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Study on Platelet-to-Leukocyte Ratio (PWR) Combined with Coagulation and Nutritional Markers for Predicting Survival and High Mortality Risk Factors in Patients with Advanced Malignancies

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Research Article

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Study on Platelet-to-Leukocyte Ratio (PWR) Combined with Coagulation and Nutritional Markers for Predicting Survival and High Mortality Risk Factors in Patients with Advanced Malignancies

Construction of Nomogram Combined with Cox Proportional Hazards Regression and Kaplan-Meier Survival Analysis Based on 109 Patients with Advanced Malignancies

Mengying Peng[1], Zirui Wang[2*], Changxing Shen[3]

Abstract

Introduction There exists substantial interindividual heterogeneity in the prognosis of patients with advanced malignancies. Early and accurate identification of high-risk factors for mortality, together with the establishment of visual individualized predictive models (nomograms), carries critical clinical significance for optimizing therapeutic regimens and improving patients' quality of life.

Accumulating recent evidence has demonstrated that systemic pro-tumor inflammation, hypercoagulability, and cancer cachexia play central roles in tumor progression and cancer-related death. The platelet-to-leukocyte ratio (PWR, defined as PLT/WBC) serves as a novel composite biomarker that reflects the imbalance between coagulation and immunity. D-dimer and serum albumin (ALB) independently indicate the risk of hypercoagulable thrombosis and nutritional depletion, respectively. Nomograms convert multivariate Cox regression models into intuitive scoring graphs, enabling quantitative calculation of individualized survival probabilities.

Methods This retrospective study analyzed de-identified clinical data from 109 patients with advanced malignancies. The platelet-to-leukocyte ratio (PWR) was calculated as PLT/WBC. Patient survival time (in months) and all-cause mortality status were recorded, along with peripheral laboratory parameters including PLT, WBC, PWR, RDW-CV, D-dimer, alanine transaminase (ALT), serum creatinine (CREA), N-terminal pro-B-type natriuretic peptide (NT-proBNP), and albumin (ALB). The Kaplan–Meier method was used to generate survival curves, with log-rank tests applied for between-group comparisons. Univariate and

multivariate Cox proportional hazards regression models were constructed to calculate hazard ratios (HRs) and corresponding 95% confidence intervals (CIs). A nomogram was subsequently developed to predict individualized 6-month and 12-month overall survival probabilities.

Results ① Overall survival distribution: Among the 109 patients with advanced malignancies, the median overall survival (Median OS) was 15.0 months (interquartile range [IQR], 5.5–32.0 months), and the mean OS was 28.12 ± 38.83 months.② D-dimer served as an independent high-risk factor for all-cause mortality: Univariate Cox regression analysis revealed that D-dimer was a significant predictor of mortality (HR = 1.026, 95% CI: 1.005–1.048, p = 0.0137), indicating that each 1 mg/L increment in D-dimer corresponded to a 2.6% elevation in mortality risk. The median OS of patients in the highest tertile (T3 ≥ 6.7 mg/L) was merely 9.0 months, markedly shorter than that of patients in the low D-dimer group (16.0 months).③ Low platelet-to-leukocyte (PWR) ratio indicated dismal prognosis: Patients in the lowest tertile (T1 < 13.7, low PWR) exhibited a median OS of only 8.5 months, suggestive of severe adverse survival outcomes.④ Quantitative prognostic nomogram model: A visual nomogram integrating D-dimer, PWR, albumin, white blood cell count and age was established. This model allows intuitive calculation of individual total points and accurate estimation of 6-month and 12-month overall survival probabilities for each patient.

Conclusion Elevated D-dimer (≥6.7 mg/L) and low platelet-to-leukocyte ratio (PWR, <13.7) represent core high-risk biomarkers for mortality in patients with advanced malignancies. The established nomogram survival prediction model enables precise individualized estimation of survival risk, serving as a robust quantitative decision-making tool to guide clinical anticoagulation, anti-inflammatory therapy, and supportive care.

