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Analysis of Serum 25-Hydroxyvitamin D Status in Non-Elderly Adults (18-64 yrs) Working Indoors at 40° North Latitude-A Cross Sectional Study of Falls and their Related Physical Performance

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Abstract

Background: Vitamin D has a key role to prevent falls in the elderly. Does it play the same function in the non-elderly (18-64 yrs)?

Objective and methods: A cross-sectional survey was addressed to investigate associations between falls, its related physical performances, and 25[OH]D_3 status in 256 non-elderly adults regularly work indoors at latitude 40° north region.

Results: The mean value of the serum 25[OH]D_3 was 15.6 ± 7.0 ng/ml. We divided the serum 25[OH]D_3 levels into 3 groups. The deficient, inadequate, and adequate group was as a level of <12.0 ng/ml, 12.0 ng/ml to <20 ng/ml and ≥ 20 ng/ml. Percentage of each group was 35%, 38%, and 27%. Falls prevalence of the past 12 months was 8.9%, 5.1%, and 11.8%. Among the 3 groups, no significant differences were found in falls incidence, its related physical performances, spinal alignment, bone, muscle status, and laboratory findings. The mean age of the 3 groups was 37.2 ± 12.5, 39.7 ± 13.2 and 42.0 ± 13.4 years and it was significantly older in the adequate group (p<0.01).

Conclusion: No associations found among the prevalence of falls, its related physical performances, spinal alignment, bone, muscle status, laboratory data, and the 25[OH]D_3 levels. Therefore, for Vitamin D deficiency, assessment of Vitamin D status in the non-elderly (18-64 yrs) workers may be less valuable as far as falls were concerned. But 73% of the 256 non-elderly adults working indoors did not have adequate serum 25[OH] D_3. A further longitudinal study is mandatory.

Keywords: 25[OH]D_3; Falls incidence; Non-elderly indoor workers

Introduction

Vitamin D or cholecalciferol is a collective structure related to metabolites obtained from dietary foods, supplements and sunlight. It regulates calcium and phosphorus levels in the blood by promoting their absorption from the intestine and also stimulates bone formation and mineralization. The importance of Vitamin D is well recognized in the skeleton. 25-hydroxyvitamin D (25[OH]D) is a stable form of Vitamin D metabolized in the liver, and it sharply reflects the nutritional status of Vitamin D. Lack of 25[OH]D easily leads to osteopenia or osteoporosis because of secondary hyperparathyroidism which induces increasing flow-out of calcium from the bone tissue. Recently, lots of new functional aspects of 25[OH]D in the human body are being investigated. Moreover, several potential links between lack of 25[OH] D and general health problems are also proposed, though they are not conclusive [1,2].

Lack of 25[OH]D has a possibility to result in myopathy, sarcopenia, neurological impairment, and secondarily limits physical performance. It has already been demonstrated that 25[OH]D plays a key role to prevent falls directly or indirectly in the elderly (≥ 65-years-old), but the mechanism is still controversial. Falls are serious events in elderly populations, and even minor falls lead to hip, vertebral fracture, and spinal cord injury without bone damage, which finally lead to disused syndrome or mortality. The proportion of elderly cases has been increasing in our globe. Out of all the advanced countries, Japan, in terms of the aging society phenomenon, is at the center of this problem. The rate of people over 65 years is rapidly increasing and estimated to rise to 32.8% by 2035; even though the total population of Japan is going to naturally decrease. This is unsurprising data, and one we must confront. Undoubtedly, the current situation of Japan is bound to develop in other countries in the near future [3,4]. Therefore, prevention of falls is considerably crucial to establish well-being and lessen medical costs in aging societies [5,6]. It has been disclosed that 25[OH]D is crucial to prevent falls in the elderly, but there still remains a question whether it plays the same function in the non-elderly (18-64yrs) who are normally not associated with osteoporosis and/or sarcopenia. If 25[OH]D has the same function for falls and the related physical performance in the non-elderly, it is very beneficial to keep serum 25[OH]D concentrations in their normal range, which is still debatable, before they turn 65 years old or more [7]. To our knowledge, very few systemic studies have been done to investigate relationships between falls, their related physical performances, and 25[OH]D status in the non-elderly. To address this question, the current study was introduced in the same sun light exposure setting. The aim of the current cross-sectional survey is to investigate whether there are associations between falls, their related physical performances, and 25[OH]D status in non-elderly populations who regularly work indoors at a latitude of 40° North in Japan.

