Prognostic Factors and Survival in Nasopharyngeal Cancer: A Single Center Experience

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ABSTRACT

Our aim was to evaluate patients with nasopharyngeal carcinoma and determine the prognostic factors and overall survival. 154 patients who were diagnosed with nasopharyngeal carcinoma and referred to our clinic between 1996 and 2022 were retrospectively analyzed. 150 patients were treated with 70 Gy of radiotherapy, 4 patients did not receive treatment. Patients were stratified by tumor stage and histology. Survival analysis was conducted on 150 patients who received treatment. Of 150 patients who received treatment, 102 patients were male and 48 were female. The mean age was 49.45±15.75 (range: 12-82) years. Mean follow up time was 76.3 ± 76.1 (range: 1-278) months. The median overall survival time was 118 months (95% CI 34.4-201.59). The 2- and 5-year survival rates were 72.7% and 57.5%, respectively. On univariate analysis, T stage (p= 0.006), M stage (p< 0.0001), stage (p< 0.0001), histology (p< 0.001), radiotherapy treatment technique (p< 0.01), treatment modality (p< 0.0001) and metastasis status (p< 0.0001) were found to be prognostic factors influencing overall survival. The multivariate analysis revealed that stage (p< 0.0001), histology (p< 0.001), RT technique (p= 0.012), and metastasis status (p= 0.008) were prognostic independent factors. Nasopharyngeal carcinoma is a severe malignancy with relatively good outcomes. Concomitant chemoradiotherapy is a reliable treatment regimen and with developing radiotherapy techniques such as IMRT/VMAT, prolonged survival is one step closer. The majority of locoregional recurrence and metastatic cases occur four to five years following radiotherapy. More studies are in need with larger populations, as some countries has seen an increase in incidence recently.

Keywords: Nasopharyngeal carcinoma, Radiotherapy, Survival

INTRODUCTION

Nasopharyngeal Carcinoma (NPC) is a rare tumor usually seen in the 4th and 5th decades; the male/female ratio is 3/2. The number of new cases worldwide is approximately 80.000 annually, and the mortality rate is 50.000. Some areas, such as Southern China and Hong Kong, are considered endemic for NPC, where the incidence of NPC is mostly associated with tobacco use.[1] Additionally, the consumption of salted fish in the diet, the use of homemade harissa spice, and Epstein-Barr Virus (EBV) infection have been identified as contributing factors.[2,3] Its incidence is 1.2/100.000 in Turkey and is mostly observed between the ages of 50-70. It accounts for 0.7% of all cancer cases and 0.5% of cancer-related deaths.[4]

NPC presents diagnostic and staging challenges due to its location near structures like the oral cavity, nasal cavity, skull base, paranasal sinuses, and orbit.[5] Furthermore, these anatomical neighborhoods affect treatment planning and implementation processes. Preservation of functional and anatomical structures is as important as disease control.

Therefore, in the treatment of NPC, a multidisciplinary approach is essential. The primary treatment for early-stage and locally-advanced disease is usually radiotherapy (RT) and chemoradiotherapy (CRT), respectively.[6-7] Because of the risk of morbidity and mortality, surgery for NPC is limited to diagnosis and salvage treatment.

In recent years, it has been shown that the incidence has gradually decreased while the survival rate has significantly increased, which can be attributed to the better understanding of pathogenesis and risk factors, advances in imaging techniques, the widespread use of intensity-modulated radiotherapy (IMRT), and the development of chemotherapy strategies (induction, concomitant, and adjuvant). Also, breakthroughs have been achieved due to the use of second-series RT and new immune checkpoint agents to treat recurrent or metastatic disease, which also show promise in NPC.[8]

In this study, our aim was to evaluate local control, metastasis, and overall survival (OS) in T1N0 patients to whom we applied RT only, and ≥ T2 or ≥ N1, M0 patients to whom we applied CRT, and compare them with literature data.

PATIENTS AND METHODS

Patient Selection

We retrospectively reviewed the patients treated with the NPC diagnosis in our clinic between 1996 and 2022. Patients with pre- or concurrent malignancies were excluded at the start of the study. The study population included 154 patients with histopathological diagnoses between January 1996 and December 2022. Four patients refused the treatment. The survival analysis included 150 NPC pati-ents treated with curative intent. All patients underwent a routine detailed physical examination before treatment. Complete blood count and biochemical tests were performed. Routine clinical staging and scanning were performed, including thoracic computed tomography (CT), and brain and neck magnetic resonance imaging (MRI) scans and 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET-CT) was available for some patients. Pre-RT dental examinations were routinely performed. The patients were staged, according to the American Joint Committee on Cancer (AJCC).

