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Article

Real-World Treatment Practice and Survival Outcomes in Elderly Patients With Nasopharyngeal Carcinoma

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Abstract

Aims/Background: Elderly patients with nasopharyngeal carcinoma (NPC) generally experience inferior treatment outcomes compared to the younger population. Understanding the complex interplay among age, treatment modalities, and clinical outcomes is critical for developing evidence-based clinical guidelines for this demographic. This study aimed to evaluate treatment patterns, compliance, and clinical outcomes in elderly NPC patients within a real-world setting. **Methods:** We retrospectively included elderly patients (≥65 years) with NPC who received radiotherapy between January 2015 and December 2022. The primary endpoints were progression-free survival (PFS) and overall survival (OS). Statistical analyses were performed using the chi-square test, Kaplan-Meier method with log-rank test, and Cox proportional hazards model. **Results:** A total of 95 patients were included. Forty-two patients (44.2%) received induction chemotherapy (IC) followed by concurrent chemoradiotherapy (CCRT), 22 patients (23.2%) received CCRT alone, and 31 patients (32.6%) underwent radiotherapy alone. The CCRT completion rates were comparable between the IC group (64.3%) and the non-IC group (68.2%) ($p = 0.755$). Notably, 91 patients (95.7%) completed the recommended course of radiotherapy. The 5-year PFS and OS rates were 54.9% and 66.2%, respectively. Multivariate analysis identified age, gender, Adult Comorbidity Evaluation-27 score, Epstein-Barr Virus-deoxyribonucleic acid status, and treatment modality as independent prognostic factors. The results of multivariate prognostic analysis also showed that patients who did not receive CCRT had worse PFS ($p = 0.029$) and OS ($p = 0.005$) compared to those who received CCRT. However, no significant differences in PFS ($p = 0.274$) and OS ($p = 0.594$) were observed between the IC+CCRT and CCRT alone groups. **Conclusion:** Despite high adherence to recommended radiotherapy regimens, survival outcomes in elderly NPC patients remain suboptimal. Our findings indicate that CCRT significantly improves survival compared to radiotherapy alone. However, the addition of IC to CCRT did not confer a survival benefit over CCRT alone. These findings underscore the importance of individualized treatment planning and the necessity of considering the comprehensive health status of elderly NPC patients in clinical practice.

Keywords: nasopharyngeal carcinoma; elderly; intensity-modulated radiation therapy; survival; chemotherapy

1. Introduction

Nasopharyngeal carcinoma (NPC) is a unique head and neck malignancy with a distinct geographical distribution, particularly prevalent in Southeast China. While NPC is frequently diagnosed in younger and middle-aged adults, the highest incidence rates are observed among middle-aged and elderly individuals, specifically in the 65–69 age group, with a predominance of male patients [1]. Approximately 10–30% of NPC cases are diagnosed in elderly patients [2,3]. Despite significant advancements in radiotherapy, chemotherapy, and targeted therapies [4], managing NPC in elderly patients remains challenging due to age-related physiological changes, decreased tolerance to aggressive treatments, and competing health risks compared to younger patients. Elderly patients often exhibit poor tolerance to radiotherapy, and treatment-related early deaths are not uncommon [3]. These factors highlight the need for personalized therapeutic strategies that balance efficacy and safety in this vulnerable population.

For the majority of NPC patients, regardless of age, the disease presents as a locally advanced disease. The pattern of stage distribution in elderly NPC patients has been shown to align closely with trends in the general population [3,5]. Although several guidelines exist for managing NPC [6,7,8], none are specifically designed for elderly patients. Current guidelines are primarily based on studies involving younger individuals, resulting in a significant knowledge gap regarding the optimal therapeutic approach for the elderly. Consequently, less aggressive management is typically selected for this population, largely due to late-stage detection, multiple comorbidities, and suboptimal physical function. Elderly patients with NPC generally have poorer survival outcomes compared to the overall population [9,10]. Understanding the interaction between age, treatment modalities, and outcomes is critical to devel-

oping evidence-based guidelines for this group. Here, we present a real-world experience regarding treatment modalities, treatment compliance, and clinical outcomes in elderly patients with NPC.

2. Methods

2.1 Patients

This study included NPC patients aged ≥65 years who underwent intensity-modulated radiation therapy (IMRT) between January 2015 and December 2022. The inclusion criteria were as follows: (1) age ≥65 years; (2) stage I–IVA NPC patients; (3) receipt of IMRT with or without chemotherapy; and (4) availability of complete clinicopathologic and treatment data. Exclusion criteria were as follows: (1) presence of distant metastasis at the time of diagnosis; (2) history of prior malignancy or other concurrent malignancies; (3) incomplete medical records or missing follow-up data.

2.2 Variables

The following variables were analyzed: age, gender, smoking history, alcohol consumption, histology, clinical stage, tumor (T) stage, nodal (N) stage, body mass index (BMI), Adult Comorbidity Evaluation-27 (ACE-27) scores [11], Epstein-Barr Virus (EBV)-deoxyribonucleic acid (DNA) status, and treatment modality. Staging was determined according to the eighth edition of the American Joint Committee on Cancer staging system [12]. Based on World Health Organization (WHO) definitions specific to Asian populations, patients were categorized into four BMI groups: underweight (<18.5 kg/m^2), normal weight (18.5–22.9 kg/m^2), overweight (23.0–24.9 kg/m^2), and obese (≥25 kg/m^2) [13].

2.3 Radiotherapy

The gross target volume for the primary nasopharyngeal tumor (GTVnx) and the gross tumor volume of involved cervical lymph nodes (GTVnd) encompassed all gross disease identified clinically and via imaging. The clinical target volume (CTV) was delineated based on consensus guidelines from international experts [14]. All patients underwent IMRT. The planning target volume (PTV) was constructed by automatically expanding the CTV by a 3-mm margin in three dimensions to account for setup variability. The prescribed doses were as follows: 70.29 Gray (Gy) (in 32–33 fractions) to planning GTVnx (PGTVnx) and planning GTVnd (PGTVnd); 62 Gy (in 32–33 fractions) to planning CTV1 (PCTV1) and planning clinical target volume of nodal disease (PCTVnd) (high-risk regions); and 56 Gy (in 32–33 fractions) to planning CTV2 (PCTV2) (low-risk regions). Treatment was administered once daily, five days per week.

2.4 Chemotherapy

The decision to administer induction chemotherapy (IC) was at the discretion of the treatment physician. Concurrent chemotherapy consisted of cisplatin (75–80 mg/m^2), nedaplatin (80–100 mg/m^2), or lobaplatin (30–40 mg/m^2) administered every three weeks for two cycles, commencing on the first day of IMRT. Adjuvant chemotherapy was not typically recommended for elderly patients at our institution.

2.5 Assessment of Adverse Effects During Radiotherapy

Adverse effects occurring during IMRT were graded using the National Cancer Institute Common Terminology Criteria for Adverse Events (version 5.0) [15] and the Acute and Late Radiation Morbidity Scoring Criteria of the Radiation Therapy Oncology Group [16].

