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RESEARCH

Long-term results of locoregionally advanced nasopharyngeal carcinoma treated with cisplatin and 5-fluorouracil induction chemotherapy with or without docetaxel in young and middle aged adults

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Abstract

Purpose This study aims to evaluate the efficacy and toxicity of the two induction chemotherapy (IC) regimens (TPF: docetaxel, cisplatin and 5-fluorouracil, and PF: cisplatin and 5-fluorouracil) combined with radiotherapy in young and middle aged patients with locoregionally advanced nasopharyngeal carcinoma (LA-NPC).

Methods A retrospective analysis was conducted on 329 cases with stage III-IVA nasopharyngeal carcinoma from September 2005 to February 2017. Of the 329 cases, 253 cases underwent TPF (docetaxel: 60 mg/m^2 on day 1, cisplatin: 25 mg/m^2 on days 1–3, 5-fluorouracil: 500 mg/m^2 on days 1–5, intravenous 120-h infusion), while 76 cases received the PF regimen (cisplatin: 25 mg/m^2 on days 1–3, 5-fluorouracil: 500 mg/m^2 on days 1–5, intravenous 120-h infusion) every 3 weeks. Radiotherapy was administered after IC with or without concurrent chemotherapy. The survival rates were assessed by Kaplan–Meier analysis, and the survival curves were compared using a log-rank test.

Results The 5-year and 8-year overall survival (OS) rates of the PF group and TPF group were 80.1% and 72.1%, 87.3% and 78.4% respectively ($p = 0.405$). There were no statistical differences in regional recurrence-free survival (RRFS) and distant metastasis-free survival (DMFS) rates between PF and TPF groups($p = 0.585$ and 0.500, respectively).The 5-year and 8-year estimated local recurrence free survival (LRFS) rates for patients in PF and TPF group were 91.1% and 78.0%, 96.2% and 93.7%, respectively ($p = 0.026$). Moreover, The OS, LRFS, RRFS and DMFS rates were comparable between the non CCRT or CCRT subgroup ($p = 0.542$, 0.319, 0.070, 0.986, respectively). Compared with PF group, the TPF group significantly increased the occurrence of grade 3 or 4 neutropenia and leukopenia ($p < 0.001$).

Conclusion PF and TPF followed by radiotherapy with or without concurrent chemotherapy performed encouraging antitumor effects in LA-NPC, there was no statistical significance in 5-year and 8-year OS, RRFS, and DMFS rates between two chemotherapy regimens. Compared with PF, TPF induction chemotherapy achieved more satisfactory LRFS rate in LA-NPC with acceptable toxicity.

Keywords Nasopharyngeal Carcinoma (NPC) · Induction Chemotherapy (IC) · TPF · PF

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Introduction

Compared with early stage nasopharyngeal carcinoma (NPC), locoregionally advanced NPC (LA-NPC) is associated with high risk of local–regional recurrence and distant metastasis, which is the primary cause of treatment failure. Studies over past decades disclosed that 63.3–81.6% of Chinese NPC has developed into locoregionally advanced disease at the time of pathological confirmed (Jiang et al. 2015; Ou et al. 2015; Zhao et al. 2016; Wu et al. 2017; Au et al. 2018; Xu et al. 2021). After treated with multimodality therapy, patients diagnosed with LA-NPC Querysuffered metastasis in approximately 15.2–22.7%, and 9.0–22.2% of patients eventually developed locoregional recurrences (Jamshed et al. 2014; Kong et al. 2018; Yang et al. 2019; Xu et al. 2023). Treatment outcomes for LA-NPC remain unsatisfactory, different treatment methods are being explored to improve the efficacy.

Induction chemotherapy (IC) followed by radiotherapy (RT) has recommended as category 1 for T3-4N1-3M0 or T1-4N2-3M0 NPC in the National Comprehensive Cancer Network guidelines (version 3. 2024). IC holds significant advantages of acquiring better overall survival (OS) and progress free survival (PFS) in LA-NPC (Nazeer et al. 2022; Zhang et al. 2022), which may own to better treatment tolerability and early eradication of micro metastasis. Chemotherapy administered before initiation of radiotherapy could relieve the patient's symptoms, shrink tumor load, increase the distance between tumor and critical organs at risk and reduce incidence of radiation-induced toxicity (Kong et al. 2022). Platinum-based chemotherapy regimens are standard of care for patients with LA-NPC (Du et al. 2013; Wu et al. 2018, 2020; Tao et al. 2021). Li et al. reported that TPF followed by concurrent chemoradiotherapy (CCRT) group significantly improved 5-year failure-free survival (77.4% vs. 66.4%, P = 0.019), 5-year OS (85.6% vs. 77.7%, P = 0.042), 5-year distant failure-free survival (88.0% vs. 79.8%, P = 0.030), and 5-year locoregional failure-free survival (90.7% vs. 83.8%, P = 0.044) in stage LA-NPC (excluding N0 disease) compared with the CCRT alone group (Li et al. 2019). Similarly, Cao et al. found that induction cisplatin plus fluorouracil (PF) followed by CCRT achieved higher 3-year disease-free survival rate (82.0%, 95% CI = 0.77–0.87) than the CCRT alone arm (74.1%, 95% CI = 0.68–0.80, P = 0.028) (Cao et al. 2017). In Hong Kong, a randomized phase II trial reported that the 3-year progression-free survival rates for docetaxel and cisplatin (TP) plus CCRT versus CCRT alone arm were 88.2% and 59.5% (HR = 0.49, 95% CI = 0.20–1.19, P = 0.12). The 3-year OS rate for TP plus CCRT versus CCRT alone arm were 94.1% and 67.7% (HR = 0.24, 95% CI = 0.078–0.73, P = 0.012) (Hui et al. 2009). Gemcitabine plus cisplatin (GP) showed its superiority as IC regimen in later randomized phase III trial NCT01872962. Patients received induction chemotherapy with GP had better 3-year OS than those in CCRT alone group (94.6% vs. 90.3%, HR = 0.43, 95% CI = 0.24–0.77). The 3-year recurrence-free survival was 85.3% in GP followed by CCRT group and 76.5% in the CCRT alone group (P = 0.001) (Zhang et al. 2019a, b). Currently, several studies directly compared the efficacy and safety profiles during different IC regimens were reported. Zhu et al. found that in LA-NPC, the GP induction chemotherapy regimen was comparable to TPF in treatment outcomes (Zhu et al. 2019). Jin et al. conducted a multi-center, open-label, randomized, non-inferiority trial and revealed that there was no statistically significant difference in PFS between the TPF and PF induction chemotherapy in stage III-IV NPC (without distant metastases) (Jin et al. 2019). Peng et al. found that TPF plus CCRT and TP plus CCRT achieved significantly better OS and DFS than PF plus CCRT alone in stage III-IVA NPC (P = 0.045 and P = 0.029, respectively), while PF regimen achieved the lowest grade 3–5 toxicities (Peng et al. 2021a, b). The efficacy and safety for different IC regimen are still inconsistent. Hence, the optimal IC regimen is still not established (De Felice et al. 2022).

