



Abant Tıp Dergisi

Abant Medical Journal

Abant Med J 2026;15(2):165-173, doi:10.47493/abantmedj.1940302



Prognostic Value of Baseline Serum 25-Hydroxyvitamin D in High-Risk Resected Cutaneous Melanoma

Yüksek Riskli Rezekte Kutanöz Melanomda Bazal Serum 25-Hidroksivitamin D Düzeyinin Prognostik Değeri

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Geliş Tarihi (Received): 30.04.2026

Kabul Tarihi (Accepted): 20.06.2026

Yayın Tarihi (Published): 28.08.2026

Abstract

Objective: Vitamin D has been proposed as a prognostic biomarker in melanoma, but its significance in the postoperative setting remains unclear. We examined whether perioperative serum 25-hydroxyvitamin D [25(OH)D] status provides prognostic information on recurrence-free survival (RFS) in high-risk stage II–III cutaneous melanoma treated by complete resection.

Materials and Methods: In this retrospective multicenter study, 154 patients with resected cutaneous melanoma and baseline serum 25(OH)D measured within 3 months of surgery were included. Patients were categorized as low (≤ 20 ng/mL) or high (> 20 ng/mL) vitamin D. RFS was assessed using Kaplan–Meier analysis and Cox proportional hazards models.

Results: Of 154 patients, 81 (52.6%) had high and 73 (47.4%) had low vitamin D levels. Median follow-up was 65 months, during which 67 relapses occurred. Median RFS was 54.1 months (95% CI: 35.2–73.0) in the low and 89.2 months (95% CI: 68.3–110.2) in the high vitamin D group ($p < 0.001$). In univariate Cox analysis, stage III disease (HR: 3.30, 95% CI: 1.84–5.90, $p < 0.001$), absence of adjuvant therapy (HR: 1.98, 95% CI: 1.21–3.23, $p = 0.006$), low vitamin D (HR: 2.68, 95% CI: 1.59–4.51, $p < 0.001$), and higher Breslow thickness (HR: 1.04, 95% CI: 1.01–1.09, $p = 0.048$) were associated with poorer RFS. In multivariate analysis, stage III disease (HR: 3.05, 95% CI: 1.52–6.11, $p = 0.002$) and low vitamin D (HR: 2.61, 95% CI: 1.52–4.49, $p < 0.001$) remained independent predictors.

Conclusion: Baseline serum 25(OH)D status may reflect a clinically relevant host-related component of recurrence risk in resected stage II–III cutaneous melanoma, supporting its potential as a complementary prognostic marker, although prospective validation is warranted.

Keywords: Cutaneous Melanoma, High-Risk Resected Melanoma, Prognostic Biomarker, Recurrence-Free Survival, Vitamin D Status

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Öz

Amaç: Vitamin D, melanomda potansiyel bir prognostik biyobelirteç olarak öne sürülmüş olmakla birlikte, postoperatif dönemdeki klinik önemi henüz netlik kazanmamıştır. Bu çalışma, komplet cerrahi rezeksiyon uygulanan yüksek riskli evre II–III kutanöz melanom hastalarında perioperatif serum 25-hidroksivitamin D [25(OH)D] durumunun nüksüz sağkalım (RFS) açısından prognostik bilgi sağlayıp sağlamayacağını araştırdı.

Gereç ve Yöntemler: Bu retrospektif çok merkezli çalışmaya, cerrahi öncesi veya sonrası 3 ay içinde bazal serum 25(OH)D ölçümü bulunan 154 rezekte kutanöz melanom hastası dahil edildi. Hastalar vitamin D düzeyine göre düşük (≤ 20 ng/mL) ve yüksek (> 20 ng/mL) olmak üzere iki gruba ayrıldı. Klinikopatolojik değişkenler ile vitamin D durumu arasındaki ilişkiler değerlendirildi. RFS, Kaplan–Meier analizi ve Cox orantısız risk regresyon modelleri kullanılarak incelendi.

