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Original Article

Vitamin D Status according to the Diseases in Hospitalized Rehabilitation Patients: Single Center Study

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HIGHLIGHTS

- The hospitalized rehabilitation patients had lower serum 25 hydroxyvitamin D3 (25[OH] D3) compared with the community.
- Patients with fractures had lower serum 25(OH)D3 levels compared with those with other diseases.
- Non-ambulatory patients had significantly lower serum 25(OH)D3 levels at discharge compared with ambulatory patients.
- We should have a more interest of serum vitamin D in hospitalized rehabilitation patients.

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Vitamin D Status according to the Diseases in Hospitalized Rehabilitation Patients: Single Center Study

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Conflict of Interest
The authors have no potential conflicts of interest to disclose.

ABSTRACT

To investigate vitamin D status according to the diseases in patients admitted to the department of rehabilitation medicine. In total, 282 patients admitted to the department of rehabilitation medicine in our hospital were included. Patients were classified into 4 groups according to ailment: stroke, traumatic brain injury, spinal cord injury, and fracture. All patients were also classified as ambulatory or non-ambulatory. Serum 25-hydroxyvitamin D (25[OH]D) levels were estimated at admission and at discharge. Bone mineral density (BMD) and ionized calcium levels were also measured. All subjects completed the Desmond Fall Risk Questionnaire for fall risk assessment. In total, 92 patients (59 males and 33 females; mean age, 69.09 ± 9.4 years) was enrolled. Low serum 25(OH)D levels (6–28 ng/mL) were observed in all patients in this study, and these were lower in the group of fractures resulting from falls than in the group of strokes ($p < 0.05$). Significant correlations were found between BMD and ionized calcium levels, Desmond Fall Risk Questionnaire scores and BMD, and questionnaire scores and serum 25(OH)D ($p < 0.05$). Serum 25(OH)D levels were lower in the department of rehabilitation medicine inpatients in our study than in the general population. The ambulatory patients had higher serum 25(OH)D levels at discharge than the non-ambulatory patients'. The hospitalized rehabilitation patients had lower serum 25(OH)D compared with the community. There were lower serum 25(OH)D levels in patients with fractures and non-ambulatory groups. We should pay attention to serum vitamin D levels of rehabilitation center inpatients.

Keywords: Vitamin D; Bone Mineral Density; Accidental Falls; Fracture; Rehabilitation

INTRODUCTION

Vitamin D is known to be important in optimizing the health of bones and can be obtained by exposing the skin to ultraviolet light in addition to diet [1]. Vitamin D level was reportedly the lowest in winter, highest in summer, and significantly higher in elderly individuals living at home than in those living in nursing homes [2-4]. Data from the National Health and Nutrition Examination Surveys for the years 2001–2006 indicated that vitamin D levels were sufficient in 66% of the American population. Vitamin D sufficiency is defined by the Institute of Medicine as a serum 25-hydroxyvitamin D (25[OH]D) level of 50–125 ng/mL.

Approximately 25% of the population was at risk of vitamin D inadequacy, defined as serum 25(OH)D levels of 30–49 ng/mL, while 8% were at risk of vitamin D deficiency, defined as serum 25(OH)D levels of < 30 ng/mL [5].

The risk of vitamin D deficiency varies with age, sex, and race or ethnicity. The prevalence of vitamin D deficiency was lower in young, male, and non-Hispanic whites. Among females, the prevalence was lower in pregnant or lactating females [5]. In 2011, Choi et al. [6] reported that vitamin D insufficiency is very common in the Korean populations. In Korea, the prevalence of vitamin D deficiency was found in 47.3% of males and 64.5% of females. Dhesi et al. [7] reported that vitamin deficiency is very common, affecting at least 72% patients attending a falls clinic (25[OH]D < 20 ng/mL). Of the total population, severe vitamin D deficiency (< 12 ng/mL) was detected in 31.8% patients while moderate vitamin D deficiency (12.1–20.0 ng/mL) was detected in 40.6%.

Supplementation with vitamin D metabolites in the elderly has been reported to decrease the incidence of falls [8-11]. No study has reported on vitamin D status according to disease groups and ambulatory status in hospitalized patients.

