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Original Article

Diagnostic and prognostic value of coagulation markers and platelet-derived growth factor-BB in evaluating intensity-modulated radiotherapy efficacy in nasopharyngeal carcinoma

Haizhong Zhang[1], Deli Ye[2]

[1]*Laboratory Center, Longyou County People's Hospital, Quzhou 324400, Zhejiang, China;* [2]*Laboratory Center, Zhejiang Provincial People's Hospital, Hangzhou 310000, Zhejiang, China*

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Abstract: Objectives: To evaluate the diagnostic and prognostic value of coagulation markers - including activated partial thromboplastin time (APTT), prothrombin time (PT), fibrinogen (FIB), platelet count (PLT), and D-dimer (DD) - and platelet-derived growth factor-BB (PDGF-BB) in patients with nasopharyngeal carcinoma (NPC) undergoing intensity-modulated radiotherapy (IMRT). Methods: A total of 210 NPC patients receiving IMRT and 160 healthy controls were enrolled. Baseline levels of PDGF-BB and coagulation markers were compared between groups. The association of PDGF-BB with clinical staging was analyzed, and receiver operating characteristic (ROC) curve analysis was used to assess its diagnostic performance. Cox regression analyses were performed to identify independent predictors of five-year survival. A dynamic nomogram was developed to provide individualized survival predictions. Results: NPC patients exhibited significantly higher levels of PDGF-BB, APTT, PT, FIB, PLT, and DD compared to healthy controls (all $P < 0.001$). PDGF-BB was positively correlated with TNM stage (stage III/IV vs. I/II, $P < 0.001$), T stage ($P = 0.005$), and N stage ($P = 0.020$). Multivariate Cox regression identified low PDGF-BB (< 628.18) (HR = 0.492, $P = 0.009$), low DD (< 746.1) (HR = 0.456, $P = 0.002$), age 51-64 years (HR = 2.057, $P = 0.032$) and ≥ 65 years (HR = 4.138, $P < 0.001$), EBV DNA negativity (HR = 0.273, $P = 0.012$), and TNM stage III/IV (HR = 3.042, $P = 0.023$) as independent prognostic factors. Conclusions: PDGF-BB and DD, alongside age, EBV DNA status, and TNM stage, are promising biomarkers for NPC prognosis. A dynamic nomogram integrating these factors offers accurate survival prediction and supports personalized treatment strategies in NPC management.

Keywords: Nasopharyngeal carcinoma, intensity-modulated radiotherapy, PDGF-BB, coagulation markers, prognosis

Introduction

Nasopharyngeal carcinoma (NPC), a malignancy arising in the nasopharyngeal epithelium, exhibits a distinct geographic distribution, with high prevalence in Southeast Asia-particularly in southern China, where incidence rates reach 20-50 per 100,000 in regions such as Guangdong, Hong Kong, and Macao [1, 2]. Its pathogenesis is multifactorial, involving genetic predisposition, environmental exposure, Epstein-Barr virus (EBV) infection, and lifestyle factors including smoking and alcohol consumption [3]. Intensity-modulated radiotherapy (IMRT) remains the cornerstone of NPC treatment due to its ability to deliver precise radiation doses to the tumor while minimizing damage to adjacent healthy tissues [4, 5]. However, the insidious onset and non-specific early symptoms often result in late-stage diagnoses, complicating treatment and worsening prognosis [6].

Despite advances in imaging and molecular diagnostics, early detection and accurate prognostic assessment of NPC remain challenging [7]. Current diagnostic modalities, such as computed tomography (CT), magnetic resonance imaging (MRI), and EBV DNA quantification, provide essential information but have limited util-

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ity for early-stage identification and real-time disease monitoring [8, 9]. Traditional prognostic indicators-such as TNM staging and patient age-demonstrate variable predictive power across populations [10, 11]. Recent studies have highlighted the potential involvement of coagulation markers and platelet-derived growth factor-BB (PDGF-BB) in tumor biology, implicating them in cancer progression, metastasis, and treatment responsiveness [12]. This study aims to evaluate the diagnostic and prognostic value of coagulation markers and PDGF-BB in NPC patients undergoing IMRT, with the goal of improving individualized treatment strategies.

The role of the coagulation system extends beyond hemostasis and into cancer biology. Emerging evidence indicates that it contributes to multiple stages of tumorigenesis, including initiation, progression, and metastasis [13]. PDGF-BB, a growth factor secreted by platelets and certain tumor cells, plays a crucial role in cell proliferation, migration, and angiogenesis [14]. In malignancies, PDGF-BB acts as a double-edged sword: it promotes tumor angiogenesis and sustains tumor growth by enhancing vascularization, while also remodeling the tumor microenvironment to facilitate metastasis and therapy resistance [15]. Previous research has suggested associations between PDGF-BB levels and tumor aggressiveness, metastatic potential, and treatment outcomes, positioning it as a promising biomarker for diagnosis and prognosis [16].

Although prior studies have explored the roles of coagulation indices and PDGF-BB in various malignancies, their specific functions in NPC remain unclear. This study investigates the relationships between these biomarkers and NPC clinical characteristics, treatment responses, and 5-year survival outcomes by comparing their levels in NPC patients and healthy controls. The findings are expected to provide new insights into the diagnostic and prognostic utility of coagulation markers and PDGF-BB in NPC, potentially informing more effective and personalized management strategies.

Methods and materials

Sample size calculation

Based on a previously reported 5-year mortality rate of approximately 30% for nasopharyngeal carcinoma (NPC) [17], the required sample size was calculated using the formula: $N = Z^2 [P (1-P)]/E^2$, where $P = 0.30$, $E = 0.05$, $Z = 1.96$. The calculated sample size was approximately 323. However, the actual number of participants was determined by the availability of eligible clinical samples.

General information

This study included 210 patients diagnosed with NPC and treated at Longyou County People's Hospital between January 2017 and December 2019. Additionally, 160 healthy individuals undergoing routine physical examinations during the same period were enrolled as the control group. The study was approved by the Medical Ethics Committee of Longyou County People's Hospital (**Figure 1**).

Inclusion and exclusion criteria

Inclusion criteria: (1) Histopathological confirmation of NPC [18]. (2) Age between 18 and 70 years. (3) Scheduled to receive IMRT. (4) Availability of complete clinical, imaging, and pathological data required for the study.

Exclusion Criteria: (1) Presence of severe cardiovascular or cerebrovascular disease, hepatic/renal dysfunction, diabetes, or other conditions affecting coagulation function. (2) History of primary or secondary coagulation disorders. (3) History of malignancies other than NPC. (4) Pregnancy or lactation. (5) Current use of anticoagulant or antiplatelet medications. (6) Stage IVB NPC.

Treatment regimens

Patients received IMRT via linear accelerators (e.g., Varian TrueBeam). Treatment protocols varied by clinical stage:

Stage I (T1N0M0): Radical radiotherapy alone; 66-70 Gy to the nasopharynx and 54-60 Gy to the cervical lymph nodes.

Stage II (T0-2N0-1M0): For T2N1 cases, concurrent chemoradiotherapy (typically cisplatin-based) is recommended; others may receive radiotherapy alone or in combination with chemotherapy. Radiation doses are the same as in Stage I.

Stages III-IVA (locally advanced): Induction chemotherapy (e.g., TP or GP regimen) followed by concurrent chemoradiotherapy, or concurrent chemoradiotherapy plus adjuvant chemothera-

