BMC Pediatrics

RESEARCH Open Access

# Prognosis of nasopharyngeal carcinoma in children and adolescents: a population-based analysis

Yi Shi[1,2†], Yang Wu[2†], Jiezhi He[3], Yinjie Ling[2*] and Wenyuan Liu[2*]

## Abstract

**Objectives** The purpose of this study is to use a population-based cohort to examine the clinicopathological features and survival outcomes of nasopharyngeal cancer (NPC) in children and adolescents.

**Methods** Demographic and clinicopathological variables of pediatric patients diagnosed with NPC were extracted from the Surveillance, Epidemiology, and End Results database (2000–2018). The survival rates were calculated using Kaplan-Meier analysis. Univariate survival analysis used the log-rank test, whereas multivariate analysis used Cox proportional-hazards regression to find factors impacting overall survival (OS).

**Results** A total of 233 pediatric patients were analyzed, with a median age at diagnosis of 16 years (range: 7–19 years). The cancers primarily affected males (70.0%). In terms of grade, 8 (3.5%) patients were well and moderately differentiated, 31 (13.3%) patients were poorly differentiated, and 134 (57.5%) patients were undifferentiated. TNM stage and radiotherapy were significant independent predictors of overall survival. The risk of death was higher for M1 stage (hazard ratio (HR) 20.1, 95% confidence interval (CI), 8.0-50.5; $P < 0.001$) as compared to M0 stage. Furthermore, multivariate analysis revealed a significant survival advantage for radiotherapy treatment (HR 0.24, 95% CI, 0.09–0.68; $P = 0.007$).

**Conclusion** NPC in children is rare and should be studied independently. This study found that TNM stage and radiotherapy were the most significant survival predictors, emphasizing the importance of these parameters in the prediction and treatment of pediatric NPC.

**Level of evidence** 3.

**Keywords** Nasopharyngeal carcinoma, Overall survival, Pediatric, SEER, Radiotherapy

†Yi Shi and Yang Wu contributed equally to the work.

*Correspondence:
Yinjie Ling
50411@zjhu.edu.cn
Wenyuan Liu
liuwenyuanhuzhou@126.com
[1]School of Medicine, Huzhou university, Huzhou 313000, Zhejiang, China
[2]Department of Pediatrics, First Affiliated Hospital of Huzhou University, the First People's Hospital of Huzhou, Huzhou 313000, China
[3]Department of nursing, Wenzhou Central Hospital, Wenzhou 325000, Zhejiang, China

## Introduction

Nasopharyngeal carcinoma (NPC) is an uncommon type of pediatric cancer which mainly occurs in adults [1–2]. Despite its rarity, it comprises 20–50% of all nasopharyngeal tumors found in children [3]. The age distribution shows two peaks: primarily in adults during their fifties and sixties, and a smaller, earlier peak among adolescents aged 15 to 19 years [4]. It remains uncertain whether a combination of genetic and environmental elements contributes to increased risk in certain young individuals. For pediatric cases, the average age of diagnosis ranges from 12 to 15 years, and these cases are frequently identified at an advanced stage involving the retronasal area and nearby lymph nodes [5–6]. Typically, the treatment protocols for pediatric NPC are adapted from those used for adults, even though the disease's origins may differ [7–8].

To enhance our comprehension of NPC in pediatric population, our study utilizes data from the Surveillance, Epidemiology, and End Results (SEER) program to examine the clinical characteristics and prognostic indicators of NPC in children and adolescents.

## Methods

### Study population

Using SEER∗Stat software (version 8.4.3), we extracted detailed data on pediatric and adolescent patients (aged ≤ 19 years) diagnosed with NPC from the SEER program of the National Cancer Institute. The SEER program provides comprehensive cancer incidence and survival data across the United States. NPC cases were classified according to the International Classification of Diseases for Oncology, Third Edition (ICD-O-3), including the following histologic subtypes: undifferentiated nonkeratinizing carcinoma (codes 8010, 8020), lymphoepithelial carcinoma (code 8082), and squamous cell carcinoma (codes 8070, 8071, 8072, 8073).

