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Prognostic value of the PLACE score in a Turkish cohort of metastatic pleural mesothelioma

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ABSTRACT

Aims: Pleural mesothelioma is an aggressive malignancy with poor prognosis and limited therapeutic options. Reliable prognostic models are essential for risk stratification and clinical decision-making. The recently developed PLACE score has shown promising results in Chinese populations; however, its generalizability remains uncertain. This study aimed to externally validate the PLACE prognostic score in a Turkish cohort of patients with metastatic epithelioid pleural mesothelioma.

Methods: This retrospective cohort study included patients diagnosed with metastatic epithelioid pleural mesothelioma at a single tertiary center between January 2016 and September 2025. Clinical and laboratory data at diagnosis were collected, and the PLACE score was calculated for each patient. Overall survival (OS) was analyzed using the Kaplan–Meier method, and differences between risk groups were compared using the log-rank test. Cox proportional hazards regression analysis was performed to evaluate the association between prognostic variables and survival. The discriminative ability of the PLACE score was assessed using receiver operating characteristic (ROC) curve analysis.

Results: A total of 48 patients were included, with a median age of 66 years. According to the PLACE score, 33.3% of patients were classified as low-risk and 66.7% as high-risk. The median OS was 21.06 months. Patients in the low-risk group had significantly longer survival compared to the high-risk group (37.98 vs. 15.6 months, p=0.033). Time-dependent ROC analysis demonstrated increasing discriminative ability over time, with AUC values ranging from 0.554 at 6 months to 0.717 at 24 months. In Cox regression analysis, high-risk patients had a significantly increased risk of mortality (HR: 2.28, 95% CI: 1.04–4.95, p=0.037). In multivariable analysis, the PLACE risk group remained significantly associated with OS.

Conclusion: The PLACE score retains prognostic significance in Turkish patients with metastatic pleural mesothelioma but demonstrates reduced discriminative performance compared to the original study. These findings emphasize the need for external validation and potential population-specific recalibration of prognostic models.

Keywords: Mesothelioma, PLACE score, prognostic score, survival

INTRODUCTION

Pleural mesothelioma is a rare but aggressive malignancy primarily associated with asbestos exposure, characterized by poor prognosis and limited therapeutic options.[1,2] The median survival typically ranges from 12 to 18 months from diagnosis, making accurate prognostic assessment crucial for clinical decision-making, treatment planning, and patient counseling.[3,4] The heterogeneous nature of the disease and variable patient outcomes underscore the need for reliable prognostic tools that can stratify patients into meaningful risk categories.

Turkiye is recognized as one of the endemic regions for malignant pleural mesothelioma, primarily due to environmental asbestos exposure, particularly in certain rural areas where asbestos-containing soil has been traditionally utilized for domestic purposes.[5-7] Previous epidemiological studies have indicated a higher incidence of mesothelioma in regions such as Central Anatolia and Southeastern Turkiye, where environmental exposure, rather than occupational exposure, predominates.[8] This distinctive exposure pattern differentiates Turkiye from many Western countries and highlights the necessity of evaluating prognostic models within this specific population. Consequently, the validation of prognostic scoring systems in Turkish cohorts is crucial to ensure their clinical applicability and reliability in real-world settings.

All patients received first-line systemic therapy consisting of pemetrexed, cisplatin, and bevacizumab.[9,10] Immunotherapy-based combination regimens were not included, as these

treatments were not reimbursed in our national healthcare system for an extended period and only became available more recently.[11-13]

Several prognostic scoring systems have been developed for pleural mesothelioma, including the CALGB (Cancer and Leukemia Group B) score, EORTC (European Organisation for Research and Treatment of Cancer) score, and more recently, the LENT and BRIMS scores.[4,14-16] However, these models have shown variable performance across different populations and healthcare settings, highlighting the challenges in developing universally applicable prognostic tools for this complex malignancy.

