West Texas Journal *of* Medicine

Original Article

The Role of Vitamin D Deficiency in Predicting Secondary Osteoporosis Among Geriatric Patients in West Texas Community: A Cross-Sectional Multi-Center Study

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Abstract

Background: Vitamin D deficiency has been associated with osteoporosis and fracture risk. However, its role in secondary osteoporosis among community-dwelling elderly patients remains unclear.
Objectives: This study aimed to examine the relationships between vitamin D deficiency, bone mineral density, and fracture risk in elderly outpatients in West Texas.
Methods: In this cross-sectional multi-center study, 115 patients aged 65-89 years were recruited from outpatient clinics. Serum 25(OH)D levels, dual-energy x-ray absorptiometry scans, and Fracture Risk Assessment Tool (FRAX) scores were obtained. Patients were categorized by vitamin D status and the presence of secondary osteoporosis. Differences in bone health outcomes were analyzed.
Results: Patients with secondary osteoporosis (n=34) had significantly lower mean serum 25(OH)D levels (24.48 ng/mL) compared to patients without secondary osteoporosis (n=81, 39.90 ng/mL, $p<0.01$). This difference persisted across 23/26 subgroups. Hispanic patients also had lower 25(OH)D levels than non-Hispanics ($p=0.032$). No significant correlations existed between 25(OH)D and other risk factors. 25(OH)D level demonstrated good diagnostic ability for secondary osteoporosis (AUC 0.826).
Conclusion: Vitamin D deficiency appears strongly associated with secondary osteoporosis risk among community-dwelling elderly outpatients. Routine screening and correcting of deficiency may reduce this risk. Larger studies should validate these findings and further examine the mechanisms of this relationship.

Keywords: Vitamin D, Bone Health, Osteoporosis

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Introduction

Osteoporosis is a chronic condition characterized by progressive loss of bone mass and deterioration of bone tissue, resulting in increased bone fragility.[1] Low bone density meeting diagnostic requirements for osteoporosis and osteopenia is common among elderly patients. Dual-energy x-ray absorptiometry (DXA) scans are used clinically to measure spinal and hip bone mineral density (BMD), with World Health Organization (WHO) T-scores between -1 and -2.5 meeting criteria for osteopenia and less than -2.5 for osteoporosis.[2] An estimated 43.4 million American adults over the age of 50 have low bone mass, while 10.2 million older American adults meet the diagnostic criteria for osteoporosis.[3] Fracture is the primary complication among patients with osteoporosis, and patients with osteoporotic fractures suffer increased morbidity, risk of additional fractures, disability, and mortality.[4]

Osteoporosis is also of significant financial burden on the American healthcare system, with costs of osteoporosis and associated fractures projected to be $22 billion annually.[5] Fracture Risk Assessment Tool (FRAX) from the WHO is used clinically to estimate 10-year major osteoporotic fracture risk based on risk factors and DXA score results.[6] Osteoporotic fracture risk factors include drug use, cigarette smoking, low physical activity, and low intake of vitamin D.[7] Managing low bone density is of importance to the healthcare system in reduction of cost, morbidity, and mortality, and vitamin D supplementation to correct deficiency has been explored for its potential to cost-effectively reduce osteoporotic fracture risk.[8]

Vitamin D is a fat-soluble vitamin essential to proper calcium homeostasis and bone metabolism, and its role in human health has been of significant interest to researchers and clinicians.[9] Vitamin D is obtained either through synthesis by skin cells exposed to ultraviolet B radiation or obtained through the diet, and the risk of deficiency is highest among people with insufficient sun exposure, oral intake, or absorption.[10] Its active form calcitriol (1,25(OH)2D3) is involved in human immune, musculoskeletal, cardiac, and nervous systems, and deficiency has been linked to clinical issues including bone demineralization and fracture susceptibility.[11] Vitamin D deficiency is estimated to be at 42% in adults in the US, and 50% of post-menopause women are estimated to have severe vitamin D deficiency.[12,13] This prevalence is likely higher among elderly patients.[14] Race is also a risk factor, with African American adults having the highest prevalence of vitamin D deficiency followed by Hispanic adults.[15]