### Inclusion and exclusion criteria

To ensure a robust and representative cohort, we applied the following inclusion criteria: (1) Histologically confirmed NPC, including undifferentiated nonkeratinizing carcinoma, lymphoepithelial carcinoma, and squamous cell carcinoma; (2) Age at diagnosis ≤ 19 years; (3) Availability of detailed demographic and clinical data, including follow-up duration, survival status (in months), and cause of death; (4) Complete information on clinical stage, histopathological subtypes, and treatment modalities (e.g., radiotherapy and chemotherapy). Patients were excluded if they met any of the following criteria: (1) Lack of pathological confirmation of NPC; (2) Missing or unknown SEER stage, surgery status, or incomplete follow-up information; (3) Insufficient data on key variables such as TNM staging or treatment details.

### Data extraction and variables

Demographic, tumor, and treatment variables were extracted, including gender, race, TNM stage (UICC/AJCC 6th edition), tumor grade, and treatment modalities (radiotherapy, chemotherapy). Patients were stratified into two age groups (0–14 years and 15–19 years) based on biological/developmental differences, age-specific treatment protocols, and alignment with prior literature. The primary outcome was overall survival (OS), measured from diagnosis to death or last follow-up.

**Ethical approval** was waived by the Huzhou First People's Hospital IRB, as the study used de-identified, publicly available data. All procedures complied with relevant guidelines and regulations. These revisions enhance the clarity, transparency, and scientific rigor of the study.

### Statistical analysis

Statistical analyses were performed using SPSS software (version 22.0, SPSS Inc., Chicago, IL, USA). Survival outcomes were analyzed using Kaplan-Meier curves for 1-, 3-, and 5-year OS intervals, and differences between groups were compared using the log-rank test. To identify prognostic risk factors, a Cox proportional hazards model was employed. Variables with a $P$-value < 0.05 in univariate analysis were included in the multivariate analysis. A two-tailed $P$-value < 0.05 was considered statistically significant for all analyses.

## Results

### Patient characteristics

From 2000 to 2018, a total of 233 pediatric and adolescent patients diagnosed with nasopharyngeal carcinoma were recorded, as shown in Table 1. The median age at diagnosis was 16 years, with an age range of 7 to 19 years. Among these patients, 86 (36.9%) were 14 years or younger, while 147 (63.1%) were older than 14. The majority of the cases (70.0%) occurred in males. In terms of tumor differentiation, 8 (3.5%) patients had well or moderately differentiated tumors, 31 (13.3%) had poorly differentiated tumors, and 134 (57.5%) had undifferentiated tumors. The predominant histological type was undifferentiated nonkeratinizing carcinoma, accounting for 51.9%, followed by squamous cell carcinoma at 24.0%, lymphoepithelial carcinoma at 20.2%, and other types at 3.9%. The distribution of disease stages was as follows: Stage I (26.6%), Stage II (12.9%), Stage III (19.7%), and Stage IV (40.8%). Treatment primarily involved radiotherapy, administered to 88.8% of patients, and chemotherapy, received by 93.5% of the cohort.

### Survival and prognosis analysis

The 1-, 3-, and 5-year survival rates of the entire cohort were 66.7%, 57.9%, and 44.2%, respectively, as shown in

