

Evaluation of Prognostic Factors In Nasopharyngeal Cancers

Nazofaringeal Kanserlerde Prognostik Faktörlerin Değerlendirilmesi

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ABSTRACT

Aim: We aimed to examine prognostic factors that affect the survival of patients with nasopharyngeal cancer (NPC) who were diagnosed and treated in our clinic. .

Method: Patients with nasopharyngeal cancer, who were diagnosed and treated in our clinic between 2009-2013, were examined retrospectively.

Results: In our study, 33 patients were male (%73.3), 12 patients were female (%26.6), and male/female ratio was 2.75. Mean age was 50,8; the youngest patient was 14 and the oldest one was 84 years old. The most common presenting cause was cervical lymph node metastasis (%66,7). %66,6 of our patients had advanced stage tumor (Stage 3-4). Longer survival was detected in low T-stage patients, whereas no relation was determined between N-stage and survival. No statistical relation was determined between histopathological types and 2-year survival. Longer survival was observed in young age group and male patients; however, this was not statistically significant.

Conclusion: Younger age are good prognostic factors, however, the advanced T and N stages at diagnosis are poor prognostic factors. Therefore, early diagnosis is important in terms of treatment and survival.

Keywords: Nasopharynx, Prognostic factors, Retrospective

ÖZET

Amaç: Kliniğimizde teşhis ve tedavi edilen nazofaringeal kanserli (NPC) hastaların hayatta kalmasını etkileyen prognostik faktörleri incelemektir.

Yöntem: Kliniğimizde 2009-2013 yılları arasında teşhis ve tedavi edilen nazofaringeal kanserli hastalar geriye dönük olarak incelendi.

Bulgular: Çalışmamızda 33 hasta erkek (% 73.3), 12 hasta kadın (% 26.6), erkek / kadın oranı 2.75 idi. Ortalama yaş 50,8; En genç hasta 14 ve en yaşlısı 84 yaşında idi. En sık görülen neden servikal lenf nodu metastazı (% 66,7) idi. Hastalarımızın %66,6'sında ileri evre tümör vardı (Evre 3-4). Düşük T evresi hastalarında daha uzun sağkalım süresi saptanırken, N-evresi ile sağkalım arasında ilişki saptanmadı. Histopatolojik tiplerle 2 yıllık sağkalım arasında istatistiksel olarak bir ilişki saptanmadı. Genç yaş grubu ve erkek hastalarda daha uzun sağkalım süresi gözlemlendi fakat bu istatistiksel olarak anlamlı değildi.

Sonuç: Genç yaş iyi prognostik faktörlerdir, ancak tanıdaki ilerlemiş T ve N evreleri kötü prognostik faktörlerdir. Bu nedenle erken teşhis, tedavi ve sağkalım açısından önemlidir.

Anahtar kelimeler: nazofarenks, prognostik faktörler, retrospektif

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Nasopharyngeal cancers occur at younger ages compared to the other head and neck malignancies. They are challenging in terms of diagnosis and treatment because of complicated anatomic structure of the tumor region and proximity to structures such as oral cavity, paranasal sinuses and skull base. The incidence of the disease increases at adolescence period and shows a peak at ages of 40-50 [1,2]. Nasopharyngeal cancers are observed more often in young age group and the most common presenting cause is lymph node involvement. Advanced T and N stages at diagnosis are poor prognostic factors. Therefore, early diagnosis is important in terms of treatment and survival.

In this study, we aimed to evaluate the prognosis factors affecting the survival of the patients with nasopharyngeal cancer who were diagnosed and treated in our clinic between 2009-2013.

MATERIALS AND METHODS

In our study, 45 patients with nasopharyngeal carcinoma who presented to Akdeniz University Faculty of Medicine Otolaryngology and Radiation Oncology Clinic between 2009-2013 and treated in our clinic were investigated retrospectively. Fiber optic nasal endoscopy was performed on all the patients and diagnosis was made by punch biopsy. The cases were classified histopathologically according to World Health Organization (WHO) 2005. Computer tomography (CT), Magnetic resonance imaging (MRI) and Positron emission tomography (PET) examinations were performed for staging and The American Joint Committee on Cancer (AJCC) / The Universal Integrated Circuit Card (UICC) Classification of Malignant Tumours (TNM) 2009 staging system version 7 was used. Patients were examined in terms of age and gender characteristics, histopathological types, TNM stage, duration of Radiation therapy (RT), parameters for response to chemotherapy and post-treatment local, regional recurrence and distant metastasis.

