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Efficacy and Safety of Nimotuzumab Plus Radiotherapy With or Without Cisplatin-Based Chemotherapy in an Elderly Patient Subgroup (Aged 60 and Older) With Nasopharyngeal Carcinoma

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Abstract

OBJECTIVE: This study was conducted to assess the efficacy and safety of nimotuzumab combined with radiotherapy (RT) in elderly patients with nasopharyngeal carcinoma. *MATERIALS AND METHODS:* The clinical data of 75 nasopharyngeal carcinoma patients, who were initially treated with nimotuzumab combined with RT, were collected and retrospectively reviewed from December 2008 to April 2014. They were aged 60 to 81 years (median 64 years). The distribution of disease was stage II in 10 (13.3%), stage III in 33 (44.0%), and stage IV in 32 (42.7%). Among these patients, 59 cases received cisplatin-based chemotherapy. Survival outcomes and treatment toxicity were analyzed using IBM SPSS 19.0 software. *RESULTS:* With a median follow-up of 45 months (range, 13-78 months), the estimated 3-year local recurrence-free survival (LRFS), regional recurrence-free survival (RRFS), distant metastasis-free survival (DMFS), progression failure-free survival (PFS), and overall survival (OS) rates were 95.6%, 95.5%, 98.6%, 89.7%, and 89.2%, respectively. In the subgroup, 3-year OS rate in the patients with concurrent chemotherapy was 90.5% and 77.4% in patients without concurrent chemotherapy (Log-Rank = 1.795, $P = .180$). Univariate analysis showed that T stage and clinical stage were correlated with OS. Multivariate analysis indicated that age, T stage and tumor response at the end of treatment were independent prognosticators. Nine patients experienced grade 3 to 4 acute mucositis and 26 patients experienced grade 3-4 leukocytopenia, with no cases of skin rash and infusion reaction. Twelve patients developed mild liver function damage. No serious gastrointestinal or renal toxicities were observed. *CONCLUSION:* The efficacy of combined

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nimotuzumab with RT in elderly NPC patients was encouraging and the toxicities were accepted. In addition, nimotuzumab provides a better option for elderly patients who cannot be tolerate chemotherapy.

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Introduction

The incidence of nasopharyngeal carcinoma (NPC) is relatively high in Southern China, Singapore and Malaysia, which varying with age, ethnic and geographical origin [1]. The peak age of NPC occurrence in endemic areas is from 40 to 60 years and subsequently reduced [2]. With the increase in the aging population and the extension of life expectancy, elderly NPC patients increased gradually in the future.

Radiotherapy (RT) is the standard treatment for NPC owing to the anatomical location and the high radiosensitivity. According to meta-analyses of randomized studies, combination with radiotherapy and chemotherapy reduce the risk of mortality by 18% and increases 5-year survival by 4% to 6% [3]. Chemoradiotherapy (CRT) with or without adjuvant chemotherapy, which establishes a benefit in overall survival, has become the standard treatment strategy for loco-regionally advanced nasopharyngeal carcinoma (LA NPC), although with acute toxicities [4–6]. The evidence that CRT is the optimal treatment regimen for the elderly NPC patients remains controversial because the number of elderly patients in these studies is small. The tolerance to CRT could be crucial for the elderly patients who are related with comorbidities, poorer performance status, less social support and reduced organ function. Two previous studies showed that CRT regimen achieved a reasonable treatment outcome and acceptable acute toxicities in the elderly NPC patients with good performance status [7,8]. The result that chemotherapy induced a higher rate of grade 3 and 4 side effects for cancer patients with comorbidities was reported by a systemic review [9]. After weighing therapeutic benefits and chemotherapy-induced toxicities, most oncologists choose RT alone to treat elderly patients because it had been proven to be tolerable [10,11]. However, some patients may not achieve advantage from this treatment option. So, elderly NPC patients need to be treated with new and effective regimens with tolerable toxicity.

