Journal of Southeast Asian Orthopaedics
ISSN 2821-9848 (Print)
ISSN 2821-9864 (Online)
https://doi.org/10.56929/jseaortho-2026-0273 https://jseaortho.org

Functional and Symptomatic Effects of Vitamin D Supplementation Following Carpal Tunnel Release: A Randomized Controlled Trial

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Purpose: Carpal tunnel release (CTR) is the standard surgery for patients with carpal tunnel syndrome (CTS) who do not respond to conservative management. Vitamin D is implicated in musculoskeletal and neurological health; evidence suggests it has neuroprotective effects, influencin pain and functional outcomes. This randomized controlled trial aimed to evaluate the impact of postoperative vitamin D supplementation on functional and symptomatic outcomes after CTR.

Methods: Seventy patients with CTS who underwent CTR were randomly assigned to receive postoperative vitamin D supplementation (40,000 IU/week for 4 weeks) or none. Patients were assessed at baseline and 12 weeks postoperatively. The primary outcomes included pain intensity measured using the Visual Analog Scale (VAS), grip strength, and the Thai version of the Boston Carpal Tunnel Questionnaire (Symptom Severity Scale [SSS] and Functional Status Scale [FSS]). Baseline characteristics were compared between groups.

Results: Of the 70 patients, 54 (79.4%) were female, with a mean age of 53.02±8.52 years and mean body mass index of 24.24±3.62 kg/m². Most (93.8%) were right-handed, with right-sided disease in 38 (55.1%) and severe CTS in 39 (57.4%) patients. Baseline characteristics were similar between groups. At 12 weeks, there were no statistically significant differences between the vitamin D and control groups in the VAS scores, grip strength, SSS, or FSS. No vitamin D toxicity or hypervitaminosis-related complications were observed.

Conclusions: Postoperative vitamin D supplementation at 40,000 IU/week for 4 weeks did not significantly improve pain, functional status, or symptom severity after CTR. Supplementation was well tolerated with no adverse effects.

Keywords: carpal tunnel syndrome, functional outcome, hypovitaminosis D, pain, carpal tunnel release, neuropathic pain

Article history:
Received September 16, 2025 Revised: April 12, 2026
Accepted: May 11, 2026
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Median nerve compression within the carpal tunnel, referred to using the diagnostic term carpal tunnel syndrome (CTS) is a common upper limb neuropathy that is more prevalent in individuals aged 30–50 years and in women. It is associated with repetitive wrist use and flexor retinaculum thickening, leading to sensory symptoms in the median nerve distribution and thenar muscle weakness in advanced cases.

Management includes conservative and surgical approaches, with carpal tunnel release (CTR) recommended by the American Academy of Orthopaedic Surgeons (AAOS) for severe cases, failed nonoperative treatment, or thenar atrophy; however, surgery may result in complications such as postoperative pain, scar-related issues, and, rarely, complex regional pain syndrome [1,2]. Postoperative pain, a key determinant of patient satisfaction, is typically managed with analgesics; however, opioid overuse remains a concern, with prolonged use reported in 6–13% of patients [3,4].

Given these limitations, adjunctive strategies to improve postoperative outcomes are garnering increasing interest. Vitamin D has been widely studied in orthopedic and neurological conditions for pain reduction due to its neuroprotective and neurotrophic effects, including the promotion of nerve myelination and increased secretion of neurotrophic factors [5]. It also reduces oxidative stress and inflammation through modulation of immune pathways and cytokine activity [13,16] and may decrease inflammatory fibrosis relevant to CTS [5-7].

Clinical evidence suggests potential benefits of vitamin D supplementation in patients with CTS. A cohort study demonstrated that supplementation with 1,000 IU/day for six months improved the Disabilities of the Arm, Shoulder, and Hand (DASH) scores, although no effects were observed on motor or strength outcomes [8]. A systematic review has reported reduced pain, improved function, and increased sensory conduction velocity [9]. However, no standardized dosing regimen exists, with studies using 7,000–60,000 IU/week for 12–24 weeks [8,10]. Although high doses of vitamin D may cause toxicity, including hypercalcemia after prolonged excessive intake [11], no adverse effects have been reported in CTS studies, even at 50,000 IU/week [10].