Patients and Treatment

Among the patients, those with T1N0M0 received only RT, and those with ≥ T2 or ≥ N1 and M0 received CRT. The chemotherapy regimen consisted of three cycles of cisplatin 100 mg/m^2 (days 1, 22, and 43) or 40 mg/m^2 weekly. However, 3 cycles of induction chemotherapy (100 mg/m^2 cisplatin on day 1, 22, and 43 followed by 750 mg/m^2 5-fluorouracil as continuous 24 h infusion for 5 days on day 1, 22, and 43) were given to 13 patients since healthy tissue tolerance doses could not be achieved. Five of these patients were stage III, seven were stage IVA, and one was stage IVB. A fraction of the patients were aged ≤ 18, and despite their age, they underwent treatment following the same protocols as others.

Between 1996 and 2010, patients were treated with 2-Dimensional (2D) -RT, and between 2010 and 2022, with Intensity-Modulated Radiation Therapy (IMRT). All patients were immobilized in the supine position using a customized thermoplastic head-neck-shoulder mask.

RT areas were defined as follows: primary tumor and positive lymph nodes were given a margin of 5-10 mm (1 mm margin is accepted in the spinal cord, brainstem, optic nerve, and chiasm), and 70 Gray (Gy) RT was applied from 2 Gy/fraction to this area. The entire nasopharynx, skull base, clivus, pterigoid fossa, parapharyngeal space, posterior ethmoid sinuses, sphenoid sinus, posterior 1/3 of the nasal cavity and maxillary sinuses, bilateral cervical lymph nodes (For N+ disease, Level 1b–4; for N0 disease, Level 1b was skipped), and retropharyngeal lymph nodes were administered 60 Gy RT from 2 Gy/fraction.

Follow-up

Follow-up visits were scheduled every three months for the first three years and every six months for the following years. Fine-needle aspiration or biopsy was used to confirm distant metastasis or locoregional recurrence, whenever possible. Detailed physical examination, complete blood count, and biochemical tests were repeated at each visit, and brain and neck MRI and thoracic and abdominal CT were performed for clinical indications. Follow-up visits continued from the initial diagnosis to the last follow-up or date of death.

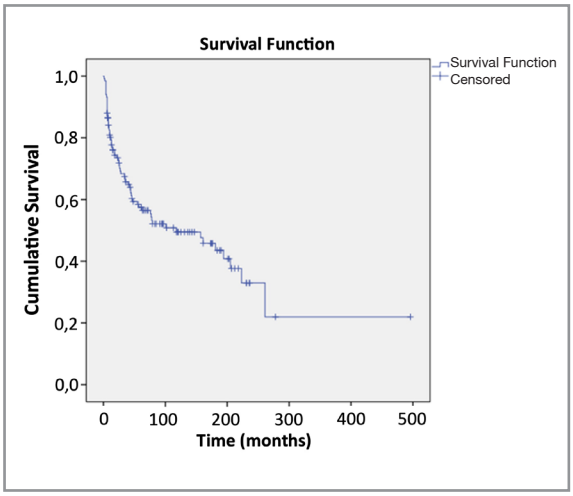

Figure 1. Kaplan Meier survival curve of patients with nasopharyngeal cancer

The institutional review board approved this retrospective analysis. (Karadeniz Technical University Faculty of Medicine Scientific Research Ethics Committee, Project No: 2017-77; May 08, 2017).

Statistical Analysis

The obtained data were subjected to statistical analysis using IBM SPSS Statistics (Version 23, Chicago, USA). Clinical outcomes were evaluated according to the time to locoregional recurrence, development of metastasis, or death after RT or CRT. OS and disease-free survival (DFS) were calculated using the Kaplan-Meier method. A bilateral log-rank test was used to analyze differences between subgroups to predict factors with independent prognostic significance on survival. All significant tests and statistical significance were considered as the calculated p value <0.05 statistical significance limit.

RESULTS

Between 1998 and 2022, we retrospectively analyzed 154 patients. Survival analysis was conducted on 150 patients; 4 patients were excluded, since they did not receive treatment. Our mean follow-up time was 76.3 ± 76.1 months (range: 1-278). The median survival time was 118 months (95% CI 34.4-201.59). The 2- and 5-year survival rates were 72.7% and 57.5%, respectively (Figure 1).

