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Retrospective Analysis of 5-Year Survival Rate of Nasopharyngeal Carcinoma: Correlation with Clinical Features and Prognosis

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Abstract

Main Objective: This study was designed to evaluate the epidemiological characteristics of NPC and their prognostic value, with a goal to correlate with Clinical Features and Prognosis.

Results: The 5-year overall survival (OS) rates for patients in stages I, II, III and IV were 66.7%, 55.6%, 41.8% and 25.9%, respectively (P=0.026), while the respective 5-year progression-free survival (PFS) rates were 60.0%, 51.1%, 36.6% and 18.6% (P=0.044). Clinical staging appears to be the most important prognostic factor for NPC. As the stage number increases, both the 5-year OS and PFS significantly decrease.

The respective 5-year OS rates, according to stage, for the group that received radiotherapy combined with chemotherapy (Concurrent Chemotherapy-CCRT or Neo-adjuvant Chemotherapy-NAC-) and for the group that received radiotherapy only were as follows: stages I and II, 62.7% and 58.7% (P=0.450); stage III, 34.0%, 28.6% (P=0.460); stage IV, 36.7%, and 0.0% (P=0.036). The respective 5-year PFS rates in these groups were as follows: stages I and II, 56.0% and 50.2% (P=0.550); stage III, 26.9% and 15.0% (P=0.025); stage IV, 23.6% and 0.0% (P=0.008). Patients with stages I or II NPC will likely not benefit from the addition of chemotherapy, in terms of long-term survival and PFS. However, for patients with stage III NPC, adding chemotherapy can improve PFS to a certain degree though it may not improve OS and in patients with stage IV NPC, the addition of chemotherapy can significantly prolong both OS and PFS.

Keywords: Retrospective analysis; nasopharyngeal carcinoma (NPC); Treatment; Prognosis

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Introduction

NPC is a much more common malignancy in Southeast Asia, especially in the southern coastal area of Mainland China and in Hong Kong, Macao, and Taiwan. The annual incidence rate among the male population in Hong Kong is about 20/100,000 [1]. The incidence of NPC gradually increases with age, peaking at 50-59 years of age, and then tends to decrease [1]. Furthermore, the prognosis for those with NPC tends to worsen with age [1]. There is a notable difference in the pathological types of NPC that occur within different regions. The keratinizing type of NPC (WHO Type I) mainly occurs in Western countries with overall low incidences of NPC. However, NPC tends to be of an undifferentiated, non-keratinizing subtype (WHO Type III) in South China and in Southeast Asian countries where the overall incidence of NPC is higher [1]. Patient survival rates also differ depending on the different pathological type of NPC. Patients with Type III have significantly better survival rates compared to those with Type I [2,3].

Surgical resection is very difficult due to the fact that NPC is anatomically deep and occurs close to important neurovascular structures. Thus, the mainstay strategies for the treatment of NPC are radiotherapy-based, comprehensive therapies, including concurrent chemoradiotherapy, as well as induction or adjuvant chemotherapy and palliative chemotherapy following radiotherapy [4]. Prognosis is affected by treatment approach, race, histological type, and disease stage [3,5,6] Many factors that impact the long-term survival of NPC patients have not yet been fully clarified [7-9]. In the current study, the clinical data from NPC patients in the Hainan Province was retrospectively analyzed in order to clarify epidemiological characteristics, influencing factors and patient survival.

The main purpose of the study was to know the overall five-year survival rate of Nasopharyngeal Carcinoma cases. It is significance study; this would indicate all the favorable and poor prognostic factors which determine the OS and PFS for NPC.

The aim of the study was achieved during the analysis of the below factors; through the indicators used and their prognosis. The study reveals that clinical stage is the most important factor for NPC. As the stage number increases, both the 5-year OS and PFS significantly decrease. The study further reveals females have favorable prognostic factors; gender is a major factor in the incidence of NPC and slightly indicative an independent prognostic factor affecting OS and PFS. In the current study, the five-year survival rate in patients older than 50 years of age was significantly lower than in patients younger than 50 years of age. Less than 50-year is an advantage prognostic factor. The addition of chemotherapy to radiotherapy improves the outcome of the treatment.

Patients and Methods

Ethical Consideration Issues

Prior to conducting the study approval of the head of ethics committee, Head of Research Management Institute, Head of Department Otorhinolaryngology Head and Neck, Head of Department Radiotherapy, Head of Department Oncology, Head of Department Medical Records was sought before activities carried out. Upon applying through the research department then further to the ethical consideration committee, the committee, however, verified the purposes and significance of the study. Additionally, the committee verified each researcher information thoroughly and their capability to participate and conduct the study. The ethics consideration committee further organized a meeting with the researchers and the importance of the study was explained to the committee and their full consent sought and approved.

Data collection

Clinical data was collected from all histologically confirmed, new cases of 183 NPC, which occurred between 2007 and 2011, including 135 males and 48 females, aged 12-85 year old, with an average age as (47.94 ±13.250) years at Hainan Medical College First Affiliated Hospital. Patients that had been previously diagnosed with NPC and treated, but who had relapsed during this period, were excluded. However, the study did include patients that had been diagnosed with NPC outside of First Affiliated Hospital between 2007 and 2011, who then underwent subsequent treatment and follow-up at Hainan Medical College First Affiliated Hospital.