It has shown that overexpression of EGFR is observed in many different cancers, including gliomas, sarcomas and head and neck cancers [12]. Moreover high EGFR expression was associated with poor prognosis [13,14]. Several inhibitors of the EGFR, e.g., cetuximab, panitumumab, erlotinib, and gefitinib, have shown favorable results in clinical trials [15,16]. Cetuximab, the most commonly used anti-EGFR antibody, combined with radiotherapy (RT), has been shown to improve survival in patients with loco-regionally advanced head and neck squamous cell carcinoma (LA HNSCC) [17]. In NPC, cetuximab with concurrent chemoradiotherapy is tolerable and has shown promising advantage for NPC prognosis [18]. However, the relatively high rate of mucositis and acne-like skin rash limited its clinical application [18,19].

Nimotuzumab is a blocking monoclonal antibody against EGFR without intrinsic stimulating activity [20]. In the preclinical studies, nimotuzumab has demonstrated remarkably antiproliferative, pro-apoptotic, and antiangiogenic activities [21]. And nimotuzumab displayed a longer half-life and elevated area under the curve than cetuximab at the same dose level [22]. Besides, nimotuzumab improve the quality of life because it rarely caused severe dermatological toxicity, which is the most common adverse events resulting from cetuximab and panitumumab [23].

Now, nimotuzumab has marketing approval for the treatment of advanced NPC [24,25]. However, nimotuzumab combined with chemoradiotherapy or RT alone was not found to be used for elderly

Table 1. Characteristics of Elderly NPC Patients Treated With Nimotuzumab Plus Radiotherapy With or Without Chemotherapy

Characteristic	N (%)
Gender	
Male	58 (77.3)
Female	17 (22.7)
Age (years)	
Range	60-81
Median	64
60-69	53 (70.7)
≥70	22 (29.3)
WHO pathology	
Type I	2 (2.7)
Type II	2 (2.7)
Type III	71 (94.5)
ECOG performance status	
0	38 (50.7)
1	30 (40.0)
2	7 (9.3)
T stage *	
T1	6 (8.0)
T2	9 (12.0)
T3	30 (40.0)
T4	30 (40.0)
N stage *	
N0	9 (12.0)
N1	27 (36.0)
N2	36 (48.0)
N3	3 (4.0)
Clinical stage *	
II	10(13.3)
III	33 44.0)
IV	32 (42.7)
Comorbidity	
No	37 (49.3)
Yes	38 (50.7)
Cycle of h-R3	
<6 weeks	17 (22.7)
≥6 weeks	58 (77.3)
Fractional dose of h-R3	
100 mg	8 (10.7)
200 mg	67 (89.3)
Total dose of h-R3	
<1200 mg	24 (32.0)
≥1200 mg	51 (68.0)

Abbreviations: WHO World Health Organization, ECOG Eastern Cooperative Oncology Group, h-R3 nimotuzumab; * The 7th AJCC/UICC staging system.

NPC patients. Therefore, we retrospectively investigate the safety and efficacy of nimotuzumab plus RT with or without chemotherapy in elderly NPC patients.

Patients and Methods

Patients and Pretreatment

The patients enrolled into this study were hospitalized from May 2008 to February 2013 in the Department of Radiation Oncology, Zhejiang Cancer Hospital. The retrospective study was approved by the medical ethics committee of Zhejiang Cancer Hospital. All patients signed written informed consent before participating in this study. The eligible patients should met the following criteria including: (i) Patients aged ≥ 60 years; (ii) Histologically proven nonmetastatic NPC; (iii) ECOG (Eastern Cooperative Oncology Group) performance status ≤2; (iv) Completion of radical RT; (v) Without previous anti-cancer treatment.

They had a pretreatment evaluation including complete history, physical examination, hematology and biochemistry profiles, chest radiographs, sonography of the abdomen, bone scan, magnetic response imaging of nasopharynx and nasopharyngoscope. All patients were staged according to 2010 AJCC staging system. Tumor histology was classified according to the World Health Organization classification.

Totally 505 elderly NPC patients were registered at Zhejiang Cancer Hospital. Finally, a total of 75 elderly patients (median 64 years; range 60-81 years) with histology-proven nonmetastatic NPC were enrolled into this study. All patients were treated with nimotuzumab plus definitive RT with or without chemotherapy. All patients signed written informed consent before participating in this study. Clinical characteristics of the patients are listed in Table 1.