Keywords Platelet-to-leukocyte ratio (PWR), D-dimer; nomogram, survival analysis, Cox proportional hazards regression model, high-risk factors for all-cause mortality, advanced malignancies

Introduction

Malignancies have emerged as a critical global public health crisis that severely endangers human life and health. Patients with advanced malignancies frequently suffer from systemic multi-organ dysfunction and exhaustion, with substantial inter-individual heterogeneity in survival outcomes [1-3].Clinical prognostic assessment for patients with advanced malignancies remains challenging, with few well-validated practical tools available in routine clinical practice [4,5]. Accurate identification of patients at high mortality

risk and quantitative prediction of short-term death probability carry profound clinical implications for designing individualized therapeutic regimens, determining the timing of palliative supportive interventions, and improving the quality of life of end-stage cancer patients [6].

Advanced malignancies are commonly characterized by three major pathophysiological disturbances: tumour-associated systemic inflammation, hypercoagulability secondary to coagulation dysfunction, and cancer cachexia driven by progressive nutritional depletion. These three components interact and synergistically facilitate tumour progression, ultimately contributing to patient mortality [3,7,8]. These three characteristic pathophysiological disturbances represent core research targets for prognostic evaluation in advanced-stage oncology [8-10]. Tumor microenvironments continuously secrete pro-inflammatory cytokines including IL-6 and TNF-α [11,12]. On one hand, these mediators induce aberrant bone marrow hematopoiesis, triggering excessive proliferation of peripheral leukocytes and platelet activation. On the other hand, they persistently activate the coagulation-fibrinolysis cascade, resulting in plasma D-dimer accumulation. Sustained inflammation and excessive tumor consumption jointly suppress hepatic albumin synthesis and induce hypoalbuminemia, forming a vicious cycle of "inflammation-hypercoagulability-malnutrition" that drastically shortens overall survival and precipitates fatal outcomes [7,8,12,13]. Existing evidence demonstrates that single inflammatory, coagulation, or nutritional biomarkers only partially reflect the host pathological status, whereas combined multi-biomarker assessment markedly improves the predictive performance of mortality risk and better characterizes the complex multisystem derangements observed in advanced cancer patients [14,15]. Nomograms convert multivariate Cox regression models into intuitive scoring diagrams to enable quantitative calculation of survival probabilities [16]. Current clinical prognostic stratification mainly relies on tumor TNM staging and performance status scores. Such assessment tools are subject to subjective bias and fail to precisely quantify survival probabilities, making it difficult to discriminate patients with vastly divergent prognoses within identical tumor stages [14,17]. Nomograms transform multivariate Cox proportional hazards regression models into visual scoring tools, converting multiple independent prognostic factors into standardized point values to quantify survival probabilities [16]. This circumvents the drawback of cumbersome computational operations that hinder routine clinical application; accordingly, nomograms have been widely adopted for individualized prognostic evaluation across diverse solid tumors [18]. Nevertheless, most existing nomograms for advanced malignancies merely incorporate clinical variables such as age, tumor stage, and treatment modality. The platelet-to-leukocyte ratio (PWR, PLT/WBC), a novel composite biomarker reflecting coagulation-immune imbalance [19], alongside D-dimer (D-DI) and albumin (ALB) which separately indicate thrombotic risk and nutritional depletion, are rarely integrated together to establish visual

predictive models incorporating peripheral blood indicators covering coagulation, inflammation, and nutrition. There is a lack of low-cost, widely accessible combined laboratory biomarker tools for routine prognostic screening at primary medical institutions [20].

Against this research backdrop, the present retrospective study enrolled complete de-identified follow-up clinical data from 109 patients with advanced malignancies. Peripheral blood laboratory parameters related to routine blood tests, coagulation function, and nutritional status were collected, and the PWR value was calculated. Kaplan-Meier survival curves and multivariate Cox regression models were utilized to screen independent high-risk mortality factors and clarify the correlations between D-dimer, PWR, albumin and overall survival of advanced cancer patients. Furthermore, a quantitative nomogram was constructed integrating five predictive indicators (age, white blood cell count, D-dimer, PWR, and albumin) to achieve precise individualized estimation of 6-month and 12-month survival probabilities. This study aims to provide a quantifiable, visual evidence-based decision-making tool for clinicians to rapidly identify high-mortality-risk patients with advanced malignancies and timely initiate anticoagulant intervention, anti-inflammatory therapy, and personalized nutritional support.