**Table 1** Clinical characteristics of pediatric nasopharyngeal carcinoma (NPC)

| Characteristics | Frequency, *n* (%) |
|---|---|
| Age at diagnosis (years) | |
| > 14 | 147 (63.1) |
| ≤ 14 | 86 (36.9) |
| Gender | |
| Male | 163 (70.0) |
| Female | 70 (30.0) |
| Race | |
| White | 112 (48.0) |
| Black | 89 (38.2) |
| Asian/Pacific Islander | 32 (13.8) |
| Grade | |
| Well and moderate differentiated | 8 (3.5) |
| Poorly differentiated | 31 (13.3) |
| Undifferentiated | 134 (57.5) |
| Unknown | 60 (25.7) |
| Histological type | |
| Others | 9 (3.9) |
| Undifferentiated nonkeratinizing carcinoma | 121 (51.9) |
| Lymphoepithelial carcinoma | 47 (20.2) |
| Squamous cell carcinoma | 56 (24.0) |
| TNM stage | |
| I | 62 (26.6) |
| II | 30 (12.9) |
| III | 46 (19.7) |
| IV | 95 (40.8) |
| T stage | |
| T1 | 53 (22.7) |
| T2 | 53 (22.7) |
| T3 | 66 (28.3) |
| T4 | 61 (26.3) |
| N stage | |
| N0 | 43 (18.4) |
| N1 | 68 (29.3) |
| N2 | 79 (33.9) |
| N3 | 43 (18.4) |
| M stage | |
| M0 | 154 (69.0) |
| M1 | 79 (31.0) |
| Radiotherapy | |
| No | 26 (11.2) |
| Yes | 207 (88.8) |
| Chemotherapy | |
| No | 15 (6.5) |
| Yes | 218 (93.5) |

Table 2. Univariate analysis showed no significant association between overall survival (OS) and variables such as age at diagnosis, gender, grade, or histological type. However, TNM category, T category, and N category emerged as independent prognostic factors for OS. Notably, patients at M0 stage had higher survival rates than those with distant metastases, with 5-year OS rates of 92.7% for

**Table 2** 1-, 3- and 5-year survival for entire cohort and by subgroup

| Feature | 1-Year OS (%) | 3-Year OS (%) | 5-Year OS (%) |
|---|---|---|---|
| Overall | 96.0 | 89.8 | 87.1 |
| TNM stage | | | |
| I | 98.2 | 98.2 | 98.2 |
| II | 96.7 | 96.7 | 96.7 |
| III | 97.8 | 91.3 | 91.3 |
| IV | 93.7 | 83.0 | 77.3 |
| T stage | | | |
| T1 | 93.7 | 86.1 | 86.1 |
| T2 | 97.9 | 95.8 | 93.5 |
| T3 | 96.8 | 88.6 | 85.1 |
| T4 | 91.6 | 86.4 | 80.6 |
| N stage | | | |
| N0 | 100 | 97.3 | 97.3 |
| N1 | 95.3 | 91.9 | 91.9 |
| N2 | 94.8 | 93.4 | 88.6 |
| N3 | 88.3 | 71.4 | 64.0 |
| M stage | | | |
| M0 | 98.6 | 94.3 | 92.7 |
| M1 | 89.8 | 79.1 | 74.2 |
| Radiotherapy | | | |
| No | 88.1 | 68.6 | 68.6 |
| Yes | 97.0 | 92.2 | 89.3 |

M0 versus 74.2% for M1 ($P < 0.001$) (Fig. 1). Radiotherapy also correlated with improved survival outcomes compared to absence of radiotherapy ($P = 0.018$), as illustrated in Fig. 2.

Table 3 summarizes the results from the Cox regression multivariate analysis. Multivariate analysis of the entire cohort revealed that TNM stage and radiotherapy were significant independent predictors of overall survival. Specifically, patients in M1 stage had a significantly higher risk of death (hazard ratio (HR) 20.1, 95% confidence interval (CI) 8.0-50.5; $P < 0.001$) compared to those in M0 stage. Additionally, the analysis demonstrated a significant survival benefit from radiotherapy, with a hazard ratio of 0.24 (95% CI, 0.09–0.68; $P = 0.007$).

## Discussion

While previous studies have explored the prognosis of nasopharyngeal carcinoma (NPC) patients, few have specifically addressed prognostic factors related to overall survival (OS) in pediatric populations [9–10]. Our study aims to bridge this knowledge gap by examining various epidemiological factors and their impact on survival rates, highlighting TNM stage and radiotherapy as key predictors of OS through both univariate and multivariate analyses.

Histologically, pediatric NPC predominantly manifests as non-keratinizing or undifferentiated carcinoma, similar to adult NPC. This subtype exhibits high radiosensitivity and an association with EBV infection.