2.6 Follow-Up

Patients were followed up every three months. Each visit included a comprehensive assessment comprising blood tests, EBV-DNA quantification, physical examination of the nasopharynx and neck nodes, nasopharyngoscopy, and imaging studies (magnetic resonance of the nasopharynx and neck, chest computed tomography, and abdominal ultrasound). Locoregional failure-free survival (LRFS) was defined as the time from diagnosis to local recurrence in the nasopharynx and/or regional recurrence in the cervical lymph nodes, or to the last follow-up. Distant metastasis-free survival (DMFS) was defined as the time from diagnosis to distant metastasis or the last follow-up. Progression-free survival (PFS) was measured from the date of diagnosis to disease progression or death from any cause. Overall survival (OS) was defined as the time from diagnosis to death from any cause. The primary endpoints were PFS and OS.

2.7 Statistical Analysis

Categorical variables were compared using the Chi-square test. Survival estimates were generated and compared using Kaplan-Meier analysis and the log-rank test. Variables with a significance threshold of $p < 0.1$ in univariate Cox regression were included in a multivariate Cox proportional model to identify independent prognostic factors for PFS and OS. These independent factors served as the basis for developing predictive nomograms. The predictive accuracy and discrimination of the nomograms were verified using calibration plots, Harrell's C-index, receiver operating characteristic (ROC) curves, and assessment of discrimination ability. Decision curve analysis (DCA) was utilized to appraise the clinical utility of the model. To account for heterogeneity in baseline characteristics, inverse probability of treatment weighting (IPTW) was utilized to minimize confounding biases between subgroups. An absolute standardized mean difference (ASMD) of <0.20 after adjustment indicated sufficient balance. All statistical anal-

yses were conducted using the R program (version 4.4.2) (R Foundation for Statistical Computing, Vienna, Austria), SPSS version 25.0 (IBM Corporation, Armonk, NY, USA), and MedCalc Statistical Software version 18.2.1 (MedCalc Software bvba, Ostend, Belgium). A p-value < 0.05 was considered statistically significant.

3. Results

3.1 Patient Characteristics

A total of 782 patients were diagnosed during the study period. Of these, 95 patients (12.1%) aged ≥65 years met the inclusion criteria and were included in the final analysis (Table 1). The median age was 68 years (range, 65–88 years). The cohort was predominantly male (67.4%, n = 64), with 45.3% (n = 43) reporting a history of smoking and 18.9% (n = 18) a history of alcohol consumption. Regarding stage distribution, the majority of patients were classified as stage III (45 patients, 47.4%) or stage IVA (37 patients, 38.9%), whereas only 1 (1.1%) and 12 (12.6%) patients were diagnosed with stages I and II disease, respectively. The median BMI was 21.8 kg/m^2 (range 15.3–30.5 kg/m^2), with 17.9% (n = 17) of patients classified as underweight. The ACE-27 scores were distributed as follows: 0 for 32 patients (33.7%), 1 for 35 patients (36.8%), 2 for 21 patients (22.1%), and 3 for 7 patients (7.4%). Among the patients, 49 (51.6%) had EBV-DNA levels <4000 copies/mL, 24 (25.3%) exhibited EBV-DNA levels ≥4000 copies/mL, and EBV-DNA data at diagnosis were missing for 22 patients (23.2%).

3.2 Treatment Compliance

Details regarding treatment compliance are summarized in Table 2. Forty-two patients (44.2%) received IC followed by concurrent chemoradiotherapy (CCRT), 22 patients (23.2%) received CCRT alone, and 31 patients (32.6%) underwent radiotherapy alone. Among those who received IC, 2 patients (4.8%) completed one cycle, 14 patients (33.3%) completed two cycles, and 26 patients (61.9%) completed three cycles. Within the IC group (n = 42), 15 patients (35.8%) received one cycle of CCRT and 27 patients (64.3%) received two cycles. In the CCRT alone group, 7 (31.8%) received one cycle and 15 (68.2%) received two cycles. The CCRT completion rates were comparable between patients who received IC (n = 27, 64.3%) and those who did not (n = 15, 68.2%) (p = 0.755). Of the 64 patients treated with CCRT (42 received IC + CCRT and 22 received CCRT alone), 31 (48.4%) received cisplatin-based regimens, 17 (26.6%) received nedaplatin-based regimens, and 16 (25.0%) received lobaplatin-based regimens.

Regarding radiotherapy, 91 patients (95.7%) completed the prescribed treatment course. Four patients did not receive the full dosage: one received 25 fractions, one received 28 fractions, and two received 16 fractions before refusing further treatment. Radiotherapy interruptions were experienced by 53 patients (55.8%), with the interruptions

Table 1. Baseline characteristics of the patients.

Variables	N (%)
Age (years)	
65–69	63 (66.3)
≥70	32 (33.7)
Gender	
Male	64 (67.4)
Female	31 (32.6)
Smoking history	
No	52 (54.7)
Yes	43 (45.3)
Alcohol consumption	
No	77 (81.1)
Yes	18 (18.9)
Histology	
WHO I–II	12 (12.6)
WHO III	83 (87.4)
Tumor stage	
T1	5 (5.3)
T2	20 (21.1)
T3	46 (48.4)
T4	24 (25.3)
Nodal stage	
N0	9 (9.5)
N1	34 (35.8)
N2	35 (36.8)
N3	17 (17.9)
Clinical stage	
I	1 (1.1)
II	12 (12.6)
III	45 (47.4)
IVA	37 (38.9)
ACE-27	
0	32 (33.7)
1	35 (36.8)
2	21 (22.1)
3	7 (7.4)
BMI	
Underweight	17 (17.9)
Normal weight	61 (64.2)
Overweight	16 (16.8)
Obese	1 (1.1)
EBV-DNA status	
<4000 copies/mL	49 (51.6)
≥4000 copies/mL	24 (25.3)
Unknown	22 (23.2)
Chemotherapy	
No	31 (32.6)
CCRT	22 (23.2)
IC+CCRT	42 (44.2)

IC, induction chemotherapy; CCRT, concurrent chemoradiotherapy; EBV, Epstein-Barr Virus; DNA, deoxyribonucleic acid; BMI, body mass index; ACE-27, Adult Comorbidity Evaluation-27; T, tumor; N, nodal; WHO, World Health Organization.

Table 2. Treatment compliance of the patients.

Treatment data	N (%)
Treatment (n = 95)	
IC +CCRT	42 (44.2)
CCRT alone	22 (23.2)
Radiotherapy alone	31 (32.6)
IC cycles (n = 42)	
One cycle	2 (4.8)
Two cycles	14 (33.3)
Three cycles	26 (61.9)
Chemotherapy cycles during CCRT in patients receiving IC (n = 42)	
One cycle	15 (35.7)
Two cycles	27 (64.3)
Chemotherapy cycles during CCRT in patients receiving CCRT alone (n = 22)	
One cycle	7 (31.8)
Two cycles	15 (68.2)
Completion of radiotherapy (n = 95)	
No	4 (4.2)
Yes	91 (95.8)
Radiotherapy interruption (days) (n = 95)	
0	42 (44.2)
<3	27 (28.4)
3–6	16 (16.8)
>6	10 (10.5)
Weight loss during IMRT (kg)	
<5	62 (65.3)
≥5	33 (34.7)

IC, induction chemotherapy; CCRT, concurrent chemoradiotherapy; IMRT, intensity-modulated radiation therapy.

lasting less than 3 days in 27 patients (28.4%), 3–6 days in 16 patients (16.8%), and more than 6 days in 10 patients (10.5%). The median weight loss during IMRT was 4 kg (range, 3–10 kg), with 34.7% of patients (n = 33) experiencing a weight loss of 5 kg or more.