With the prolongation of survival, RT-related toxicities, such as xerostomia, mucositis, dysphagia and osteoradionecrosis are gradually attracted attention in clinical management (De Felice et al. 2016; Koch et al. 2025). RT-related toxicity prediction relies heavily on dosimetric parameters of radiotherapy, clinical factors and treatment compliance at present. An increasing interest was shown in identifying potential biomarkers for significant toxicities prediction (Koch et al. 2025).

In general, the choice of IC regimens should be made on the balance of improving survival and reducing treatment-related toxicity. In this study, we aimed to retrospectively evaluate the treatment outcomes and side effects of different IC regimens (PF vs. TPF) plus RT in LA-NPC patients.

Materials and methods

Patients

The current retrospective study reviewed the patients with pathologically confirmed non-metastatic NPC at Fudan University Shanghai Cancer center from September 2005 and February 2017. There were the inclusion criteria: (1) NPC confirmed by histopathology; (2) stage III-IVA disease; (3) age 22–55 years; (4) Karnofsky score more than 70; (5) received PF or TPF induction chemotherapy; (6) adequate organ function and hematologic function. The exclusion

criteria were as follows: (1) evidence of distant metastasis; (2) other previously diagnosed or concomitant cancer; (3) prior radiotherapy to the head and neck region; (4) presence of an uncontrolled concomitant illness. For this trial, the 8th Edition of American Joint Committee on Cancer (AJCC) staging system was used to re-staged all enrolled patients according to initial magnetic resonance imaging (MRI) imageological examination of the nasopharynx. Positron Emission Tomography-Computed Tomography (PET-CT) or a combination of chest CT, abdominal ultrasound/CT/MRI and bone scintigraphy were performed to exclusion of metastasis. The study was approved by our institutional Ethics Review Board and all patients signed a written consent.

Chemotherapy

Enrolled patients received TPF (docetaxel: 60 mg/m^2 on day 1; cisplatin: 25 mg/m^2/day on day 1- day 3; 5-fluorouracil: 500 mg/m^2/day on day 1- day 5, given in a 120-h continuous intravenous infusion) or PF (cisplatin: 25 mg/m^2 on day 1- day 3; 5-fluorouracil: 500 mg/m^2 on day 1- day 5, given in a 120-h continuous intravenous infusion) regimens during induction course. RT was implemented 3 weeks after IC. Concurrent chemotherapy consisted of cisplatin 30 mg/m^2 weekly during RT. Four weeks after the completion of RT without CCRT, AC consistent with previous regimen was administered for tolerable patients. Blood routine and blood biochemical parameters were examined before each chemotherapy cycle. The IC/AC was scheduled every 3 weeks based on well tolerance and eligible hematological examination. Otherwise, the next course will be cancelled or postponed until hematologic parameters of patients were qualified. Furthermore, the dose of the next cycle would be reduced by 20% in case of grade 4 hematological toxicity.

Radiotherapy

Patients were immobilized by a head, neck and shoulders mask in supine position. Intravenous contrast-enhanced CT planning scans were performed and contiguous slices 5 mm thick were obtained from the vertex to 2 cm below the clavicle head. The gross tumor volume (GTV) was defined as all primary nasopharyngeal tumors and metastasis lymph nodes determined by imaging and clinical findings. Clinical target volume (CTV) included GTV and subclinical lesions, which divided into CTV1 and CTV2. CTV1 included the nasopharynx, retropharyngeal lymph node, skull base, anterior one-third of the clivus, pterygoid fossae, parapharyngeal space, inferior sphenoid sinus, posterior one-third of the nasal cavity and maxillary sinus, upper neck lymphatic region and lower neck lymphatic region with positive lymph nodes. CTV2 included lower neck lymphatic region without positive lymph nodes. Finally, 5 mm expansion on the basis of the CTV was outlined as planning target volume (PTV) and then modified. According to T classification, the prescribed dose of primary tumor was 66 Gy/30 fractions and 70.40 Gy/32 fractions for T1-2 and T3-4, respectively. The prescribed dose was 66 Gy for positive cervical lymph nodes, 60 Gy for high-risk area and 54 Gy for low-risk area in the same fraction of the primary tumor. All patients received irradiation 5 days per week, one fraction daily.

Assessment and follow-up

Patients were assessed weekly during radiation therapy. After treatment completion, follow-ups occurred every 3 months for the first 2 years, every 6 months during the year 3–5 and annually thereafter. Routine follow-up included medical history, nasopharyngoscopy and physical examination. Enhanced MRI of the nasopharynx was performed every 6–12 months. Chest CT and abdominal ultrasonography were conducted once yearly. Additional tests were ordered whenever there was any clinical indication. Acute and late RT-related toxicities were graded according to the Radiation Therapy Oncology Group (RTOG).

Statistics

SPSS 26.0 (SPSS Inc, Chicago, IL, USA) software was used for statistical analysis in this study. Chi-square test for occurrence rates and categorical variables. They were performed in the baseline comparison, Student's t test for continuous variables and Rank Sum test for ordinal categorical variable. The overall survival (OS), local recurrence free survival (LRFS), regional recurrence free survival (RRFS) and distant metastasis free survival (DMFS) rates were estimated by Kaplan–Meier method. Survival differences between groups were calculated with log-rank tests. A two-sided $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

Between September 2005 and February 2017, a total of 329 patients were newly diagnosed as LA-NPC and received IC plus CCRT (n = 59) or IC plus RT ± AC (n = 270) were analyzed. This study enrolled 241 males and 88 females (male: female≈2.74: 1), 253 patients received TPF regimen chemotherapy while 76 patients received PF. In total, 90 patients were classified as T4, of which 19 patients (25.0%) in PF group and 71 patients (28.1%) in TPF group. One hundred and seven patients were diagnosed with N3 stage, of which 20 patients (26.3%) in PF group and 87 patients (34.4%) in TPF group. Thirty-seven patients (48.7%) were

diagnosed with stage IVA in PF group and 145 (57.3%) in TPF group. There were no statistic differences in distribution of T stage, N stage and clinical stage between PF and TPF groups (p = 0.618, 0.377 and 0.185, respectively).

Completion of treatment

All patients received IC in this study. In PF and TPF group, there were 59 patients (77.6%) and 233 patients (92.1%) completed two cycles of IC, respectively; 8 patients (10.5%) and 9 patients (3.6%) completed three cycles of IC, respectively; 3 patients (4.0%) and 3 patients (1.2%) completed four cycles of IC, respectively; and 6 patients (7.9%) and 8 patients (3.2%) only underwent one course of IC due to grade 4 myelosuppression with a poor personal performance. All patients completed radical radiotherapy, except for one patient in TPF group who discontinued radiotherapy for non-medical reasons at doses of 63.8 Gy/29F. Forty patients (52.6%) in the PF group and 175 patients (69.2%) in the TPF group received RT ± AC.

Survival analysis

The median follow-up time was 75 (range, 8–183) months, which were 70 (range, 8–183) months and 77 (range, 8–153) months for PF and TPF groups, respectively. By the last follow-up visit, 71 (21.6%) patients died, the causes of death were as follows: 17 patients died from recurrence, 31 patients died from metastasis, 10 patients died from recurrence and metastasis, 3 patients died from second primary tumor and 10 patients died from non-neoplastic diseases, unexplained deaths or treatment complications, distant metastasis is the commonest site of failure.