Recently, Zhang and colleagues[17] developed the PLACE prognostic score specifically for patients with pleural mesothelioma. The PLACE score incorporates five readily available clinical and laboratory parameters: platelet count (PLT) >289.5×10^9/L (+1 point), lymphocyte count >1.785×10^9/L (-1 point), age >73 years (+1 point), calcium >2.145 mmol/L (-1 point), and Eastern Cooperative Oncology Group performance status (ECOG PS) >2 (+2 points).[17] Patients are classified as low-risk (score <0) or high-risk (score 0-3) based on the total score.[17]

In the original development study, the PLACE score demonstrated excellent discriminative ability with an area under the curve (AUC) of 0.900 at 6 months in the development cohort (n=95) and 0.761 in the validation cohort (n=23).[17] High-risk patients showed significantly worse survival compared to low-risk patients, with hazard ratios of 3.878 and 3.574 in the development and validation cohorts, respectively.[17] However, the original study was conducted exclusively in Chinese patients at two hospital centers in Beijing, and the authors acknowledged that "the proposed model can only be applied to patients of Chinese ethnicity now and not currently generalizable to the overall global population".[17]

The generalizability of prognostic models across different populations, healthcare systems, and geographic regions is a critical consideration for clinical implementation. Ethnic, genetic, environmental, and healthcare delivery differences can significantly impact model performance, necessitating external validation studies in diverse populations. The original PLACE score developers emphasized the need for "multi-centre and large sample studies worldwide" to establish broader applicability.[17]

Given the promising initial results of the PLACE score and the recognized need for validation in non-Chinese populations, we conducted this study to evaluate the prognostic performance of the PLACE score in a Turkish cohort. Our objectives were to: (1) assess the discriminative ability of the PLACE score in our cohort, (2) evaluate the survival differences between PLACE-defined risk groups, and (3) determine the clinical utility of this scoring system in our patient population. This validation study aims to contribute to the growing evidence base for prognostic tools in pleural mesothelioma and inform clinical decision-making across diverse healthcare settings.

METHODS

Ethics

The study was initiated after obtaining an approval from Kocaeli University Ethics Committee for Non-interventional Clinical Researches (Date: 09.04.2026, Decision No: 2026/99). The study was conducted in accordance with the Declaration of Helsinki.

Study Design and Population

This retrospective cohort study was conducted at Kocaeli University Medical Center to validate the prognostic performance of the PLACE score in patients with pleural mesothelioma. We reviewed electronic medical records of patients diagnosed with pleural mesothelioma between January 2016 and September 2025.

Patient Selection

Inclusion criteria were: (1) histologically confirmed pleural mesothelioma with epithelioid subtype, (2) de novo metastatic disease at presentation, (3) age ≥18 years, (4) treatment with first-line pemetrexed, cisplatin, and bevacizumab combination therapy, and (5) availability of complete clinical and laboratory data required for PLACE score calculation. Exclusion criteria included: (1) non-epithelioid histological subtypes, (2) locally advanced disease without distant metastases, (3) previous treatment for mesothelioma, (4) incomplete medical records, and (5) loss to follow-up within 30 days of diagnosis.

A total of 48 patients met the inclusion criteria and were included in the final analysis.

Data Collection

Clinical and laboratory data were extracted from electronic medical records at the time of diagnosis, prior to initiation of systemic therapy. The following variables were collected: demographic characteristics (age, gender), Eastern Cooperative Oncology Group performance status (ECOG PS), sites of metastatic disease, and laboratory parameters including complete blood count (platelet count, lymphocyte count), serum chemistry panel (calcium, albumin), and other relevant biomarkers.

PLACE Score Calculation

The PLACE score was calculated for each patient using the original scoring system developed by Zhang et al.[17] The score incorporates five parameters: platelet count >289.5×10^9/L (+1 point), lymphocyte count >1.785×10^9/L (-1 point), age >73 years (+1 point), serum calcium >2.145 mmol/L (-1 point), and ECOG performance status >2 (+2 points). The total score was calculated by summing individual component scores, and patients were classified into risk groups according to the original criteria: low-risk (total score <0) and high-risk (total score 0-3).[17]

Treatment Protocol

All patients received first-line systemic therapy consisting of pemetrexed (500 mg/m^2), cisplatin (75 mg/m^2), and bevacizumab (15 mg/kg) administered intravenously every 21 days.[9,10] Treatment continued until disease progression,

unacceptable toxicity, or patient withdrawal of consent. Standard premedication with folic acid and vitamin B12 supplementation was provided according to institutional protocols.[9]

Follow-up and Outcome Assessment

Patients were followed from the date of diagnosis until death, loss to follow-up, or the end of the study period. Overall survival (OS) was defined as the time from diagnosis to death from any cause. Progression-free survival (PFS) was defined as the time from treatment initiation to radiological or clinical disease progression or death, whichever occurred first. Survival status was determined through medical record review, hospital databases, and when necessary, contact with patients or family members.