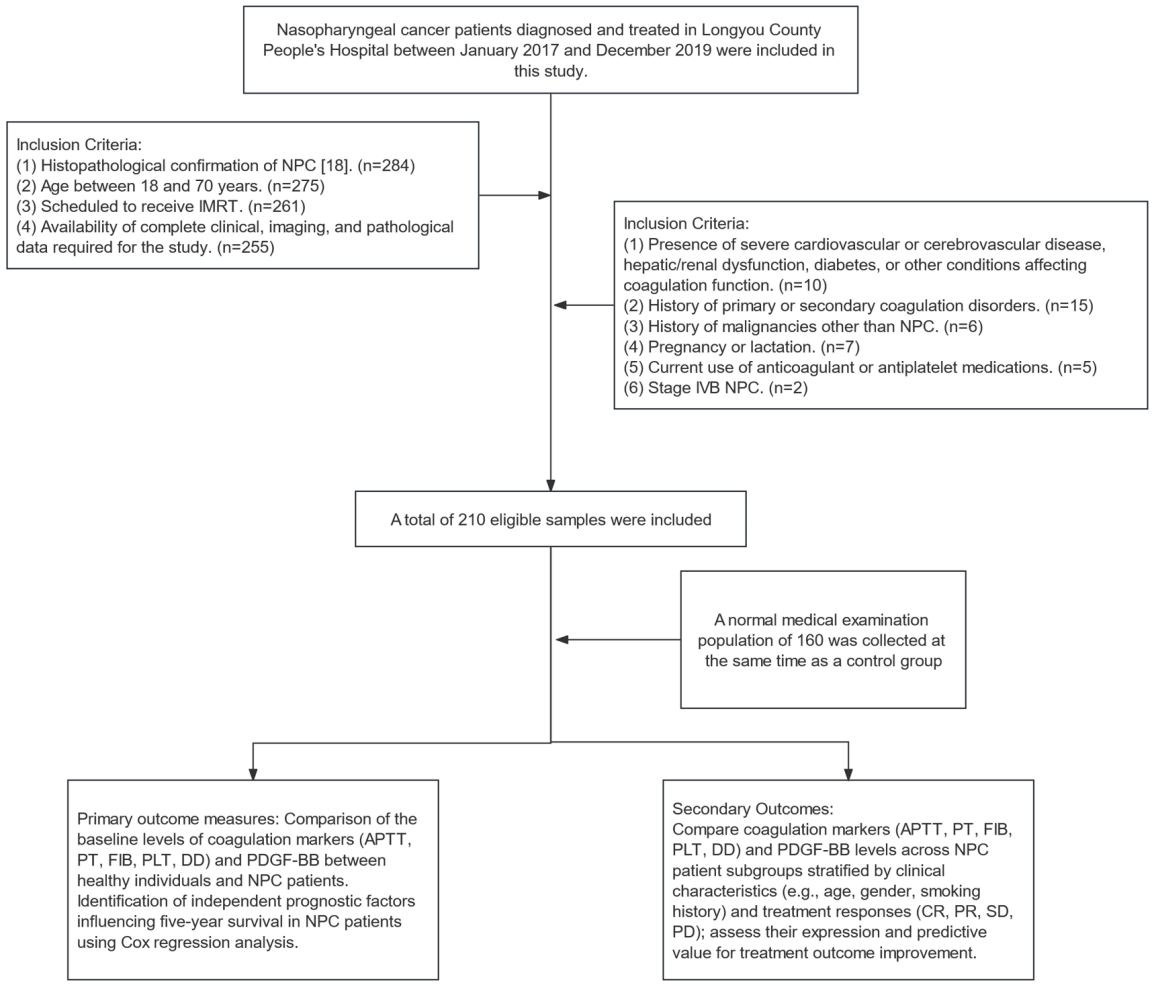

Figure 1. Sample screening flow chart.

py. Radiation doses are 66-70 Gy for the nasopharynx and 54-60 Gy for the cervical lymph nodes, including bilateral retropharyngeal and level II-Vb lymph nodes.

Clinical data collection

Comprehensive baseline data were collected to compare clinical characteristics between NPC patients and healthy controls, providing a foundation for subsequent analysis.

Demographic and behavioral variables included age, sex, education level, smoking history, alcohol consumption history, TNM stage, tumor differentiation, and EBV DNA status.

All data were obtained from the hospital's electronic medical records to ensure accuracy and completeness.

Laboratory indicator collection and testing

Laboratory indicators - including PDGF-BB, activated partial thromboplastin time (APTT), prothrombin time (PT), fibrinogen (FIB), platelet count (PLT), and D-dimer (DD), were measured using standardized protocols and equipment.

(1) PDGF-BB (pg/mL): Measured by ELISA (ELISA Bio, Shanghai; Batch No. ml105299). (2) PLT was determinedusing an automated hematology analyzer (Sysmex XN-9000, Japan). (3) APTT, PT, FIB, and DD were measured using a coagulation analyzer (Sysmex CS-5100, Japan).

All blood samples were collected upon patient admission, and processed and stored following standardized protocols to ensure reliability.

Clinical prognosis follow-up

Five-year survival outcomes were determined through structured follow-up. Patients were followed every 6 months for the first year, and annually thereafter, up to 5 years post-treatment. Survival status and clinical progress were recorded at each visit.

Outcome measurements

Primary outcome measures: Comparison of the baseline levels of coagulation markers (APTT, PT, FIB, PLT, DD) and PDGF-BB between healthy individuals and NPC patients.

Identification of independent prognostic factors influencing five-year survival in NPC patients using Cox regression analysis.

Secondary outcome measures: Comparison of coagulation markers and PDGF-BB levels among NPC patients with different clinical characteristics (e.g., age, gender, smoking history, etc.).

Comparison of expression levels of coagulation markers and PDGF-BB in patients with varying treatment responses (complete response [CR], partial response [PR], stable disease [SD], and progressive disease [PD]).

Evaluation of the expression and predictive value of coagulation markers and PDGF-BB in patients with improved treatment outcomes.

Statistical analysis

Statistical analyses were conducted using SPSS 26.0 and R 4.3.3. The Kolmogorov-Smirnov (K-S) test was first applied to assess data normality. For normally distributed continuous variables presented as (mean ± SD) deviation, independent samples t-tests were used to compare differences between groups. Continuous variables with non-normal distribution were expressed as median with interquartile range (IQR, 25th-75th percentile), and group comparisons were performed using the Mann-Whitney U test.

Categorical variables expressed as numbers (percentages) (e.g., sex, EBV DNA status) were analyzed using the chi-square test.

Cox proportional hazards regression (using the survival package in R) was employed to identify independent prognostic factors for five-year survival. Hazard ratios (HRs) and corresponding *P*-values were reported. A dynamic nomogram was constructed using the DynNom package in R to integrate clinical and laboratory variables, enabling real-time, individualized survival prediction. All tests were two-sided, and $P < 0.05$ was considered statistically significant.

Results

Comparison of baseline characteristics

There were no significant differences in age ($P = 0.849$), gender ($P = 0.541$), education level ($P = 0.653$), smoking history ($P = 0.234$), or alcohol consumption ($P = 0.270$) between NPC patients and healthy controls. Tumor-related characteristics such as T stage, N stage, TNM stage, and differentiation degree also showed no significant differences. However, the EBV DNA positivity rate was significantly higher in the NPC group than in controls (all $P < 0.001$; **Table 1**).

Comparison of the baseline levels of coagulation markers and PDGF-BB

NPC patients showed significantly elevated levels of PDGF-BB compared to healthy controls ($P < 0.001$). Similarly, APTT, PT, FIB, PLT, and DD levels were all significantly higher in the NPC group (all $P < 0.001$), suggesting notable coagulation and platelet-related changes in NPC pathophysiology (**Table 2**).

Comparison of coagulation markers and PDGF-BB in NPC patients with different clinical characteristics

NPC patients were stratified into low and high PDGF-BB expression groups. No significant differences were found in age, sex, education level, smoking, alcohol consumption, EBV DNA status, or tumor differentiation (all $P > 0.05$). However, significant associations were observed with TNM stage ($P < 0.001$), T stage ($P = 0.005$), N stage ($P = 0.020$), and receipt of chemotherapy ($P < 0.001$), suggesting a potential link between PDGF-BB expression and disease severity or treatment need (**Table 3**). Comparisons for other coagulation markers are shown in Tables S1, S2, S3, S4, S5.

Table 1. Comparison and presentation of clinical characteristics

Variable	Total	Control group (n = 160)	NPC group (n = 210)	χ^2	*P*
Age					
≤ 50	135	61	74	0.327	0.849
51-64	152	64	88		
≥ 65	83	35	48		
Gender					
Male	234	104	130	0.374	0.541
Female	136	56	80		
Educational level					
≤ Junior high school	149	61	88	0.852	0.653
Senior high school	152	70	82		
≥ University	69	29	40		
Smoking history (cigarettes/day)					
< 10	202	93	109	1.417	0.234
≥ 10	168	67	101		
Alcohol consumption history (ml/d)					
< 1000	224	102	122	1.216	0.270
≥ 1000	146	58	88		
T staging					
T1			80		
T2			66		
T3			55		
T4			9		
N staging					
N0			46		
N1			38		
N2			80		
N3			46		
TNM staging					
I			18		
II			32		
III			105		
IV			55		
Differentiation degree					
Well differentiated			40		
Moderately differentiated			47		
Poorly differentiated			123		
EBV DNA positivity					
Yes	184	16	168	177.994	< 0.001
No	186	144	42		

Notes: TNM, Tumor, Node, Metastasis; T, Tumor; N, Node; EBV, Epstein-Barr Virus.

Comparison of coagulation markers and PDGF-BB expression across clinical stages

PDGF-BB levels differed significantly across TNM stages, with stage IV patients showing significantly higher levels than stage I patients (P < 0.001). In contrast, APTT, PT, FIB, PLT, and DD levels showed no significant differences among stages (all P > 0.05; **Figure 2**).