Bulgular: Toplam 154 hastanın 81’inde (%52.6) yüksek, 73’ünde (%47.4) düşük vitamin D düzeyi saptandı. Ortanca izlem süresi 65 ay olup bu süre içinde 67 nüks olayı gözlemlendi. Medyan RFS, düşük vitamin D grubunda 54,1 ay (%95 güven aralığı [GA]: 35,2–73,0), yüksek vitamin D grubunda ise 89,2 ay (%95 GA: 68,3–110,2) olarak bulundu ($p < 0,001$). Tek değişkenli Cox analizinde evre III hastalık (hazard oranı [HR]: 3,30, %95 GA: 1,84–5,90, $p < 0,001$), adjuvan tedavi almama (HR: 1,98, %95 GA: 1,21–3,23, $p = 0,006$), düşük vitamin D düzeyi (HR: 2,68, %95 GA: 1,59–4,51, $p < 0,001$) ve daha yüksek Breslow kalınlığı (HR: 1,04, %95 GA: 1,01–1,09, $p = 0,048$) daha kötü RFS ile ilişkili bulundu. Çok değişkenli analizde ise evre III hastalık (HR: 3,05, %95 GA: 1,52–6,11, $p = 0,002$) ve düşük vitamin D düzeyi (HR: 2,61, %95 GA: 1,52–4,49, $p < 0,001$) kötü RFS’nin bağımsız belirleyicileri olarak kaldı.

Sonuç: Bazal serum 25(OH)D durumu, rezekte evre II–III kutanöz melanomda nüks riskinin klinik açıdan anlamlı konak ilişkili bir yönünü yansıtabilir. Düşük vitamin D düzeyine sahip hastalarda daha kısa RFS ile ilişkili olması, prospektif doğrulama halen gerekli olmakla birlikte, bu parametrenin tamamlayıcı bir prognostik belirteç olarak potansiyel değerini desteklemektedir.

Anahtar Kelimeler: Kutanöz Melanom, Yüksek Riskli Rezekte Melanom, Prognostik Biyobelirteç, Nüksüz Sağkalım, Vitamin D Durumu

Atıf/Cite as: Ekin Ö, Butun O, İzgor RB, Karabulut B, Aktepe OH. Prognostic Value of Baseline Serum 25-Hydroxyvitamin D in High-Risk Resected Cutaneous Melanoma. Abant Med J. 2026;15(2):165-173.

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Introduction

Cutaneous melanoma remains a clinically relevant malignancy, and pathologic staging continues to be essential for prognostic stratification and postoperative treatment planning after complete surgical resection (1). However, patients with resected stage II–III melanoma remain at meaningful risk of recurrence, and clinical outcomes may vary considerably even within the same stage group (2). This heterogeneity has driven ongoing interest in simple, clinically accessible biomarkers that may refine recurrence risk beyond conventional clinicopathologic factors (3).

Recent advances in adjuvant systemic therapy have transformed the therapeutic landscape of resected melanoma. Anti-programmed cell death protein 1 (Anti-PD-1) therapy has improved recurrence-free survival (RFS) in high-risk resected disease (4–7), and BRAF/mitogen-activated protein kinase kinase (MEK) inhibition has demonstrated benefit in patients with resected BRAF V600-mutant stage III melanoma (8). Despite these advances, a substantial proportion of patients still relapse after curative-intent surgery, highlighting the need for additional prognostic markers that are inexpensive, reproducible, and readily available in routine clinical practice.

Vitamin D may serve as a clinically relevant prognostic biomarker for recurrence in resected melanoma. Serum 25-hydroxyvitamin D [25(OH)D], the main circulating measure of vitamin D status, has been implicated in several biological processes, including the regulation of cell proliferation, differentiation, and immune function (9, 10). In melanoma, evidence from observational studies indicates that reduced circulating 25(OH)D concentrations may be linked to unfavorable clinicopathologic features and poorer survival outcomes (11–14). However, these findings have not been entirely consistent across studies, and randomized trials of vitamin D supplementation have not demonstrated a clear survival benefit (15–17). Taken together, the prognostic significance of baseline vitamin D status in resected melanoma remains to be better defined. Thus, we aimed to explore whether perioperative serum 25(OH)D status may be related to RFS in patients with high-risk stage II–III cutaneous melanoma after complete surgical resection.