RT

All patients were immobilized in the supine position with thermoplastic masks. Computed tomography scans with intravenous contrast (2.5 mm slices from the head to 2 cm below the sternoclavicular joints) were performed for planning. Target volumes were delineated according to the recommendations of the International Commission on Radiation Units and Measurements CTV delineation protocol for head and neck malignancies [35, 36]. Gross tumor volume (GTV) referred to the extent of the tumor found in clinical and imaging examinations. The extent of the primary tumor, including metastatic retropharyngeal lymph nodes, was defined as GTVnx, and the metastatic lymph nodes of the neck as GTVnd.

The CTV was defined individually according to the GTV, and the potential regions at risk surrounding the nasopharyngeal cavity. The CTV for GTVnx included CTVnx for the high-risk CTV and CTV1 when invasion was present. The CTVnx was defined as GTVnx plus a 7 mm margin that encompassed the nasopharyngeal mucosa plus 5 mm submucosal volume. For CTV1, the anatomic regions that were potentially involved were the entire nasopharyngeal cavity, the anterior one- to two-thirds of the clivus (when invasion is present, the whole clivus should be covered), the skull base, the pterygoid plates, the parapharyngeal space, the inferior sphenoid sinus (the entire sphenoid sinus should be covered for stage T3 and T4 NPC), the posterior one-quarter to one-third of the nasal cavity, and the maxillary sinus, were included. High-risk nodes included level Ib nodes in patients with metastatic lymph nodes in level IIa, and any lymph nodes in drainage pathways containing metastatic lymph nodes. Low-risk areas for prophylactic neck irradiation areas were referred as CTV2. These low-risk areas included levels IV and Vb without metastatic cervical lymph nodes.

The PTV was constructed automatically based on each volume with an additional 3-mm margin in three dimensions to account for set-up variability. All of the PTVs, including PGTVnx, PTVnx, PTV1, and PTV2, were not delineated outside of the skin surface.

All patients underwent radical RT with 6 MV photons. Among those patients, only 4 patients were treated with conformal RT, while 94.7% (71/75) of patients received intensity-modulated radiation therapy (IMRT) with simultaneous integrated boost technique. The prescribed radiation dose was 69 or 72 Gy to PGTVnx, 66 to 69 Gy to PGTVnd, 63 to 66 Gy to PTVnx, 60 to 63 Gy to PTV1, and 51 to 54 Gy to PTV2, delivered in 30 or 33 fractions. Radiation was delivered once daily, five fractions per week, over 6 to 6.5weeks for IMRT planning. Conformal RT was given 66 to 70 Gy to primary tumor and neck metastatic node, 60 to 63 Gy to high risk region and 50 to 54 Gy to low risk region with 2Gy/day.

Target Treatment

Nimotuzumab was administered concomitantly with induction chemotherapy and /or RT at a dose of 100 mg or 200 mg weekly, which was diluted in 250 mL saline to obtain a 100 mg or 200 mg suspension and intravenously infused over 1 hour. All patients received 4 to 12 cycles of nimotuzumab during the treatment.

Chemotherapy

Fifty-one patients were given one to four cycles of platinum-based induction chemotherapy. The most common induction regimens included TPF (docetaxel 60 mg/m^2/day on day 1, cisplatin 25 mg/m^2/day on days 1-3, and 5-fluorouracil 500 mg/m^2/day on days 1-3), TP (docetaxel 60 mg/m^2/day on day 1, cisplatin 25 mg/m^2/day on days 1-3), GP regimen (gemcitabine 1,000 mg/m^2/day on days 1 and 8, cisplatin 25 mg/m^2/day on days 1-3), and FP (cisplatin 25 mg/m^2/day on days 1-3, and 5-fluorouracil 500 mg/m^2/day on days 1-3).

Forty-eight patients underwent 2 cycles concurrent chemotherapy with cisplatin (80mg /m^2) for 3 days. 22 patients received 2 to 3 courses of adjuvant chemotherapy with FP regimen 3 weeks after RT.

Patient Evaluation and Follow-Up

The assessment of tumor response was performed thrice after the completion of induction chemotherapy, at the end of IMRT, and 3 months after radiation, which was based on MRI and nasopharynx fiberscope according to Response Evaluation Criteria for Solid Tumors criteria. Systemic chemotherapy adverse effects were graded using the National Cancer Institute Common Toxicity Criteria (NCI CTCAE, version 3.0), whereas RT-induced toxicities were scored according to the Acute and Late Radiation Morbidity Scoring Criteria of the Radiation Therapy Oncology Group (RTOG).