Table 2. Comparison of the distribution of baseline levels of coagulation markers and PDGF-BB

Variable	Total	Control group (n = 160)	NPC group (n = 210)	Statistic	*P*
PDGF-BB (pg/mL)	284.40 ± 251.34	30.08 ± 10.04	478.17 ± 155.61	36.354	< 0.001
APTT (s)	37.56 ± 4.51	35.33 ± 2.94	39.26 ± 4.76	9.198	< 0.001
PT (s)	12.50 [11.90, 13.10]	12.10 [11.50, 12.50]	12.90 [12.30, 13.50]	9.886	< 0.001
FIB (g/L)	3.57 ± 0.99	3.12 ± 0.53	3.91 ± 1.13	8.121	< 0.001
PLT (×10^9/L)	230.82 ± 66.69	203.11 ± 42.51	251.93 ± 73.76	7.477	< 0.001
DD (ng/mL)	342.75 [216.95, 626.59]	226.10 [170.05, 285.28]	593.92 [394.48, 827.78]	12.991	< 0.001

Notes: PDGF-BB, Platelet-Derived Growth Factor-BB; APTT, Activated Partial Thromboplastin Time; PT, Prothrombin Time; FIB, Fibrinogen; PLT, Platelet Count; DD, D-dimer.

Comparison of coagulation markers and PDGF-BB expression between early- and advanced-stage NPC patients

PDGF-BB levels were significantly higher in advanced-stage (III/IV) than in early-stage (I/II) patients (P < 0.001). PT and FIB also showed significant differences between these groups (both P < 0.05). However, no significant differences were observed in APTT, PLT, or DD (all P > 0.05; **Figure 3**).

Comparison of coagulation markers and PDGF-BB expression across different treatment responses

No significant differences were observed in the expression levels of PDGF-BB, APTT, PT, FIB, PLT, or DD among patients with different treatment responses (all P > 0.05; **Figure 4**).

Comparison of coagulation markers and PDGF-BB expression in patients with improved therapeutic outcomes

Similarly, no statistically significant differences were found in the levels of PDGF-BB, APTT, PT, FIB, PLT, or DD between patients who showed improved treatment outcomes and those who did not (all P > 0.05), as shown in **Figure 5**.

Prognostic value of coagulation markers and PDGF-BB for five-year survival

Overall survival outcomes: During the five-year follow-up period, 72 patients died, yielding a mortality rate of 34.29%. The average time to death was 19.83 months. These findings provided a foundation for assessing the prognostic significance of coagulation markers and PDGF-BB in NPC.

Univariate cox regression analysis: Univariate Cox regression revealed several significant predictors of five-year survival:

Each 1-unit increase of PDGF-BB levels was associated with a higher mortality risk (HR = 1.004, P < 0.001). DD also showed significant prognostic value (HR = 1.001, P < 0.001) Increased risk was observed in patients aged 51-64 years (HR = 1.998, P = 0.039) and ≥ 65 years (HR = 5.801, P < 0.001). EBV DNA positivity was associated with worse survival (HR = 0.201, P = 0.002). TNM stage III/IV: Significantly worse prognosis (HR = 5.486, P < 0.001). As for T stage T3/T4, increased mortality risk (HR = 1.855, P = 0.010).

Other variables - including sex, education level, smoking history, alcohol consumption, tumor differentiation, N stage, and chemotherapy-did not significantly impact survival (all P > 0.05; **Table 4**).

Kaplan-Meier survival curve analysis

Kaplan-Meier survival curves confirmed the prognostic significance of several factors. Significant survival differences (all P < 0.001) were observed based on the following items. Patients ≥ 65 years had notably lower survival than younger groups.

Positive EBV DNA status was associated with poorer survival outcomes. Patients with advanced TNM and T stages exhibited worse prognoses. High expression levels of PDGF-BB and DD were significantly associated with reduced survival. Detailed curves are presented in **Figure 6**.

Multivariate cox regression analysis

Multivariate analysis identified the following independent predictors of five-year survival:

PDGF-BB levels < 628.18 were associated with better survival compared to ≥ 628.18 (HR = 0.492, P = 0.009). DD levels < 746.1 showed significant protective effect compared to ≥ 746.1 (HR = 0.456, P = 0.002). Strong indepen-

Table 3. Analysis of differences in clinical characteristics stratified by PDGF-BB expression levels

Variable	Total	PDGF-BB (pg/mL)		χ^2	*P*
		Low expression (n = 105)	High expression (n = 105)		
Age					
≤ 50	74	37	37	4.636	0.098
51-64	88	50	38		
≥ 65	48	18	30		
Gender					
Male	130	68	62	0.727	0.394
Female	80	37	43		
Educational level					
≤ Junior high school	88	45	43	0.884	0.643
Senior high school	82	38	44		
≥ University	40	22	18		
Smoking history (cigarettes/day)					
< 10	109	60	49	2.308	0.129
≥ 10	101	45	56		
Alcohol consumption history (ml/d)					
< 1000	122	66	56	1.956	0.162
≥ 1000	88	39	49		
EBV DNA positivity					
Yes	168	81	87	1.071	0.301
No	42	24	18		
Differentiation degree					
Well differentiated	40	17	23	1.320	0.517
Moderately differentiated	47	23	24		
Poorly differentiated	123	65	58		
TNM staging					
I	18	18	0	21.534	< 0.001
II	32	18	14		
III	105	45	60		
IV	55	24	31		
T staging					
T1	80	47	33	12.955	0.005
T2	66	37	29		
T3	55	20	35		
T4	9	1	8		
N staging					
N0	46	32	14	9.791	0.020
N1	38	16	22		
N2	80	34	46		
N3	46	23	23		
Receive chemotherapy					
Yes	165	64	85	10.189	0.001
No	45	41	20		

Notes: PDGF-BB, Platelet-Derived Growth Factor-BB; EBV, Epstein-Barr Virus; TNM, Tumor, Node, Metastasis; T, Tumor; N, Node.

dent effect for age 51-64 years (HR = 2.057, P = 0.032) and ≥ 65 years (HR = 4.138, P < 0.001). EBV DNA negativity was associated with better survival compared to positivity (HR

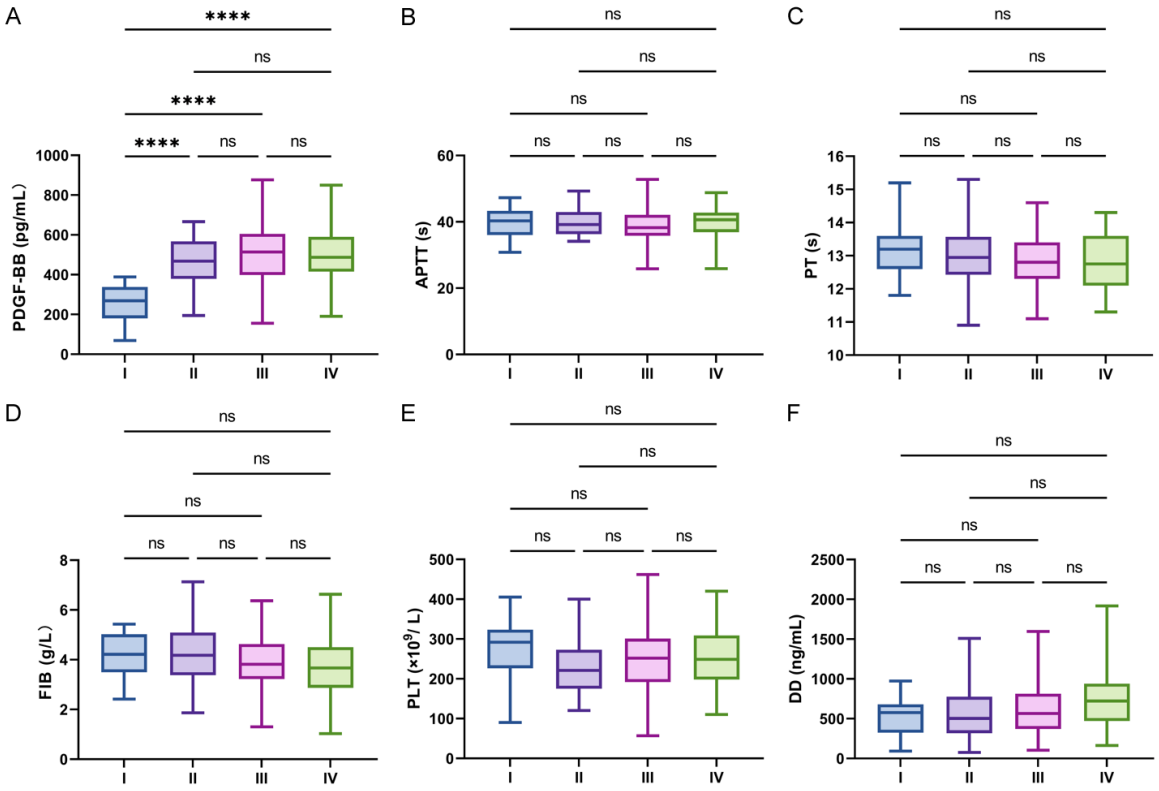

Figure 2. Expression of coagulation markers and PDGF-BB across clinical stages. A: Distribution of PDGF-BB levels across different TNM stages. B: Distribution of APTT levels across different TNM stages. C: Distribution of PT levels across different TNM stages. D: Distribution of FIB levels across different TNM stages. E: Distribution of PLT levels across different TNM stages. F: Distribution of DD levels across different TNM stages. Notes: PDGF-BB, Platelet-Derived Growth Factor-BB; APTT, Activated Partial Thromboplastin Time; PT, Prothrombin Time; FIB, Fibrinogen; PLT, Platelet Count; DD, D-dimer. ****$P < 0.0001$.