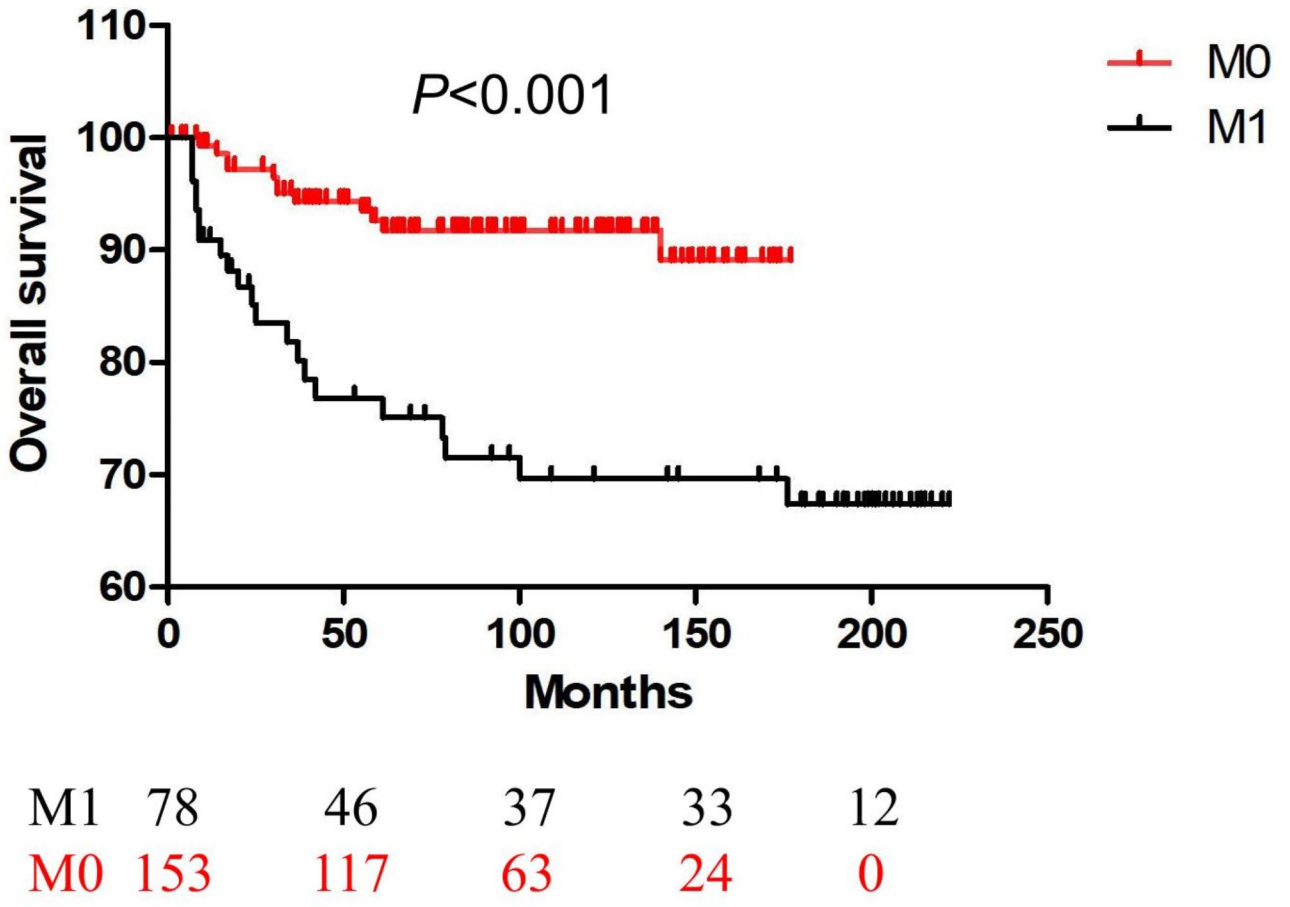


**Fig. 1** Kaplan–Meier survival curves of children and adolescents with NPC. M1 vs. M0, $P < 0.001$