Vitamin D deficiency has also been found to be higher among rural populations compared to urban populations in Ireland and Iran.[16,17] Deficiency in vitamin D has been associated with lower BMD and higher fracture incidence while supplementation studies have demonstrated increased BMD with improvement of vitamin D status.[18] Serum 25(OH)D levels are used clinically to indicate vitamin D level.[19] Current bone-centric vitamin D guidelines recommend serum 25-hydroxyvitamin D (25(OH)D) of at least 20 ng/mL with daily vitamin D doses of 400-800 IU per day.[20] Patients with 25(OH)D less than 20ng/dL are classified as having a deficiency, and patients with less than 30ng/dL are classified as having insufficiency.[21] Vitamin D supplementation risk characterization has demonstrated its safety, with minimal risk of toxicity or adverse outcomes.[22]

Historical meta-analysis of randomized controlled clinical trials demonstrated the value of vitamin D supplementation in reducing risk for hip and nonvertebral fractures.[23] However, an updated study has returned mixed results. Among interventional studies, seven found decreased fracture incidence with vitamin D supplementation compared to nine studies that did not find significant changes between the control and treatment groups.[18] Vitamin D supplementation for osteoporosis prevention in community-dwelling adults has been called into question in the past decade.[24] Meanwhile, any benefit of vitamin D supplementation may be smaller in community-dwelling elderly and postmenopausal women compared to institutionalized elderly.[25]

The role of vitamin D deficiency and supplementation in the prevention of osteoporotic fracture is of clinical importance and relevance among physicians treating elderly patients. Demonstrated reduction of fracture risk with vitamin D supplementation has historically been inconsistent, and potential benefit may be relatively reduced for noninstitutionalized, community-dwelling elderly. Our study was conducted to assess the relationships between Vitamin D deficiency, bone density, and fracture risk among American rural out-patient elderly patients at our institution. We endeavor to delineate the relative benefits of vitamin D in the prevention of osteoporosis and osteoporotic fractures among community-dwelling rural elderly.

Materials and Methods

Study Population

This is a non-randomized, multi-center cross-sectional study. The study population is comprised of patients 115 between the ages of 65 and 89 years old recruited from Texas Tech University Health Sciences Center outpatient clinics in Odessa, TX from 01/03/2018-01/12/2021.

Inclusion and Exclusion Criteria

Patients included in the study were between ages 65 and 89 at the start of the study and meet at least one of the following criteria: diagnosis of osteopenia, history of fracture, history of falls, low body mass index, chronic steroid use, lack of sun exposure, low activity level, and/or generalized weakness/deconditioning. Study participants can qualify if they live at home, in an assisted living facility, or at a nursing home (if they receive <100% of their outpatient care at a nursing home facility). All subjects included were able to consent to participation or have a patient proxy or power of attorney who could consent on their behalf. Exclusion criteria are patients with active cancer not including squamous and basal cell carcinomas, chronic kidney disease stage IV or greater (GFR less than 30ml/L per 1.73 m^2, on dialysis, with recent fracture 2ithin 2 months, and/or a history of bilateral lower extremity amputation about the ankle. Patients unable to tolerate DEXA scans, home-bound patients, and nursing home patients who receive 100% of outpatient care at nursing home facilities are also excluded from the study.

Data Collection

Interview forms were administered to consenting patients who met inclusion criteria to collect data on demographics, ethnicity, co-morbid diseases, present medications and vitamins, history of fracture, DEXA scan, and other components of the FRAX scoring system. Results from DEXA scans done within 2 years of recruitment were extracted for the study. Age, sex,

weight, height, previous fracture history, parent hip fracture history, current smoking, glucocorticoids, rheumatoid arthritis, secondary osteoporosis, use of 3 or more alcohol units per day, and femoral neck BMD estimated through DEXA are used to calculate FRAX score, as an estimate of risk for both major osteoporotic and hip fractures.

The initial subject study visit entailed obtaining informed consent, filling out questionnaires, obtaining a medical history, and measuring vitamin D levels. A second visit for a DEXA scan was indicated if not obtained on the initial visit or if results were not already on file from the past 2 years. DEXA scans are done every two years as a standard of care for the study population aged 65 to 89 years and are typically covered by insurance.

