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Association Between Serum 25-Hydroxyvitamin D3 and Disease Activity in Pediatric Crohn's Disease: A Cross-Sectional Study With Bone Age Stratification

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Abstract

Background

Vitamin D deficiency is prevalent in pediatric Crohn's disease (CD) and linked to inflammation. We evaluated the correlation between serum 25-hydroxyvitamin D3 (25(OH)D3) and disease activity across distinct bone age stages in Chinese children.

Methods

53 pediatric CD patients were categorized by 25(OH)D3 levels (deficiency ≤ 20 ng/mL vs. non-deficiency>20 ng/mL). Activity and skeletal development were assessed via PCDAI and bone age minus chronological age (BA–CA). Spearman correlation and multivariate regression identified 25(OH)D3 predictors. ROC curves evaluated predictive performance for clinical activity.

Results

The deficient group (n = 32) showed higher rates of diarrhea, fever, and oral ulcers, and lower albumin, calcium, and hemoglobin levels compared to the non-deficient group (n = 21). Delayed bone age incidence was 21.9% (P = 0.034). Multivariate regression showed 25(OH)D3 independently correlated negatively with PCDAI and positively with BA-CA. The combined 25(OH)D3 and hemoglobin model achieved an AUC of 0.845. Subgroup analysis revealed 25(OH)D3 was associated with disease activity in children without delayed bone age, but this significance was not reached in those with delayed bone age.

Conclusion

Serum 25(OH)D3 is an auxiliary biomarker for pediatric CD activity. Its association with disease activity may be influenced by bone age development status.

1. Introduction

Crohn's disease (CD), a segmental and transmural chronic inflammatory condition of the gastrointestinal tract with complex etiology, is characterized by clinical manifestations including diarrhea, abdominal pain, anemia, oral ulcers, and systemic malnutrition [1]. Since the 21st century, the epidemiological profile of CD has undergone significant evolution globally, particularly in East Asian countries such as China, where incidence rates have shown a marked upward trend [2]. Compared to adult-onset cases, pediatric CD occurs during a critical growth and development window. The chronic inflammatory burden, prolonged nutritional insufficiency, and malabsorption frequently result in severe growth retardation, delayed skeletal maturation, and delayed puberty onset [3, 4]. Previous studies have demonstrated delayed bone age development in pediatric CD patients. Therefore, bone age assessment should be

incorporated as a routine examination for these patients to facilitate precise evaluation of growth status and adjustment of treatment regimens [5].

In the pathophysiology of pediatric CD, vitamin D deficiency is considered to result from the combined effects of impaired bone maturation and disrupted immune tolerance. Research by Palmer and Weaver indicates that vitamin D functions not only as a liposoluble hormone regulating calcium and phosphorus metabolism but also as a critical immunomodulator [6]. Its active form, by binding to vitamin D receptors (VDR) distributed across various immune cells, suppresses Th1 and Th17-mediated proinflammatory responses and enhances the structural integrity of the intestinal epithelial barrier (e.g., by upregulating Claudin-1 and ZO-1 expression). However, within the inflammatory microenvironment of CD, proinflammatory cytokines can conversely downregulate VDR expression, forming a harmful feedback loop that weakens immunomodulatory efficacy and exacerbates mucosal damage [7].

Epidemiological data indicate that the prevalence of vitamin D deficiency is significantly higher among CD patients than in healthy individuals [6]. Although its association with disease activity has been extensively studied, its clinical predictive value remains controversial [8, 9, 10]. This may be attributed to the heterogeneity of study populations, and evidence from pediatric cohorts in China remains scarce. Traditional growth assessment metrics such as height-for-age z-score (HAZ) or weight-for-age z-score (BMIZ) are susceptible to short-term nutritional deficiencies and absorption disorders, making them inadequate for reflecting the long-term impact of chronic inflammation on impaired growth and development [11]. In contrast, delayed bone age better reflects the long-term impact of growth retardation [5]. Given that CD often manifests as multidimensional abnormalities—such as chronic anemia reflected by reduced hemoglobin (Hb), which frequently coexists with vitamin D deficiency—these findings collectively reveal the overall nutritional depletion and inflammatory burden in affected children [1]. However, the association between 25(OH)D3 and delayed bone age development, as well as the predictive efficacy of a combined model incorporating Hb in Chinese children with CD, remains unexplored.