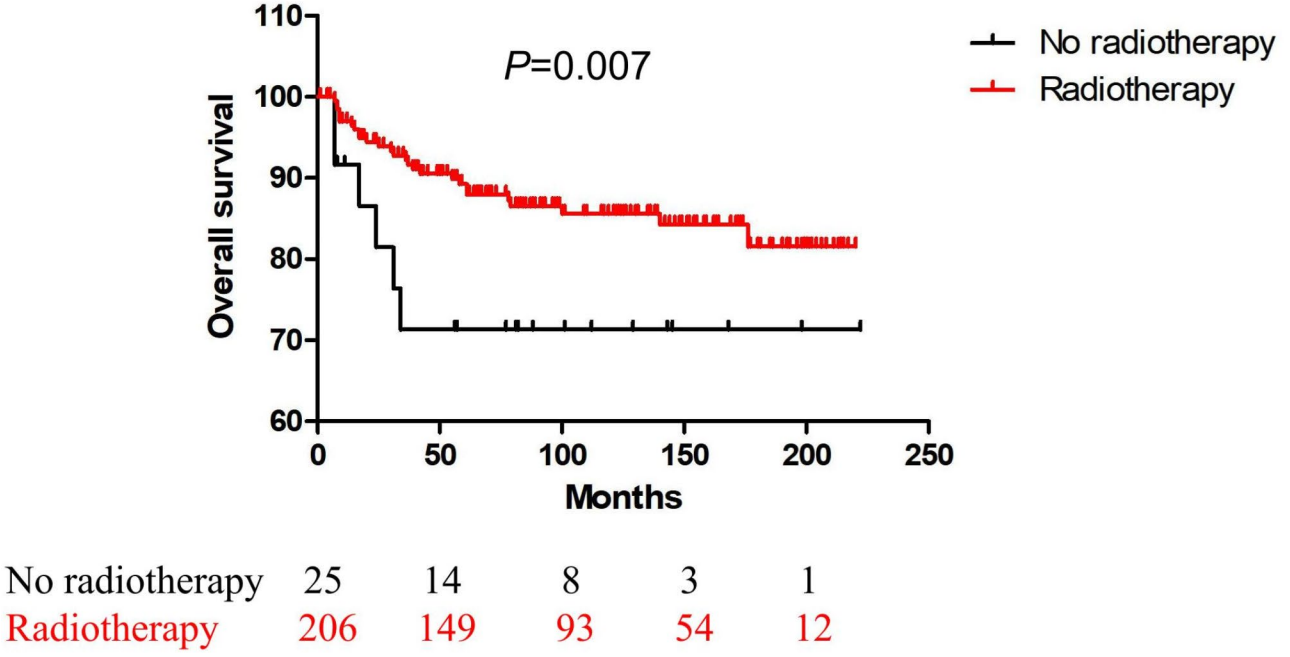


**Fig. 2** Kaplan–Meier survival curves for children and adolescents with NPC. Radiotherapy vs. No radiotherapy, $P = 0.007$