= 0.273, P = 0.012). TNM stage III/IV was associated with increased mortality risk (HR = 3.042, P = 0.023). No sig- nificant effect was found in T stage (P = 0.624; **Table 5**).

Application of the dynamic nomogram in predicting five-year survival

Figures 7 and **8** illustrate the dynamic nomogram developed using the DynNom package in R. This tool enables real-time prediction of five-year survival probabilities based on individual patient characteristics, including age, EBV DNA status, TNM stage, T stage, and PDGF-BB level.

By inputting specific values for these variables, clinicians can dynamically calculate and visualize personalized survival probabilities. For example, a patient aged ≥ 65 years with EBV DNA negativity, TNM stage III/IV, T3/T4 staging, and high PDGF-BB levels would generate a survival curve reflecting a lower five-year survival probability.

This dynamic nomogram provides an intuitive, interactive platform for individualized survival prediction, enhancing clinical decision-making in the management of NPC.

Discussion

NPC is highly prevalent in Southeast Asia, particularly in Guangdong, Hong Kong, and Macao [19]. Coagulation abnormalities within the tumor microenvironment are closely associated with cancer progression [20]. PDGF-BB, a key regulator of cell proliferation, migration, and angiogenesis, has been strongly implicated in the development of various solid tumors [21]. This study compared PDGF-BB levels and coagulation parameters between NPC patients and healthy controls, aiming to investigate their roles in diagnosis, disease staging, treatment efficacy, and prognosis, thereby providing a foundation for precision diagnosis and individualized treatment strategies in NPC.

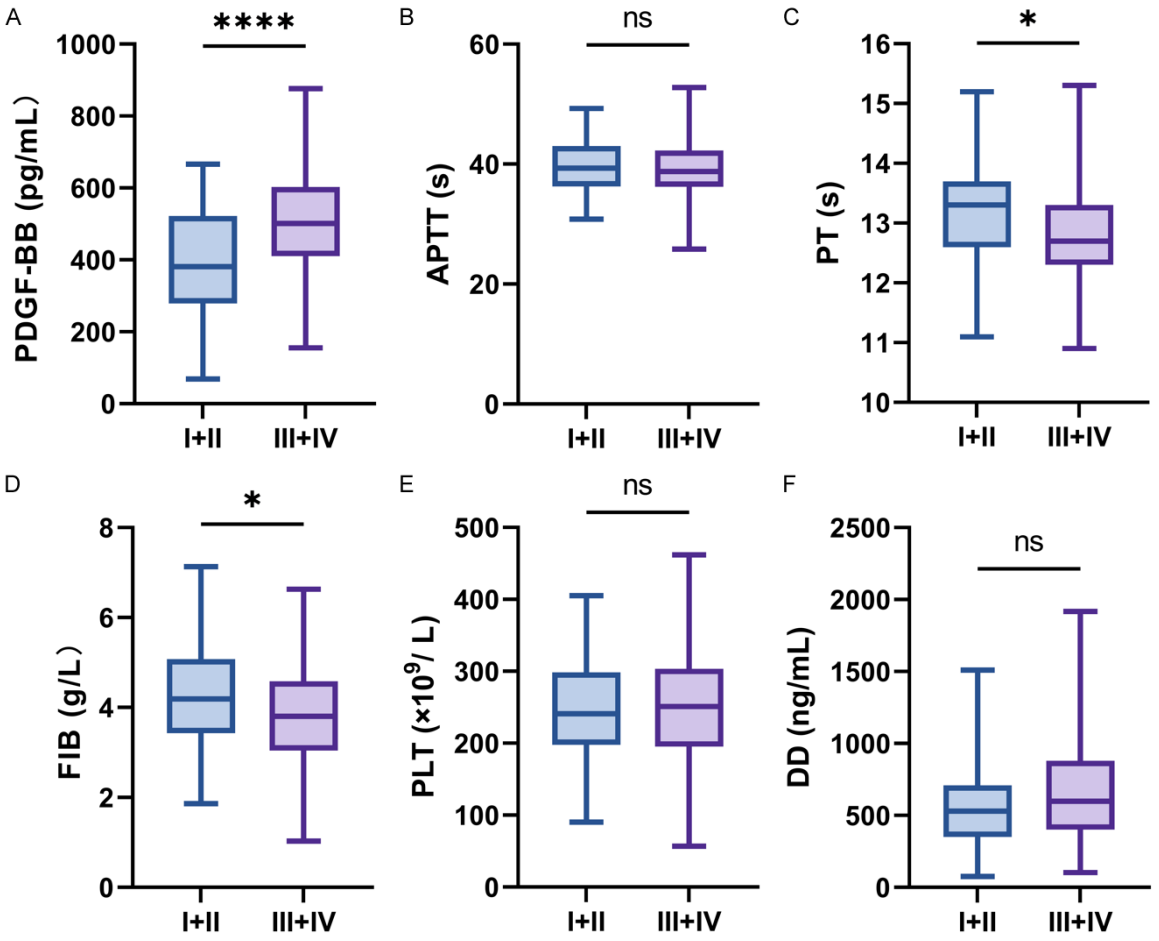

Figure 3. Expression differences of coagulation markers and PDGF-BB in early- and advanced-stage patients. A: Distribution of PDGF-BB in Stage I/II and Stage III/IV patients. B: Distribution of APTT in Stage I/II and Stage III/IV patients. C: Distribution of PT in Stage I/II and Stage III/IV patients. D: Distribution of FIB in Stage I/II and Stage III/IV patients. E: Distribution of PLT in Stage I/II and Stage III/IV patients. F: Distribution of DD in Stage I/II and Stage III/IV patients. Notes: PDGF-BB, Platelet-Derived Growth Factor-BB; APTT, Activated Partial Thromboplastin Time; PT, Prothrombin Time; FIB, Fibrinogen; PLT, Platelet Count; DD, D-dimer. *$P < 0.05$, ****$P < 0.0001$.

Our findings revealed significantly elevated PDGF-BB levels in NPC patients compared to healthy individuals, highlighting its important role in tumor initiation and progression [22]. PDGF-BB secreted by tumor cells promotes proliferation and migration, while its interaction with PDGF receptors on vascular endothelial cells activates the MAPK and PI3K/Akt pathways, facilitating neovascularization. This vascular remodeling supplies oxygen and nutrients to the tumor, enhancing its growth [22]. Additionally, NPC patients exhibited significantly higher levels of coagulation markers-APTT, PT, FIB, PLT, and DD, reflecting a dysregulated coagulation system within the tumor microenvironment [23]. These abnormalities may result from tumor-derived procoagulant factors, local inflammatory responses, and extracellular matrix remodeling, all of which promote microthrombus formation and help tumor cells evade immune surveillance [23].

Previous studies have shown that coagulation markers, with the exception of thrombin time, are associated with NPC stage and metastatic risk [24]. Elevated PDGF-BB levels derived from platelets have also been observed in breast cancer, underscoring its role in tumor angiogenesis and metastasis across multiple solid tumors [25, 26]. With the development of advanced detection technologies such as surface-enhanced Raman scattering-lateral flow assay biosensors, PDGF-BB can now be detected in prostate cancer plasma at pico-

