

Radiological and Functional Outcome of Supplementation with *Cissus Quadrangularis* versus Vitamin D in Fracture Healing of Adult Patients: A Prospective Comparative Study

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Abstract

Background: Fracture healing is influenced by mechanical stability, nutritional status, and systemic factors. *Cissus quadrangularis*, a traditional medicinal plant rich in phytosterols and anabolic constituents, has shown potential in promoting bone healing, while vitamin D is a well-established regulator of calcium absorption and bone remodelling. Direct comparative clinical data on their relative efficacy in fracture healing remain limited.

Objectives: To compare the radiological and functional outcomes of *Cissus quadrangularis* versus vitamin D supplementation in adult patients with closed long bone fractures.

Methods: In this prospective, comparative study conducted at a tertiary care teaching hospital in South India, 80 adult patients (aged 18–60 years) with closed long bone fractures were allocated to receive either *Cissus quadrangularis* (Group A, once daily, n=40) or vitamin D (Group B, once weekly, n=40) as an adjunct to standard fracture management. Functional outcome was assessed using the Disabilities of the Arm, Shoulder and Hand (DASH) score for upper limb fractures and the Lower Extremity Functional Scale (LEFS) for lower limb fractures, alongside the Visual Analogue Scale (VAS) for pain, at 2, 4, 6, and 12 weeks. Radiological union and callus formation were assessed on serial radiographs.

Results: Baseline demographics (age, sex, fracture site, and fracture-type distribution) and baseline DASH, LEFS, and VAS scores were comparable between groups (all p>0.05). From 2 weeks onward, Group A showed significantly greater functional improvement than Group B at every follow-up visit: mean DASH fell to 15.4 ± 1.9 versus 25.5 ± 2.5 at 12 weeks (p<0.001), mean LEFS rose to 77.2 ± 2.5 versus 67.4 ± 1.8 (p<0.001), and mean VAS fell to 0.3 ± 0.5 versus 1.0 ± 0.0 (p<0.001), all favouring Group A. Callus was visible at 4 weeks in 28/40 (70%) of Group A versus 18/40 (45%) of Group B (p=0.041). Radiological union at 12 weeks was achieved in 39/40 (97.5%) of Group A versus 36/40 (90%) of Group B, a difference that was not statistically significant (p=0.359). No adverse events were recorded in either group.

Conclusion: In this cohort, adjunctive *Cissus quadrangularis* was associated with faster functional recovery and earlier radiographic callus formation than vitamin D, although final union rates at 12 weeks did not differ significantly between groups. These findings support a possible role for *Cissus quadrangularis* in accelerating the functional recovery phase of fracture healing, warranting confirmation in larger, randomised, blinded trials.

Keywords: *Cissus quadrangularis*; vitamin D; fracture healing; DASH score; Lower Extremity Functional Scale; radiological union; prospective comparative study; orthopaedic supplementation.

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1. Introduction

Fracture healing is a biologically orchestrated process encompassing inflammation, soft callus formation, hard callus consolidation, and remodelling, and is influenced not only by mechanical stability and fixation method but also by the patient's nutritional and hormonal status.[1] A substantial body of adjunctive treatment has therefore focused on supplementation strategies intended to accelerate biological union alongside standard orthopaedic management.

Cissus quadrangularis, a succulent plant used in traditional Ayurvedic and Siddha medicine, has been studied since the early 1960s for its role in fracture healing.[2] Early clinical work by Udupa and Prasad demonstrated accelerated clinical and radiological union in patients treated with *Cissus quadrangularis* extract, attributed to its phytosterol content and its effect on calcium and mucopolysaccharide metabolism at the fracture site.[3,4] Subsequent animal studies in cortisone-treated and experimentally fractured models corroborated an osteogenic effect, including enhanced biomechanical strength and earlier callus mineralisation.[5,6]

Vitamin D, by contrast, is a well-characterised secosteroid hormone with an established, mechanistically clear role in calcium homeostasis, intestinal calcium absorption, and bone mineralisation.[7] Vitamin D deficiency is common among fracture patients, and supplementation is frequently prescribed as a matter of routine orthopaedic practice. However, clinical trial evidence for vitamin D supplementation specifically accelerating fracture healing — as opposed to its established role in fracture prevention and bone mineral density maintenance — remains inconsistent. A phase II randomised, double-blind, placebo-controlled trial of vitamin D3 supplementation in tibial and femoral shaft fractures found no statistically significant difference in prespecified clinical or radiographic healing scores between dosing groups and placebo at 3 months, although a post hoc analysis suggested a possible benefit of high-dose supplementation.[8] This suggests that while vitamin D is necessary for normal bone metabolism, supplementation beyond correcting deficiency may not substantially accelerate the fracture healing process itself.