**Table 3** Univariate and multivariate analysis of prognostic factors in pediatric NPC

| Characteristics | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | Hazard ratio (95% CI) | *P* value | Hazard ratio (95% CI) | *P* value |
| Age at diagnosis (years) | | | | |
| > 14 | Reference | | Reference | |
| ≤ 14 | 0.519 (0.235–1.148) | 0.105 | 0.673 (0.267–1.700) | 0.402 |
| Gender | | | | |
| Male | Reference | | | |
| Female | 0.904 (0.422–1.937) | 0.795 | | |
| Race | | | | |
| White | Reference | | | |
| Black | 0.884 (0.406–1.925) | 0.756 | | |
| Asian/Pacific Islander | 1.925 (0.816–4.543) | 0.135 | | |
| Grade | | | | |
| Well and moderate differentiated | Reference | | | |
| Poorly differentiated | 2.177 (0.268–17.696) | 0.467 | | |
| Undifferentiated | 1.379 (0.186–10.218) | 0.753 | | |
| Unknown | 0.508 (0.053–4.890) | 0.558 | | |
| Histological type | | | | |
| Others | Reference | | | |
| Undifferentiated nonkeratinizing carcinoma | 1.319 (0.175–9.926) | 0.788 | | |
| Lymphoepithelial carcinoma | 1.499 (0.190–11.834) | 0.701 | | |
| Squamous cell carcinoma | 1.229 (0.151–10.004) | 0.847 | | |
| TNM stage | | | | |
| I | Reference | | Reference | |
| II | 1.914 (0.119–30.804) | 0.647 | 6.052 (0.286–127.882) | 0.247 |
| III | 6.143 (0.641–58.911) | 0.116 | 147.421 (10.572–2055.620) | < 0.001 |
| IV | 23.518 (2.908–190.176) | 0.003 | 367.157 (28.749–4688.992) | < 0.001 |
| T stage | | | | |
| T1 | Reference | | Reference | |
| T2 | 0.344 (0.085–1.388) | 0.134 | 0.376 (0.083–1.712) | 0.206 |
| T3 | 1.108 (0.402–3.052) | 0.842 | 0.288 (0.086–0.959) | 0.043 |
| T4 | 1.913 (0.740–4.945) | 0.181 | 0.183 (0.059–0.570) | 0.003 |
| N stage | | | | |
| N0 | Reference | | Reference | |
| N1 | 3.376 (0.406–28.063) | 0.260 | 3.119 (0.339–28.721) | 0.315 |
| N2 | 4.500 (0.570–35.556) | 0.154 | 2.027 (0.222–18.484) | 0.531 |
| N3 | 19.003 (2.529–142.801) | 0.004 | 1.434 (0.151–13.660) | 0.754 |
| M stage | | | | |
| M0 | Reference | | Reference | |
| M1 | 3.901 (1.915–7.945) | < 0.001 | 20.129 (8.019–50.524) | < 0.001 |
| Radiotherapy | | | | |
| No | Reference | | Reference | |
| Yes | 0.366 (0.159–0.842) | 0.018 | 0.244 (0.088–0.677) | 0.007 |
| Chemotherapy | | | | |
| No | Reference | | | |
| Yes | 0.455 (0.160–1.292) | 0.139 | | |

Several SEER data suggest that histological subtype is an independent prognostic marker for NPC [11–12], with nonkeratinizing tumors often linked to better survival [13–14]. However, our findings did not show significant survival differences among histological subtypes, possibly due to our study's limited sample size. This underscores the need for larger, multi-center trials to further evaluate the relationship between histological subtypes and survival in pediatric NPC. Previous study noted that patients with advanced T stage have a higher likelihood of local recurrence, whereas those with advanced N stage primarily show distant metastases [15]. In our cohort, advanced T stage was associated with increased mortality, but N stage did not significantly affect OS.

Additionally, patients with distant metastases exhibited a higher risk of death.

Recent decades have seen a surge in prospective studies improving the understanding and treatment of pediatric NPC [16–17], with a high success rate of long-lasting remissions exceeding 80–90%, aligning with our findings [18–19]. Treatment predominantly involves combined chemoradiotherapy, as surgical removal is generally infeasible due to the tumor's typical location. Prior research in both adult and pediatric populations has shown that combined chemotherapy and radiotherapy are associated with superior survival outcomes compared to radiotherapy alone [20]. However, our findings did not demonstrate a significant survival benefit from chemotherapy in pediatric NPC patients. This observation may be attributed to the fact that the majority of patients in our study received chemotherapy as part of their treatment regimen. Radiotherapy remains the cornerstone of NPC treatment, as these tumors are typically highly radiosensitive. Consistent with this, our data indicated that pediatric NPC patients who received radiotherapy had improved survival rates. Nevertheless, while high doses of radiotherapy can achieve high cure rates, they are also associated with severe and debilitating long-term side effects. These include dental caries, hypothyroidism, impaired facial growth in younger children, hearing loss, and an increased risk of secondary malignancies [21–22]. These outcomes suggest potential for reducing radiation doses in patients responding well to induction chemotherapy.