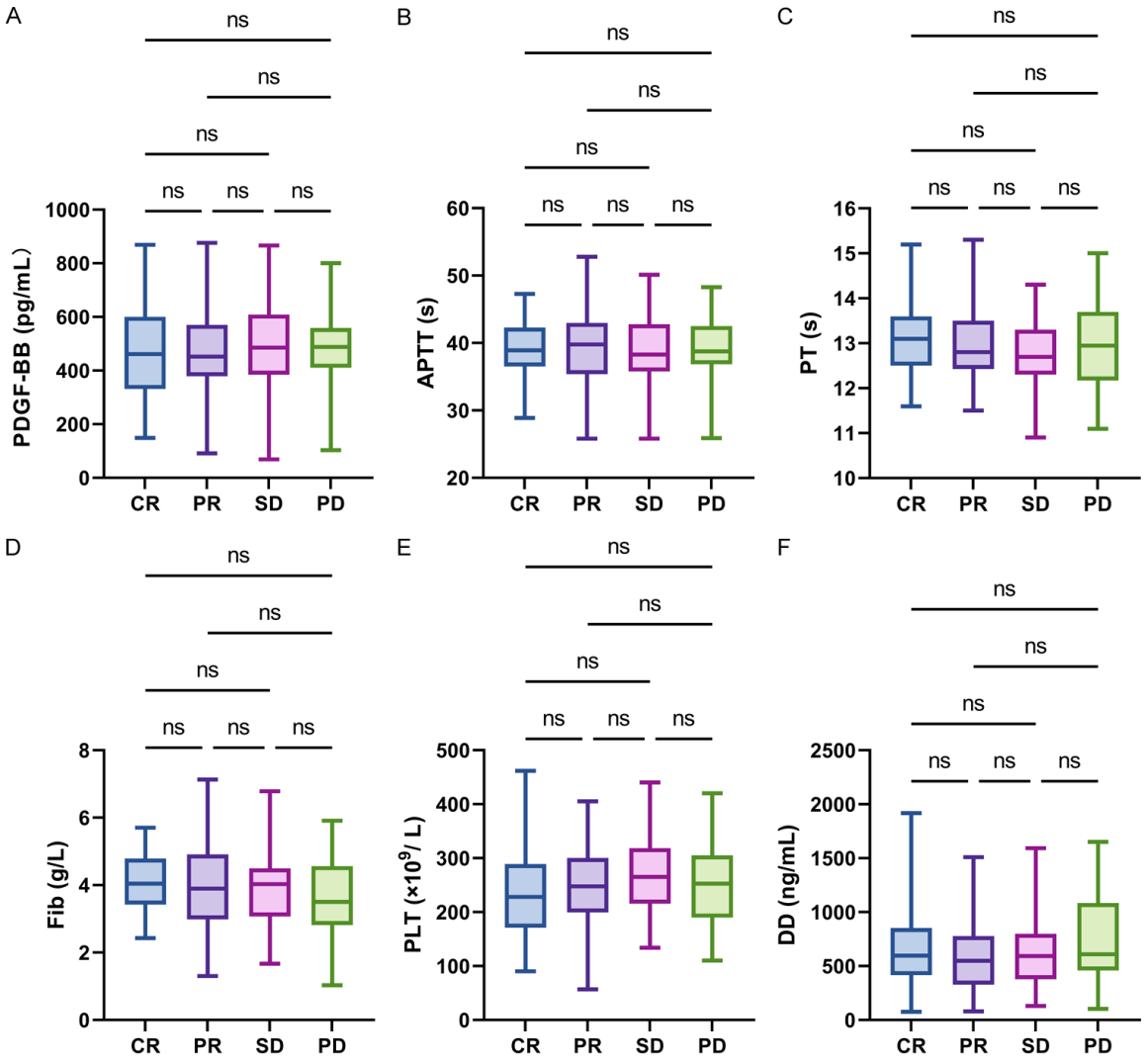

Figure 4. Expression of coagulation markers and PDGF-BB in patients with different treatment responses. A: Expression of PDGF-BB in patients with different treatment outcomes. B: Expression of APTT in patients with different treatment outcomes. C: Expression of PT in patients with different treatment outcomes. D: Expression of FIB in patients with different treatment outcomes. E: Expression of PLT in patients with different treatment outcomes. F: Expression of DD in patients with different treatment outcomes. Notes: PDGF-BB, Platelet-Derived Growth Factor-BB; APTT, Activated Partial Thromboplastin Time; PT, Prothrombin Time; FIB, Fibrinogen; PLT, Platelet Count; DD, D-dimer; CR, Complete Response; PR, Partial Response; SD, Stable Disease; PD, Progressive Disease.

gram-per-milliliter levels, supporting its potential as an early diagnostic biomarker for NPC [27].

Further analysis revealed a strong positive correlation between PDGF-BB levels and TNM, T, and N stages, with higher expression observed in patients with advanced-stage NPC. Tumor-derived PDGF-BB facilitates angiogenesis and extracellular matrix remodeling by activating downstream signaling in endothelial and stromal cells, thereby promoting tumor invasiveness and metastatic potential [28, 29]. Although APTT, PT, FIB, PLT, and DD showed stage-dependent variation trends, their collective alterations reflect underlying coagulation dysfunction and inflammation during tumor progression. Notably, He et al. [30] reported that elevated preoperative plasma FIB levels were positively associated with TNM stage and metastatic risk, highlighting the utility of multimarker panels for tumor staging and prognostic evaluation.

To assess treatment response, this study systematically compared biomarker profiles across

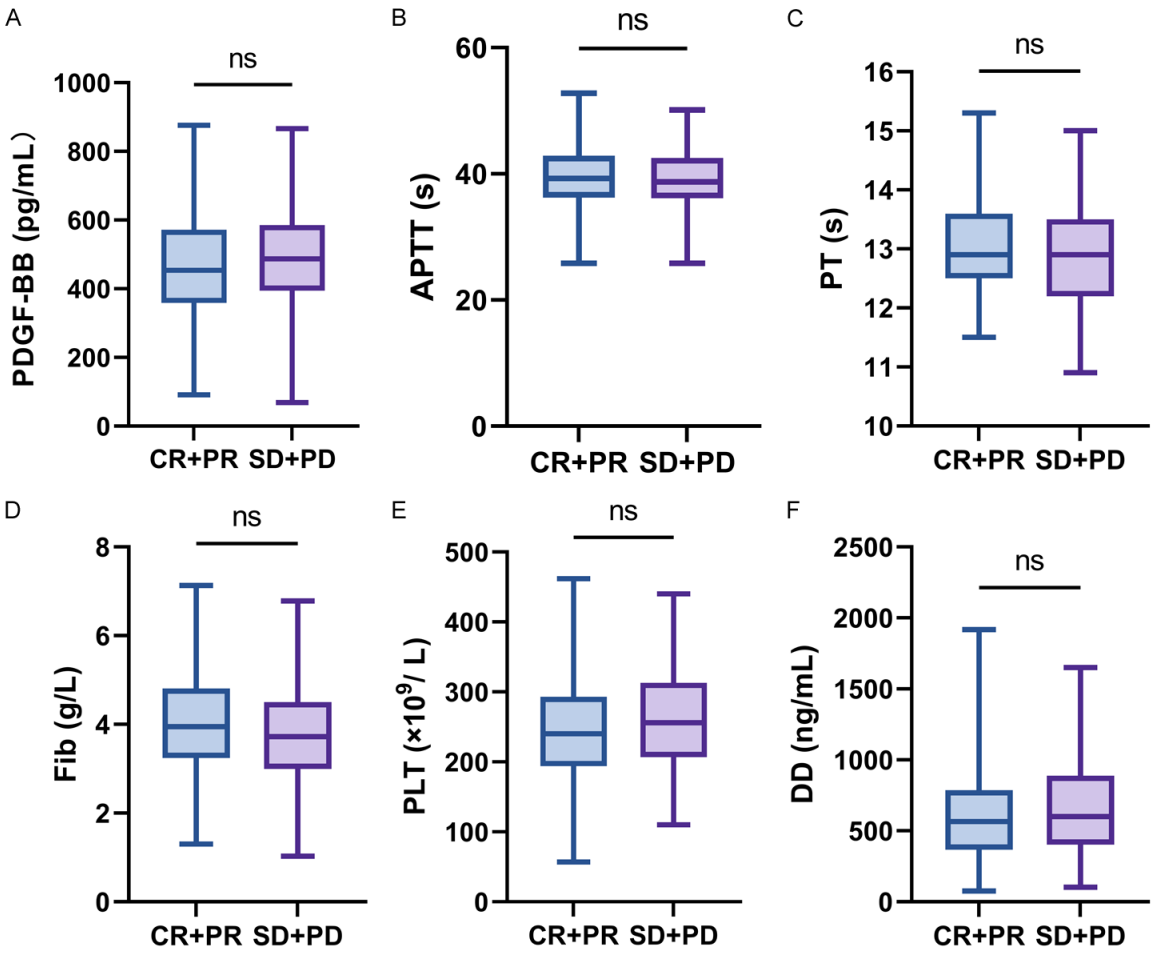

Figure 5. Expression of coagulation markers and PDGF-BB in patients with different treatment responses. A: Expression of PDGF-BB in patients with improved outcomes versus disease progression. B: Expression of APTT in patients with improved outcomes versus disease progression. C: Expression of PT in patients with improved outcomes versus disease progression. D: Expression of FIB in patients with improved outcomes versus disease progression. E: Expression of PLT in patients with improved outcomes versus disease progression. F: Expression of DD in patients with improved outcomes versus disease progression. Notes: PDGF-BB, Platelet-Derived Growth Factor-BB; APTT, Activated Partial Thromboplastin Time; PT, Prothrombin Time; FIB, Fibrinogen; PLT, Platelet Count; DD, D-dimer; CR, Complete Response; PR, Partial Response; SD, Stable Disease; PD, Progressive Disease.

patient groups stratified by clinical efficacy. Despite thorough statistical analysis, no significant differences were found in PDGF-BB or coagulation marker levels (APTT, PT, FIB, PLT, DD) between patients with treatment response and those with disease progression. Nevertheless, ROC analysis indicated that PDGF-BB retained predictive value in identifying treatment-related improvement. The complexity of clinical efficacy assessment may limit the ability of individual coagulation markers to reflect therapeutic outcomes, which are often influenced by diverse treatment protocols, tumor heterogeneity, and patient-specific factors such as therapy tolerance.