Materials and Methods

Workers employed in an indoor medical equipment factory in Odate were considered candidates. Odate is geographically located at approximately 40° North latitude and 140° East longitude in Japan and

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is one of the cities that annually have the shortest time of solar exposure in Japan. It has been estimated at approximately 1526.0 hours per year (1981-2010) [8]. The total number of workers in the medical equipment factory was 1,489. A questionnaire was delivered and was collected from 1,452 out of 1,489 workers (collection rate: 97.5%). Age, gender, body height and weight were ascertained in the questionnaire. Experience of falls in the past 12 months was ascertained as well. Definition of falls was 'an unintentional change in position resulting in coming to rest at a lower level or on the ground [9]. The forty-eight individuals who had not completed the full items in the questionnaire were excluded. Therefore, 1,404 employees were considered participants. Out of the 1,404 workers, 310 were randomly selected for further assessment. The past history of 310 participants was taken by direct interview. Physical conditions including the lumbar spine, hips, knees and ankle joints were checked by 3 independent orthopaedic doctors after the initial interview. A cross sectional study about the related physical performance to falls, spinal alignment, bone, skeletal muscle status, and laboratory data including serum concentration of 25[OH]D was carried out. Twenty-five participants taking drugs that might negatively affect the nerve system were excluded. No one had supplementation of Vitamin D and or calcium. Twenty-three participants with past histories of cranial, spinal diseases, major joint disorders of the lower extremities, and diabetes mellitus were also excluded. Three individuals who had not accurately completed items about falls and their past history were also excluded at this point. Three participants who could not complete the physical performance test were excluded. Finally, 256 of 310 participants were enrolled in the final analysis (Figure 1). To evaluate spinal coronal and sagittal balance of the spine, C7-central sacral ventral line (C7-CSVL) and C7 sagittal vertical axis (C7-SVA) were measured on the radiograms of the total spine [10,11] The radiograms were taken in neutrally standing position with the arms resting on the chest. Measurement of C7-CSVL and C7-SVA were done by 3 radiographers, and the mean value was used for the evaluation. Body mass index (BMI, kg/m2) was calculated by dividing their weight in kilograms by the square of their height in metres. Bone mineral density of the whole body (BMD, mg/cm2), and skeletal muscle index (SMI : [arm muscle mass + leg muscle mass] / body height squared, kg/m2) were simultaneously measured using Dual Energy X-ray Absorptiometry Hologic DISCOVERY A, Bedford, MA.

Physical performance test

Grip power (GP, kgf) test was done alternatively in the right and the left hand. Participants were asked to stand with their arms outstretched away from the body and to squeeze as hard as possible. The maximum value in kilogram force (kgf) with PIP joints flexed in 90° was assessed, using a hydraulic hand dynamometer (Takei Scientific Instruments Co., Ltd., Niigata City, Japan). Back muscle extensor strength (BMES, kgf) was measured based on the report by Limburg et al. [12]. A strain-gauge dynamotor (Biotec, Akita City, Japan) was attached to the frame and maximum extension force was measured at the T4 to T7 level in the supine position with the hips and knees extended, and the arms at rest next to the body on the bed (Figure 2). Functional reach test (FRT, cm) was done by placing a tape measure on the wall, parallel to the floor at the height of the acromion of the dominant arm. The participants were asked to stand with their feet at a comfortable distance apart and to make a fist, and forward flex the dominant shoulder joint to approximately 90°, and to reach forward as far as possible without taking a step or touching the wall. The distance between the start and end point is then measured using the tip of the metacarpal of the middle finger as the reference point (cm) [13]. In timed up and go test (TUGT, second), the participant sat correctly in a chair with armrests. A marker was put on the floor 3 meters away from the chair. The participant was asked on the word 'Go' to stand up, walk at regular pace to the line on the floor, turn around at the marker and walk back to the chair and sit down. The time from start to stop was measured [14]. All physical performance tests were done 3 times under supervision of physical therapists. The third performance data was used for statistical analysis.