3.3 Treatment Toxicity During Radiotherapy

In the entire cohort (n = 95), 68 patients (71.6%) experienced grade 3–4 adverse events, with some individuals experiencing multiple events. The most frequent grade 3–4 adverse event during IMRT was oral mucositis (n = 33, 34.7%), followed by leucopenia (n = 18, 18.9%), neutropenia (n = 13, 13.7%), thrombocytopenia (n = 12, 12.6%), xerostomia (n = 12, 12.6%), and dermatitis (n = 10, 10.5%). We further compared treatment-related toxicities among the three platinum-based regimens used in CCRT (n = 64) (31 patients of cisplatin-based regimens, 17 patients of nedaplatin-based regimens, and 16 patients of lobaplatin-based regimens) (Table 3). The incidence of grade 1–2 and grade 3–4 toxicities, including leucopenia, neutropenia, anemia, oral mucositis, hepatic dysfunction, and renal dysfunction, was similar across the three groups. However, patients treated with lobaplatin-based (grade 1–2, 18.8% [n = 3]; grade 3–4, 0% [n = 0]) and nedaplatin-based CCRT (grade 1–2, 17.6% [n = 3]; grade 3–4, 5.9% [n = 1]) experienced significantly less grade 1–2 ($p = 0.004$) and grade 3–4 ($p = 0.029$) nausea/vomiting compared to those receiving cisplatin-based CCRT (grade 1–2, 58.1% [n = 18]; grade 3–4, 25.8% [n = 8]). In addition, a higher frequency of grade 1–2 thrombocytopenia was observed in the lobaplatin (n = 7, 43.8%) and nedaplatin groups (n = 7, 41.2%) compared to the cisplatin-based group (n = 5, 16.1%), although this difference was of borderline statistical significance ($p = 0.070$).

3.4 Survival Analysis

The median follow-up duration for the entire cohort was 44 months (range, 5–102 months), while the median follow-up for surviving patients was 52 months (range, 7–102 months). Disease recurrence occurred in 28 patients, including 5 (17.9%) with locoregional recurrence, 18 (64.3%) with distant metastasis, and 5 (17.9%) with both locoregional recurrence and distant metastasis (Fig. 1A). A total of 34 patients died, with 24 (70.6%) deaths due to disease progression, 2 (5.9%) deaths due to other secondary cancers, 5 (14.7%) deaths due to other diseases, and 3 (8.8%) deaths due to complications (mainly malnutrition) (Fig. 1B). The 3-year and 5-year LRFS rates were 88.6%

Table 3. The treatment-related toxicities during concurrent chemoradiotherapy among three platinum-based drugs (n = 64).

Toxicities	Cisplatin (n = 31)		Lobaplatin (n = 16)		Nedaplatin (n = 17)		*p*-value for events grades 1–2	*p*-value for events grades 3–4
	Grade 1–2 (%)	Grade 3–4 (%)	Grade 1–2 (%)	Grade 3–4 (%)	Grade 1–2 (%)	Grade 3–4 (%)		
leucopenia	19 (61.3)	8 (25.8)	8 (50.0)	4 (25.0)	9 (52.9)	4 (23.5)	0.723	0.985
Neutropenia	16 (51.6)	5 (16.1)	7 (43.8)	3 (18.8)	7 (41.2)	3 (17.6)	0.754	0.973
Thrombocytopenia	5 (16.1)	4 (12.9)	7 (43.8)	4 (25.0)	7 (41.2)	3 (17.6)	0.070	0.580
Anemia	24 (77.4)	3 (9.7)	10 (62.5)	2 (12.5)	12 (70.6)	2 (11.8)	0.554	0.950
Nausea/vomiting	18 (58.1)	8 (25.8)	3 (18.8)	0 (0)	3 (17.6)	1 (5.9)	0.004	0.029
Oral mucositis	18 (58.1)	13 (41.9)	9 (56.3)	7 (43.8)	10 (58.8)	7 (41.2)	0.988	0.988
Liver dysfunction	3 (9.7)	0 (0)	2 (12.5)	0 (0)	2 (11.8)	0 (0)	0.950	NA
Kidney dysfunction	2 (6.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.333	NA

NA, not available.

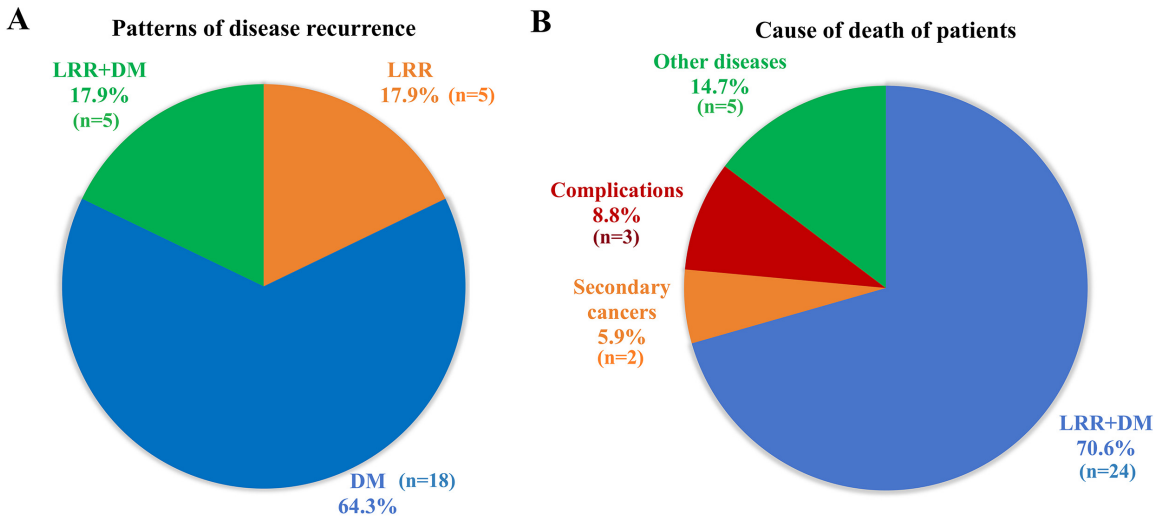

Fig. 1. Patterns of disease recurrence (A) and cause of death (B) in patients with elderly nasopharyngeal carcinoma. LRR, locoregional recurrence; DM, distant metastasis.

and 85.8% (Fig. 2A), respectively; the 3-year and 5-year DMFS rates were 75.3% and 73.1% (Fig. 2B), respectively; the 3-year and 5-year PFS rates were 61.3% and 54.9% (Fig. 2C), respectively; and the 3-year and 5-year OS rates were 72.2% and 66.2% (Fig. 2D), respectively.

