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CARCINOMA OF THE NASOPHARYNX

A retrospective analysis of treatment results in 125 patients

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Abstract

From 1958 to 1982, 125 patients with histologically verified carcinoma of the nasopharynx were treated with external radiotherapy as the sole curative intent. The 5-year actuarial survival rates by stage were as follows: stage I 68%, stage II 64%, stage III 44%, and stage IV 20%. Primary control rate by T-category was 71% in T1, 67% in T2, 52% in T3, and 64% in T4. Regional control rate was 96% in N0, 76% in N1, 61% in N2, and 63% in N3. The T-category was found to be an important prognostic parameter for survival.

Key words: Nasopharynx, carcinoma, radiotherapy, staging, prognosis.

Malignant neoplasm of the nasopharynx is relatively uncommon in the western world, and only some 20 to 30 new cases are diagnosed each year in Finland (population 4.9 million) (1). The treatment of choice is radiation therapy due to surgical inaccessibility of the tumour location. This study is a retrospective analysis of treatment results of patients with carcinoma of the nasopharynx seen at our department during the period 1958–1982.

Material and Methods

During the period 1958–1982, 139 new patients with histologically verified carcinoma of the nasopharynx were treated with external radiotherapy alone in the department of radiotherapy and oncology, University Central Hospital, Helsinki. Of the 139 patients, 14 were treated palliatively only and excluded from the present study. All remaining 125 patients were treated with curative intent and had a 5-year minimum follow-up (mean 12.7 years).

Patients' characteristics. The series comprised 47 females and 78 males. The mean age of the patients at the beginning of treatment was 51 years (SD ± 18 years, range 19–87 years). The histological types of carcinomas were as follows: poorly differentiated squamous cell carcinoma in 56 patients (45%), lymphoepithelioma in 39 patients (31%), anaplastic carcinoma in 19 patients (15%), transitional cell carcinoma in 7 patients (6%), and adenocarcinoma in 4 patients (3%). The pathology reports of all patients were reviewed in the division of pathology of the hospital.

Staging. The tumours were retrospectively staged according to the TNM classification (2) (Table 1). The distribution of the tumours by stage was as follows: stage I (T1 N0) 10 (8%), stage II (T2 N0) 16 (13%), stage III (T3 N0, T1–3N1) 44 (35%) and stage IV (T1–3 N2–3, T4 N0–3) 55 (44%). For further analysis of treatment results the tumours were divided into early tumours (T1–2 N0, or stage I and stage II) (26 cases, 21%) and advanced tumors (T1–2 N1–3, T3–4 N0–3, or stage III and stage IV) (99 cases, 79%). Of the 22 patients with T4 disease, 14 had radiographic evidence of destruction of the base of the skull. Fifty patients (40%) were clinically N0 at the beginning of treatment.

Radiation treatment. One hundred and three patients (83%) were treated with telecurie machines, 14 patients (11%) with 20 MV photons from a betatron and 8 patients (6%) with 6 MV photons from a linear accelerator. All patients were irradiated with individually shaped fields, as a rule two lateral parallel opposing fields supplemented with an anterior suborbital or nasal field according to a dose plan to ensure adequate tumour coverage. The dose was calculated at the midplace in nasopharynx. The mean

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Table 1

Distribution of patients according to the TN-classification (UICC, 1982)

	T1	T2	T3	T4	Total
N0	10	16	15	9	50
N1	8	13	8	4	33
N2	7	7	3	6	23
N3	3	6	7	3	19
Total	28	42	33	22	125

height of the treatment fields was 9.0 cm (SD ± 0.3 cm) and the mean field size 72 cm^2 (SD ± 5.6 cm^2). Continuous treatment was given to 53 (42%) patients with a median tumour dose of 58.1 Gy (range 46.7 to 71.8 Gy) and a median daily dose of 2.2 Gy (range 1.5 to 2.9 Gy) given in five fractions per week over 5.8 weeks (range 4.5 to 6.8 wk). A randomized clinical trial was performed from 1964 to 1967 to compare the therapeutic results of split-course external beam radiotherapy with that of continuous treatment. The result of this study has already been published (3) and the efficacy of these two treatment modalities is not further compared in the present report. Split-course therapy has been used in our department since 1967 and only three patients have been treated with continuous therapy after 1967. To compensate for the split-course pause, the total dose was increased by 5–10% (4). The planned tumour dose in split-course therapy was 66 Gy with a daily fraction of 2.2 Gy given in five fractions per week and with a 2–3 weeks' rest in the middle of the treatment. Split-course therapy was given to 72 (58%) patients with a median tumour target dose of 62.4 Gy (range 56.6 to 74.8 Gy) and a median daily dose of 2.1 Gy (range 1.7 to 2.5 Gy) given in five fractions per week in 8.2 weeks (range 6.6 to 9.1) with a 2.6 weeks' rest (range 1.8 to 3.1) in the middle of the treatment.