Biochemical assessment

Blood samples were collected in a non-fasting state and in a sitting position. Serum calcium, phosphorus, albumin were analysed by a fully automatic biochemistry analyser (TBA 120FR®, Canon, Tokyo)

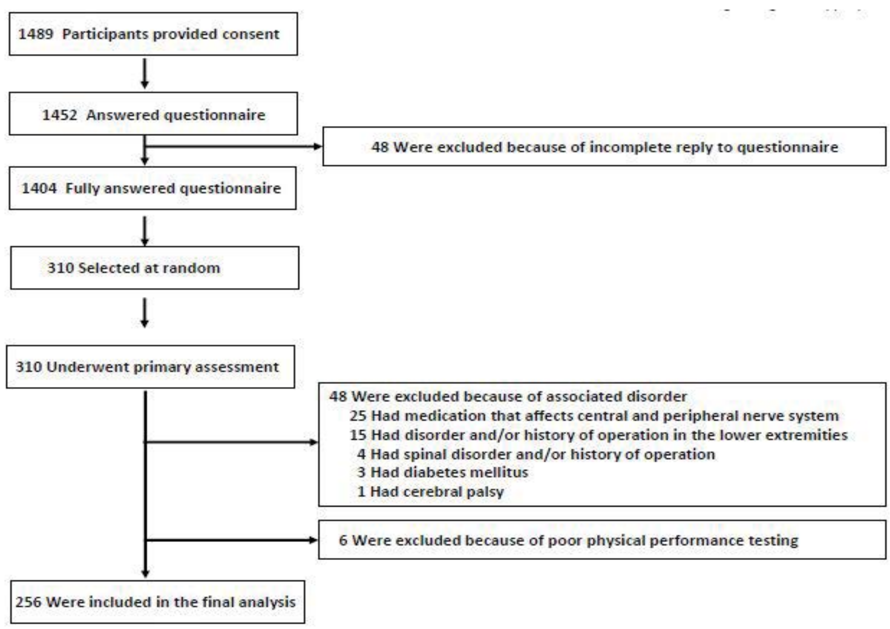

Figure 1: Enrolment and outcome.

Figure 2: Back muscle extensor strength (BMES, kgf) measurement based on the report by Limburg et al. [12].

using commercially available kits. HgA1C was analysed by high performance liquid chromatography. To evaluate metabolic status of the bone, type I procollagen N-terminal propeptide, (total P1NP), and type I collagen cross-linked N-telopeptide (NTx) were measured with electro chemiluminescent immunoassay and enzyme immunoassay, respectively. Blood samples for 25[OH]D (25[OH]D_2, 25[OH]D_3) were temporarily stored at- 20° C, and measured by liquid chromatography-mass spectrometry/mass spectrometry method with an RIT 2 kit® (Dia Sorin, Stillwater, MN, USA). The RIT 2 method is based on an antibody specific to 25[OH] D (the CV was <1%).

Statistical analysis

Associations between 25[OH]D concentrations and all investigated items were statistically analysed (cut-off, p<0.05). The one-way ANOVA test for ordinal data and the chi-square test for nominal data were used. All analysis was performed by the Statistical Package for Bioscience (SPBSware Ver 9.6®) [15].