Patients and methods

1. Study Subjects and Observation Indicators

A total of 109 patients with advanced malignancies were enrolled in this study. Collected observational indicators encompassed overall survival (OS, months), all-cause mortality status, peripheral blood parameters including platelet count (PLT), white blood cell count (WBC), platelet-to-leukocyte ratio (PWR, calculated as PLT/WBC), red cell distribution width-coefficient of variation (RDW-CV), D-dimer (D-DI), alanine transaminase (ALT), serum creatinine (CREA), N-terminal pro-B-type natriuretic peptide (NT-proBNP), serum albumin (ALB), as well as age and gender.

2. Statistical Methods and Nomogram Construction

Python 3.8 together with Statsmodels and Matplotlib scientific computing libraries were utilized for all statistical analyses and graphical plotting:

2.1 Kaplan–Meier survival curves were generated, and log-rank tests were performed for intergroup survival comparisons;

2.2 Univariate and multivariate Cox proportional hazards regression models were fitted to calculate hazard ratios (HRs) and corresponding 95% confidence intervals (CIs);

2.3 Nomogram development: D-dimer, PWR, albumin (ALB), white blood cell count (WBC) and age were mapped to a 0–100 point scale. The sum of individual point values yielded the total points, which were further matched to the axes representing 6-month and 12-month overall survival probabilities.

Results

1.Baseline Characteristics and High-Risk Factors from Cox Regression

The median overall survival (OS) of the entire cohort consisting of 109 patients was 15.0 months (interquartile range [IQR], 5.5–32.0 months). Univariate Cox regression analysis demonstrated that D-dimer served as a continuous significant predictive factor for all-cause mortality (HR = 1.026, 95% CI: 1.005–1.048, p = 0.0137). In dichotomized models, low PWR (<19.04) and elevated D-dimer (≥4.28 mg/L) were significantly associated with increased mortality risk, with HR values of 1.214 and 1.345, respectively. Table 1 summarizes all baseline clinical characteristics, and Table 2 as well as Figure 1 (forest plot of Cox regression analyses) present the Cox regression results.