Supporting this view, Yang et al. [31] reported that reductions in PDGF-BB levels after treatment were associated with better clinical outcomes, reinforcing its potential as a response biomarker. Therefore, while no significant group differences were observed in this cohort, PDGF-BB may still play a critical role in monitoring therapeutic efficacy. Future studies incorporating broader clinical variables, diverse treatment regimens, and extended follow-up are warranted to further clarify its role in efficacy evaluation.

Using multivariate Cox regression analysis, this study identified PDGF-BB as an independent

Table 4. Univariate Cox regression analysis: prognostic value of coagulation markers and PDGF-BB for five-year survival

Variable	Beta	Std Err	*P*	HR	Lower	Upper
PDGF-BB	0.004	0.001	< 0.001	1.004	1.003	1.006
APTT	0.001	0.024	0.981	1.001	0.954	1.049
PT	0.069	0.150	0.647	1.071	0.799	1.436
FIB	-0.093	0.104	0.369	0.911	0.744	1.116
PLT	-0.001	0.002	0.683	0.999	0.996	1.002
DD	0.001	< 0.001	< 0.001	1.001	1.001	1.002
Age						
≤ 50						
51-64	0.692	0.336	0.039	1.998	1.035	3.858
≥ 65	1.758	0.332	< 0.001	5.801	3.024	11.127
Gender						
Male						
Female	-0.202	0.248	0.414	0.817	0.503	1.327
Educational level						
≤ Junior high school						
Senior high school	0.026	0.265	0.921	1.027	0.611	1.726
≥ University	0.109	0.318	0.731	1.116	0.598	2.081
Smoking history (cigarettes/day)						
< 10						
≥ 10	0.317	0.237	0.181	1.373	0.863	2.182
Alcohol consumption history (ml/d)						
< 1000						
≥ 1000	0.228	0.237	0.336	1.256	0.790	1.996
EBV DNA positivity						
Yes						
No	-1.603	0.515	0.002	0.201	0.073	0.552
Differentiation degree						
Well differentiated						
Moderately differentiated	-0.202	0.392	0.607	0.817	0.379	1.763
Poorly differentiated	0.210	0.314	0.504	1.234	0.667	2.284
TNM staging						
I + II						
III + IV	1.702	0.464	< 0.001	5.486	2.210	13.622
T staging						
T1 + T2						
T3 + T4	0.618	0.239	0.010	1.855	1.160	2.965
N staging						
N0						
N1-3	0.598	0.328	0.068	1.819	0.957	3.457
Receive chemotherapy						
Yes						
No	-0.357	0.287	0.213	0.700	0.399	1.227

Notes: PDGF-BB, Platelet-Derived Growth Factor-BB; APTT, Activated Partial Thromboplastin Time; PT, Prothrombin Time; FIB, Fibrinogen; PLT, Platelet Count; DD, D-dimer; EBV, Epstein-Barr Virus; TNM, Tumor, Node, Metastasis; T, Tumor; N, Node; HR Hazard Ratio.

risk factor for five-year survival in NPC patients, with each unit increase in PDGF-BB levels associated with a proportional rise in mortality risk. In univariate analysis, DD also demonstrated

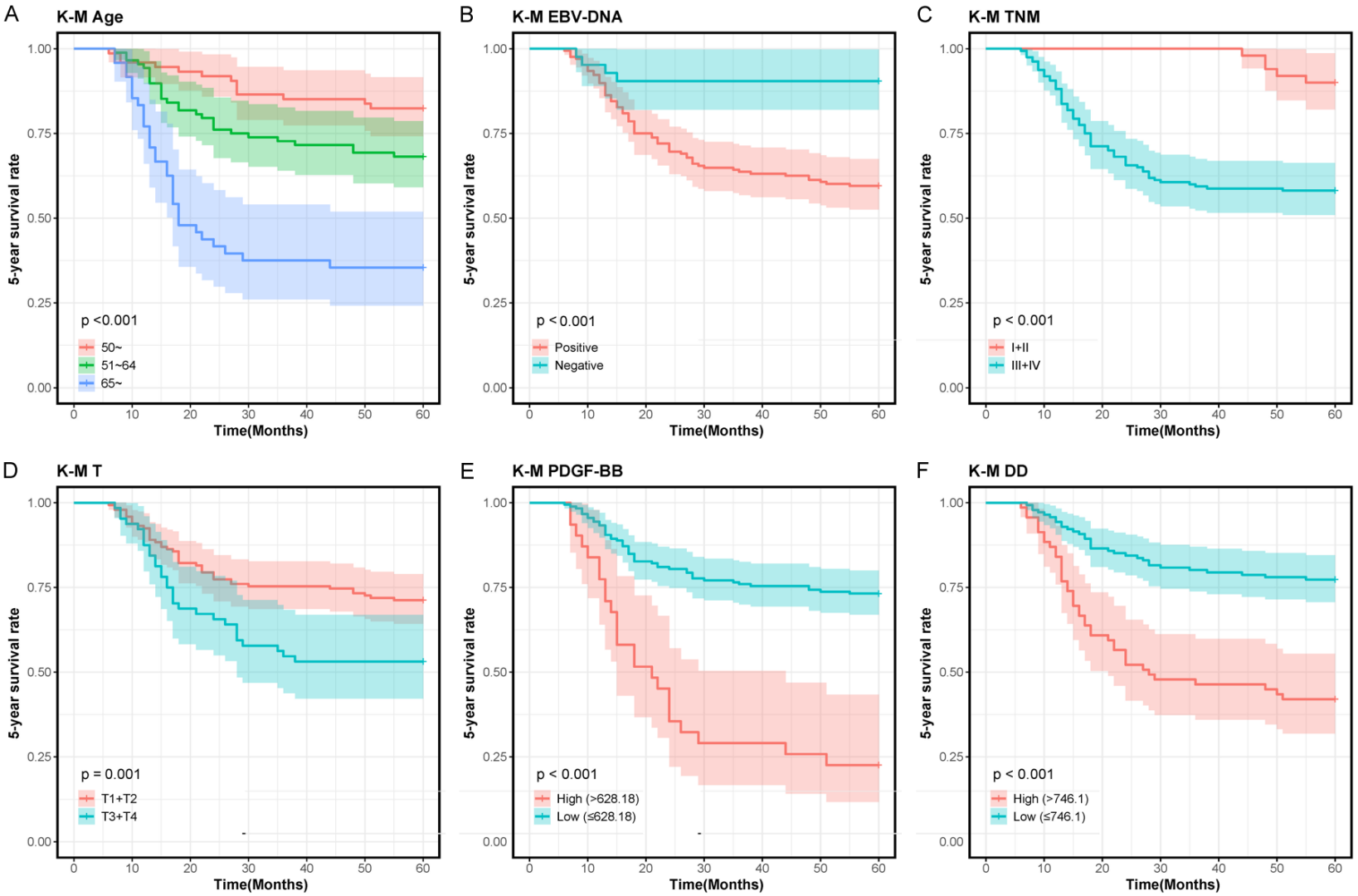

Figure 6. KM survival curves: influence of different clinical characteristics on five-year survival. A: Survival curves grouped by age. B: Survival curves grouped by EBV-DNA. C: Survival curves of patients with different TNM stages. D: Survival curves of patients with different T stages. E: Survival curves of patients with high vs. low PDGF-BB expression. F: Survival curves of patients with high vs. low DD expression. Notes: K-M, Kaplan-Meier; EBV, Epstein-Barr Virus; PDGF-BB, Platelet-Derived Growth Factor-BB; DD, D-dimer.

Table 5. Multivariate Cox regression analysis: prognostic value of coagulation markers and clinical characteristics for five-year survival

Variable	Beta	Std Err	*P*	HR	Lower	Upper
PDGF-BB						
≥ 628.18						
< 628.18	-0.710	0.273	0.009	0.492	0.288	0.840
DD						
≥ 746.1						
< 746.1	-0.785	0.249	0.002	0.456	0.280	0.743
Age						
≤ 50						
51-64	0.721	0.337	0.032	2.057	1.064	3.979
≥ 65	1.420	0.350	< 0.001	4.138	2.084	8.215
EBV DNA						
Positive						
Negative	-1.300	0.519	0.012	0.273	0.098	0.754
TNM staging						
I + II						
III + IV	1.113	0.491	0.023	3.042	1.163	7.958
T staging						
T1 + T2						
T3 + T4	0.122	0.250	0.624	1.130	0.692	1.845

Notes: PDGF-BB, Platelet-Derived Growth Factor-BB; DD, D-dimer; EBV, Epstein-Barr Virus; TNM, Tumor, Node, Metastasis; T, Tumor; HR, Hazard Ratio.