Data collected included patient demographics, NPC stage, histological type, treatment modalities, treatment efficacy, and survival time. Patient demographic characteristics included gender, age, and marital status. Age data were divided into two groups: those younger than 50 years of age and those 50 years of age and older. The disease was restaged in accordance with the eighth edition of the American Joint Committee of Cancer (AJCC) TNM staging system [10] and

the tumor pathological types were determined according to the WHO's NPC classification [11].

Radiotherapy Modalities

The treatment modalities were radiotherapy alone, neoadjuvant chemotherapy followed by radiotherapy, concurrent chemoradiotherapy plus adjuvant chemotherapy, or palliative treatment. The agents used in neo-adjuvant chemotherapy were cisplatin combined with 5-FU. The concurrent chemoradiotherapy and adjuvant chemotherapy treatments were the same as those used by Zhang et al. [12]. Palliative treatment of advanced tumors included single-agent chemotherapy or combined chemotherapy and radiotherapy.

All patients in the three groups underwent radiotherapy with Cobalt 60 gamma photons using conventional techniques. Two laterally opposed fields were used to treat the nasopharynx and the upper neck and an anterior cervical field with a midline shield were used to treat the lower neck to 38.4– 40 Gy. Thermoformable mask was used for contention. The remainder dose of irradiation was delivered via an anterior nasal field which included the nasopharynx and a large anterior cervical field treating all cervical nodes.

External beam radiotherapy was delivered with two modalities. One hundred and twenty-seven patients were treated with conventional fractionation and 56 patients with hyperfractionated radiotherapy (1.6 Gy × 2/day with an interval of 6 hours, 5 days per week). The hyperfractionated schedule was used in a previous randomized phase III trial [13]. The total dose to the nasopharynx and involved neck areas was 70–75 Gy and was 50–55 Gy to the remaining cervical areas from level II to level V.

Examinations and Follow-up

Patients were examined prior to treatment and during the follow-up period after treatment. Examinations included a complete medical history and physical examination, a craniofacial examination (including dental and cranial nerve exams), nasopharyngo-fiberscope, a complete blood count, serum biochemistry, a chest X-ray, and a CT or MRI examination of the nasopharynx, skull base and any suspicious metastatic sites, including the paranasal sinuses. Treatment efficacy was evaluated using the WHO criteria [14]. After treatment, the patients were asked to return to the clinic once every three months, for two years and then every six months until relapse or death. The follow-up period was defined as the period from the date of diagnosis until death or until the last follow-up time. Patients with disease recurrence, progression, and those that were lost to follow-up were considered to have died on the day of their last follow-up. Local recurrence was confirmed by examination of the nasopharynx, head, and neck and was verified by needle aspiration biopsy or MRI. Distant metastases were identified by clinical symptoms, physical examination, or bone scans and verified by CT or MRI scan(s).

Assessment and Statistical Analysis

Prognostic factors for NPC patients were determined by analyzing the associations between patient survival and the following: age, gender, disease-stage, NPC histological type, treatment modalities, and primary therapeutic effects. Overall survival (OS) was defined as the time from diagnosis to the time of death from any cause. The cut-off time for patients who survived was defined as the time of the last visit. Progression-free survival (PFS) referred to the time from the start of treatment until recurrence, disease progression or death from any cause. The cut-off time for the cases without disease progression was defined as the time of the last visit. SPSS 19.0 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. The survival curves were analyzed using the Kaplan-Meier method and the survival curves of different groups of patients were compared using a log-rank test. The Cox proportional hazard model was used for multivariate analysis of the prognostic factors, including the patient, tumor and treatment modalities. A total of 183 newly diagnosed cases of NPC were treated in Hainan Medical College First Affiliated Hospital between January 1, 2007, and December 31, 2011. The age of disease onset was similar to the normal distribution, with a median age of 48.0 years (Table 1).

Patients were followed every 3 months during the first 2 years, every 6 months for the next 3 years, and then every year until death). The 5-year survival rate for all patients that underwent follow-up was 49.8%, however, the median survival (5-year) was not reached and could not be calculated. The 5-year survival rates for patients with stages I, II, III, and IV NPC were 66.7%, 55.6%, 41.8%, and 25.9%, respectively. There was a significant difference in the survival curves among patients in different clinical stages (P=0.026) (Figure1). The prognostic significances of age, gender, T stage, M stage, primary treatment modality, and therapeutic effect were evaluated by univariate analysis (Table 2). Favorable prognostic

Characteristics	Number	%
Age(year)	47.94±13.250	
Range	1 2-85	
Median	48. 00	
Male: Female	135:48	
Histology		
WHOType I	20	10.9
WHOType II	41	22.4
WHOType III	122	6.7
Stage(AJCC2010)		
StageI	15	8.2
StageII	45	24.6
StageIII	96	52.5
StageIV	27	14.8
T Classification		
T1	35	19.1
T2	73	39.9
T3	56	30.6
T4	19	10.4
N Classification		
N0	43	23.5
N1	83	45.4
N2	48	26.2
N3	9	4.9
M Classification		
M0	178	97.3
M1	5	2.7
Primary Treatment		
RT	20	11. 0
NAC+RT+CCRT	14	24. 0
CCRT+RT+AC	119	65. 0