The study population consisted of 48 (32%) female and 102 (68%) male patients. For females, the median survival time was 181 months (95% CI 74.67-287.32). The 2- and 5-year survival rates were 80.4% and 61.8%, respectively. For males, the median survival time was 79 months (95% CI 0-178.25). The 2- and 5-year survival rates were 68.9% and 55.4%, respectively. There was no statistically significant difference in survival between genders (p= 0.492).

Our patients had a mean age of 49.45±15.75 years (range: 12-82). Under the age of 18, there were 8 patients (5%), while above the age of 19, there were 142 patients (95%). There was no statistically significant difference in survival between age groups (p= 0.053).

According to the T stage; T1, T2, T3, and T4 tumors was present in 38 (25%), 44 (29%), 31 (21%), and 37 (25%) patients, respectively. There was a statistically significant difference in survival between T stages (p= 0.006).

According to the N stage, 31 (21%) patients were classified as N0, 22 (15%) as N1, 87 (58%) as N2, and 10 (6%) as N3. There was no statistically significant difference in survival between the N stages (p= 0.243).

According to the M stage, 144 (96%) patients were M0, and 6 (4%) were M1 at initial diagnosis. There was a statistically significant difference in survival between M stages (p< 0.0001).

When patients were analyzed for stage, 4 (3%) patients were stage I, 28 (18%) were stage II, 70 (47%) were stage III, 42 (28%) were stage IVA and 6 (4%) were stage IVB. Stage I patients had a mean survival time of 11.75 ± 2.88 months (95% CI: 6.1-17.39) and a median survival time of 10 months (95% CI: 2.51-17.48). The 2- and 5-year survival rates were 37.5% and 37.5%, respectively. Stage II patients had a mean survival time of 235.33 ± 21.28 months (95% CI: 193.61-277.05). The 2- and 5-year survival rates were 100% and 81.9%, respectively. Stage III patients had a mean survival time of 145.56 ± 15.99 months (95% CI: 114.22-176.9) and a median survival time of 181 months (95% CI: 57.57-304.42). The 2- and 5-year survival rates were 78.4% and 61.4%, respectively. Stage IVA patients had a mean survival time

Table 1. Patients characteristics and survival analysis

		n (%)	Mean (95%CI)	Median (95%CI)	2 y (%)	5 y (%)	p
General		150 (100%)	137.19±11.31	118	72.7	57.5	
			115.01-159.37	34.4-201.59			
Gender	Female	48 (32%)	145.43±18.69	181	80.4	61.8	
			108.79-182.07	74.67-287.32			0.492
	Male	102 (68%)	135.13±13.96	79	68.9	55.4	
			107.79-162.52	0-178.25			
Age			49.45±15.75 (range: 12-82) years				
	≤18	8 (5%)	203.71±29.89		85.7	85.7	
			145.12-262.3				0.053
	>19	142 (95%)	134.07±11.72	118	74.7	57.5	
			111.09-157.05	38.98-197.02			
T	I	38 (25%)	160.17±19.15		85.8	68.6	
			122.62-197.71				0.006
	II	44 (29%)	175.33±19.88	205	82.9	70.7	
			136.35-214.3	140.87-269.12			
	III	31 (21%)	95.43±20.3	55	73.5	44.1	
			55.63-135.23	30.31-79.68			
	IV	37 (25%)	92±119.04	34	50.8	46.9	
			54.67-129.32	0-108.23			
N	0	31 (21%)	135.07±23.97	161	71.6	62	
			88.09-182.06	43.35-278.65			0.243
	1	22 (15%)	170.09±24.14		94.4	81	
			122.76-217.42				
	2	87 (58%)	134.68±15.27	101	69.5	54.8	
			104.73-164.62	0-228.82			
	3	10 (6%)	74.87±26.29	45	77.8	25.9	
			23.33-126.4	22.73-67.26			
M	0	144 (96%)	200±30.97	161	78.8	62.3	
			139.3-260.71	70.58-251.42			0.0001
	1	6 (4%)	6.5±1.97	4	–	–	
			2.62-10.37	0-8.8			
Stage	I	4 (3%)	11.75±2.88	10	37.5	37.5	
			6.1-17.39	2.51-17.48			0.0001
	II	28 (18%)	235.33±21.28		100	81.9	
			193.61-277.05				
	III	70 (47%)	145.56±15.99	181	78.4	61.4	
			114.22-176.9	57.57-304.42			
	IVA	42 (28%)	98.39±17.31	45	67.1	46	
			64.45-132.33	0-98.83			
	IVB	6 (4%)	6.5±1.97	4	–	–	
			2.62-10.37	0-8.8			