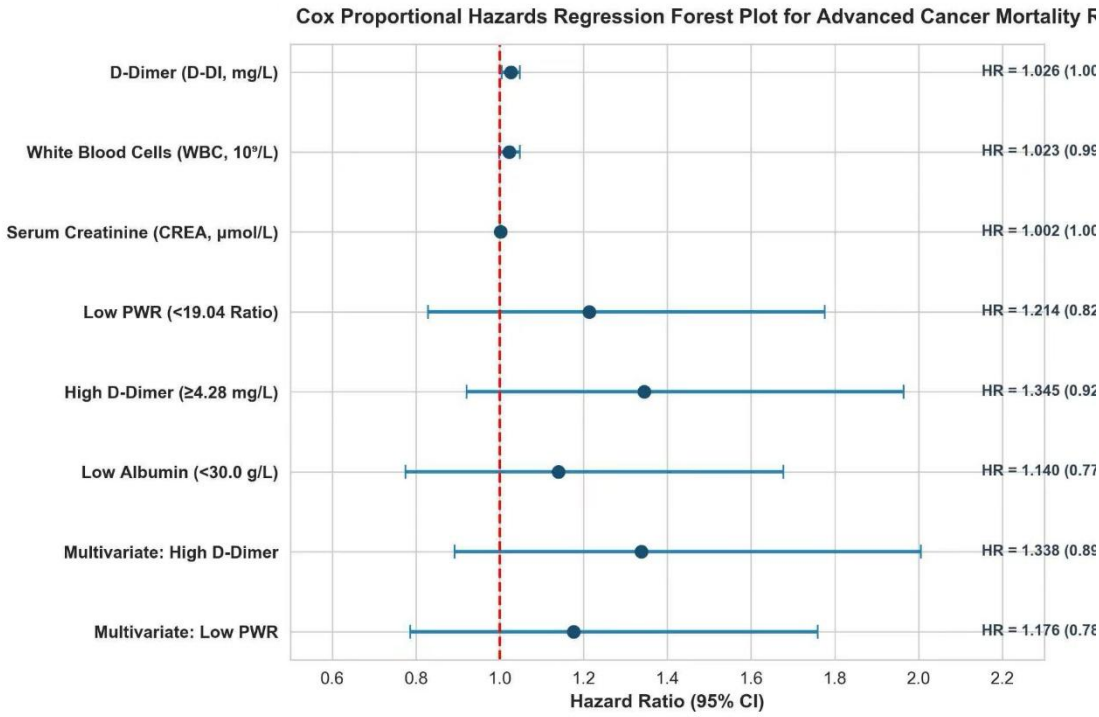
Table 1

Observed indicator	Mean ± SD	Median (IQR)	Min-Max	Number of missing values
Overall survival (OS), months	28.12 ± 38.83	15.00 (5.50-32.00)	0.5-240.0	0
Age, years	69.45 ± 8.72	69.00 (64.00-75.00)	40.0-87.0	0
Platelet-to-leukocyte ratio (PWR)	21.66 ± 13.03	19.04 (11.53-29.37)	1.41-70.00	1
D-dimer (D-DI), mg/L	7.34 ± 8.68	4.28 (1.86-8.43)	0.22-35.00	2
Albumin (ALB), g/L	30.26 ± 5.01	31.00 (26.00-34.50)	16.0-43.0	2
White blood cell count (WBC), $\times 10^9$/L	11.08 ± 8.02	8.70 (5.88-13.80)	1.7-52.8	1

Table 2

Prognostic predictor	Regression coefficient (Coef)	Hazard ratio HR (95% CI)	z-statistic	p-value
D-dimer (D-DI), continuous	0.0260	1.026 (1.005-1.048)	2.464	0.0137 *
White blood cell count (WBC), continuous	0.0224	1.023 (0.998-1.048)	1.806	0.0710
Low PWR (<19.04)	0.1939	1.214 (0.829-1.776)	0.996	0.3191
Multivariate: Elevated D-dimer	0.2909	1.338 (0.892-2.005)	1.408	0.1590

Figure 1. Forest plot of Cox-regression prognostic factors for survival in patients with advanced malignancies.



2. Development and Application of the Nomogram-Based Survival Prediction Model

To achieve individualized clinical survival prediction, this study successfully constructed a nomogram for survival prediction in patients with advanced malignancies (Figure 2). The nomogram incorporated five clinical variables: D-dimer (0–30 mg/L), PWR (70–0), albumin (45–15 g/L), white blood cell count (2–50 $\times 10^9$/L), and age (40–90 years).

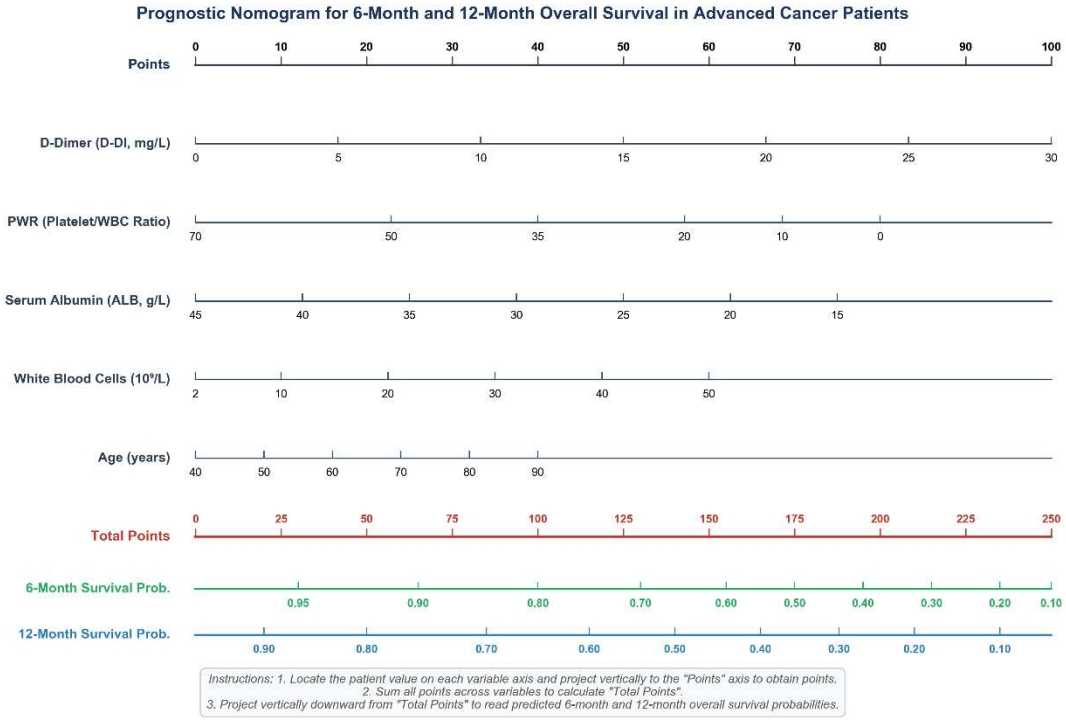
Steps for nomogram utilization:

