Vitamin D Deficiency is Common at the Time of Fragility Fracture and Can Persist Despite Supplementation: Implications for Correction and Monitoring

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INTRODUCTION: Osteoporosis affects more than 200 million people worldwide and causes an estimated 9 million fractures annually, imposing major disability and healthcare costs. Adequate vitamin D is essential for calcium absorption and bone mineralization, and supplementation is routinely prescribed for both prevention and management of osteoporosis. Vitamin D status is assessed by measuring serum 25-hydroxyvitamin D [25(OH)D] levels, with deficiency defined as <75 nmol/L in high-risk populations. Although supplementation regimens are widely used, 25(OH)D levels are often only assessed at the time of diagnosis or initiation of therapy, with repeated testing typically reserved for when there is a change in clinical status or poor response to therapy. A lack of routine serum 25(OH)D assessment to monitor the adequacy of vitamin D supplementation may represent a care gap in the management of patients with osteoporosis and fragility fractures. The objective of this study was to examine the relationship between prior vitamin D supplementation dose and duration with serum 25(OH)D levels in patients presenting with fragility fractures, and to assess whether follow-up measurements after treatment adjustment provide clinically meaningful information.

METHODS: Patients were enrolled in the Personalized Osteoporosis with Early Recognition (POWER) program, a virtual outpatient Fracture Liaison Service (FLS) that facilitates treatment for patients with new fragility fractures. Eligible participants were 50 years and older, provided informed consent, and enrolled within six weeks of a low-energy fragility fracture (pelvis, hip, proximal humerus, distal radius, or ankle). Personalized bone health baseline assessments included demographics, comorbidities, lifestyle factors, medications, vitamin D supplementation history, bone mineral density using dual X-ray absorptiometry (DEXA), and a Fracture Risk Assessment (FRAX) score. A baseline serum 25(OH)D measurement for most patients was obtained within three months of enrollment, and follow-up measurements were conducted as needed, based on clinical judgment. An independent t-test was used to compare serum 25(OH)D levels in patients who previously took vitamin D supplements and those who did not. A paired t-test was used to compare baseline serum levels with the follow-up level at six months among patients with more than one 25(OH)D measurement during follow-up. Patients were stratified by prior daily vitamin D dosage (0 IU, <1000 IU, 1000–3000 IU, >3000 IU) and by supplementation duration/adherence (no vitamin D, intermittent use, consistent use for <1 year, and consistent use for >1 year). Chi-square tests were used to assess intergroup differences in demographics and FRAX score, and one-way ANOVAs were used to compare serum 25(OH)D levels across dosage and duration/adherence groups. The study was approved by the University of Calgary Research Ethics Board.

RESULTS: A total of 336 patients (mean age 66.4 ± 9.4 years, 86% female) were enrolled. At baseline, mean serum 25(OH)D was 93.6 ± 41.8 nmol/L (n=296), with 34.1% of patients being deficient. Patients reporting vitamin D supplementation (n=102) had significantly higher baseline 25(OH)D levels compared with non-supplement users (n=53) ($p<0.05$; Figure 1). Across dosage categories, mean 25(OH)D significantly increased in a stepwise manner from no supplementation to 1000–3000 IU/day ($p<0.05$). There was no significant difference in serum 25(OH)D levels between the 2000–3000 IU/day and >3000 IU/day groups ($p=0.86$; Figure 2). However, 12% of patients taking daily high-dose supplementation (>3000 IU/day) remained below the recommended threshold (<75 nmol/L). Across duration/adherence categories, patients with no vitamin D supplementation had significantly lower serum 25(OH)D compared with those with consistent supplementation for <1 year ($p<0.05$) and >1 year ($p<0.01$). No significant difference was observed between the no supplementation and intermittent use groups, or between the <1 year and >1-year groups. At six months, follow-up 25(OH)D levels (n=20) increased significantly compared with baseline ($p<0.05$). Demographics and FRAX scores did not differ across supplementation or adherence groups ($p>0.05$).

DISCUSSION: In this cohort, vitamin D supplementation was associated with higher serum 25(OH)D levels, and consistent supplementation for <1 year was sufficient to distinguish patients from those not taking vitamin D. However, one-third of patients were vitamin D deficient at the time of fracture, including many already taking supplements, and some of those on high-dose therapy (>3000 IU/day) remained below sufficiency thresholds. These findings highlight variability in individual response and suggest supplementation history alone is insufficient to ensure adequate vitamin D status. Follow-up testing revealed significant increases in serum 25(OH)D, further supporting the clinical utility of repeat measurement to guide personalized vitamin D supplementation in patients with osteoporosis. Limitations include the observational design and reliance on patient-reported supplementation and adherence.

SIGNIFICANCE/CLINICAL RELEVANCE: A substantial proportion of patients with fragility fractures presented with vitamin D deficiency and remained vitamin D deficient despite supplementation, underscoring that single baseline testing may be inadequate. Routine follow-up 25(OH)D measurement could enable more personalized supplementation and better fracture prevention in this high-risk population.

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IMAGES AND TABLES:

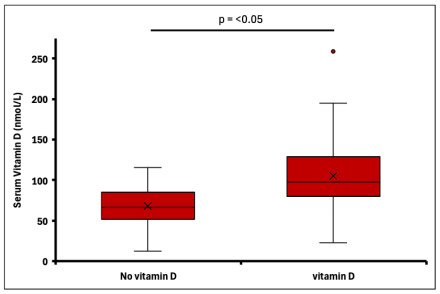

Figure 1: Serum 25(OH)D in patients who used daily vitamin D supplements prior to fragility fracture and those who did not.

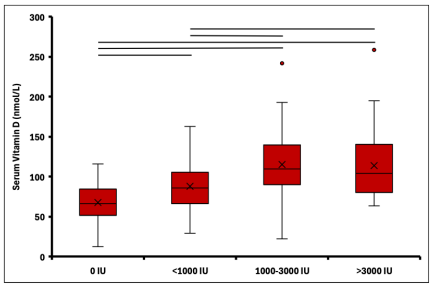

Figure 2: Serum 25(OH)D in patients who used daily vitamin D supplements prior to fragility fracture by dosage of supplement taken. Lines indicate significance ($p<0.05$).