of 98.39 ± 17.31 months (95% CI: 64.45-132.33) and a median survival time of 45 months (95% CI: 0-98.83). The 2- and 5-year survival rates were 67.1% and 46%, respectively. Stage IVB patients had a mean survival time of 6.5 ± 1.97 months (95% CI: 2.62-10.37) and a median survival time of 4 months (95% CI: 0-8.8). The one-year survival rate was 16.7%. There was a statistically significant difference between the stages in survival ($p< 0.001$). Patients characteristics and survival analysis are shown on Table 1.

Table 2. Survival rates by histology and EBV status

	n (%)	Mean (95%CI)	Median (95%CI)	2 y (%)	5 y (%)	p
Histology						
I	12 (8%)	56.66±18.21 20.96-92.36	35 0-78.71	60.6	34.6	0.001
IIA	12 (8%)	81.6±27.17 28.33-134.86	35 6.94-63.06	72.7	37.7	
IIB	94 (63%)	170.06±13.94 142.73-197.4	261 125.11-396.88	78	67.3	
Anaplastic	1 (1%)	34	34	-	-	
Unknown	31 (20%)	98±35.19 29.02-166.97	11 0-83.82	50	40	
EBV						
Negative	5 (3%)	156±48.06 61.78-250.21	194	80	80	0.757
Positive	26 (17%)	67.88±8.01 52.16-83.59		76	69.1	
Unknown	120 (80%)	136.71±12.36 112.48-160.94	118 22.09-213.9	71.9	51.4	

Stage I patients were found to have shorter survival times. This could be attributed to the fact that one out of our four Stage I patients was a 16-year-old boy who died 10 months after treatment due to fungal sepsis, and another one of the four Stage I patients, a 76-year-old male, died 5 months after treatment due to cardiac comorbidities (coronary artery disease).

According to histology, 12 (8%) patients had WHO Type I, 12 (8%) had WHO Type IIA, 94 (63%) had WHO Type IIB, 1 (1%) had anaplastic, and 31 (20%) had unknown histology. WHO Type 1 patients had a mean survival time of 56.66 ± 18.21 months (95% CI: 20.96-92.36) and a median survival time of 35 months (95% CI: 0-78.71). The 2- and 5-year survival rates were 60.6% and 34.6%, respectively. WHO Type 2 patients had a mean survival time of 81.6 ± 27.17 months (95% CI: 28.33-134.86) and a median survival time of 35 months (95% CI: 6.94-63.06). The 2- and 5-year survival rates were 72.7% and 37.7%, respectively. WHO Type 2 patients had a mean sur-vival time of 170.06 ± 13.94 months (95% CI: 142.73-197.4) and a median survival time of 261 months (95% CI: 125.11-396.88). The 2- and 5-year survival rates were 78% and 67.3%, respecti-vely. The only patient with the anaplastic histology had a survival of 34 months. Patients with the unknown histology had a mean survival time of 98±35.19 months (95% CI: 29.02-166.97) and a median survival time of 11 months (95% CI: 0-83.82). The 2- and 5-year survival rates were 50% and 40%, respectively. There was a statistical significance between types of histology in survival (p< 0.001).

When patients were analyzed for EBV status, 5 (3%) were EBV-negative, 26 (17%) were EBV-positive, and 120 (80%) were unknown. There was no statistically significant difference in survival between EBV status groups (p= 0.757). Survival by histology and EBV status are shown on Table 2.

In terms of treatment, 150 (97%) patients received treatment, and 4 (3%) patients did not. Patients who received treatment had a mean survival time of 141.38±11.48 months (95% CI: 118.87-163.88) and a median survival time of 157 months (95% CI: 64.01-249.98). The 2- and 5-year sur-vival rates were 72.7% and 57.5%, respectively. For patients who did not receive treatment, the mean survival time was 6.75 ± 2.28 months (95% CI: 2.26-11.23) and the median survival time was 6 months (95% CI: 0-12.86). There was no patient who lived 1 year. There was a statistically signi-ficant difference in survival between patients who received treatment and those who did not (p< 0.0001).