Results

The basic characteristics of the 256 participants are shown in Table 1. In fall incidence, 8.2% of participants (21/256) experienced it at least once over the previous year. The mean age, BMI, BMD, SMI, male sex, and smoking percentage were 39.4 ± 13.1 (means ± SD) years old, 23.1 ± 3.5 kg/m^2, 1.053 ± 0.093 g/cm^2, 7.4 ± 1.2 kg/m^2, 69.1% (177/256), and 29.7% (76/256), respectively. The mean value of calcium, phosphorus, albumin, HgA1C, total P1NP, and NTx were 9.4 ± 0.4 mg/dl, 3.1 ± 0.6 mg/dl, 4.4 ± 0.3 g/dl, 5.5 ± 0.3%, 46.3 ± 16.9 ng/dl, and 15.3 ± 4.5 nmol BCE/L, respectively. In terms of serum concentrations of 25[OH] D, 25[OH]D_2 were below the limitation of detecting (<4 ng/mL) in all participants. The mean value of the serum 25[OH]D_3 concentrations was 15.6 ± 7.0 ng/ml. The mean value of C7-CSVL and SVA were 8.5 ± 6.6 mm and -1.97 ± 24.5 mm. The mean value of GP was 33.1 ± 9.2 kgf and 31.5 ± 8.7 kgf in the right and the left hand. The mean value of BMES was 387.5 ± 156.3 kgf. The mean value of TUGT and FRT were 6.9 ± 0.8 sec. and 41.9 ± 7.0 cm.

Subgroup Analysis According to Serum 25[OH]D_3: We summarized the serum 25[OH]D_3 levels of these subjects into 3 groups according to NIH proposal [7]. The deficient group was defined as a level of <12.0 ng/ml (30 nmol/L). The inadequate group was defined as a level of 12.0 ng/ml (30 nmol/L) to <20 ng/ml (50 nmo/Ll). The adequate group was defined as a level of ≥ 20ng/ml (50 nmo/Ll). The male percentage in the 3 groups was 63.3% (57/90), 75.5% (74/98), and 67.6% (46/68). The smoking percentage in the 3 groups was 32.2% (29/90), 29.6% (29/98), and 25% (17/68). No significant differences were found in terms of the male and smoking percentage. The mean 25[OH]D_3 of each group was 8.7 ± 2.3, 15.5 ± 2.4, and 24.7 ± 4.8 ng/mL. Percentages of the participants categorized as deficient, inadequate and adequate groups were 35% (90/256), 38% (98/256), and 27% (68/256) respectively. The prevalence of falls in the 3 groups was 8.9% (8/90), 5.1% (5/98), and 11.8% (8/68). No significant difference was found among the prevalence of falls. The mean age of the deficient, inadequate and adequate group was 37.2 ± 12.5, 39.7 ± 13.2 and 42.0 ± 13.4 years old. The mean age in the adequate group was significantly older than the deficient and inadequate groups (p<0.01). As a total result, there were no statistical differences found among the 3 groups in all evaluated items of spinal alignment, bone, muscle status, the physical performance test and biochemical assessment (Table 2).

Discussion

Vitamin D is a kind of essential hormone to maintain normal muscle function *in vitro* although its biochemical mechanism has not been completely unveiled. Vitamin D receptors (VDR) are also expressed in the muscle tissue of the entire human body. The action of vitamin D is affected by allelic variance of the VDR. The main action is directly mediated through 1, 25$(OH)_2D_3$ binding VDR in skeletal muscle tissue. There are numerous articles about biochemical positive function of Vitamin D in the skeletal muscle. Hamilton has summarized both the genomic and non-genomic function of vitamin D in a review article. According to Hamilton, 1, 25$(OH)_2D_3$ binding VDR rapidly regulates membrane calcium channels in the skeletal muscle cells as a non-genetic function. Meanwhile, the binding of 1, 25$(OH)_2D_3$ to VDR results in enhanced protein transcription in the skeletal muscle cells as a genomic function [2]. There is a unique article simultaneously describing biomechanical and histological function of Vitamin D in the skeletal muscle. Miyakoshi et al. has demonstrated that a vitamin D analog (alfacalcidal) had an effect of strengthening muscle tonus as well as bone mineral density in glucocorticoid-treated rats [16]. Furthermore, Endo et al. have demonstrated that normal differentiation of the myocytes