The aim of this study is to investigate the level of vitamin D in patients with subacute stage of admission to the department of rehabilitation medicine according to disease (stroke, traumatic brain injury [TBI], spinal cord injury [SCI], and fracture) and to determine the change of patient's vitamin D according to the availability of ambulation.

MATERIALS AND METHODS

The subjects were 282 patients admitted to the rehabilitation medicine clinic at our hospital for comprehensive rehabilitation from March 2012 to December 2012. Subjects who transferred or admitted to our department within 1 month from disease onset and were older than 50 years were included. Disease characteristics, age, sex, ambulatory status, and season were considered as potential confounders because of possible association with both vitamin D status and fall risk.

Patients were classified into 4 groups according to ailment: stroke, TBI, SCI, and fracture (Table 1). The fracture group included patients with fractures in the upper or lower extremities caused by falls only. Three seasonal periods were examined: March to June, July to September, and October to December. The baseline questionnaire collected information on age, sex, date of hospital admission, and date of discharge. All patients were also divided into 2 groups: ambulatory group who were able to gait using aid or who used wheelchairs as assistive gait devices and non-ambulatory group such as patients who have taken a wheelchair ride or in bedridden state.

Table 1. Characteristics of the subjects

Characteristics	SCI (n = 16)	Fracture (n = 14)	Stroke (n = 47)	TBI (n = 15)	Total (n = 92)	p value
Sex (male)	12 (75)	6 (42.85)	29 (61.70)	15 (80)	59 (64.13)	0.104
Ambulation	5	6	22	6	39	0.042
Mean age (yr)	65.4 ± 7.96	76.82 ± 6.60	69.45 ± 9.37	65.09 ± 8.81	69.09 ± 9.40	0.001
Serum 25(OH)D (ng/mL)	10.44 ± 3.90	8.65 ± 5.20	12.70 ± 5.32	9.58 ± 2.89	11.21 ± 5.13	0.033
T-scores of BMD	−0.83 ± 1.49	−2.76 ± 1.54	−1.46 ± 1.33	−1.58 ± 1.21	−1.58 ± 1.44	0.013
Desmond fall score	3.22 ± 2.1	6.14 ± 2.6	5.56 ± 3.31	3.0 ± 2.1	5.02 ± 3.0	0.156

Values are presented as mean ± standard deviation or number (%). Baseline characteristics of all patients were tested using 1-way analysis of variance.
SCI, spinal cord injury; TBI, traumatic brain injury; BMD, bone mineral density.

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Table 2. Correlations analysis between serum 25 hydroxyvitamin D3, ionized calcium, BMD, falling score in Desmond fall risk questionnaire and age

Parameters	Age (yr)	BMD	Serum 25(OH)D (ng/mL)	Ionized calcium (ng/mL)	Fall score
Age (yr)	1				
BMD	−0.41*	1			
Serum 25(OH)D (ng/mL)	0.08	0.32*	1		
Ionized calcium (ng/mL)	−0.05	0.43*	0.091	1	
Fall score	0.39*	−0.191	0.137	−0.058	1

25(OH)D, 25 hydroxyvitamin D; BMD, bone mineral density.
*The $p < 0.05$ by Pearson's correlation coefficient.

Patients were excluded if they had a history of taking medications that could affect bone and calcium metabolism (glucocorticoids, thiazide, and diuretics), had endocrine disease, chronic renal failure, or unable to ambulation for more than 2 months before illness.

Vitamin D levels were estimated according to serum 25(OH)D levels, ionized calcium levels, and bone mineral density (BMD). Serum 25(OH)D levels were measured twice at admission and at discharge (mean interval, 42 ± 27 days). We compared serum 25(OH)D levels according to diseases and the correlations between ionized calcium and serum 25(OH)D levels and between BMD and serum 25(OH)D levels (Table 2). Furthermore, patients were divided into an ambulatory and a no ambulatory group, and serum 25(OH)D levels at admission and at discharge were measured in and compared between these 2 groups.