Response to therapy, local control, survival and prognostic factors were evaluated. Data was analyzed by SPSS 16 software.

RESULTS

In our study, 33 patients were male (%73.3), 12 were female (%26.6), and male/female ratio was 2.75. Mean age was 50,8; the youngest patient was 14 and the oldest was 84 years old.

Cervical lymph node metastasis is the most common presenting cause when the patients were examined in terms of presenting symptoms (%66,7). Other presenting symptoms were nasal congestion, headache, hearing loss, otalgia and dizziness, respectively. Cranial nerve involvement rate was found as %8,9 in our study.

In our study, follow-up length was minimum 6 months and maximum 60 months. Three patients were excluded from our assesment of survival for not having regular checks. The number of patients evaluated for two-year survival was 42. Nine of 42 patients died during two-year follow-up. Two-year overall survival rate was %78,6.

Advanced stage (Stage 3-4) tumor was present in %66,6 of our patients (Table1). Rate of T stage1-3 rate was %86,4 and patients with node involvement of 0-1 was %57,8. No statistically significant findings were determined between tumor, N stage and age, gender. ($p=0.97$ $p=0.34$).

Table 1. Distribution of patients according to AJCC/UICC staging system.

Stage	Number of patients (n)	Percentage (%)
I	3	6,7
II	12	26,7
III	24	53,3
IV	6	13,3
Total	45	100,0

In our study, 2 patients (%4,4) were classified as type 1 (well-differentiated keratinized squamous), 5 patients (%11,1) as type 2 (differentiated non-keratinized squamous) and 38 patients (%84,4) as type 3 (undifferentiated). No significant relation between histopathologic type and gender and age groups was determined (Table2).

Table 2. Distribution of patients according to WHO classification.

Histopathology	Number of Cases	Lymph Node Involvement
WHO TYPE I	2	4,4%
WHO TYPE II	5	11,1%
WHO TYPE III	38	84,4%
Total	45	100%

Meandose of 70 Gy was administered to nasopharynx region in all patients. Cisplatin-based regimens were

chosen for the chemotherapy receivers. When the relation between histopathologic characteristics and response to treatment was evaluated, complete response was not observed in any of the type I patients, whereas %86,8 of the type III patients obtained complete response, however, histopathologic characteristics had no effect on prognosis statistically.

2-year survival rate of patients aged below 30 was %100, whereas that of the patients aged above 30 was 75,7%. 2-year survival was %83,9 in male patients and %63,6 in female patients. Longer survival length was observed in younger age group and male gender; however, it was not statistically significant (Table3).

Table3. Evaluation of age, gender and histopathology groups in terms of two-year survival rates.

	2-year survival rates %	
	Number of patients (n)	Percentage (%)
WHO TYPE I	1	100,0
WHO TYPE II	4	100,0
WHO TYPE III	28	75,7
Male patients	26	83,9
Female patients	7	63,6
Patients aged <30	5	100,0
Patients aged >30	28	75,7

Longer survival length was determined in low T stage patients, whereas there was no relation between N stage and survival.

DISCUSSION

Nasopharyngeal cancers occurs at younger ages compared to the other head and neck malignancies. They are challenging in terms of in diagnosis and treatment because of complicated anatomic structure of the tumor region and proximity to structures such as oral cavity, paranasal sinuses and skull base. The incidence of the disease increases at adolescence period and shows a peak at ages of 40-50. Nasopharyngeal cancers have been reported 4-5 times more in males in the literature. In our study, mean age was 50,8 and male/female patient ratio was 2,75 [1].

The most common presenting cause is cervical lymph node involvement and a ratio between 60-87 % has been reported in the literature [1,2]. Nasopharynx has an anatomically rich lymphatic network; therefore, nasopharynx cancers show early and frequent metastasis.

In our study, the most common presenting symptom was cervical lymph node metastasis at a rate of 66,7 % which was compatible with the literature and the other presenting symptoms were nasal congestion, headache, hearing loss, otalgia and dizziness, respectively. Intracranial spread may be observed infiltrating skull base due to its anatomical adjacency, therefore it may cause neurological findings. In literature, cranial nerve involvement rate has been reported as 20%[1,2]. We observed cranial nerve involvement in 8,9% of our cases.