This study has several limitations. First, its retrospective design introduces the potential for selection bias and limits the availability of detailed treatment data. Second, while radiotherapy was identified as a significant prognostic marker for survival, the SEER database does not provide specific details on radiotherapy techniques (e.g., volumetric modulated arc therapy [VMAT] or proton therapy) or doses, which may influence treatment outcomes. This omission is a notable limitation that should be considered when interpreting the results. Additionally, we were unable to evaluate the impact of factors such as EBV infection, genetic predispositions, or tumor biomarkers, which could further refine prognostic models. These limitations underscore the need for future research, particularly in regions where pediatric NPC is prevalent, to validate our findings and explore these critical aspects in greater depth.

## Conclusion

Pediatric NPC is a rare malignancy with distinct clinicopathological features compared to its adult counterpart. TNM stage and radiotherapy emerged as the most significant survival predictors, emphasizing the implications of these factors on the prognosis and management of pediatric NPC.

**Acknowledgements**
We thank the National Cancer Institute for providing the SEER dataset.

**Author contributions**
Yi Shi. MD. Conception and design of study, acquisition of data, drafting and revising the manuscript. Yang Wu. MD. Conception and design of study, acquisition of data, drafting the manuscript. Jiezhi He. BS. Conception and design of study, acquisition of data, drafting the manuscript. Yinjie Ling. MD. Conception and design of study, acquisition of data, drafting and revising the manuscript. Wenyuan Liu. MD. Conception and design of study, acquisition of data, analysis and/or interpretation of data, drafting the manuscript. All authors read and approved the final manuscript as submitted.

**Funding**
This study was supported by Huzhou Municipal Bureau of Science and Technology, Zhejiang Province (Grant number 2021GYB55 to Yinjie Ling).

**Data availability**
The dataset used and analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

**Ethics approval and consent to participate**
Because the data utilized in the current study were de-identified and openly accessible, Huzhou first People's Hospital's Institutional Review Board permission was waived. The Huzhou first People's Hospital's Institutional Review Board disregarded the requirement for written informed consent due to the study's retrospective nature. All processes were carried out in conformity with the applicable norms and legislation.

**Consent for publication**
None.

**Competing interests**
The authors declare no competing interests.

Received: 14 December 2024 / Accepted: 31 March 2025
Published online: 21 April 2025

**References**

1. Sultan I, Casanova M, Ferrari A, et al. Differential features of nasopharyngeal carcinoma in children and adults: a SEER study. Pediatr Blood Cancer. 2010;55:279–84.
2. Dourthe ME, Bolle S, Temam S, et al. Childhood nasopharyngeal carcinoma: state-of-the-art, and questions for the future. J Pediatr Hematol Oncol. 2018;40:85–92.
3. Person L, Lacour B, Faure L, et al. Childhood head and neck cancer in France: incidence, survival and trends from 2000 to 2015. Int J Pediatr Otorhinolaryngol. 2021;150:110858.
4. Bray F, Haugen M, Moger TA, et al. Age-incidence curves of nasopharyngeal carcinoma worldwide: bimodality in low-risk populations and aetiologic implications. Cancer Epidemiol Biomarkers Prev. 2008;17:2356–65.
5. Mertens R, Granzen B, Lassay L, et al. Nasopharyngeal carcinoma in childhood and adolescence: concept and preliminary results of the cooperative GPOH study NPC-91. Gesellschaft fur padiatrische onkologie und hamatologie. Cancer. 1997;80:951–9.
6. Casanova M, Bisogno G, Gandola L, et al. A prospective protocol for nasopharyngeal carcinoma in children and adolescents: the Italian rare tumors in pediatric age (TREP) project. Cancer. 2012;118:2718–25.
7. Rodriguez-Galindo C, Krailo MD, Krasin MJ, et al. Treatment of childhood nasopharyngeal carcinoma with induction chemotherapy and concurrent chemoradiotherapy: results of the children's oncology group ARAR0331 study. J Clin Oncol. 2019;37:3369–76.