Table 1: Patients Characteristics

AJCC, America Joint Committee on Cancer; RT, Radiotherapy, NAC, Neo-adjuvant Chemotherapy, CCRT, Concurrent Chemotherapy

Univariate analysis of prognostic factors for OS and PFS							
Factors	n()	5-year OS rate (%)	x2	*P value	5year PFS rate(%)	x2	*P value
Age-group							
<50 50 and above	103 80	58.3 **41.3**	5.208	0.022	53.4 **32.5**	4.773	0.029
Gender							
Male Female	135 48	43.8 60.3	4.15	0.042	39.6 59.3	4.38	0.036
Stage (AJCC 2014)							
Stage I Stage I I Stage I I I Stage IV	15 45 96 27	66.7 55.6 41.8 25.9	9.275	0.026	60.0 51.1 36.6 18.6	8.103	0.044
T classification							
T1 T2 T3 T4	35 73 56 19	57.1 54.4 41.4 21.3	9.113	0.028	51.4 50.7 35.7 15.8	9.737	0.021
M classification							
M0 M1	178 5	50.6 0.00	4.975	0.026	48.3 0.00	4.558	0.035
Primary treatment							
RT NAC+RT+CCRT CCRT+RT+AC	20 44 119	42.1 50.4 69.7	8.921	0.012	36.8 45.5 67.2	10.50	0.005
Treatment	Effects						
NC PD PR CR	11 14 34 124	9.1 14.4 47.1 56.5	16.567	0.001	0.0 7.1 41.2 52.4	20.061	0.000

Table 2: Univariate analysis of prognostic factors for OS and PFS

AJCC, America Joint Committee on Cancer; RT, Radiotherapy, NAC, Neo-adjuvant Chemotherapy; AC, Adjuvant Chemotherapy, CCRT, Concurrent Chemotherapy; CR, complete response; PR , partial response; NC, no change; PD, progression disease; OS, overall survival; PFS, progression free survival

	No. of	OS				PFS	
Variable	Patients	Hazard ratio	95% CI	*P value	Hazard ratio	95% CI	*P value
Age group <50	103	1.12	1.41- 3.82	0.043	2.052	1.20-3.05	0.017
50 and above	80						
Gender							
Male	135	0.35	0.147-0.817	0.01	0.383	0.189-0.776	0.07
Female	48						
Histology							
WHO Type I	20	2.57	0.841-1.853	0.088	1.408	0.667-2.969	0.368
WHO Type II	41						
WHO Type III	122						
Stage (AJCC 2010)							
Stage I	15	0.748	0.317-1.764	0.034	1.008	0.502-2.025	0.029
Stage II	45						
Stage III	96						
Stage IV	27						
T classification							
T1	35	1.427	0.610-3.337	0.025	1.05	0.54-2.039	0. 000
T2	73						
T3	56						
T4	19						
N classification							
N0	43	0.904	0.464-1.758	0.765	1.232	0.622-2.437	0.547
N1	83						
N2	48						
N2	9						
M classification							
M0	178	4.278	0.679-26.940	0.019	4.304	0.697-26.576	0.046
M1							
Primary treatment							
RT	20	2.114	1.123 -3.978	0. 000	0.636	0.322-1.254	0.01 0
NAC+RT+CCRT	44						
CCRT+RT+CCRT	119						
Treatment Effects							
NC	14	1.165	0.611-2.224	0.004	1.364	0.696- 2.674	0.03 0
PD	17						
PR	34						
CR	118						

Table 3: Multivariate analysis prognostic factors for OS and PFS

AJCC, America Joint Committee on Cancer; RT, Radiotherapy, NAC, Neo-adjuvant Chemotherapy, CCRT, Concurrent Chemotherapy; CR, complete response; PR , partial response; NC, no change; PD, progression disease; OS, overall survival; PFS, progression free-survival; CI, confidence interval.

Factors	N=183	RT(n=20)	NAC+RT+CCRT(n=44)	CCRT+RT+AC(n=119)	x2	*P value
Age group						
Less than 50	103	13	20	65	1.961	0.375
50 and above	80	7	23	54		
Gender						
Male	135	10	34	91	1.201	0.319
Female	48	7	10	31		
Histology						
WHO Type I	20	1	5	14	3.374	0.497
WHO Type II	41	7	7	27		
WHO Type III	122	12	32	78		
Stage(AJCC2010)						
Stage I	15	15	2	28	70.487	0. 000
Stage II	45	3	24	30		
Stage III	96	1	2	47		
Stage IV	27	1	16	14		
T classification						
T1	35	15	2	28	49.873	0. 000
T2	73	3	17	37		
T3	56	1	9	40		
T4	19	1	16	14		
M classification						
M0	178	20	44	119	8.434	0 .004
M1	5		1	4		

Table 4: Characteristics of patients' different primary treatment modalities

AJCC, America Joint Committee on Cancer; RT, Radiotherapy, NAC, Neo-adjuvant Chemotherapy, CCRT, Concurrent Chemotherapy; M0 , no distance metastasis; M1 , distance metastasis

