient evidence that current multifactorial falls prevention programs could prevent falls and related injuries [25], it must be kept in mind that great majority of fall-prone older adults has more than one risk factor for falls. Randomized controlled trials suggest that exercise may effectively improve many risk factors of falling, such as muscle strength, flexibility, balance, coordination, proprioception, reaction time and gait [26–28] and prevent falls and fractures [29–31].

In this study we evaluated the separate and combined effects of multimodal exercise training and vitamin D supplementation in reducing falls and injurious falls, and in improving bone mass and physical functioning among older women at risk for falling. In addition, we evaluated the effects of both factors on quality of life and fear of falling.

Design

This study was a 2-year double-blind placebo-controlled vitamin D and open exercise intervention trial with four arms (Fig. 22.1). The trial was done between April 2010 and March 2013. Eligibility criteria and recruitment of participants have been described in detail previously [32, 33]. Briefly, 70–80-year old home-dwelling women living in the City of Tampere, Finland, were eligible if they had fallen at least once during the previous 12 months, did not use vitamin D supplements, and had no contraindications to exercise. The criterion for exclusion was participation in moderate to vigorous exercise more than 2 h per week.

The study protocol was approved by the Ethics Committee of the Tampere University Hospital, Finland (R09090). Each participant provided her written informed consent prior to randomization. The study protocol is registered at ClinicalTrial.gov (NCT00986466).

Participants

Four-hundred and nine participants were randomly assigned to one of four groups using a computer-generated list based on simple randomization with random allocation sequence to ensure equal group sizes: (1) vitamin D 800 IU/day and exercise (D^+Ex^+) (2) placebo and exercise (D^-Ex^+) (3) vitamin D 800 IU/day without exercise (D^+Ex^-) (4) placebo without exercise (D^-Ex^-).

Participants received one daily pill containing either 800 IU (20 μg) vitamin D_3 or placebo for 24 months [32]. All tablets were provided by Oy Verman Ab (Kerava, Finland) and were similar in size, appearance and taste. Each participant received a pack of pills for 6 months at a time. Used packs were returned at the time of laboratory measurements every 6 months, and new full packs were given. The compliance was confirmed by pill counts.

Exercise consisted of supervised, progressive group training classes two times a week for the first 12 months, and once a week for the remaining 12 months of the 24-month intervention [32]. Training sessions were carried out in 8-week periods, alternating between the exercise hall and gym by physiotherapists who also monitored attendance. Sessions in the exercise hall focused on balance challenging, weight bearing, strengthening, agility, and functional exercises. Gym sessions included a combination of pin-loaded weight machines, pulleys, and free weights; beginning with 30–60 % of one repetition maximum (1RM), progressing to a target level of 60–75 % of 1RM. The non-exercising groups were asked to maintain their pre-study level of physical activity.

Outcome Measures

The primary outcome was falls, and injurious falls, fallers and injured fallers were analyzed as secondary outcomes. In addition, changes in bone mass, physical functioning (muscle strength, balance and mobility), quality of life (QoL) and fear of falling were evaluated.

The number of falls was obtained from prospective fall diaries returned monthly via mail, and details of each registered fall were ascertained by a telephone call. A fall was defined "an unexpected event in which the participant comes to rest on the ground, floor or lower level" [34]. Injurious falls were those for which participants sought medical care (nurse, physician, or hospital). These included injuries, such