Therefore, this study aims to evaluate the association between serum 25(OH)D3 levels and disease activity in Chinese pediatric patients with CD. By integrating dual dimensions of compromised immune, nutritional, and hematopoietic systems, we developed a novel diagnostic model combining 25(OH)D3 and Hb to predict disease activity. We further explored the independent association between 25(OH)D3 deficiency and delayed bone age—a core indicator reflecting long-term growth impairment. Furthermore, stratified analysis across different bone age subgroups validated the robustness of these findings, aiming to provide more precise clinical evidence for risk stratification and growth intervention in pediatric CD.

2. Methods

2.1 Ethics Statement

The study was approved by the Ethics Committee of the First Affiliated Hospital of Fujian Medical University (Approval No. MRCTA, ECFAH FMU [2019] 219). Written informed consent was obtained from the parents or caregivers. This study was conducted in accordance with the ethical principles of the 1964 Declaration of Helsinki and its later amendments. Clinical trial number: not applicable.

2.2. Patients

This retrospective study included 53 pediatric Crohn's disease (CD) patients admitted to and followed up at the Department of Pediatrics, The First Affiliated Hospital of Fujian Medical University between July 2017 and August 2025. Diagnosis was based on the revised Porto criteria of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) [12]. Patients were divided into two groups based on serum 25-hydroxyvitamin D3 [25(OH)D3] levels at admission: vitamin D deficiency group (≤ 20 ng/mL, n = 32) and non-deficiency group (> 20 ng/mL, n = 21).

Inclusion criteria:

 Age ≤ 18 years;

 Meeting CD diagnostic criteria with complete clinical follow-up data;

 Complete baseline serum 25(OH)D3 measurement data;

 Clear anteroposterior wrist radiograph obtained within one week of admission, enabling bone age assessment;

 Traceable clinical data (gender, chronological age, disease duration, mode of delivery, laboratory parameters, etc.).

Exclusion Criteria:

 Concurrent congenital growth disorders, congenital nutritional/metabolic diseases, endocrine disorders, malignancies, or other conditions severely affecting bone metabolism;

 Prior vitamin D supplementation or long-term high-dose glucocorticoid therapy before initial diagnosis;

 Missing clinical data or critical assessment images ≥ 20%, rendering statistical analysis impossible.

2.3 Data Collection

2.3.1. General Characteristics and Anthropometry

Baseline data collected included patient gender, age (years), time from symptom onset to diagnosis (days), positive family history, extraintestinal manifestations, Montreal classification, body mass index z-score, age-specific height z-score (calculated using the World Health Organization [WHO] Child Growth Standards [13]), and serum 25(OH)D3 levels at initial diagnosis.

2.3.2 Bone Assessment

All pediatric patients underwent an anteroposterior radiograph of the left wrist within one week of admission to measure bone age. Bone age interpretation was performed by two experienced radiologists under double-blind conditions using the TW3 scoring system (Tanner-Whitehouse 3) combined with China-05 standards [14, 15, 16, 17]. Scores were calculated separately for carpal bones and radius, as well as metacarpal/phalangeal bones, based on the child's sex, and ultimately converted into bone age values. To eliminate the influence of chronological age and gender on growth assessment, this study employed the difference between bone age and chronological age (BA-CA) as a standardized developmental indicator. Following commonly used clinical criteria, BA-CA < -1 year was defined as a significant bone age delay, indicating that the child's bone age maturity lagged significantly behind their chronological age.

2.3.3. Laboratory and Disease Assessment

This study systematically evaluated indicators reflecting disease activity, bone metabolism, and nutritional status by collecting fasting venous blood and stool samples from pediatric patients. Hematological and inflammatory markers included white blood cell count (WBC), hemoglobin (Hb), hematocrit (HCT), platelet count (PLT), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). Nutritional and bone metabolism indicators included albumin (ALB), serum calcium (Ca), serum phosphorus (P), and alkaline phosphatase (ALP). Serum 25-hydroxyvitamin D3 levels were used to determine pediatric vitamin D status, with 25(OH)D3 ≤ 20 ng/mL defined as vitamin D deficiency. Concurrently, fecal occult blood testing (FOBT) and fecal calprotectin (FC) assessed intestinal inflammatory burden. For disease severity assessment, the Pediatric Crohn's Disease Activity Index (PCDAI) [18] and the Simplified Endoscopic Score for Crohn's Disease (SES-CD) [19] were used to represent disease activity. This study defined moderate-to-severe clinical activity, defined as PCDAI ≥ 30 points, as the primary predictive outcome.