Characteristic	Value
Age	39.4 ± 13.1 years old
BMI	23.1 ± 3.5
BMD	1.053 ± 0.093
SMI	7.4 ± 1.2
Male sex number (%)	177 (69.1)
Smoking number (%)	76 (29.7)
Falls incidence number (%)	21 (8.2)
Laboratory Data	
Calcium (mg/dl)	9.4 ± 0.4
Phosphorus (mg/dl)	3.1 ± 0.6
Albumin (g/dl)	4.4 ± 0.3
HgA1C (%)	5.5 ± 0.3
Total P1NP (ng/dl)	46.3 ± 16.9
NTx (nmol BCE/L)	15.3 ± 4.5
25[OH]D_3 (ng/ml)	15.6 ± 7.0
Spinal Alignment	
C7-CSVL	8.5 ± 6.6
SVA	-1.97 ± 24.5
Physical Performance Test	
GP (Right and Left)	33.1 ± 9.2 and 31.5 ± 8.7
BMES	387.5 ± 156.3
FRT	6.9 ± 0.8
TUGT	41.9 ± 7.0

*Plus-minus values are means ± SD. BMI: Body Mass Index (kg/m^2), BMD: Bone Mineral Density (g/cm^2), SMI: Skeletal Muscle Index (kg/m^2), C7-CSVL: c7-Central Sacral Ventral Line (mm), SVA: C7 Sagittal Vertical Axis (mm), GP: Grip Power (kgf), BMES: Back Muscle Extension Strength (kgf), FRT: Functional Reach Test (cm), TUGT: Timed Up and Go Test (second)

Table 1: Characteristics of the 256 Participants.

was not observed in VDR knockout mice, and as a result, a formation of the small myocytes was observed [17]. Falls are regulated by various intrinsic and extrinsic factors. As for the intrinsic factors, central and peripheral nerve system, visual, vestibular organs, skeletal tissues, and so forth are interacting in a complex form to prevent falls in the human body. Skeletal muscle function is considered as one of the important intrinsic factors that affect falls and its related physical performances. When the function of Vitamin D in the experimental models *in vitro* is positively supported, it is presumed that the influence of Vitamin D would be very crucial to prevent falls and keep the related physical performance well *in vivo*. It is generally recognized that muscle volume and strength is negatively associated with aging. Keller and Engelhardt have clearly demonstrated that muscle strength declined from people ages<40 years to those >40 years between 16.6% and 40.9% although the study was done in a very small number of participants with healthy legs [18]. Moreover, Bischoff-Ferrari et al. concluded that aging was significantly associated with decreased VDR expression, independent of biopsy location and serum 25[OH]D levels in human body [19]. Therefore, serum 25[OH]D would be more significant in the elderly than the non-elderly in regard to falls. Some epidemiological reports have already shown the significance of Vitamin D to maintain physical performances and prevent falls in the elderly population. In 2001, Pfeifer et al. demonstrated that serum 25[OH]D had a negative correlation with trunk sway and fall incidence in 237 postmenopausal women [20]. In 2004, Bischoff-Ferrari et al. demonstrated that lower 25[OH]D concentration (<40 nml/L) are associated with weaker lower-extremity functions in both active and inactive persons aged 60 years and above [21]. Menant et al. also disclosed that the lower serum 25[OH]D was associated with an increased risk of falls in elderly men (aged 70-90 years) [22]. Suzuki et al. also concluded that the lower serum 25[OH] D, cut-off level <20 ng/mL, was associated with an increased risk of falls among 1393 community-dwelling elderly women aged 75 years or older [9].