				OS rate (%)					PFS rate (%)		
Variable No. of	RT	NAC +RT+ CCRT	CCRT +RT+ AC	RT		NAC+ RT+ CCRT					C CRT+ RT+ AC
Patients=183		(n=20)	(n=44)	(n=119)	x2	*P value	(n=20)	(n=44)	(n=119)	x2	*P value
Stage (AJCC2010)											
Stage I	60	34	58.3	62.7	62.451	0. 00	26.9	43.9	56	61.202	0. 000
Stage II	96	28.6	44.3	58.7			15. 0	36.1	50.2		
Stage III	27	0. 0	20. 0	36. 7			0. 0	10. 5	23. 6		
T classification											
T1	35	28.9	47.54	60 .0	0. 028	0.06 0	25.36	44.32	54.4	0.025	0.067
T2	73	20.9	34.6	47.3			19.6	26	45.7		
T3	59	17.1	26.1	45. 0			15.3	17.2	33.6		
T4	19	5.26	22.9	44. 4			4.9	12.3	30		
N classification											
N0	43	39.2	44.4	52.1	0.165	0.059	30.2	38.3	47.8	0.122	0.07 0
N1	83	30.2	38.6	46.9			28.3	23.3	46.5		
N2	48	14.5	29.5	44.1			10.4	21.6	22.7		
N3	9	8.3	11.1	12.6			1.2	2. 0	7. 6		
M classification											
M0	178	29.21	54.8	60.6	0.629	0.73	11.7	32.02	46.4	4.957	0.175
M1	5	0	8. 87	10.2			0. 0	1.53	5. 70		

Table 5: Five –year OS and PFS rates of different stages and treatment modalities

AJCC, America Joint Committee on Cancer; RT, Radiotherapy, NAC, Neo-adjuvant Chemotherapy, CCRT, Concurrent Chemotherapy; OS, overall survival; PFS, progression free-survival; M0 , no distance metastasis; M1 , distance metastasis.

indicators for relatively longer OS included being less than 50 years of age, being female, having an earlier T stage, the absence of distant metastases, having had treatment with Concurrent Chemotherapy combined with radiotherapy and Neo-Adjuvant Chemotherapy, and achieving remission after first-line treatment (P<0.05). Age, gender, T stage, M stage, primary treatment modality, and initial therapeutic effect were all independent prognostic factors for OS, as indicated by multivariate Cox regression analysis (Table 3).

as 50–55 Gy to the remaining cervical areas from level II to level V.

The 5-year PFS rate was 42.95% for all patients. The PFS rates for patients with stages I, II, III, and IV NPC were 60.0%, 51.1%, 36.6%, and 18.6%, respectively. Just like the median survival, the median PFS (5-year) was not reached either. Clinical stage was found to be a significant prognostic indicator for PFS (P<0.05) (Figure 2). Univariate analysis showed that gender, T stage, M stage, primary treatment modality, and treatment efficacy were all prognostic factors for PFS in patients (Table 2). Favorable prognostic indicators for relatively long PFS included being a woman, having an earlier T stage, having no distant metastases, having had concurrent Chemotherapy combined with radiotherapy and achieving remission after primary treatment (P<0.05). Age, gender, T stage, M stage, the primary treatment modality, and the efficacy of first-line therapy were all independent prognostic factors for PFS, as indicated by multivariate analysis (Table 3).

The 5-year OS and PFS rates were significantly better in the combined radiotherapy (Concurrent Chemotherapy-CCRT or Neo-adjuvant Chemotherapy-NAC-) groups compared with the group that received the only radiotherapy. The effect of treatment modality on long-term survival was further examined via sub-group analysis of the demographic characteristics, pathological type and stage of NPC in these two patient groups (Table 4). The group treated with a combination of chemotherapy and radiotherapy (Concurrent Chemotherapy-CCRT or Neo-adjuvant Chemotherapy-NAC-) groups was again at a significantly later stage of NPC, on average, than the group that was treated with radiotherapy alone, indicating that the patients were not randomly assigned to each group and that more late-stage patients received radiotherapy combined with chemotherapy. Long-term survival was further analyzed according to different subgroups excluding interference due to unbalanced stage distribution between the three groups (Table 5). When comparing the treatment modalities, there was no significant difference in the 5-year OS and PFS of patients with stages I and II NPC (P=0.450 and P=0.550, respectively) (Figure 3). The 5-year PFS in stage III patients treated with a combination of radiotherapy and chemotherapy was significantly better than stage III patients that were treated with radiotherapy alone (P=0.025), however, there was no significant difference in the 5-year OS of stage III patients when comparing these treatment modalities (P=0.460) (Figure 4). The 5-year OS and PFS were both significantly better for stage IV patients that received combined chemotherapy and radiotherapy compared with stage IV patients that were treated with radiotherapy alone (P=0.036 and P=0.008) (Figure 5).

Results

Gender indicates a major factor incidence of nasopharyngeal carcinoma: from the study occurrence of nasopharyngeal carcinoma, males (135) and females (48) had shown as NPC in males is 2 – 3 times than in females in (Table 2, Table 3).