Statistical Analysis

The project is an observational and cross-sectional study based on convenience sampling. Statistical analyses used two-sided p-values and a significance level of $\alpha = 0.05$. Adjustments to p-values for multiple comparisons are not made since the study intends to evaluate the plausibility of significant differences. Continuous variables are summarized using the mean and standard deviation. Categorical variables are summarized using counts and percentages. Standardized effect sizes are reported using the standardized mean difference (SMD). Statistical significance of differences is computed using the permutational unequal variance t-test and Fisher's test.[26] 95% confidence intervals for mean differences are computed using Monte-Carlo simulation.[27] The consistency of significant differences is reviewed using subgroup analyses. Power analyses for the t-test, Fisher test, and correlation tests are provided in supplementary figure 1.[28] Statistical analyses were completed using R version 4.1.1 and RStudio version 1.4.1717

Results

Characteristics and Outcomes of Patients

Table 1 summarizes the characteristics and outcomes of the patients included in the study. Continuous variables are summarized using the mean and standard deviation. Categorical variables are summarized using counts and percentages.

Table 1. Characteristics and Outcomes of Subjects

Continuous Covariates	**Mean (SD)**
Age (years)	72.71 (6.52)
Weight (kg)	77.60 (17.76)
Height (cm)	162.74 (9.32)
Neck BMD	0.68 (0.14)
Major Osteoporotic	15.57 (12.53)
Hip Fx	5.47 (9.55)
Vitamin D (ng / ml)	35.34 (14.61)
Categorical Covariates	**count / total no. (%)**
Ethnicity	
Non-Hispanic	71/115 (61.7)
Hispanic	37/115 (32.2)
African American	7/115 (6.1)
Sex (male)	88/115 (76.5)
Previous Fracture	55/115 (47.8)
Parent Fracture	14/115 (12.2)
Smoking	16/115 (13.9)
Gluco Cortiods	16/115 (13.9)
Rheumatoid Arthritis	7/115 (6.1)
Secondary Osteoporosis	34/115 (29.6)
Alcohol	7/115 (6.1)
Supplementation	49/115 (42.6)
Dex Scan	71/115 (61.7)

Association of Vitamin D Level with Categorical Covariates

Figure 1(a) displays 95% confidence intervals for the mean differences in Vitamin D levels. Secondary osteoporosis patients had lower mean vitamin D levels compared to patients without secondary osteoporosis (*Δm = -15.42 (ng/ml), 95% CI -19.44 to -*

11.40, P< 0.001), Hispanics had lower mean vitamin D levels compared to non-Hispanics (*Δm = -6.00 (ng/ml), 95% CI -11.05 to -1.10, P=0.032*), and patients with supplementation had higher mean vitamin D level compared to patients without supplementation (*Δm = 6.82(ng/ml), 95% CI 1.49 to 12.03, P=0.013*).

Association of Vitamin D Level with Continuous Covariates

Figure 1(b) displays 95% confidence intervals for the Spearman correlation of Vitamin D levels with continuous covariates. No correlations were identified as practically or statistically significant.

