Liu *et al. Infectious Agents and Cancer* (2025) 20:10
https://doi.org/10.1186/s13027-025-00638-2

Infectious Agents and Cancer

RESEARCH Open Access

Impact of Epstein-Barr virus and CD lymphocytes on the prognosis of patients with advanced nasopharyngeal carcinoma

Fangchu Liu[1], Yonghua Peng[2], Xintao Wang[1], Weili Long[3] and Zhenhe Huang[1*]

Abstract

Background Understanding the factors influencing the occurrence and progression of nasopharyngeal carcinoma (NPC) is critical for reducing incidence rates and improving patient outcomes. The objective of this study is to preliminarily investigate the impact of Epstein-Barr virus (EBV) and cluster of differentiation (CD) lymphocytes on the prognosis of patients with advanced NPC.

Method A prospective cohort study design was employed, involving newly diagnosed patients with NPC confirmed by pathological diagnosis. Patients received standard radiotherapy and chemotherapy according to treatment guidelines, with regular follow-up assessments conducted. Prior to treatment initiation, patients underwent testing for EBV, blood biochemistry, and other parameters, while baseline data including patient age, pathology, and tumor node metastasis classification (TNM) staging were also collected. The primary outcome measure focused on disease progression.

Results The analysis included a total of 99 cases, with a median age of 52 years, all of whom were stage III or IV patients. The median progression-free survival time for the patients was 45.53 months. After adjusting for confounding factors such as age, T stage, and metastasis, patients with low levels of B cells exhibited a 1.503-fold increased risk of progression compared to those with high levels of B cells (adjusted hazard ratio [HR] = 2.503; 95% confidence interval [CI]: 1.062–5.899). Patients infected with EBV had a 1.739-fold increased risk of progression compared to uninfected patients (adjusted HR = 2.739; 95% CI: 1.222–6.125).

Conclusion This study observed that patients with advanced nasopharyngeal carcinoma, infected with EBV and exhibiting diminished B cell levels, display heightened susceptibility to disease deterioration and progression.

Keywords Nasopharyngeal carcinoma, EBV, B cells, Progression-free survival

*Correspondence:
Zhenhe Huang
380809727@qq.com
[1]Otolaryngology head and neck surgery, Ganzhou People's Hospital, No. 16, Meiguan Avenue, Zhanggong District, Ganzhou City, Jiangxi Province, China
[2]Medical examination center, Ganzhou People's Hospital, No. 16, Meiguan Avenue, Zhanggong District, Ganzhou City, Jiangxi Province, China
[3]Operating room, Ganzhou People's Hospital, No. 16, Meiguan Avenue, Zhanggong District, Ganzhou City, Jiangxi Province, China

Background

Nasopharyngeal carcinoma (NPC) is a malignant tumor that arises from the epithelium of the nasopharyngeal mucosa and represents the most prevalent head and neck malignancy in Southeast Asia [1]. Over recent decades, there has been a substantial surge in both incidence and mortality rates of NPC among Chinese residents. The annual number of new cases escalated from approximately 42,000 in 2013 to around 62,000 by 2020, while deaths increased from about 21,000 to approximately 34,000 [2, 3]. Projections indicate a continued rise in NPC incidence rate within China over the next two decades [4]. Due to its inconspicuous onset location, NPC often manifests with indistinct early symptoms. Patients typically present clinical manifestations such as epistaxis with blood discharge through the nose, cervical lymphadenopathy enlargement, and secretory otitis media during advanced stages of metastasis. The combined treatment utilizing intensity-modulated radiotherapy has demonstrated an overall survival (OS) rate of approximately 80% at the 5-year mark and a locoregional control rate exceeding 90% for newly diagnosed non-metastatic NPC. However, despite these advancements, local and/or regional recurrence still occurs in around 10–15% of patients post-treatment, with distant metastasis emerging as the primary cause of treatment failure [5]. The management outcomes for metastatic NPC remain suboptimal, with a median survival time ranging from 1 to 2 years [1]. Recent advancements in technologies, such as intensity-modulated radiotherapy, novel adjuvant chemotherapy approaches, synchronous chemoradiotherapy, and molecular targeted therapy, have contributed to improvements in both the local control rate and overall survival rate of patients with NPC. However, despite these advancements, a somewhat pessimistic outlook still persists. Therefore, early detection and treatment strategies are crucial for reducing the incidence rate and enhancing prognosis by identifying factors influencing the occurrence and progression of NPC.

Epstein-Barr virus (EBV), the first human carcinogenic virus discovered, has the ability to persistently and asymptomatically infect the human body for life. It is associated with various diseases, including benign conditions, multiple sclerosis, numerous lymphoid malignancies and epithelial cancers, as well as gastric cancer [6, 7]. In vitro studies have demonstrated that EBV can transform quiescent B lymphocytes into Lymphoblastoid cell lines (LCL) [8, 9]. Furthermore, a higher prevalence of EBV infection in NPC patients has been observed in several studies, suggesting a potential link to disease onset [10, 11]. The impact of EBV infection on the survival prognosis of patients with NPC, particularly those in intermediate and advanced stages, remains unclear. Immune system deficiencies and dysfunctions play a critical role in mediating persistent viral infections and are also significant factors in tumor development. Further investigation is required to explore the influence of CD lymphocytes [12], essential components of the immune