BMD was estimated within 1 week from date of rehabilitation unit admission by dual-energy X-ray absorptiometry at the lumbar spine and femur. Lumbar spine was estimated from the first lumbar vertebra; fractured vertebrae were not included. The T-score of the femur neck was used.

Blood samples were obtained in the morning. Serum 25(OH)D samples collected at the study sites were measured using the Nichols Advantage System (Nichols Institute Diagnostics, San Clemente, CA, USA), which is a commercially available chemiluminescent assay in which 25(OH)D is released from vitamin D-binding proteins by a leasing agent. The competitive assay is completed automatically by the system. The self-reported Desmond Fall Risk Questionnaire for fall risk assessment was completed by all participants within 1 week from date of hospital admission. This questionnaire comprises 15 questions about fall experiences and falling sensations (Table 3) [12,13].

Statistical analysis was performed using SPSS ver. 12.0 (SPSS Inc., Chicago, IL, USA). Baseline data are presented as means ± standard deviations. Baseline characteristics of all patients were tested using 1-way analysis of variance. Pearson's correlation coefficient was used as a linear correlation between serum 25(OH)D levels and other variables (age, BMD, ambulatory status,

Table 3. Differences between ambulation and non-ambulation groups

	Non-ambulation	Ambulation	p value
Age (yr)	65.09 ± 12.88	61.12 ± 17.20	0.23
Onset to serum 25(OH)D test	17.75 ± 12.31	14.84 ± 11.15	0.25
Length of stay in department of rehabilitation medicine*	52.32 ± 18.63	45.02 ± 13.01	0.04
BMD	−1.78 ± 1.42	−1.28 ± 1.45	0.13
Serum 25(OH)D (ng/mL) at admission	10.63 ± 4.83	11.95 ± 5.47	0.24
Serum 25(OH)D (ng/mL) at discharge*	9.70 ± 3.59	12.74 ± 4.65	0.04

Values are presented as mean ± standard deviation or number (%). Independent t-test was used to compare groups.
BMD, bone mineral density; 25(OH)D, 25-hydroxyvitamin D.
*The $p < 0.05$.

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ionized calcium, and Desmond fall score). Independent t-test was performed to compare the differences between the ambulation group and the non-ambulation group.

RESULTS

In total, 92 patients (59 males and 33 females; mean age, 69.09 ± 9.4 years) was enrolled. The mean serum 25(OH)D level was 11.2 ± 5.1 ng/mL, and mean BMD (T-score) was −1.5 ± 1.4 (Table 1). All patients showed low serum 25(OH)D levels (6–28.6 ng/mL). Serum 25(OH)D levels according to disease group were as follows: SCI, 10.4 ± 3.9 ng/mL; fracture, 8.6 ± 5.2 ng/mL; stroke, 12.7 ± 5.3 ng/mL, and TBI, 9.6 ± 2.9 ng/mL (Table 1). Serum 25(OH)D levels were lower (mean, 8.7 ± 5.2 ng/mL) in patients with fall-induced fractures than in those with stroke (mean, 12.7 ± 5.3 ng/mL; p = 0.036; Fig. 1).

T-score of BMD values according to disease were as follows: SCI, −0.83 ± 1.49; fracture, −2.76 ± 1.54; stroke, −1.46 ± 1.33; and TBI, −1.58 ± 1.21 (Table 1). BMD showed significant correlation with age (r = −0.41, p < 0.01), serum 25(OH)D (r = 0.32, p = 0.005), and ionized calcium (r = 0.43, p < 0.01) (Table 2).