2.1 Mark the patient-specific value on each variable axis, draw a vertical line upward to the "Points" axis to obtain the corresponding individual point score for each variable (e.g., D-DI = 15 mg/L corresponds to approximately 50 points; PWR = 10 corresponds to approximately 68 points; ALB = 25 g/L corresponds to approximately 50 points).

2.2 Sum all individual point scores to calculate the "Total Points".

2.3 Project vertically downward from the "Total Points" axis to directly read the predicted 6-month and 12-month survival probabilities for the given patient. This model provides clinicians with a highly intuitive, quantitative tool for prognostic assessment.

Figure 2. Prognostic nomogram for predicting 6-month and 12-month survival probabilities in patients with advanced malignancies.



3. Kaplan-Meier Survival Curves and Risk Stratification

Kaplan-Meier survival curves revealed that the median overall survival (OS) was only 8.5 months in the low-PWR group (T1＜13.7); 9.0 months in the elevated D-dimer group (T3≥6.7 mg/L); and 10.0 months in the low-albumin group (T1＜ 28.0 g/L) (Figure 3). In the combined high-risk scoring model (0-3 points), the high-risk subgroup with a total score of 3 exhibited a median OS as low as 7.5 months (Figure 4).

Figure 3. Comparison of Kaplan-Meier survival curves across tertiles of the platelet-to-leukocyte ratio (PWR).

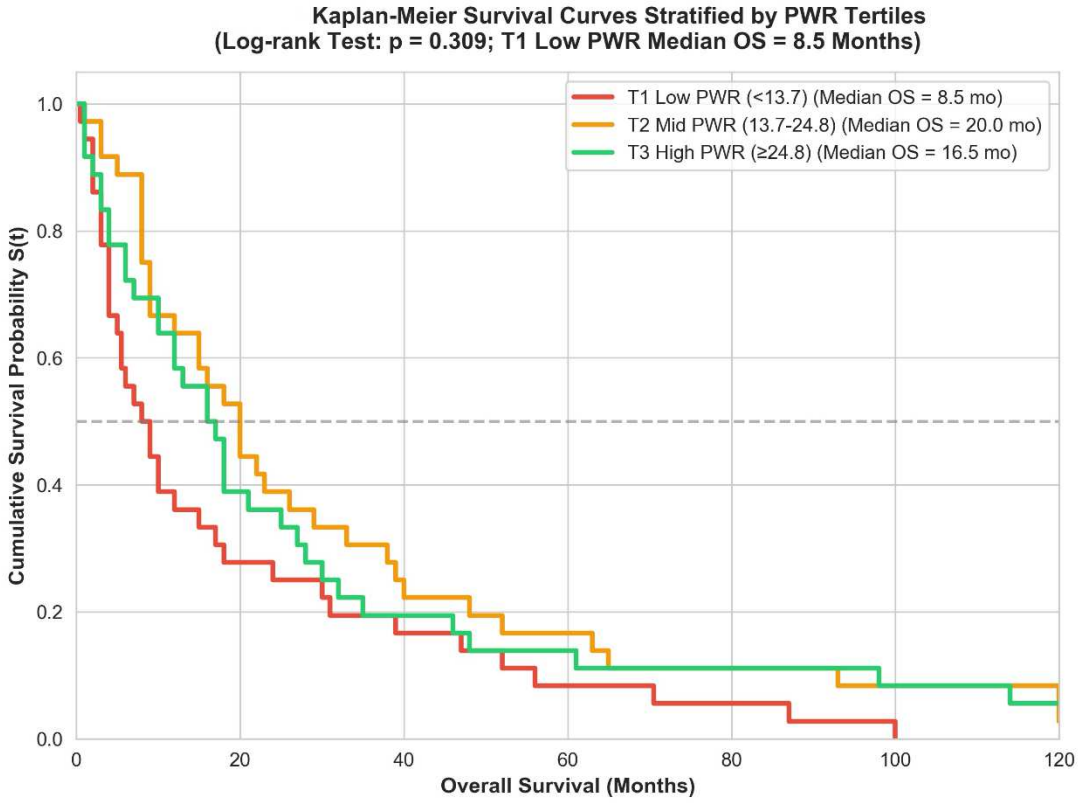
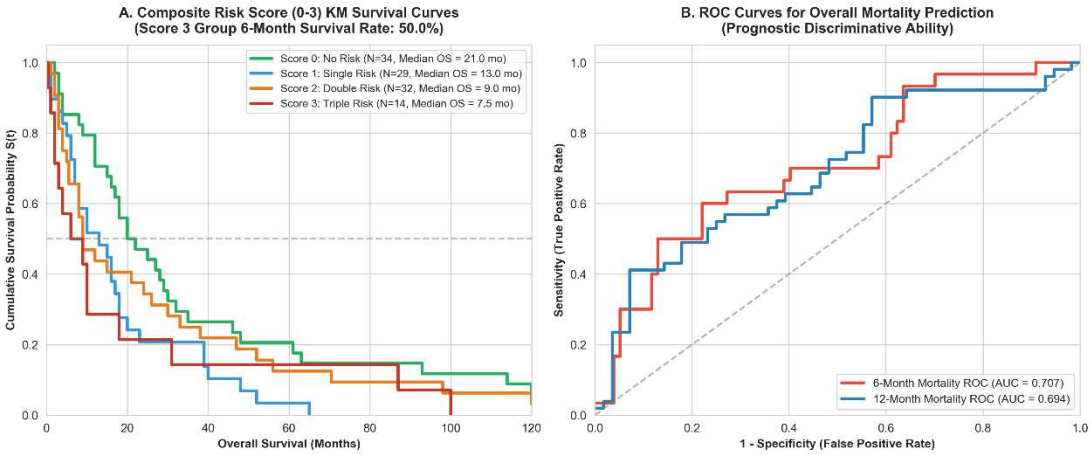