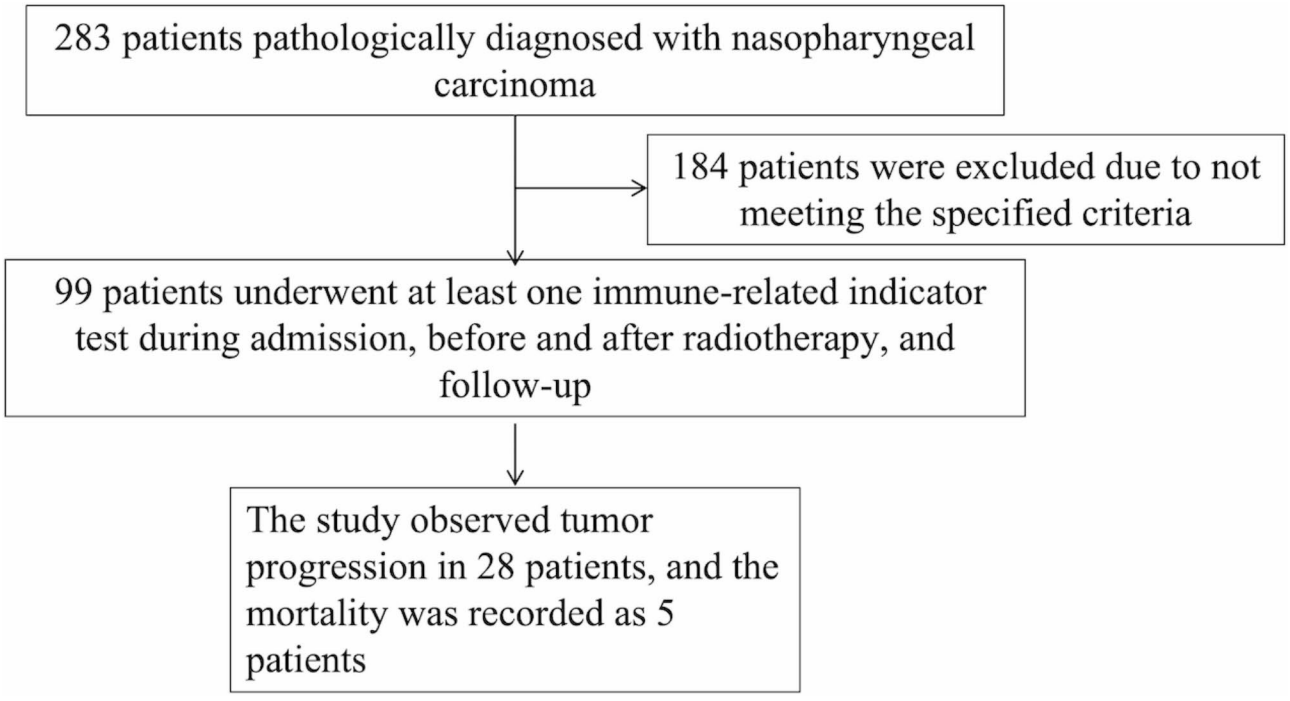

Fig. 1 Inclusion exclusion screening flowchart

Table 1 General condition of the patient during the initial consultation

Variable	*n*(%)
Gender	
Male	80 (80.81)
Female	19 (19.19)
Drinking History	
Yes	15 (15.15)
No	84 (84.85)
Smoking History	
Yes	29 (29.29)
No	70 (70.71)
Age(years old)	
≥60	22 (22.22)
< 60	77 (77.78)
T staging	
T1-2	7 (7.07)
T3-4	92 (92.93)
N staging	
N1-2	46 (46.46)
N3	53 (53.54)
TNM staging	
III	25 (25.25)
IV	74 (74.75)
Metastasis	
Metastasis of lymph nodes	90 (90.91)
Metastasis beyond the lymphatic system	9 (9.09)
Pathological classification	
Undifferentiated non-keratinizing squamous cell carcinoma	75 (75.76)
Differentiated non-keratinizing squamous cell carcinoma	24 (24.24)
Progress	
No	71 (71.72)
Yes	28 (28.28)
Death	
No	94 (94.95)
Yes	5 (5.05)
Induction chemotherapy	
No	9(9.09)
Yes	90(90.91)

system, on the occurrence, progression, and prognosis of NPC. This cohort study involved newly diagnosed patients with advanced NPC to preliminarily examine the effects of EBV infection and CD lymphocytes on patient prognosis.

Object and method

Research design and patient selection

This study employed a prospective cohort study design. It included patients with NPC who were initially diagnosed and treated at our Hospital between August 2019 and July 2021. The inclusion criteria encompassed patients with comprehensive clinical, imaging, and laboratory examination data, those without prior treatment for NPC or other tumor types, and individuals who provided informed consent to undergo routine radiotherapy and chemotherapy treatments. Exclusion criteria comprised patients with severe infections or mental illnesses, those unable to complete radiotherapy and chemotherapy, individuals with immune system diseases undergoing immunotherapy, as well as patients lost to follow-up due to relocation or unrelated causes of death. Approval from the hospital ethics committee was obtained for this study.

Diagnosis and treatment of NPC

All patients were diagnosed with NPC based on pathological examination, using squamous differentiation as the diagnostic criteria. According to the 1991 World Health Organization (WHO) classification, NPC was classified into two types: type I, keratinizing squamous cell carcinoma or squamous cell carcinoma (KSCC), and type II, non-keratinizing carcinoma, which includes differentiated non-keratinizing carcinoma (NKDC) and undifferentiated carcinoma (NKUC) [13]. The TNM [14] staging was performed in accordance with the 8th edition of the Union for International Cancer Control/American Joint Committee on Cancer (UICC/AJCC) staging system.

The patients in this study received curative radiotherapy according to the "Chinese Nasopharyngeal Carcinoma Radiation Guidelines" [15]. The induction chemotherapy regimen consisted of a platinum-based two or three-drug combination, including cisplatin plus gemcitabine, cisplatin plus docetaxel, or docetaxel plus cisplatin plus fluorouracil. The dosages were as follows: intravenous administration of 75 mg/m^2 of docetaxel on day 1, 75 mg/m^2 of cisplatin on days 1–3, and 500 mg/m^2 of fluorouracil on days 1–5. Each cycle lasted for three weeks with a total duration of 2–3 cycles. Synchronous chemotherapy drugs included either docetaxel plus cisplatin or monotherapy with intravenous administration of 75 mg/m^2 of cisplatin on days 1–3, with or without intravenous administration of 75 mg/m^2 of docetaxel on day 1 every three weeks per cycle. Alternatively, weekly intravenous administration could be done using a dosage of 30 mg/m^2 for cisplatin. Efficacy assessment after systemic therapy was conducted according to the WHO Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1).