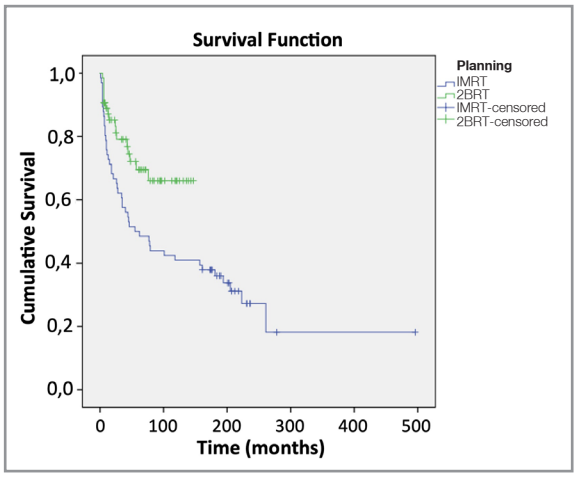

Figure 2. Survival by radiotherapy technique

When radiotherapy treatment techniques were compared, 76 (51%) patients were planned with 2DRT and 74 (49%) patients were planned with IMRT/VMAT. For 2D-RT, patients had a mean survival time of 107.02 ± 8.1 months (95% CI: 91.14-122.9). The 2- and 5-year survival rates were 66.7% and 50%, respectively. For IMRT/VMAT, patients had a mean survival time of 117.77 ± 14.01 months (95% CI: 90.31-145.23) and a median survival time of 55 months (95% CI: 16.18-93.81). The 2- and 5-year survival rates were 83.2% and 69.5%, respectively. There was a statistical significance between 2DRT and IMRT/VMAT in survival (p< 0.01) (Figure 2). Survival rates by radiotherapy technique are shown on Table 3.

When patients were compared according to treatment modality, 30 (20%) received RT and brachytherapy (BRT), 106 (70%) received CRT, 4 (3%) patients received RT, 6 (4%) were palliative patients and 4 (3%) patients did not receive any treatment. RT and BRT patients had a mean survival time of 115.27±19.39 months (95% CI: 77.25-153.28) and a median survival time of 62 months (95% CI: 9.66-114.33). The 2- and 5-year survival rates were 70% and 53.3%, respectively. CRT patients had a mean survival time of 165.28±15.32 months (95% CI: 135.24-195.32) and a median survival time of 194 months. The 2- and 5-year survival rates were 81.4% and 65%, respectively. Patients who received RT alone had a mean survival time of 46 months (95% CI: 0-46) and a median survival time of 46 months. The 2- and 5-year survival rates were 100% and 0%, respectively. Palliative patients had a mean survival time of 6.5±1.97 months (95% CI: 2.62-10.37) and a median survival time of 4 months (95% CI: 0-8.8). The 2- and 5-year survival rates were 0% and 0%, respectively. There was a statistical significance in survival between the treatment intension groups (p< 0.0001). Survival by treatment intention are shown on Table 4.

When patients were analyzed for the induction chemotherapy administration, 13 (9%) patients were given induction chemotherapy and 137 (91%) patients were not. There was no statistical significance in terms of survival between induction chemotherapy groups (p= 0.968).

In our study, locoregional recurrence was seen in 13 (9%) patients after a mean time of 65 ± 49.61 months (range:5-149). There was no statistical significance in survival between locoregional recurrence status (p= 0.093).

In our study, 17 (13%) patients developed metastasis after a median time of 45 (range: 2-223) months. Metastasis sites were Liver (2 patients), Lungs (5 patients), Bones (6 patients), Brain (2 patients) and Distant Lymph Nodes (2 patients). Patients who developed metastasis had a mean survival time of 69 ± 23.07 months (95% CI 23.77-114.24) and a median survival time of 45 months (95% CI: 0-95.7). The 2- and 5-year survival rates

Table 3. Survival by Radiotherapy technique

	n (%)	Mean (95% CI)	Median (95% CI)	2 y (%)	5 y (%)	p
2D-RT	76 (51%)	107.02±8.1 91.14-122.9		66.7	50	0.01
IMRT/VMAT	74 (49%)	117.77±14.01 90.31-145.23	55 16.18-93.81	83.2	69.5	