2.4 Statistical Data

Data analysis was performed using IBM SPSS version 26.0 and R version 4.2.0. Discrete data are presented as frequencies and percentages. Continuous variables are expressed as mean ± standard deviation (for normally distributed variables) or median and interquartile range (for non-normally distributed variables). Intergroup comparisons were conducted using chi-square tests, independent samples t-tests, or Mann-Whitney U tests. Spearman's rank correlation analysis explored associations between 25(OH)D3 and PCDAI, SES-CD, BA-CA, CRP, ESR, HGB, ALB, and FC. Multivariate logistic regression assessed the relationship between 25(OH)D3 and moderate-to-severe disease activity, adjusting for age, sex, BMI-Z, CRP, hemoglobin, and disease phenotype. The predictive performance of 25(OH)D3 and the combined model (25(OH)D3 + Hb) was assessed using ROC curves and AUC. The DeLong test was used to compare AUC differences between models. Subgroup ROC analyses based on BA-CA status were performed to compare AUC across subgroups and validate model robustness. All statistical tests were two-sided, with $P < 0.05$ indicating statistical significance.

3. Results

3.1. Baseline Demographic and Clinical Characteristics

As shown in Table 1, no significant differences were observed between groups in age at diagnosis, gender, disease duration, or family history ($P > 0.05$). The vitamin D ≤ 20 ng/mL group exhibited significantly higher rates of diarrhea (37.5% vs. 9.5%, $P = 0.029$), fever (62.5% vs. 23.8%, $P = 0.011$), and oral ulcers (37.5% vs. 9.5%, $P = 0.029$) were significantly higher than in the vitamin D > 20 ng/mL group. Paris classification revealed a lower proportion of non-stricture/non-penetrating type (B1) in the vitamin D ≤ 20 ng/ml group (50.0% vs. 90.5%, $P = 0.003$), while the proportions of stenotic type (B2) (46.9% vs. 9.5%, $P = 0.006$) and growth retardation (G1) (43.8% vs. 9.5%, $P = 0.013$) were higher.

Table 1
Demographic and clinical characteristics.

Variables	Group with 25(OH)D3 > 20 ng/ml (n = 21)	Group with 25(OH)D3 ≤ 20 ng/ml (n = 32)	Statistics (H/χ2/t)	P value
Median age, years, (IQR)	12.0 (10.0, 13.0)	11.5 (10.0, 13.0)	0.271	0.602
Gender, Male, n (%)	15 (71.4)	16 (50.0)	2.398	0.159
Time from onset to diagnosis, (IQR)	246 (70.5, 696.0)	186 (90.5, 767.5)	0.167	0.682
Positive family history, n (%)	1 (4.8)	5 (15.6)	1.490	0.384
Extra-intestinal manifestation				
Abdominal pain, n (%)	12 (57.1)	24 (75.0)	1.856	0.232
Diarrhea, n (%)	2 (9.5)	12 (37.5)	5.105	**0.029**
Hematochezia, n (%)	3 (14.3)	8 (25.0)	0.885	0.494
Fever, n (%)	5 (23.8)	20 (62.5)	7.616	**0.011**
Weight loss, n (%)	5 (23.8)	8 (25.0)	0.010	0.922
Oral ulcers, n (%)	2 (9.5)	12 (37.5)	5.105	**0.029**
Anemia, n (%)	2 (9.5)	3 (9.4)	0.000	0.986
HAZ, mean ± SD	-0.53 ± 0.97	-0.80 ± 1.03	0.967	0.338
BMIZ, mean ± SD	-1.28 ± 1.00	-0.98 ± 0.96	1.092	0.280
PCDAI score, (IQR)	20.0 (12.3, 38.5)	32.5 (15.5, 40.0)	2.020	0.155
SES-CD score, (IQR)	26.0 (5.0, 34.5)	19.5 (9.8, 26.8)	0.339	0.560
Paris classification				
A1a (Age < 10y), n (%)	6 (28.6)	3 (9.4)	3.811	0.136
A1b (Age 10-17y), n (%)	15 (71.4)	29 (90.6)	3.314	0.131
L1 (terminal ileum), n (%)	5 (23.8)	3 (9.4)	2.061	0.240
L2 (colon), n (%)	0 (0.0)	2 (6.3)	1.364	0.512

