Clinical and Translational Science

ARTICLE OPEN ACCESS

Vitamin D Supplementation Improves Muscle Mass, Physical Function, and Quality of Life in Patients With Degenerative Lumbar Disease

Sinsuda Dechsupa[1] | Wicharn Yingsakmongkol[2] | Worawat Limthongkul[2] | Weerasak Singhatanadgige[2] | Suvichada Assawakosri[1,3] | Sittisak Honsawek[1]

[1]Center of Excellence in Osteoarthritis and Musculoskeleton, Department of Biochemistry, Faculty of Medicine, King Chulalongkorn Memorial Hospital, Chulalongkorn University, Bangkok, Thailand | [2]Center of Excellence in Biomechanics and Innovative Spine Surgery, Department of Orthopaedics, Faculty of Medicine, King Chulalongkorn Memorial Hospital, Chulalongkorn University, Bangkok, Thailand | [3]Department of Pharmacology, Faculty of Science, Mahidol University, Bangkok, Thailand

Correspondence: Sittisak Honsawek (sittisak.h@chula.ac.th)

Received: 18 April 2025 | **Revised:** 25 June 2025 | **Accepted:** 21 July 2025

Funding: This work was supported by Ratchadaphisek Somphot Fund, the Center of Excellence in Osteoarthritis and Musculoskeleton (CE67_113_3000_042), Thailand Science Research and Innovation Fund Chulalongkorn University (HEA_FF_68_088_3000_014), and the Second Century Fund (C2F), Chulalongkorn University.

Keywords: degenerative lumbar disease | muscle strength | physical performance | vitamin D_2 supplementation

ABSTRACT

Degenerative lumbar disease is a significant contributor to acute or chronic musculoskeletal issues in the elderly, often associated with low serum 25-hydroxyvitamin D (25(OH)D) levels. The effect of vitamin D_2 supplementation on muscle mass, strength, and physical performance remains unclear. This study aimed to determine the effect of vitamin D_2 supplementation on these parameters in patients with degenerative lumbar disease and low vitamin D status. A total of 115 patients with serum 25(OH)D levels < 30 ng/mL were administered 40,000 IU of vitamin D_2 (ergocalciferol) weekly for 6 months. Body composition, serum 25(OH)D, parathyroid hormone (PTH) levels, muscle strength, and physical performance were examined before and after 6 months of vitamin D_2 supplementation. Baseline median serum 25(OH)D was 24.9 ng/mL; 79.1% had vitamin D insufficiency, and 20.9% had vitamin D deficiency. After supplementation, median 25(OH)D increased to 43.1 ng/mL ($p < 0.001$), with a significant reduction in PTH ($p < 0.001$). Significant improvements were observed in muscle mass ($p = 0.04$), balance test ($p = 0.01$), gait speed ($p = 0.009$), chair stand test ($p < 0.001$), short physical performance ($p < 0.001$), Oswestry disability index ($p < 0.001$), and visual analog scale (VAS) scores ($p < 0.001$). Post-supplementation 25(OH)D levels correlated negatively with body mass index ($\rho = -0.187$, $p = 0.045$), fat mass ($\rho = -0.219$, $p = 0.019$), fat percentage ($\rho = -0.199$, $p = 0.033$), and VAS score ($\rho = -0.313$, $p < 0.001$). Six months of vitamin D_2 supplementation significantly improved vitamin D status, muscle mass, physical performance, and quality of life in patients with degenerative lumbar disease.

Abbreviations: 1, 25 (OH)D, 1, 25-dihydroxyvitamin D; 25(OH)D, 25- hydroxyvitamin D; ASM, appendicular skeletal muscle mass; BIA, bioelectrical impedance analysis; BMI, body mass index; EQ-5D-5L, EuroQol-5 dimension-5 level; IQR, interquartile ranges; IU, international units; LDD, lumbar disc degeneration; LDH, lumbar disc herniation; LSS, lumbar spinal stenosis; ODI, Oswestry Disability Index; PTH, parathyroid hormone; SD, standard deviation; SMI, skeletal muscle index; SPPB, Short Physical Performance Battery; SPSS, Statistics Package for Social Science; TUG, Timed Up and Go; VAS, Visual Analog Scale; VDR, vitamin D receptor; WC, waist circumference.

Study Highlights

- What is the current knowledge on the topic?
  - Vitamin D deficiency is highly prevalent among older adults and has been implicated in the pathophysiology of degenerative lumbar disease. Previous studies have demonstrated that vitamin D supplementation can improve musculoskeletal health, reduce the risk of falls, and alleviate pain.
- What question did this study address?
  - This study aimed to evaluate whether vitamin D_2 supplementation improves muscle mass, muscle strength, physical performance, and quality of life in patients with degenerative lumbar disease and low vitamin D status. It also examined the association between serum 25(OH)D levels and body composition, pain intensity, and functional outcomes.
- What does this study add to our knowledge?
  - Vitamin D_2 supplementation improves serum 25(OH)D levels and reduces PTH concentrations. It also leads to statistically significant improvements in body composition (reduced fat mass and waist circumference), muscle mass, physical performance, and quality of life.
- How might this change clinical pharmacology or translational science?
  - This study underscores the clinical relevance of vitamin D_2 as a viable therapeutic agent for improving musculoskeletal health and physical function in patients with degenerative lumbar disease. Given its cost-effectiveness and availability, especially in settings where ergocalciferol is the standard form of supplementation, vitamin D_2 could serve as a practical intervention to alleviate disability, reduce pain, and enhance quality of life in older adults. These findings may influence treatment guidelines and support broader implementation of vitamin D_2 supplementation in musculoskeletal and rehabilitation medicine.

1 | Introduction

Degenerative lumbar disease is one of the leading causes of both acute and chronic musculoskeletal disorders worldwide, affecting individuals across the lifespan, especially adolescents and older adults. It is estimated that around 80% of adults will experience low back pain at some point in their lives [1]. The primary causes of degenerative lumbar disease include conditions such as lumbar spinal stenosis (LSS), lumbar disc degeneration (LDD), and lumbar disc herniation (LDH). Symptoms commonly associated with these degenerative changes include low back pain, difficulty walking, and reduced muscle content [2]. The progression of these conditions is influenced by various factors, including aging, gender, mechanical stress, environmental factors, and inadequate vitamin D levels. These factors are believed to contribute a significant role in the development of degenerative lumbar conditions [3, 4].

