Cancer of the Nasal Cavity and Paranasal Sinuses

A Clinico-pathological Study of 277 Patients

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In the period 1963–1991, a total of 277 consecutive patients with malignant tumours of the nasal cavity and paranasal sinuses were treated at Aarhus University Hospital. The major histological types included squamous cell carcinoma (46%), lymphoma (14%), adenocarcinoma (13%), and malignant melanoma (9%). Kaplan-Meier estimates of 5-year corrected survival (death from cancer) showed the best prognosis for adenoid cystic carcinoma (87%), adenocarcinoma (65%) and lymphoma (56%), and the poorest prognosis for undifferentiated carcinoma (17%) and malignant melanoma (24%). The 5-year corrected survival for squamous cell carcinoma was 35%. Of the 180 patients with treatment failure, the vast majority occurred locally (n = 166); a minor proportion was regional (n = 23) or distant (n = 30). For the 195 patients with carcinoma, the following parameters were of statistical prognostic significance (5-year corrected survival): histological differentiation (moderate-well 65% vs. poor 22%), primary T-site (nasal cavity 56% vs. maxillary antrum 39% vs. other sinuses 24%), tumour stage (T2 68% vs. T3 37% vs. T4 29%), nodal stage (N0 48% vs. N1-3 21%), treatment (radiotherapy + surgery 56% vs. radiation alone 35%).

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Malignant tumours of the nasal cavity and paranasal sinuses are relatively rare, accounting for only 0.4% of all new malignant cases in Denmark (1). The treatment strategy at our institution has been the following: Small, resectable tumours were surgically removed, and adjuvant radiotherapy applied in case of non-radicality or poor differentiation. Primary curative radiotherapy was used for larger, unresectable tumours, which constitutes the majority of these cancers. In case of residual tumour two months after primary radiotherapy, salvage surgery was attempted. The advantage of this strategy lies in the avoidance of excessive tissue removal, as surgery in this area may lead to major functional and cosmetic defects. In the last decade the large mutilating surgical procedures, e.g. orbital exenteration have been abandoned, but otherwise the treatment principles have remained unchanged during the last 30 years.

In 1984, a paper from our centre, studying classification and prognosis for 180 malignant tumours in the nasal cavity and paranasal sinus, was published (2). This material has been thoroughly re-evaluated and is included in the present series.

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This retrospective study evaluates the significance of histological classification, degree of differentiation, tumour site, clinical stage, and treatment for corrected survival in a consequtive series of 277 patients treated in a single institution, with special emphasis on the major group of 195 carcinomas.

MATERIAL AND METHODS

From January 1, 1963 to December 31, 1991 a total of 277 consecutive patients with malignant tumours of the nasal cavity and the paranasal sinuses were treated at Aarhus University Hospital, Aarhus, Denmark. The population basis was 1.7 million (1963–1973) and 1.4 million (1974–1991). All patients are included in the present analysis, even patients with advanced disease. Most patients (90%) have been treated with curative attempt. Patients with cancers of the nasal vestibule were not included.

Tumour histology included carcinoma, lymphoma, malignant melanoma, soft tissue sarcoma, and other types. The carcinomas included squamous cell carcinoma, adenocarcinoma, undifferentiated carcinoma, adenoid cystic carcinoma and salivary gland carcinoma; and for these tumours the degree of differentiation was scored. Detailed information about the distribution of tumours in anatomical sites and histological types are crosstabulated in Table

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1. The median patient age was 65 years (range 21–91 years) and the male/female ratio was 1.7 (Table 1). Sarcoma patients were younger (median 55 years) and lymphoma patients older (median 72 years), with a majority of women.

Primary symptoms included swelling of the cheek/nose (59%), pain (34%), nasal obstruction or chronic sinusitis (22%) and vision disturbances (11%). Occupational risk factors were not routinely recorded during the entire period, but for the 37 patients with adenocarcinomas, at least 21 had a history of occupational exposure to wood dust.

Carcinomas of the maxillary antrum were classified retrospectively according to recommended UICC classification (3). From 1963 to 1980 the staging was based on clinical examination and x-ray tomography. From 1981 to 1991 the staging was based on CT-scans. Determination of the exact site of origin in bulky tumours was difficult. Whenever the tumor extended to the maxillary antrum it was classified accordingly. There is no generally accepted classification of tumours in the other sinuses or the nasal cavity.