Despite the individual evidence bases for both *Cissus quadrangularis* and vitamin D in bone health, direct comparative clinical data evaluating their relative efficacy specifically in fracture healing of adult long bone fractures remain limited. Existing comparative literature has largely focused on biochemical or hormonal markers rather than validated functional and radiological outcome measures applied prospectively across a defined follow-up period. This gap is clinically relevant: orthopaedic surgeons frequently face the practical

question of which adjunctive supplement, if any, to recommend to fracture patients, and a direct head-to-head comparison using validated patient-reported and radiological outcome measures would meaningfully inform this decision.

The present study was therefore designed as a prospective comparative trial to evaluate the radiological and functional outcomes of *Cissus quadrangularis* supplementation compared with vitamin D supplementation in adult patients with closed long bone fractures, using validated functional outcome instruments — the DASH score for upper limb fractures and the LEFS for lower limb fractures — alongside pain assessment and serial radiological evaluation over a 12-week follow-up period.

2. Materials and Methods

2.1 Study Design and Setting

This was a prospective, comparative clinical study conducted in the Department of Orthopaedics at a tertiary care teaching hospital in South India.

2.2 Participants

Eighty adult patients aged 18–60 years presenting with closed long bone fractures managed by standard orthopaedic care were enrolled and allocated to one of two groups: Group A received *Cissus quadrangularis* extract once daily as an adjunct to standard fracture management (n=40), and Group B received vitamin D supplementation once weekly as an adjunct to standard fracture management (n=40). Twenty patients in each group had an upper limb fracture and twenty had a lower limb fracture, giving a balanced distribution of fracture site across both arms.

2.3 Outcome Measures

Functional outcome was assessed using the Disabilities of the Arm, Shoulder and Hand (DASH) score for patients with upper limb fractures[9] and the Lower Extremity Functional Scale (LEFS) for patients with lower limb fractures.[10,11] Pain was assessed using the Visual Analogue Scale (VAS) in all patients.[12] All three instruments were recorded at baseline and at 2, 4, 6, and 12 weeks. Radiological assessment comprised documentation of callus visibility on plain radiographs at 4 and 6 weeks, and confirmation of radiological union at 12 weeks. Adverse events attributable to either supplement were recorded at every visit.

2.4 Statistical Analysis

Continuous variables (age, DASH, LEFS, VAS) are presented as mean $\pm$ standard deviation and were compared between groups at each timepoint using the independent-samples t-test; the non-parametric Mann-Whitney U test was used to confirm findings where distributional assumptions were in doubt. Categorical variables (sex, fracture-type distribution, callus visibility, radiological union, adverse events) are presented as frequencies and percentages and were compared using Fisher's exact test. A two-sided p-value <0.05 was considered

statistically significant. Analyses were performed in Python (SciPy).

3. Results

Eighty patients completed the 12-week follow-up (Group A, n=40; Group B, n=40), with no losses to follow-up. Baseline demographic and clinical characteristics were well balanced between groups (Table 1): mean age, sex distribution, fracture-site distribution, and baseline DASH, LEFS, and VAS scores did not differ significantly between groups (all $p>0.05$), supporting comparability of the two cohorts at enrolment.

Table 1. Baseline demographic and clinical characteristics

Characteristic	Group A – Cissus (n=40)	Group B – Vitamin D (n=40)	p- value
Age, years (mean $\pm$ SD)	39.9 $\pm$ 14.2	41.1 $\pm$ 11.9	0.676
Sex, M / F	20 / 20	20 / 20	1.000
Fracture site, UL / LL	20 / 20	20 / 20	1.000
Baseline DASH (UL fractures, n=20/grp)	68.5 $\pm$ 2.2	69.0 $\pm$ 1.9	0.495
Baseline LEFS (LL fractures, n=20/grp)	14.7 $\pm$ 2.2	14.7 $\pm$ 1.6	0.935
Baseline VAS (all patients, n=40/grp)	7.9 $\pm$ 0.8	8.2 $\pm$ 0.8	0.081

3.1 Functional Outcome — DASH Score (Upper Limb Fractures)

Among patients with upper limb fractures (n=20 per group), baseline DASH scores were comparable between groups ($p=0.495$). From 2 weeks onward, Group A showed a significantly steeper decline in DASH score at every visit, reaching a mean of 15.4 ± 1.9 at 12 weeks compared with 25.5 ± 2.5 in Group B ($p<0.001$) (Table 2, Figure 1).