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as median with interquartile range (IQR) or mean with standard deviation, as appropriate. Survival curves were constructed using the Kaplan-Meier method, and differences between risk groups were compared using the log-rank test. Hazard ratios (HR) with 95% confidence intervals (CI) were calculated using Cox proportional hazards regression analysis. The multivariable model included two covariates, yielding an events-per-variable (EPV) ratio of 17.0, which satisfies the recommended minimum threshold of ≥10. The discriminative ability of the PLACE score was assessed using time-dependent ROC analysis. An incident/dynamic definition was applied: cases were defined as patients experiencing the event (death) before a predefined time point t, and controls were patients alive at time t. AUC values were calculated at 6, 12, 18, and 24 months. For comparison with the original PLACE study, a binary ROC analysis based on OS status (alive vs. deceased) was also performed as a supplementary analysis. Statistical significance was set at $p<0.05$. All statistical analyses were performed using IBM SPSS Statistics for Windows version 29.0 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 48 patients participated in the study. The median age was 66 years (IQR: 59.8–71.0), with 66.7% (n=32) being male and 33.3% (n=16) female. Regarding smoking status, 54.2% (n=26) of patients were smokers and 45.8% (n=22) were non-smokers. The ECOG performance status was 0-1 in 85.4% (n=41) of patients and ≥2 in 14.6% (n=7). Regarding comorbidities, diabetes mellitus was present in 22.9% (n=11), hypertension in 56.3% (n=27), COPD in 20.8% (n=10), and coronary artery disease in 31.3% (n=15). According to the PLACE risk classification, 33.3% (n=16) of patients were categorized as low-risk, while 66.7% (n=32) were classified as high-risk. Laboratory parameters were reported as median (IQR). Urea was 33.5 (26.9-40.3) mg/dl, creatinine 0.80 (0.668-0.915) mg/dl, and GFR 90.0 (82.7-100.0) ml/min/1.73 m^2. Albumin was 38.0 (34.7-40.0) g/L, calcium 2.11 (2.03-2.18) mmol/L, AST 17.0 (12.8-28.0) U/L, ALT 14.2 (10.9-23.3) U/L, and LDH 164 (130-213) U/L. Inflammatory and hematological parameters included CRP 28.8 (6.4-46.5) mg/L, WBC 7870 (6528-9665)×10^3/µL, neutrophils 5380 (3668-6795)×10^3/µL, hemoglobin 12.5 (11.2-13.6) g/dl, lymphocytes 1700 (1380-2100)×10^3/µL, and platelets 304 (252-428)×10^3/µL. **Table 1** presents the clinical and demographic characteristics of the study population. (n=48).

Table 1. Baseline characteristics of the study population (n=48)

Variable	Value n (%) or median (IQR)
Age, years (median, IQR)	66 (59.8-71.0)
Sex (male/female)	32 (66.7%)/16 (33.3%)
Smoking status (yes/no)	26 (54.2%)/22 (45.8%)
ECOG performance status	
0–1	41 (85.4%)
≥2	7 (14.6%)
Comorbidities	
Diabetes mellitus	11 (22.9%)
Hypertension	27 (56.3%)
COPD	10 (20.8%)
Coronary artery disease	15 (31.3%)
Sites of metastasis	
Lung metastasis (yes/no)	21 (43.8%)/27 (56.2%)
Liver metastasis (yes/no)	4 (8.3%)/44 (91.7%)
Bone metastasis (yes/no)	8 (16.7%)/40 (83.3%)
Brain metastasis (yes/no)	3 (6.3%)/45 (93.7%)
Mediastinal lymph node metastasis (yes/no)	27 (56.3%)/21 (43.7%)
PLACE risk group	
Low risk	16 (33.3%)
High risk	32 (66.7%)
Laboratory parameters	**(Median, IQR)**
Urea (mg/dl)	33.5 (26.9-40.3)
Serum creatinine (mg/dl)	0.80 (0.668-0.915)
GFR (ml/min/1.73 m^2)	90.0 (82.7-100.0)
Albumin (g/L)	38.0 (34.7-40.0)
Calcium (mmol/L)	2.11 (2.03-2.18)
AST (U/L)	17.0 (12.8-28.0)
ALT (U/L)	14.2 (10.9-23.3)
LDH (U/L)	164 (130-213)
CRP (mg/L)	28.8 (6.4-46.5)
WBC (×10^3/µL)	7870 (6528-9665)
Neutrophils (×10^3/µL)	5380 (3668-6795)
Hemoglobin (g/dl)	12.5 (11.2-13.6)
Lymphocytes (×10^3/µL)	1700 (1380-2100)
Platelets (×10^3/µL)	304 (252-428)