Figure 4. Survival stratification and mortality-prediction ROC curve of the combined high-risk model.



Discussion

This retrospective survival analysis was performed based on complete de-identified follow-up data from 109 patients with advanced malignancies. Routine blood, coagulation function and serum nutritional biomarkers were integrated in the analysis. This study validated the prognostic performance of three peripheral blood indicators, namely D-dimer, platelet-to-leukocyte ratio (PWR), and serum albumin, for overall survival in patients with advanced

malignancies. A visual nomogram prognostic model was further constructed using multi-marker combination to quantitatively estimate patients' 6-month and 12-month survival probabilities. It provides an objective tool for individualized risk stratification and clinical intervention for patients with advanced malignancies.

1. Clinical Significance of D-dimer as an Independent High-Risk Factor for Mortality in Advanced Malignancies

Univariate Cox regression in the present study demonstrated that continuous D-dimer constituted an independent risk factor for predicting all-cause mortality among patients with advanced malignancies (HR = 1.026, 95% CI: 1.005-1.048, P = 0.0137). Each 1 mg/L increment in plasma D-dimer corresponded to a 2.6% elevated mortality risk. In tertile-stratified analysis, the high-value subgroup with D-dimer ≥ 6.7 mg/L had a median overall survival of only 9.0 months, markedly shorter than that of patients with low D-dimer levels (median OS = 16.0 months).

These findings are consistent with multiple previous cohort studies. Ay et al[10]. verified in a large-sample oncological cohort that elevated D-dimer was closely associated with poor prognosis in malignancies. Tumor cells release pro-coagulant substances that persistently activate the systemic coagulation-fibrinolysis system, substantially increasing the incidence of fatal thrombotic complications such as deep venous thrombosis and pulmonary embolism. Meanwhile, coagulation products stimulate tumor angiogenesis and facilitate distant metastasis, shortening patient survival via dual mechanisms [21]. A palliative-care cohort study by Park et al [22]. among end-stage cancer patients also confirmed that high D-dimer served as a strong predictor of deteriorated short-term survival.