Based on these findings, we hypothesized that vitamin D supplementation after CTR might reduce pain and improve functional outcomes. This study aimed to evaluate these effects using a randomized controlled trial design.

PATIENTS AND METHODS

Following approval from the Institutional Review Board (IRB), this prospective randomized controlled trial was conducted in 70 patients diagnosed with mild-to-severe CTS.

Sample Size

The sample size was calculated based on the primary outcome (Boston Symptom Severity Scale; SSS). Expected values were obtained from Samant and Sane (2021), with mean±SD of 2.22±0.43 at baseline and 1.37±0.20 at 3 months. Using a two-sided significance level of $\alpha = 0.01$ and 95% power, the required sample size was 32 participants per group. Allowing for 10% attrition, the final target sample size was 35 participants per group (N = 70). Outcomes were measured at baseline and 3 months in both groups.

Participants

Patients with CTS who met the indications for CTR were eligible for enrollment. The study employed a block-of-four randomization technique and the outcome was analyzed according to the intention-to-treat principle.

The inclusion criteria were patients aged 18–70 years with a confirmed diagnosis of CTS requiring CTR. Surgical intervention was considered in patients with persistent symptoms despite adequate conservative treatment, functional impairment affecting daily activities, or patient preference following shared decision-making, including cases classified as mild CTS.

The exclusion criteria were:

- Underlying conditions requiring vitamin D supplementation (e.g., osteoporosis)
- Diabetes mellitus
- Rheumatoid arthritis
- Patients with abnormal liver or renal function
- Pregnancy or breastfeeding
- Use of medications such as anticonvulsants, thrombolytics, or rifampicin
- History of CTR or wrist fracture on the operative side

- Known allergy to vitamin D or corn starch
- Planned concomitant opponensplasty at the time of CTR

Method

Vitamin D supplementation within 12 weeks prior to enrollment was an exclusion criterion. The data were collected between March 2022 and October 2023. Baseline preoperative data obtained within one month before CTR included demographic characteristics (age, sex, and body mass index [BMI]), occupation, allergy and medication history, comorbidities, dominant hand, affected side, disease severity, disease duration, and prior treatments.

All surgeries were performed by the same team of hand surgeons, using a standardized technique. The procedures were performed under local anesthesia using 1% lidocaine without sedation. A pneumatic tourniquet was inflated to 250 mm Hg. A mini-open approach was used, involving a 2-cm longitudinal incision beginning distal to the Kaplan cardinal line and extending proximally toward the distal wrist crease. The transverse carpal ligament was released using standard surgical instruments to decompress the median nerve. Internal neurolysis was induced as previously described. The skin was closed with 4-0 nylon sutures and the tourniquet was deflated.

Postoperative management was standardized for both groups. All patients received the same postoperative regimen, including antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and local anesthetics. The intervention group received oral vitamin D_3 at a dose of 40,000 IU per week, whereas the control group received an identical-appearing placebo. The sutures were removed 10–14 days after surgery.

Participants were randomly allocated to the intervention or control group using block randomization with a block size of four. The participants were unaware of their treatment allocations. The outcome assessors were blinded to group assignment during data collection. Owing to the nature of the intervention, the surgeons were not blinded to the treatment allocation.

Data Collection

Patients were evaluated 10–14 days, 4 weeks, and 12 weeks postoperatively. Outcome measures included pain intensity, assessed using the Visual Analog Scale (VAS) and scored from 0 (no pain) to 10 (worst imaginable pain). Symptom severity and functional status were evaluated using the Thai version of the Boston Carpal Tunnel Questionnaire, which comprises the Symptom Severity Scale (SSS) and Functional Status Scale (FSS). Each item is scored on a 1–5 Likert scale, with higher scores indicating greater symptom severity or functional impairment. Grip strength was measured using a calibrated Jamar hand dynamometer, with the mean of three trials recorded in kilograms (kg). Postoperative complications, and signs or symptoms suggestive of vitamin D toxicity were systematically monitored and recorded at each follow-up visit throughout the study period.