ECOG: Eastern Cooperative Oncology Group, COPD: Chronic obstructive pulmonary disease, GFR: Glomerular filtration rate, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, CRP: C-reactive protein, WBC: White blood cell count, IQR: Interquartile range

Time-dependent ROC analysis demonstrated increasing discriminative ability over time, with AUC values of 0.554 (95% CI: 0.378–0.707) at 6 months, 0.576 (95% CI: 0.440–0.712) at 12 months, 0.669 (95% CI: 0.541–0.785) at 18 months, and 0.717 (95% CI: 0.572–0.844) at 24 months. For supplementary comparison with the original PLACE study, binary ROC analysis yielded an AUC of 0.617 (95% CI: 0.413–0.821) (**Figure 1**).

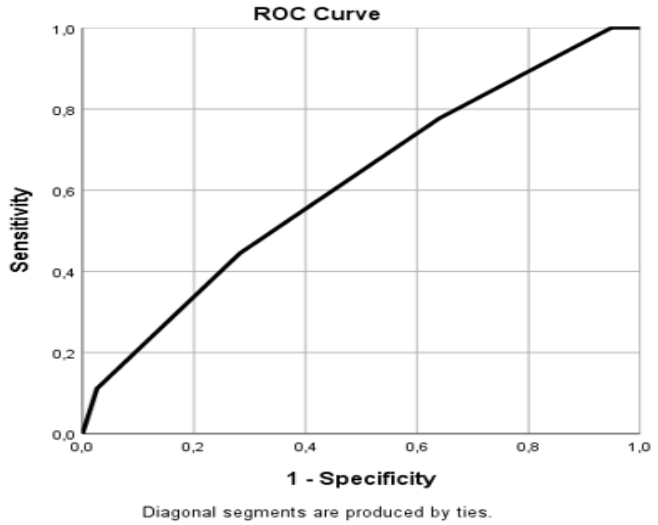

Figure 1. Receiver operating characteristic (ROC) curve of the PLACE score for predicting survival status (alive vs. deceased), shown for supplementary comparison with the original PLACE study. The area under the curve (AUC) was 0.617 (95% CI: 0.413–0.821). Primary discrimination analysis using time-dependent ROC is reported in the text.

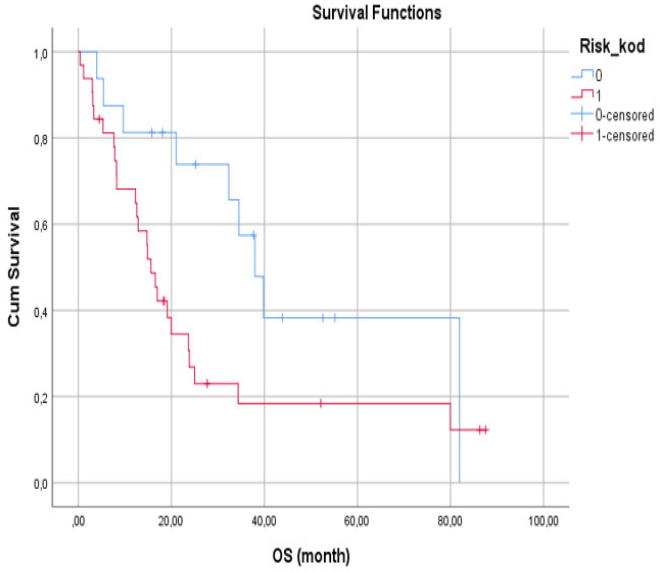

Figure 3. Kaplan–Meier survival curves according to PLACE risk groups. Patients in the low-risk group demonstrated significantly longer survival compared to the high-risk group (37.98 vs. 15.6 months, p=0.033).