Data collection and follow-up

The clinical data, including gender, age, presence of chronic diseases, smoking and drinking history, diagnosis time, and treatment data, were collected from medical records. Prior to treatment initiation, all patients underwent routine testing for EBV serology using DNA analysis and CD lymphocyte subsets on the first day of admission. Plasma EBV DNA, which the cutoff value for EB DNA is set at $< 5.0 \times 102$ copies, the units are copies per ml, was detected using a real-time fluorescence quantitative PCR method, Circulating immune cell subsets

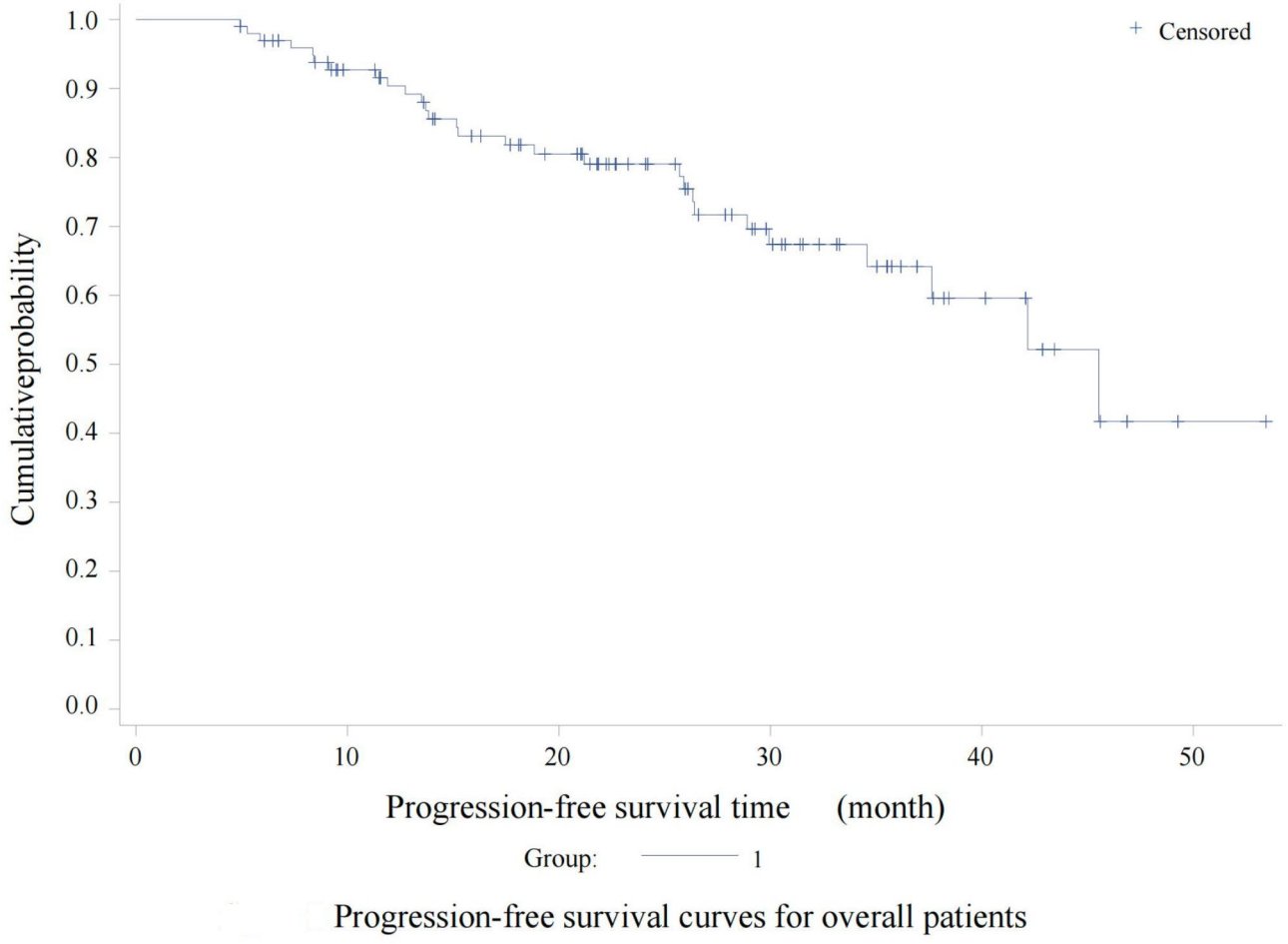

Fig. 2 Progression-free survival curves for overall patients

and NK cells in peripheral blood were analyzed using flow cytometry prior to treatment.

The treatment cycle lasted for a duration of 2 years, during which follow-up visits were scheduled at intervals of the first day of every 3 months for the first 2 years post-treatment, the first day of every 6 months from year 2 to year 5, and annually thereafter. Each follow-up cycle encompassed comprehensive assessments including blood routine and biochemical tests, nasopharyngoscopy, nasopharyngeal MRI, low-dose chest CT scan, abdominal ultrasound examination, and bone scan.

Outcome measures

The primary endpoint of this study is the progression of NPC, which encompasses tumor recurrence, infiltration, metastasis, or invasion of distant tissues and organs.

Statistical analysis

The chi-square test or Fisher's exact probability method was employed to compare categorical variables between groups, while Student's t-test or rank sum test was used for comparing quantitative variables. Survival curves were generated using the Kaplan-Meier method and compared using the log-rank test. A Cox model with progression as the endpoint event was utilized for multivariate analysis of survival time. Statistical analysis was performed using SAS 9.4 software with a two-tailed test, considering a p-value < 0.05 as indicative of statistical significance.