Although the relationship between vitamin D falls and their related physical performance in the elderly have been recently disclosed, there are very few reports focusing on a role of Vitamin D in falls and their related physical performances in the non-elderly (18-64) years. The current study was performed in non-elderly adults with the mean age of 39.4 ± 13.1 yrs., and has demonstrated that no significant difference was found in fall prevalence, SMI, muscle strength, the related physical performance, and other parameters among deficient serum 25[OH]D_3 [<12.0 ng/ml (30 nmol/L)], inadequate serum 25[OH]D_3 [12.0 ng/ml (30 nmol/L) to <20ng/ml (50 nmo/Ll)] and adequate serum 25[OH] D_3 (≥ 20 ng/ml(50 nmo/Ll)) groups. The current results are completely opposed to the established conclusions of elderly populations. Does Vitamin D play the same role in the non-elderly populations or not? It is speculated that the participants with deficient and inadequate serum 25[OH]D_3 still have enough muscle volume and/or ability to compensate for a low level of serum 25[OH]D status, and as a result, the participants do not easily fall down as the elderly do. Does the status of low serum 25[OH]D (<20 ng/ml (50 nmo/Ll) still remain in subclinical or insignificant conditions in comparison to the elderly population? The current result is pretty controversial. Pfeifer et al. demonstrated that body gravity sway velocity was negatively associated with the level of serum 25[OH]D in the elderly [20]. If body gravity sway is analysed in all participants, similar findings with the elderly might be disclosed. Further biomechanical research is very crucial. Furthermore, it is presumed that the quality of muscle fibers is remarkably different between the non-elderly and the elderly. In 2007, McNeil et al. suggested that age-related reductions in specific strength and power indicated that muscle mass volume alone could not account for the loss of strength and power in the elderly [23]. Nilwik et al. has also demonstrated that reduced muscle mass with aging is mainly attributed to a reduction in type II muscle fiber size and is unlikely accompanied by substantial muscle fiber loss [24]. Also, it could not be denied that rich VDR expression in the muscle tissue still compensates for low serum 25[OH]

Characteristics	25[OH]D<12	12 ≤ 25[OH]D<20	20 ≤ 25[OH]D
25[OH]D_3 (ng/ml)	8.7 ± 2.3	15.5 ± 2.4	24.7 ± 4.8
Participants number (%)	90 (35)	98 (38)	68 (27)
Falls incidence number (%)	8 (8.9)	5 (5.1)	8 (11.8)
Age (years old)	37.2 ± 12.5	39.7 ± 13.2	42.0 ± 13.4*
BMI	22.4 ± 4.4	23.1 ± 3.3	22.3 ± 3.0
BMD	1.053 ± 0.088	1.052 ± 0.099	1.056 ± 0.092
SMI	7.3 ± 1.3	7.6 ± 1.2	7.4 ± 1.1
Male Sex number (%)	57 (63.3)	74 (75.5)	46 (67.6)
Smoking number (%)	29 (32.2)	29 (29.6)	17 (25)
Laboratory Data			
Calcium (mg/dl)	9.3 ± 0.3	9.4 ± 0.4	9.4 ± 0.4
Phosphorus (mg/dl)	3.0 ± 0.5	3.1 ± 0.6	3.2 ± 0.5
Albumin (g/dl)	4.5 ± 0.3	4.3 ± 0.4	4.4 ± 0.3
HgA1C (%)	5.5 ± 0.3	5.6 ± 0.4	5.6 ± 0.3
Total P1NP (ng/dl)	45.1 ± 17.6	47.5 ± 17.3	46.4 ± 15.6
NTx (nmol BCE/L)	14.9 ± 4.2	15.5 ± 4.4	15.7 ± 4.9
Spinal Alignment			
C7-CSVL	8.9 ± 7.5	7.6 ± 5.5	9.1 ± 6.7
SVA	-3.7 ± 23.2	-2.0 ± 25.8	0.4 ± 25.2
Physical Performance Test			
GP Right	32.3 ± 9.2	34.3± 8.6	32.8 ± 10.1
Left	30.4 ± 8.8	32.2± 8.4	32.0 ± 9.1
BMES	380.4 ± 151.2	392.5 ± 156.7	389.6 ± 164.1
FRT	41.9 ± 6.4	42.2 ± 7.1	41.4 ± 7.7
TUGT	7.0 ± 0.8	6.8 ± 0.9	6.8 ± 0.8