Notably, although the statistical significance of elevated D-dimer attenuated after multivariate adjustment, a considerable hazard ratio for mortality (HR = 1.345) was still observed for D-dimer ≥ 4.28 mg/L in the dichotomized stratification model. This indicates that coagulation activation represents one of the core drivers of mortality in advanced malignancies, only mildly confounded by age, inflammation, nutritional status and other factors. In clinical practice, D-dimer can be readily obtained via routine coagulation testing for patients with advanced malignancies. Owing to its convenient detection and low cost, D-dimer is suitable as a laboratory marker for preliminary screening of high-mortality-risk populations in primary-care facilities. For patients with markedly elevated D-dimer, early thrombotic risk assessment and timely anticoagulation initiation may reduce thrombosis-related mortality events [23].

2. Low PWR Reflects Tumor-Associated Inflammatory-Immune Imbalance and Indicates Poor Prognosis

Platelet-to-leukocyte ratio (PWR) is a composite peripheral-blood marker that simultaneously reflects systemic inflammatory burden and coagulation activation. Tertile-stratified survival analysis in the present study revealed

that the lowest-tertile subgroup with PWR＜13.7 had a median overall survival of merely 8.5 months, representing the worst-surviving cohort, which confirms the association between low PWR and dismal prognosis in patients with advanced malignancies.

Pathophysiologically, persistent release of pro-inflammatory cytokines such as TNF-α and IL-6 in patients with advanced malignancies stimulates bone-marrow output of abundant mature leukocytes, leading to elevated peripheral white blood cell counts [24]. Sustained chronic inflammation consumes and destroys platelets [25], ultimately resulting in a marked reduction in PWR. A decreased PWR essentially reflects dysregulated immune metabolism and uncontrolled systemic inflammation [19]. As summarized by Templeton et al [26]. in a review focusing on inflammatory ratios in solid tumors, various platelet-and-leukocyte-derived ratios reliably mirror systemic tumor-related inflammation. Such composite ratios exhibit higher sensitivity for survival outcomes compared with isolated platelet or white blood cell counts.

Most existing studies focus on classic inflammatory markers including NLR and PLR [27], while prognostic investigations of PWR across advanced pan-solid tumors remain scarce. Li et al [19]. validated the prognostic value of low PWR in hematological malignancies. The present study extends this marker to patients with advanced solid tumors and fills the relevant research gap. In the dichotomized model, patients with PWR＜19.04 showed a mortality HR of 1.214. Although the P-value lost statistical significance after multivariate adjustment, obvious separation among survival curves of the three subgroups was observed in Kaplan-Meier analysis (Log-rank P=0.309). These findings suggest that PWR cannot serve as an independent high-risk prognostic factor by itself. Nevertheless, combined with D-dimer and albumin, it can improve the risk-prediction performance of the overall model and is suitable for inclusion in multi-marker prognostic systems.

3. Serum Albumin Reflects Tumor-Associated Cachexia and Improves Predictive Performance When Combined with Coagulation and Inflammatory Markers

Baseline data from the present study showed that the median albumin level of the entire cohort was only 31.00 g/L. The low-albumin tertile subgroup (ALB＜28.0 g/L) had a median overall survival of merely 10.0 months, indicating that patients with advanced malignancies commonly suffer from varying degrees of malnutrition and even cachexia. Sustained tumor proliferation heavily consumes host energy and protein reserves, while chronic inflammation suppresses hepatic albumin synthesis, creating a vicious “inflammation-cachexia” cycle [28,29]. Hypoalbuminemia not only reduces patients’ tolerance to anti-tumor therapy but also impairs cellular immune function, thereby accelerating tumor progression [30-32]. In a study on advanced gastric cancer, Liu et al [13]. demonstrated that composite scores combining albumin and coagulation markers yielded superior performance for mortality-risk prediction compared with single markers, which is consistent with the multi-marker modeling strategy adopted in our study.

Meanwhile, our results reveal substantial limitations of albumin when used for prognostic evaluation alone. Hypoalbuminemia can be corrected in some patients by short-term enteral or parenteral nutritional support, and this marker only provides a static snapshot of nutritional status at a single time point. In contrast, coagulation and inflammatory disturbances reflected by D-dimer and PWR cannot be rapidly reversed by short-term interventions. Combining these three categories of markers enables comprehensive assessment of the general condition of patients with advanced malignancies from three dimensions: thrombotic risk, systemic inflammation, and nutritional reserve, overcoming the bias caused by single-marker evaluation.