Results

Overall patient characteristics and prognosis

A total of 99 cases were included for analysis (see Fig. 1). The age range of the participants was from 18 to 82 years, with a median age of 52 years (interquartile range: 45–59 years). Among them, there were 80 males and 19 females, all in advanced stages (III + IV) of the disease. Detailed baseline characteristics of the patients can be found in Table 1 and Table 1-1. The median total doses administered in the tumor target area, subclinical target area, and lymphatic drainage area were recorded as approximately 70–73 Gy, 60–66 Gy, and 50–54 Gy respectively. Out of these cases, induction chemotherapy followed by synchronous radiotherapy and chemotherapy was given

Table 2 The EB DNA positive or negative

Variable		EB DNA(+)	EB DNA(-)	*p* value
Progress	No	12 (52.17)	59 (77.63)	0.018
	Yes	11 (47.83)	17 (22.37)	
Using anti-HBV drugs	No	19 (82.61)	73 (96.05)	0.049
	Yes	4 (17.39)	3 (3.95)	
HBV infection	No	16 (69.57)	69 (90.79)	0.017
	Yes	7 (30.43)	7 (9.21)	
Gender	No	19 (82.61)	61 (80.26)	1.000
	Yes	4 (17.39)	15 (19.74)	
Smoking	No	13 (56.52)	57 (75.00)	0.088
	Yes	10 (43.48)	19 (25.00)	
Drinking	Yes	20 (86.96)	64 (84.21)	1.000
	No	3 (13.04)	12 (15.79)	
Death	No	20 (86.96)	74 (97.37)	0.080
	Yes	3 (13.04)	2 (2.63)	
B cells upon admission(%)	1.<12	12 (52.17)	36 (47.37)	0.686
	2. ≥12	11 (47.83)	40 (52.63)	
NK cells upon admission(%)	1.<19	13 (56.52)	38 (50.00)	0.583
	2. ≥19	10 (43.48)	38 (50.00)	
	2. ≥8	10 (43.48)	39 (51.32)	
T cells upon admission(%)	1.<65	8 (34.78)	37 (48.68)	0.241
	2. ≥65	15 (65.22)	39 (51.32)	
Tc upon admission	1.<25	10 (43.48)	41 (53.95)	0.379
	2. ≥25	13 (56.52)	35 (46.05)	
Th upon admission	1.<38	12 (52.17)	38 (50.00)	0.855
	2. ≥38	11 (47.83)	38 (50.00)	
Th/Tc upon admission	1.<1.5	14 (60.87)	37 (48.68)	0.306
	2. ≥1.5	9 (39.13)	39 (51.32)	
Hypertension	No	22 (95.65)	68 (89.47)	0.680
	Yes	1 (4.35)	8 (10.53)	
TNM staging	IV	18 (78.26)	56 (73.68)	0.658
	III	5 (21.74)	20 (26.32)	
Pathological type	Differentiated non-keratinizing squamous cell carcinoma	3 (13.04)	21 (27.63)	0.153
	Undifferentiated non-keratinizing squamous cell carcinoma	20 (86.96)	55 (72.37)	

to a majority of patients (90 out of total), involving cycles ranging from two to four before treatment initiation; while nine patients received synchronous radiotherapy and chemotherapy directly without prior induction therapy. During follow-up period, progression occurred in twenty-eight patients (28.28%), with a median progression-free survival time (PFS) estimated at approximately 45.53 months. Please refer to Fig. 2 for visualization on patient survival curve.

Comparison between patients infected with EBV or not

The baseline characteristics of patients infected and uninfected with EBV are presented in Table 2. Significant differences were observed between the two groups regarding progression, the value of Th(CD3 + CD4+)/Tc (CD3 + CD8+) before the patient's admission, use of immune-related drugs, and hepatitis B infection (HBV) ($p < 0.05$). No significant differences were found in terms of gender, smoking, alcohol consumption, hypertension, TNM grade, pathological type, death, and the levels of peripheral blood CD lymphocyte subsets such as B cells (CD19+) and NK cells (CD16 + CD56+) ($p > 0.05$). However, patients infected with **EBV** exhibited a shorter median progression-free survival time compared to uninfected patients (25.90 vs. 45.53 months; $p = 0.001$; Fig. 3).

Comparison of different levels of peripheral blood CD lymphocyte subsets in patients

The baseline characteristics of patients with low B cell levels (< 12% of lymphocytes) and high B cell levels (≥ 12% of lymphocytes) are presented in Table 3. Patients with low B cell levels demonstrated significantly higher levels of T (CD3+), Tc, and NK cells ($p < 0.05$), as well as a higher proportion of lymph node metastasis ($p < 0.05$). There were no statistically significant differences observed in terms of age, gender, smoking, alcohol consumption, and TNM staging between the two groups. Furthermore, patients with low B cell levels exhibited a shorter median progression-free survival time compared to those with high B cell levels (37.63 vs. 42.17 months; see Fig. 4).

No statistically significant differences were observed in the progression-free survival time of various peripheral blood CD lymphocyte subsets at different levels, including pathological pattern, lymph node metastasis, anti-HBV drugs use, the level of NK cells, T cells, Tc cells, Th cells.

Multivariate analysis

The Cox multivariate analysis model demonstrated that, after adjusting for age, T stage, and confounding factors of metastasis, patients with a low level of B cells exhibited an increased risk of progression compared to those with a high level (HR = 2.503, 95% CI: 1.062–5.899). Furthermore, patients infected with the EBV showed an elevated risk of progression in comparison to uninfected patients (HR = 2.739, 95% CI: 1.222–6.125). Moreover, the results were further supported by additional multivariate model analyses (refer to Table 4).