3.5 Prognostic Analysis

We first analyzed prognostic factors affecting PFS (Table 4). Univariate analysis identified age, clinical stage, EBV-DNA status, ACE-27 score, and treatment modality as significant prognostic factors for PFS. Gender was also a potential factor ($p = 0.071$). Variables with a p-value < 0.10 in the univariate analysis were entered into the multivariate model, which indicated that age, gender, ACE-27 score, EBV-DNA status, and treatment modality remained independent prognostic factors for PFS. Specifically, patients aged ≥70 years (vs. 65–69 years, hazard ratio [HR] 2.168, 95% confidence interval [CI] 1.100–4.272, $p = 0.025$) ($p = 0.005$, log-rank test) (Fig. 3A), those with an ACE-27 score 2–3 (vs. 0–1, HR 2.163, 95% CI 1.122–4.167, $p = 0.021$) ($p < 0.001$, log-rank test) (Fig. 3B), and those with EBV-DNA levels ≥4000 copies/mL (vs. <4000 copies/mL, HR 2.431, 95% CI 1.112–5.316, $p = 0.026$) ($p = 0.020$, log-rank test) (Fig. 3C) had significantly poorer PFS. Furthermore, patients who did not receive CCRT (vs. CCRT, HR 3.029, 95% CI 1.119–8.197, $p = 0.029$) exhibited worse PFS than those who received CCRT and patients who received IC+CCRT had comparable PFS to those receiving CCRT alone (HR 1.763, 95% CI 0.638–4.869, $p = 0.274$) ($p = 0.051$ among the three treatment groups, log-rank test) (Fig. 4A). However, female patients had significantly better PFS than male patients (HR 0.372, 95% CI 0.168–0.824, $p = 0.015$) ($p = 0.066$, log-rank test) (Fig. 3D).

Finally, we analyzed prognostic factors associated with OS (Table 5). Univariate analysis indicated that age, gender, clinical stage, ACE-27 score, EBV-DNA status, and treatment modality were prognostic factors for OS. Variables yielding a p-value below 0.10 in the univariate analysis were entered into the multivariate model, which indicated that age, gender, ACE-27 score, EBV-DNA sta-

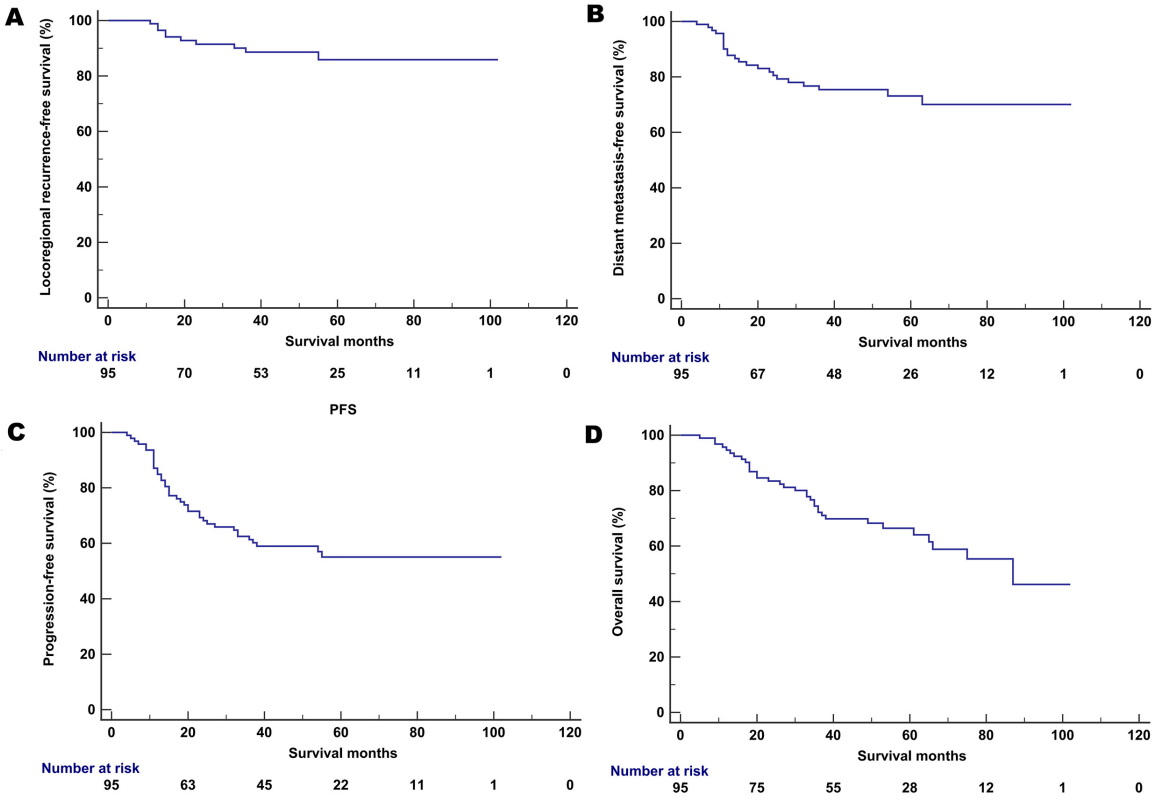

Fig. 2. Locoregional failure-free survival (A), distant metastasis-free survival (B), progression-free survival (C), and overall survival (D) in patients with elderly nasopharyngeal carcinoma.