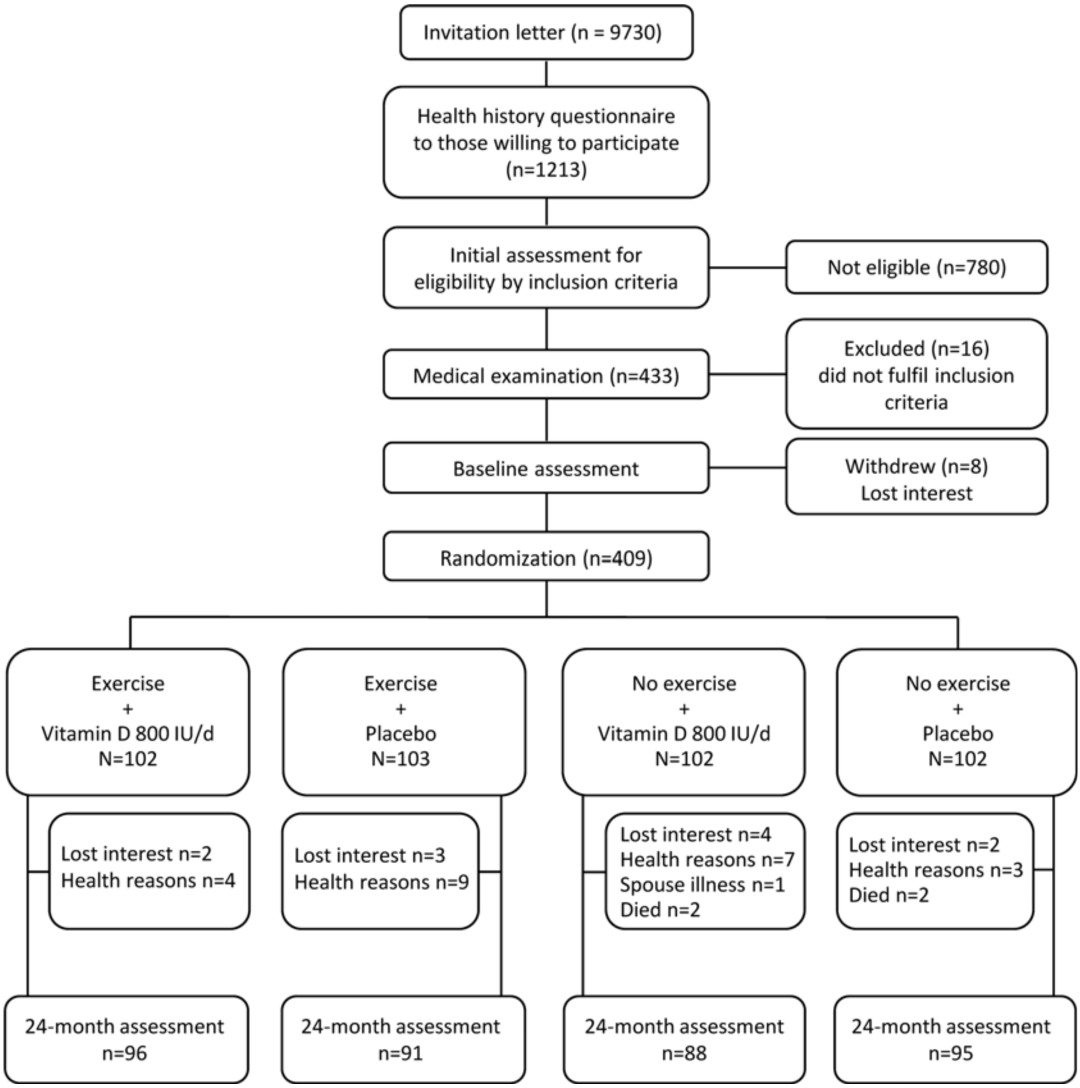

Fig. 22.1 Flowchart of the study

as bruises, abrasions, contusions, sprains, fractures, and head injuries.

Data Collection

All measurements were done at baseline, 12-, and 24-months. Blood samples and physical functioning were also assessed at 6-, and 18-months.

Height and weight were monitored with standard methods. Body composition and bone mineral content (BMC, g) of the total body and left proximal femur were assessed using dual-energy X-ray absorptiometry (DXA) (Lunar Prodigy Advance, GE Lunar, Madison, WI, USA) [35]. Distal site (5 %) and the mid-diaphysis (50 %) of the tibia were assessed with peripheral quantitative computed tomography (pQCT) (Norland/Stratec XCT 3000, Pforzheim, Germany) [36].

Disability scores in activities of daily living (ADL) (range 6–36), instrumental ADL (IADL) (range 8–48) and mobility (range 4–24) were calculated using validated questionnaires [37]. Physical functioning was assessed by the Short Physical

Performance Battery (SPPB) [38], which comprised static balance, 4 m normal walking speed and five-time chair stand tests, and by the Timed up and go (TUG) test [39]. Dynamic balance was assessed using backwards walking [40]. Maximal isometric leg-extensor strength at a knee angle 110° was measured by a strain gauge dynamometer (Tamtron, Tampere, Finland). Each participant recorded her daily steps with a pedometer (Omron HJ-112-E) over the entire 24-month study period.

Fasting Serum 25-hydroxy-vitamin D [(25OH) D] was measured as a marker of vitamin D metabolism with OCTEIA immunoenzymometric assay (IDS, Bolton, UK). Reproducibility was ensured by adhering to the Vitamin D External Quality Assessment Scheme, DEQAS (deqas.kpmd.co.uk). Interassay variation was avoided by measuring all samples from the same subject in the same series. Serum intact parathyroid hormone (S-iPTH) was measured with an Immulite 1000 automated immunoassay (Siemens Healthcare Diagnostics, Malvern, PA). Dietary intake of calcium and vitamin D were assessed with a validated food frequency questionnaire [41].