HAZ,height-for-age z-score; BMIZ,body mass index-for-age z-score; PCDAI, Pediatric Crohn's Disease Activity Index; SES-CD, Simple Endoscopic Score for Crohn's Disease;

Variables	Group with 25(OH)D3 > 20 ng/ml (n = 21)	Group with 25(OH)D3 ≤ 20 ng/ml (n = 32)	Statistics (H/χ2/t)	P value
L3 (ileocolon), n (%)	15 (71.4)	28 (87.5)	2.139	0.169
L4a (upper GI, proximal to ligament of Treitz), n (%)	1 (4.8)	4 (12.5)	0.889	0.637
L4b (upper GI, distal to ligament of Treitz), n (%)	9 (42.9)	15 (46.9)	0.083	0.787
B1 (Non-stricturing), n (%)	19 (90.5)	16 (50.0)	9.262	**0.003**
B2 (Stricturing), n (%)	2 (9.5)	15 (46.9)	8.119	**0.006**
B3 (Penetrating), n (%)	0 (0.0)	1 (3.1)	0.669	1.000
G1 (Growth delay), n (%)	2 (9.5)	14 (43.8)	7.048	**0.013**
P (Perianal modifier), n (%)	8 (38.1)	12 (37.5)	0.002	0.965

HAZ,height-for-age z-score; BMIZ,body mass index-for-age z-score; PCDAI, Pediatric Crohn's Disease Activity Index; SES-CD, Simple Endoscopic Score for Crohn's Disease;

3.2. Comparison of Disease Laboratory Markers

Laboratory and bone development indicators (Suppl Table 1) revealed significantly lower levels of HB (P = 0.012), HCT (P = 0.003), ALB (P = 0.001), serum calcium (P = 0.019), and BA-CA values (-0.15 vs. 0.82, P = 0.001) were significantly lower. Additionally, the fecal calcitonin-positive rate (100.0% vs. 85.7%, P = 0.028) and incidence of delayed bone age (21.9% vs. 0.0%, P = 0.034) were significantly higher in the vitamin D ≤ 20 ng/mL group.

3.3. Correlations Between 25(OH)D3 Levels and Disease Activity and Clinical Indicators

Spearman correlation analysis (Suppl Table 2 and Suppl Fig. 1) revealed that serum 25(OH)D3 levels were negatively correlated with PCDAI (rs = − 0.47, P < 0.001), SES-CD (rs = − 0.39, P = 0.004), ESR (rs = − 0.27, P = 0.050), and PLT (rs = − 0.29, P = 0.038). Concurrently, 25(OH)D3 showed significant positive correlations with ALB (rs = 0.44, P = 0.001) and serum calcium (Ca) (rs = 0.41, P = 0.002).

3.4. Independent Factors Associated with 25(OH)D3 Levels

Logistic regression analysis (Table 2) revealed a significant association between serum 25(OH)D3 levels and disease activity in pediatric Crohn's disease. In the unadjusted model (Model 1), higher 25(OH)D3 levels were associated with a lower risk of active disease (OR = 0.839, 95% CI: 0.745–0.922, P = 0.001). After adjusting for age and sex (Model 2: OR = 0.815, 95% CI: 0.716–0.905, P < 0.001) and further

adjustment for BMIZ score, CRP, hemoglobin, and disease behavior (Model 3: OR = 0.842, 95% CI: 0.723–0.953, P = 0.012).

Table 2
Association between serum 25(OH)D3 and disease activity

Model	OR (95% CI)	P value
Model 1	0.839 (0.745–0.922)	0.001
Model 2	0.815 (0.716–0.905)	< 0.001
Model 3	0.842 (0.723–0.953)	0.012
Model 1: unadjusted.		
Model 2: adjusted for age and sex.		
Model 3: adjusted for age, sex, BMI-Z, CRP, hemoglobin, and disease behavior.		

3.5. The Restricted Cubic Spline Analysis

RCS analysis (Suppl Fig. 2) revealed a negative correlation between serum 25(OH)D3 levels and the probability of disease clinical activity occurrence (p = 0.042). This indicates an approximately linear relationship between 25(OH)D3 and disease clinical activity. As 25(OH)D3 levels increase, the predicted probability of disease clinical activity gradually decreases.