Age group has an impact on survival: Overall survival and Progression-free survival is worse in >50yrs. than < 50yrs. (P value 0.022 and 0.029). The 5-year Overall survival and Progression-free survival for all patients were 49.8% and 42.9% and 5-year OS rate; male and females 43.8% and 60.8% (P-value 0.042), 5-year PFS rate; male and female 39.6% and 59.3% (P-value 0.044) captioned as shown elsewhere and reported in (Table 2, Figure 1 and Figure 2).

The findings on 5-year Overall survival and Progression-free survival stages I, II, III, IV were 66.7%, 55.6%, 41.8% and 25.9% and 60.0%, 51.1%, 36.6%, and 18.6% observed in (Table 2, Figure 3 A and B) respectively.

The study indicated the results obtained according to stages and treatment modalities for overall survival and Progression-free survival as indicated below;

Overall survival for CCRT+RT+ AC stages I and II: 62.7% and 58.7%, NAC +RT +CCRT stages II and III: 43.6% and 20.0%, RT alone for stages III & IV: 36.7% and 0.0%. The Progression-free survival for CCRT+RT+ AC stages I and II: 56.0% and 50.2%, NAC +RT +CCRT stages II and III: 36.1% and 10.1%, RT alone for stages III & IV: 23.6% and 0.0%, the CR (complete remission) were 56.5%, PR Partial remission) of 47.1% with significant 5-year OS and PFS (p-value: 0.001 and 0.000) captioned and shown elsewhere and reported (Table 2), Figure 3A), (Figure 4 A, B), and (Figure 5 A, B).

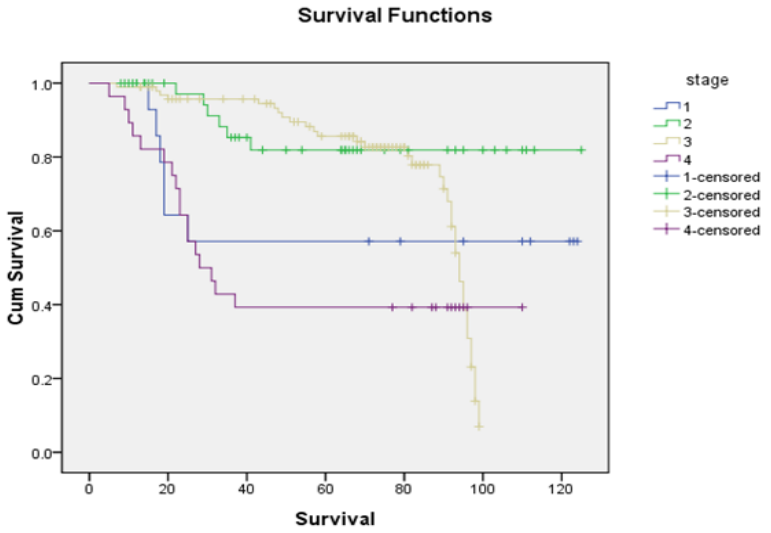

Figure: 1 Comparison of OS among AJCC stages. OS, overall survival; AJCC, American Joint Committee on Cancer

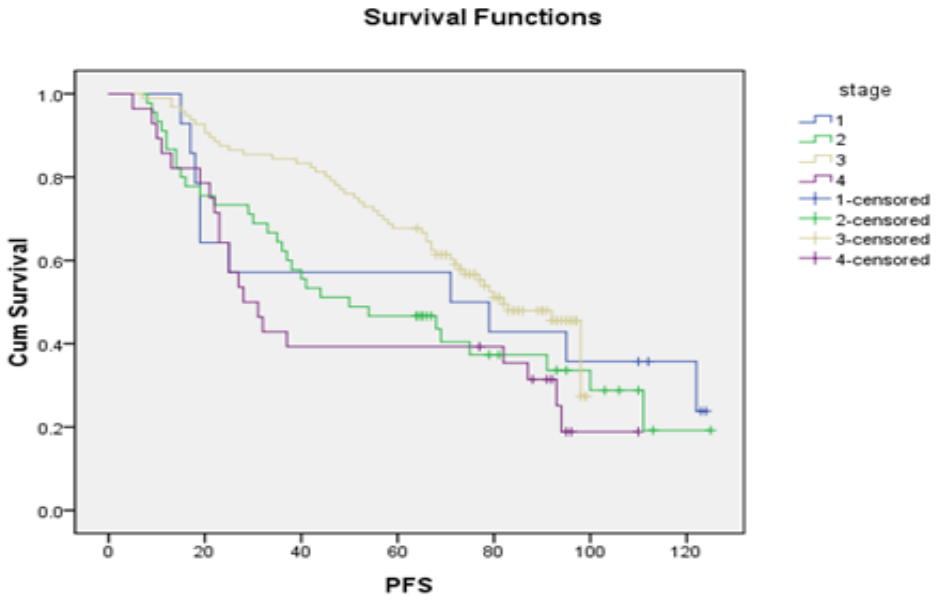

Figure: 2 Comparison of PFS among AJCC stages. PFS, progression free survival; AJCC, American Joint Committee on Cancer