Vitamin D is a fat-soluble steroid that exists in various forms, including through ultraviolet light exposure, dietary intake, and supplements. It plays a crucial role in regulating calcium deposition in bones and supporting bone metabolism [5, 6]. The activity of human skeletal muscle precursor cells is influenced by the binding of 1, 25-dihydroxyvitamin D (1, 25 (OH)D), also known as calcitriol, the active form of vitamin D, to the vitamin D receptor (VDR). This interaction regulates calcium channel activation via both direct and indirect pathways [7, 8]. Vitamin D deficiency, which tends to increase with age, affects approximately 70% of older individuals in both Asian and Caucasian populations [9]. Zolfaghari et al. reported that vitamin D insufficiency and deficiency are common among patients with lumbar spinal stenosis (LSS), with a prevalence rate of 29% in this population [10]. Kim et al. reported that patients with preoperative LSS exhibited low vitamin D levels [11]. Therefore, evidence from previous studies suggests that vitamin D deficiency may be linked to bone and musculoskeletal diseases, including LSS.

Vitamin D supplementation is a therapeutic approach for managing vitamin D deficiency in older adults. It contributes to bone mineralization and improves muscle strength [12]. Numerous studies have demonstrated that vitamin D supplementation enhances serum 25-hydroxyvitamin D (25(OH)D) levels, improves muscle function and physical activity, and reduces the risk of falls in older adults with vitamin D insufficiency and deficiency [13, 14]. In addition, a prior study demonstrated that increased vitamin D levels following surgery were associated with reduced pain, as indicated by the Oswestry Disability Index (ODI) and health-related quality of life assessments [11]. Additionally, the study suggested that vitamin D supplementation elevated serum 25(OH)D concentrations, leading to a reduction in pain severity and an improvement in physical function [15].

Although both vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol) are available as over-the-counter dietary supplements without a prescription, according to the National List of Essential Medicines in Thailand, ergocalciferol is utilized as the first-line treatment for vitamin D deficiency in public health services and hospitals across the country [16]. However, the effect of vitamin D_2 (ergocalciferol) supplementation on muscle strength and physical performance in patients with degenerative lumbar disease is still unclear. Hence, the objectives of the current study were to examine its role in enhancing muscle strength and physical performance in degenerative lumbar disease patients and explore the association between body composition, muscle strength, and physical performance in these patients. We hypothesize that vitamin D supplementation could offer valuable clinical insights for the treatment or prevention of physical impairment in those patients.

2 | Materials and Methods

2.1 | Study Design and Participants

This prospective cohort study was conducted at the outpatient clinic of the Department of Orthopaedics at King Chulalongkorn Memorial Hospital from January to December 2023. This study was approved by the Institutional Review Board of Faculty of

Medicine, Chulalongkorn University (IRB No. 427/65). This study follows the principles of the Declaration of Helsinki (COA No. 1685/2022). All patients who are participants in this study provided informed consent.

Three hundred and sixty-nine patients aged 50–80 years who were diagnosed with degenerative lumbar disease consented to participate. The inclusion criteria were that participants had symptomatic degenerative lumbar disease (i.e., LSS, LDD, and LDH), a positive response to conservative medical treatment, and low vitamin D levels (25(OH)D < 30 ng/mL). The diagnosis is based primarily on patient history and physical examination. The exclusion criteria encompassed a history of spinal surgery, primary hyperparathyroidism, steroid injections, liver disease, metabolic bone disorders, prior use of drugs affacted vitamin D metabolism, vitamin D_3 analogues (i.e., anticonvulsant and anti-tuberculosis medication), or declined physical capability (patients who impaired to perform physical performance).

One hundred and fifty patients fulfilled the study criteria and were included. Thirty-five of the enrolled patients were excluded from the final analysis due to loss to follow-up. We assessed 115 degenerative lumbar disease patients who completed the study protocol (Figure 1).

2.2 | Interventions

The Endocrine Society guidelines recommend administering 50,000 international units (IU) of vitamin D_2 weekly for 8 weeks to consistently achieve serum 25(OH)D levels reaching 30 ng/mL in adults [17]. In Thailand, the sole commercial formulation of vitamin D_2 (ergocalciferol) is described as 20,000 IU per capsule. Consequently, each patient was given the instructions to take 40,000 IU of vitamin D_2 (two capsules of 20,000 IU ergocalciferol; the British Dispensary, Bangkok, Thailand) weekly for 6 months to investigate the effect of vitamin D_2 supplementation on muscle mass, muscle strength, and physical performance.

2.3 | General Information

The medical history of participants was acquired through interviews. All participants were assessed for back and leg pain using the Visual Analog Scale (VAS) score instrument. The scale presents an ordinal range of scores from 0 to 10. A higher score signifies more pain intensity. The participants were instructed to express their current pain intensity by marking a line.

Pain and functional disability were assessed using the Thai version of the Oswestry Disability Index (ODI) questionnaire (version 1.0), which is recommended for evaluating spinal disorders [18]. The questionnaire consists of 10 items, each with 6 response options, covering the following domains: pain intensity, personal care, lifting, walking, sitting, standing, sleeping, sexual activity, social life, and traveling. Each item is scored on a scale from 0 to 5, with the total score converted to a percentage out of 100 [11, 18]. In this study, ODI scores were categorized into three levels: mild disability (0–40), moderate disability (41–60), and severe disability (61–100). Higher scores indicate greater pain intensity and functional impairment.