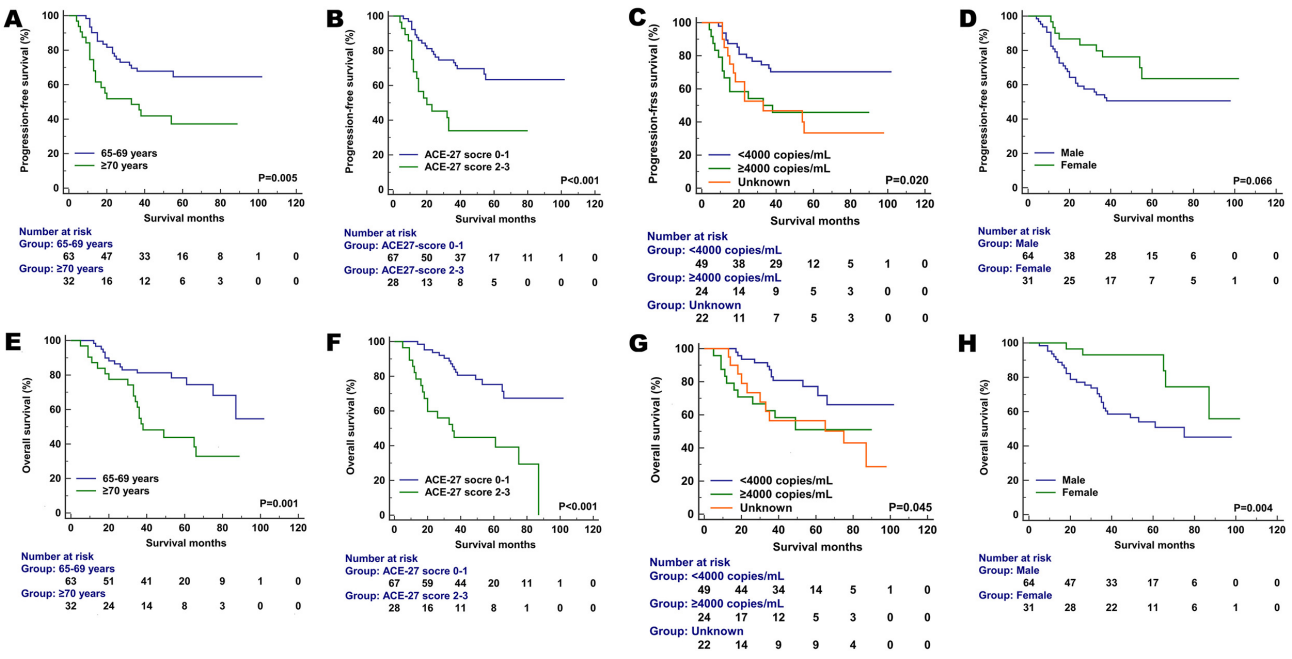

Fig. 3. Kaplan-Meier survival curves according to aged groups (progression-free survival [PFS], A; overall survival [OS], E), Adult Comorbidity Evaluation-27 (ACE-27) status (PFS, B; OS, F), Epstein-Barr Virus-deoxyribonucleic acid levels (PFS, C; OS, G), and gender groups (PFS, D; OS, H).

tus, and treatment modality remained independent prognostic factors for OS. Worse OS were observed in patients aged ≥70 years (vs. 65–69 years, HR 2.438, 95% CI 1.120–5.307, $p = 0.025$) ($p = 0.001$, log-rank test) (Fig. 3E), those

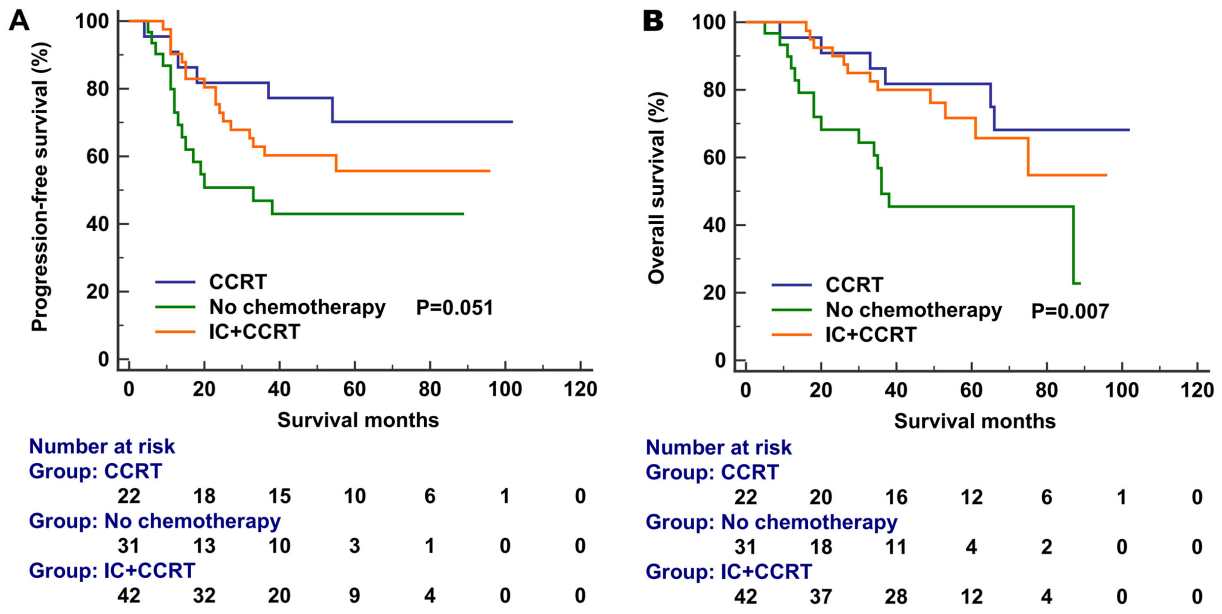

Fig. 4. Kaplan-Meier survival curves of progression-free survival (A) and overall survival (B) curves according to treatment receipt. IC, induction chemotherapy; CCRT, concurrent chemoradiotherapy.

with an ACE-27 score 2–3 (vs. 0–1, HR 3.574, 95% CI 1.695–7.537, $p < 0.001$) ($p < 0.001$, log-rank test) (Fig. 3F), those with EBV-DNA levels ≥4000 copies/mL (vs. <4000 copies/mL, HR 3.345, 95% CI 1.392–8.036, $p = 0.007$) (Fig. 3G) ($p = 0.045$, log-rank test). Furthermore, patients who did not receive CCRT (vs. CCRT, HR 4.435, 95% CI 1.559–12.615, $p = 0.005$) exhibited worse OS than those received CCRT and patients who received IC+CCRT had comparable OS to those receiving CCRT alone (HR 1.355, 95% CI 0.444–4.136, $p = 0.594$) ($p = 0.007$ among the three treatment groups, log-rank test) (Fig. 4B). However, female patients had significantly better OS than male patients (HR 0.130, 95% CI 0.043–0.398, $p < 0.001$) ($p = 0.004$, log-rank test) (Fig. 3H).

To address potential imbalances in baseline characteristics among the treatment groups, IPTW was performed to adjust for age, ACE-27, and EBV-DNA status. Following IPTW adjustment, the ASMD was significantly reduced, indicating well-balanced pretreatment covariates across the groups. After adjustment, patients receiving IC+CCRT did not demonstrate significantly superior survival compared to those receiving CCRT alone in terms of PFS (HR 1.360, 95% CI 0.756–2.446, IPTW-adjusted $p = 0.305$) and OS (HR 1.206, 95% CI 0.619–2.351, IPTW-adjusted $p = 0.582$) after IPTW adjustment (Fig. 5).

3.6 Nomogram Construction

Based on the independent predictors such as age, gender, ACE-27, EBV-DNA status, and chemotherapy regimen, two nomograms were generated to estimate 5-year PFS (Fig. 6A) and OS (Fig. 6B). By assigning weights to each factor according to its regression coefficient, the models convert total scores into an individual's survival probabilities. Discrimination analysis yielded C-indices of 0.747 (95% CI: 0.645–0.849) for PFS and 0.814 (95% CI: 0.759–0.869) for OS. Additionally, calibration curves confirmed good agreement between the predicted survival rates and the actual observed outcomes (**Supplementary Fig. 1**). Since the AJCC staging system is the most widely used clinical tool for prognosis evaluation in current practice, we compared the performance of the novel nomogram against this established standard. The area under the curve (AUC) for the nomogram was significantly higher than that for the 8th AJCC staging system in PFS (0.771 vs. 0.632, $p = 0.029$) and OS (0.845 vs. 0.609, $p < 0.001$) (**Supplementary Fig. 2**). The nomogram was used to calculate cutoff scores for risk stratification. There was a significant difference in the 5-year PFS between the high-risk (>191 points) and low-risk groups (≤191 points) (26.0% vs. 76.9%, $p < 0.001$), showing that high-risk patients had significantly worse survival outcomes (**Supplementary Fig. 3A**). And similarly, the low-risk (≤190 points) patients had significantly better 5-year OS than high-risk (>190 points) group (86.4% vs. 32.2%, $p < 0.001$) (**Supplementary Fig. 3B**). Subsequently, DCA further demonstrated that decision-making guided by this model could significantly improve clinical net benefit (**Supplementary Fig. 4**). These results indicated that the nomograms have good predictive performance.