Quality of Life (QoL)

The Leipad questionnaire was used to assess QoL [42]. The core instrument constructed for use with older people has six subscales: physical function (5 items), self-care (6 items), depression and anxiety (4 items), cognitive functioning (5 items), social relations (3 items), and life satisfaction (6 items). Items are scored on a 4-point scale ranging from 0 to 3, with 0 indicating the best condition and 3 the worst. Two questions about sexual functioning were excluded, which reduced the maximum possible total score by six points. A summed index of all items was used as an indicator of overall QoL, higher scores indicating worse QoL (range 0–87).

Fear of Falling

Fear of falling was assessed with the Falls Efficacy Scale International (FES-I) questionnaire, which contains items scored on a 4-point scale (1 = not at all concerned to 4 = very concerned). It assesses concern about falling, a term that is closely related to fear, but is less intense and emotional, and therefore may be more socially acceptable for older people to disclose [43]. Higher scores indicate worse outcome (range 16–64).

Statistical Methods

Power calculations indicated that a sample size of 260 (130 in exercisers and non-exercisers) would have an 80 % power to detect a 30 % between-group difference in the rate of falls during the two-year intervention with a significance level of $\alpha = 0.05$. However, in order to eliminate the role of chance in detecting the possible interaction of vitamin D and exercise, a total number of 400 participants (100 participants in each group) were recruited into the study.

All data were analyzed on an intention-to-treat basis. Follow-up time for falls and fallers were calculated from the beginning to the end of the 24-month intervention unless the participant withdrew from the study or died. Falls incidence rates were calculated as the total number of falls divided by the time over which falls were monitored (100 person-years) in each group. Negative binomial regression was used to estimate the incidence rate ratios (IRR) for falls and injurious falls. Cox-regression models were used to calculate hazard ratios (HR) for fallers and injured fallers in each group, with the $D^{-}Ex^{-}$ group as reference.

For physical functioning and bone traits, between-group differences in time were estimated by linear mixed models for normally distributed outcomes, and generalized linear mixed models with gamma distribution and log link function for non-normally distributed outcomes using age, height, weight and use of hormone therapy as covariates. Pairwise multiple comparisons with Sidak adjustment were used to test the differences among treatment groups and interaction between vitamin D and exercise. All statistical analyses were conducted using IBM SPSS statistics software version 22 (Chicago, IL).

Table 22.1 Baseline characteristics of the study groups, mean (SD)

Characteristic	D^-Ex^- N = 102	D^+Ex^- N = 102	D^-Ex^+ N = 103	D^+Ex^+ N = 102
Age, years	73.8 (3.1)	74.1 (3.0)	74.8 (2.9)	74.1 (2.9)
Height, cm	160.7 (5.4)	159.2 (5.8)	159.4 (6.1)	159.7 (5.9)
Weight, kg	72.0 (12.4)	73.0 (13.1)	70.9 (10.6)	73.2 (10.5)
Fat, %	41.1 (6.7)	42.0 (7.2)	41.3 (6.4)	42.8 (5.3)
Dietary Calcium intake, mg/day	1040 (345)	1125 (420)	1119 (346)	1109 (385)
Dietary Vitamin D intake, μg/day	10.2 (4.1)	10.9 (4.2)	10.3 (3.6)	10.4 (3.9)
S-25(OH)D, nmol/L	67.6 (18.8)	65.8 (17.1)	69.5 (18.0)	65.5 (17.5)
S-PTH, pmol/L	5.0 (2.7)	5.0 (2.2)	4.7 (2.0)	5.2 (2)
Disability scores[a], (range)				
ADL score (6–36)	6.7 (1.6)	7.0 (2.2)	6.8 (1.9)	6.9 (1.8)
IADL score (8–48)	9.8 (2.6)	10.7 (4.8)	9.9 (3.8)	10.3 (4.0)
Mobility score (4–24)	4.76 (1.85)	5.11 (2.58)	4.71 (1.79)	4.78 (1.63)
SPPS, range (0–12)[b]	10.6 (3–12)	10.7 (1–12)	10.9 (7–12)	10.8 (5–12)
Isometric leg extensor muscle strength, N/kg	23.1 (6.1)	23.4 (7.7)	23.6 (6.0)	22.2 (6.6)
Normal walking speed, m/s	1.04 (0.21)	1.00 (0.21)	1.01 (0.19)	1.03 (0.20)
5*Chair-stand, s	12.6 (2.4)	12.6 (3.3)	12.5 (2.8)	12.4 (2.5)
TUG-time, s	9.3 (2.1)	9.7 (6.4)	8.9 (1.9)	8.9 (1.6)
Backwards walking, proportion of those able to do 6.1 m, %	41.8	30.3	45.8	51.0
Quality of life, Leipad[a]				
Total score, (0–87)	14.9 (7.0)	16.6 (8.1)	15.8 (7.7)	15.7 (8.5)
Fear of falling, FES-I[a] (16–64)	22.9 (5.7)	24.2 (6.7)	22.7 (6.4)	23.4 (6.0)