The health-related quality of life was assessed using the Thai version of the EuroQol-5 dimension-5 level (EQ-5D-5L) questionnaire, comprising mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The questionnaire is

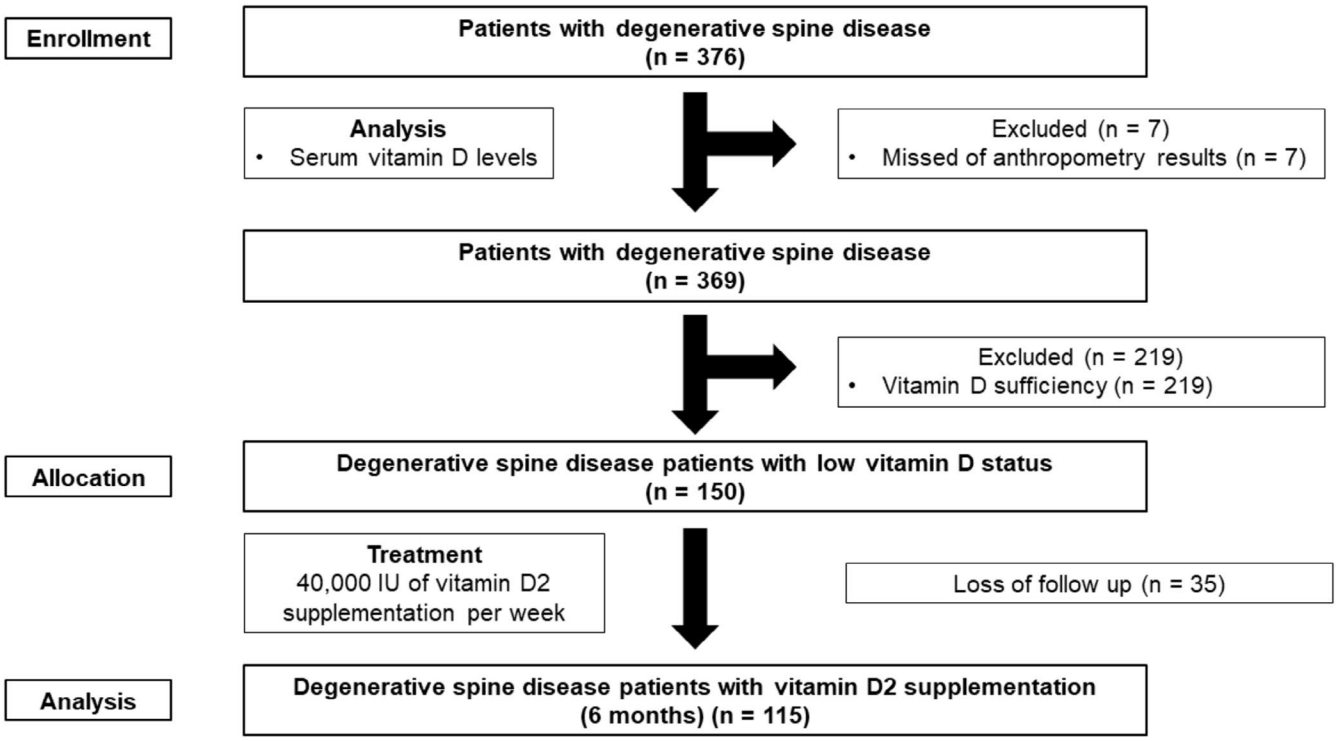

FIGURE 1 | Flowchart of study protocol.

evaluated on a five-point scale ranging from no problems to extreme problems [19].

2.4 | Anthropometric and Body Composition Measurements

Weight and height were assessed using standard measurements. Body mass index (BMI) was calculated by dividing weight (kg) by the square of the height (m^2). Waist circumference (WC) was measured at the midpoint between the lower ribs and the upper hips with the arms relaxed at the sides, using a measuring tape.

Muscle mass, appendicular skeletal muscle mass (ASM), percentage of fat mass, and fat mass were evaluated using bioelectrical impedance analysis (BIA) (BC-418 Segmental Body Composition Analyzer; Tanita Corporation, Tokyo, Japan). BIA was used to estimate muscle mass (kg) using an equation that incorporates height, electrical resistance, gender, and age. The formula applied was: muscle mass (kg) = [(height^2/resistance $\times 0.401$) + (3825 × gender) + (age $\times -0.071$)] + 5.102, where height is measured in centimeters, resistance (R) in ohms, gender is coded as 0 for males and 1 for females, and age is in years. ASM was determined by summing the skeletal muscle mass of the arms and legs in kilograms. The skeletal muscle index (SMI) was calculated as the percentage of ASM divided by body weight (%).

2.5 | Muscle Strength and Physical Performance

Muscle strength and physical performance were examined by physical therapists at baseline and after 6 months. Handgrip strength was evaluated using a handgrip dynamometer (kg) (Takei Scientific Instruments Co. Ltd., Tokyo, Japan), which is the most widely used instrument.

Short Physical Performance Battery (SPPB) was employed to determine physical performance. It comprised three assessments. The first test was a four-meter gaited speed test, which measures the time twice and calculates the average time. The second test was a balance test, which evaluates body balance without using the support of a walker or cane, using three standing positions: (i) a side-by-side stand (stand with feet together), (ii) a semi-tandem stand (stand with the side of the heel of one foot touching the big toe of the other foot), and (iii) a tandem stand (stand with the heel of one foot positioned in front of and touching the toes of the other foot) for 10 s. The final test was the chair stand test, which measured the time in seconds taken to rise from a chair at stand height five times as fast as possible while crossing the arms over the chest. Each of the three tests is scored on a scale from 0 to 4 points, with a higher score indicating better performance, resulting in a total score of 0 to 12 points [20].

Additionally, patients were evaluated using the Timed Up and Go test (TUG), which determined the time required to stand up from a chair, walk three meters, turn around, walk back, and sit on the chair (sec).

2.6 | Hydroxyvitamin D and Parathyroid Hormone Measurements

Fasted early morning venous blood samples were obtained from patients both at baseline and after 6 months of vitamin D_2 supplementation. The blood was drawn by trained clinical staff according to standard protocols, using serum tubes with gel to allow for coagulation. The samples were then centrifuged at 4000 rpm for 10 min at room temperature to separate the serum and plasma. The serum was transferred to centrifuge tubes and stored at −80°C until further analysis. All samples were anonymized using an ID-log that linked participants to their biological samples. Serum concentrations of 25(OH)D were determined using a chemiluminescent immunoassay (DiaSorin Inc., Stillwater, MN, USA). Vitamin D deficiency was defined as a serum concentration of <20 ng/mL, insufficiency as $20-<30$ ng/mL, and vitamin D sufficiency as ≥ 30 ng/mL. Parathyroid hormone (PTH) levels were analyzed using an electrochemiluminescence method (Roche Diagnostic GmbH, Mannheim, Germany).