Materials and Methods

This retrospective multicenter study included consecutive adult patients with histologically confirmed, completely resected high-risk stage II–III cutaneous melanoma who were treated and followed at the participating centers. Patients were identified retrospectively from the institutional oncology and pathology databases of each center. During the screening process, patients were considered eligible if they had undergone curative-intent complete surgical resection and had an available baseline serum 25(OH)D measurement obtained within 3 months before or after surgery. Patients with evidence of recurrent disease at the time of vitamin D assessment were not included.

Postoperative treatment decisions were made by the treating multidisciplinary oncology teams according to the tumor stage, pathological risk factors, BRAF mutation status when available, patient preference, comorbidities, reimbursement conditions, and the treatment standards available at the time of diagnosis. Adjuvant systemic therapy, including anti-PD-1 therapy or BRAF/MEK inhibition when appropriate, was administered according to contemporary clinical practice. Patients who did not receive adjuvant therapy were followed with routine surveillance. Because of the retrospective design and long study period, treatment selection was not standardized by a predefined protocol.

Clinical, demographic, pathological, treatment-related, and follow-up data were retrieved from institutional medical records. Collected variables included age, sex, Breslow thickness, Clark level, mitotic rate, ulceration status, tumor stage, primary tumor location, and receipt of adjuvant therapy. Tumor stage was determined according to routine pathological staging records. Ethical approval for the study was obtained from the Ethics Committee of Dokuz Eylul University (date: 20.04.2026, approval number: 2026/16-29), and all study-related procedures were performed in line with the ethical principles of the Declaration of Helsinki.

Patients were excluded if they had stage I disease, stage IV disease, or melanoma not fulfilling the predefined study definition of high-risk resected stage II–III disease. Additional exclusion criteria were mucosal or uveal melanoma, incomplete surgical resection, unavailable baseline serum 25(OH)D measurement within the

predefined perioperative period, missing essential clinicopathological or follow-up data, or evidence of recurrent disease at the time of baseline vitamin D assessment.

There is no universally accepted cutoff for vitamin D deficiency or sufficiency; however, serum 25(OH)D status is generally described as deficient when levels are below 12 ng/mL, insufficient between 12 and 20 ng/mL, and sufficient when levels exceed 20 ng/mL (18). However, in the present study, patients were classified into two groups according to baseline vitamin D status: low vitamin D (≤ 20 ng/mL) and high vitamin D (> 20 ng/mL). This dichotomized approach was preferred because the limited number of recurrence events was considered insufficient to support a more granular three-group analysis. In addition, the use of a 20 ng/mL threshold allowed a clinically interpretable distinction between patients with low vitamin D status and those with relatively adequate levels.

Statistical Analysis

Continuous variables were described using median values and interquartile ranges (IQRs). For comparisons of non-normally distributed continuous data, the Mann–Whitney U test was applied. Group differences in categorical parameters were examined with the chi-square test or Fisher’s exact test, depending on cell frequencies. RFS was estimated using the Kaplan–Meier method and compared with the log-rank test, and Kaplan–Meier curves were generated using R software (R Foundation for Statistical Computing, Vienna, Austria). Univariate and multivariate Cox proportional hazards regression models were applied to identify factors associated with RFS. Variables with a p value ≤ 0.20 in univariate analysis were entered into the multivariate model. The final multivariate Cox model was constructed by incorporating these candidate variables while taking into account clinical relevance and the number of relapse events. To reduce the risk of overfitting, the number of variables included in the final model was restricted according to the available number of events. Hazard ratios (HRs) and 95% confidence intervals (CIs) were reported. To assess the incremental prognostic contribution of baseline vitamin D status beyond conventional clinicopathologic factors, receiver operating characteristic (ROC) curve analysis was performed, and the area under the curve (AUC) was reported. All other analyses were conducted using SPSS software version 27.0 (IBM Corp., Armonk, NY, USA), and a two-sided p value < 0.05 was considered statistically significant.