*Plus-minus values are means ± SD. BMI: Body Mass Index (kg/m^2), BMD: Bone Mineral Density (g/cm^2), SMI: Skeletal Muscle Index (kg/m^2), C7-CSVL: C7-Central Sacral Ventral Line (mm), SVA: C7 Sagittal Vertical Axis (mm), GP: Grip Power (kgf), BMES: Back Muscle Extension Strength (kgf), FRT: Functional Reach Test (cm), TUGT: Timed Up and Go Test (second), * p<0.01

Table 2: Characteristics of the participants according to NIH vitamin D subgroup.

D status in the non-elderly. In 2010, Priemel et al. demonstrated that pathologic mineralization defects of iliac bone occur in 675 individuals (with 401 males (mean age 58.72 ± 16.99 years) and 274 females (mean age: 68.26 ± 17.27 years)) with a serum 25[OH]D below 75 nmol/L. Their results have suggested a lower 25[OH]D subclinical influence for skeletal health [25]. There is no data whether the participants with low serum 25[OH]D_3 below 20 ng/ml (50 nmo/Ll) are destined to fall down easily and become frail several decades later, but there is a possibility that a similar pathologic change is already present in the muscle tissue of the participants of which a serum 25[OH]D is less than 12 ng/ml or 20 ng/ml. Further discussion and consensus based on the non-biased epidemiological and scientific research are very important.