Note: D^-Ex^- placebo, D^+Ex^- 800 IU vitamin D daily, D^-Ex^+ placebo + exercise, D^+Ex^+ 800 IU vitamin D daily + exercise

[a]Lower score indicates better functioning

[b]Higher score indicates better functioning

Results

The main results are previously reported [33]. There were no clinically relevant between-group differences in age or anthropometry at baseline (Table 22.1). Body composition or disability scores did not change significantly during the trial. Mean (SD) daily dietary calcium intake was sufficient, being 1098 (378) mg at baseline and 1212 (400) mg at 24 months, while respective values for dietary vitamin D intake were 10.4 (3.9) μg and 10.5 (4.3) μg. Of the participants 356 women (87 %) had at least one diagnosed chronic disease, most commonly cardiovascular, and 79 (19 %) used hormone therapy currently.

Thirty-nine women (9.5 %) did not complete the end point measurements, most of them due to health reasons, and four died (Fig. 22.1). Mean pill compliance (range) was 98 % (42–100 %), while mean exercise compliance measured as attendance at all offered training sessions for group and home training was 73 % (0–97 %) and 66 % (0–100 %), respectively. In general, the training program was well tolerated. There were no severe adverse effects or injuries due to the training. Twenty-two participants from the Ex^+ and one from the Ex^- groups had musculoskeletal complaints, mainly mild overuse symptoms, and three injuries occurred during the gym training.

Vitamin D concentrations differed significantly between D^- and D^+ groups. Mean S-25(OH)D levels remained stable in the D^- groups, being 68.6 (18.4) nmol/L at baseline and 68.6 (17.2) nmol/L at 24 months with small seasonal variations,

Table 22.2 Rate of falls per 100 person-years in each study group during the 24-month intervention, and incidence rate ratios (IRR) (95 % CI) for falls and injurious falls

Outcome	D^-Ex^-	D^+Ex^-	D^-Ex^+	D^+Ex^+
Falls, all	118.2	132.1	120.7	113.1
Injurious falls	13.2	12.9	6.5	5.0
Falls with fractures	2.9	3.0	2.4	1.5
IRR				
All falls	1	1.08 (0.78–1.52)	1.07 (0.77–1.45)	0.99 (0.72–1.39)
Injurious falls	1	0.84 (0.45–1.57)	0.46 (0.22–0.95)	0.38 (0.17–0.81)
Multiple falls	1	1.05 (0.60–1.86)	1.11 (0.63–1.94)	1.14 (0.65–1.99)
Multiple injurious falls	1	1.04 (0.56–1.96)	1.10 (0.59–2.05)	1.54 (0.84–2.81)

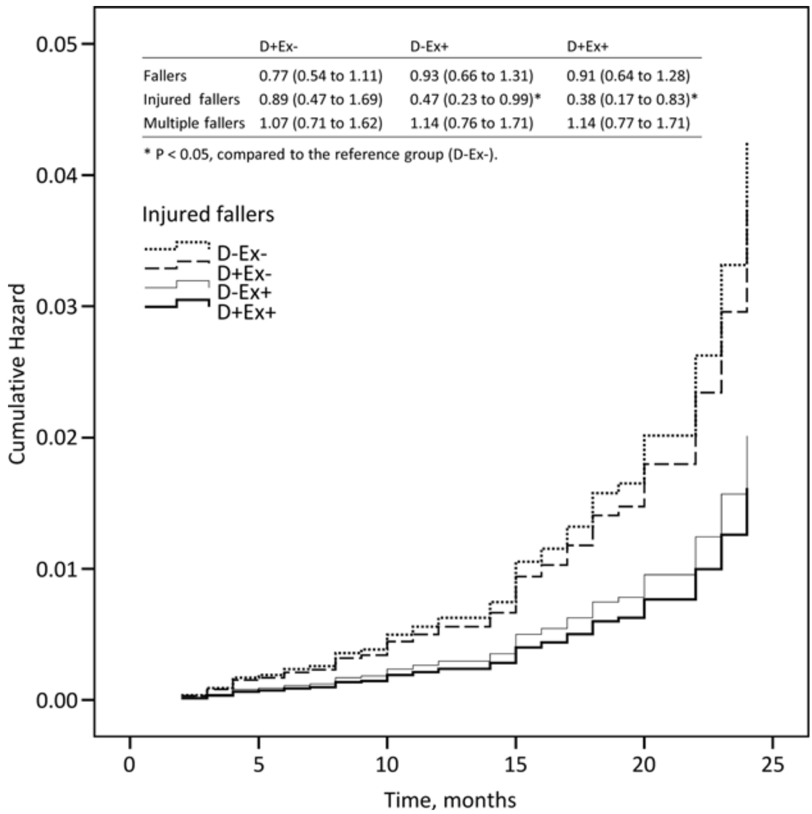

Fig. 22.2 Hazard ratios (95 % CIs) for fallers, injured fallers, and multiple fallers using the D^-Ex^- group as a reference