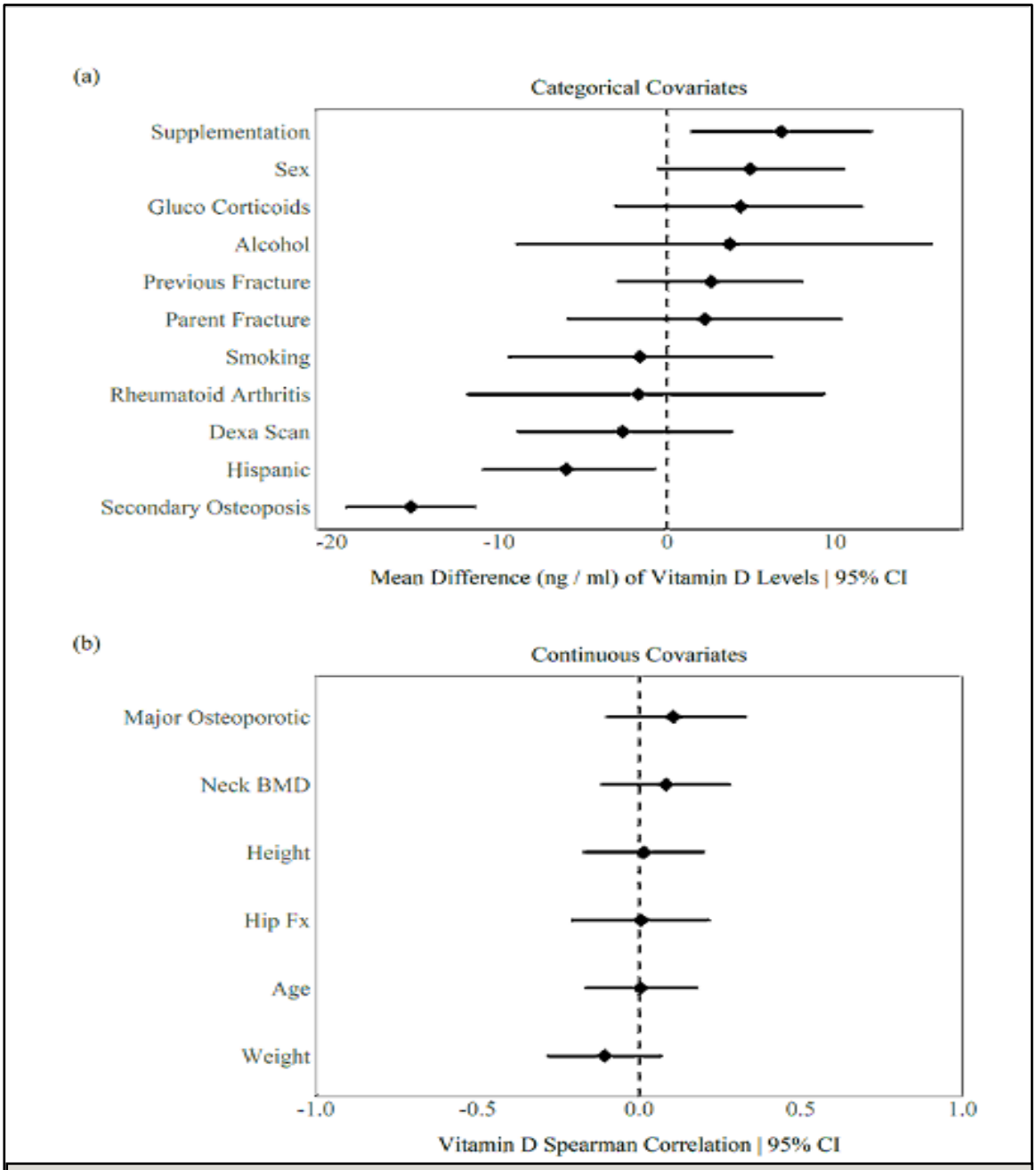


Figure 1. Associations of Vitamin D Level with Categorical and Continuous Covariates

Characteristics and Outcomes of Patients with and without Secondary Osteoporosis

Table 2 summarizes the characteristics and outcomes of patients with and without secondary osteoporosis.

Vitamin D level is the only variable identified as significantly different between the groups. Figure 2 displays the practical and statistical significance of the difference in vitamin D levels between patients with and without secondary osteoporosis.

Table 2. Characteristics and Outcomes of Patients with and without secondary osteoporosis