8. Romer T, Franzen S, Kravets H, et al. Multimodal treatment of nasopharyngeal carcinoma in children, adolescents and young adults-extended follow-up of the NPC-2003-GPOH study cohort and patients of the interim cohort. Cancers (Basel). 2022;14:1261.
9. Wu SG, Liao XL, He ZY, et al. Demographic and clinicopathological characteristics of nasopharyngeal carcinoma and survival outcomes according to age at diagnosis: A population-based analysis. Oral Oncol. 2017;73:83–7.
10. Wu J, Zhou Q, Pan Z, et al. Development and validation of a nomogram for predicting long-term overall survival in nasopharyngeal carcinoma: A population-based study. Med (Baltim). 2020;99(4):e18974.
11. Vazquez A, Khan MN, Govindaraj S, et al. Nasopharyngeal squamous cell carcinoma: a comparative analysis of keratinizing and nonkeratinizing subtypes. Int Forum Allergy Rhinol. 2014;4(8):675–83.
12. Burt RD, Vaughan TL, McKnight B. Descriptive epidemiology and survival analysis of nasopharyngeal carcinoma in the united States. Int J Cancer. 1992;52(4):549–56.
13. Shi W, Pataki I, MacMillan C, et al. Molecular pathology parameters in human nasopharyngeal carcinoma. Cancer. 2002;94(7):1997–2006.
14. Petersson F. Nasopharyngeal carcinoma: a review. Semin Diagn Pathol. 2015;32(1):54–73.
15. Au KH, Ngan RKC, Ng AWY, et al. Treatment outcomes of nasopharyngeal carcinoma in modern era after intensity modulated radiotherapy (IMRT) in Hong Kong: A report of 3328 patients (HKNPCSG 1301 study). Oral Oncol. 2018;77:16–21.
16. Buehrlen M, Zwaan CM, Granzen B, et al. Multimodal treatment, including interferon beta, of nasopharyngeal carcinoma in children and young adults: preliminary results from the prospective, multicenter study NPC-2003-GPOH/DCOG. Cancer. 2012;118:4892–900.
17. Luo DH, Li XY, Guo SS, et al. Paclitaxel liposome, cisplatin and 5-fluorouracil-based induction chemotherapy followed by de-escalated intensity-modulated radiotherapy with concurrent cisplatin in stage IVA-IVB childhood nasopharyngeal carcinoma in endemic area: a phase II, single-arm trial. Lancet Reg Health West Pac. 2023;40:100895.
18. Ben-Ami T, Ash S, Ben-Harosh M, et al. Nasopharyngeal carcinoma in children and young adults-beyond 5-year survival. Pediatr Blood Cancer. 2020;67:e28494.
19. Sahai P, Mohanti BK, Sharma A, et al. Clinical outcome and morbidity in pediatric patients with nasopharyngeal cancer treated with chemoradiotherapy. Pediatr Blood Cancer. 2017;64:259–66.
20. Sun Y, Li WF, Chen NY, et al. Induction chemotherapy plus concurrent chemoradiotherapy versus concurrent chemoradiotherapy alone in locoregionally advanced nasopharyngeal carcinoma: a phase 3, multicentre, randomised controlled trial. Lancet Oncol. 2016;17:1509–20.
21. Küpeli S, Varan A, Ozyar E, et al. Treatment results of 84 patients with nasopharyngeal carcinoma in childhood. Pediatr Blood Cancer. 2006;46(4):454–8.
22. Qiu WZ, Peng XS, Xia HQ, et al. A retrospective study comparing the outcomes and toxicities of intensity-modulated radiotherapy versus two-dimensional conventional radiotherapy for the treatment of children and adolescent nasopharyngeal carcinoma. J Cancer Res Clin Oncol. 2017;143:1563–72.

## Publisher's note