Treatment modalities included radiotherapy and surgery. Chemotherapy was given only in one case. Of the 195 patients with carcinomas, the majority were treated with a combination of radiotherapy and surgery. Radiotherapy was delivered by external photon beam with ^{60}Co or 4 MV x-rays. A total dose of 57–66 Gy (median 60 Gy) in 30–33 fractions was delivered to the tumour and positive regional lymph nodes. No elective treatment of the neck was given. Eight weeks after the end of radiotherapy, the patients were evaluated for residual tumour with x-ray tomography and surgical biopsy (in 1963–1980) or by CT-scans with or without biopsy (after 1980). If a residual tumour was found, a surgical resection was performed in most of the cases. Exceptions were large residual tumours where radical surgery was either technically impossible or would result in unacceptable cosmetic and functional results.

The patients were followed for 5 to 10 years at the University Hospital, and the tumour and nodal status was recorded at each visit. Survival informations were cross-checked and updated in January 1995 by the National Population Register. Survival data were analyzed by the Kaplan-Meier method using the BMDP 1L computer program. The difference between groups were evaluated by log-rank test with a two-sided significance level of $p < 0.05$.

RESULTS

Tumour histology

The corrected (cancer specific) 5 and 10-year survival according to tumour histology are listed in Table 2. The overall actuarial corrected survival was 46% at 5 years and 36% at 10 years for all sites and histological subtypes. Malignant lymphoma and adenocarcinoma was associated with the best long term prognosis, and the worst prognosis was found for undifferentiated carcinoma and melanoma. Patients with adenoidcystic carcinoma had the best 5-year prognosis (87%), but these patients had very late relapses, leading to a 10-year survival of only 27%.

Failure patterns

A total of 180 patients (65%) failed after the initial treatment. The vast majority of these failures occurred loco-regionally (Fig. 1). Failure in regional lymph nodes without local (T) failure was seen in only 2 out of 23 nodal failures, whereas distant metastasis occurred without T-failure in 12 out of 30 cases. The failure pattern for the histological subgroups are listed in Table 2. Adenocarcinomas, soft tissue sarcomas and lymphomas had low distant metastasis rate, especially when compared to undifferentiated and salivary gland carcinoma.

Table 1

The median age, sex ratio, and the number of patients according to histological subtypes and tumour site

	Age	Sex	Tumour localization			Total	
	Median years	Male/female	Nasal cavity	Maxillary sinus	Other sinus	n	%
Squamous cell carcinoma	64	2.1	43	75	8	126	46%
Adenocarcinoma	65	4.3	31	3	3	37	13%
Undifferentiated carcinoma	63	5.0	3	2	1	6	2%
Adenoid cystic carcinoma	60	1.0	8	8	0	16	6%
Salivary gland carcinoma	66	2.3	3	7	0	10	4%
Lymphoma	72	0.7	15	24	1	40	14%
Malignant melanoma	65	2.3	24	2	0	26	9%
Soft tissue sarcoma	55	1.3	1	8	0	9	3%
Miscellaneous	63	0.4	3	4	0	7	3%
Total	65	1.7	131	133	13	277	100%

Table 2

The corrected survival rate at 5 and 10 years according to histological subtypes and the failure pattern, i.e. the frequency of relapse: at the site of the primary tumour (T), in regional lymph nodes (N), or by distant metastasis (M). Some patients had more than one relapse site. The number of patients are listed in Table 1

	Corrected survival (%)		Failure frequency (% of patients in the group)		
	5-year	10-year	T position	N position	M position
Squamous cell carcinoma	35	30	62	12	11
Adenocarcinoma	65	52	54	0	5
Undifferentiated carcinoma	17	0	67	0	17
Adenoid cystic carcinoma	87	27	63	2	13
Salivary gland carcinoma	48	48	50	13	20
Lymphoma	56	56	40	3	5
Malignant melanoma	24	15	81	12	15
Soft tissue sarcoma	56	56	56	11	0
Miscellaneous	57	43	71	14	0
Overall	46	36	59	8	10

Primary nodal involvement

Primary nodal involvement was found in 19/195 of the carcinoma patients (10%) and 2/26 patients with malignant melanoma (8%). Other histological types did not present with positive nodes. Patients with positive nodes had a significantly reduced 5-year corrected survival compared to node-negative patients (21% vs. 48%; Fig. 2). Primary distant metastases were a problem only in 8 of 277 patients (5 squamous cell carcinoma, 2 undifferentiated carcinoma and 1 sarcoma).