The current survey was performed in a non-elderly population with the mean age of 41 ± 13 yrs (18-64) in a city at 40° North latitude in Japan. The mean value of the serum 25[OH] D_3 was 15.1 ± 7.0 ng/ml (Male; 15.0 ± 6.8 ng/ml, Female; 13.5 ± 6.4 ng/ml). The mean age of the participants (42.0 ± 13.4 years) in the adequate 25[OH]D_3 group was significantly older than of those (37.0 ± 12.5, 39.7 ± 13.1 years) in the deficient and the inadequate 25[OH]D_3 group ($p<0.01$). The result of this current survey does not match previous reports which demonstrated that Vitamin D status was negatively correlated with aging, but it is very similar to the result of a cross sectional study of 77 young, healthy women, aged 19-66 years in Japan. According to the report, the mean serum 25(OH)D in women younger than 30 years old was 34.0 ± 11.0 nmol/L and significantly lower than that in women 30 years old and older (50.0 ± 14.4 nmol/L), and the proportion of subjects younger than 30 years old who had serum 25(OH)D less than 30 nmol/L was 42.1%, and was significantly higher than the proportion of those 30 years old and older (10.3%) ($p<0.001$). The author has speculated that low fish intake, peculiar dieting, and less outdoor activity are the main reasons of lower serum 25(OH)D in young, healthy Japanese women [26]. There was another cross-sectional study done in North-western Russia. The study showed a high prevalence of Vitamin D insufficiency and deficiency in adults and adolescent population and an association of low serum 25[OH]D level with female gender, obesity and a low fish diet [27]. The current survey was carried out in Odate, a region located at 40° North latitude. The Japan Meteorological Agency reported that Odate has the shortest sunlight duration in Japan (1526.0 hours per year in 2010). The less sunlight exposure in the indoor working field might negatively affect production of 25[OH]D_3 in the non-elderly. A further assessment about the status of serum 25[OH] D of Japanese populations is mandatory to disclose the issue. Influence of low serum 25[OH]D on individual health is a serious concern in developed western countries. In the United States, NIH, World Health Organization, Institute of Medicine, Centre for Disease Control and other organizations have suggested variable kinds of risks caused by lack of Vitamin D. Especially, NIH has clearly proposed a guideline for the serum 25[OH] for bone and overall health [7]. In the current survey, the mean value of the serum 25[OH]D_3 of the participants is defined as being 'inadequate' according to the NIH proposal. If a cut-off value of 20 ng/mL (50 nmol/L) is adopted, 73% of the participants (188/256) are categorized into the insufficient status of serum 25[OH] D. Dawson-Hughes et al. have reported that 90% of Japanese and Korean populations have serum 25[OH]D concentrations below 30ng/mL (75 nmol/L) of which this level is defined as an elderly threshold level for falls [28]. If a cut-off value of 30 ng/mL (50 nmol/L) is adapted for fall risk in the non-elderly as well, 98% of the participants (251/256) in the current survey would be categorized into the high risk group for falls. In the current survey, totally, 8.2% of participants (21/256) have experienced falls over the previous year. It is a fact that Asian populations easily fall down in comparison to Caucasians. Aoyagi et al. reported that the proportion of falls in the previous year after age standardization for Japanese (65 years and over) was about twice as high for Caucasians in 1998 [29]. But it is pretty controversial that the 25[OH]D guideline for falls mentioned above are also pragmatic for young Japanese population without osteoporosis and/or sarcopenia. There is a possibility of ethnic and age-related difference in Vitamin D function for falls and physical performance. It seems to be beneficial that a racial and age-related difference of serum 25[OH]D status should be reconsidered to establish the consensus for fall prevention in whole–spectrum age populations [30,31]. In regards to the supplementation of Vitamin D, the validity is much more controversial. Broe et al. reported that a dose of vitamin D (800 IU/day) supplementation dramatically reduced the risk of falls of nursing home residents [32]. Preifer et al. strongly argued that in conjunction with a sufficient calcium intake, the dose of vitamin D supplementation should ensure that circulating levels of 25(OH)D reach this minimum threshold (75 nmol/L or 30 ng/mL) to maintain skeletal health [20]. Whereas, there is a report that proves no efficacy of the vitamin D supplementation, Khaw et al. have reported that high-dose bolus vitamin D supplementation of 100 000 IU colecalciferol monthly over 2.5-4.2 years did not prevent falls or fractures in this healthy, ambulatory, adult population [33,34]. As far as fall risk is concerned, is it really necessary for non-elderly, healthy individuals to mandatorily check Vitamin D status and take the Vitamin D supplementation when they have low serum 25[OH]D below 30 ng/mL (75 nmol/L)? Further research is also needed to ascertain the effects of daily Vitamin D dosing with or without calcium for fall prevention.

Conclusion and Limitation

This study is a unique survey describing the relationships between falls, their related physical performance, and Vitamin D status in the non-elderly (18-64 yrs). However, limitations to the current study should also be noted. First, the survey was done for duration of 1 year due to limited capacity of our institute to evaluate 256 participants. Therefore, it could not be denied that a seasonal change of 25[OH]D_3 concentrations effects on fall incidence and its related physical performance in each participant. Second, bias or inaccuracy about recall of falls in the previous year of the participants, could not be completely excluded through the current interview technique although the interviewers had had no information of the 25[OH]D_3 status of the participants before the interview. Uncertainty of the definition about falls should also be acknowledged. Third, the survey is absolutely cross-sectional. There is no data in regard to the period of the deficient, inadequate serum 25[OH]D_3 or adequate serum 25[OH]D_3 status of the participants in the past and future. A longitudinal influence of lower serum 25[OH]D_3 could not be discussed from the view point of the current results.

Ethics

This survey was approved by the ethics committee of our institute on 7 August 2015 according to the 1964 Helsinki Declaration. The approval number was 32 in our institute. All patients were asked to give their consent to participate in the current survey. On completion, the survey team will submit the current results for publication in a peer-reviewed scientific journal.

Contributors

NM was a co-investigator and involved in the design of the current survey protocol. KT played a key role of the statistical analysis of the current data. TK was one of the main investigators who had checked the physical findings of the participants. YS orchestrated the whole project of the current survey and contributed to draft the manuscript. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the current survey.

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