Results

Baseline Patient Characteristics

A total of 154 patients with high-risk resected cutaneous melanoma were included in the study. The median age of the overall cohort was 61 years (IQR: 49–68), and 90 patients (58.4%) were male. The median Breslow thickness was 3.3 mm (IQR: 1.8–6.1), and the median mitotic rate was 6 (IQR: 3.9–14.1). Ulceration was present in 87 patients (56.5%), while Clark level IV–V disease was observed in 118 patients (76.6%). Regarding stage distribution, 86 patients (55.8%) had stage III disease and 68 (44.2%) had stage II disease. Primary tumor location was most commonly the extremities (44.8%), followed by the trunk (31.8%) and the head and neck region (23.4%). Adjuvant therapy was administered to 53 patients (34.4%). Among patients receiving adjuvant treatment, 31 (58.5%) received anti-PD-1 therapy with nivolumab or pembrolizumab, 9 (17.0%) received BRAF/MEK inhibition with dabrafenib plus trametinib, and 13 (24.5%) received other adjuvant treatments used during earlier treatment periods, including interferon or ipilimumab.

When stratified according to vitamin D status, 81 patients (52.6%) were classified in the high vitamin D group and 73 (47.4%) in the low vitamin D group. Baseline demographic characteristics were broadly comparable between the two groups. The median age was 63 years (IQR: 49–69) in the high vitamin D group and 58 years (IQR: 47–67) in the low vitamin D group ($p = 0.359$). Male sex was observed in 61.7% and 54.8% of patients, respectively ($p = 0.383$). Likewise, median Breslow thickness was similar between the high and low vitamin D groups at 3.4 mm (IQR: 1.4–6.1) and 3.1 mm (IQR: 2.2–5.8), respectively ($p = 0.770$). Clark level IV–V disease was present in 74.1% of patients with high vitamin D and 79.5% of those with low vitamin D ($p = 0.431$).

Among clinicopathological variables, only mitotic rate differed significantly according to vitamin D status. The median mitotic rate was 5 (IQR: 3–11.7) in the high vitamin D group and 7 (IQR: 4–13.7) in the low vitamin D group ($p = 0.007$). Ulceration was numerically more frequent in the low vitamin D group than in the high vitamin D group (64.4% vs. 49.4%, $p = 0.061$). Similarly, stage III disease was more common in the low vitamin

D group (61.6% vs. 50.6%), but the difference was not statistically significant ($p = 0.169$). Primary tumor location was distributed similarly across groups ($p = 0.661$), and the proportion of patients receiving adjuvant therapy was also comparable between the low and high vitamin D groups (37% vs. 32.1%, $p = 0.524$) (Table 1).

Table 1

Baseline Clinical, Pathological, And Demographic Variables Stratified According to Vitamin D Level.

Characteristics	All patients (n = 154)	High vitamin D (n = 81, 52.6%)	Low vitamin D (n = 73, 47.4%)	P value
Age, years, (IQR)	61 (49–68)	63 (49–69)	58 (47–67)	0.359
Sex				0.383
Female	64 (41.6%)	31 (38.3%)	33 (45.2%)	
Male	90 (58.4%)	50 (61.7%)	40 (54.8%)	
Breslow, (IQR)	3.3 (1.8–6.1)	3.4 (1.4–6.1)	3.1 (2.2–5.8)	0.770
Clark				0.431
II-III	36 (23.4%)	21 (25.9%)	15 (20.5%)	
IV-V	118 (76.6%)	60 (74.1%)	58 (79.5%)	
Mitotic rate, (IQR)	6 (3.9–14.1)	5 (3–11.7)	7 (4–13.7)	0.007
Ulceration				0.061
No	67 (43.5%)	41 (50.6%)	26 (35.6%)	
Yes	87 (56.5%)	40 (49.4%)	47 (64.4%)	
Tumor stage				0.169
II	68 (44.2%)	40 (49.4%)	28 (38.4%)	
III	86 (55.8%)	41 (50.6%)	45 (61.6%)	
Tumor location				0.661
Trunk	49 (31.8%)	28 (34.6%)	21 (28.8%)	
Extremity	69 (44.8%)	36 (44.4%)	33 (45.2%)	
Head and neck	36 (23.4%)	17 (21%)	19 (26%)	
Adjuvant therapy				0.524
No	101 (65.6%)	55 (67.9%)	46 (63%)	
Yes	53 (34.4%)	26 (32.1%)	27 (37%)	