Carcinoma differentiation

The histological grading was determined in 145 of the 195 carcinomas (Fig. 3). The 5-year corrected survival for patients with moderate and well differentiated carcinomas were significantly better than that of patients with poorly differentiated tumours (65% vs. 22%, $p < 0.0001$).

Tumour site

Fig. 4 shows the survival among the carcinoma patients according to subsite. The 5-year survival rate was significantly better for nasal cavity (56%) compared to maxillary sinus (39%) tumours. This difference seems to be related to the distribution of histological subtypes at the different sites. For squamous cell carcinoma, the survival was similar at all sites, and the favourable prognosis for nasal cavity tumour may be related to the large proportion of adenocarcinomas at this site. Tumours in the frontal, ethmoid and/or sphenoid sinuses were associated with a significantly worse 5-year survival (24%).

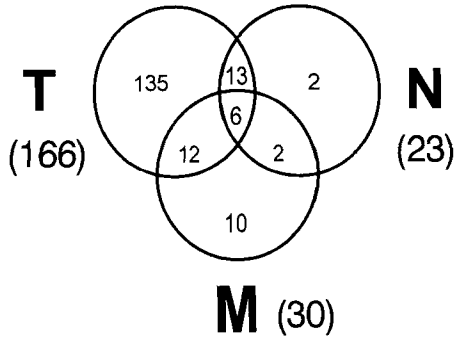

Fig. 1. The failure pattern for 180 patients presenting with one or more primary failure sites, either locally (T), regionally (N) or distant (M).

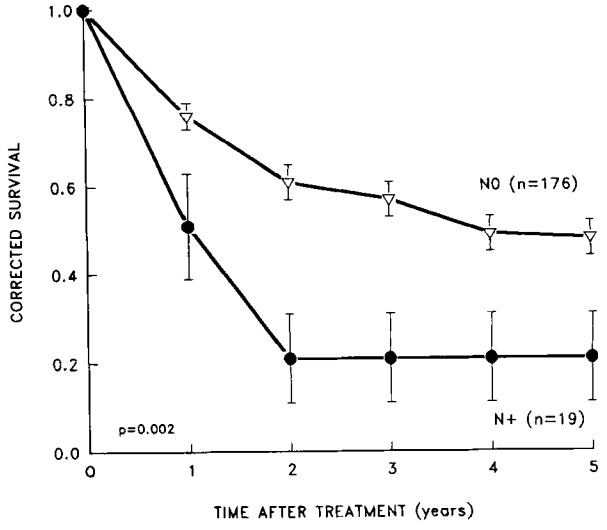

Fig. 2. The corrected survival for 195 carcinoma patients presenting with either positive (N+) or negative (N0) regional lymph nodes. Error bars are ±S.E.

Tumour stage

Data on tumour stage are difficult to evaluate since there has been no uniform or accepted topological classification for the different tumour types in these regions. The retrospective classification of the 94 carcinomas of the maxillary antrum according to the UICC classification (3)

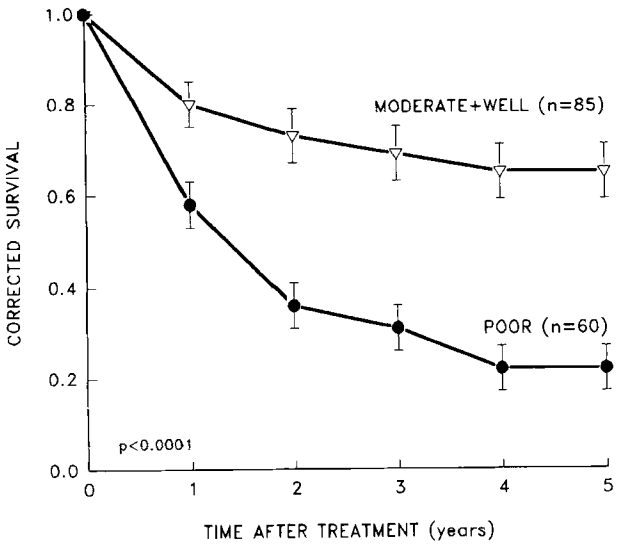

Fig. 3. The corrected survival for 145 carcinoma patients with either well-moderately or poorly differentiated tumours. Error bars are ±S.E.