3.6. Predictive Performance of 25(OH)D3 for Clinical Activity

ROC analysis (Suppl Table 3 and Fig. 1) showed that serum 25(OH)D3 had an AUC of 0.792 for predicting disease clinical activity. Hemoglobin alone demonstrated comparable predictive performance (AUC = 0.787). The combined model incorporating 25(OH)D3 and hemoglobin yielded a higher AUC of 0.845. However, the DeLong test indicated no statistically significant difference between the combined model and 25(OH)D3 alone (P = 0.135).

3.7. Subgroup Analysis Based on Bone Age

Subgroup analysis (Table 3) revealed that serum 25(OH)D3 levels remained significantly associated with disease activity in patients without bone age delay (OR = 0.858, 95% CI: 0.747–0.987, P = 0.032), whereas no significant association was observed in patients with delayed bone age (OR = 0.752, 95% CI: 0.425–1.330, P = 0.325). However, the interaction between 25(OH)D3 and delayed bone age was not statistically significant (P for interaction = 0.613).

Table 3
Subgroup analysis according to bone age delay

Subgroup	OR (95% CI)	P value	P for interaction
No bone age delay	0.858 (0.747–0.987)	0.032	
Bone age delay	0.752 (0.425–1.330)	0.325	0.613
Adjusted for age, sex, BMIZ, CRP, hemoglobin and disease behavior.			

Discussion

This study evaluated the clinical characteristics and predictive value of serum 25(OH)D3 levels in Chinese pediatric CD patients. Findings revealed widespread vitamin D deficiency in pediatric CD, closely associated with more aggressive disease phenotypes such as stricturing lesions and growth retardation. Multivariate regression analysis demonstrated significant independent correlations between serum 25(OH)D3 levels and PCDAI as well as BA-CA. Furthermore, this study demonstrated that a combined model of 25(OH)D3 and hemoglobin (AUC = 0.845) showed higher predictive efficacy for clinical activity assessment, though this difference did not reach statistical significance compared to using a single indicator. Most critically, we found that bone age development status may influence the association between 25(OH)D3 and disease activity.

In inflammatory bowel disease, vitamin D is one of the markers that fluctuates significantly due to multiple factors, such as genetic predisposition, seasonal variations, physical activity levels, disease status, and whether vitamin D supplements are taken orally[33]. Our analysis revealed that over half (60.4%, n = 32) exhibited vitamin D deficiency (levels below 20 ng/mL). Results indicate that children in the vitamin D-deficient group were more likely to exhibit the stricture-prone (B2) and growth-delayed (G1) phenotypes. Previous studies confirm that vitamin D deficiency reduces vitamin D receptor (VDR) expression on immune cell surfaces. Since VDR is a key regulator suppressing intestinal fibrosis, vitamin D deficiency may increase the risk of intestinal stricture formation [20, 34]. Meta-analyses further confirm that vitamin D deficiency disrupts calcium-phosphorus homeostasis and enhances inflammation-mediated growth hormone resistance, closely correlating with growth retardation [21]. Notably, this study found significant negative correlations between 25(OH)D3 and PCDAI, SES-CD, and ESR, consistent with numerous other studies [22, 23, 24, 25, 26, 27, 28, 29]. However, one Swedish study reported no significant association with SES-CD [30]. This discrepancy may stem from 25(OH)D3's ability to regulate the balance of T cell subsets (Th1, Th2, and Th17) by suppressing systemic proinflammatory factors TNF-α and IL-6 release, thereby improving systemic inflammatory status. In contrast, endoscopic scores solely reflect localized mucosal damage within the gut [21]. Vitamin D levels also showed a negative correlation with fecal calprotectin, consistent with previous studies [8, 31].

In this study, we further investigated whether combining 25(OH)D3 with hemoglobin could enhance predictive ability for pediatric CD disease activity. ROC analysis showed that the AUC for the combined 25(OH)D3 and Hb model was higher than that for the 25(OH)D3 model alone, though the difference was

not statistically significant. Previous studies suggest vitamin D levels may negatively correlate with ferritin, thereby affecting hemoglobin levels [32]. This study similarly found that patients with vitamin D deficiency had significantly lower HB levels than those with adequate vitamin D status. Pathophysiologically, chronic intestinal inflammation may impair fat-soluble vitamin absorption due to ileal involvement, while simultaneously triggering anemia by disrupting iron metabolism and causing gastrointestinal blood loss. Thus, the combined 25(OH)D3 and Hb model holds potential as a biomarker for assessing disease activity in pediatric CD.