The 5-year and 8-year estimated OS rates for the whole group were 85.7% and 77.0%, which were 80.1% and 72.1%, 87.3% and 78.4% for patients in PF and TPF group, respectively (p = 0.405; Table 1). The 5-year and 8-year estimated OS rates for patients with classifications of T1-3 and T4 were 87.8% and 80.8%, 80.0% and 66.9%, respectively (p = 0.007; Table 1). The 5-year and 8-year estimated OS rates for patients with classifications of N0-2 and N3 were 88.7% and 82.4%, 79.4% and 65.6%, respectively (p = 0.008; Table 1). The 5-year and 8-year estimated OS rates for patients with classifications of stage III and stage IVA were 91.1% and 86.3%, 81.3% and 69.6%, respectively (p = 0.001; Table 1). The 5-year and 8-year estimated LRFS rate for the whole group were 95.0% and 90.5%, which were 91.1% and 78.0%, 96.2% and 93.7% for patients in PF and TPF group, respectively (p = 0.026; Table 2). The 5-year and 8-year estimated LRFS rates for patients with classifications of T1-3 and T4 were 97.2% and 93.2%, 89.2% and 83.2%, respectively (p = 0.004; Table 2). The 5-year and 8-year estimated RRFS rates for the whole group were 96.7% and 87.9%, which were 94.2% and 83.7%, 97.4% and 89.1% for patients in PF and TPF group, respectively (p = 0.585; Table 3). The 5-year and 8-year estimated RRFS rates for patients with classifications of N0-2 and N3 were 98.1% and 91.1%, 93.8% and 80.4%, respectively (p = 0.022; Table 3). The 5-year and 8-year estimated DMFS rates for the whole group were 91.3% and 84.9%, which were 87.9% and 87.9%, 92.3% and 84.4% for patients in PF and TPF group, respectively (p = 0.500; Table 4). The 5-year and 8-year estimated DMFS

Table 2 The 5-year and 8-year estimated local recurrence free survival rate among various groups

		Cases	5-year	8-year	p
T stage	T1-3	14/239	97.2	93.2	**0.004**
	T4	14/90	89.2	83.2	
Chemotherapy strategy	non-CCRT	22/270	95.2	91.7	0.319
	CCRT	6/59	94.4	81.4	
Chemotherapy regimens	PF	11/76	91.1	78.0	**0.026**
	TPF	17/253	96.2	93.7	

Bold means p < 0.05, difference between groups was statistically significant

Table 1 The 5-year and 8-year estimated overall survival rate among various groups

		Cases	5-year (%)	8-year(%)	p value
T stage	T1-3	42/239	87.8	80.8	**0.007**
	T4	29/90	80.0	66.9	
N stage	N0-2	39/222	88.7	82.4	**0.008**
	N3	32/107	79.4	65.6	
Stage	III	19/147	91.1	86.3	**0.001**
	IVA	52/182	81.3	69.6	
Chemotherapy strategy	non-CCRT	62/270	85.9	76.2	0.542
	CCRT	9/59	84.4	84.4	
Chemotherapy regimens	PF group	18/76	80.1	72.1	0.405
	TPF group	53/253	87.3	78.4	

Bold means p < 0.05, difference between groups was statistically significant

Table 3 The 5-year and 8-year estimated regional recurrence free survival among various groups

		Case	5-year	8-year	p value
N stage	N0-2	17/222	98.1	91.1	**0.022**
	N3	15/107	93.8	80.4	
Chemotherapy strategy	non-CCRT	25/270	96.8	89.1	0.070
	CCRT	7/59	96.4	80.7	
Chemotherapy regimens	PF	8/76	94.2	83.7	0.585
	TPF	24/253	97.4	89.1	

Bold means $p < 0.05$, difference between groups was statistically significant

Table 4 The 5-year and 8-year estimated distant metastasis free survival among various groups

		Cases	5-year	8-year	p value
T stage	T1-3	31/239	91.9	87.8	**0.031**
	T4	20/90	89.5	77.1	
N stage	N0-2	22/222	94.9	91.3	**< 0.001**
	N3	29/107	83.7	71.6	
Stage	III	11/147	95.2	94.1	**< 0.001**
	IVA	40/182	88.1	77.6	
Chemotherapy strategy	non-CCRT	44/270	92.0	84.8	0.986
	CCRT	7/59	87.9	87.9	
Chemotherapy regimens	PF	10/76	87.9	87.9	0.500
	TPF	41/253	92.3	84.4	

Bold means $p < 0.05$, difference between groups was statistically significant

Table 5 The 5-year and 8-year estimated survival rate among non-CCRT and CCRT groups

		cases	5-year	8-year	p value
OS	non-CCRT	62/270	85.9	76.2	0.542
	CCRT	9/59	84.4	84.4	
LRFS	non-CCRT	22/270	95.2	91.7	0.319
	CCRT	6/59	94.4	81.4	
RRFS	non-CCRT	25/270	96.8	89.1	0.070
	CCRT	7/59	96.4	80.7	
DMFS	non-CCRT	44/270	92.0	84.8	0.986
	CCRT	7/59	87.9	87.9	

Bold means $p < 0.05$, difference between groups was statistically significant

Table 6 The adverse effects among PF and TPF groups

Adverse Effects	TPF group (%)	PF group (%)	P
During IC			
Grade 3–4 leukopenia	24.9 (63/253)	3.9 (3/76)	**0.000**
Grade 3–4 neutropenia	37.5 (95/253)	5.2 (3/76)	**0.000**
Liver dysfunction	4.3 (11/253)	2.6 (2/76)	0.736
Renal dysfunction	0.8 (2/253)	0.0 (0/76)	1.000
During RT			
Grade 3–4 mucosal reaction	28.5 (72/253)	22.4 (17/76)	0.295
Median weight loss	9.1 (0–26.7)	9.0 (0–27.9)	0.273
Median intravenous nutritional support duration (days)	3 (0–20)	3 (0–14)	0.471

Bold means $p < 0.05$, difference between groups was statistically significant

rates for patients with classifications of T1-3 and T4 were 91.9% and 87.8%, 89.5% and 77.1%, respectively ($p = 0.031$; Table 4). The 5-year and 8-year estimated DMFS rates for patients with classifications of N0-2 and N3 were 94.9% and 91.3%, 83.7% and 71.6%, respectively ($p < 0.001$; Table 4). The 5-year and 8-year estimated DMFS rates for patients with classifications of III and IVA stage were 95.2% and 94.1%, 88.1% and 77.6%, respectively ($p < 0.001$; Table 4). Finally, the 5-year and 8-year OS, LRFS, RRFS and DMFS rates were similar in with or without CCRT subgroups ($p = 0.542$, 0.319, 0.070 and 0.986, respectively; Table 5).