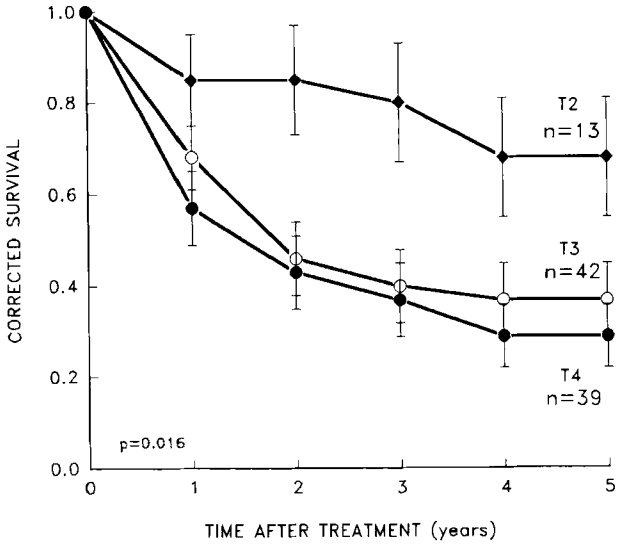

Fig. 5. The corrected survival for 94 patients with carcinoma of the maxillary sinus classified according to UICC. The one T1 tumour is not shown.

showed that most of the tumours were T3 (44%) or T4 (41%). The introduction of CT scanning in 1980 caused a considerable up-staging, resulting in a reduction in T3 tumours from 55% (1963–1979) to 21% (1980–1991) and a concurrent increase in T4 tumours from 30% to 68% ($p < 0.05$). Fig. 5 shows the significant correlation between T-stage and risk of death from cancer. The 5-year corrected survival rates were 68% (T2), 37% (T3) and 29% (T4).

Treatment

Accurate data on treatment modalities have been recorded for the 195 patients with carcinoma. Of these were 20 were 20 patients either not treated or had only palliative treatment. Of the 175 patients treated with curative intent, 11 patients (6%) were treated with surgery only, external radiotherapy alone was given in 60 cases (34%); radiotherapy followed by surgery in 94 cases (54%) and postoperative radiotherapy in 10 cases (6%). The corrected survival for the two radiotherapy groups has been compared in Fig. 6. Patients receiving the combined approach had a significantly better prognosis compared with those given radiotherapy alone (56% vs. 35%, $p < 0.0001$).

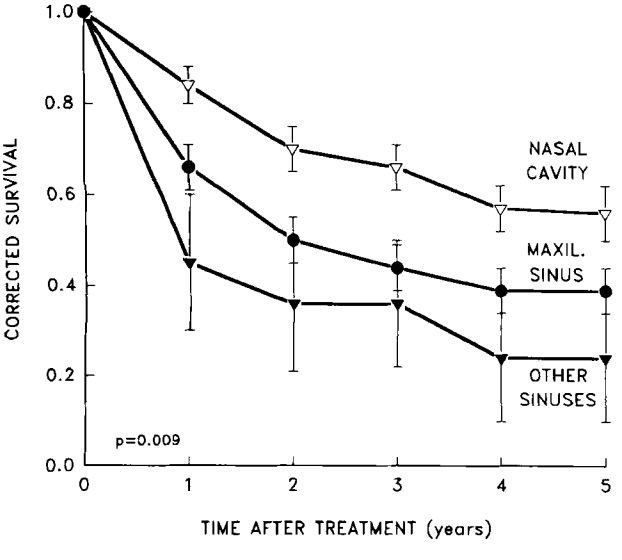

Fig. 4. The corrected survival for 195 carcinoma patients according to site of the primary tumour. Error bars are ±S.E.

DISCUSSION

Malignant tumours in the nasal cavity and paranasal sinuses are so rare, that a study of the clinicopathological features require data sampling over a very long time period. The present study, including 277 patients treated at a single institution over a 30-year period, represents one of the larger reported series in the literature. In the present report, univariate analysis have suggested a range of prognostic parameters. These include histology, differentiation, size, site, nodal involvement, and treatment type.