whereas mean levels increased in the D^+ groups from 65.7 (17.3) nmol/L at baseline to 92.3 (18.5) nmol/L at 24 months. There were small seasonal variations in S-PTH in the D^- groups, while in the D^+ groups PTH declined slightly from baseline, remaining stable thereafter.

In total, there were 928 falls and 281 fallers with no between-group differences and no interaction between vitamin D and exercise (rate of falls given in Table 22.2). However, hazard ratios (HR; 95 % CI) for injured fallers were lower in both Ex^+ groups compared with D^-Ex^- group: 0.47 (0.23–0.99) for the D^-Ex^+ group, and 0.38 (0.17–0.83) for the D^+Ex^+ group. The D^+Ex^- group did not differ from D^-Ex^- group (Fig. 22.2). Results were similar concerning the IRRs of injurious falls (Table 22.2). The number of multiple fallers (190) and multiple injured

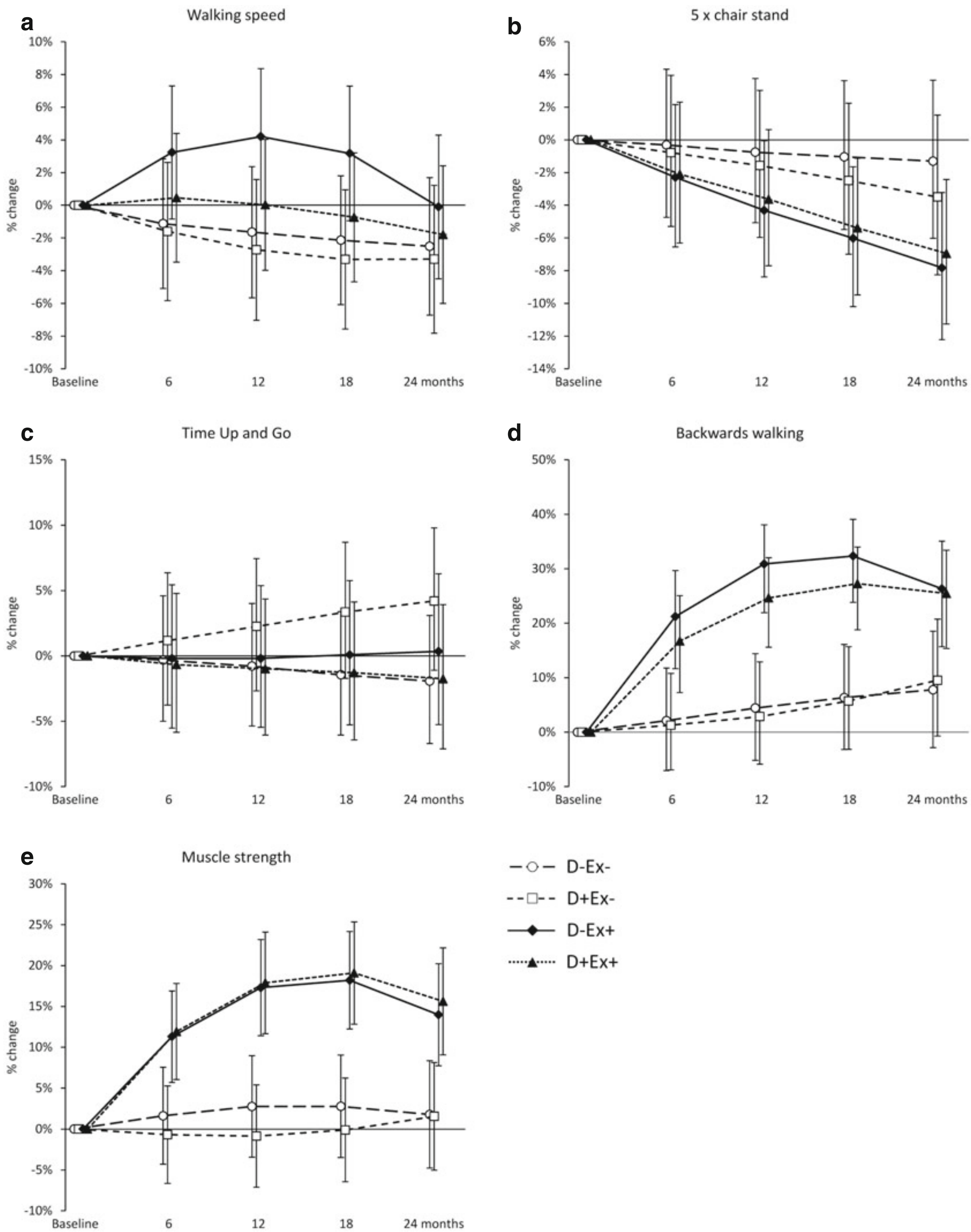

Fig. 22.3 Mean percentage changes (95 % CI) from baseline for normal walking speed (**a**), chair-stand test (**b**), Timed up and go (TUG) (**c**), Backwards walking (**d**), and lower limb extension muscle strength (**e**). In backwards walking, the %-change describes the change in proportion of those women able to walk 6.1 m. Figure legend: Placebo without exercise ($D^{-}Ex^{-}$); Vitamin D without exercise ($D^{+}Ex^{-}$); Placebo and exercise ($D^{-}Ex^{+}$); and vitamin D with exercise ($D^{+}Ex^{+}$)

Table 22.3 Baseline values (SD) and mean changes (95 % CI) in bone traits, quality of life and fear of falling in each study group

Outcome	Absolute value, mean (SD)	Change at 12 months, %	Change at 24 months, %	P compared with D^-Ex^-
Total body BMC, g/cm^2				
D^-Ex^-	2395 (410)	−0.37 (−2.33 to 1.58)	−0.59 (−2.58 to 1.41)	