The Kaplan–Meier survival curve for OS is shown in Figure 2, with a median OS of 21.06 months (95% CI: 12.99–29.13). The analysis of OS across different risk groups demonstrated a statistically significant difference. Patients in the low-risk group exhibited a longer median OS of 37.98 months (95% CI: 30.26–45.69), whereas those in the high-risk group had a shorter median OS of 15.6 months (95% CI: 12.62–18.59) (p=0.033). These findings are summarized in Figure 3.

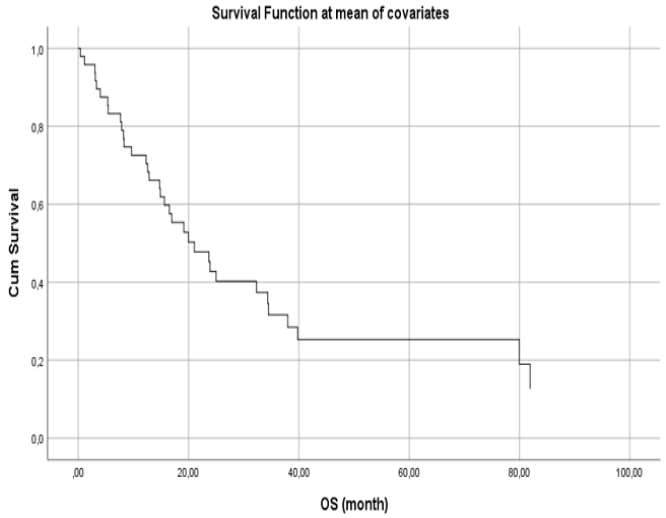

Figure 2. Kaplan–Meier survival curve for overall survival (OS). The median overall survival was 21.06 months (95% CI: 12.99–29.13).

During follow-up, 34 patients (70.8%) died, while 14 patients (29.2%) were alive at the time of analysis. Univariable Cox regression analysis revealed a significant association between the PLACE risk group and OS. Specifically, patients classified within the high-risk group exhibited a markedly elevated risk of mortality compared to those in the low-risk group (HR: 2.28, 95% CI: 1.04–4.95, p=0.037). Among the clinical variables examined, the presence of liver metastasis (HR: 2.21, 95% CI: 1.06–4.62, p=0.035), bone metastasis (HR: 3.00, 95% CI: 1.55–5.83, p=0.001), and brain metastasis (HR: 2.46, 95% CI: 1.14–5.32, p=0.022) were also significantly correlated with poorer OS outcomes. Conversely, elevated calcium levels (HR: 0.18, 95% CI: 0.08–0.39, p<0.001) and albumin levels (HR: 0.92, 95% CI: 0.86–0.98, p=0.011) were associated with enhanced survival outcomes. Variables such as age, sex, ECOG performance status, lung metastasis, mediastinal lymph node involvement, lymphocyte count, platelet count, hemoglobin, LDH, and CRP levels did not demonstrate a significant association with OS in the univariable analysis. Univariable Cox regression analysis results are summarized in Table 2.

Table 2. Univariable Cox regression analysis for overall survival

Variable	HR (95% CI)	p-value
PLACE risk group (high vs low)	2.28 (1.04–4.95)	0.037
Age (years)	1.01 (0.98–1.04)	0.495
Sex (male vs female)	1.16 (0.55–2.46)	0.692
ECOG performance status	1.14 (0.78–1.68)	0.502
Lung metastasis	1.78 (0.92–3.45)	0.087
Liver metastasis	2.21 (1.06–4.62)	0.035
Bone metastasis	3.00 (1.55–5.83)	0.001
Brain metastasis	2.46 (1.14–5.32)	0.022
Mediastinal lymph node metastasis	1.64 (0.86–3.13)	0.134
Calcium (mmol/L)	0.18 (0.08–0.39)	<0.001
HGB (g/dl)	1.09 (0.922–1.303)	0.518
Lymphocyte count (×10³/μL)	1.00 (0.999–1.000)	0.518
Platelets (×10³/μL)	1.00 (0.998–1.004)	0.477
Albumin (g/L)	0.92 (0.86–0.98)	0.011
LDH (U/L)	1.002 (0.999–1.005)	0.117
CRP (mg/L)	1.002 (0.994–1.01)	0.637