	Non-Secondary Osteoporosis	Secondary Osteoporosis	SMD	P Value
Age (years)	72.48 (6.53)	73.26 (6.54)	0.12	0.56
Weight (kg)	76.52 (17.09)	80.18 (19.27)	0.20	0.34
Height (cm)	161.88 (8.43)	164.76 (11.03)	0.29	0.18
Ethnicity			0.18	0.63
Non-Hispanic	52/81 (64.2)	19/34 (55.9)		
Hispanic	24/81 (29.6)	13/34 (38.2)		
Asian	5/81 (6.2)	2/34 (5.9)		
Sex (male)	62/81 (76.5)	26/34 (76.5)	<0.01	1.00
Previous Fracture	41/81 (50.6)	14/34 (41.2)	0.19	0.42
Parent Fracture	9/81 (11.1)	5/34 (14.7)	0.11	0.76
Smoking	10/81 (12.3)	6/34 (17.6)	0.15	0.56
Gluco Corticoids	10/81 (12.3)	6/34 (17.6)	0.15	0.56
Rheumatoid Arthritis	4/81 (4.9)	3/34 (8.8)	0.15	0.42
Alcohol	4/81 (4.9)	3/34 (8.8)	0.15	0.42
Neck BMD	0.70 (0.16)	0.64 (0.10)	0.50	0.02
Major Osteoporotic (%)	14.91 (12.97)	16.77 (11.78)	0.15	0.49
Hip FX (%)	5.39 (10.92)	5.62 (6.51)	0.03	0.90
Vitamin D (ng / ml)	39.90 (14.56)	24.48 (7.14)	1.35	<0.01
Supplementation	40/81 (49.4)	9/34 (26.5)	0.49	0.03
Dexa Scan	41/81 (50.6)	30/34 (88.2)	0.89	<0.01

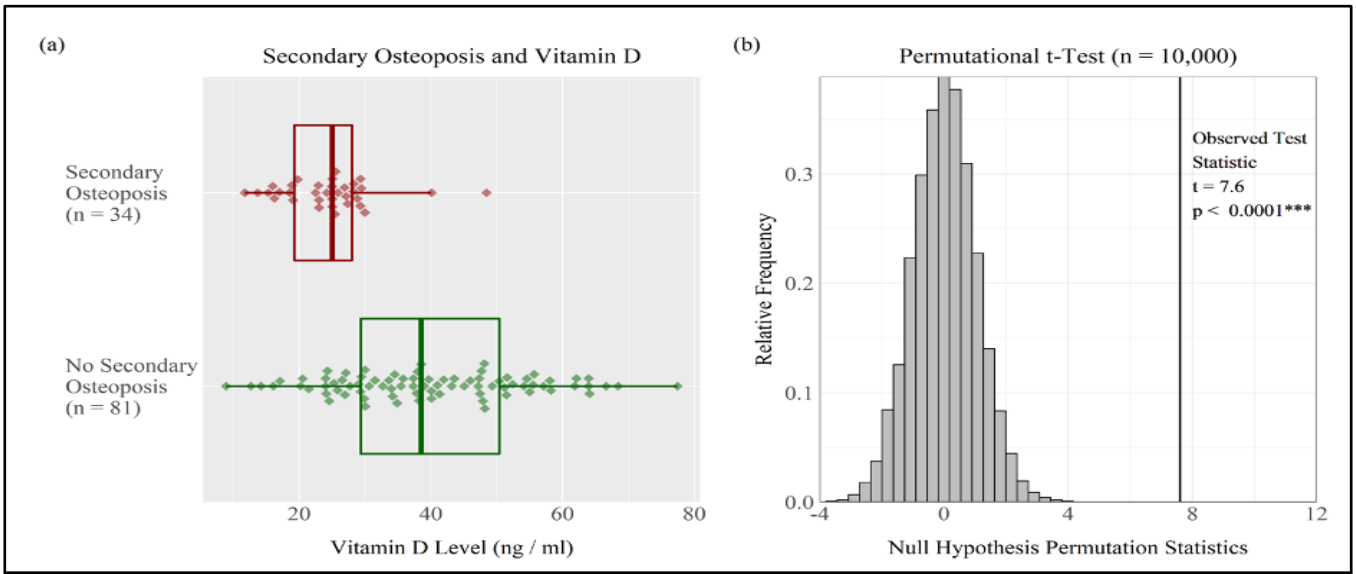


Figure 2. Mean vitamin D levels are significantly different based on secondary osteoporosis.

Subgroup Analyses for Association of Vitamin D Level and Secondary Osteoporosis

Table 3 summarizes the results of subgroup analyses for the association of vitamin D level and secondary osteoporosis.