All the subjects underwent weekly examinations for treatment response and toxicities during radiation therapy. Patients were followed-up every 3 months in the first 2 years; every 6 months from the third to the fifth year, and then annually. Each follow-up included careful examination of the nasopharynx and neck nodes by an experienced doctor, MRI scan of the nasopharynx, nasopharynx fiberscope, chest computed tomography radiograph, and ultrasound of abdomen were performed 3 months after the completion of RT and every 6 to 12 months thereafter. Additional examinations were

performed when it is indicated to evaluate local relapse or distant metastasis.

Statistical Analysis

Survival curves were generated using the Kaplan-Meier method. The curves were compared using log-rank tests. Multivariate analysis was performed using Cox regression models to identify significant prognostic factors. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated for each prognostic factor. IBM SPSS Statistics version 19.0 was used for all data analysis. A $P < .05$ was considered statistically significant. Survival time was calculated from the date of diagnosis to the most recent follow-up or to either the date of relapse (event-free, local recurrence-free, or distant metastasis-free) or death (overall survival). After recurrence or metastasis, patients were given salvage therapy as determined by their physicians.

Results

Tumor Response

The overall response rates for lesions of the nasopharynx and cervical lymph nodes were 100% (complete remission [CR] 88.0%) and 100% (CR 94.7%), respectively at the end of treatment. 96% of patients experienced CR of primary tumor and 100% at the neck region 3 months after RT.

Survival

The median follow-up time was 45 months (range, 13–78). The estimated 3-year local recurrence-free survival (LRFS), regional recurrence-free survival (RRFS), distant metastasis-free survival (DMFS), progression failure-free survival (PFS), and overall survival (OS) rates were 95.6%, 95.5%, 98.6%, 89.7%, and 89.2%, respectively (Figure 1). The 3-year OS rates were 80%, 100.0%, 95.8%, and 73.0% for patients with stage T1, T2, T3, and T4, respectively (log-rank = 9.945, $P = .019$) (Figure 2*A*). The 3-year OS rates were 87.5%, 96.2%, and 74.8% for patients with stage II, III, and IV, respectively (log-rank = 8.080, $P = .018$) (Figure 2*B*). The 3-year PFS rate of CR patients was higher than that of non-CR patients (91.3% vs. 80.0%, log-rank = 4.247, $P = .039$, Figure 2*C*).

For the role of chemotherapy in these elderly NPC patients, it is noteworthy that either NAC or CC did not improve OS (3-year OS of 92.1% in patients with NAC vs. 82.1% in patients without NAC, log-rank = 0.044, $P = .835$, Figure 3*A*; 3-year OS of 90.5% in patients with CC vs. 77.4% in patients without CC, log-rank = 1.795, $P = .180$, Figure 3*B*).

Altogether, fourteen patients experienced treatment failure: four patient had local recurrence only; Three had regional recurrence and one loco-regional recurrence; Two developed ≥1 distant metastasis who died because of disease progression; One patient had both regional and distant failure who was still alive. These details are shown in Table 2.

Identification of Prognostic Factors

We evaluated several potential prognostic factors including patient age, gender, clinical stage, adjusted tumor (T) and lymph node (N) stage, neoadjuvant chemotherapy, concurrent chemotherapy, adjuvant chemotherapy, comorbidities, cycles of nimotuzumab, dose of nimotuzumab, and tumor response at the end of treatment.