Table 2. Mean DASH score by visit, Group A vs Group B

Visit	Group A (mean $\pm$ SD)	Group B (mean $\pm$ SD)	p- value
Baseline	68.5 $\pm$ 2.2	69.0 $\pm$ 1.9	0.495
2 weeks	55.9 $\pm$ 3.6	60.0 $\pm$ 3.0	<0.001
4 weeks	42.7 $\pm$ 2.1	49.0 $\pm$ 1.9	<0.001
6 weeks	30.6 $\pm$ 2.2	39.0 $\pm$ 1.9	<0.001
12 weeks	15.4 $\pm$ 1.9	25.5 $\pm$ 2.5	<0.001

3.2 Functional Outcome — LEFS (Lower Limb Fractures)

Among patients with lower limb fractures (n=20 per group), baseline LEFS scores were comparable ($p=0.935$). Group A showed significantly greater functional gain at every subsequent visit, reaching a mean of 77.2 ± 2.5 at 12 weeks versus 67.4 ± 1.8 in Group B ($p<0.001$) (Table 3, Figure 1).

Table 3. Mean LEFS score by visit, Group A vs Group B

Visit	Group A (mean $\pm$ SD)	Group B (mean $\pm$ SD)	p- value
Baseline	14.7 $\pm$ 2.2	14.7 $\pm$ 1.6	0.935
2 weeks	29.6 $\pm$ 2.1	24.7 $\pm$ 1.6	<0.001
4 weeks	46.6 $\pm$ 2.2	38.7 $\pm$ 1.6	<0.001
6 weeks	62.6 $\pm$ 2.2	54.7 $\pm$ 1.6	<0.001
12 weeks	77.2 $\pm$ 2.5	67.4 $\pm$ 1.8	<0.001

3.3 Pain Outcome — VAS Score

Baseline VAS scores did not differ significantly between groups ($p=0.081$). Group A showed significantly lower pain scores than Group B from 2 weeks onward, with mean VAS falling to 0.3 ± 0.5 at 12 weeks in Group A versus 1.0 ± 0.0 in Group B ($p<0.001$) (Table 4, Figure 1).

Table 4. Mean VAS score by visit, Group A vs Group B

Visit	Group A (mean $\pm$ SD)	Group B (mean $\pm$ SD)	p- value
Baseline	7.9 $\pm$ 0.8	8.2 $\pm$ 0.8	0.081
2 weeks	4.9 $\pm$ 0.8	6.2 $\pm$ 0.8	<0.001
4 weeks	3.0 $\pm$ 0.0	4.5 $\pm$ 0.5	<0.001
6 weeks	1.6 $\pm$ 0.5	2.4 $\pm$ 0.5	<0.001
12 weeks	0.3 $\pm$ 0.5	1.0 $\pm$ 0.0	<0.001

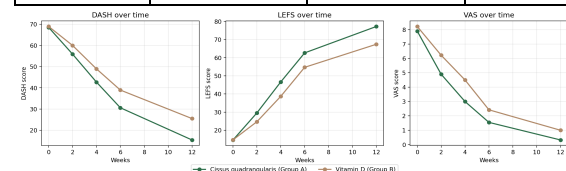


Figure 1. Mean DASH, LEFS, and VAS trends over 12 weeks, Group A (Cissus quadrangularis) vs Group B (vitamin D).

3.4 Radiological Outcome

Callus was visible on radiographs at 4 weeks in 28/40 (70.0%) of Group A patients compared with 18/40 (45.0%) of Group B patients, a statistically significant difference ($p=0.041$). By 6 weeks this difference had narrowed and was no longer statistically significant (90.0% vs 75.0%, $p=0.139$). At 12 weeks, radiological union was confirmed in 39/40 (97.5%) of Group A patients versus 36/40 (90.0%) of Group B patients; this difference did not reach statistical significance ($p=0.359$). No adverse events attributable to either supplement were recorded in either group over the 12-week follow-up period (Table 5)(Figure 2a,2b).