Discussion

This prospective cohort study enrolled patients who were newly diagnosed with advanced NPC. After receiving standardized systemic radiotherapy and chemotherapy treatment, followed by subsequent follow-up, it was observed that the presence of EBV infection and low levels of B cells prior to treatment were associated

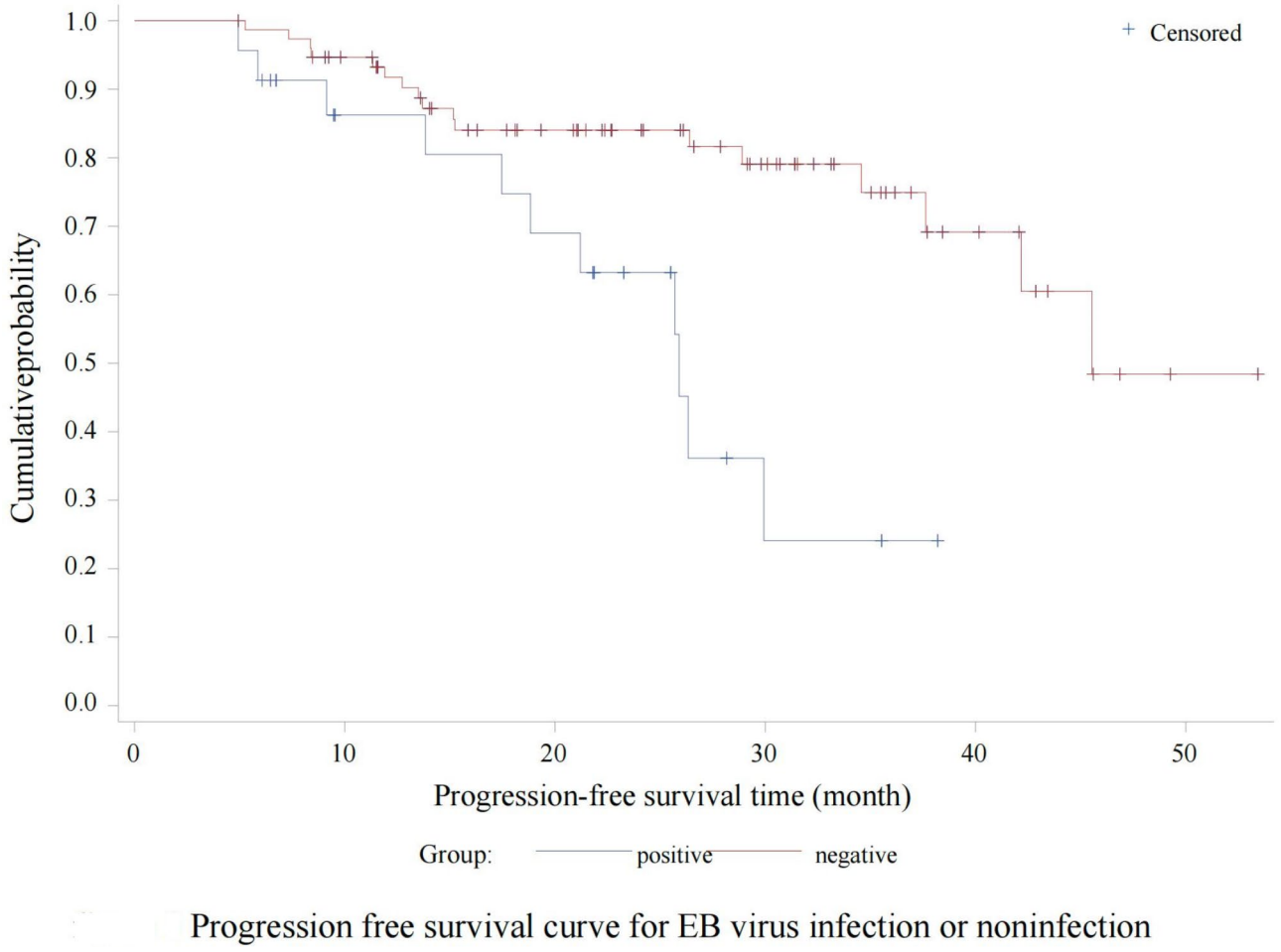

Fig. 3 Progression free survival curve for EBV infection or noninfection

with an increased likelihood of deterioration and disease progression.

A study investigating patients with pure bone metastasis and EBV infection undergoing platinum-based first-line chemotherapy for NPC reported a significantly higher proportion of EBV positivity in patients who experienced disease progression during follow-up compared to those who did not progress [16]. Despite the limitations in study design and conclusions, the observed phenomena suggest a potential association between EBV infection and disease progression. Another study focusing on newly diagnosed patients with non-metastatic nasopharyngeal non-keratinizing carcinoma found that a higher EBV DNA load was associated with an increased risk of disease progression [17]. This comprehensive study encompassed both metastatic and non-metastatic, undifferentiated, and differentiated patients, further indicating an elevated risk of EBV infection-related progression across all types of NPC.

The in vitro cell study has demonstrated that EBV infection diminishes the susceptibility of NPC cells to ferroptosis through activation of the p62-Keap1-NRF2 signaling pathway and upregulation of SLC7A11 and GPX4 expression, thereby impacting tumor sensitivity and resistance to chemotherapy drugs. Genetic knockout or specific inhibition of endogenous GPX4 can augment the chemical sensitivity of EBV-infected NPC cells. Moreover, GPX4 depletion impedes the proliferation and colony formation ability of NPC cells [13, 18]. Jianmin Hu et al. have discovered that EBV induces high oxidative stress, promoting its reactivation and resulting in radiation resistance. EBV stimulates a "redox reset" process in nasopharyngeal carcinoma cells by increasing expression levels of ROS-producing enzyme NOX2 and major antioxidant regulator Nrf2, leading to a new redox state characterized by elevated ROS accumulation and a stronger antioxidant system. Additionally, the EBV-encoded motor protein LMP1 facilitates viral reactivation through ROS generation [19]. However, heightened oxidative stress and EBV reactivation are inversely associated with overall survival rate following radiotherapy. They exhibit significant correlations with recurrence risk and clinical stage among patients with NPC. Consequently, EBV may elevate progression risk by enhancing drug resistance