Abbreviations: IQR: interquartile range

RFS and Prognostic Factors

For the overall cohort, the median follow-up was 65 months (95% CI: 52.9–77.1), and 67 relapse events were observed during this period. The median RFS was 73.4 months (95% CI: 55.8–90.9). Kaplan–Meier analysis showed that, across the overall cohort as well as within both the stage II and stage III subgroups, low vitamin D status was consistently associated with poorer RFS. In the entire cohort, median RFS was 54.1 months (95% CI: 35.2–73.0) in the low vitamin D group and 89.2 months (95% CI: 68.3–110.2) in the high vitamin D group ($p < 0.001$). In the stage II subgroup, median RFS was 81.5 months (95% CI: 61.1–102.0) among patients with low vitamin D, while the median was not reached in the high vitamin D group ($p < 0.001$). In stage III disease, the corresponding median RFS values were 41.7 months (95% CI: 18.3–65.1) and 72.0 months (95% CI: 60.5–83.6), respectively ($p = 0.029$) (Figure 1).

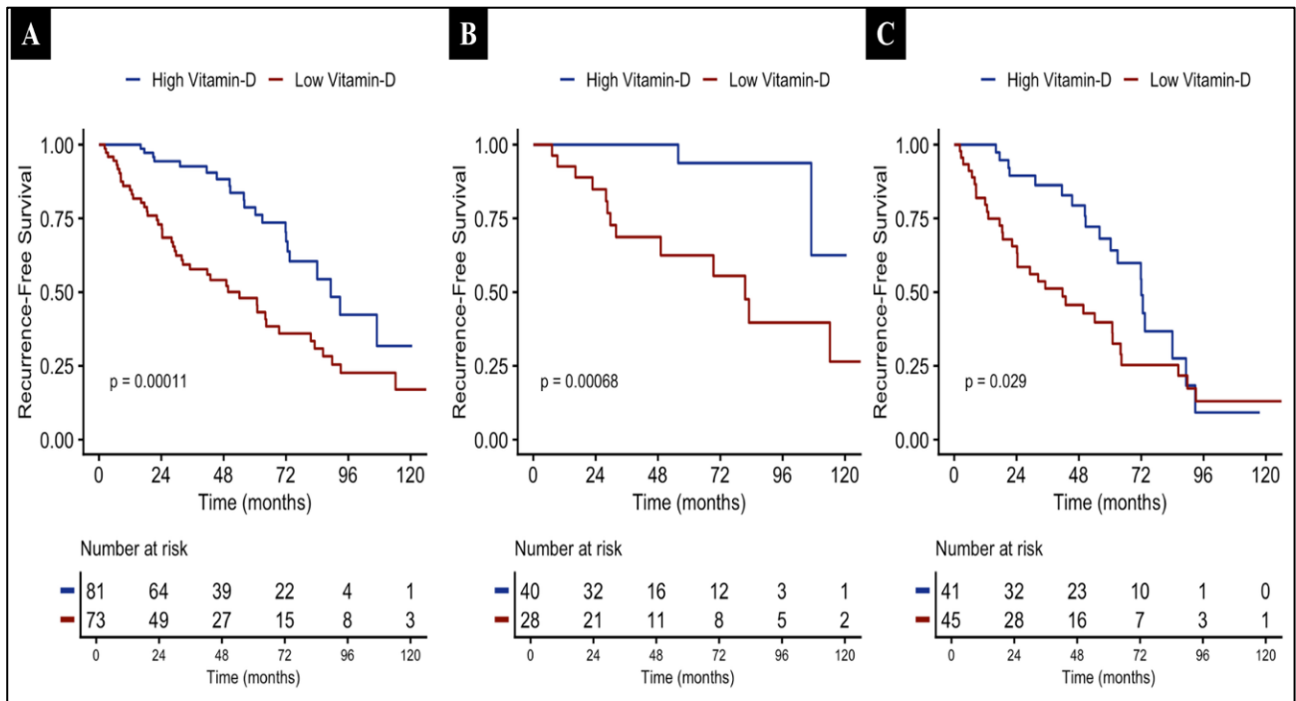


Figure 1. Kaplan–Meier curves for RFS according to vitamin D status in the overall cohort (A), stage II subgroup (B), and stage III subgroup (C).

In the univariate Cox regression analysis for RFS, stage III disease, absence of adjuvant therapy, low vitamin D level, and higher Breslow thickness were associated with poorer outcomes, while mitotic rate showed borderline significance. Compared with stage II disease, stage III melanoma was linked to an increased relapse risk (HR: 3.30, 95% CI: 1.84–5.90, $p < 0.001$). Likewise, lack of adjuvant therapy was related to poorer RFS (HR: 1.98, 95% CI: 1.21–3.23, $p = 0.006$). Low vitamin D level was also significantly associated with inferior RFS (HR: 2.68; 95% CI: 1.59–4.51, $p < 0.001$). In addition, higher Breslow thickness was significantly associated with worse RFS in univariate analysis (HR: 1.04, 95% CI: 1.01–1.09, $p = 0.048$), whereas mitotic rate showed borderline significance (HR: 1.01, 95% CI: 1.00–1.01, $p = 0.056$). Age and sex were not significantly associated with RFS. In the multivariate analysis, stage III disease (HR: 3.05, 95% CI: 1.52–6.11, $p = 0.002$) and low vitamin D level (HR: 2.61, 95% CI: 1.52–4.49, $p < 0.001$) remained independent predictors of worse RFS, whereas Breslow thickness, mitotic rate, and adjuvant therapy were no longer statistically significant after adjustment (Table 2).

Table 2

Univariate And Multivariate Cox Regression Analyses For RFS

Variable	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Age, years	0.98 (0.97–1.00)	0.138	0.99 (0.97–1.01)	0.335
Gender (male vs female)	1.21 (0.73–2.00)	0.449	NA	NA
Breslow	1.04 (1.01–1.09)	0.048	1.04 (0.98–1.10)	0.123
Mitotic rate	1.01 (1.00–1.01)	0.056	1.00 (0.99–1.02)	0.131
Stage (III vs II)	3.30 (1.84–5.90)	<0.001	3.05 (1.52–6.11)	0.002
Adjuvant therapy (no vs yes)	1.98 (1.21–3.23)	0.006	1.11 (0.62–2.01)	0.713
Vitamin D (low vs high)	2.68 (1.59–4.51)	<0.001	2.61 (1.52–4.49)	<0.001

Abbreviations: CI: confidence interval; HR: hazard ratio; NA: not applicable; RFS: recurrence-free survival.

To evaluate the incremental prognostic contribution of vitamin D, ROC curve analysis was performed for two models (Figure 2). Model 1, based on tumor stage, Clark level, and Breslow thickness, yielded an AUC of 0.73 (95% CI: 0.66–0.81). After addition of baseline vitamin D status, Model 2 achieved an AUC of 0.81 (95% CI: 0.74–0.87), suggesting improved discrimination beyond conventional clinicopathologic parameters.