Interestingly, subgroup analysis based on bone age suggests that the association between serum 25(OH)D3 levels and disease activity may vary depending on bone age development status. In children without delayed bone age, 25(OH)D3 levels remained significantly correlated with moderate-to-severe disease activity; however, this association failed to reach statistical significance in children with markedly delayed bone age. Previous studies have demonstrated an increased risk of metabolic bone disease in pediatric Crohn's disease patients, potentially attributable to the combined effects of multiple factors, including calcium and vitamin D deficiency, persistent chronic inflammation, inadequate nutritional intake, reduced physical activity, and glucocorticoid therapy [35, 36]. Persistent inflammation can impair bone metabolism by affecting osteoblast and osteoclast function through proinflammatory cytokines such as IL-6, TNF-α, and IL-1, thereby disrupting bone remodeling processes [37]. Inflammation also indirectly contributes to reduced physical activity. Numerous studies confirm that decreased physical activity leads to lower bone mineral density (BMD) and skeletal muscle index (SMI), while poor appetite results in reduced calcium and mineral intake, malabsorption, and increased energy requirements [38, 39, 40]. Glucocorticoid therapy alleviates systemic and local inflammation but may indirectly contribute to skeletal disease. While effective, this treatment significantly impacts bone health and development, creating a vicious cycle [41]. Concurrently, prolonged disease burden, diminished appetite, and malabsorption may further exacerbate calcium and vitamin D deficiency or absorption disorders. Consequently, delayed bone age may reflect chronic exposure to systemic inflammation and nutritional deficiency in children with CD. In this context, serum 25(OH)D3 levels may persistently remain low, partially explaining why its association with disease activity failed to reach statistical significance in this subgroup. Clinically, this suggests that a single 25(OH)D3 measurement may inadequately reflect disease activity in children with pronounced bone age delay, necessitating comprehensive evaluation using multidimensional clinical and laboratory indicators. It should be noted that the small sample size in the bone age delay subgroup may have limited the statistical power of this subgroup analysis; therefore, these findings require further validation in larger-scale studies.

This study has certain limitations. First, as a single-center retrospective study, we confirmed correlations between variables but could not establish a definitive causal relationship between 25(OH)D3 levels and disease activity in pediatric CD. Second, the sample size was relatively limited, and we were unable to dynamically track changes in various indicators following vitamin D supplementation therapy. Future large-scale prospective cohort studies are needed to validate this combined model and to investigate the molecular mechanisms underlying the impact of different bone age states on disease activity.

Conclusion

In summary, serum 25(OH)D3 levels correlate with disease activity and bone age development in Chinese children with CD. Models incorporating both 25(OH)D3 and Hb demonstrate superior predictive performance. The association between 25(OH)D3 and disease activity may vary across different bone age development stages. In CD patients with delayed bone age development, disease status should be assessed using multidimensional clinical and laboratory indicators.

Abbreviations

CD
Crohn's disease
BA
bone age
CA chronological age
25(OH)D3
25-hydroxyvitamin D3
TW3
Tanner-Whitehouse 3
ALB
albumin
Ca
calcium
P,phosphorus
ALP
alkaline phosphatase
WBC
white blood cell count
CRP
c-reactive protein
PLT
platelet count
HCT
hematocrit
ESR
erythrocyte sedimentation rate
Hb
hemoglobin
HAZ
height-for-age Z-score
BMIZ

body mass index Z-score
FC
fecal calprotectin
FOBT
fecal occult blood test
VDR
vitamin D receptor
BMD
bone mineral density
SMI
skeletal muscle index

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the First Affiliated Hospital of Fujian Medical University (Approval No. MRCTA, ECFAH FMU [2019] 219). Written informed consent was obtained from the parents or caregivers. This study was conducted in accordance with the ethical principles of the 1964 Declaration of Helsinki and its later amendments. Clinical trial number: not applicable.

Consent for publication

Consent for publication was obtained from the children's parents or legal guardians.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare no competing interests.