2.7 | Statistical Analysis

Data were analyzed using the Statistics Package for Social Science (SPSS) software, version 22.0 for Windows (SPSS Inc., Chicago, IL, USA). Figures were generated using GraphPad Prism version 9.0 (GraphPad software, San Diego, CA, USA). The demographic category data of patients was analyzed by Chi-squared test. While the quantitative variable was analyzed by paired *t*-test and Wilcoxon signed-rank test where appropriate, comparing baseline and after 6 months of vitamin D_2 supplementation. The comparison of pre- and post-vitamin D_2 supplementation data was conducted using paired *t*-test or Wilcoxon signed-rank test. The data were presented as *n* (%), mean ± standard deviation (SD), or median (interquartile ranges (IQR)). Spearman's rank correlation coefficient test was used to examine the association between serum 25(OH)D levels, body composition, muscle mass, muscle strength, and physical performance. A *p*-value less than 0.05 was used to determine statistical significance for differences and correlations.

3 | Results

A total of 376 participants were initially screened at the outpatient clinic of the Department of Orthopaedics at King Chulalongkorn Memorial Hospital. Of these, 369 participants were invited for a clinical screening visit (Figure 1), provided consent, and completed a clinical screening visit. Among them, 150 participants satisfied all eligibility criteria. However, 35 participants lost follow-up, resulting in 115 participants in the vitamin D insufficiency and deficiency group who completed the study.

At baseline, participants had a mean age of 63.2 ± 9.6 years; 71.3% were female, and 28.7% were male. No significant differences were observed between participants before and after

vitamin D_2 supplementation in terms of age, gender, weight, BMI, ASM, and SMI.

3.1 | Effects on Body Composition, Pain, and Quality of Life

After receiving vitamin D_2 supplementation, there were significant reductions in WC, percentage of fat mass, and fat mass, while muscle mass demonstrated a significant increase compared to before supplementation ($p < 0.05$) (Table 1). Additionally, both VAS and ODI scores significantly decreased after vitamin D_2 treatment ($p < 0.001$ for both), indicating improvements in pain and disability. The EQ-5D-5L, reflecting quality of life, also showed significant improvement post-supplementation ($p < 0.001$).

3.2 | Effects on Vitamin D and PTH Status

At baseline, the median serum 25(OH)D level in individuals with degenerative lumbar disease was 24.9 (20.9–27.4) ng/mL. Among the participants, 24 (20.9%) were classified as vitamin D deficiency, while 91 patients (79.1%) had vitamin D insufficiency. Following 6 months of weekly supplementation with 40,000 IU of vitamin D_2, there was a statistically significant increase in the median serum 25(OH)D level. A total of 98 participants (85.2%) exhibited serum 25(OH)D concentrations exceeding 30 ng/mL which reached 43.1 (33.9–56.0) ng/mL ($p < 0.001$), whereas 17 individuals (14.8%) demonstrated vitamin D insufficiency, as detailed in Table 1. Furthermore, plasma PTH levels showed a significant decrease ($p < 0.001$) following the supplementation.

TABLE 1 | Demographic data degenerative lumbar disease patients before and after vitamin D_2 supplementation for 6 months.

	Vitamin D_2 supplementation ($N = 115$)		
Variables	**Before supplementation**	**After 6 months**	***p***
Age (years)	63.2 ± 9.6	63.2 ± 9.6	
Gender; *n* (%)			
Females	82 (71.3)	82 (71.3)	
Males	33 (28.7)	33 (28.7)	
Body composition			
Weight (kg)	60.8 (56.1–70.2)	61.0 (55.7–71.0)	0.87
BMI (kg/m^2)	25.0 ± 3.9	25.1 ± 4.0	0.44
WC (cm)	87.8 ± 11.6	84.7 ± 11.7	**< 0.001**[a]
Muscle mass (kg)	22.1 (19.0–26.3)	22.3 (19.9–26.0)	**0.04**[b]
Percentage of fat mass (%)	33.4 (27.1–38.8)	32.8 (25.6–37.9)	**0.03**[b]
Fat mass (kg)	21.4 (16.6–24.7)	20.1 (15.7–24.5)	**0.02**[b]
ASM (kg)	16.7 (15.4–19.8)	16.4 (15.3–20.0)	0.07
SMI (%)	27.8 ± 3.6	27.6 ± 3.6	0.15
VAS (0–10)	5.0 (3.0–7.0)	3.0 (1.0–6.0)	**< 0.001**[b]
ODI score	24.0 (16.0–32.0)	14.0 (8.0–22.0)	**< 0.001**[b]
Mild disability, *n* (%)	99 (86.1)	111 (96.5)	
Moderate disability, *n* (%)	16 (13.9)	3 (2.6)	
Severe disability, *n* (%)	0 (0)	1 (0.9)	
EQ-5D-5L	0.74 (0.54–0.84)	0.80 (0.65–0.89)	**< 0.001**[b]
Biochemical markers			
Serum 25(OH)D (ng/mL)	24.9 (20.9–27.4)	43.1 (33.9–56.0)	**< 0.001**[b]
PTH (pg/mL)	40.2 (29.0–50.6)	34.4 (37.6–46.3)	**< 0.001**[b]
SPPB (points)	10.0 (9.0–12.0)	11.0 (10.0–12.0)	**< 0.001**[b]

Note: Values are reported as mean ± standard deviation (SD) and medians (interquartile range; IQR). Significant results are shown in bold. $p < 0.05$ before vs. after 6 months.

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; ASM, appendicular skeletal muscle mass index; BMI, body mass index; EQ-5D-5L, EuroQol-5 dimensions-5 level; ODI, Oswestry disability index; PTH, parathyroid hormone; SMI, skeletal muscle index; SPPB, short physical performance battery; VAS, Visual analogue scale; WC, waist circumference.

[a]Paired *t*-test.

[b]Wilcoxon signed-rank test.

TABLE 2 | Muscle strength and physical performance at baseline and after supplementation with vitamin D_2.