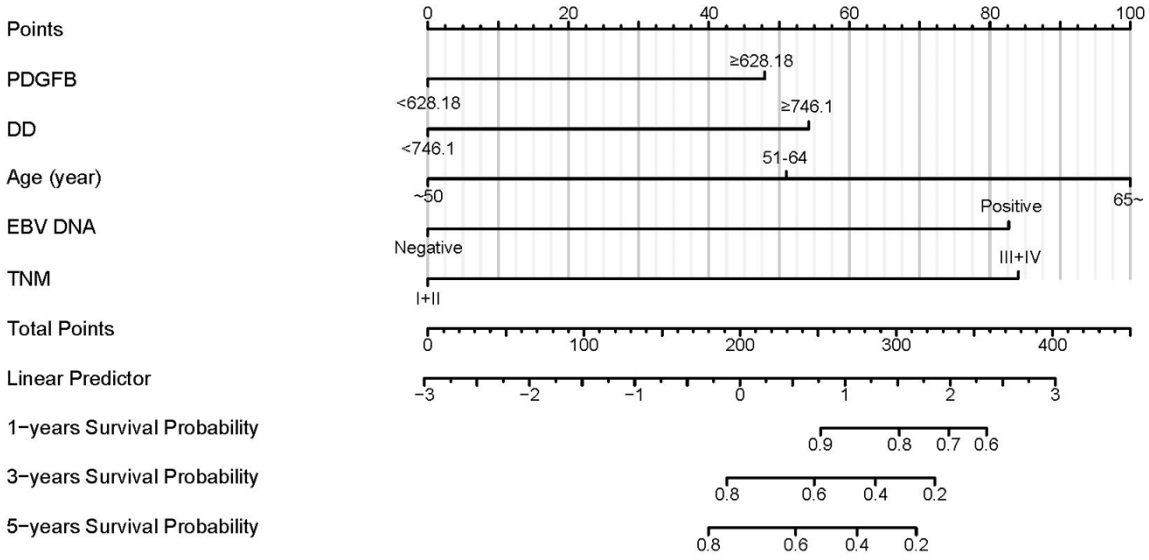

Figure 7. Patient 5-year prognosis nomogram. Notes: DynNom, Dynamic Nomogram; PDGF-BB, Platelet-Derived Growth Factor-BB; EBV, Epstein-Barr Virus; TNM, Tumor, Node, Metastasis; T, Tumor.

significant prognostic value. Additionally, age, EBV DNA status, and TNM stage were found to significantly influence survival outcomes, with elderly patients, EBV DNA-positive individuals, and those with advanced-stage disease exhibiting poorer prognoses [32].

Among coagulation markers, DD was notably elevated in NPC patients and has been widely validated as a prognostic biomarker. Chen et al. [33] reported that elevated DD reflects a hypercoagulable state and is significantly associated with worse disease-free survival, distant

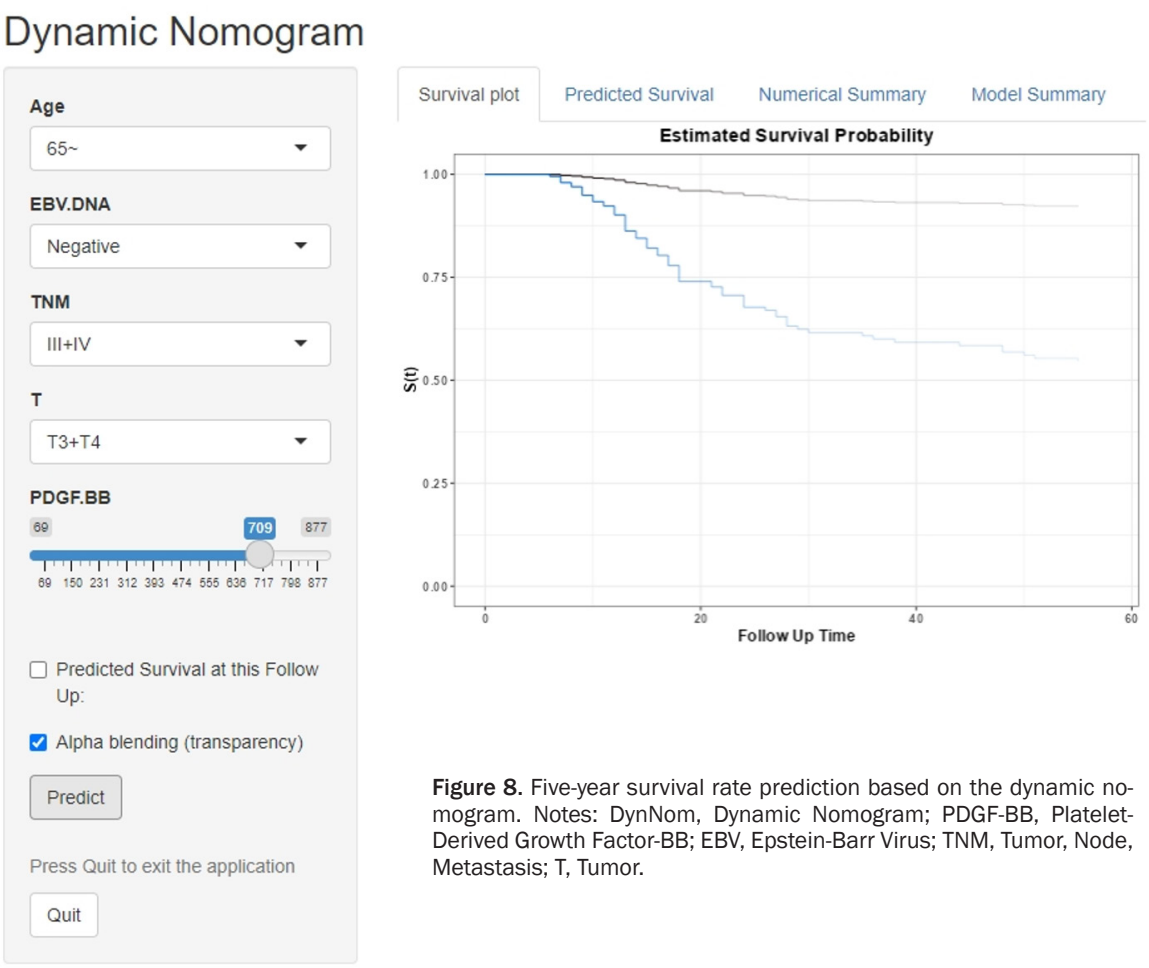

Figure 8. Five-year survival rate prediction based on the dynamic nomogram. Notes: DynNom, Dynamic Nomogram; PDGF-BB, Platelet-Derived Growth Factor-BB; EBV, Epstein-Barr Virus; TNM, Tumor, Node, Metastasis; T, Tumor.

metastasis-free survival, and overall survival, findings that align with our results. He et al. [34] further demonstrated that combined detection of DD and albumin enhances prognostic accuracy in NPC. DD levels are closely related to tumor invasiveness and metastatic potential, reinforcing their utility as a prognostic marker. Moreover, when integrated with traditional clinical factors such as TNM stage and age, survival prediction accuracy is further improved.

PDGF-BB also plays a central role in both coagulation and tumor biology. As highlighted by Liang et al. [35], PDGF-BB facilitates tumor proliferation, migration, and angiogenesis, and is strongly associated with aggressive behavior and metastatic capacity. Our study further supports this role in the NPC microenvironment.

In our analysis, age, EBV DNA status, and TNM stage emerged as strong independent prognostic indicators. Specifically, older patients, EBV DNA-positive cases, and advanced-stage tumors were consistently linked to reduced survival. EBV DNA is an established biomarker in NPC, and the study by Mazurek et al. [36] emphasized its dual value in diagnosis and prognosis. Elevated EBV DNA levels are linked to poor local control and a markedly increased risk of distant metastasis.

TNM staging remains the cornerstone of prognostic evaluation in clinical practice. However, integrating TNM stage with emerging biomarkers such as PDGF-BB and DD can significantly enhance survival prediction accuracy. Kaplan-Meier survival curves in our study demonstrated that high PDGF-BB and DD levels were strongly correlated with poorer five-year survival, validating their prognostic utility.

Interestingly, studies in other cancers also support PDGF-BB's prognostic value. For example, in esophageal cancer, post-radiotherapy reduc-

tions in PDGF-BB levels were significantly associated with longer survival durations [37]. This finding supports the potential application of PDGF-BB in monitoring treatment efficacy and survival outcomes in NPC as well.

Based on multivariate Cox regression results, we developed a dynamic nomogram incorporating PDGF-BB, age, EBV DNA status, TNM stage, and T stage to predict individualized five-year survival. This model offers a user-friendly, interactive platform for real-time survival prediction and risk assessment, enabling clinicians to tailor treatment strategies according to patient-specific clinical profiles. With further validation in multi-center cohorts, this model holds promise for broader application in NPC and other malignancies, contributing to the advancement of precision oncology.

This study has several limitations. First, its single-center, retrospective design and limited sample size may restrict the generalizability of findings. Second, variability in detection technologies and sample processing may have reduced the sensitivity of certain coagulation parameters in predicting treatment response, limiting the utility of single-marker analysis.

Future studies should aim to conduct multi-center, prospective trials with larger cohorts to validate the diagnostic and prognostic value of PDGF-BB and coagulation biomarkers in NPC. Investigating combined biomarker panels, dynamic changes during treatment, and the molecular mechanisms underlying PDGF-BB and coagulation dysregulation will improve predictive models and guide therapeutic interventions. Integration of clinical, molecular, and imaging data will be essential for enhancing early detection, personalized treatment, and overall clinical outcomes in NPC patients.