In 30 patients (24%) the primary tumour received a total dose ranging from 50 to 60 Gy. The majority (87 patients, 69%) received a total dose ranging from 60 to 70 Gy, while 8 patients (7%) received more than 70 Gy. The clinically negative lower neck (N0) was irradiated through one anterior field to a maximum dose (d_{max}) of 51 Gy in 17 fractions. Patients with N1–N2 disease received 60–66 Gy (target dose). The treatment of N3 disease was individualized based on the extent of the lymph node metastases and each side of the neck was often treated separately.

The regression of the tumour was evaluated by inspection and palpation. Local control means complete disappearance of the primary tumour and regional nodes, persisting for the 5-year follow-up or until the death of the patient. The local control rate was calculated both as the proportion of all patients and as the proportion of patients at risk at three years.

Follow-up of the patients. All patients were regularly seen at three months' intervals during the first three years after the termination of radiotherapy at the department. Thereafter the patients were seen at six months' intervals until five years, when they were sent for controls to their regional health centers.

Statistics. Actuarial survival time was determined without age correction from the date of initiation of radiotherapy until the date of the last follow-up examination or death respectively. These rates were computed by using the product-limit estimator of Kaplan & Meier (5). The statistical difference between survival curves was calculated according to the Mantel-Cox's test, the χ^2 test was used to compare response rates and the Student's t-test for comparing doses (6). The term 'overall p' was used for global test which examines if all the mentioned groups were equivalent. Data were analyzed using the BMDP (Biomedical Computer Programs-P series) statistical package at the computer center of the Helsinki University Central Hospital.

Results

The 5-year acturial survival rate was 68% for stage I, 64% for stage II, 44% for stage III, and 20% for stage IV (overall $p < 0.001$, Figure). The 5-year survival rate was 64% for the group of early tumours (stages I and II) and 32% for the group of advanced tumours (stages III and IV).

The primary control rate was 71% in T1, 67% in T2, 52% in T3 and 64% in T4 (Table 2). Regional control rate was 96% in N0, 76% in N1, 61% in N2 and 63% in N3 (Table 2). The control rate as percentage of patients at risk at three years was 87% in T1, 83% in T2, 42% in T3, 0% in T4 and 70% in N0, 78% in N1, 70% in N2 and 100% in N3 (Table 2).

The 5-year actuarial survival rates for T1, T2 and T3 were 60, 52 and 24% respectively. There were no long-term survivors in the T4 group which had a median survival

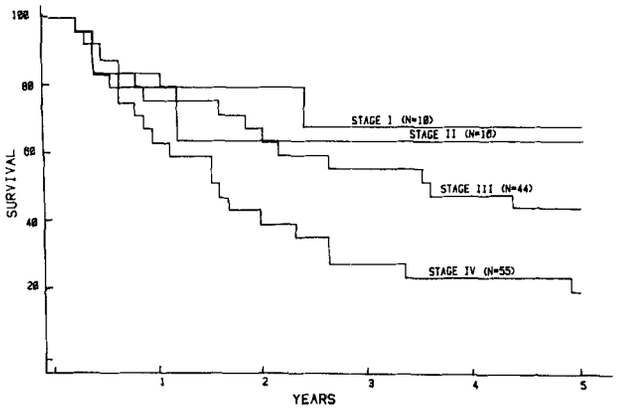

Figure. 5-year survival rate by stage.