Statistical Analysis

Baseline demographic and clinical characteristics, including mean age, sex, BMI, disease duration, affected side, and disease severity, were compared between the vitamin D and control groups using the chi-square test or Fisher's exact test for categorical variables, as appropriate. Preoperative treatment history was also analyzed using the chi-square or Fisher's exact tests to assess between-group differences. For continuous outcome measures, including VAS scores, SSS, FSS, and grip strength, between-group comparisons were conducted using the independent t-test for normally distributed data or the Mann–Whitney U test for non-normally distributed data. The incidence of postoperative complications and signs of vitamin D toxicity were compared between the groups using the chi-square test or Fisher's exact test, depending on the distribution of the categorical data. All statistical analyses were performed using a two-sided significance level of $p < 0.05$.

RESULTS

The flow of participants throughout the study is shown in Figure 1. Seventy patients were

enrolled, most of whom were female (n = 54; 79.4%). The mean age of participants was 53.02 ± 8.52 years, and the mean BMI was 24.24 ± 3.62 kg/m², which is within the healthy weight range for the general population. Most of the participants were right-handed (n = 61, 93.8%). Regarding the affected side, the right hand was involved in 38 patients (55.1%) and the left hand in 31 patients (44.9%). Disease severity was classified as severe in 39 patients (57.4%), with the remainder presenting moderate or mild CTS.

There were no statistically significant differences between the vitamin D and control groups with respect to prior treatments, including kinesio taping, splinting, nonsteroidal anti-inflammatory drug (NSAID) use, and rehabilitation therapy. Similarly, baseline demographic and clinical characteristics did not differ significantly between the groups ($p > 0.05$).

A detailed comparison of demographic and baseline variables is presented in Table 1.

Table 1 Baseline characteristics.

Factors (n=70)	**Overall, (n=70) n (%)**	**control, (n=34) n (%)**	**Vitamin D (n=36), n (%)**	***P*† value**
Age (year), mean±s.d.	53.02 ±8.52	52.85 ±9.14	53.17 ±8.03	0.877
Sex				
Male	14 (20.6)	8 (24.2)	6 (17.1)	0.469
Female	54 (79.4)	25 (75.8)	29 (82.9)	
Weight (kg), mean±s.d.	62.59 ±9.09	61.06 ±10.17	64.03 ±7.81	0.180
Hight (m), mean±s.d.	1.61 ±0.08	1.59 ±0.08	1.63 ±0.07	0.081
BMI (kg/m²), mean±s.d.	24.24 ±3.62	24.16 ±4.10	24.32 ±3.16	0.854
Underweight (<18.5)	2 (2.9)	2 (5.9)	0 (0.0)	0.510
Normal range (18.5 -22.9)	22 (31.4)	12 (35.3)	10 (27.8)	
Overweight (23.0 – 24.9)	16 (22.9)	6 (17.6)	10 (27.8)	
Obesity grade 1 (25.0 – 29.9)	24 (34.3)	11 (32.4)	13 (36.1)	
Obesity grade 2 (≥30.0)	6 (8.6)	3 (8.8)	3 (8.3)	
Underlying disease				
No	44 (62.9)	23 (67.6)	21 (58.3)	0.420
Yes	26 (37.1)	11 (32.4)	15 (41.7)	
Atrial fibrillation (AF)	1 (1.4)	1 (2.9)	0 (0.0)	0.300
Dyslipidemia (DLP)	10 (14.3)	5 (14.7)	5 (13.9)	0.922
Diabetes mellitus (DM)	7 (10.0)	4 (11.8)	3 (8.3)	0.632
Hypertension (HT)	14 (20.0)	7 (20.6)	7 (19.4)	0.905
Asthma	1 (1.4)	0 (0.0)	1 (2.8)	0.328
Spondylosis	2 (2.9)	0 (0.0)	2 (5.6)	0.163
Occupational				0.201
Hand dominant				0.317
Right	61 (93.8)	30 (90.9)	31 (96.9)	
Left	4 (6.2)	3 (9.1)	1 (3.1)	
Site of disease				0.171
Right	38 (55.1)	21 (63.6)	17 (47.2)	
Left	31 (44.9)	12 (36.4)	19 (52.8)	
Severity				0.577
Mild	2 (2.9)	1 (3.0)	1 (2.9)	

Table 1 Baseline characteristics. (Cont.)