Table 3 B cells at admission were divided into two groups for comparison

Variable	B cells < 12% of lymphocytes	B cells ≥ 12% of lymphocytes	*p* value
Age(years old)	50.06 ± 11.42	53.16 ± 10.54	0.082
Smoking duration(year)	23.82 ± 14.13	26.85 ± 9.56	0.670
Drinking duration(year)	32.50 ± 15.00	35.00 ± 5.77	0.868
Ki2	0.47 ± 0.18	0.44 ± 0.14	0.345
Survival time with no progress(year)	23.03 ± 13.05	23.93 ± 10.85	0.482
T cells upon admission(%)	68.52 ± 9.35	64.77 ± 8.55	0.040
Tc cells upon admission(%)	29.13 ± 10.58	23.32 ± 5.74	0.003
Th cells upon admission(%)	37.52 ± 10.71	38.70 ± 9.38	0.561
Th/Tc upon admission	1.58 ± 1.02	1.82 ± 0.94	0.021
NK cells upon admission(%)	21.78 ± 9.97	17.59 ± 9.52	0.029
T cells before radiation therapy and chemotherapy(%)	71.12 ± 9.19	68.29 ± 7.95	0.103
Tc cells before radiation therapy and chemotherapy(%)	31.75 ± 10.70	31.75 ± 10.70	0.032
Th cells before radiation therapy and chemotherapy(%)	36.90 ± 11.00	39.06 ± 7.55	0.214
Th/Tc before radiation therapy and chemotherapy	1.40 ± 0.89	1.57 ± 0.59	0.047
B cells before radiation therapy and chemotherapy (%)	6.28 ± 2.93	10.64 ± 5.01	0.000
NK cells before radiation therapy and chemotherapy(%)	21.45 ± 8.89	20.41 ± 10.34	0.313
T cells after radiation therapy and chemotherapy(%)	67.02 ± 12.93	66.42 ± 11.48	0.807
Tc cells after radiation therapy and chemotherapy(%)	32.30 ± 12.17	31.62 ± 13.14	0.559
Th cells after radiation therapy and chemotherapy(%)	31.61 ± 12.87	29.62 (21.86,42.23)	0.592
Th/Tc after radiation therapy and chemotherapy	1.21 ± 0.78	1.61 ± 2.38	0.327
B cells after radiation therapy and chemotherapy (%)	7.36 ± 6.28	10.22 ± 8.09	0.107
NK cells after radiation therapy and chemotherapy (%)	24.43 ± 13.25	21.88 ± 11.80	0.334
T cells of follow-up(%)	58.94 ± 11.25	54.07 ± 9.77	0.023
Tc cells of follow-up(%)	31.63 ± 10.13	26.79 ± 8.51	0.007
Th cells of follow-up(%)	24.03 ± 7.30	25.36 ± 7.09	0.482
Th/Tc of follow-up	0.99 ± 0.94	1.05 ± 0.50	0.059
B cells of follow-up(%)	10.44 ± 7.30	17.32 ± 9.14	0.000
NK cells of follow-up(%)	28.59 ± 11.12	26.49 ± 9.37	0.300

mechanisms as well as inducing high oxidative stress within tumor cells.

B cells (CD19+) are specialized lymphocytes that produce antibodies and perform humoral immune functions to eliminate free infectious pathogens. The EBV activates the pro-inflammatory signaling pathway in B cells, leading to viral gene expression and cytokine release [20]. The genetic locus of the BHLF1 gene of the EBV contributes to the progression of EBV latency, promoting sustained growth of B lymphocytes and enhancing its carcinogenic potential [17, 21]. However, no significant differences were observed in CD lymphocyte subsets between patients infected with EBV and uninfected patients in this study. This may be attributed to the duration of infection and variations in testing time. Despite being newly diagnosed with NPC, these patients were not recently infected with EBV. Further comprehensive research is needed to investigate the persistence of EBV infection and its impact on cytokine expression closely associated with CD lymphocyte subsets.

In addition to the observation in this study that low-level B cells are more susceptible to deterioration and

Table 4 COX analysis of risk factors for progression

Variables	Class	Crude		Adjusted in model 1		Adjusted in model 2	
		HR(95%CL)	*p*	HR (95%CL)	*p*	HR(95%CL)	*p*
Age	≥ 60 vs. <60	2.189 (0.988,4.852)	0.054	1.739 (0.772,3.918)	0.182		
T staging	T3 vs..T1-2	3.642 (1.147,11.565)	0.028	4.099 (1.191,14.101)	0.025	4.457 (1.318,15.073)	0.016
	T4 vs. T1-2	7.368 (2.311,23.489)	< 0.001	7.522 (2.230, 25.377)	0.001	7.906 (2.359,26.491)	< 0.001
Extra-lymph node metastasis	No vs. Yes	0.379 (0.142,1.009)	0.052	0.576 (0.202,1.643)	0.302		
B cells (%)	< 12 vs. ≥ 12	2.253 (1.008,5.035)	0.048	2.503 (1.062,5.899)	0.036	2.800 (1.226,6.399)	0.015
EB DNA	Positive vs. Negative	3.513 (1.592,7.753)	0.002	2.739 (1.222,6.135)	0.014	2.678 (1.202,5.970)	0.016

Notation: Multivariate COX model included variables with $p < 0.05$ in the comparison results of progression-free survival curves as independent variables. On the basis of model 1, the independent variable with $p > 0.05$ was eliminated