In our study, follow-up length was minimum 6 months and maximum 60 months. The number of patients evaluated for two-year survival was 42 and the two-year survival rate of these patients was 78,6%. 9 of 42 patients died during the treatment. Sutton et. al. have reported that 5 and 10-year survival rates were 54% and 38% in 126 patients who received curative radiotherapy [3]. Sanguineti et al. have reported these rates as 48% and 34%, respectively [4]. We determined higher survival rates compared to the literature. We attributed this finding to short follow-up length.

Parameters related to the patient, disease and treatment are the factors that affect prognosis in nasopharyngeal cancers[5]. Race, age and gender are patient-dependent prognostic factors, while T and N stages, histopathological type, parapharyngeal invasion are disease-dependent. Prognosis is better in female patients compared to male patients [5]. We observed better 2-year survival in male patients, however, this difference was not statistically significant. Gender differences in prognosis of NPC may be due to genetic variants affected by the hormonal environment. Nasr reported VEGF polymorphisms in patients with NPC and found that male patients carrying the VEGF-2578C allele had higher risk for NPC than female patients [6].

There are many studies reporting higher survival rates in young patients [7]. In a study, longer survival was observed in young group, however, the results were similar at ninth year [8]. We found better survival rates in young patients, however, this difference was not statistically significant. Ma and his friends have reported that patients younger than 40 have lower survival in their study [9]. The long survival length in young patients has been attributed to different histologic subtype distribution in different age groups. But these studies were not adjusted to account for other prognostic factors; tumor size, stage, therapeutic differences

and performance. All of these variables must be considered with age.

It is reported that there is a direct relationship between the stage at diagnosis and prognosis in head and neck malignancies[1,2,5]. T-stage has been reported as an important prognostic factor for survival. Kaasa et. al. have reported longer survival length in T1-2 patients without statistical significance, and in another study, T stage has been suggested as an important prognostic factor for local non-recurring survival [10,11]. Otherwise Han et al. showed that the T stage didn't affect the survival [12]. We determined longer survival in T1-2 patients compared to T3-4 patients in conformity with the literature, however, this difference was not statistically significant ($p=0.97$).

Bilateral cervical involvement may be observed in 1/3 of the patients due to rich nasopharynx lymphatic draining network[1,2,5]. Number and size of lymph nodes are taken in consideration rather than involved lymph node level when staging is performed. When the lymph nodes are evaluated in nasopharyngeal carcinomas, lower cervical involvement, fixed, >6 cm lymph node, bilateral involvement are the poor prognostic parameters [3,10]. The survival rates decrease significantly as the N status increase. There is a close relationship particularly between N status and distant metastasis incidence. The prognosis of nodal involvement extended to middle cervical region is not worse than involvement limited to upper cervical, however, prognosis is significantly worse in nodal involvement extended to lower cervical region [13]. Differently from the other head and neck tumors, supraclavicular lymph node involvement is considered as N3 regardless of the size. Kaasa et. al. have demonstrated that relative mortality risk is 2,1 times higher in N2-3 stage compared to N0-1 stage in lymph node involvement. They have suggested that N stage is a stronger prognostic factor than T stage for survival.. Zietek has found the 5-year survivals as 69% in N0-1 patients and as 52% in N2-3 patients [10,14]. We did not determined any significant difference between the N0-1 and N2-3 patients in terms of survival.

90% of the histologic subtypes of nasopharyngeal cancers are WHO type 2 and WHO type 3. There are different opinions about the effect of the histopathological type on the survival length and local recurrence. It has been reported that survival and local control rates are better in WHO type 3. WHO type 3 has the most

favorable prognosis because of its high degree of radiosensitivity, and type 1 has the worst prognosis because of its low radiosensitivity[15]. In Chinese series the great majority of patients had WHO type 3 tumors, no significant difference in survival [16,17]. We have detected no statistically significant relation between histopathological type, survival and local control.

Nasopharyngeal cancers are observed mostly in younger age group and the most common presenting cause is neck lymph node involvement. Advanced T and N stages at diagnosis are poor prognostic factors, whereas female gender and young age are the good prognostic factors. Therefore, early diagnosis is important in terms of treatment and survival..

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