Factors (n=70)	**Overall, (n=70) n (%)**	**control, (n=34) n (%)**	**Vitamin D (n=36), n (%)**	***P*† value**
Moderate	27 (39.7)	11 (33.3)	16 (45.7)	
Severe	39 (57.4)	21 (63.6)	18 (51.4)	
Duration (month), mean±s.d.	9.64 ±6.00	9.03 ±4.35	10.24 ±7.27	0.415
Previous steroid injection				0.866
Yes	39 (56.5)	19 (57.6)	20 (55.6)	
No	30 (43.5)	14 (42.4)	16 (44.4)	
Previous slab				0.896
Yes	8 (11.6)	4 (12.1)	4 (11.1)	
No	61 (88.4)	29 (87.9)	32 (88.9)	
Previous NSAIDS				0.809
Yes	45 (65.2)	22 (66.7)	23 (63.9)	
No	24 (34.8)	11 (33.3)	13 (36.1)	
Rehabilitation				0.446
Yes	30 (44.1)	13 (39.4)	17 (48.6)	
No	38 (55.9)	20 (60.6)	18 (51.4)	

Abbreviations: n, frequency; %, percentage; mean, average; s.d., standard deviation; BMI, body mass index; NSAIDS, Non-Steroidal Anti-inflammatory Drugs; kg, kilogram; cm, centimeter; m, meter; m^2 , square meter; †, p-value calculated using Pearson chi-square test or, Likelihood chi-square test for comparison of proportion among categorical variables more than 2 groups, and independent t-test or Wilcoxon rank-sum test (the Mann – Whitney two-sample test for comparison of mean between 2 independent groups.

Primary Outcomes

The primary outcomes are summarized in Table 2.

Pain, assessed using the Visual Analog Scale (VAS), improved significantly in both groups over the study period. The baseline VAS score was 6 (interquartile range [IQR], 4–8), which decreased to 2 (IQR, 1–4) at the first postoperative follow-up (10–14 days) ($p < 0.001$). No statistically significant differences in VAS scores were observed between the control and vitamin D groups at any follow-up. Grip strength also improved postoperatively in both groups. The baseline grip strength was 16 kg (IQR: 14–19), which increased to 18 kg (IQR: 16–20) at 4 weeks postoperatively ($p < 0.001$). However, there was no statistically significant difference in grip strength gain between the vitamin D and control groups. Functional outcomes measured using the Thai Boston SSS and FSS, showed consistent improvements in both groups across all follow-up visits. No statistically significant differences were observed between the groups at any time point.

- Thai Boston SSS

Baseline: 2.50 (IQR: 2.18–3.36) in the control group vs. 2.86 (IQR: 2.00–3.45) in the vitamin D group

10–14 days: 1.64 (IQR: 1.18–2.18) vs. 1.36 (IQR: 1.09–2.23) ($p = 0.378$)

4 weeks: 1.36 (IQR: 1.18–1.64) vs. 1.18 (IQR: 1.09–1.59) ($p = 0.403$)

12 weeks: 1.09 (IQR: 1.00–1.18) vs. 1.00 (IQR: 1.00–1.55) ($p = 0.914$)

- FSS:

Baseline: 2.18 (IQR: 1.75–2.88) vs. 2.06 (IQR: 1.69–3.31)

10–14 days: 1.75 (IQR: 1.50–2.38) vs. 1.50 (IQR: 1.31–2.56) ($p = 0.625$)

4 weeks: 1.25 (IQR: 1.00–1.63) vs. 1.50 (IQR: 1.31–2.56) ($p = 0.182$)

12 weeks: 1.13 (IQR: 1.00–1.38) vs. 1.00 (IQR: 1.00–1.25) ($p = 0.165$)

Overall, both groups demonstrated significant postoperative improvements in pain, grip strength, and functional scores; however, no statistically significant differences were found between the vitamin D and control groups at any time point. Importantly, no adverse effects or signs of vitamin D toxicity, including hypercalcemia, gastrointestinal symptoms, or neurological complications, were observed in any participant during the 12-week follow-up period.