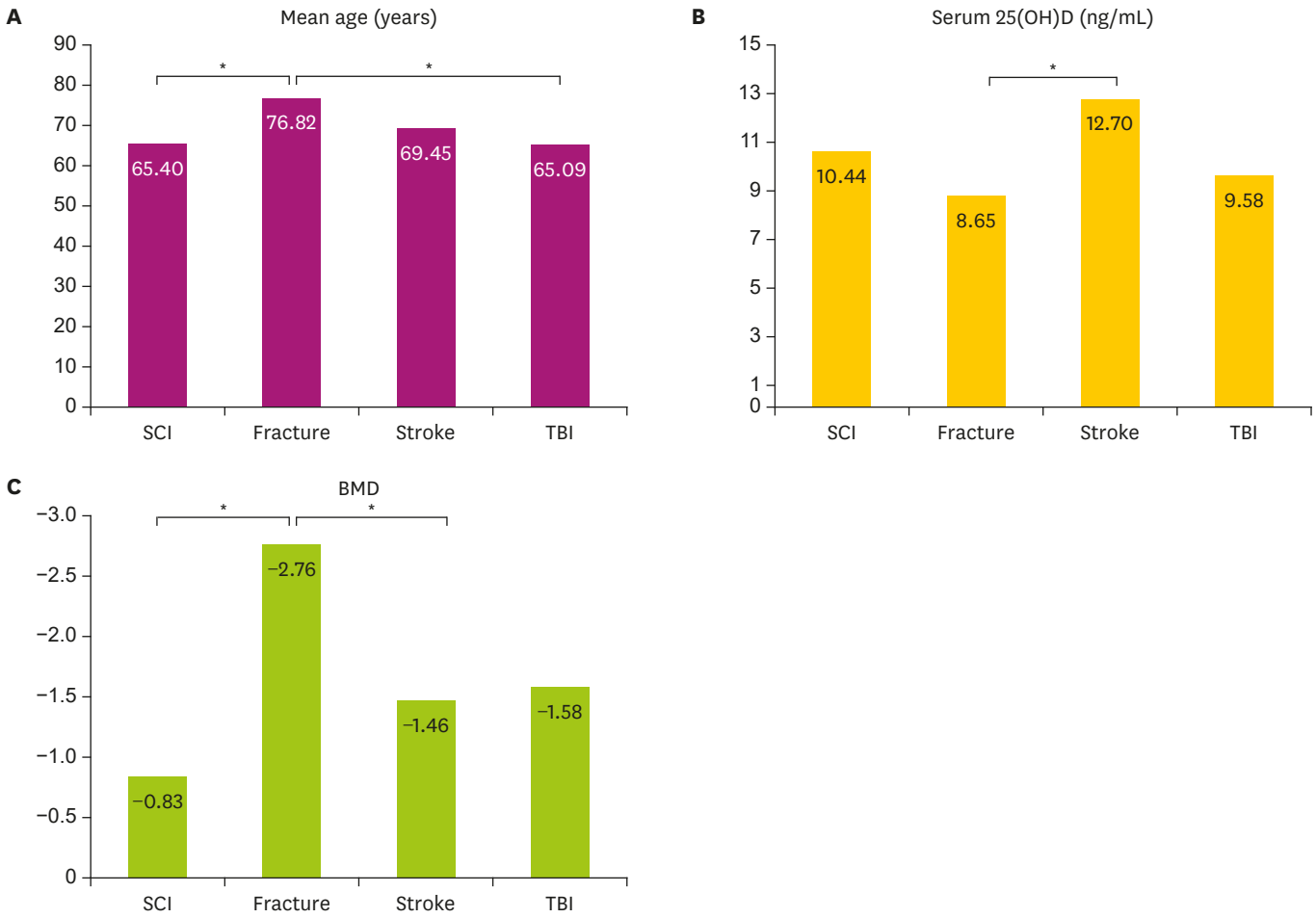

Fig. 1. Baseline characteristics of 4 groups of disease at admission; 1 (A), mean age; 1 (B), serum 25(OH)D; 1 (C), BMD.
25(OH)D, 25-hydroxyvitamin D; BMD, bone mineral density; SCI, spinal cord injury; TBI, traumatic brain injury.
*The p < 0.05 by Tukey honestly significant difference in 1 way analysis of variance.

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Desmond Fall Risk Questionnaire score according to disease were as follows: SCI, 3.2 ± 2.1; fracture, 6.1 ± 2.6; stroke, 5.6±3.3; and TBI, 3.0 ± 2.1 (Table 1). Desmond Fall Risk Questionnaire score was not significantly associated with characteristics of disease in patients admitted to a department of rehabilitation medicine.