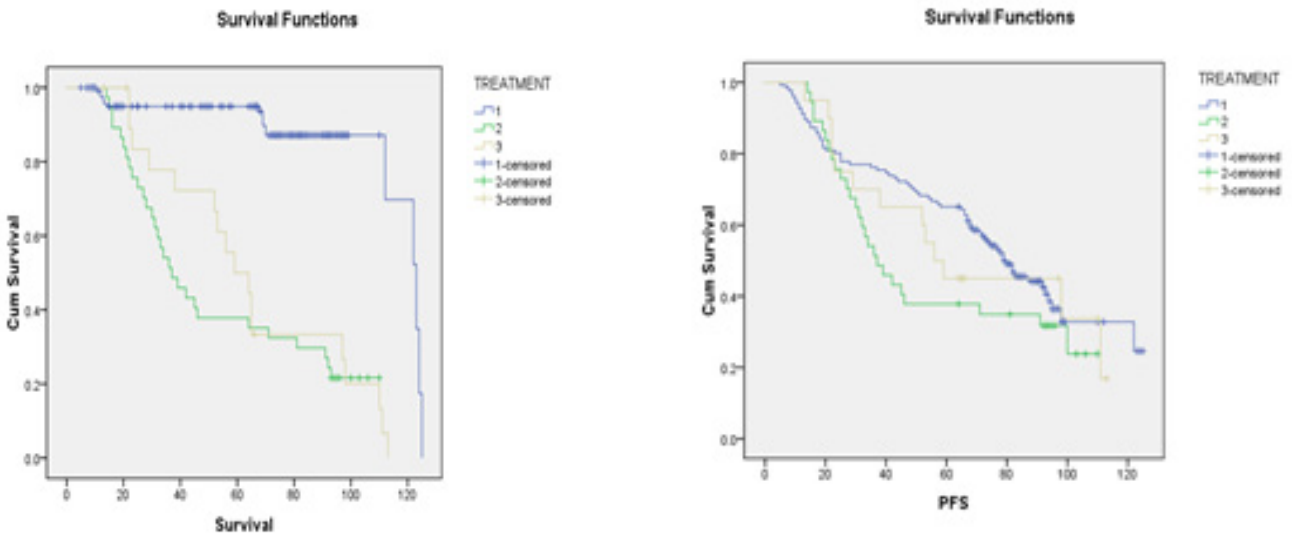

Figure: 3 Comparison of OS (A) and PFS (B) between the treatment methods in stage I-II. OS, overall survival; PFS progression-free survival.

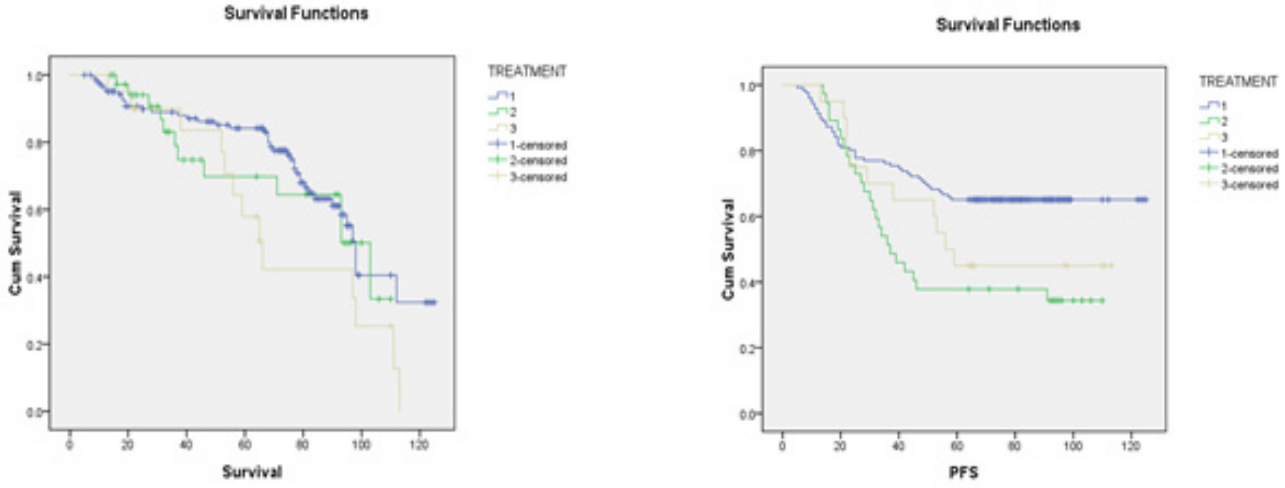

Figure: 4 Comparison of OS (A) and PFS between the treatment methods in stage III. OS, overall survival; PFS, progression-free survival.