Treatment complications

No treatment-induced death occurred in the whole group. During IC, most common adverse event of grade 3 or 4 were neutropenia in 98 patients (29.8%) followed by leukopenia in 66 patients (20.1%). Those received TPF course had a higher incidence of grade 3 or 4 adverse event, with neutropenia in 95 patients (37.5%), leukopenia in 63 patients (24.9%). Thrombopenia rate was low and mainly in grade 1 or 2. The incidence of liver and renal dysfunction were also rare. The acute and late RT toxicities were recorded in accordance with the RTOG. The incidence of grade 3–4 mucositis during radiotherapy was 28.5% and 22.4% in TPF and PF group, respectively ($p = 0.295$). A total of 182 patients received fluid support in the entire group, with a median fluid support duration of 3 days (ranging from 0 to 20 days), and a median weight loss rate of 9.0% (ranging from 0–27.9%). None of the case required gastric tube placement (Table 6).

Late reactions included grades 3–4 xerostomia, hearing loss and dental caries, with respective incidence of 4.3%, 11.1% and 19.4%. There were 13 cases of cranial neuropathy, 7 cases of temporal lobe necrosis, and 13 cases of secondary primary tumors.

Discussion

NPC owns sensitive response to radiotherapy and chemotherapy. With the progression of imaging and radiation technology, a significantly higher overall survival rate for NPC patients was observed in the era of IMRT. The existed researches showed that the 5-year OS rates were 82.0%−93.0% for LA-NPC using IMRT as radiation treatment. The primary failure pattern was distant metastasis, followed by local and regional recurrence (Li et al. 2019; Xia et al. 2019; Wang et al. 2020). A greater improvement of locoregional control with IMRT was demonstrated. It's mainly due to the reduction of locoregional recurrence in NPC patients by delivering a higher and more accurate dose to tumor target while conforming a low dose to normal tissues (Lai et al. 2011). The prognosis of LA-NPC is also related to T and N category. It has been revealed in HKNPCSG 1301 study from Hong Kong that IMRT yields excellent 8-year LRFS rates of 87.2–91.7% in T1–T3 category but 71.6% for T4 tumors ($p < 0.001$). While excellent regional control could be achieved in N0-2 with 5-year and 8-year RRFS rates exceeding 90%, the treatment of N3 disease remained highly challenging ($p < 0.001$) (Au et al. 2018). Other literature revealed that T4 was a prognostic indicator of poor OS and PFS, and N3 was a prognostic indicator of poor OS (Fangzheng et al. 2017a, b). Similar conclusions were proposed in this research. Our study showed that T stage was significantly associated with OS, LRFS and DMFS (all $p < 0.05$; Table 7), and N stage was significantly associated with OS, RFFS and DMFS (all $p < 0.05$; Table 8). The analysis showed after stratifying the overall patients by T stage, the 5-year and 8-year OS, LRFS and DMFS rates for T4 patients were 80.0% and 66.9%, 89.2% and 83.3%, 89.5% and 77.1%, respectively (Table 7). We also did a subset analysis regarding the different N stages, the 5-year and 8-year OS, RRFS and DMFS rates for N3 patients were 79.4% and 65.6%, 93.8% and 80.4%, 83.7% and 71.6%, respectively (Table 8). Obviously worse prognosis in patients with T4 or N3 diseases was observed. In addition, Huang et al. suggests that stage T4 and N3 were closely associated with distant metastasis (Huang et al. 2021). IMRT failed to meliorate the main failure pattern of distant metastasis, looking for effective chemotherapy method is crucial (Peng et al. 2012; Zhang et al. 2015).

Table 7 The 5-year and 8-year estimated survival rate among T1-3 and T4 groups

		Cases	5-year	8-year	p value
OS	T1-3	42/239	87.8	80.8	**0.007**
	T4	29/90	80.0	66.9	
LRFS	T1-3	14/239	97.2	93.2	**0.004**
	T4	14/90	89.2	83.3	
DMFS	T1-3	31/239	91.9	87.8	**0.031**
	T4	20/90	89.5	77.1	

Bold means $p < 0.05$, difference between groups was statistically significant

Table 8 The 5-year and 8-year estimated survival rate among N0-2 and N3 groups

		Cases	5-year	8-year	p value
OS	N0-2	39/222	88.7	82.4	**0.008**
	N3	32/107	79.4	65.6	
RRFS	N0-2	17/222	98.1	91.1	**0.022**
	N3	15/107	93.8	80.4	
DMFS	N0-2	22/222	94.9	91.3	**< 0.001**
	N3	29/107	83.7	71.6	

Bold means $p < 0.05$, difference between groups was statistically significant

The addition of IC to radiotherapy is associated with significant survival improvement in LA-NPC, which precisely due to the reduction of distant metastasis (Sun et al. 2016; Chen et al. 2018, 2021; Zhang et al. 2019a, b). IC followed by CCRT was associated with a significantly lower rate of distant failure than CCRT alone (HR = 0.68, 95% CI: 0.51–0.90, P = 0.008), 9.3% and 5.5% improvement of 5-year OS and PFS, respectively (for OS: HR = 0.75, 95% CI: 0.57–0.99, P = 0.04; for PFS: HR = 0.70, 95% CI: 0.56–0.86, P = 0.0009) (Chen et al. 2018). Chen et al. conducted a meta-analysis on five studies involving 759 LA-NPC patients, and found TPF presented a pronounced efficacy on improving OS (HR = 0.53, 95% CI: 0.35–0.81, P = 0.003), PFS (HR = 0.63, 95% CI: 0.46–0.86, P = 0.004), DMFS (HR = 0.58, 95% CI: 0.39–0.86, P = 0.008), and LRFFS (HR = 0.62, 95% CI: 0.43–0.90, P = 0.01) than CCRT alone (Chen et al. 2021).

The optimal chemotherapy pattern in combination with IMRT needs further investigation. Some studies have shown that the induction efficacy of PF is not inferior to TPF with mild side effects (Fangzheng et al. 2017a, b; Wang et al. 2022). Jin et al. undertook a multi-center, open-label, randomized, non-inferiority trial and didn't observe significant difference in OS and PFS when docetaxel was added to cisplatin and fluorouracil in patients with LA-NPC ($P > 0.05$). On the contrary, significantly more patients in the TPF group required treatment delays and dose modifications because of grade 3 or 4 neutropenia and diarrhea (Jin et al. 2019). In our retrospective investigation, both TPF and PF performed encouraging anti-tumor effects in LA-NPC. Compare to precious study, our research, with a significantly longer median follow-up period (75 months), further validated that there was no statistical significance in 5-year and 8-year OS rates between two chemotherapy regimens ($p = 0.405$; Table 9),

Table 9 The 5-year and 8-year estimated survival rate among PF and TPF groups

		Cases	5-year	8-year	p value
OS	PF	18/76	80.1	72.1	0.405
	TPF	53/253	87.3	78.4	
LRFS	PF	11/76	91.1	78.0	**0.026**
	TPF	17/253	96.2	93.7	
RRFS	PF	8/76	94.2	83.7	0.585
	TPF	24/253	91.5	89.1	
DMFS	PF	10/76	87.9	87.9	0.500
	TPF	41/253	92.3	84.4	

Bold means $p < 0.05$, difference between groups was statistically significant

similar consequence was also observed in RRFS ($p = 0.585$; Table 9) and DMFS ($p = 0.500$; Table 9).