Table 4. Survival by treatment modality

	n (%)	Mean (95% CI)	Median (95% CI)	2 y (%)	5 y (%)	p
None	4 (3%)	6.75±2.28 2.26-11.23	6 0-12.86	0	0	0.0001
Palliative	6 (4%)	6.5±1.97 2.62-10.37	4 0-8.8	0	0	
RT	4 (3%)	46 0-46	46	100	0	
CRT	106 (70%)	165.28±15.32 135.24-195.32	194	81.4	65	
RT+BRT	30 (20%)	115.27±19.39 77.25-153.28	62 9.66-114.33	70	53.3	

were 58.8% and 33.6%, respectively. Patients who did not develop metastasis had a mean survival time of 201.92±22.26 (95% CI: 158.29-245.56). The 2- and 5-year survival rates were 86.2% and 80.5%, respectively. There was a statistically significant difference in survival between patients who developed metastasis and those who did not (p< 0.0001). Survival by locoregional recurrence, metastasis, and induction chemotherapy are shown on Table 5.

In order to identify independent prognostic factors, multivariate analysis was performed. Stage (p< 0.0001), histology (p< 0.001), RT modality (p= 0.012), and metastasis status (p= 0.008) were found to be independent prognostic factors. Multivariate analysis of prognostic factors are shown on Table 6.

During the follow-ups, 2 patients developed acute myeloid leukemia, 1 patient developed the syndrome of inappropriate antidiuretic hormone (ADH) secretion, secondary adrenal failure, and central hypothyroidism, and 1 patient developed glioblastoma multiforme.

Table 5. Survival by Locoregional recurrence, metastasis, and induction chemotherapy

	n (%)	Mean (95% CI)	Median (95% CI)	2 y (%)	5 y (%)	p
Locoregional recurrence						
No	137 (91%)	139.86±12.43 115.49-164.22	161 45.82-276.17	70.5	54.3	0.093
Yes	13 (9%)	69.91±24.37 22.13-117.69	49 0-186.69	53.8	43.1	
Metastasis						
No	133 (87%)	201.92±22.26 158.29-245.56	86.2	80.5		0.0001
Yes	17 (13%)	69±23.07 23.77-114.24	45 0-95.7	58.8	33.6	
Induction chemotherapy						
No	137 (91%)	137.47±12 113.93-161.01	118 35.4-200.59	72.6	58.7	0.968
Yes	13 (9%)	118.14±30.17 59.01-177.28	47 0-274.14	73.3	45.8	

Table 6. Multivariate analysis for prognostic factors

Factor	Hazard Ratio (95% CI)	p
Age	5.611 (0.774-40.669)	0.088
Gender	0.835 (0.497-1.403)	0.496
Stage		0.0001
I	0.063 (0.010-0.391)	0.003
II	0.245 (0.056-1.073)	0.062
III	0.396 (0.089-1.762)	0.224
IV	3.248 (0.652-16.182)	0.150
Histology		0.001
I	1.571 (0.615-4.008)	0.345
IIA	0.967(0.359-2.609)	0.948
IIB	0.436 (0.192-0.987)	0.046
Anaplastic	1.685 (0.204-13.891)	0.628
RT modality	0.480 (0.271-0.850)	0.012
Metastasis	3.172 (1.343-7.489)	0.008

DISCUSSION

NPC develops from the nasopharyngeal epithelium and is a severe malignancy. Thanks to the improvement of treatment modalities, NPC patients who are early-stage often have an improved out-come and longer life span than those with other malignancies.[9]

NPC is known to be radiosensitive; therefore, RT with or without chemotherapy has been the primary approach, with gemcitabine/cisplatin being the first-line chemotherapy regimen.[10] A prescribed dose of 70 Gy should be delivered over 33-35 fractions (2.12 Gy per fraction) or 35-39 fractions (1.8-2 Gy per fraction) within 7 weeks. The treatment should be given once daily, five fracti-ons per week, with or without cisplatin chemotherapy. This treatment has been proven effective with acceptable toxicity in Intergroup 0099 and RTOG 0225 trials, and should be offered to all patients with NPC.[11] It is worth noting that the Intergroup 0099 trial was carried out in the era of conventional RT, where the rate of locoregional failure was high, however, with the shift to IMRT, failure patterns have changed, and with concurrent chemoradiotherapy has now led to excellent locoregional control, while also reducing long-term side effects. In the KROG 11-06 study; 2D-RT, 3-Dimensional Conformal RT (3D-CRT) and IMRT were compared, and 3D-CRT and IMRT were associated with better 5-year OS than 2D-RT (73.6%, 76.7% and 59.7%, respectively, p< 0.001).[12] In our study, 76 (51%) patients were treated with conformal 2D-RT and 74 (49%) patients were treated with IMRT/VMAT. A significant survival benefit was observed in the IMRT/VMAT group (p< 0.01).