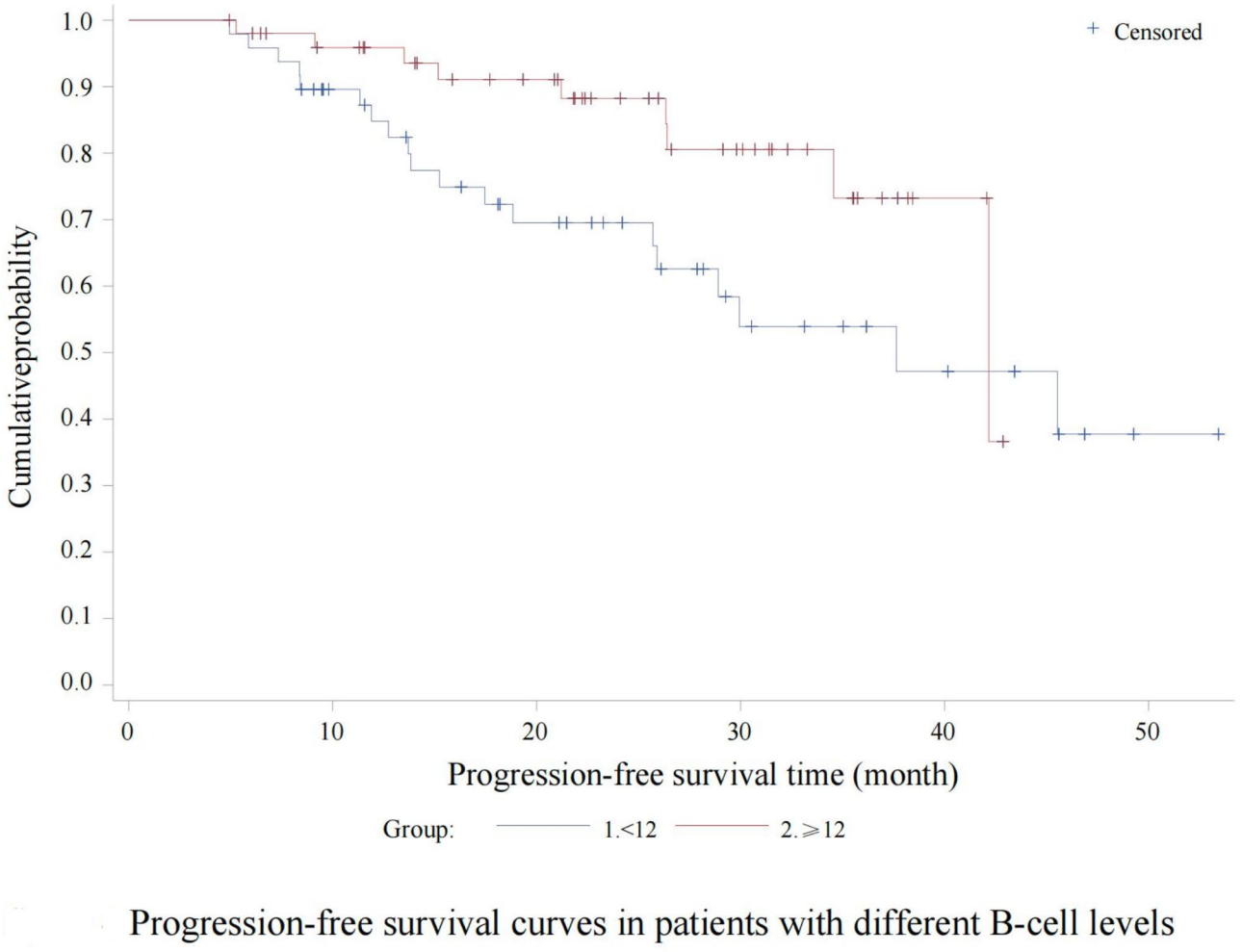

Fig. 4 Progression-free survival curves in patients with different B-cell levels

progression, similar findings have also been reported in other cancer patients. Patients with gastric cancer who have fewer circulating CD19 + lymphocytes exhibit shorter disease-free survival, while those with low expression of B cell-specific markers in head and neck squamous cell carcinoma and cervical cancer demonstrate shorter overall survival rates [22, 23]. The tumor microenvironment of NPC is characterized by an infiltration of more dendritic cells (DCs) and gamma-delta T cells, whereas there is a scarcity of B cells. The interaction between PKP1 and TIL-B cells plays a role in the development of NPC. TIL-B cells may produce immunoglobulin G (IgG) against tumor antigens and exert antitumor capabilities through DCs and T cells. In response, NPC cells express proteins such as PKP1 (which is normally deficient in nasopharynx), inducing the expansion of bone marrow-derived suppressor cells that subsequently impair B cell proliferation leading to B cell death via iNOS and NOX2 production [24]. Therefore, a lower count of B cells may also result from increased activity within the tumor itself. This suggests that the number of B cells could serve as a potential biomarker for predicting tumor cell vitality.

Limitations

It is a preliminary investigation conducted on a small sample size with short follow-up time; additionally, no other pathogenic microorganisms potentially affecting the prognosis of NPC were detected.

Conclusion

In summary, this study observed that patients with advanced NPC, who are infected with the EBV and exhibit low levels of B cells, demonstrate a heightened susceptibility to deterioration and disease progression.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13027-025-00638-2.

Supplementary Material 1

Author contributions
Yonghua Peng: Data curation, Writing-original draft. Fangchu Liu: Investigation, Writing-review & editing. Xintao Wang: Data curation. Weili Long: Investigation, Data curation. Zhenhe Huan: Project administration Writing-original draft.

Funding
There was no funding for the study.

Data availability
Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate
The study was reviewed and approved by the Ethics Committee of Ganzhou People's Hospital. (TY-ZKY2024-069-01).

Consent for publication
Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Competing interests
The authors declare no competing interests.

Received: 5 November 2024 / Accepted: 17 January 2025
Published online: 19 February 2025