The mean vitamin D level was consistently lower in secondary osteoporosis patients across all subgroups and twenty-three of the twenty-six subgroups demonstrated a statistically significant difference in vitamin D levels.

Table 3. Subgroup Analyses for Vitamin D Level and Secondary Osteoporosis

Subgroup	total no. (%)	Control Group	Study Group	Difference	P Value
All Data	115/115 (100.0)	39.90	24.48	-15.52	<0.01
Age (years)					
< 72	64 / 115 (55.7)	39.25	23.99	-15.26	< 0.01
73 - 79	32 / 115 (27.8)	39.55	23.31	-16.24	< 0.01
≥ 80	19 / 115 (16.5)	42.82	27.92	-14.91	0.05
Sex					
Male	88 / 115 (76.5)	33.26	27.36	-5.89	0.22
Female	27 / 115 (23.5)	41.94	23.59	-18.35	< 0.01
Race / Ethnicity					
White	71 / 115 (61.7)	41.44	25.88	-15.56	< 0.01
Hispanic	37 / 115 (32.2)	34.91	23.16	-11.76	< 0.01
Black	7 / 115 (6.1)	47.90	19.76	-28.14	0.14
Smoking					
Nonsmoker	99 / 115 (86.1)	40.16	23.95	-16.21	< 0.01
Smoker	16 / 115 (13.9)	38.11	26.98	-11.13	0.12
Parent Fracture					
No	101 / 115 (87.8)	39.38	24.41	-14.96	< 0.01
Yes	14 / 115 (12.2)	44.12	24.86	-19.26	0.02
Previous Fracture					
Yes	60 / 115 (52.2)	41.50	22.72	-18.79	< 0.01
No	55 / 115 (47.8)	38.26	25.71	-12.55	< 0.01
Alcohol					
No	108 / 115 (93.9)	39.31	24.70	-14.61	< 0.01
Yes	7 / 115 (6.1)	51.33	22.19	-29.15	0.03
Rheumatoid Arthritis					
No	108 / 115 (93.9)	39.72	24.84	-14.88	< 0.01
Yes	7 / 115 (6.1)	43.43	20.75	-22.68	0.03
Gluco Corticoids					
No	99 / 115 (86.1)	38.89	24.21	-14.68	< 0.01
Yes	16 / 115 (13.9)	47.10	25.76	-21.35	< 0.01
Supplementation					
No	66 / 115 (57.4)	37.17	24.76	-12.42	< 0.01
Yes	49 / 115 (42.6)	42.70	23.71	-18.99	< 0.01
Height (cm)					
< 157	33 / 115 (28.7)	38.64	22.49	-16.15	< 0.01
157 - 167	40 / 115 (34.8)	41.12	21.61	-19.52	< 0.01
≥ 167	40 / 115 (34.8)	40.28	27.18	-13.10	< 0.01
Weight (kg)					
< 70	42 / 115 (36.5)	41.08	23.39	-17.69	< 0.01
70 - 80	31 / 115 (27.0)	40.34	25.53	-14.82	< 0.01
≥ 80	42 / 115 (36.5)	38.42	24.70	-13.72	< 0.01

Diagnostic Ability of Vitamin D Level as Binary Classifier for Secondary Osteoporosis

The diagnostic ability of vitamin D level as a binary classifier for secondary osteoporosis is visualized with a receiver operating characteristic curve in Figure 3. The area under the curve, AUC = 0.826, suggests that vitamin D level has good diagnostic ability as a binary classifier for secondary osteoporosis.