Table 2 Clinical outcomes and intra-group comparisons at baseline and follow-up visits in the control and vitamin D supplementation groups.

Outcome	Time point	Control group Median (IQR)	Vitamin D group Median (IQR)	Between-group p value
VAS score	Baseline (W0)	6 (4–8)	7 (4–9)	0.128
	10–14 days (W1)	2 (1–4)	2 (0–4)	0.816
	4 weeks (W4)	0 (0–1)	0 (0–1)	NS
	12 weeks (W12)	0 (0–0)	0 (0–0)	NS
Grip strength	Baseline (W0)	16 (14–19)	16 (13–18)	NS
	10–14 days (W1)	15 (12–18)	15 (14–16)	NS
	4 weeks (W4)	18 (16–20)	20 (17–22)	NS
	12 weeks (W12)	19 (16–22)	22 (20–24)	< 0.05*
Thai Boston SSS	Baseline (W0)	2.50 (2.18–3.36)	2.86 (2.00–3.45)	0.378
	10–14 days (W1)	1.64 (1.18–2.18)	1.36 (1.09–2.23)	NS
	4 weeks (W4)	1.36 (1.18–1.64)	1.18 (1.09–1.59)	NS
	12 weeks (W12)	1.09 (1.00–1.18)	1.00 (1.00–1.55)	NS
Thai Boston FSS	Baseline (W0)	2.18 (1.75–2.88)	2.06 (1.69–3.31)	NS
	10–14 days (W1)	1.75 (1.50–2.38)	1.50 (1.31–2.56)	NS
	4 weeks (W4)	1.25 (1.00–1.63)	1.06 (1.00–1.50)	NS
	12 weeks (W12)	1.13 (1.00–1.38)	1.00 (1.00–1.25)	NS

Abbreviations: IQR, Interquartile range (3rd Quartile –1st Quartile); VAS, Visual analog scale (0 –10 scores); SSS, symptom severity scores; FSS, functional status scale; †, p-value calculated using (a) Repeated measurement ANOVA or (b) Friedman F-test for comparison of mean among continuous variables more than 2 groups, and (c) paired (dependent) sample t-test or (e) Wilcoxon matched-pairs signed-rank test for comparison of median between two periods. *Statistically significant differences between groups ($p < 0.05$). NS: not statistically significant.

Within-group analyses showed significant improvements from baseline to week 12 in both the control and vitamin D groups across all outcomes, including VAS score, grip strength, Thai Boston SSS, and Thai Boston FSS (all $p < 0.001$). Improvements were observed as early as 10–14 days postoperatively and persisted for 12 weeks. Although both groups demonstrated similar recovery patterns following CTR, the vitamin D group did not show statistically superior within-group outcomes compared to the control group.

Figure 1 A–1 D. Changes in clinical outcomes over time in the control and vitamin D supplementation groups. (A) VAS pain score, (B) grip strength, (C) Thai Boston Symptom Severity Scale (SSS), and (D) Thai Boston Functional Status Scale (FSS) measured at baseline (W0), 10–14 days (W1), 4 weeks (W4), and 12 weeks (W12) postoperatively. Data are presented as median values. *$p < 0.05$ between groups at W12 (grip strength).

While both the control and vitamin D groups demonstrated significant postoperative improvements across all measured outcomes, no statistically significant intergroup differences were observed in the VAS score, SSS, or FSS throughout the study period. A statistically significant

between-group difference in grip strength was observed 12 weeks postoperatively (p = 0.012), whereas no significant differences were found in other clinical outcome measures.