Other previous studies indicated that TPF is more effective than PF in some subgroups. Results from patients in IVA stage and high-risk group (pre-EBV DNA ≥ 1500 copies) showed that TPF was associated with significantly better DMFS than PF regimen ($p = 0.050$ and $p = 0.025$) (Liu et al. 2020). Peng et al. stratified LA-NPC into low-risk and high-risk groups by a prognostic nomogram and discovered that TPF was associated with significantly improved 3-year DFS (76.2% vs. 67.5%), OS (88.3% vs. 84.1%), DMFS (81.9% vs. 75.0%) and LRFS (92.0% vs. 87.5%; all $P < 0.05$) compared with PF within high-risk group (Peng et al. 2021a, b). In another retrospective study, TPF was found to have a higher 5-year DMFS in stage IVA and N2-3 patients (Xiong et al. 2021). In our study, improvement of LRFS in the TPF group for LA-NPC was remarkable than PF ($p = 0.026$; Table 8). We further stratified patients with T stage and found that patients receiving TPF regimen had better 5-year and 8-year LRFS rates than others receiving PF regimen in T1-3 subgroup ($p = 0.012$; Fig. 1A), there were no statistically significant difference in LRFS rates between two IC regimens for T4 subgroup ($p = 0.468$; Fig. 1B).

Our studies also revealed that OS, LRFS, RRFS and DMFS rates were comparable between IC followed by CCRT and non-CCRT group ($p = 0.235$, 0.130, 0.148, 0.718, respectively). Past retrospective study showed the combination of IC and IMRT without concurrent chemotherapy is an effective method for LA-NPC. Wei et al. found that patients received TPF plus CCRT did not make a difference in 3-year OS, LRFS, RRFS and DMFS compared with TPF plus RT alone in LA-NPC ($p = 0.286$, 0.142, 0.156 and 0.567, respectively) (Wei et al. 2019). Similar conclusions have been obtained on Chang's literature, after receiving neoadjuvant chemotherapy of ≥ 3 cycles, patients received IMRT alone were observed reducing treatment-related side effects while without compromising survival outcomes (Chang et al. 2019). Our previous research revealed that deleting concurrent chemotherapy could achieve satisfactory 5-year and 10-year OS and LPFS rates (73.8% and 59.3%, 87.5% and 79.3%, respectively) in T4 non-metastatic NPC (Zheng et al. 2024).

In terms of treatment-related side effects, obviously, docetaxel-based regimen produced more grade 3–4 acute toxicities. Compared with PF, the incidence of grade 3 or 4 leukopenia and neutropenia were more common in the TPF group ($p = 0.000$ and $p = 0.000$, respectively), which was consistent as previously reported (Peng et al. 2021a, b). Almost no severe hepatic and renal toxicities were found. During the period of IMRT, this study recorded similar incidence of grade 3–4 mucosal reaction in both the PF and TPF groups ($p = 0.295$; Table 5).

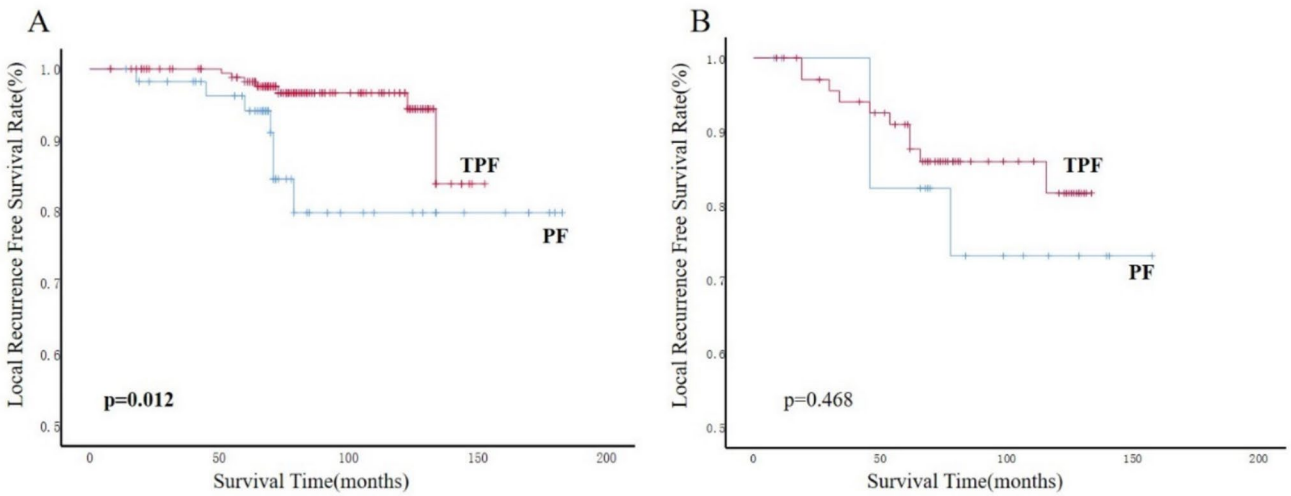

Fig. 1 Kaplan–Meier curves showing local progression free survival (LPFS) rates in different T stage among PF and TPF groups. A T1-3, B T4

Median weight loss and median intravenous nutritional support duration were also approximate in two groups ($p = 0.273$ and $p = 0.471$, respectively). Radiation-related late toxicities emerge as significant problems during the follow-up surveillance of NPC survivors. A retrospective analysis of 3328 cases in Hong Kong showed that 5.1% patients had cranial nerve palsies, 7.1% had hearing loss requiring hearing aids, 3% had dysphagia requiring long-term tube feeding, and 0.9% had symptomatic temporal lobe necrosis at a median follow-up time of 80 months (Au et al. 2018). In our cohort, 4.0% patients had cranial neuropathy, 2.1% had temporal lobe necrosis, 4.3% had grades 3–4 xerostomia, 11.1% had hearing loss and 19.4% had dental caries. None of the patients experienced osteoradionecrosis during follow-up. The incidence of the second primary tumor after IMRT in NPC patients was 3.0%−9.2% in previous reports (Zhang et al. 2019a, b; Chow et al. 2020; Svärd et al. 2023), 13 cases of secondary primary tumors were observed in our study.

Whereas, there are also some limitations in this study. The study is a retrospective analysis in a single center and with a small sample size, plasma EBV-DNA data was lacking as tests were not conduct at the time. Further multicenter, large-sample, prospective randomized controlled trials are needed to comprehensively compare the effects of different IC regimens on the efficacy and prognosis in LA-NPC patients.

Conclusion

In summary, this analysis indicated that TPF or PF induction treatment followed by RT obtained equally satisfactory efficiency in OS, LRFS and DMFS among patients with LA-NPC. TPF provided improved LRFS than PF regimen. Patients underwent TPF regimen experience higher myelosuppression, but most were endurable.