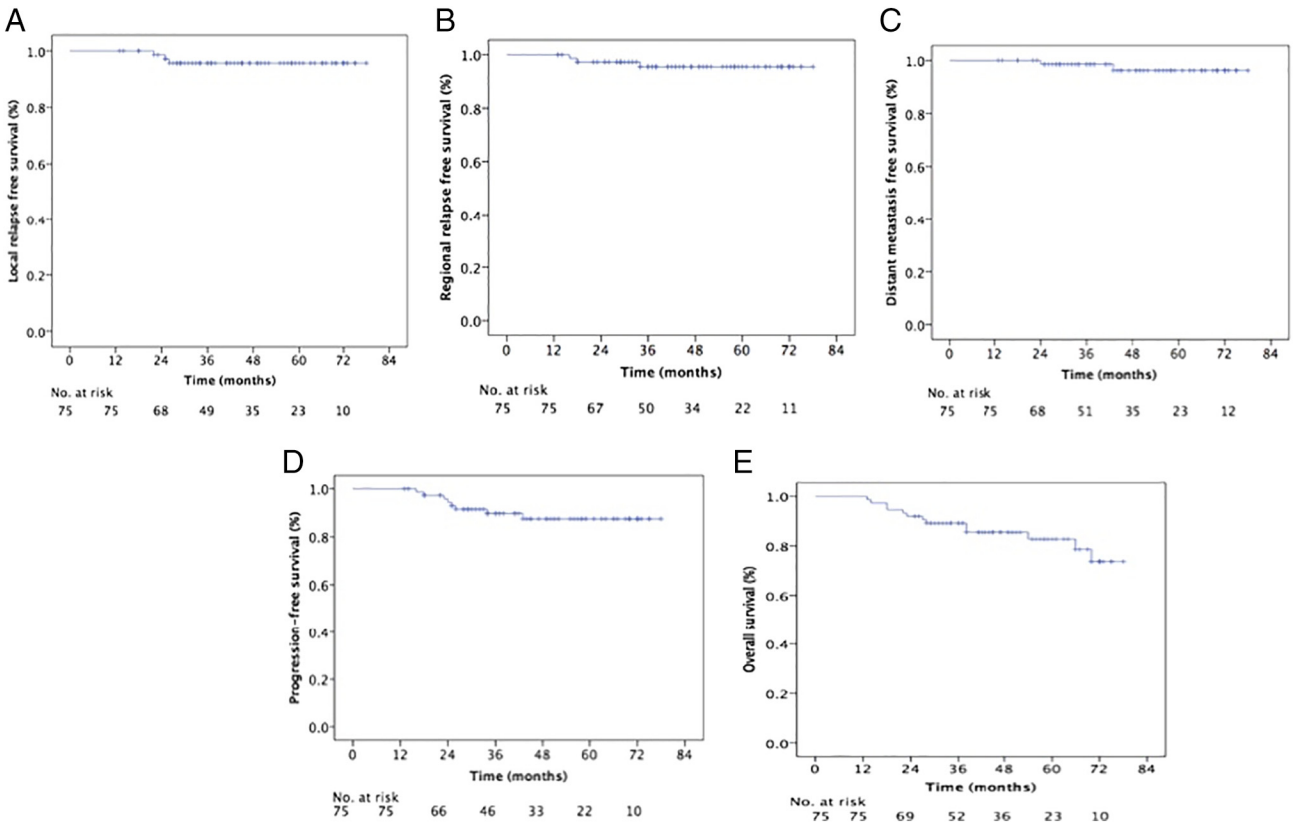

Figure 1. Kaplan-Meier estimates of the survival of elderly patients with nasopharyngeal carcinoma. (A) local recurrence-free survival; (B) regional recurrence-free survival; (C) distance metastasis-free survival; (D) progress-free survival; (E) overall survival.