In conclusion, PDGF-BB and key coagulation markers, particularly DD, represent promising biomarkers for prognostic assessment in nasopharyngeal carcinoma. When combined with clinical factors such as age, EBV DNA status, and TNM staging, these biomarkers can significantly enhance the accuracy of personalized survival predictions, offering valuable guidance for clinical decision-making in NPC patients receiving IMRT.

Disclosure of conflict of interest

None.

Address correspondence to: Deli Ye, Laboratory Center, Zhejiang Provincial People's Hospital, Hangzhou 310000, Zhejiang, China. Tel: +86-0571-85893889; E-mail: yedeli2003@163.com

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Table S1. The relationship between high and low expression of APTT and baseline data of patients

Variable	Total	APTT (s)		χ^2	*P*
		Low expression (n = 105)	High expression (n = 105)		
Age					
≤ 50	74	38	36	0.796	0.672
51-64	88	41	47		
≥ 65	48	26	22		
Gender					
Male	130	63	67	0.323	0.570
Female	80	42	38		
Educational level					
≤ Junior high school	88	42	46	3.121	0.210
Senior high school	82	38	44		
≥ University	40	25	15		
Smoking history (cigarettes/day)					
< 10	109	49	60	2.308	0.129
≥ 10	101	56	45		
Alcohol consumption history (ml/day)					
< 1000	122	62	60	0.078	0.780
≥ 1000	88	43	45		
EBV DNA positivity					
Yes	168	88	80	1.905	0.168
No	42	17	25		
Differentiation degree					
Well differentiated	40	17	23	1.750	0.417
Moderately differentiated	47	22	25		
Poorly differentiated	123	66	57		
TNM staging					
I	18	7	11	4.629	0.201
II	32	15	17		
III	105	60	45		
IV	55	23	32		
T staging					
T1	80	37	43	0.785	0.853
T2	66	34	32		
T3	55	29	26		
T4	9	5	4		
N staging					
N0	46	23	23	3.045	0.385
N1	38	21	17		
N2	80	43	37		
N3	46	18	28		
Chemotherapy treatment					
With	149	75	74	0.023	0.879
Without	61	30	31		

Notes: APTT, Activated Partial Thromboplastin Time; EBV, Epstein-Barr Virus; TNM, Tumor, Node, Metastasis; T, Tumor; N, Node.

Table S2. The relationship between high and low expression of PT and baseline data of patients

Variable	Total	PT (s)		χ^2	*P*
		Low expression (n = 105)	High expression (n = 105)		
Age					
≤ 50	74	39	35	0.345	0.842
51-64	88	43	45		
≥ 65	48	23	25		
Gender					
Male	130	68	62	0.727	0.394
Female	80	37	43		
Educational level					
≤ Junior high school	88	44	44	0.595	0.743
Senior high school	82	43	39		
≥ University	40	18	22		
Smoking history (cigarettes/day)					
< 10	109	47	62	4.292	0.038
≥ 10	101	58	43		
Alcohol consumption history (ml/day)					
< 1000	122	61	61	0.000	1.000
≥ 1000	88	44	44		
EBV DNA positivity					
Yes	168	91	77	5.833	0.016
No	42	14	28		
Differentiation degree					
Well differentiated	40	19	21	0.705	0.703
Moderately differentiated	47	26	21		
Poorly differentiated	123	60	63		
TNM staging					
I	18	4	14	13.010	0.005
II	32	11	21		
III	105	55	50		
IV	55	35	20		
T staging					
T1	80	37	43	1.513	0.679
T2	66	32	34		
T3	55	31	24		
T4	9	5	4		
N staging					
N0	46	18	28	8.319	0.040
N1	38	15	23		
N2	80	42	38		
N3	46	30	16		
Chemotherapy treatment					
With	149	81	68	3.905	0.048
Without	61	24	37		

Notes: PT, Prothrombin Time; EBV, Epstein-Barr Virus; TNM, Tumor, Node, Metastasis; T, Tumor; N, Node.

Table S3. The relationship between high and low expression of FIB and baseline data of patients

Variable	Total	FIB (g/L)		χ^2	*P*
		Low expression (n = 105)	High expression (n = 105)		
Age					
≤ 50	74	41	33	1.380	0.502
51-64	88	42	46		
≥ 65	48	22	26		
Gender					
Male	130	63	67	0.323	0.570
Female	80	42	38		
Educational level					
≤ Junior high school	88	50	38	2.956	0.228
Senior high school	82	36	46		
≥ University	40	19	21		
Smoking history (cigarettes/day)					
< 10	109	53	56	0.172	0.679
≥ 10	101	52	49		
Alcohol consumption history (ml/day)					
< 1000	122	59	63	0.313	0.576
≥ 1000	88	46	42		
EBV DNA positivity					
Yes	168	91	77	5.833	0.016
No	42	14	28		
Differentiation degree					
Well differentiated	40	21	19	0.495	0.781
Moderately differentiated	47	25	22		
Poorly differentiated	123	59	64		
TNM staging					
I	18	7	11	1.478	0.687
II	32	15	17		
III	105	53	52		
IV	55	30	25		
T staging					
T1	80	35	45	3.783	0.286
T2	66	32	34		
T3	55	32	23		
T4	9	6	3		
N staging					
N0	46	25	21	0.740	0.864
N1	38	18	20		
N2	80	38	42		
N3	46	24	22		
Chemotherapy treatment					
With	149	77	72	0.578	0.447
Without	61	28	33		

Notes: FIB, Fibrinogen; EBV, Epstein-Barr Virus; TNM, Tumor, Node, Metastasis; T, Tumor; N, Node.

Table S4. The relationship between high and low expression of PLT and baseline data of patients

Variable	Total	PLT (×10^9/L)		χ^2	*P*
		Low expression (n = 105)	High expression (n = 105)		
Age					
≤ 50	74	34	40	0.752	0.687
51-64	88	46	42		
≥ 65	48	25	23		
Gender					
Male	130	60	70	2.019	0.155
Female	80	45	35		
Educational level					
≤ Junior high school	88	46	42	0.377	0.828
Senior high school	82	39	43		
≥ University	40	20	20		
Smoking history (cigarettes/day)					
< 10	109	56	53	0.172	0.679
≥ 10	101	49	52		
Alcohol consumption history (ml/day)					
< 1000	122	61	61	0.000	1.000
≥ 1000	88	44	44		
EBV DNA positivity					
Yes	168	84	84	0.000	1.000
No	42	21	21		
Differentiation degree					
Well differentiated	40	20	20	2.382	0.304
Moderately differentiated	47	19	28		
Poorly differentiated	123	66	57		
TNM staging					
I	18	6	12	5.381	0.146
II	32	21	11		
III	105	50	55		
IV	55	28	27		
T staging					
T1	80	46	34	2.911	0.406
T2	66	30	36		
T3	55	25	30		
T4	9	4	5		
N staging					
N0	46	16	30	7.029	0.071
N1	38	24	14		
N2	80	41	39		
N3	46	24	22		
Chemotherapy treatment					
With	149	72	77	0.578	0.447
Without	61	33	28		

Notes: PLT, Platelet Count; EBV, Epstein-Barr Virus; TNM, Tumor, Node, Metastasis; T, Tumor; N, Node.

Table S5. The relationship between high and low expression of DD and baseline data of patients

Variable	Total	DD (ng/mL)		χ^2	*P*
		Low expression (n = 105)	High expression (n = 105)		
Age					
≤ 50	74	39	35	3.943	0.139
51-64	88	48	40		
≥ 65	48	18	30		
Gender					
Male	130	67	63	0.323	0.570
Female	80	38	42		
Educational level					
≤ Junior high school	88	50	38	10.039	0.007
Senior high school	82	30	52		
≥ University	40	25	15		
Smoking history (cigarettes/day)					
< 10	109	55	54	0.019	0.890
≥ 10	101	50	51		
Alcohol consumption history (ml/day)					
< 1000	122	61	61	0.000	1.000
≥ 1000	88	44	44		
EBV DNA positivity					
Yes	168	82	86	0.476	0.490
No	42	23	19		
Differentiation degree					
Well differentiated	40	22	18	0.494	0.781
Moderately differentiated	47	23	24		
Poorly differentiated	123	60	63		
TNM staging					
I	18	9	9	2.683	0.443
II	32	19	13		
III	105	54	51		
IV	55	23	32		
T staging					
T1	80	38	42	0.875	0.832
T2	66	36	30		
T3	55	27	28		
T4	9	4	5		
N staging					
N0	46	22	24	2.728	0.435
N1	38	19	19		
N2	80	45	35		
N3	46	19	27		
Chemotherapy treatment					
With	149	71	78	1.132	0.287
Without	61	34	27		

Notes: DD, D-dimer; EBV, Epstein-Barr Virus; TNM, Tumor, Node, Metastasis; T, Tumor; N, Node.