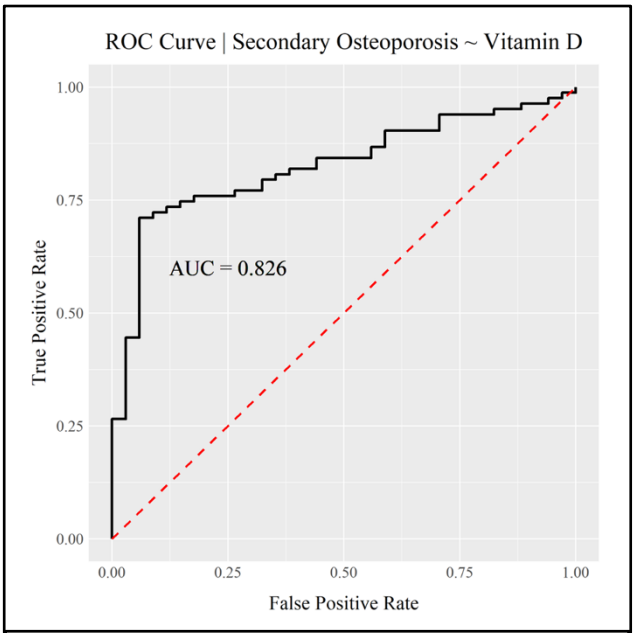


Figure 3. Receiver Operator Characteristics Curve

Summary of Key Findings:

1. Secondary osteoporosis patients had significantly lower mean vitamin D levels than those without the condition.

2. Hispanics had lower mean vitamin D levels compared to non-Hispanics.

3. Patients with vitamin D supplementation had higher mean vitamin D levels than those without.

4. No significant correlations were found between vitamin D levels and continuous covariates.

5. Vitamin D level was the only significant differentiating variable between patients with and without secondary osteoporosis.

6. In twenty-three out of twenty-six subgroups, secondary osteoporosis patients had statistically significantly lower vitamin D levels.

7. Vitamin D level demonstrated good diagnostic ability as a binary classifier for secondary osteoporosis with an AUC of 0.826.

Discussion

This study examined the potential link between vitamin D levels and secondary osteoporosis. The study was non-randomized and multi-centered, with patients aged 65 to 89 years old participating. The results revealed significant disparities in vitamin D levels across major categorical variables. A significant discovery was that patients with secondary osteoporosis consistently had lower mean vitamin D levels than those who did not have secondary osteoporosis. This crucial discovery suggests a probable link between low vitamin D levels and an increased risk of subsequent osteoporosis.

Furthermore, ethnicity was discovered to play an essential role in vitamin D levels, with Hispanics having lower mean vitamin D levels than non-Hispanics. This variation could be due to genetic, nutritional, or environmental variables influencing vitamin D synthesis and metabolism in various ethnic groups. Furthermore, the study found that patients who took vitamin D supplements had higher mean vitamin D

levels than those who did not, confirming the importance of vitamin D in bone health and the potential benefits of supplementation.

Despite these categorical differences, no significant correlations were discovered between vitamin D levels and many variables investigated in the study. In this patient population, variables such as age, gender, weight, height, previous fracture history, parent hip fracture history, current smoking habits, glucocorticoid use, presence of rheumatoid arthritis, and femoral neck BMD estimated via DEXA scans did not show a strong relationship with vitamin D levels. This finding shows that these factors may not significantly influence vitamin D levels or that their influence is overshadowed by other, more potent factors not investigated in this study. When comparing patients with and without secondary osteoporosis, vitamin D level emerged as the only variable significantly different between the two groups. This further underscores the potential role of vitamin D in secondary osteoporosis. More specifically, in almost all subgroups, vitamin D levels were distinctly lower in patients with secondary osteoporosis, suggesting a pervasive pattern regardless of other factors.

The study also shed light on the potential of vitamin D levels as a diagnostic tool and a binary secondary osteoporosis classifier. Using a receiver operating characteristic (ROC) curve, the area under the curve (AUC) was estimated to be 0.826. It supported the hypothesis that vitamin D levels have a significant diagnostic ability for recognizing secondary osteoporosis, potentially functioning as a valuable tool in therapeutic settings.