Variables	Vitamin D_2 supplementation ($N=115$)		
	Before supplementation	After 6 months	*p*
Grip strength			
Dominant (kg)	21.5 (17.2–26.3)	22.6 (18.0–27.8)	0.06
Physical performance			
Balance test (points)	3.5 (3.2–3.6)	4.0 (4.0–4.0)	**0.01**
Gait speed (s)	3.5 (2.9–4.2)	3.3 (2.8–3.9)	**0.009**
Chair stand test (s)	13.2 (10.5–17.7)	11.7 (9.3–14.4)	**<0.001**
TUG (s)	7.1 (6.0–9.2)	6.8 (5.8–8.6)	0.08

Note: Values are reported as medians (interquartile range; IQR). Significant results are shown in bold. $p<0.05$ before supplementation vs. after 6 months. Results were determined using the Wilcoxon signed-rank test.
Abbreviation: TUG, timed up and go.

3.3 | Effects on Muscle Strength and Physical Performance

Administration of vitamin D_2 supplementation resulted in significant improvements in overall physical performance, including better outcomes in the balance test ($p=0.01$), gait speed ($p=0.009$), chair stand test ($p<0.001$), and SPPB score ($p<0.001$). However, there were no significant differences observed for dominant grip strength and TUG test before and after supplementation ($p>0.05$), as reported in Table 2.

3.4 | Association of Serum 25(OH)D, Body Composition, and Pain Intensity

As illustrated in Table 3, our results indicate a significant negative correlation between serum 25(OH)D level and BMI ($\rho=-0.187$, $p=0.045$), fat mass ($\rho=-0.219$, $p=0.019$), percentage of fat mass ($\rho=-0.199$, $p=0.033$), and VAS ($\rho=-0.313$, $p<0.001$) in patients with degenerative lumbar disease following vitamin D_2 supplementation (Figure 2). However, no significant changes were observed in muscle strength or physical performance, as the correlation between serum 25(OH)D levels and these parameters did not differ significantly before and after supplementation ($p>0.05$).

4 | Discussion

Degenerative lumbar disease is a frequent source of acute or chronic spinal issues, contributing to various musculoskeletal disorders. Vitamin D deficiency has been implicated in the pathogenesis of these degenerative lumbar conditions. The aims of this study were to evaluate the effect of vitamin D_2 supplementation (ergocalciferol) on muscle mass, physical performance, and quality of life in patients with degenerative lumbar disease and low vitamin D levels, as well as to explore the relationship between body composition, muscle strength, and physical

TABLE 3 | Correlation between serum 25(OH)D after vitamin D_2 supplementation and different parameters ($n=115$).

Variables	ρ	*p*	95% CI
Age (years)	0.181	0.053	(−0.008 to 0.357)
Weight (kg)	−0.180	0.054	(−0.357 to 0.008)
BMI (kg/m^2)	−0.187	**0.045**	(−0.363 to 0.001)
WC (cm)	−0.128	0.173	(−0.309 to 0.062)
Muscle mass (kg)	−0.081	0.389	(−0.265 to 0.109)
Fat mass (kg)	−0.219	**0.019**	(−0.391 to −0.032)
Percentage of fat mass (%)	−0.199	**0.033**	(−0.373 to −0.011)
ASM (kg)	−0.113	0.229	(−0.295 to 0.077)
SMI (%)	0.134	0.153	(−0.056 to 0.315)
VAS	−0.313	**<0.001**	(−0.474 to −0.132)
ODI score	−0.151	0.107	(−0.330 to 0.039)
EQ-5D-5L	0.077	0.415	(−0.113 to 0.261)
PTH (pg/mL)	−0.105	0.264	(−0.288 to 0.085)
Grip strength (kg)	0.088	0.348	(−0.102 to 0.272)
Balance test (points)	0.074	0.429	(−0.116 to 0.259)
Gait speed (s)	0.021	0.824	(−0.168 to 0.209)
Chair stand test (s)	−0.055	0.560	(−0.241 to 0.135)
TUG test (s)	−0.018	0.852	(−0.205 to 0.171)
SPPB (points)	0.084	0.375	(−0.107 to 0.268)

Note: Statistically significant at $p<0.05$.
Abbreviations: ρ, Spearman's rho; 25(OH)D, 25-hydroxyvitamin D; ASM, appendicular skeletal mass; BMI, body mass index; EQ-5D-5L, EuroQol-5 dimensions-5 level; ODI, Oswestry Disability Index; PTH, parathyroid hormone; SMI, skeletal mass index; SPPB, short physical performance battery; TUG, timed up and go; VAS, visual analog scale; WC, waist circumference.