HR: Hazard ratio, CI: Confidence interval, ECOG: Eastern Cooperative Oncology Group performance status, HGB: Hemoglobin, LDH: Lactate dehydrogenase, CRP: C-reactive protein

Multivariable Cox regression analysis revealed that the PLACE risk group remained an independent predictor of OS, even after adjusting for serum albumin level (HR: 1.776, 95% CI: 1.192–2.648, p=0.005). In contrast, serum albumin level did not exhibit an independent association with OS (HR: 0.934, 95% CI: 0.868–1.005, p=0.069). The overall model was statistically significant (p=0.001).

DISCUSSION

This study constitutes the inaugural external validation of the PLACE prognostic score within a Turkish cohort and is among the limited investigations assessing its efficacy beyond the initial Chinese cohort. Our results indicate that, while the PLACE score maintains statistically significant prognostic utility in patients with metastatic epithelioid pleural mesothelioma, its discriminative capacity is considerably diminished in comparison to the original development study.

Performance Comparison with Original Study

In the original development study by Zhang et al.,[17] the PLACE score demonstrated excellent discriminative ability with an AUC of 0.900 in the development cohort and 0.761 in the validation cohort. The HR for high-risk versus low-risk patients were 3.878 and 3.574, respectively.[17] In contrast, our study demonstrated time-dependent AUC values ranging from 0.554 at 6 months to 0.717 at 24 months, with a hazard ratio of 2.28 (95% CI: 1.04–4.95, p=0.037). For supplementary comparison with the original study, binary ROC analysis yielded an AUC of 0.617 (95% CI: 0.413–0.821). While our results remain statistically significant, the reduced discriminative performance compared to the original Chinese cohort suggests important population-specific differences that may limit the universal applicability of the PLACE score. Notably, the time-dependent AUC improved over the follow-up period (0.717 at 24 months), suggesting that the score may have greater clinical value for longer-term prognostic stratification.

Population and Treatment Differences

Several factors may account for the diminished performance observed in our cohort. Firstly, the original PLACE score was specifically developed for Chinese patients, with the authors explicitly stating that "the proposed model can only be applied to patients of Chinese ethnicity now and not currently generalizable to the overall global population".[17] Ethnic variations in disease biology, genetic background, and baseline laboratory characteristics may contribute to the observed discrepancies in model performance across different populations.[18]

Although our results remained statistically significant, the reduced discriminative ability indicates that the model may not perform consistently across diverse populations. Furthermore, the use of a predefined threshold (score=0) for risk stratification, as established in the original study, may not be entirely optimal for our cohort and could have contributed to the observed reduction in performance. While we did not attempt to redefine alternative thresholds, our findings suggest that population-specific recalibration of risk stratification may warrant further investigation.

Secondly, our study population was more homogeneous, comprising only patients with de novo metastatic epithelioid disease treated with a uniform first-line regimen. In contrast, the original cohort included patients with stages I–III disease, with 92.6% receiving chemotherapy with or without anti-angiogenesis therapy.[17] This heterogeneity in the development dataset may have contributed to the higher discriminative performance reported in the original study.

Clinical Implications

Although discriminative performance was limited, the PLACE score retained statistically significant prognostic stratification ability in our cohort. The significant survival difference between risk groups (37.98 months vs. 15.6 months, p=0.033) suggests that the score can still inform clinical decision-making and patient counseling. However, clinicians should be aware of the limitations when applying this score to non-Chinese populations or patients with metastatic disease.

The original authors emphasized that the PLACE score relies on "commonly monitored clinical and laboratory indicators" that do not add "additional physical and economic burden to the patient".[17] This practical advantage remains valid in our validation, as all components of the score are routinely available in clinical practice. The PLACE score may serve as a practical bedside tool for risk stratification in routine clinical practice.