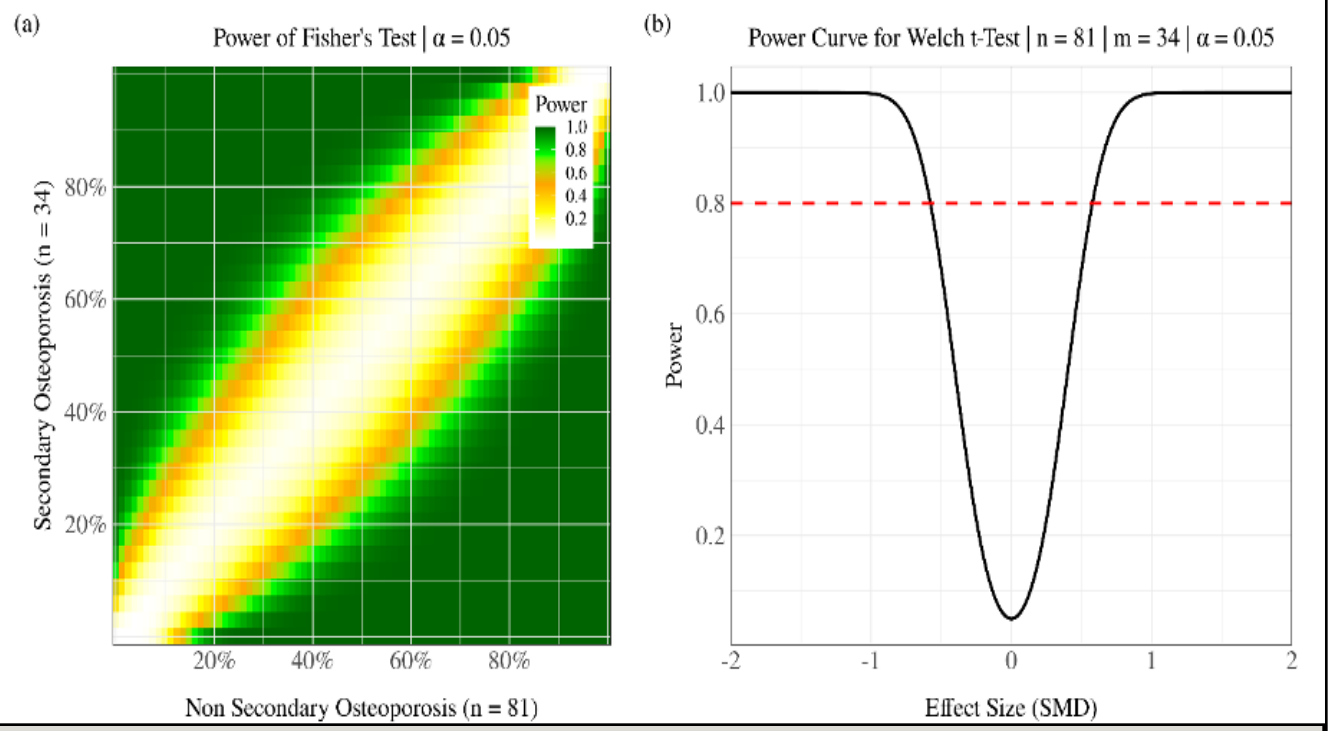
Conclusion:

Indeed, the findings of this study highlight the vital role vitamin D may play in the health of the geriatric population, particularly in the case of secondary osteoporosis. The study discovered a strong link between low vitamin D levels and secondary osteoporosis. This result highlights the significance of regular monitoring and maintaining adequate vitamin D levels in the geriatric population to prevent and manage this illness.

The study's findings shed light on vitamin D's possible impact on bone health in developing secondary osteoporosis. The persistently lower mean vitamin D levels in patients with secondary osteoporosis than those without it highlight the potential protective role of this vitamin in developing this condition. These findings not only underline the significance of prevention but also point to potential therapeutic approaches. Maintaining optimum vitamin D levels may effectively reduce the risk and progression of secondary osteoporosis. As a result, the study suggests that vitamin D could be a key component in developing novel, tailored treatments for managing and preventing secondary osteoporosis.

In terms of the future, the study provides a clear direction for additional research. It is now critical to probe deeper into these first findings. More research could be done to validate these relationships, investigate the underlying mechanisms, and investigate the significance of vitamin D supplementation in patients at risk of developing secondary osteoporosis. The possibility of developing preventive measures or therapies based on these findings throws up fascinating possibilities. Future studies must also focus on creating new dietary guidelines for the elderly population and maintaining adequate vitamin D levels in this population.

Supplementary



Supplementary Figure 1. Power Analyses

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