4. Discussion

In this study, we present a real-world analysis of treatment modalities, compliance, and clinical outcomes in elderly patients with NPC. Our findings indicate that the ma-

Table 4. Univariate and multivariate Cox proportional analysis of independent prognostic factors associated with progression-free survival.

Variables	Univariate			Multivariate		
	HR	95% CI	*p*	HR	95% CI	*p*
Age (years)						
65–69	1			1		
≥70	2.413	1.287–4.524	0.006	2.168	1.100–4.272	0.025
Gender						
Male	1			1		
Female	0.503	0.239–1.061	0.071	0.372	0.168–0.824	0.015
Smoking history						
No	1			—		
Yes	0.878	0.466–1.654	0.687	—	—	—
Alcohol consumption						
No	1			—		
Yes	1.231	0.584–2.594	0.585	—	—	—
Histology						
WHO I–II	1			—		
WHO III	1.851	0.569–6.016	0.306	—	—	—
Tumor stage						
T1–T2	1			—		
T3–T4	1.743	0.769–3.952	0.183	—	—	—
Nodal stage						
N0–1	1			—		
N2–3	1.526	0.800–2.909	0.199	—	—	—
Clinical stage						
I–II	1			1		
III	2.991	0.691–12.954	0.143	2.261	0.462–11.074	0.314
IVA	5.051	1.178–21.663	0.029	3.044	0.612–15.129	0.174
ACE-27						
0–1	1			1		
2–3	2.809	1.491–5.292	0.001	2.163	1.122–4.167	0.021
BMI						
Underweight	1			—		
Normal weight-obese	0.778	0.343–1.767	0.549	—	—	—
EBV-DNA status						
<4000 copies/mL	1			1		
≥4000 copies/mL	2.432	1.143–5.176	0.021	2.431	1.112–5.316	0.026
Unknown	2.517	1.160–5.462	0.019	2.593	1.175–5.721	0.015
Chemotherapy						
CCRT	1			1		
No	2.289	1.130–7.434	0.027	3.029	1.119–8.197	0.029
IC+CCRT	1.647	0.619–4.182	0.294	1.763	0.638–4.869	0.274

IC, induction chemotherapy; CCRT, concurrent chemoradiotherapy; EBV, Epstein-Barr Virus; DNA, deoxyribonucleic acid; BMI, body mass index; ACE-27, Adult Comorbidity Evaluation-27; T, tumor; N, nodal; HR, hazard ratio; CI, confidence interval; WHO, World Health Organization.

jority of elderly patients present with locally advanced NPC (LANPC) and receive IMRT combined with chemotherapy, although compliance with CCRT was relatively low. While CCRT was associated with improved survival, the addition of IC did not confer a significant survival benefit. Our study provides valuable insights into NPC in the elderly population and informs personalized therapeutic strategies aimed at improving both survival and quality of life.

In endemic regions, the incidence rate of NPC rises sharply between the ages of 20–25, peaking at approximately 65 years [1,17]. In large-scale radiotherapy centers, elderly patients account for approximately 5% of NPC

Table 5. Univariate and multivariate Cox proportional analysis of independent prognostic factors associated with overall survival.

Variables	Univariate			Multivariate		
	HR	95% CI	*p*	HR	95% CI	*p*
Age (years)						
65–69	1			1		
≥70	2.929	1.485–5.777	0.002	2.438	1.120–5.307	0.025
Gender						
Male	1			1		
Female	0.271	0.104–0.703	0.007	0.130	0.043–0.398	<0.001
Smoking history						
No	1			—		
Yes	1.030	0.523–2.030	0.932	—	—	—
Alcohol consumption						
No	1			—		
Yes	1.370	0.617–3.043	0.439	—	—	—
Histology						
WHO I–II	1			—		
WHO III	1.571	0.480–5.144	0.456	—	—	—
Tumor stage						
T1–T2	1			—		
T3–T4	1.891	0.782–4.573	0.157	—	—	—
Nodal stage						
N0–1	1			—		
N2–3	1.451	0.724–2.905	0.294	—	—	—
Clinical stage						
I–II	1			1		
III	2.538	0.579–11.119	0.217	2.303	0.465–11.417	0.307
IVA	4.551	1.046–19.799	0.043	3.565	0.709–17.942	0.123
ACE-27						
0–1	1			1		
2–3	3.737	1.899–7.350	<0.001	3.574	1.695–7.537	<0.001
BMI						
Underweight	1			—		
Normal weight-obese	0.524	0.226–1.218	0.133	—	—	—
EBV-DNA status						
<4000 copies/mL	1			1		
≥4000 copies/mL	2.408	1.061–5.465	0.036	3.345	1.392–8.036	0.007
Unknown	2.378	1.037–5.456	0.041	2.849	1.182–6.865	0.020
Chemotherapy						
CCRT	1			1		
No	3.363	1.302–8.683	0.012	4.435	1.559–12.615	0.005
IC+CCRT	1.340	0.499–3.604	0.562	1.355	0.444–4.136	0.594

cases [18]. However, data from the Surveillance, Epidemiology, and End Results reveal that in non-endemic areas, about 10.2% of NPC patients are diagnosed at or after the age of 65 with nonmetastatic disease and received definitive radiotherapy [19]. In our cohort, 12.1% of the patients were elderly. These variations may stem from selection bias and differences in patient population, treatment practices, and epidemiological characteristics across different healthcare settings. Elderly patients with NPC are more likely to seek treatment at local radiotherapy centers rather than large, urban tertiary centers, which could explain the differences in the distribution of elderly NPC cases. This trend also presents challenges for local centers, particularly regarding the delivery of individualized care and the evaluation of treatment outcomes in this population.