Additional Prognostic Factors

Our analysis identified several additional prognostic factors not included in the original PLACE model, including specific metastatic sites (liver, bone, brain) and serum albumin levels.[19] These findings suggest potential opportunities for model refinement or development of population-specific modifications to improve prognostic accuracy.

Limitations

Our study has several limitations that should be acknowledged. The relatively small sample size (n=48) limits the statistical power and generalizability of our findings. Given the rarity of pleural mesothelioma, our sample size is comparable to many single-center studies in the literature. The wide confidence interval of the AUC (0.413–0.821) reflects this limited sample size and should be interpreted with caution; however, this is consistent with the rarity of the disease and the sample sizes reported in similar validation studies, including the original PLACE validation cohort (n=23). Although the multivariable model achieved an adequate EPV ratio of 17.0, variable selection was not fully pre-specified, and the risk of overfitting cannot be entirely excluded in small datasets; this should be considered when interpreting the multivariable results. The retrospective design introduces potential selection bias, and the single-center nature may limit external validity. Additionally, our focus on metastatic epithelioid disease represents a subset of the broader pleural mesothelioma population, which may limit comparability with the original mixed-stage cohort.

The original study authors noted similar limitations, including "small sample sizes," "short follow-up time in validation cohort," and the need for "multi-centre and large sample studies worldwide". Our study contributes to addressing these knowledge gaps but highlights the ongoing need for larger, multicenter validation studies.[17]

The absence of immunotherapy-based regimens reflects real-world practice in our country, where such treatments were not reimbursed for a prolonged period and only recently became accessible. This limitation should be considered when interpreting survival outcomes.

The reduced performance of the PLACE score in our population underscores the importance of external validation across diverse populations before widespread clinical implementation. Future research should focus on: (1) larger multicenter validation studies in non-Chinese populations, (2) investigation of population-specific modifications to improve model performance, (3) incorporation of additional prognostic variables such as molecular markers or imaging parameters, and (4) prospective validation studies to confirm clinical utility.

The original authors acknowledged that their model "lacks relevant genetic molecular variables and imaging variables", suggesting opportunities for model enhancement. Integration of modern biomarkers, genomic data, and advanced imaging features may improve prognostic accuracy across diverse populations. Furthermore, asbestos exposure status was unknown in a substantial proportion of patients (85.4%), which may affect the generalizability of our findings; however, as asbestos exposure is not a component of the PLACE score, this does not affect the validity of the primary analyses.

CONCLUSION

This study provides the first external validation of the PLACE prognostic score in a non-Chinese population with metastatic epithelioid pleural mesothelioma. While the score maintains statistical significance for survival prediction, the reduced discriminative performance (time-dependent AUC ranging from 0.554 at 6 months to 0.717 at 24 months, compared to 0.900 in the original study) highlights important limitations in cross-population generalizability. The PLACE score retains clinical utility for risk stratification in our population, but clinicians should interpret results with caution when applying this tool to non-Chinese patients or those with metastatic disease.

Our findings emphasize the critical importance of external validation studies for prognostic models and support the original authors' call for "multi-centre and large sample studies worldwide". Future research should focus on larger validation studies, population-specific model modifications, and incorporation of additional prognostic variables to develop more universally applicable prognostic tools for pleural mesothelioma patients across diverse populations and healthcare settings.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated after obtaining an approval from Kocaeli University Ethics Committee for Non-interventional Clinical Researches (Date: 09.04.2026, Decision No: 2026/99).

Informed Consent

This retrospective study used pre-existing anonymized patient data. No additional intervention was performed, and there was no direct patient contact. The study was approved by the Ethics Committee, and the requirement for written informed consent was waived by the ethics committee.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Concept: İÇ, YBT; Design: İÇ, YBT; Control: İÇ, YBT, KU, DÇ, UK; Resources: HZ, MÖ; Materials: İÇ, YBT; Data Collection and/or Processing: HZ, MÖ, İÇ, EB; Analysis and/or Interpretation: İÇ, YBT, KU, DÇ, UK; Literature Review: İÇ, YBT, EB; Writing the Article: İÇ, YBT, KU, DÇ, UK; Critical Review: İÇ, YBT, KU, DÇ, UK.

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