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Author contributions Xiayun He and Chaosu Hu designed this study; Xiaoshuang Niu collected the clinical data; Fen Xue and Yuming Zheng performed statistical analyses; Xiayun He and Dan Ou gave critical suggestions; Yuming Zheng drafted the manuscript. All authors contributed to the article and approved the submitted version. All authors reviewed the manuscript.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

References

Au KH, Ngan RKC, Ng AWY, Poon DMC, Ng WT, Yuen KT, Lee VHF, Tung SY, Chan ATC, Sze HCK, Cheng ACK, Lee AWM, Kwong DLW, Tam AHP (2018) 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 on 77:16–21. https://doi.org/10.1016/j.oraloncology.2017.12.004

Cao SM, Yang Q, Guo L, Mai HQ, Mo HY, Cao KJ, Qian CN, Zhao C, Xiang YQ, Zhang XP, Lin ZX, Li WX, Liu Q, Qiu F, Sun R, Chen QY, Huang PY, Luo DH, Hua YJ, Wu YS, Lv X, Wang L, Xia WX, Tang LQ, Ye YF, Chen MY, Guo X, Hong MH (2017) Neoadjuvant chemotherapy followed by concurrent chemoradiotherapy versus concurrent chemoradiotherapy alone in locoregionally advanced nasopharyngeal carcinoma: a phase III multicentre randomised controlled trial. Eur J Cancer 75:14–23. https://doi.org/10.1016/j.ejca.2016.12.039

Chang H, Peng L, Tao YL, Chen C, Xiao WW, Hu YH, Gao YH (2019) Necessity of concurrent chemotherapy in N2–3 nasopharyngeal carcinoma treated with neoadjuvant chemotherapy of ≥3 cycles followed by intensity-modulated radiotherapy. Cancer Med 8(6):2823–2831. https://doi.org/10.1002/cam4.2179

Chen YP, Tang LL, Yang Q, Poh SS, Hui EP, Chan ATC, Ong WS, Tan T, Wee J, Li WF, Chen L, Ma BBY, Tong M, Tan SH, Cheah SL, Fong KW, Sommat K, Soong YL, Guo Y, Lin AH, Sun Y, Hong MH, Cao SM, Chen MY, Ma J (2018) Induction chemotherapy plus concurrent chemoradiotherapy in endemic nasopharyngeal carcinoma: individual patient data pooled analysis of four randomized trials. Clin Cancer Res 24(8):1824–1833. https://doi.org/10.1158/1078-0432.Ccr-17-2656

Chen R, Lu Y, Zhang Y, He R, Tang F, Yuan W, Li Y, Zhang X (2021) Comparison of therapeutic efficacy and toxicity of docetaxel, cisplatin, and fluorouracil (TPF)-based induction chemotherapy plus concurrent chemoradiotherapy and chemoradiotherapy alone in locally advanced nasopharyngeal carcinoma. Medicine (Baltimore) 100(42):e27475. https://doi.org/10.1097/md.0000000000027475

Chow JCH, Tam AHP, Cheung KM, Lee VHF, Chiang CL, Tong M, Wong ECY, Cheung AKW, Chan SPC, Lai JWY, Ngan RKC, Ng WT, Lee AWM, Au KH (2020) Second primary cancer after intensity-modulated radiotherapy for nasopharyngeal carcinoma: a territory-wide study by HKNPCSG. Oral Oncol 111:105012. https://doi.org/10.1016/j.oraloncology.2020.105012

De Felice F, Musio D, Tombolini V (2016) Osteoradionecrosis and intensity modulated radiation therapy: an overview. Crit Rev Oncol Hematol 107:39–43. https://doi.org/10.1016/j.critrevonc.2016.08.017

De Felice F, Cirillo A, Botticelli A (2022) Ideal regimen for induction chemotherapy in nasopharyngeal cancer: still a hot issue? Radiother Oncol 177:111–112. https://doi.org/10.1016/j.radonc.2022.10.033

Du C, Ying H, Zhou J, Hu C, Zhang Y (2013) Experience with combination of docetaxel, cisplatin plus 5-fluorouracil chemotherapy, and intensity-modulated radiotherapy for locoregionally advanced nasopharyngeal carcinoma. Int J Clin Oncol 18(3):464–471. https://doi.org/10.1007/s10147-012-0403-y

Fangzheng W, Chuner J, Quanquan S, Zhimin Y, Tongxin L, Jiping L, Sakamoto M, Peng W, Kaiyuan S, Weifeng Q, Zhenfu F, Yangming J (2017a) Addition of 5-fluorouracil to docetaxel/cisplatin does not improve survival in locoregionally advanced nasopharyngeal carcinoma. Oncotarget 8(70):115469–115479. https://doi.org/10.18632/oncotarget.23300

Fangzheng W, Quanquan S, Chuner J, Lei W, Fengqin Y, Zhimin Y, Tongxin L, Min X, Peng W, Haitao J, Aizawa R, Sakamoto M, Yuezhen W, Zhenfu F (2017b) Gemcitabine/cisplatin induction chemotherapy before concurrent chemotherapy and intensity-modulated radiotherapy improves outcomes for locoregionally advanced nasopharyngeal carcinoma. Oncotarget 8(57):96798–96808. https://doi.org/10.18632/oncotarget.18245

Huang J, Yang ZY, Wu B, Ding Q, Qin Y, Zhang ZJ, Yin ZY, Liang ZW, Han J, Wang Y, Peng ZJ, Peng G, Li Q, Wu G, Yang KY (2021) Long-term therapeutic outcome and prognostic factors of patients with nasopharyngeal carcinoma receiving intensity-modulated radiotherapy: an analysis of 608 patients from low-endemic regions of China. Curr Med Sci 41(4):737–745. https://doi.org/10.1007/s11596-021-2405-3

Hui EP, Ma BB, Leung SF, King AD, Mo F, Kam MK, Yu BK, Chiu SK, Kwan WH, Ho R, Chan I, Ahuja AT, Zee BC, Chan AT (2009) Randomized phase II trial of concurrent cisplatin-radiotherapy with or without neoadjuvant docetaxel and cisplatin in advanced nasopharyngeal carcinoma. J Clin Oncol 27(2):242–249. https://doi.org/10.1200/jco.2008.18.1545

Jamshed A, Hussain R, Iqbal H (2014) Gemcitabine and cisplatin followed by chemo-radiation for advanced nasopharyngeal carcinoma. Asian Pac J Cancer Prev 15(2):899–904. https://doi.org/10.7314/apjcp.2014.15.2.899

Jiang F, Jin T, Feng XL, Jin QF, Chen XZ (2015) Long-term outcomes and failure patterns of patients with nasopharyngeal carcinoma staged by magnetic resonance imaging in intensity-modulated radiotherapy era: the Zhejiang cancer hospital's experience. J Cancer Res Ther 11(Suppl 2):C179-184. https://doi.org/10.4103/0973-1482.168181

Jin T, Qin WF, Jiang F, Jin QF, Wei QC, Jia YS, Sun XN, Li WF, Chen XZ (2019) Cisplatin and fluorouracil induction chemotherapy with or without docetaxel in locoregionally advanced nasopharyngeal carcinoma. Transl Oncol 12(4):633–639. https://doi.org/10.1016/j.tranon.2019.01.002