The ACE-27 score, which evaluates comorbidities, was a critical factor in our study. Patients with higher ACE-27 scores had poorer outcomes, indicating that comorbidities significantly affect treatment efficacy and survival. These findings highlight the necessity of shifting to-

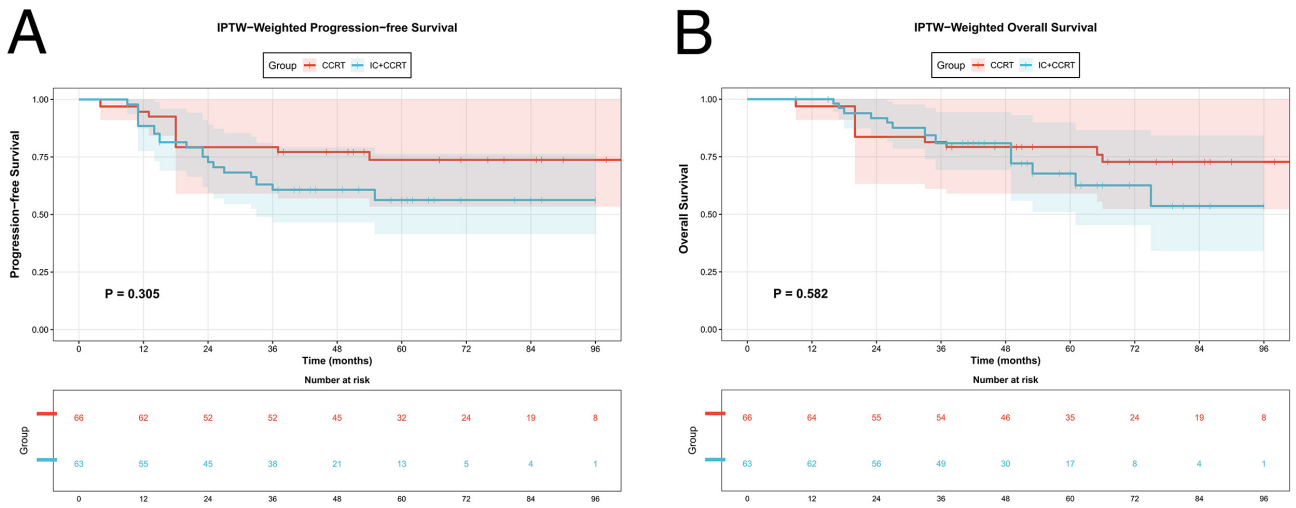

Fig. 5. Kaplan-Meier survival curves of progression-free survival (A) and overall survival (B) curves according to treatment receipt after inverse probability of treatment weighting (IPTW) adjustment. The numbers at risk are IPTW-weighted numbers at risk. IC, induction chemotherapy; CCRT, concurrent chemoradiotherapy.

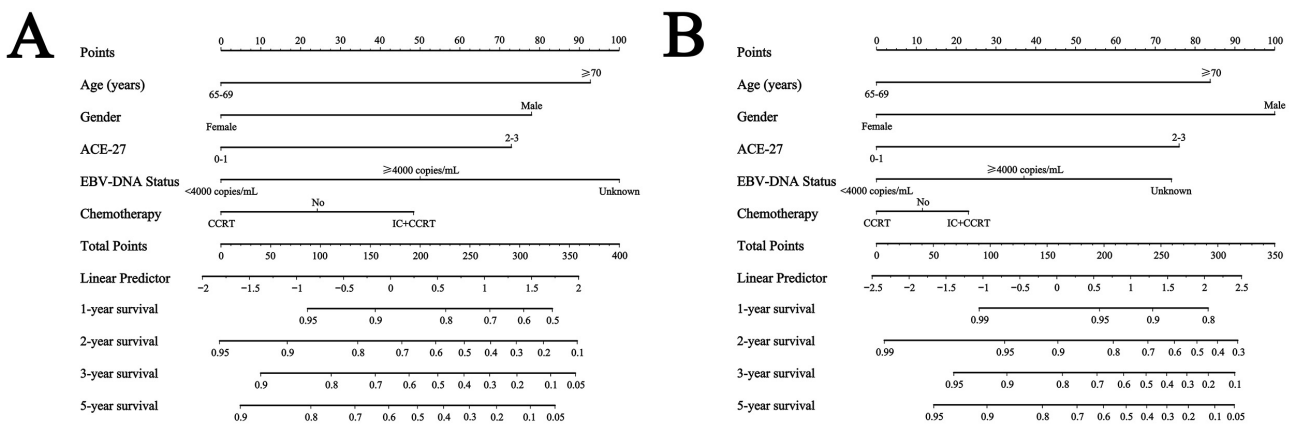

Fig. 6. Nomogram for prognostic prediction of progression-free survival (A) and overall survival (B).

ward person-centered, individualized treatment models for older adults. Comorbidities must be specifically taken into consideration during clinical decision-making, as they are known to significantly influence treatment tolerance and overall prognosis. Future management strategies should incorporate comprehensive geriatric assessments to tailor interventions to specific health profile of each patient, thereby optimizing the balance between therapeutic benefit and the risk of adverse effects.

Advancements in screening techniques have improved the detection rate of early-stage NPC [20]. Currently, approximately 80% of patients are diagnosed with LANPC [21]. Although several previous studies have suggested that the distribution of tumor stages among elderly patients aligns with that of the general population [3,5], our study found that 86.3% of elderly patients present with LANPC. This higher prevalence of advanced disease in the elderly may be attributed to delayed diagnosis or more rapid disease progression.

Elderly patients often experience metabolic changes and have a higher burden of comorbidities, predisposing them to increased treatment-related toxicities. Reduced organ function can alter the pharmacokinetics of chemotherapeutic agents, rendering toxicities less predictable [22]. A previous study indicated that among elderly NPC patients treated with IMRT, 7.9% of deaths were attributable to preventable treatment-related factors, specifically poor nutritional status and psychological condition [18]. However, no clear consensus exists regarding the optimal treatment for elderly NPC. Treatment decisions should be individualized, taking into account performance status, nutritional status, organ function, comorbidities, social support, and treatment goals [23]. For “fit” elderly patients, standard treatment including IMRT and chemotherapy may be appropriate. “Marginally fit” patients might benefit from IMRT alone, while “unfit” patients could receive optimized symptom management with or without palliative radiotherapy [23].

Our study observed a relatively high completion rate of IC, with no significant difference in the completion rate of chemotherapy during CCRT compared to CCRT alone. This suggests that the addition of IC did not substantially impair the patient's ability to complete the full course of CCRT, an important consideration given the potential for increased toxicity and treatment burden in elderly patients. However, it is noteworthy that the completion of recommended chemotherapy during CCRT was lower than that observed in younger populations [24,25]. A previous study demonstrated that radiotherapy interruptions of ≥5 days (occurring in 23.5% of patients) were associated with poorer LRFS [26]. In our study, the radiotherapy completion rate was relatively high, with only 18.9% of patients experiencing interruptions of ≥7 days. Additionally, the degree of weight loss was consistent with previous reports, with 63% of patients experiencing ≥5% weight loss [27]. Therefore, for elderly NPC patients, comprehensive nutritional and organ function assessments should be integrated into the treatment workflow, ensuring timely monitoring and appropriate interventions to optimize outcomes.

Due to variations in incidence rates and treatment modalities, there is no unified standard for prognostic factors in elderly NPC. Mi et al. [28] identified tumor stage as an independent prognostic factor affecting PFS and OS, although their study did not account for the ACE-27 or EBV-DNA status. Lyu et al. [29] found that age was an independent prognostic factor for OS, but staging, age-related comorbidity index score, and EBV-DNA status did not significantly impact survival. Kou et al. [30] reported that EBV-DNA status, T stage, N stage, and albumin levels were independent prognostic factors affecting PFS in patients. Our study highlights several key prognostic factors for elderly NPC patients. Age, particularly over 70 years, was identified as a significant negative prognostic factor for both PFS and OS, likely reflecting a general decline in physical health and reduced treatment tolerance. EBV-DNA levels, a known biomarker for NPC, were also identified as independent prognostic factors for both PFS and OS. Patients with EBV-DNA levels >4000 copies/mL had significantly poorer survival outcomes, suggesting that this biomarker can aid in risk stratification and personalized treatment planning [31,32]. Gender differences were evident in our study, with female patients demonstrating better PFS and OS compared to males, a finding consistent with previous findings and potentially attributable to hormonal factors, better overall health, and higher treatment compliance [33,34].