D^+Ex^-	2323 (371)	−0.77 (−2.91 to 1.37)	−1.27 (−3.43 to 0.88)	0.38
D^-Ex^+	2352 (403)	−1.07 (−2.98 to 0.83)	−1.44 (−3.40 to 0.51)	0.56
D^+Ex^+	2400 (363)	−0.59 (−2.40 to 1.23)	−0.80 (−2.61 to 1.02)	0.10
Femur BMC, g/cm^2				
D^-Ex^-	32.10 (5.43)	0.33 (−0.81 to 1.48)	−0.05 (−1.22 to 1.11)	
D^+Ex^-	30.59 (4.53)	0.22 (−1.16 to 1.61)	−0.27 (−1.65 to 1.11)	0.30
D^-Ex^+	31.28 (4.99)	0.05 (−1.11 to 1.20)	−0.19 (−1.38 to 1.00)	0.49
D^+Ex^+	32.02 (4.94)	0.42 (−0.71 to 1.54)	0.20 (−0.92 to 1.32)	0.06
Distal tibia TrD, mg/cm^3				
D^-Ex^-	220.3 (34.8)	−0.25 (−3.54 to 3.03)	−0.49 (−3.77 to 2.80)	
D^+Ex^-	217.9 (28.6)	−0.09 (−3.50 to 3.32)	0.03 (−3.36 to 3.42)	0.12
D^-Ex^+	224.5 (29.4)	−0.13 (−3.39 to 3.13)	−0.16 (−3.43 to 3.11)	0.41
D^+Ex^+	224.4 (31.4)	0.17 (−3.05 to 3.39)	0.19 (−3.04 to 3.42)	*0.021*
Tibial shaft CoD, mg/cm^3				
D^-Ex^-	1104.6 (37.0)	−0.07 (−0.78 to 0.64)	−0.13 (−0.85 to 0.58)	
D^+Ex^-	1106.3 (38.0)	0.05 (−0.65 to 0.75)	0.11 (−0.60 to 0.82)	0.08
D^-Ex^+	1106.5 (33.6)	−0.04 (−0.72 to 0.65)	−0.08 (−0.77 to 0.62)	0.68
D^+Ex^+	1114.4 (34.0)	−0.06 (−0.75 to 0.63)	−0.12 (−0.82 to 0.58)	0.93
Total Leipad score (scale 0–87)				
D^-Ex^-	14.9 (7.0)	−1.8 (−12.1 to 9.7)	−0.9 (−11.7 to 11.2)	
D^+Ex^-	16.6 (8.1)	1.2 (−9.4 to 13.2)	5.3 (−6.3 to 18.3)	0.30
D^-Ex^+	15.8 (7.7)	−0.2 (−10.4 to 11.3)	2.4 (−8.6 to 14.8)	0.58
D^+Ex^+	15.7 (8.5)	−1.4 (−11.6 to 9.9)	−0.2 (−10.9 to 11.8)	0.95
FES-I score (scale 16–64)				
D^-Ex^-	22.9 (5.7)	2.0 (−4.1 to 8.5)	−0.7 (−6.8 to 5.9)	
D^+Ex^-	24.2 (6.7)	−4.9 (−10.7 to 1.3)	−1.2 (−7.4 to 5.4)	*0.02*
D^-Ex^+	22.7 (6.4)	−4.2 (−9.9 to 2.0)	0.9 (−5.3 to 7.5)	*0.02*
D^+Ex^+	23.4 (6.0)	−4.4 (−10.0 to 1.7)	−1.3 (−7.3 to 5.1)	*0.03*

fallers (117) were distributed similarly between the groups.