References

1. Chen YP, Chan ATC, Le QT et al. Nasopharyngeal carcinoma[J]. The Lancet, 2019;394(10192):64–80.https://doi.org/10.1016/S0140-6736(19)30956-0
2. Wei KR, Zheng RS, Zhang SW. Analysis of the incidence and mortality of nasopharyngeal carcinoma in China in 2013 [J]. Cancer, 2018(4):9. CNKI: SUN: AIZH. 0.2018-04-005.
3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer statistics 2020: GLOBOCAN estimates of incidence and Mortality Worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209–49. https://doi.org/10.3322/caac.21660.
4. Zhu WP, Han MQ, Wang YX, et al. Study on the Trend and Prediction of Nasopharyngeal Cancer incidence and death in China from 1990 to 2019 [J]. Chin J Gen Pract. 2023;26(34):4269–76. https://doi.org/10.12114/j.issn.1007-9572.2023.0247.
5. He ML, Yi JL. Current status of treatment for recurrent nasopharyngeal carcinoma [J]. Chin J Radiation Oncol. 2021;30(11):7. https://doi.org/10.3760/cmA.j.cn113030-20200220-00065.
6. Soldan SS, Lieberman PM. Epstein-Barr virus and multiple sclerosis. Nat Rev Microbiol. 2023;21(1):51–64. https://doi.org/10.1038/s41579-022-00770-5.
7. Yang J, Liu Z, Zeng B, et al. Epstein-Barr virus-associated gastric cancer: a distinct subtype[J]. Cancer Lett. 2020;495. https://doi.org/10.1016/j.canlet.2020.09.019.
8. Damania B, Kenney SC, Raab-Traub N. Epstein-Barr virus: Biology and clinical disease. Cell. 2022;185(20):3652–70. https://doi.org/10.1016/j.cell.2022.08.026.
9. Yu H, Robertson ES. Epstein-Barr Virus History and Pathogenesis. Viruses. 2023;15(3):714. https://doi.org/10.3390/v15030714.
10. He JR, Shen GP, Ren ZF, Qin H, Cui C, Zhang Y, Zeng YX, Jia WH. Pretreatment levels of peripheral neutrophils and lymphocytes as independent prognostic factors in patients with nasopharyngeal carcinoma. Head Neck. 2012;34(12):1769–76. https://doi.org/10.1002/hed.22008.
11. Jiang Y, Qu S, Pan X, Huang S, Zhu X. Prognostic value of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in intensity modulated radiation therapy for nasopharyngeal carcinoma. Oncotarget. 2018;9(11):9992–10004. https://doi.org/10.18632/oncotarget.24173.
12. Medical Immunology/Gong Feili (Ed.-4). Beijing, China. Science Press. 2014.8. ISBN 978-07-03-041594-3.
13. Badoual C. Update from the 5th Edition of the World Health Organization Classification of Head and Neck tumors: Oropharynx and Nasopharynx. Head Neck Pathol. 2022;16(1):19–30. https://doi.org/10.1007/s12105-022-01449-2.
14. Pan JJ, Ng WT, Zong JF, et al. Proposal for the 8th edition of the AJCC/UICC staging system for nasopharyngeal cancer in the era of intensity-modulated radiotherapy. Cancer. 2016;122(4):546–58. https://doi.org/10.1002/cncr.29795.
15. Chinese Medical Association Radiation Oncology Therapy Physician Branch, Chinese Medical Association Radiation Oncology Therapy Branch. Chinese nasopharyngeal Cancer Radiotherapy Guidelines (2022 Edition) [J]. Chin J Cancer Prev Treat, 2022(009):029.
16. Liu GY, Xia WX, Bi ZF, Lu N, Li WZ, Bei WX, Liang H, Xie JZ, Liu YM, Yao HR, Xiang YQ. Plasma circulating Tumor Epstein-Barr Virus for the Surveillance of Cancer Progression in bone-only metastatic nasopharyngeal carcinoma. Front Oncol. 2022;12:860700. https://doi.org/10.3389/fonc.2022.860700.
17. Wei XL, Lan M, Peng XH, et al. The correlation between immune function status and EBV DNA in nasopharyngeal carcinoma patients and its impact on prognosis [J]. Cancer Prev Treat Res. 2021;48(6):7. https://doi.org/10.3971/j.issn.1000-8578.2021.20.1402.
18. Yuan L, Li S, Chen QY, et al. EBV infection-induced GPX4 promotes chemoresistance and tumor progression in nasopharyngeal carcinoma[J]. Cell Death Differ. 2022;29:1513–27. https://doi.org/10.1038/s41418-022-00939-8.
19. Hu J, Li Y, Li H, Shi F, Xie L, Zhao L, Tang M, Luo X, Jia W, Fan J, Zhou J, Gao Q, Qiu S, Wu W, Zhang X, Liao W, Bode AM, Cao Y. Targeting Epstein-Barr virus oncoprotein LMP1-mediated high oxidative stress suppresses EBV lytic reactivation and sensitizes tumors to radiation therapy. Theranostics. 2020;10(26):11921–11937. doi: 10.7150/thno.46006. Erratum in: Theranostics. 2022;12(8):3609. https://doi.org/10.7150/thno.73630
20. Baccianti F, Masson C, Delecluse S, Li Z, Poirey R, Delecluse H-J. Epstein-Barr virus infectious particles initiate B cell transformation and modulate cytokine response. mBio. 2023;14(5):e0178423. https://doi.org/10.1128/mbio.01784-23.
21. Yetming KD, Lupey-Green LN, Biryukov S, Hughes DJ, Marendy EM, Miranda JL, Sample JT. The BHLF1 locus of Epstein-Barr Virus contributes to viral latency and B-Cell immortalization. J Virol. 2020;94(17):e01215–20. https://doi.org/10.1128/JVI.01215-20.
22. Kim SS, Shen S, Miyauchi S, Sanders PD, Franiak-Pietryga I, Mell L, Gutkind JS, Cohen EEW, Califano JA, Sharabi AB. B cells improve overall survival in HPV-Associated squamous cell carcinomas and are activated by Radiation and PD-1 blockade. Clin Cancer Res. 2020;26(13):3345–59. https://doi.org/10.1158/1078-0432.CCR-19-3211.
23. Yu QM, Yu CD, Ling ZQ. Elevated circulating CD19 + lymphocytes predict survival advantage in patients with gastric cancer. Asian Pac J Cancer Prev. 2012;13(5):2219–24. https://doi.org/10.7314/apjcp.2012.13.5.2219.
24. Huang YM, Wang LQ, Liu Y, Tang FQ, Zhang WL. Integrated analysis of bulk and single-cell RNA sequencing reveals the interaction of PKP1 and tumor-infiltrating B cells and their therapeutic potential for nasopharyngeal carcinoma. Front Genet. 2022;13:935749. https://doi.org/10.3389/fgene.2022.935749.

Publisher's note