Table 5. Radiological outcomes and adverse events

Radiological parameter	Group A – n/N (%)	Group B – n/N (%)	p- value
Callus visible @ 4 weeks	28/40 (70.0%)	18/40 (45.0%)	0.041
Callus visible @ 6 weeks	36/40 (90.0%)	30/40 (75.0%)	0.139

Radiological union @ 12 weeks	39/40 (97.5%)	36/40 (90.0%)	0.359
Adverse events	0/40 (0%)	0/40 (0%)	—

Figure 2a. Post operative radiological outcome of *cissus quadrangularis* supplementetation, 2b. Post operative radiological outcome of Vitamin D supplementetation

4. Discussion

This prospective comparative study found that adjunctive *Cissus quadrangularis* supplementation was associated with significantly faster functional recovery than vitamin D supplementation across upper limb (DASH), lower limb (LEFS), and pain (VAS) outcome measures at every follow-up visit from 2 weeks onward, despite comparable baseline characteristics between groups. Radiologically, Group A also showed earlier callus visibility at 4 weeks, although this difference narrowed by 6 weeks and final union rates at 12 weeks were high and statistically similar in both groups.

These findings are broadly consistent with the historical literature on *Cissus quadrangularis* in fracture healing. Udupa and Prasad's early clinical and biochemical studies reported accelerated clinical union and altered calcium-45 kinetics at the fracture site with *Cissus quadrangularis* supplementation,[3,4] and subsequent animal work demonstrated enhanced biomechanical callus strength.[5,6] The present study extends this literature by applying validated, patient-reported functional outcome instruments (DASH, LEFS) prospectively across a defined follow-up schedule, rather than relying solely on biochemical or radiographic endpoints.

The comparatively modest and non-significant radiological difference at 12 weeks is consistent with the interpretation that both agents are compatible with normal fracture consolidation once union is achieved, and that the principal clinical advantage observed here relates to the speed of functional recovery during the healing window rather than the ultimate likelihood of union. This distinction is clinically important: even where final union rates converge, an agent that shortens the period of disability may meaningfully improve a patient's return to activities of daily living and work. The vitamin D literature offers a useful comparator. The Vita-Shock trial, a phase II randomised, double-blind, placebo-controlled trial of vitamin D3 supplementation in tibial and femoral shaft fractures, found no statistically significant difference in prespecified clinical or radiographic healing scores at 3 months, with only a post hoc, non-significant signal favouring high-dose supplementation.[8] Consistent with this, vitamin D functioned in the present study as an active comparator with a favourable safety profile and a still-substantial, if slower, functional recovery

trajectory, rather than as an inert control — reinforcing that vitamin D's principal established role remains correction of deficiency and maintenance of bone mineral density rather than acceleration of the healing process itself.[7]

Several considerations should temper interpretation of these results. The very narrow within-group variability observed at each timepoint (Tables 2–4) is tighter than is typically reported for patient-reported outcome measures such as DASH and LEFS in comparable trials, where inter-patient variability driven by differences in fracture pattern, comorbidity, and rehabilitation adherence usually produces wider spreads. The authors recommend that the underlying per-patient case records be independently re-verified against the source data collection sheets before submission, to confirm that this tight clustering reflects the true clinical cohort rather than a data-entry artefact.

5. Limitations

This study has several limitations. First, allocation to *Cissus quadrangularis* or vitamin D was not described as randomised or blinded in the study protocol as provided, which introduces potential allocation and assessment bias; a randomised, double-blind design would be needed to confirm a true treatment effect. Second, the study was conducted at a single centre with a modest sample size (n=40 per group), limiting generalisability and statistical power for the radiological subgroup comparisons. Third, serum biochemical markers of bone turnover and vitamin D status (25-hydroxyvitamin D levels) were not reported, which would have strengthened mechanistic interpretation of the functional findings. Fourth, the unusually narrow variability in the recorded outcome scores, noted above, should be independently verified against original case sheets before this manuscript is submitted for publication. Finally, the CTRI trial registration number has not yet been provided and should be inserted prior to submission.

6. Conclusion

In this cohort of 80 adult patients with closed long bone fractures, adjunctive *Cissus quadrangularis* supplementation was associated with significantly faster functional recovery (DASH, LEFS) and pain reduction (VAS) than vitamin D supplementation at every follow-up visit from 2 weeks onward, and with earlier radiographic callus formation at 4 weeks. Final radiological union rates at 12 weeks were high in both groups and did not differ significantly. These findings support a possible role for *Cissus quadrangularis* in accelerating the functional recovery phase of fracture healing and warrant confirmation in a larger, randomised, double-blind trial with biochemical corroboration.

Declarations

Ethics approval was obtained at saveetha medical college and hospital

Informed consent: Written informed consent was obtained from all participants prior to enrolment.

Conflict of interest: None declared.

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