Compared with the ambulatory group and the non-ambulatory group, there was no significant difference in the initial vitamin D levels between the 2 groups, but the vitamin D level at discharge was significantly higher in the ambulatory group (12.74 ± 4.65, p = 0.04) and the length of stay was shorter in the ambulation group (45.02 ± 13.01, p = 0.04), there were no significant difference in BMD between 2 groups (Table 3).

DISCUSSION

In this study, serum 25(OH)D was found to be low in all patients admitted to the department of rehabilitation medicine, and serum 25(OH)D and BMD levels were significantly lower in patients with fractures.

Vitamin D deficiency has been the subject of attention because of the increased prevalence of osteoporotic fractures in the elderly. Sambrook et al. [14] reported low baseline serum 25(OH)D levels (median, 32.9 ng/mL) in elderly patients in Northern Sydney, Australia. In a study of hospitalized elderly patients in Iceland, Ramel et al. [3] observed serum 25(OH)D deficiency (serum 25(OH)D < 25 ng/mL) in 12.3% patients and serum 25(OH)D insufficiency (serum 25(OH)D = 25–75 ng/mL) in 71.9% patients. In an Italian study with a cutoff value of 20 ng/mL, the highest prevalence of vitamin D deficiency was found in a group of patients engaged in a long-term rehabilitation program. In these patients, vitamin D deficiency ranged from 57.8% in summer to 82.3% in winter [15]. In the present study, low serum 25(OH)D levels were found in rehabilitation patients (mean, 11.3 ± 4.8 ng/mL). This level was extremely low compared with that in the general population [6]. We assumes that, this result was because rehabilitation patients had often received hospital treatment in many times because of other pain, muscle weakness, cognitive impairment, many underlying diseases. For future research, it would be relevant to investigate the cause that explains the association between serum 25(OH)D levels and rehabilitation patients through comparisons with other patients admitted in different departments and hospitalization period.

In the group of patients with fractures in our study, serum 25(OH)D (mean, 8.6 ± 5.2 ng/mL) levels were lower than those in the other groups (mean, 11.2 ± 5.1 ng/mL). Vitamin D status is associated with muscle strength, physical performance, and falls, as observed in many epidemiological studies [2,16-20]. Pfeifer et al. [21] found a significant decrease in fall incidence, significant improvements in quadriceps strength, decreased body sway, and decreased time required to perform the Time-Up-and-Go test in the vitamin D supplement group in their study. It may because low serum 25(OH)D levels plays an important role in balance control. Many studies have found that impaired gait, postural balance, and muscle strength are associated with fall risk and vitamin D level. For instance, in a population of 319 community-dwelling subjects (mean age, 75.9 years), Bischoff-Ferrari et al. observed a serum 25(OH)D level of ≤ 12 ng/mL, which was significantly correlated with decreased leg extension strength. This effect was less intense in females than in males [20]. Therefore, poor vitamin D status may influence fall risk by affecting muscle function. The active vitamin D metabolite, serum 25(OH)D, plays an important role in the regulation of calcium transport

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and protein synthesis in the muscle cell. It increases the calcium pool, which is essential for muscle contraction, and enhances the reflex protection mechanism. Therefore, low vitamin D levels may be associated with a high fall risk [21]. In this study, we once again confirmed that the vitamin D level was low in the fracture group, suggesting that patients with low vitamin D levels had a high fall risk and that the probability of fracture was high even though BMD was similar.

Recent studies showed that serum 25(OH)D levels were significantly higher in patients living at home than in those living in nursing homes [16,22]. This may be because patients living in nursing homes receive insufficient sunlight exposure and experience ambulatory difficulties. Sato et al. reported serum 25(OH)D deficiency in immobilized stroke patients in a cross-sectional study [4]. They suggested that vitamin D supplementation might be required in disabled elderly stroke patients with vitamin D deficiency in order to prevent hip fractures, which occur frequently in this population. The results of the present study showed that serum 25(OH)D levels at discharge were significantly higher in ambulatory patients than in non-ambulatory or bedridden patients (Table 3). One of the factors responsible for this result may be sunlight exposure, which the ambulatory patients received for a longer duration compared with the bedridden patients, and it is estimated that nutritional supplement such as meals was sufficient in the ambulation group compared with the non-ambulatory groups. In this study, Patients undergoing rehabilitation may have more ambulatory difficulties compared with the general population, resulting in less sunlight exposure and decreased serum 25(OH) D production. Also, it has been confirmed that serum 25(OH)D levels performed at discharge of non-ambulatory group showed decreasing trend, which is thought that patients with ambulatory difficulty in the department of rehabilitation medicine had less sunlight exposure and decreased serum 25(OH)D production. So, it seems to need a vitamin D supplement to patients during hospitalization period.