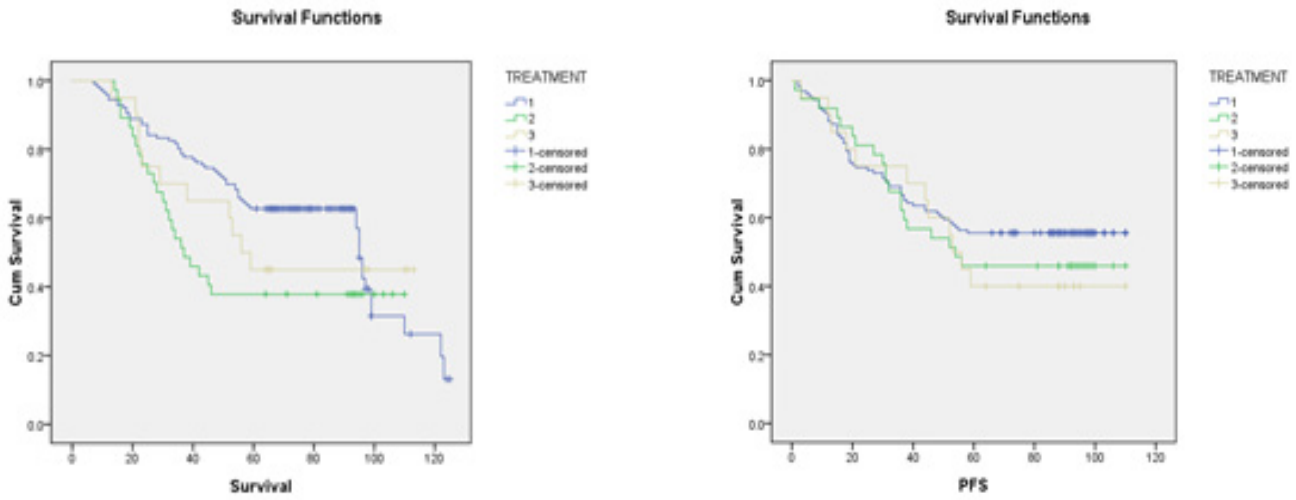

Figure 5: Comparison of OS (A) and PFS between the treatment methods in stage IV. OS, overall survival; PFS, progression-free survival.

WHO type I & II; accounts for 33.3%, WHO type III; recorded 6.7%, the Overall survival (p-value: 0.088), (P value 0.388) respectively. 5- Year Overall survival and Progression-free survival rates indicate that T1: 35 were 2.68 and 3.25 times that of patients with T4: 19 in (Table 1, 2, 3, 4 and 5).

Discussion

In the current study, the five-year survival rate in patients older than 50 years of age was significantly lower than in patients younger than 50 years of age (P=0.022), similarly there was also a significant difference in 5-year PFS between the two age groups (P=0.029), this indicates that the prognosis for OS in older patients is worse than in younger patients. Age was also found to be an independent prognostic factor affecting the long-term survival of patients with NPC. On the other hand, a retrospective study done in Malaysia reported that the risk of death within five years for NPC patients older than 70 years of age was 3.18 times that of patients younger than 50 years of age [15].

Existing epidemiological data demonstrate that gender is a major factor in the incidence of NPC. The occurrence of NPC in males is 2-3 times that in females; this is similar to the results found in the current study [16, 17]. Previous studies have reported slightly better, though not significant, long-term survival rates in women with NPC than in men [15]. However, in one Japanese retrospective study, a significantly higher 5-year survival rate was reported for female patients compared to male patients (P=0.484), through multivariate analysis showed that gender was not an independent prognostic factor for survival in this study [16]. In sharp relations studies done in Macau respectively, suggesting that gender was an independent prognostic factor [17]. Similarly, in the current study, the 5-year OS rate for male and female patients was 43.8% and 60.3% (P=0.042) and the 5-year PFS rate was 39.6% and 59.3% (P=0.044), slightly indicative for gender been also an independent prognostic factor affecting OS and PFS.

Some studies have demonstrated that patients with WHO Type III NPC are more sensitive to radiotherapy, and survive longer, than those with Type I [18]. However, there is not yet enough evidence that supports the idea that patients with different pathological types of NPC require different treatment modalities [1, 19]. In the current study, patients with WHO Type III NPC accounted for only 6.7% of cases, while those with Types I and II accounted for only 33.3% of cases. No statistically significant difference found in OS (P=0.088) or PFS (P=0.368) among the different pathological types in the current study, though this is contrary to previously published results [15, 16]. A retrospective study conducted in Malaysia showed that the risk of death was 1.97 times greater in patients with WHO Types I and II NPC than in patients with type III [15]. Similarly, in a retrospective Japanese study, patients with the non-keratinizing type of NPC (WHO Types III and II)

were found to have higher 5-year OS and PFS rates than those with the keratinizing type (WHO Type I) [16]. Two studies, conducted in Brazil, and Macao reported results similar to the current study and concluded that there was no significant difference in the 5-year disease-specific survival rates among different histological types of NPC [20, 21]. Many studies have confirmed a clear association between long-term survival and NPC clinical stage [15,16,19,20,21]. Results of the current study also demonstrated that, as the disease stage increased, the 5-year OS and PFS rates gradually and significantly decreased P = 0.000. Multivariate analysis established AJCC staging as an independent prognostic indicator for OS and PFS. Further analysis demonstrated that tumor size (T) and distant metastases (M) are decisive factors for OS and PFS, but that lymph node metastasis (N) staging has no independent prognostic significance for OS or PFS. The 5-year OS and PFS rates in patients with stage T1 were 2.68 and 3.25 times that of patients with T4, respectively. Whiles, in patients with M1, the risk of death was 4.28 times higher, similar to the risk of recurrence and progression 4.30 times higher than in patients with M0.