Koch A, Reinhardt P, Elicin O, Aebersold DM, Schanne DH (2025) Predictive biomarkers of radiotherapy- related dermatitis, xerostomia, mucositis and dysphagia in head and neck cancer: a systematic review. Radiother Oncol 203:110689. https://doi.org/10.1016/j.radonc.2024.110689

Kong M, Lim YJ, Kim Y (2018) Concurrent chemoradiotherapy for loco-regionally advanced nasopharyngeal carcinoma: treatment outcomes and prognostic factors. Asian Pac J Cancer Prev 19(6):1591–1599. https://doi.org/10.22034/apjcp.2018.19.6.1591

Kong FF, Ni MS, Zhai RP, Ying HM, Hu CS (2022) Local control and failure patterns after intensity modulated radiotherapy with reduced target volume delineation after induction chemotherapy for patients with T4 nasopharyngeal carcinoma. Transl Oncol 16:101324. https://doi.org/10.1016/j.tranon.2021.101324

Lai SZ, Li WF, Chen L, Luo W, Chen YY, Liu LZ, Sun Y, Lin AH, Liu MZ, Ma J (2011) How does intensity-modulated radiotherapy versus conventional two-dimensional radiotherapy influence the treatment results in nasopharyngeal carcinoma patients? Int J Radiat Oncol Biol Phys 80(3):661–668. https://doi.org/10.1016/j.ijrobp.2010.03.024

Li WF, Chen NY, Zhang N, Hu GQ, Xie FY, Sun Y, Chen XZ, Li JG, Zhu XD, Hu CS, Xu XY, Chen YY, Hu WH, Guo L, Mo HY, Chen L, Mao YP, Sun R, Ai P, Liang SB, Long GX, Zheng BM, Feng XL, Gong XC, Li L, Shen CY, Xu JY, Guo Y, Chen YM, Zhang F, Lin L, Tang LL, Liu MZ, Ma J, Sun Y (2019) Concurrent chemoradiotherapy with/without induction chemotherapy in locoregionally advanced nasopharyngeal carcinoma: long-term results of phase 3 randomized controlled trial. Int J Cancer 145(1):295–305. https://doi.org/10.1002/ijc.32099

Liu SL, Sun XS, Xie HJ, Chen QY, Lin HX, Liang H, Liang YJ, Li XY, Yan JJ, Lin C, Yang ZC, Guo SS, Liu LT, Tang QN, Du YY, Tang LQ, Guo L, Mai HQ (2020) Comparing three induction chemotherapy regimens for patients with locoregionally advanced nasopharyngeal carcinoma based on TNM stage and plasma Epstein-Barr virus DNA level. BMC Cancer 20(1):89. https://doi.org/10.1186/s12885-020-6555-7

Nazeer F, Poulose JV, Kainickal CT (2022) Induction chemotherapy in nasopharyngeal carcinoma- a systematic review of phase III clinical trials. Cancer Treat Res Commun 32:100589. https://doi.org/10.1016/j.ctarc.2022.100589

NCCN Clinical Practice Guidelines in Oncology (NCCN): head and neck cancers. Version 3.2024.

Ou X, Zhou X, Shi Q, Xing X, Yang Y, Xu T, Shen C, Wang X, He X, Kong L, Ying H, Hu C (2015) Treatment outcomes and late toxicities of 869 patients with nasopharyngeal carcinoma treated with definitive intensity modulated radiation therapy: new insight into the value of total dose of cisplatin and radiation boost. Oncotarget 6(35):38381–38397. https://doi.org/10.18632/oncotarget.5420

Peng G, Wang T, Yang KY, Zhang S, Zhang T, Li Q, Han J, Wu G (2012) A prospective, randomized study comparing outcomes and toxicities of intensity-modulated radiotherapy vs. conventional two-dimensional radiotherapy for the treatment of nasopharyngeal carcinoma. Radiother Oncol 104(3):286–293. https://doi.org/10.1016/j.radonc.2012.08.013

Peng H, Chen B, He S, Tian L, Huang Y (2021a) Efficacy and toxicity of three induction chemotherapy regimens in locoregionally advanced nasopharyngeal carcinoma: outcomes of 10-year follow-up. Front Oncol 11:765378. https://doi.org/10.3389/fonc.2021.765378

Peng H, Chen L, Mao YP, Tian L, Liu LZ (2021b) Nomogram-aided individual induction chemotherapy regimen selection in advanced nasopharyngeal carcinoma. Oral Oncol 122:105555. https://doi.org/10.1016/j.oraloncology.2021.105555

Sun Y, Li WF, Chen NY, Zhang N, Hu GQ, Xie FY, Sun Y, Chen XZ, Li JG, Zhu XD, Hu CS, Xu XY, Chen YY, Hu WH, Guo L, Mo HY, Chen L, Mao YP, Sun R, Ai P, Liang SB, Long GX, Zheng BM, Feng XL, Gong XC, Li L, Shen CY, Xu JY, Guo Y, Chen YM, Zhang F, Lin L, Tang LL, Liu MZ, Ma J (2016) Induction chemotherapy plus concurrent chemoradiotherapy versus concurrent chemoradiotherapy alone in locoregionally advanced nasopharyngeal carcinoma: a phase 3, multicentre, randomised controlled trial. Lancet Oncol 17(11):1509–1520. https://doi.org/10.1016/s1470-2045(16)30410-7

Svärd F, Alabi RO, Leivo I, Mäkitie AA, Almangush A (2023) The risk of second primary cancer after nasopharyngeal cancer: a systematic review. Eur Arch Otorhinolaryngol 280(11):4775–4781. https://doi.org/10.1007/s00405-023-08144-0

Tao HY, Zhan ZJ, Qiu WZ, Liao K, Yuan YW, Yuan TZ, Zheng RH (2021) Clinical value of docetaxel plus cisplatin (TP) induction chemotherapy followed by TP concurrent chemoradiotherapy in locoregionally advanced nasopharyngeal carcinoma. J Cancer 12(1):18–27. https://doi.org/10.7150/jca.49944

Wang F, Jiang C, Wang L, Yan F, Sun Q, Ye Z, Liu T, Fu Z, Jiang Y (2020) Influence of concurrent chemotherapy on locoregionally advanced nasopharyngeal carcinoma treated with neoadjuvant chemotherapy plus intensity-modulated radiotherapy: a retrospective matched analysis. Sci Rep 10(1):2489. https://doi.org/10.1038/s41598-020-59470-w

Wang Y, Wang C, He S, Bai L, Kong F, Wang S, Cui L, Qin Q, Yang Y, Xiao W, Zhu M, Zhang Z, Lai Y, Bao W, Peng Z, Chen Y (2022) Induction chemotherapy regimen of docetaxel plus cisplatin versus docetaxel, cisplatin plus fluorouracil followed by concurrent chemoradiotherapy in locoregionally advanced nasopharyngeal carcinoma: preliminary results of an open-label, noninferiority, multicentre, randomised, controlled phase 3 trial. EClinicalMedicine 53:101625. https://doi.org/10.1016/j.eclinm.2022.101625