Kazemian et al. conducted a study in Iran, where the incidence of NPC is rising. A total of 106 patients who received definitive radiotherapy with 70 Gy in 2 Gy fractions were included in the study. Twenty-nine patients developed locoregional or distant metastasis. Their 2-year and 5-year OS rates were 81% and 76%, respectively.[13] In our study, 13 (9%) patients developed locoregional recurrence and 17 (13%) developed metastasis, with 5-year survival rates of 43.1% and 33.6%, respectively. There was a survival benefit in patients who did not develop metastasis (p< 0.0001).

Wu et al., retrospectively analyzed 614 patients with NPC diagnoses who received IMRT. The 10-year OS rates were 100% for stage I, 87.1% for stage II, 75.5% for stage III, and 55.6% for stage IV (p< 0.05, except for stages I and II). Multivariate analysis revealed that tumor stage and age were independent prognostic factors.[14] Our study suggests that late-stage disease negatively affects survival, which is compatible with the current literature (p< 0.0001).

Farias, et al., also investigated prognostic factors in their retrospective analysis with a population of 173 patients with a diagnosis of NPC.[15] Locoregional advanced disease was present in most patients (88.5%) and most patients (53.4%) had a NKCC. Approximately ¾ of patients were treated with RT (median dose of 66 Gy) and ¼ of patients with concomitant CRT with adjuvant CT (cisplatin combined with 5-fluorouracil) (median dose, 68 Gy). They found that 5 year disease specific survival was 32.3%. Adverse outcomes were associated with factors such as age > 40 years at the time of treatment and advanced TNM stage.[15] In our study, we were not able to draw any conclusions.

Although there is no agreement on the prognostic importance of NPC histological subtypes, several studies have suggested that they have an impact on treatment outcomes or patient survival. Ou et al. examined the survival of 2436 Chinese patients diagnosed with NPC. RT (versus none, $p< 0.0001$) and UNKC (versus KSCC, $p< 0.0001$) were found to be associated with improved survival among other variants.[16] Wu et al. investigated if the histological subtype of NPC affected survival outcomes after extensive follow-up. A total of 2845 patients were identified in the study, including 42.8%, 29.8%, and 27.3% with KSCC, DNKC, and UNKC, respectively. They found a significant difference between the histological subtypes of hazard rate patterns for NPC-related mortality.[17] A similar study was conducted by Pan et al. Their study identified 4085 patients with NPC, including 1929 with KSCC, 2203 with UNKC, and 53 with BSCC. They concluded that KSCC was associated with worse cause-specific survival than UNKC was.[18] Our study showed a significant survival difference between histological types. Patients with the UNKC subtype had the longest mean survival time. In contrast, patients with the KSCC subtype had the shortest survival time if the patient with the anaplastic carcinoma was excluded ($p< 0.001$).

In a tertiary referral hospital in Malaysia, Siti-Azrin et al. investigated the prognostic factors of NPC patients in a retrospective cohort study. The mean age was 48.12 years. Stage IV was observed in 40.6% of the patients and stage III in 39.1% of the patients. They found that the median OS time was 31.30 months. Older age and stage IV disease were significant prognostic factors influencing survival.[19] In our study, 70 patients (47 %) had stage III disease. Our findings also suggest that stage influences survival ($p< 0.0001$).

Our study has limitations, including a relatively small cohort size, its retrospective nature, and the rare incidence of NPC in our area, all of which could have influenced the results. Therefore, these results should be carefully interpreted.

Conclusion

Concomitant chemoradiotherapy and the development of radiotherapy techniques, such as IMRT/VMAT, has been found to be highly effective in the treatment of nasopharyngeal cancer, resulting in high survival rates. However, it has been observed that the majority of cases of locoregional recurrence and metastatic cancer tend to occur between four to five years following radiotherapy. The stage and the WHO Type 2B histology are important prognostic factors for overall survival. The 2- and 5-year OS, DMFS, and LRRFS survival rates are 72.7% and 57.5%, 86.2% and 80.5%, and 70.5% and 54.3%, respectively. While the retrospective data obtained were consistent with existing literature, further studies with larger patient cohorts are needed to validate these findings.

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