During the intervention, total body BMC declined slightly in all groups, but remained stable at the femur with no between-group differences (Table 22.3). There were also no statistically significant between-group differences in changes at tibial shaft cortical density. Vitamin D increased trabecular bone density at the distal tibia slightly, the mean difference being statistically significant between D^+Ex^+ and D^-Ex^- ($p=0.021$) (Table 22.3).

Changes in physical functioning are presented in Fig. 22.3. Normal walking speed was maintained in D^-Ex^+ compared to D^-Ex^- ($p=0.007$), while declined similarly in other groups. Chair-stand time improved in both Ex^+ groups, showing over 6 % improvement compared to D^-Ex^- but reaching statistical significance only in D^-Ex^+ ($p=0.027$). TUG time deteriorated significantly more in D^+Ex^- ($p=0.011$) compared to D^-Ex^-, while other groups did not differ from D^-Ex^-. Backwards walking improved significantly among exercisers; the difference compared to D^-Ex^- was statistically significant in D^-Ex^+ ($p=0.001$) and D^+Ex^+ ($p=0.026$). Irrespective of vitamin D, exercise increased muscle strength, while vitamin D alone had no effect. The predicted mean increase in the lower limb extension strength was nearly 15 % in both Ex^+ groups and differed significantly from D^-Ex^- ($p<0.001$).

There was a small but insignificant improvement in perceived QoL during the first 6 months in all four groups. However, when comparing with the D^-Ex^- group, there were no statistically significant between-group differences in changes in QoL. The improvement seen at 6 months was no longer apparent at 12 months (Table 22.3). The median FES-I score at baseline was 21 suggesting moderate fear about falling. However, according to the FES-I, 16 (3.9 %) women reported no fear of falling at all at baseline, 89 (21.9 %) women had high (FES-I score 28–64), and 186 (45.8 %) had moderate (FES-I score 20–27) fear for falling, respectively. All three intervention groups (D^+Ex^-, D^-Ex^+ and D^+Ex^+) showed reduced fear for falling during the first 12 months, and differed significantly compared with the D^-Ex^- control group (Table 22.3). However, this reduction in fear of falling was not maintained at the end of the intervention.

Discussion

This large randomized controlled clinical trial of vitamin D and exercise showed that exercise training reduced injurious falls among home-dwelling older women, while the rate of falls was not affected by either treatment. Exercise improved physical functioning, but against initial expectations vitamin D did not. However, vitamin D increased trabecular density at the distal tibia slightly.

Current evidence for the effectiveness of vitamin D in falls prevention is inconsistent, most likely because of varying study designs and baseline 25(OH)D concentrations, and different doses or type of vitamin D supplement used. According to some experts, adequate serum 25(OH)D concentration should be ≥75 nmol/L [44], while many guidelines consider 50 nmol/L to be sufficient [45]. A recent paper showed that although very high vitamin D doses increased calcium absorption, benefits for bones, physical functioning, or falls were small [46].

There is also inconclusive evidence on whether vitamin D could modulate physical functioning [9, 47]. A recent meta-analysis suggested that vitamin D had no effect on muscle strength with vitamin D levels over 25 nmol/L [19]. In a population-based survey of men and women aged 60 year or older, a higher concentration of 25(OH)D was associated with better neuromuscular function [14]. Surprisingly, chair-stand test performance appeared to decline at the highest 25(OH) D concentrations (>120 nmol/L), possibly due a small number of observations in the highest category [14]. This finding needs confirmation, since in trials using high doses of vitamin D, high 25(OH)D concentrations have increased the risk of falls and fractures suggesting negative influences on balance and mobility [48, 49]. Very little is known about the combined effects of vitamin D and exercise, and two pilot studies have suggested a positive influence [50, 51].

In the present trial, exercise training, irrespective of vitamin D supplementation, reduced injurious falls and injured fallers. Apparently this effect was attributable to improved physical functioning. Muscle strength and balance training have earlier been shown to prevent falls in community-dwelling older adults, and recent meta-analyses have confirmed that such exercise programs are effective in preventing fall-induced injuries, too [8, 52].