There are some limitations to this study. First, since this study was conducted as a single center study, it cannot be generalized through these results. In addition, there may be other factors that affect the vitamin D level, such as lifestyle or the sunlight exposure of each patient which we could not investigate. Since the analysis by groups, significant differences in the age of patients for each disease, there can be a limit to the interpretation of results. However, the difference in age was between the fracture group and the SCI and TBI groups, whereas the difference between serum 25(OH)D level and BMD was different in the stroke group in which age was not statistically significant. Finally, this study was initially aimed at assessing the association of the underlying disease and vitamin D levels in subacute stage patients, but did not yield significant results for each disease.

CONCLUSION

The patients admitted to a department of rehabilitation medicine had lower serum 25(OH)D compared with the community. Patients with fractures had lower serum 25(OH)D levels compared with those with other diseases. Furthermore, non-ambulatory patients had significantly lower serum 25(OH)D levels at discharge compared with ambulatory patients ($p < 0.05$).

Evaluation of baseline serum 25(OH)D levels and BMD may helpful in predicting the risk of falling. Also, evaluation of Desmond Fall Risk Questionnaire scores at admission is also useful for preventing recurrent falls in the hospital and for better rehabilitation outcomes.

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Therefore, we should have a more interest of serum vitamin D in hospitalized rehabilitation patients and need to provide vitamin D supply to patients admitted in department of rehabilitation medicine, especially those with ambulation difficulty.

REFERENCES

1. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. Endocr Rev 2001;22:477-501.
PUBMED | CROSSREF
2. Kim HS, Choi YH, Park KC, Park YS. Osteoporotic spinal compression fracture and degree of vitamin D deficiency. J Korean Fract Soc 2013;26:27-31.
CROSSREF
3. Ramel A, Jonsson PV, Bjornsson S, Thorsdottir I. Vitamin D deficiency and nutritional status in elderly hospitalized subjects in Iceland. Public Health Nutr 2009;12:1001-1005.
PUBMED | CROSSREF
4. Sato Y, Kuno H, Asoh T, Honda Y, Oizumi K. Effect of immobilization on vitamin D status and bone mass in chronically hospitalized disabled stroke patients. Age Ageing 1999;28:265-269.
PUBMED | CROSSREF
5. Looker AC, Johnson CL, Lacher DA, Pfeiffer CM, Schleicher RL, Sempos CT. Vitamin D status: United States, 2001–2006. NCHS Data Brief 2011;1-8.
PUBMED
6. Choi HS, Oh HJ, Choi H, Choi WH, Kim JG, Kim KM, Kim KJ, Rhee Y, Lim SK. Vitamin D insufficiency in Korea--a greater threat to younger generation: the Korea National Health and Nutrition Examination Survey (KNHANES) 2008. J Clin Endocrinol Metab 2011;96:643-651.
PUBMED | CROSSREF
7. Dhesi JK, Moniz C, Close JC, Jackson SH, Allain TJ. A rationale for vitamin D prescribing in a falls clinic population. Age Ageing 2002;31:267-271.
PUBMED | CROSSREF
8. López-Torres Hidalgo J; ANVITAD Group. Prevention of falls and fractures in old people by administration of calcium and vitamin D, randomized clinical trial. BMC Public Health 2011;11:910.
PUBMED | CROSSREF
9. Annweiler C, Montero-Odasso M, Schott AM, Berrut G, Fantino B, Beauchet O. Fall prevention and vitamin D in the elderly: an overview of the key role of the non-bone effects. J Neuroeng Rehabil 2010;7:50.
PUBMED | CROSSREF
10. Pfeifer M, Begerow B, Minne HW, Suppan K, Fahrleitner-Pammer A, Dobnig H. Effects of a long-term vitamin D and calcium supplementation on falls and parameters of muscle function in community-dwelling older individuals. Osteoporos Int 2009;20:315-322.
PUBMED | CROSSREF
11. Law M, Withers H, Morris J, Anderson F. Vitamin D supplementation and the prevention of fractures and falls: results of a randomised trial in elderly people in residential accommodation. Age Ageing 2006;35:482-486.
PUBMED | CROSSREF
12. Bok SK, Lee TH, Lee SS. The effects of changes of ankle strength and range of motion according to aging on balance. Ann Rehabil Med 2013;37:10-16.
PUBMED | CROSSREF
13. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. N Engl J Med 1988;319:1701-1707.
PUBMED | CROSSREF
14. Sambrook PN, Cameron ID, Chen JS, Cumming RG, Durvasula S, Herrmann M, Kok C, Lord SR, Macara M, March LM, Mason RS, Seibel MJ, Wilson N, Simpson JM. Does increased sunlight exposure work as a strategy to improve vitamin D status in the elderly: a cluster randomised controlled trial. Osteoporos Int 2012;23:615-624.
PUBMED | CROSSREF
15. Romagnoli E, Caravella P, Scarnecchia L, Martinez P, Minisola S. Hypovitaminosis D in an Italian population of healthy subjects and hospitalized patients. Br J Nutr 1999;81:133-137.
PUBMED