Table 2

Local control as a function of T and N categories

	Percentage of all patients	Percentage of patients at risk at 3 years
T-category		
T1 (n = 28)	71	87
T2 (n = 42)	67	83
T3 (n = 33)	52	42
T4 (n = 22)	64	0
Total (n = 125)		
N-category		
N0 (n = 50)	96	70
N1 (n = 33)	76	78
N2 (n = 23)	61	70
N3 (n = 19)	63	100
Total (n = 125)		

time of 14 months (overall $p < 0.001$). The 5-year survival rates for N0, N1, N2 and N3 groups were 44, 40, 28 and 24% respectively (overall $p = 0.167$).

Serious complications and side effects were documented. Concerning late side effects mucosal atrophy or oedema were observed in 36% of the patients (45/125), all of whom received at least 63 Gy midline tumour dose. Soft tissue necrosis occurred in 4% of the patients (5/125). This corresponds to 54% of the patients surviving at three years and 53% of the patients surviving at five years showing mucosal atrophy or oedema, and to 8% of the patients surviving at three years and 8% of the patients surviving at five years showing soft tissue necrosis. Brain tissue damage was observed in two patients (1.6%), both with T4-tumour and receiving a dose of 64 Gy in the brain tissue. One patient developed quadriparesis during follow-up after a spinal dose of 56 Gy. No significant differences in the frequency of mucosal reactions or soft tissue necrosis were noted between patients treated with split-course vs. continuous technique.

Discussion

An absence of correlation between the T and N group has been observed in many reviews of carcinoma of the nasopharynx (7–9). For this reason, the survival rates in the present report were also analyzed in relation to stage groupings, which are based on both T and N.

It is well known that patients with carcinoma of the nasopharynx have a high rate (62–72%) of cervical adenopathy (10–12). The majority of patients seek medical attention because of a neck mass. In our material 64% (89/139) presented at the beginning of the treatment with cervical adenopathy, which did not significantly differ from other reports (10, 12, 13).

The 5-year survival rate was 64% for the group of early tumours (stages I and II) and 32% for the group of advanced tumours (stages III and IV). These results are comparable with other reports (7, 10, 12). In the study by Bedwinek et al. (7) the relapse-free 5-year survival for the T1–2 N0–1 category was 69% but only 20% for the other T and N categories. The observed 5-year survival and NED survival rates in the patients of Schabinger et al. (12) were 38% and 37% respectively. The 5-year actuarial and relapse-free survival rates for the entire group of patients of Chu et al. (10) were 36% and 33% respectively. When the survival was analyzed in relation to integrated T and N category, the prognosis was good only for patients who had both small primary tumours (T1 or T2) and minimal neck disease (N0 or N1).

Our primary control rates by T category were comparable with results published in the literature (10, 14) except for T4-tumours. In our study, 14 patients had radiographic evidence of destruction of the base of skull before treatment. During the time of our study (1958–1982), CT scans were not performed, whereas it is nowadays a routine staging procedure (15). The frequency of local failures raises the suspicion of geographic miss or inadequate dose in the tumour area, which are common causes of radiotherapy failure (16). The base of the skull is most often the site of a local recurrence (11), and CT scans provide valuable information of the tumour extent.

The overall regional control rate of neck node metastases was inferior to some published results (7, 10, 14). In the present study the dose in the regional nodes was rather low. A dose in the entire neck of 50 Gy in 5 weeks, and in palpable nodes of 65 to 70 Gy in $6\frac{1}{2}$ to 7 weeks has been recommended (17).

Survival correlated well with initial extent of local (T-category) disease (overall $p < 0.001$). Patients with clinically uninvolved or unilaterally involved neck nodes did slightly better (44% and 40% 5-year survival rates) than patients with bilateral nodal involvement or fixed nodes (28% and 24% 5-year survival rates). The difference was, however, not statistically significant (overall $p = 0.167$). This is in agreement with Hoppe et al. (9) who reported that T-category is an important prognostic parameter whereas Chu et al. (10) found no significant relationship between the extent of the primary tumour and survival.

Due to the early deaths of some patients and the incomplete follow-up, the frequency of serious complications associated with radiotherapy was low in our series. The occurrence of late complications was dose-related both in the split-course and in the continuous treatment group. To avoid spinal cord damage the dose in this structure should be very carefully measured, as pointed out by Mesic et al. (11).

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