Our results indicated that vitamin D may not improve neuromuscular function, at least when vitamin D intake is sufficient at baseline. Exercise improved muscle strength, balance, and mobility, except the TUG test time. Similarly, though normal walking speed was maintained in both exercise groups with or without vitamin D, the vitamin D-treated group without exercise (D^+Ex^-) showed the greatest decline. Exercisers on vitamin D supplementation showed consistently smaller benefits than placebo-treated exercisers.

Despite improved physical performance exercise conferred no effect on the overall fall rate. Some recent studies have also provided similar results [53, 54]. More falls have been reported among exercisers despite improved muscle strength and physical performance [53]. Nevertheless, in our study the rate of injurious falls and injured fallers more than halved among exercisers. Good physical condition may help prevent injuries when falling, perhaps via better and safer landing techniques. This trend fully concurs with recent meta-analyses [8, 52].

The exercise training was primarily intended to improve balance, muscle strength and mobility rather than bone density, since limited physical capacity or co-morbidities of participants were likely to restrict the intensity or type of loading needed to strengthen bone. Nevertheless both vitamin D groups showed increased trabecular bone density in the tibia suggesting that mean 25(OH)D levels were sufficient for a skeletal effect (85 % of the participants in both vitamin D groups exceeded the target level ≥75 nmol/L) [44].

There is inconsistent evidence about the association between low vitamin D levels and low quality of life among generally healthy populations [21, 55, 56]. Positive associations found between vitamin D concentrations and physical functioning could explain better QoL. In a large Dutch cohort, physical performance explained the largest part of the association between lower 25(OH)D and lower QoL scores [21]. However, in our study QoL scores reacted similarly in all four groups despite clear positive changes in physical functioning among exercise groups with or without vitamin D. Minor but short-term benefits in change in QoL in the exercise groups compared with non-exercisers are in accordance with previous results of similarly aged women [57]. In our study, QoL seemed to improve slightly during the first 6 months, but the trend was similar in all four groups suggesting an attention effect, rather than the effect of added vitamin D or exercise. It is also not known which particular time point during training would be optimal for the perception of changes [58], and it is possible that the participants adapted to successive minor changes due to the treatments (vitamin D or exercise) well before the first follow-up measurement which did not reflect these adequately.

While it has been suggested that multifactorial programs, community-based Tai Chi and home-based exercise interventions are effective in reducing fear of falling in community-dwelling older people [59], our result supports the recent Cochrane review (30 studies, n = 2878), which found that exercise interventions regardless of type, frequency or duration probably reduce fear of falling only to a limited extent immediately after the intervention, with insufficient evidence to determine whether this reduction lasts beyond the intervention [6]. We found a slight but temporary reduction in the mean FES-I score in exercisers compared with controls (3 % net difference in mean values) at 12 months, which was no longer apparent at 24 months.

To our knowledge, there are no RCTs assessing effects of vitamin D supplementation on fear of falling. It may be speculated that if vitamin D affects mood or anxiety, it may also have an influence on fear of falling.

The strength of this study is the randomized controlled design with two years' duration. While it was not possible to blind for exercise, the study was double-blinded for vitamin D. Assessors of physical functioning and falls were, however, blinded to exercise group allocation. The trial was population-based, and the drop-out percent was very low (9.5 %) with good participation in exercise training and excellent pill compliance. Falls were collected monthly using falls diaries, and all reported falls were scrutinized by the investigators. Also, physical functioning and bone traits were comprehensively assessed.

There are also some limitations. Very few participants had insufficient vitamin D levels (S-25OHD < 50 nmol/L), and none were deficient (<25 nmol/L) at baseline. Vitamin D may have a threshold over which supplementation does not give an additional benefit, and therefore these results may not account for possible benefits in those with vitamin D deficiency. It may also be possible that the measured outcomes were not sufficiently sensitive to changes in mental well-being, and minute changes may not be easily recognized by healthy, community-living participants in their daily lives. Although our trial is population-based, it is possible that the women willing to participate in the study may have been more physically active and motivated to exercise than the general population of older women, and our findings may overestimate the effects of the exercise intervention. Also, our findings cannot be generalized to institutionalized people or men.

Conclusions

Given the fact that fall risk is multifactorial, exercise may be the most effective and feasible strategy for preventing injurious falls in community-dwelling older adults replete with vitamin D. Vitamin D increased tibial trabecular density slightly and exercise clearly improved physical functioning. While neither treatment reduced the rate of falling, injurious falls more than halved among exercisers with or without vitamin D. Vitamin D or exercise neither improved quality of life, nor reduced fear of falling. Our participants were vitamin D replete with sufficient calcium intake. Future research is needed to elaborate the effects of interventions on people with varying baseline levels of vitamin D and physical functioning, especially when changes in wellbeing parameters are subtle.

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