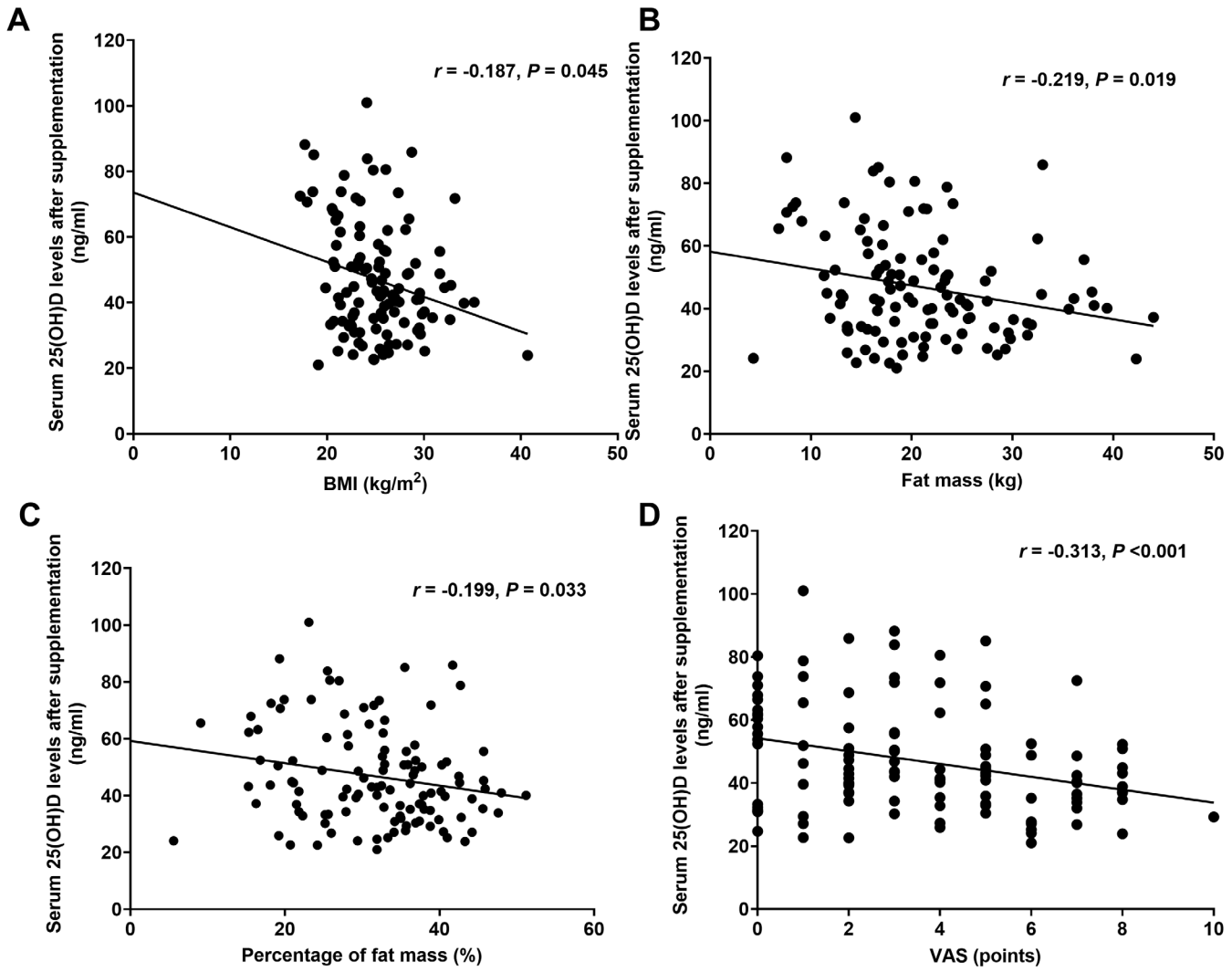

FIGURE 2 | The negative correlation between serum 25(OH)D levels, body composition, and pain score in patients after vitamin D_2 supplementation; (A) BMI, (B) fat mass, (C) percentage of body fat, and (D) VAS. *r*: Spearman's coefficient; statistically significant at $p < 0.05$.

performance. The findings indicated that while vitamin D_2 supplementation enhanced physical performance and overall quality of life in these patients, it did not result in improvements in muscle strength.

Following 6 months of supplementation with 40,000 IU of vitamin D_2 per week, 85.2% of patients reached sufficient levels of vitamin D, while 14.8% remained insufficient. In general, vitamin D_2 (ergocalciferol), which is primarily derived from plants or plant-based sources, differs from vitamin D_3 (cholecalciferol), which is produced by animals through diet and sunlight exposure [21]. Both ergocalciferol and cholecalciferol are employed in the treatment of vitamin D insufficiency and deficiency. Although some studies suggested that dosage equivalency between vitamin D_2 and D_3 may vary, it is likely that vitamin D_2 is prescribed at a sufficiently high dose relative to body weight to ensure proper bone mineral metabolism [22].

Our study found that PTH levels were significantly lower in the group after vitamin D_2 supplementation compared to the baseline group. This finding aligns with the research by Thimachai et al., which revealed that PTH levels significantly decreased in the patients with chronic kidney disease stages III–IV who received high-dose ergocalciferol (50,000 IU per week) for 8 weeks [23]. A previous study has established a link between low vitamin D levels and increased bone turnover. This is because long-term vitamin D deficiency contributes to higher PTH levels, which subsequently enhances the risk of falls, fractures, and frailty [3]. PTH activation enhances the differentiation of pro-osteoclasts into mature osteoclasts, thereby promoting bone turnover [4]. Maintaining adequate vitamin D levels may help lower PTH levels and reduce the bone turnover rate, thereby decreasing the risk of fractures, falls, and declines in physical function.

After supplementation with vitamin D_2, there was a notable reduction in body composition and anthropometric parameters, including WC, fat mass, and body fat percentage. Additionally, muscle mass showed a significant increase following the six-month intervention. This could partially be explained by the fact that VDR plays a key role in regulating gene expression across multiple human tissues and cell types, including skeletal muscle cells. Upon binding with the active form of vitamin D, the VDR forms a heterodimeric complex with the retinoid-X-receptor

within the nucleus. This complex subsequently translocates and activates the vitamin D response element, thereby enhancing the transcription of genes associated with muscle cell proliferation, differentiation, and the production of calcium-binding proteins [7, 24]. Following the administration of vitamin D_2, we observed a mild negative correlation between serum 25(OH)D levels and BMI, fat mass, and body fat percentage after the administration of vitamin D_2. In line with our findings, Manoy et al. [13] reported a significant decrease in fat mass and body fat percentage in knee osteoarthritis patients receiving 40,000 IU of vitamin D_2 weekly for 6 months. The results of our study further suggest that participants may have experienced improvements in their lifestyle, along with notable gains in physical function, as reflected by a reduction in the ODI score and an increase in the EQ-5D-5L score.

The findings from VAS, ODI, and EQ-5D-5L scores indicated that self-reported pain and functional outcomes improved following vitamin D_2 supplementation. Furthermore, we observed a slight negative correlation between serum 25(OH)D levels and the VAS score after vitamin D_2 administration. This aligns with the results of two studies, which reported a significant reduction in VAS scores following a 10-day supplementation of 60,000 IU of vitamin D_3 in patients with mechanical low back pain [25]. Additionally, Sandoughi et al. demonstrated that patients with nonspecific chronic low back pain who received 50,000 IU of vitamin D_3 per week for 8 weeks experienced a significant reduction in VAS scores compared to baseline values [26]. These findings suggest that vitamin D supplementation provides effective pain relief and functional improvement without notable adverse effects. The influence of vitamin D on pain pathways is attributed to the expression of VDR and enzymes that regulate vitamin D activity in tissues involved in pain modulation, such as the skin, dorsal root ganglia, and spinal cord [27]. A previous in vitro study highlighted that vitamin D could suppress the production of prostaglandin E2, a molecule involved in proinflammatory signaling [28]. Moreover, 1,25-$(OH)_2D_3$ has been shown to reduce inflammation in macrophage by enhancing the synthesis of interleukin-10 and decreasing inflammatory cytokines [29]. In summary, vitamin D supplementation appears to effectively alleviate pain by attenuating inflammatory signaling and reducing pain sensitivity in patients with degenerative lumbar disease.