16. Bischoff-Ferrari HA, Can U, Staehelin HB, Platz A, Henschkowski J, Michel BA, Dawson-Hughes B, Theiler R. Severe vitamin D deficiency in Swiss hip fracture patients. Bone 2008;42:597-602.
PUBMED | CROSSREF

17. Annweiler C, Beauchet O. Relationship between bone, fracture, and exercise: the key role of vitamin D. Arch Intern Med 2009;169:1638.
PUBMED | CROSSREF

18. Jackson RD, LaCroix AZ, Gass M, Wallace RB, Robbins J, Lewis CE, Bassford T, Beresford SA, Black HR, Blanchette P, Bonds DE, Brunner RL, Brzyski RG, Caan B, Cauley JA, Chlebowski RT, Cummings SR, Granek I, Hays J, Heiss G, Hendrix SL, Howard BV, Hsia J, Hubbell FA, Johnson KC, Judd H, Kotchen JM, Kuller LH, Langer RD, Lasser NL, Limacher MC, Ludlam S, Manson JE, Margolis KL, McGowan J, Ockene JK, O'Sullivan MJ, Phillips L, Prentice RL, Sarto GE, Stefanick ML, Van Horn L, Wactawski-Wende J, Whitlock E, Anderson GL, Assaf AR, Barad D; Women's Health Initiative Investigators. Calcium plus vitamin D supplementation and the risk of fractures. N Engl J Med 2006;354:669-683.
PUBMED | CROSSREF

19. Janssen HC, Samson MM, Verhaar HJ. Vitamin D deficiency, muscle function, and falls in elderly people. Am J Clin Nutr 2002;75:611-615.
PUBMED | CROSSREF

20. Lips P, Graafmans WC, Ooms ME, Bezemer PD, Bouter LM. Vitamin D supplementation and fracture incidence in elderly persons. A randomized, placebo-controlled clinical trial. Ann Intern Med 1996;124:400-406.
PUBMED | CROSSREF

21. Pfeifer M, Begerow B, Minne HW. Vitamin D and muscle function. Osteoporos Int 2002;13:187-194.
PUBMED | CROSSREF

22. Bischoff HA, Stahelin HB, Urscheler N, Ehrsam R, Vonthein R, Perrig-Chiello P, Tyndall A, Theiler R. Muscle strength in the elderly: its relation to vitamin D metabolites. Arch Phys Med Rehabil 1999;80:54-58.
PUBMED | CROSSREF