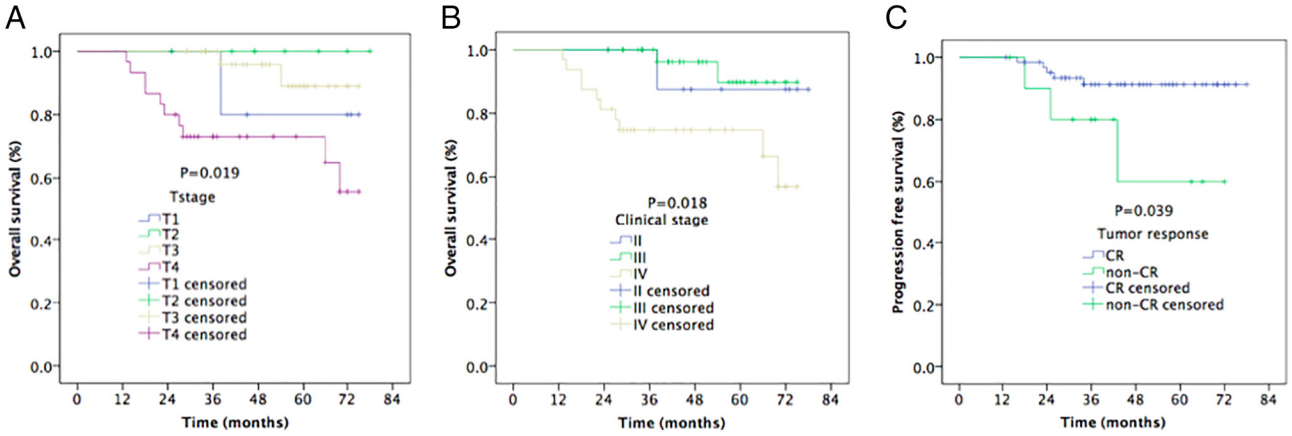

Figure 2. Kaplan-Meier estimates of the survival of elderly patients' nasopharyngeal carcinoma for different variables. (A) Overall survival for T stage; (B) Overall survival for clinical stage; (C) progress-free survival for tumor response.

Univariate analysis revealed that T stage and clinical stage were significant prognostic factors for OS, and tumor response at the end of treatment was a significant prognostic factor for PFS (Table 3). Multivariate analysis indicated that age ≥70 years, T4 and non-CR were poorer prognostic factors for OS (Table 4).

Safety and Toxicity

The most common treatment-related acute adverse events included hematologic and nonhematologic toxicity (Table 5). Hematologic toxicity was reported as grade 3 and worse in severity in 26 (34.7%) patients. Nine of these patients occurred neutropenic fever. They can be tolerated without delaying the chemotherapy and interrupting radiotherapy by GMSF treatment. The gastrointestinal toxicities were mild or moderate, and patients recovered rapidly with or without symptomatic medication. The grade 3 to 4 radiotherapy–related oral mucositis was reported in 9 (12.0%) patients. No grade 3 dermatitis was observed within the RT field. No acneiform eruptions were found among these subjects.

The long-term complication included xerostomia, dental caries, deafness, trismus, radiation encephalopathy, neck fibrosis. Xerostomia was the most common late effect, and the degree of xerostomia appeared to decrease with time. At the time of analysis, most patients developed moderate xerostomia, ten (13.3%) patients were observed with severe xerostomia. Five (6.7%) patients developed temporal lobe damage, diagnosed by MRI examination in the follow-up. Two of these patients occurred bilateral temporal lobe damage. Eight cases were found for the second primary tumor that including lung cancer, prostate cancer, gastric cancer, liver cancer, thyroid cancer, and kidney cancer. They had been treated by operation. No severe trismus, hearing impairment and neck fibrosis were found.

Discussion

As the population ages and the life expectancy extends, more and more patients has been diagnosed NPC at older age. Compared to younger NPC patients, a significantly higher risk of death and disease progression was found in elderly patients [26]. Therefore, it is a very pressing task to manage and treat elderly NPC patients. A previous study demonstrated that administrative pattern, comorbidities and staging were closely related with the improving ages and worse prognosis for elderly NPC patients [27]. In addition, the tolerability of chemotherapy and radiation therapy for elderly patients with malignancy is still unclear. No increased treatment-related adverse

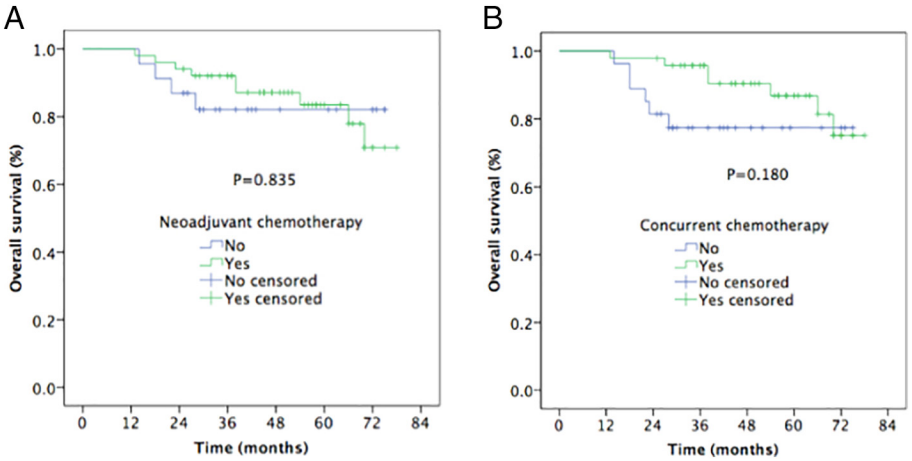

Figure 3. Kaplan-Meier estimates of the survival of elderly patients' nasopharyngeal carcinoma with or with chemotherapy. (A) Overall survival of patients with or without NAC; (B) Over survival of patients with or without CC.