The efficacy of primary treatment was also found to be an independent prognostic factor affecting long-term survival. Among all 183 patients, the complete remission (CR) rate was 56.5%, progression disease rate (PD) was 14.4% and the partial remission (PR) rate was 47.1%. The 5-year OS and PFS rates were slightly higher and significant in patients with CR and PR than in patients without remission (P=0.001 and P=0.000, respectively). Based on this, the initial treatment modality and its therapeutic efficacy are the major factors affecting the prognosis of patients in all stages of NPC. Measures should be taken to achieve CR or PR during primary treatment as this will improve the long-term survival of patients in all stages of NPC.

NPC is sensitive to radiotherapy and chemotherapy [22,23]. Since surgical resection is difficult and the efficacy is poor, the primary treatment for NPC is radiotherapy and chemotherapy is used as an adjuvant option. Surgical resection is limited to cases in which there is a residual tumor or can be used as salvage therapy in cases of local recurrences. Although NPC is relatively sensitive to radiotherapy, the long-term survival for patients with advanced NPC is not ideal [20, 24, 25, 34]. According to the literature, the five-year survival rate for patients with stage IV NPC, who received radiotherapy only, is between 12.5% and 8.0% [25,26]. Depicting from the study, the appropriate addition of chemotherapy is necessary to improve long-term survival in these patients.

Most studies have indicated that adding chemotherapy to radiotherapy can improve treatment efficacy and prolong OS in patients with intermediate or advanced NPC, though not all studies have had positive results [9,20, 28-31]. Phua et al. found no difference in the prognosis among patients with different stages of NPC whether chemotherapy was added or not [15]. Also, a retrospective analysis by Chua et al. found that radiotherapy combined with induction chemotherapy resulted in only a mild improvement in PFS and in the relapse rate and no improvement in OS when compared with radiotherapy alone [9]. A phase III clinical trial conducted in patients with locally advanced NPC in China showed that adding adjuvant chemotherapy did not result in improved OS or relapse-free survival when compared with using concurrent chemo-radiotherapy [32]. Chen et al. reported that, in a randomized phase III trial, the 5-year survival in 230 cases of stage II NPC was significantly better in the group treated with combined radiotherapy and chemotherapy compared to the group treated with radiotherapy alone [34]. The prolonged survival in the combined group was mainly attributed to a lower rate of distant metastases; however, restaging these patients according to the latest TNM classification system [2014] revealed that a considerable portion of the patients should have been categorized as stage III [11].

The group (s) that received combined chemotherapy and radiotherapy was compared with the group that received radiotherapy only to determine the effect of adding chemotherapy on patient survival in our study. The 5-year OS and PFS rates in the combined chemotherapy and radiotherapy groups (CCRT+RT+AC, NAC+RT+CCRT) were significantly higher than in the radiotherapy only group (P=0.012 and P=0.005, respectively). Also, according to AJCC stage-based subgroup analysis, there was no much difference between the three groups in the 5-year OS rate of patients with stages I, II and III NPC, although the 5-year OS rate of patients with stage IV NPC was significantly higher in the chemotherapy combined with radiotherapy groups (CCRT+RT+AC, NAC+RT+CCRT) than in the radiotherapy only group. For patients with stage I or II NPC, the 5-year PFS rate was not significantly different in the combined groups vs. the radiotherapy only group (P=0.550). Conversely, for patients with stage III or IV NPC, the rate of 5-year PFS was significantly higher in the combined groups (CCRT+RT+AC,

NAC+RT+CCRT) than in the radiotherapy only group (P=0.025 andP=0.008, respectively).

Patients with stages I or II NPC will likely not benefit from the addition of chemotherapy, in terms of long-term survival and PFS. However, for patients with stage III NPC, adding chemotherapy can improve PFS to a certain degree though it may not improve OS and in patients with stage IV NPC, the addition of chemotherapy can significantly prolong both OS and PFS. A random trial from endemic regions of China also showed the addition of concurrent and adjuvant chemotherapy to RT provides survival benefits to patients with stage III through IVB NPC [31].

Conclusions

The current study indicates that in clinical practice, it is recommended that chemotherapy be added to radiotherapy for patients with stage IV NPC. Treatment modalities may include induction chemotherapy, concurrent chemoradiotherapy, and adjuvant or palliative chemotherapy treatment after radiotherapy. In patients with stage III NPC, the treatment should be based on the individual. Chemotherapy may be considered for patients that are otherwise in good general health or for patients that have a relatively advanced stage of NPC. In patients with mid and early stages of NPC, such as stage II or lower, chemotherapy is not really recommended.

The study conducted using conventional radiotherapy during the period under review will also serve as the basis for future study in IMRT survival assessments.

The study used was a descriptive cross-sectional, retrospective analysis and the clinical stage between the three groups. Sample method used was Universal sampling. This will invariably reduce bias from the study. However, a cohort study or randomized phase III could also be used if necessary for future study.

Declarations and Acknowledgements

Authors' contributions

Clement Arthur analyzed the data and wrote the paper. Hao Ruan, Collins Koranteng Osei, and Akparibila Joseph Azure and Xun Bi prepared and calculated the data. Xiaofeng Wang, Xue Jun Zhou, Sha Liu, and Ping Zhou, data check, analysis, and information retrieval. Clement Arthur and ZhongLin Mu conceived of the study and participated in its design, Technical advice, and coordination. All authors read and approved the final manuscript.

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Competing interests

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