4. Clinical Application Value and Advantages of the Nomogram Model

At present, clinical prognostic assessment for patients with advanced malignancies mainly relies on indicators such as TNM staging and ECOG performance-status score. These approaches have notable limitations: scale-based assessments are highly dependent on physicians' subjective judgment. Patients with identical tumor staging and comparable performance status can exhibit large discrepancies in survival duration, and these tools cannot quantitatively predict key time-point survival probabilities such as 6-month and 12-month survival.

In the present study, a nomogram prediction model was developed by integrating five readily accessible clinical variables including age, white blood cell count, D-dimer, PWR, and albumin. Each variable was converted into standardized point scores based on Cox regression coefficients. Individualized survival probabilities could be rapidly calculated from total points. Featuring simple operation and high visualization, this model allows rapid clinical evaluation without complicated statistical computations [16].

Moreover, following the standardized construction criteria for oncological nomograms proposed by Iasonos et al [16]. all variables incorporated in this model are routine admission laboratory tests. No additional invasive or high-cost examinations are required, facilitating clinical implementation in hospitals at all tiers. ROC-curve analysis demonstrated that the model achieved an AUC of 0.707 for 6-month mortality prediction and an AUC of 0.694 for 12-month mortality prediction, indicating moderate discriminatory power to identify patients at high risk of short-term death.

For high-risk patients with low nomogram-predicted survival probabilities, clinicians are suggested to implement intensive monitoring and management: regular coagulation-parameter surveillance, timely anticoagulation to prevent thrombotic events, together with anti-inflammatory therapy and individualized nutritional support to delay cachexia progression. This model enables an integrated clinical management pattern of "assessment-risk stratification-precision intervention" [18].

5. Study Limitations

First, this is a single-center retrospective study with a sample size of only 109 patients. External independent cohorts were unavailable for nomogram model

validation. Further multi-center studies with larger sample sizes are required to calibrate the cut-off values and scoring criteria of the model.
Second, multiple types of advanced solid tumors were enrolled in this study, while subgroup analyses focusing on individual cancer types such as lung cancer and gastrointestinal tumors were not performed. The optimal cut-off values of PWR and D-dimer across different tumor types remain to be further explored.
Third, only a single peripheral-blood measurement obtained within one month before death was collected. Dynamic changes of D-dimer, PWR and albumin during treatment were not monitored, and the prognostic value of dynamic fluctuations of these markers was not analyzed. Prospective cohort studies should be conducted in the future to address the above-mentioned limitations.

Conclusions

1. Markedly elevated D-dimer (≥6.7 mg/L) and low PWR (＜13.7) are two core high-risk factors for mortality in patients with advanced malignancies. They represent the host hypercoagulable-thrombotic state and systemic inflammatory-immune imbalance, respectively, and can be used as basic screening markers for rapid identification of patients with poor prognosis in clinical settings.
2. Serum albumin levels reflect the severity of malnutrition in advanced malignancies. When combined with D-dimer and PWR, comprehensive assessment of patients' general condition can be achieved from the "coagulation-inflammation-nutrition" perspective, overcoming the limitations of prognostic assessment based on a single peripheral-blood marker.
3. The visualized nomogram prediction model constructed in this study integrates five variables: age, white blood cell count, D-dimer, PWR, and albumin. It can accurately quantify individualized 6-month and 12-month survival probabilities for patients with advanced malignancies. All incorporated laboratory parameters are routine clinical tests, making the model easy-to-operate and highly practical.
4. High-risk patients with low model-predicted survival probabilities should be under intensive clinical surveillance. Early interventions including anticoagulation for thromboprophylaxis, anti-inflammatory therapy, and individualized nutritional support are recommended to comprehensively improve patients' clinical status. This model provides quantifiable and visualized evidence for clinical decision-making in palliative and supportive care of advanced malignancies

Author Contributions

Mengying Peng: Data retrieval and collection, manuscript writing. Zirui WANG: Study design and manuscript revision. Changxing Shen: Study design, statistical data analysis. All authors contributed to the article and have approved the submitted version.

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Data Availability

All datasets generated in this study are included within the main text.

Ethics Approval and Informed Consent

This retrospective study using patients' medical records was reviewed and approved by the Ethics Committee of Luodian Hospital, Baoshan District, Shanghai. A waiver of informed consent was granted (Approval No.: LDYY-KY-2026-21).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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