Wei Z, Zhang Z, Luo J, Li N, Peng X (2019) Induction chemotherapy plus IMRT alone versus induction chemotherapy plus IMRT-based concurrent chemoradiotherapy in locoregionally advanced nasopharyngeal carcinoma: a retrospective cohort study. J Cancer Res Clin Oncol 145(7):1857–1864. https://doi.org/10.1007/s00432-019-02925-z

Wu LR, Liu YT, Jiang N, Fan YX, Wen J, Huang SF, Guo WJ, Bian XH, Wang FJ, Li F, Song D, Wu JF, Jiang XS, Liu JY, He X (2017) Ten-year survival outcomes for patients with nasopharyngeal carcinoma receiving intensity-modulated radiotherapy: an analysis of 614 patients from a single center. Oral Oncol 69:26–32. https://doi.org/10.1016/j.oraloncology.2017.03.015

Wu M, He X, Hu C (2018) Intensity-modulated radiotherapy combined with sequential cisplatin and fluorouracil chemotherapy for locoregionally advanced nasopharyngeal carcinoma. Medicine (Baltimore) 97(50):e13361. https://doi.org/10.1097/md.0000000000013361

Wu M, Ou D, Hu C, He X (2020) Comparing long-term survival and late toxicities of different sequential chemotherapy regimens with intensity-modulated radiotherapy in locoregionally advanced nasopharyngeal carcinoma. Transl Oncol 13(7):100765. https://doi.org/10.1016/j.tranon.2020.100765

Xia WX, Liang H, Lv X, Wang L, Ye YF, Ke LR, Xu LH, Guo X, Xiang YQ (2019) Stage-specific concurrent chemoradiotherapy with or without induction chemotherapy for locoregionally advanced nasopharyngeal carcinoma: a retrospective, population-based study. Cancer Manag Res 11:9813–9827. https://doi.org/10.2147/cmar.S179139

Xiong Y, Shi L, Zhu L, Peng G (2021) Comparison of TPF and TP induction chemotherapy for locally advanced nasopharyngeal carcinoma based on TNM stage and pretreatment systemic immune-inflammation index. Front Oncol 11:731543. https://doi.org/10.3389/fonc.2021.731543

Xu M, Zang J, Luo S, Wang J, Li X (2021) Long-term survival outcomes and adverse effects of nasopharyngeal carcinoma patients treated with IMRT in a non-endemic region: a population-based retrospective study. BMJ Open 11(8):e045417. https://doi.org/10.1136/bmjopen-2020-045417

Xu AA, Miao JJ, Wang L, Li AC, Han F, Shao XF, Mo ZW, Huang SM, Yuan YW, Deng XW, Zhao C (2023) Efficacy of concurrent chemoradiotherapy alone for loco-regionally advanced nasopharyngeal carcinoma: long-term follow-up analysis. Radiat Oncol 18(1):63. https://doi.org/10.1186/s13014-023-02247-y

Yang Q, Cao SM, Guo L, Hua YJ, Huang PY, Zhang XL, Lin M, You R, Zou X, Liu YP, Xie YL, Wang ZQ, Mai HQ, Chen QY, Tang LQ, Mo HY, Cao KJ, Qian CN, Zhao C, Xiang YQ, Zhang XP, Lin ZX, Li WX, Liu Q, Li JB, Ling L, Guo X, Hong MH, Chen MY (2019) Induction chemotherapy followed by concurrent chemoradiotherapy versus concurrent chemoradiotherapy alone in locoregionally advanced nasopharyngeal carcinoma: long-term results of a phase III multicentre randomised controlled trial. Eur J Cancer 119:87–96. https://doi.org/10.1016/j.ejca.2019.07.007

Zhang MX, Li J, Shen GP, Zou X, Xu JJ, Jiang R, You R, Hua YJ, Sun Y, Ma J, Hong MH, Chen MY (2015) Intensity-modulated radiotherapy prolongs the survival of patients with nasopharyngeal carcinoma compared with conventional two-dimensional radiotherapy: a 10-year experience with a large cohort and long follow-up. Eur J Cancer 51(17):2587–2595. https://doi.org/10.1016/j.ejca.2015.08.006

Zhang LL, Li GH, Li YY, Qi ZY, Lin AH, Sun Y (2019a) Risk assessment of secondary primary malignancies in nasopharyngeal carcinoma: a big-data intelligence platform-based analysis of 6377 long-term survivors from an endemic area treated with intensity-modulated radiation therapy during 2003–2013. Cancer Res Treat 51(3):982–991. https://doi.org/10.4143/crt.2018.298

Zhang Y, Chen L, Hu GQ, Zhang N, Zhu XD, Yang KY, Jin F, Shi M, Chen YP, Hu WH, Cheng ZB, Wang SY, Tian Y, Wang XC, Sun Y, Li JG, Li WF, Li YH, Tang LL, Mao YP, Zhou GQ, Sun R, Liu X, Guo R, Long GX, Liang SQ, Li L, Huang J, Long JH, Zang J, Liu QD, Zou L, Su QF, Zheng BM, Xiao Y, Guo Y, Han F, Mo HY, Lv JW, Du XJ, Xu C, Liu N, Li YQ, Chua MLK, Xie FY, Sun Y, Ma J (2019b) Gemcitabine and cisplatin induction chemotherapy in nasopharyngeal carcinoma. N Engl J Med 381(12):1124–1135. https://doi.org/10.1056/NEJMoa1905287

Zhang Y, Chen L, Hu GQ, Zhang N, Zhu XD, Yang KY, Jin F, Shi M, Chen YP, Hu WH, Cheng ZB, Wang SY, Tian Y, Wang XC, Sun Y, Li JG, Li WF, Li YH, Mao YP, Zhou GQ, Sun R, Liu X, Guo R, Long GX, Liang SQ, Li L, Huang J, Long JH, Zang J, Liu QD, Zou L, Su QF, Zheng BM, Xiao Y, Guo Y, Han F, Mo HY, Lv JW, Du XJ, Xu C, Liu N, Li YQ, Xie FY, Sun Y, Ma J, Tang LL (2022) Final Overall survival analysis of gemcitabine and cisplatin induction chemotherapy in nasopharyngeal carcinoma: a multicenter, randomized phase III trial. J Clin Oncol 40(22):2420–2425. https://doi.org/10.1200/jco.22.00327

Zhao W, Lei H, Zhu X, Li L, Qu S, Liang X (2016) Investigation of long-term survival outcomes and failure patterns of patients with nasopharyngeal carcinoma receiving intensity-modulated radiotherapy a retrospective analysis. Oncotarget 7(52):86914–86925. https://doi.org/10.18632/oncotarget.13564

Zheng Y, Xue F, Ou D, Niu X, Hu C, He X (2024) Deletion of concurrent chemotherapy on the basis of sequential chemoradiotherapy for non-metastatic stage T4 nasopharyngeal carcinoma in IMRT era. Cancer Med 13(4):e6578. https://doi.org/10.1002/cam4.6578

Zhu J, Duan B, Shi H, Li Y, Ai P, Tian J, Chen N (2019) Comparison of GP and TPF induction chemotherapy for locally advanced nasopharyngeal carcinoma. Oral Oncol 97:37–43. https://doi.org/10.1016/j.oraloncology.2019.08.001