The optimal treatment modality for elderly NPC remains controversial. Lu et al. [35] found no significant association between chemotherapy and PFS or OS. Mi et al. [28] reported that combining IMRT with chemotherapy did not improve survival outcomes compared to IMRT alone, although it resulted in higher grade 3 gastrointestinal and hematological toxicities. Their study included various chemotherapy subgroups, complicating the evaluation of the role of chemotherapy. Lyu et al. [29] also suggested that for patients aged ≥70 years, OS was similar between those receiving IMRT alone and those receiving IMRT plus chemotherapy. However, their chemotherapy group included both IC and adjuvant chemotherapy, making it difficult to assess the value of sequential chemotherapy. Wang et al. [36] found that CCRT significantly improved survival outcomes compared to IMRT alone in elderly patients (aged ≥60 years) with stage II NPC, without added late complications. Conversely, Miao et al. [37] did not observe a survival benefit in elderly patients (aged ≥60 years) who received CCRT compared to those who underwent IMRT alone. Kou et al. [30] reported that radiotherapy combined with chemotherapy improved PFS and OS for patients with a Charlson Comorbidity Index (CCI) of 2 and high-risk disease. Our study found that patients receiving chemotherapy had better survival outcomes, but adding IC to CCRT did not further improve the outcomes. Wu et al. [38] also found that survival outcomes with IC+CCRT were comparable to those with CCRT alone. Chen et al. [39] observed that adding IC to CCRT did not improve survival outcomes in elderly NPC patients but was associated with significant toxicities. According to previous studies [40,41], the IC+CCRT group exhibited increased CCRT compliance as well as higher rates of grade 3–4 gastrointestinal and hematological toxicities compared to the CCRT alone group. Consequently, it is crucial to screen for risk factors associated with treatment-related adverse events and to manage modifiable variables before therapy. While IMRT remains the standard of care for elderly patients with NPC, the inclusion of chemotherapy requires careful deliberation given the risk of potential toxicity.

Further exploration of highly effective and low-toxicity treatment options is warranted for elderly NPC. A previous prospective study has shown that lobaplatin-based CCRT results in lower gastrointestinal toxicity, nephrotoxicity, and weight loss compared to cisplatin-based CCRT in patients aged 18–60 years [42]. Our small-scale study found that lobaplatin-based CCRT as the primary treatment yielded favorable short-term survival outcomes and acceptable toxicity in elderly NPC patients, with 3-year LRFS, DMFS, PFS, and OS rates of 95.8%, 85.7%, 82.5%, and 100%, respectively [43]. Our phase II clinical trial on lobaplatin-based CCRT in elderly NPC is ongoing. In the current study, patients receiving lobaplatin-based or nedaplatin-based CCRT experienced significantly lower rates of nausea and vomiting compared to those receiving cisplatin-based CCRT. This finding is clinically highly relevant for geriatric oncology, as superior tolerability can significantly impact nutritional status, treatment compliance, and overall quality of life in older adults. Therefore, a personalized approach, weighing the risk of specific toxicities against the potential need for more intensive monitoring in the elderly, is warranted. Furthermore, findings from a con-

temporary prospective trial indicate that concurrent nimotuzumab alongside IMRT is both effective and tolerable for elderly individuals presenting with LANPC. Specifically, the study reported 5-year LRFS, DMFS, PFS, and OS rates of 89.4%, 86.4%, 76.5%, and 78.8%, respectively, while grade 3 mucositis was observed in 33% of the cohort [44]. Moreover, a phase 3 randomized clinical trial demonstrated that in patients with LANPC, toripalimab (a programmed death-1 inhibitor) combination therapy without concurrent cisplatin was a feasible treatment option, offering higher failure-free survival, improved quality of life, and lower toxicity [45]. Therefore, whether immunotherapy can serve as a viable alternative to chemotherapy in elderly patients with NPC represents a promising direction for future investigation.

Several limitations of this study should be acknowledged. First, the retrospective design introduces potential selection bias in treatment allocation. Second, the sample size is relatively small, and the follow-up period is relatively short. Finally, the accuracy of adverse event assessment may be limited in retrospective studies, potentially leading to an incomplete evaluation of patient toxicities.

5. Conclusion

In conclusion, our study indicates that while the completion rate of recommended radiotherapy is high, survival outcomes in elderly patients with NPC remain suboptimal. CCRT significantly improves survival outcomes compared to radiotherapy alone, while combining IC with CCRT did not yield superior survival outcomes over CCRT alone. These findings underscore the importance of individualized treatment planning and the necessity of considering the overall health status of elderly NPC patients in clinical practice. Future research should focus on refining treatment approaches to enhance outcomes in this challenging patient population.

Key Points

• This real-world study focused on elderly NPC patients (≥65 years), a vulnerable population with poorer outcomes, analyzing treatment patterns, compliance, and survival.

• Treatment was diverse: 44.2% received IC+CCRT, 23.2% CCRT alone, and 32.6% radiotherapy alone; high radiotherapy compliance (95.7%) was achieved.

• Survival outcomes were suboptimal, with 5-year PFS and OS rates of 54.9% and 66.2%, respectively.

• Independent prognostic factors for poorer survival included age ≥70, male, higher comorbidity burden, elevated EBV-DNA, and not receiving CCRT.

• The addition of IC to CCRT did not improve outcomes compared with CCRT alone.

• The findings emphasize the critical need for individualized treatment strategies tailored to the overall health status of elderly NPC patients.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding authors upon reasonable request.

Author Contributions

ZZL: Data curation, Formal analysis, Writing—original draft. LFG: Data curation, Formal analysis, Writing—original draft. ZQY: Data curation, Formal analysis, Writing—original draft. YFY: Data curation, Formal analysis, Investigation, Methodology. SGW: Supervision, Visualization, Funding acquisition. YML: Supervision, Visualization, Resources, Project administration. All authors contributed to revising the manuscript critically for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study received ethics approval from the Institutional Review Boards of The First Affiliated Hospital of Xiamen University (No. XMFHIIT-2025SL268). The requirement for written informed consent was waived for the following justifications: (1) the research involved no more than minimal risk to subjects; (2) the waiver did not adversely affect the rights and welfare of the subjects; (3) the research could not practicably be conducted without the waiver; and (4) adequate provisions were in place to protect the privacy of subjects and the confidentiality of data, in accordance with the Declaration of Helsinki. To ensure privacy, all personally identifiable information was removed from the dataset before analysis. Consequently, all analyses were conducted exclusively on anonymized data. The study was conducted in accordance with the principles of the Declaration of Helsinki.

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Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/BJHM56190.

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