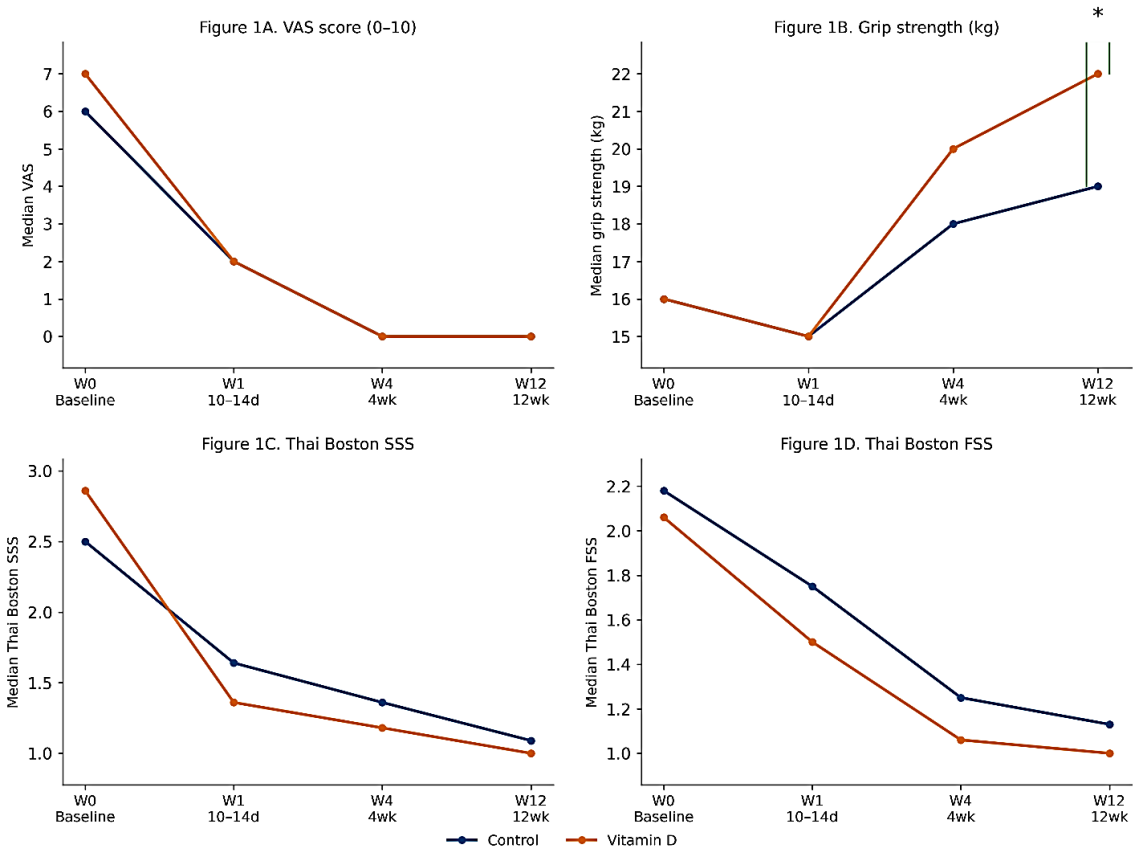

Fig. 1A–1D Changes in clinical outcomes over time in the control and vitamin D supplementation groups. (A) VAS pain score, (B) grip strength, (C) Thai Boston Symptom Severity Scale (SSS), and (D) Thai Boston Functional Status Scale (FSS) measured at baseline (W0), 10–14 days (W1), 4 weeks (W4), and 12 weeks (W12) postoperatively. Data are presented as median values. *p < 0.05 between groups at W12 (grip strength).

DISCUSSION

This randomized controlled trial evaluated the effects of high-dose vitamin D supplementation on functional and symptomatic outcomes following CTR in patients with mild-to-severe CTS. The results demonstrated that while both the control and vitamin D groups experienced significant improvements in pain, grip strength, and functional scores over the 12-week follow-up period, vitamin D supplementation did not confer statistically significant benefits in pain (VAS score), Thai Boston SSS, or FSS compared with the control group. A statistically significant difference in grip strength at 12 weeks was observed in the vitamin D group. However, this finding should be interpreted with caution in the absence of consistent differences across other outcome measures.

Our findings are partially consistent with those of previous studies that evaluated vitamin D levels in CTS. A systematic review by Anusitviwat et al. reported that vitamin D supplementation may improve pain, functional status, and sensory nerve conduction. However, the included studies were mostly non-randomized and demonstrated considerable heterogeneity in study design, patient characteristics, and dosing regimens [9]. Likewise, Samant et al. reported significant improvements in the VAS and Boston questionnaire scores following

vitamin D supplementation in patients with CTS and hypovitaminosis D, although their study used a single-arm pre–post design without a control group, limiting causal inference [10].