Many different histological tumour types are found in the nasal cavity and the paranasal sinuses. The proportion of squamous cell carcinoma (46%) is less than what is seen in other sites in the head and neck region. This has also been found in other reports (4–9). The relative distribution of undifferentiated carcinoma and adenocarcinoma differ considerably between studies. McNicoll (4) found 20% undifferentiated carcinoma and only 9% adenocarcinoma in a series of 460 patients. In another series of 624 patients, 10% were anaplastic carcinoma (5). In our series, the values were 13% adenocarcinoma and only 2% undifferentiated carcinoma. The differences in relative incidence

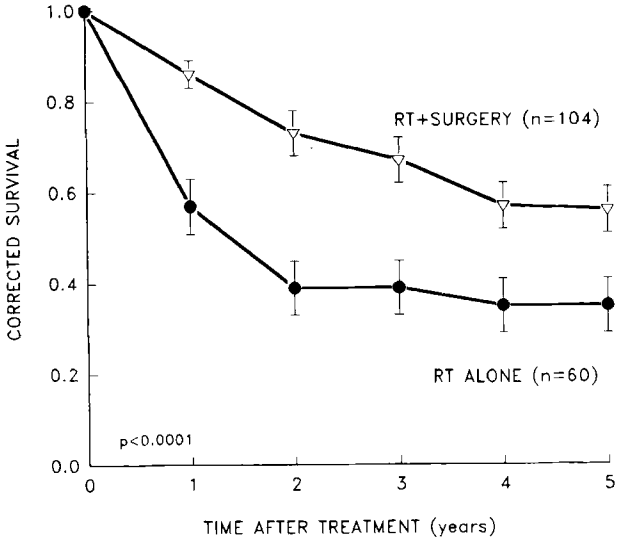

Fig. 6. The corrected survival for 164 carcinoma patients treated with curative intention with either surgery + radiotherapy (RT) or RT alone. Error bars are ±S.E.

of specific types of tumors between studies might be due partly to real differences because of different socio-economic and cultural conditions. More probably, it is due to different ways of pathological classification. The material of 277 patients are all analyzed by the same pathologist. A demand for classifying the carcinomas as squamous cell carcinomas are keratinizing and/or intercellular bridges. All squamous cell carcinomas are graded according to malignancy as well, moderate and low differentiated. This may partly explain our low proportion of undifferentiated carcinomas. The proportion of malignant melanomas is high in our material, due to immunohistochemical examination of all species, which means that unpigmented malignant melanomes are included. The proportion of adenoidcystic carcinoma in the present material is similar to that of others (4, 6, 7, 10, 11).

Present, as well as most previous, data have clearly showed that tumour stage and primary nodal involvement in maxillary carcinoma are important factors for prognosis (5, 11–13). The lack of a generally accepted staging system covering all sites makes reasonable comparison of the influence of this parameter between institutions impossible. Several authors have evaluated different classification systems (2, 10, 13–16), but none have gained widespread acceptance. Consensus on a reproducible and clinically applicable classification system constitutes one of the major issues for future clinical developments in this area.

The histological differentiation of carcinoma was found to correlate strongly with prognosis. This is in good agreement with another study on maxillary sinus and paranasal carcinoma (12), as well as other head and neck carcinomas (17–20).

Effective loco-regional tumour control in advanced head and neck cancer normally requires sufficient treatment of the neck. For nasal and paranasal cavity tumours, however, few patients had regional nodal relapse in the present series. This has also been found by most other investigators (5, 7, 11, 21). The low incidence of primary and secondary nodal involvement in carcinoma of the sino-nasal area makes it reasonable to use radical excision surgery or local radiation fields for node-negative patients, reserving treatment of the neck for patients with positive nodes (5). The low frequency of regional and distant metastases also points to the importance of optimizing local treatment for improvements in prognosis. The choice of initial local treatment is still unsettled. The univariate analysis showed that patients receiving combined surgery and radiotherapy had a considerably better prognosis compared with those receiving radiotherapy alone. This is comparable to what has been reported in most other studies (8, 10, 12, 22). However, this is most likely a result of difference in tumour stage. Patients, who are not candidates for primary surgery, and thus are treated with radiotherapy alone, tend to have large tumours with nodal involvement—factors which are known to be strongly linked to poor prognosis. The inherent relationship between co-factors will be tested in a future multivariate analysis of the data set. Recent developments in diagnostic imaging, surgical procedures (23) and radiotherapeutical techniques (24), may lead to improved local treatment, and hence better prognosis for this group of patients.

In conclusion, the present study has shown that the prognosis for patients with tumours of the sino-nasal area is dependent on tumour histology. For the large group of carcinoma patients, the prognostic factors included the histological differentiation, tumour site, tumour stage, nodal involvement and treatment modality.

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