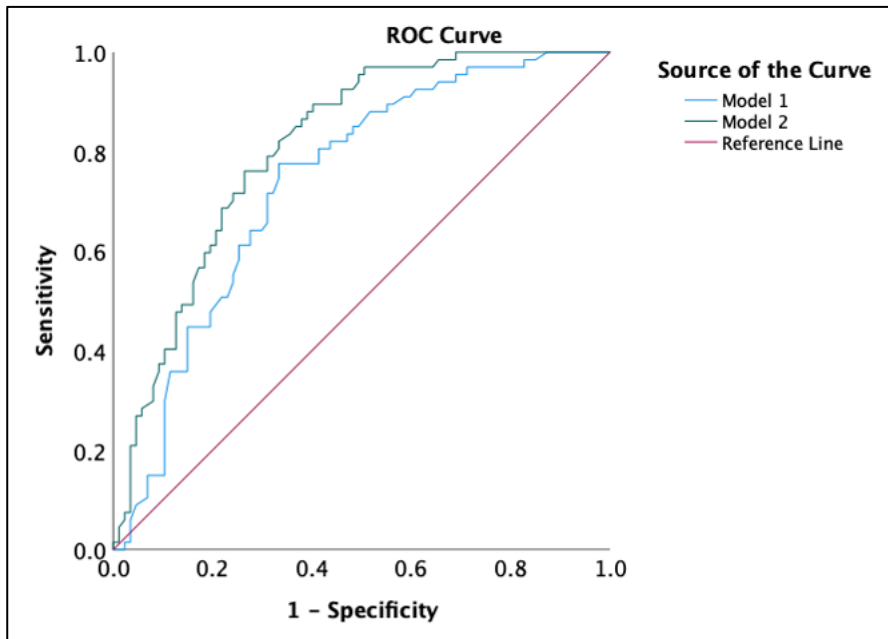


Figure 2. ROC curves comparing two prognostic models for relapse risk in high-risk resected cutaneous melanoma. Model 1 included tumor stage, Clark level, and Breslow thickness, whereas Model 2 additionally included baseline vitamin D status. The AUC was 0.73 (95% CI: 0.66–0.81) for Model 1 and 0.81 (95% CI: 0.74–0.87) for Model 2.

Discussion

The present study showed that lower baseline serum 25(OH)D levels were independently associated with shorter RFS in patients with completely resected high-risk stage II–III cutaneous melanoma. This association remained significant after adjustment for established clinicopathological variables, suggesting that vitamin D status may reflect host-related factors associated with recurrence risk in the postoperative setting.

The association between low vitamin D status and inferior RFS in melanoma is biologically plausible and may be explained by several complementary mechanisms. The vitamin D receptor (VDR) is central to vitamin D signaling, which has been implicated in several biologic processes relevant to melanoma, including regulation of cell proliferation, differentiation, apoptosis, and immune function (19). In melanoma, preserved vitamin D–VDR signaling appears to restrain tumor proliferation, support cellular differentiation, and limit invasive behavior, while impaired signaling may contribute to tumor plasticity and disease progression (19–21). Preclinical evidence suggests that 1 α ,25-dihydroxyvitamin D3 and its analogues may promote apoptosis in human melanoma cells, supporting a possible role for vitamin D signaling in restraining tumor cell survival (22). Additional experimental evidence suggests that vitamin D–VDR signaling may inhibit molecular pathways involved in melanoma progression, particularly Wnt/ β -catenin signaling (20), which has been linked to tumor proliferation, immune evasion, and metastatic behavior (23). Moreover, because vitamin D has been implicated in the regulation of oxidative stress and cellular homeostasis, deficient vitamin D status may also contribute to genomic instability and persistence of micrometastatic disease (24, 25). Collectively, these observations support the view that low vitamin D status may reflect a biologically unfavorable host milieu characterized by impaired immune control and increased susceptibility to relapse in resected melanoma.

Our findings suggest that baseline vitamin D status may be more informative as a marker of underlying host biology than as a direct driver of melanoma recurrence. Consistent with this interpretation, prior melanoma studies have yielded heterogeneous results. Bade et al. reported that reduced circulating 25(OH)D

concentrations were linked to a higher likelihood of melanoma and poorer prognostic outcomes (11), whereas Lim et al. found that higher 25(OH)D levels measured within 6 months of primary melanoma diagnosis were associated with more favorable clinicopathologic features (12). Similarly, Moro et al. reported that a vitamin D level below 9.25 ng/mL at diagnosis was linked to tumor ulceration and independently predicted poorer overall survival (OS) (13). In contrast, Befon et al. did not observe a significant relationship between vitamin D levels measured at diagnosis and established prognostic features (14), and Lippala et al., in a high-risk resected melanoma cohort from an adjuvant trial, did not identify a clear association between vitamin D levels and disease-free interval or OS (16). Such variability across studies may reflect differences in patient selection, stage distribution, treatment context, study design, and, importantly, the timing of vitamin D assessment (26, 27). In our study, assessment within a defined perioperative window may have captured clinically meaningful host-related information, although it may also have introduced some degree of heterogeneity.