Six months of weekly supplementation with 40,000 IU of vitamin D_2 resulted in significant improvements in various clinical physical performance measures, including the balance test, gait speed test, chair stand test, and SPPB score. However, no changes were observed in grip strength when compared to baseline values. These results are consistent with those of Bentes et al. who reported that 3 months of daily supplementation with 1000 IU of vitamin D_3 significantly enhanced performance on the 30-s chair stand test in postmenopausal women with type 2 diabetes [30]. It was suggested that vitamin D supplementation increased 25(OH)D levels, leading to enhanced physical performance. One potential mechanism is that the active form of vitamin D, 1,25(OH)D, plays a crucial role in skeletal muscle function. It regulates the mitogen-activated protein kinase signaling pathway and affects the expression of several genes. Through interaction with the VDR, 1,25(OH)D treatment boosts VDR activation, thereby promoting protein synthesis in skeletal muscle and preventing the atrophy of type 2 muscle fibers [31, 32].

The primary strength of this study is its particular contribution, as it is the first to examine the effect of vitamin D_2 supplementation on muscle strength, muscle mass, and physical performance of patients with degenerative lumbar disease. However, it is important to acknowledge several limitations. First, the study did not include a control group of healthy individuals without degenerative lumbar disease. Second, ergocalciferol (vitamin D_2) is the standard first-line treatment for vitamin D deficiency, as outlined in the National List of Essential Medicines, and is widely used in public health settings in Thailand. This study was not designed to establish equivalence compared to cholecalciferol (vitamin D_3). We acknowledge that vitamin D_2 and D_3 differ in pharmacokinetics and biological potency. The absence of a direct comparison between these two forms of vitamin D represents a study limitation. Additional limitations include a relatively small sample size. The proportion of male participants was low, which may reduce the statistical power of the findings. Furthermore, this study applied rigorous inclusion criteria to enroll participants with the heterogeneity of spinal conditions—encompassing LSS, LDD, and LDH may introduce variability in clinical outcomes.

Further studies should focus on the specific effects and interpretability of vitamin D_2 supplementation. A more targeted approach would facilitate a clearer understanding of its therapeutic efficacy within distinct pathophysiological outcomes. Additionally, standardized monitoring of calcium intake or supplementation is needed to elucidate the independent and synergistic effects of calcium alongside vitamin D in managing degenerative lumbar disease. Moreover, the considering factors such as overall physical activity, sun exposure, and dietary intake–potential contributors to vitamin D levels–are recommended to provide deeper insights into the vitamin D metabolic pathway.

In conclusion, our results demonstrated that administration of 40,000 IU of vitamin D_2 resulted in improvements in body composition and physical performance. Vitamin D_2 supplementation significantly alleviated pain, as assessed by the VAS score, and improved quality of life, based on the EQ-5D-5L and ODI scores. Additionally, vitamin D_2 supplementation is a safe, cost-effective approach to enhancing muscle strength and physical activity in this patient population. Based on these findings, we recommend offering vitamin D supplements to individuals with degenerative lumbar disease who experience limited physical function.

Author Contributions

S.D., S.A., and S.H. wrote the manuscript. S.D. and S.H. designed the research. S.D. performed the research. S.D. and S.H. analyzed the data. W.Y., W.L., and W.S. contributed reagents, materials, and analytical tools.

Acknowledgments

The authors would like to express sincere gratitude to all staff of the Department of Orthopaedics, King Chulalongkorn Memorial Hospital, for their assistance. The authors are thankful to Manassanan

Jitjumnong, Ladawan Vajarintarangoon, Pattana Mangnimit, and Pattanant Klunklowjeeravi for their excellent technical assistance.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

All data generated or analyzed during the present study are included in this published article. Further details are available for non-commercial purposes from the corresponding author on reasonable request.

References

1. J. W. S. Vlaeyen, C. G. Maher, K. Wiech, et al., "Low Back Pain," *Nature Reviews Disease Primers* 4 (2018): 52.

2. J. N. Katz and M. B. Harris, "Clinical Practice. Lumbar Spinal Stenosis," *New England Journal of Medicine* 358 (2008): 818–825.

3. Y. Calik and U. Aygun, "Evaluation of Vitamin D Levels in Patients With Chronic Low Back-Leg Pain," *Acta Orthopaedica et Traumatologica Turcica* 51 (2017): 243–247.

4. G. S. Maier, M. Weissenberger, M. Rudert, K. E. Roth, and K. Horas, "The Role of Vitamin D and Vitamin D Deficiency in Orthopaedics and Traumatology—A Narrative Overview of the Literature," *Annals of Translational Medicine* 9 (2021): 942.

5. M. van Driel and J. P. van Leeuwen, "Vitamin D Endocrine System and Osteoblasts," *Bone Reports* 3 (2014): 493.

6. C. Cooper, K. Javaid, S. Westlake, N. Harvey, and E. Dennison, "Developmental Origins of Osteoporotic Fracture: The Role of Maternal Vitamin D Insufficiency," *Journal of Nutrition* 135 (2005): 2728S–2734S.

7. J. W. Pike and M. B. Meyer, "Fundamentals of Vitamin D Hormone-Regulated Gene Expression," *Journal of Steroid Biochemistry and Molecular Biology* 144 (2014): 5–11.

8. K. Olsson, A. Saini, A. Stromberg, et al., "Evidence for Vitamin D Receptor Expression and Direct Effects of 1alpha,25(OH)2D3 in Human Skeletal Muscle Precursor Cells," *Endocrinology* 157 (2016): 98–111.