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Author Contributions:

Yifei Zhang: Conceptualization, methodology, software, formal analysis, original draft preparation, and visualization. Peilin Wu: Formal analysis, investigation, and data curation. XiLin Peng: Investigation and data curation. QiaoPing Wu: Investigation and data curation. WenXin Chen: Investigation and data

curation. Yuan Xie: Investigation and data curation. Suqing Chen: Writing—review and editing, supervision, and project administration.

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Figures

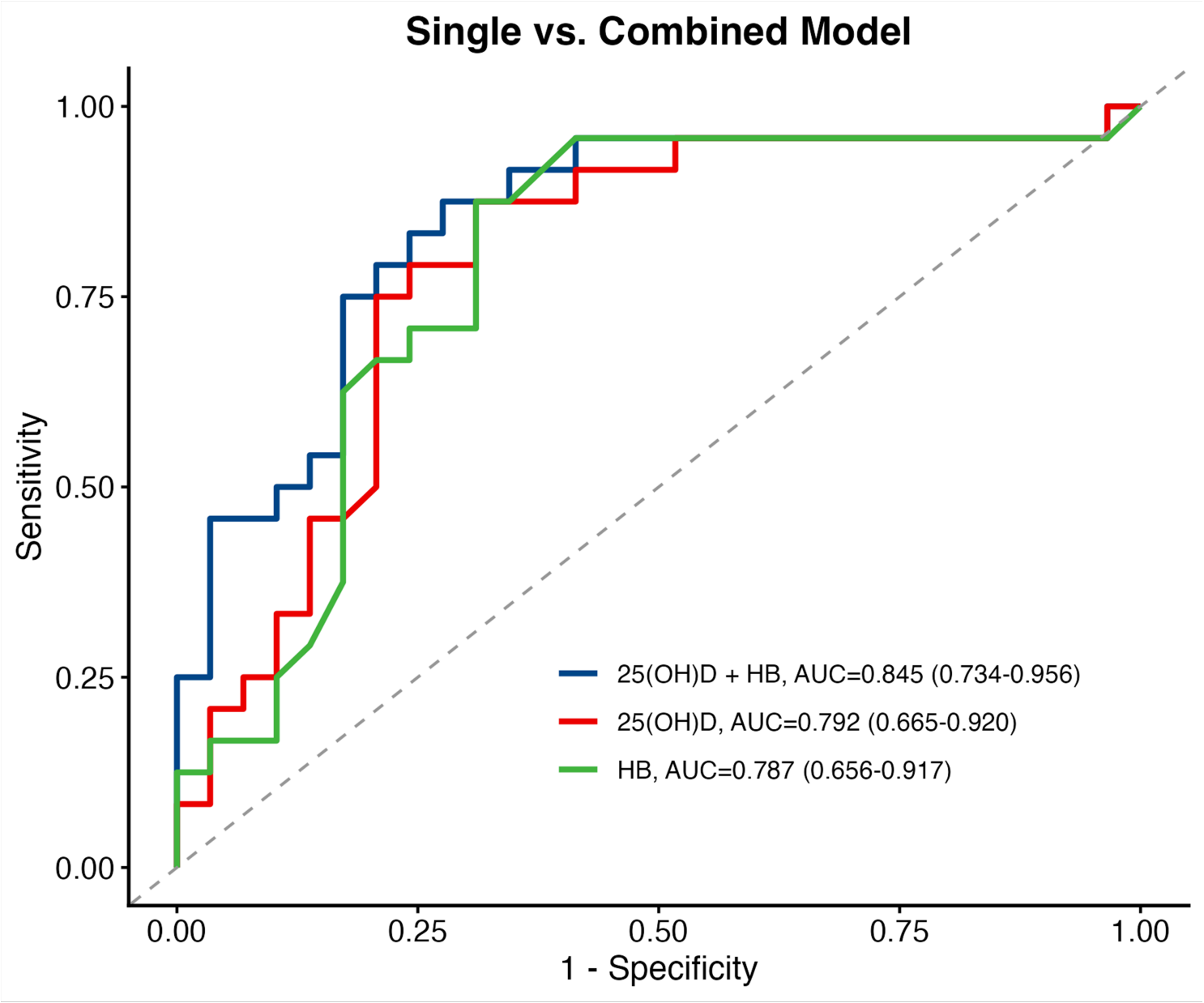


Figure 1

ROC curves for predictive performance of 25(OH)D3 for clinical activity ROC, receiver operator characteristic curve

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