The clinical implications of our findings should be interpreted cautiously. While low baseline vitamin D was associated with inferior RFS, this does not establish causality or imply that vitamin D supplementation will improve outcomes. Instead, vitamin D status should currently be considered a prognostic biomarker reflecting host-related vulnerability (28). From a practical standpoint, assessment of serum 25(OH)D is low-cost and widely available, and identification of patients with low levels may have relevance for general health optimization and survivorship care. However, its role in guiding melanoma-specific management remains to be defined.

Several limitations should be acknowledged. First, the retrospective design may have introduced selection bias and residual confounding. Serum vitamin D levels are influenced by multiple non-cancer-related factors, including seasonal variation, sunlight exposure, body mass index and obesity, physical activity, comorbidities, systemic inflammation, and vitamin D supplementation. Because these variables were not consistently available in the medical records, they could not be included in the adjusted analyses. In particular, reliable and systematic data regarding vitamin D supplementation were not available. Therefore, residual confounding related to lifestyle, metabolic status, comorbidity burden, seasonal timing of measurement, and supplementation cannot be excluded. Second, vitamin D status was assessed using a single baseline measurement, which may not fully reflect long-term vitamin D exposure. Third, the relatively modest sample size and number of relapse events may have limited statistical power and increased the risk of model instability. Finally, although dichotomization of vitamin D levels was preferred for analytical robustness, this approach may have obscured potential dose–response relationships and may limit comparability with studies using alternative thresholds or continuous modeling.

Despite these limitations, our findings support the view that host-related factors, including vitamin D status, may contribute to outcome heterogeneity in resected melanoma. Importantly, our findings extend prior observations to a clinically relevant perioperative setting and demonstrate that vitamin D remains independently associated with recurrence risk beyond established prognostic variables.

Future research should focus on prospective validation in larger multicenter cohorts, with standardized timing of vitamin D measurement and incorporation of longitudinal assessments. In addition, integration of serum vitamin D levels with tumor-specific factors, including molecular characteristics and immune profiling, may provide a more comprehensive understanding of its role in melanoma biology. Finally, randomized studies targeting vitamin D–deficient populations, rather than unselected supplementation, may help clarify whether correction of deficiency has clinically meaningful effects on melanoma outcomes.

Conclusion

In the present study, lower baseline serum 25(OH)D levels were independently associated with shorter RFS in patients with completely resected high-risk stage II–III cutaneous melanoma. These findings suggest that vitamin D status may provide complementary prognostic information in the postoperative setting. However, given the study limitations, including the modest sample size and potential residual confounding, the results should be interpreted cautiously and should not be considered evidence of a causal relationship. Further validation is needed before vitamin D status can be incorporated into routine melanoma-specific risk stratification.

Ethics Committee Approval: The study was approved by the Ethics Committee of Dokuz Eylul University (date: 20.04.2026 and approval number: 2026/16-29).

Informed Consent: Written consent was obtained from the participants.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

Data Sharing Statement: The datasets generated and/or analyzed during the current study are not publicly available due to institutional and ethical restrictions but may be obtained from the corresponding author upon reasonable request.

Author Contributions: Idea/Concept: OE, BK, OHA; Design: OE, OB, BK, OHA; Supervision: BK, OHA; Funding: None; Materials: OE, OB, OHA; Data Collection/Processing: OE, OB, RBI; Analysis/Interpretation: OE, RBI, OHA; Literature Review: OE, OB, RBI, OHA; Drafting/Writing: OE, OB, RBI, OHA; Critical Review: BK, OHA. The authors have accepted responsibility for the entire content of this manuscript and approved its submission.

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