9. P. Lips, "Vitamin D Deficiency and Secondary Hyperparathyroidism in the Elderly: Consequences for Bone Loss and Fractures and Therapeutic Implications," *Endocrine Reviews* 22 (2001): 477–501.

10. F. Zolfaghari, A. Faridmoayer, B. Soleymani, M. Taji, and M. Mahabadi, "A Survey of Vitamin D Status in Patients With Degenerative Diseases of the Spine," *Asian Spine Journal* 10 (2016): 834–842.

11. T. H. Kim, J. Y. Yoon, B. H. Lee, et al., "Changes in Vitamin D Status After Surgery in Female Patients With Lumbar Spinal Stenosis and Its Clinical Significance," *Spine* 37 (2012): E1326–E1330.

12. M. Pfeifer, B. Begerow, H. W. Minne, K. Suppan, A. Fahrleitner-Pammer, and H. Dobnig, "Effects of a Long-Term Vitamin D and Calcium Supplementation on Falls and Parameters of Muscle Function in Community-Dwelling Older Individuals," *Osteoporosis International* 20 (2009): 315–322.

13. P. Manoy, P. Yuktanandana, A. Tanavalee, et al., "Vitamin D Supplementation Improves Quality of Life and Physical Performance in Osteoarthritis Patients," *Nutrients* 9 (2017): 799.

14. S. D. Anton, R. T. Mankowski, P. Qiu, et al., "Vitamin D Supplementation Is Associated With a Reduction in Self-Reported Falls Among Older Adults With Previous Fall History—Feasibility Study," *Journal of Frailty & Aging* 11 (2022): 224–230.

15. B. Ghai, D. Bansal, R. Kanukula, et al., "Vitamin D Supplementation in Patients With Chronic Low Back Pain: An Open Label, Single Arm Clinical Trial," *Pain Physician* 20 (2017): E99–E105.

16. O. Siwamogsatham, B. Ongphiphadhanakul, and V. Tangpricha, "Vitamin D Deficiency in Thailand," *Journal of Clinical & Translational Endocrinology* 2 (2015): 48–49.

17. M. F. Holick, N. C. Binkley, H. A. Bischoff-Ferrari, et al., "Evaluation, Treatment, and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice Guideline," *Journal of Clinical Endocrinology and Metabolism* 96 (2011): 1911–1930.

18. N. Sanjaroensuttikul, "The Oswestry Low Back Pain Disability Questionnaire (Version 1.0) Thai Version," *Journal of the Medical Association of Thailand* 90 (2007): 1417–1422.

19. J. Pattanaphesaj, Health-Related Quality of Life Measure (EQ-5D-5L): Measurement Property Testing and Its Preference-Based Score in Thai Population [Doctoral Dissertation]: Mahidol University (2014).

20. C. T. Schmidt, R. E. Ward, P. Suri, et al., "Association of Neuromuscular Attributes With Performance-Based Mobility Among Community-Dwelling Older Adults With Symptomatic Lumbar Spinal Stenosis," *Archives of Physical Medicine and Rehabilitation* 98 (2017): 1400–1406.

21. M. Halfon, O. Phan, and D. Teta, "Vitamin D: A Review on Its Effects on Muscle Strength, the Risk of Fall, and Frailty," *BioMed Research International* 2015 (2015): 953241.

22. E. M. Alayed Albarri, A. Sameer Alnuaimi, and D. Abdelghani, "Effectiveness of Vitamin D2 Compared With Vitamin D3 Replacement Therapy in a Primary Healthcare Setting: A Retrospective Cohort Study," *Qatar Medical Journal* 2022 (2022): 29.

23. P. Thimachai, O. Supasyndh, A. Chaiprasert, and B. Satirapoj, "Efficacy of High vs. Conventional Ergocalciferol Dose for Increasing 25-Hydroxyvitamin D and Suppressing Parathyroid Hormone Levels in Stage III-IV CKD With Vitamin D Deficiency/Insufficiency: A Randomized Controlled Trial," *Journal of the Medical Association of Thailand* 98 (2015): 643–648.

24. D. Goltzman, G. N. Hendy, and J. H. White, "Vitamin D and Its Receptor During Late Development," *Biochimica et Biophysica Acta* 1849 (2015): 171–180.

25. M. Lakkireddy, M. L. Karra, C. Patnala, et al., "Efficiency of Vitamin D Supplementation in Patients With Mechanical Low Back Ache," *Journal of Clinical Orthopaedics and Trauma* 10 (2019): 1101–1110.

26. M. Sandoughi, Z. Zakeri, Z. Mirhosainee, M. Mohammadi, and S. Shahbakhsh, "The Effect of Vitamin D on Nonspecific Low Back Pain," *International Journal of Rheumatic Diseases* 18, no. 8 (2015): 854–858.

27. A. M. Habib, K. Nagi, N. B. Thillaiappan, V. Sukumaran, and S. Akhtar, "Vitamin D and Its Potential Interplay With Pain Signaling Pathways," *Frontiers in Immunology* 11 (2020): 820.

28. X. Liu, A. Nelson, X. Wang, et al., "Vitamin D Modulates Prostaglandin E2 Synthesis and Degradation in Human Lung Fibroblasts," *American Journal of Respiratory Cell and Molecular Biology* 50 (2014): 40–50.

29. P. J. Martens, C. Gysemans, A. Verstuyf, and A. C. Mathieu, "Vitamin d's Effect on Immune Function," *Nutrients* 12 (2020): 1248.

30. C. M. Bentes, P. B. Costa, M. Resende, et al., "Effects of 12 Months of Vitamin D Supplementation on Physical Fitness Levels in Postmenopausal Women With Type 2 Diabetes," *Journal of Functional Morphology and Kinesiology* 6 (2021): 87.

31. C. M. Girgis, N. Mokbel, K. M. Cha, et al., "The Vitamin D Receptor (VDR) is Expressed in Skeletal Muscle of Male Mice and Modulates 25-Hydroxyvitamin D (25OHD) Uptake in Myofibers," *Endocrinology* 155 (2014): 3227–3237.

32. K. R. Montenegro, V. Cruzat, R. Carlessi, and P. Newsholme, "Mechanisms of Vitamin D Action in Skeletal Muscle," *Nutrition Research Reviews* 32 (2019): 192–204.