More recent clinical evidence has shown improvements in pain severity and symptom scores after vitamin D administration, whereas functional outcomes have remained less consistent, suggesting that symptomatic relief may occur earlier than measurable functional recovery [11].

In the present trial, both groups demonstrated rapid postoperative improvement beginning at 10–14 days, which likely reflected the expected recovery trajectory following surgical decompression. This observation supports the idea that the CTR remains the main determinant of early pain relief and functional recovery. The absence of significant intergroup differences in SSS and FSS contrasts with some earlier observational studies reporting functional improvements after vitamin D supplementation, and may be explained by differences in study design, baseline vitamin D status, and the inclusion of surgery as a dominant therapeutic intervention in the current randomized model [9].

The observed gain in grip strength after 12 weeks in the vitamin D group raises the possibility of delayed neuromuscular or muscle performance effects. However, previous studies have reported inconsistent associations between vitamin D status and motor recovery after CTR. For example, correction of vitamin D deficiency after CTR has been associated with modest improvements in disability scores, but not with clear changes in grip strength or motor conduction parameters [8].

The dose of vitamin D_3 (40,000 IU/week) was selected based on previously published studies in patients with CTS, which used supplementation doses ranging from 7,000 to 60,000 IU/week and demonstrated clinical benefit without significant adverse events [9].

A weekly dose of 40,000 IU was chosen to provide sufficient biological activity to potentially enhance nerve recovery, while remaining within a range with an established safety profile. Additionally, this dosage remains below the levels previously associated with vitamin D–related adverse effects, thereby balancing efficacy and safety considerations.

Importantly, no adverse events or signs of vitamin D toxicity were detected, even at a dose of 40,000 IU/week for 12 weeks. This finding supports the short-term safety of high-dose vitamin D supplementation in CTS patients without contraindications, consistent with previous reports [11-13].

Limitations

This study had several limitations. First, serum vitamin D levels were not measured before or after treatment, which precludes analysis of whether baseline deficiency or achieved serum concentrations influenced the outcomes. However, epidemiological studies in Thailand and other Asian populations have shown that vitamin D insufficiency remains relatively common, particularly among urban residents and women, thus providing a clinical context for evaluating vitamin D supplementation. However, the absence of biochemical assessments remains an important limitation.

Second, the 12-week follow-up period may not have been sufficient to capture longer-term motor recovery or the potential delayed benefits of supplementation.

Third, the relatively small sample size may have limited the statistical power to detect subtle intergroup differences.

Clinical Implications and Future Research

The findings of this trial suggest that vitamin D supplementation at 40,000 IU/week for 12 weeks is safe but does not significantly enhance postoperative outcomes following CTR in the general patient population. Nonetheless, the observed improvement in grip strength at 12 weeks raises the possibility of a functional benefit, particularly in the vitamin D–deficient subgroups. Future studies should incorporate the monitoring of serum vitamin D concentrations, extend the follow-up period to assess longer-term effects, and stratify participants according to their deficiency status to identify those who may derive the greatest benefit from supplementation.

CONCLUSIONS

In this randomized controlled trial, vitamin D supplementation at a dose of 40,000 IU per week for 12 weeks following CTR was safe but did not result in statistically significant improvements in pain reduction, symptom severity, or functional status compared with placebo. Both groups demonstrated meaningful clinical improvement after surgery, although only grip strength at 12 weeks showed a statistically significant difference in favor of the vitamin D group, suggesting a potential delayed functional effect. These findings reinforce the effectiveness of CTR as the primary treatment for CTS and indicate that routine vitamin D supplementation may not provide additional short-term benefits to the general patient population. However, supplementation may be considered in select patients, particularly those with suspected or confirmed vitamin D deficiency. Further research with larger cohorts, longer follow-up periods, and biochemical monitoring is warranted to clarify the role of vitamin D in postoperative nerve and muscle recovery.

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