Table 2. Site and Incidence of Treatment Failure

Sites	Number of patients (n = 14)
Local only	4
Regional only	3
Local and regional	1
Loco-regional and distant	1
Distant only	5
Lung only	1
Bone only	1
Liver only	1
Lung, liver, bone and other	2

Table 3. Univariate Analysis of Prognostic Factors on OS and PFS in Elderly Patients

Characteristic	n	3-year OS(%)	*P*	3-year PFS(%)	*P*
Gender			.773		.405
Male	58	89.7		88.2	
Female	17	87.5		94.1	
Age (years)			.087		.088
60-69	53	94.3		86.2	
≥70	22	76.7		100	
T stage *			.019		.970
T1	6	80.0		83.3	
T2	9	100.0		83.3	
T3	30	95.8		90.0	
T4	30	73.0		86.6	
N stage *			.388		.053
N0	9	77.8		66.7	
N1	27	88.6		86.4	
N2	36	91.7		97.0	
N3	3	100		66.7	
Clinical stage *			.018		.782
II	10	87.5		90	
III	33	96.2		90.8	
IV	32	74.8		87.8	
Comorbidity			.793		.510
No	37	91.7		85.5	
Yes	38	86.8		94.2	
NAC			.835		.071
No	23	82.1		100	
Yes	51	92.1		85.5	
CC			.180		.233
No	27	77.4		95.7	
Yes	48	90.5		87.0	
AC			.353		.487
No	51	86.2		90.6	
Yes	22	95.2		86.4	
Cycles of h-R3			.927		.311
<6 weeks	17	94.1		81.3	
≥6 weeks	58	87.7		92.3	
Dose of h-R3			.273		.841
<1200 mg	24	86.3		87.0	
≥1200 mg	51	86.0		91.0	
Tumor response			.063		.039
CR	64	88.9		91.3	
Non-CR	11	77.9		80.0	

Abbreviations: NAC neoadjuvant chemotherapy; CC concurrent chemotherapy; AC adjuvant chemotherapy; h-R3 nimotuzumab; CR complete response; * The 7th AJCC/UICC staging system.

events in the older patients were reported by several retrospective studies [28,29], whereas elderly patients experienced more toxicities were found by other studies [30,31]. Occurrence of comorbidities and metabolic changes has been more frequently observed in the older patients [32]. And on the basis of these conditions, treatment may induce more complications [33]. A systemic review reported that chemotherapy increased grade ≥3 side effects for cancer patients with comorbidities [9]. In this study, we observed 38 (50.7%) elderly patients with comorbidities including diabetes mellitus, hypertension and cardiovascular disease. So it is necessary to introduce more effective and low toxicities drugs to involve in the comprehensive treatment for elderly NPC patients. Therefore, we evaluated the efficacy and safety of nimotuzumab plus RT with or without chemotherapy in the treatment of elderly NPC patients.

With the further research of the molecular mechanism of tumorigenesis and tumor development, molecular targeted therapy in patients with nasopharyngeal carcinoma will become the research hotspot. 94% patients with NPC were detected for over expression of EGFR [14]. Cetuximab, as a most common drugs used for anti-EGFR monoclonal antibody, has a good curative effect in the treatment of nasopharyngeal carcinoma, with 2-years PFS of 86.5% - 89.3% and 3-year OS of 90.9% [18], but severe oral mucositis and itchy acneiform rash limited its application in nasopharyngeal cancer. To minimize cetuximab-related toxicities, novel EGFR-targeted agent was warranted.

Nimotuzumab, as a humanized Immunoglobulin G1 (IgG1) isotype monoclonal antibody with unique safety profile and low skin toxicity, has been approved for the treatment of non-NPC HNSCC [12,34]. The advantage of the drug is that the affinity constant is quite lower than that of cetuximab, allowing for high tumor uptake and low normal tissues uptake [35]. Nimotuzumab requires bivalent binding for stable attachment, which renders the agent to selectively binding to tumors with moderate-to-high EGFR levels. When EGFR expression is low as on the normal tissues, cetuximab still had high ability of binding because of its higher affinity constant [35]. All of these indicated that nimotuzumab plus RT could be selected in the design of the clinical trial of NPC. Our experiment confirmed that nimotuzumab has sensitization of radiotherapy on nasopharyngeal carcinoma cell line CNE-2 in vitro, and can reduce cancer cell proliferation, induce cell apoptosis, and change in cell cycle distribution [36]. In a phase II study of nimotuzumab plus RT for stage III to IVb NPC, the nimotuzumab add-on group was superior to the placebo add-on group, resulting in a significantly higher complete remission rate (90.63% vs. 51.52%, respectively, $P = .02$) and higher 3-year overall survival rate (84.29% vs. 77.61%, respectively, $P < .05$) without increasing radiation-related adverse events [37]. Our phase II study has shown that compared with chemoradiotherapy (CRT), nimotuzumab plus CRT produced the similar efficacy without increasing the acute severe dermatitis/mucositis for LA NPC [38]. Similar results were also observed in some retrospective study where nimotuzumab was combined with concurrent CRT in treatment LA NPC [27,28]. So, nimotuzumab provides a promising option for LA NPC. But the role of nimotuzumab in the combined treatment of in elderly NPC patients remains unknown.

This study retrospectively analyzed the efficacy and safety of 75 elderly NPC patients received nimotuzumab plus RT with or without chemotherapy. Our results showed promising clinical outcomes, with 3-year LRFS of 95.6%, 3-year RRFS of 95.5%, 3-year DMFS of 98.6%, 3-year PFS of 89.7%, and 3-year OS of 89.2%. Sze et al reported that 5-year OS rate of elderly NPC patients aged >70 years was 43.9% after radical radiotherapy 39. In the current study, 3-year OS rate was 76.7% for patients aged ≥70 years. Zeng et al indicated that 5-year OS and DMFS rates were 62%, 40% and 75%, 73% in aged ≥60 years patients treated with CRT and RT alone, respectively, but the incidence of grade ≥ 3 mucositis were 46.0% and 28.7% in two group, respectively 40. In our study, 34.7% of patients experienced grade ≥3 hematologic toxicity and 12.0% developed

Table 4. Multivariate Analysis of Prognostic Factors in Elderly NPC Patients

	Characteristic	HR	95% CI	*P*
OS	Age ≥70 years	0.138	0.035-0545	.005
	T4	0.129	0.033-0.503	.003
	Non-CR	0.132	0.032-0.547	.005

Table 5. Toxicity of Nimotuzumab Plus Radiotherapy and Chemotherapy

Adverse events	0	1	2	3	4
Leucopenia	10	19	20	22	4
Neutropenia	13	20	16	20	6
Anemia	52	12	8	3	0
Thrombocytopenia	44	18	8	4	1
Liver function	53	8	4	0	0
Renal function	68	7	0	0	0
Mucositis	12	32	22	6	3
Dermatitis	12	53	10	0	0
Diarrhea	63	11	2	0	0
Nausea/vomiting	44	17	9	3	2

grade ≥3 radiotherapy–related oral mucositis. No grade 3 dermatitis was observed within the RT field. No acneiform eruptions were found among these subjects. Compared with historical data, nimotuzumab plus RT was effective and well-tolerated strategy.

Furthermore, univariate analysis revealed that T stage and clinical stage were significant prognostic factors for OS, and tumor response at the end of treatment was a significant prognostic factor for PFS. Multivariate analysis indicated that age≥70 years, T4 and non-CR were poorer prognostic factors for OS. And we found that either NAC or CC did not improve OS in elderly NPC patients (5-year OS of 83.5% in patients with NAC vs. 82.1% in patients without NAC; 5-year OS of 86.8% in patients with CC vs. 77.4% in patients without CC).

Our experiences found that nimotuzumab plus RT with or without chemotherapy in the treatment of elderly NPC patients is safely and effective. However, due to retrospective study nature and small number of cases, our results should be regarded as preliminary.

Conclusion

In conclusion, our study observed that the administration of nimotuzumab with RT in elderly NPC patients was tolerated and showed promising clinic outcomes. Further randomized, controlled, multicenter phase III clinical trials are needed to confirm the ultimate therapeutic gain.

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

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