

Cancer of the Nasal Cavity and Paranasal Sinuses¹

Prognosis and Outcome of Treatment

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A retrospective study of 121 patients, 77 men and 44 women, with sino-nasal cancer, admitted to the National University Hospital, Rigshospitalet, during the period 1983–1993, is presented. The median follow-up time was 21 months, (range 3–124). Forty-six percent of the tumors originated from the nasal cavity, 29% from the maxillary sinuses and 5% from the ethmoid sinuses. In 18% of the cases, the site of origin was not clear due to advanced local growth. Sixty-five patients received primary radiation therapy with curative intention of whom 5 underwent secondary surgery. Forty-nine patients underwent primary surgery, 38 of them received postoperative radiation therapy. The overall 5-year survival rate in this material was 35% and the disease-specific 5-year survival was 45%. Patients with well-differentiated squamous cell carcinomas had a significantly higher 5-year survival rate than patients with poorly differentiated carcinomas and patients with regional metastases had a significantly poorer 5-year survival than patients without. The 5-year local control was 48% (41/121). Six of 9 patients with regional metastases at admission were controlled locally, whereas 16 patients developed regional metastases after primary treatment.

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Cancer of the nasal cavity and paranasal sinuses is a rare disease; the incidence is 0.73 for men and 0.52 for women per 100 000 in Denmark, resulting in approximately 50 cases a year (1). The histological picture varies considerably and the nasal cavity and paranasal sinuses constitute a complex anatomical and physiological region. At time of diagnosis these tumors are often at an advanced stage as a result of late and vague symptoms leading to delay in consultation and referral (2). Many methods of treatment have been advocated, mainly as combination modalities of surgery, radiotherapy (RT), and chemotherapy (CHT). On account of the low incidence and the variable histologic pattern, it is difficult for a single institution to gain much experience in the management of these tumors. In this retrospective series, we reviewed 121 consecutive patients referred over a 10-year period (roughly 25% of the total cases in Denmark) in order to assess the results of various treatments.

MATERIAL AND METHODS

From 1983 to 1992, 121 patients with cancer of the nasal cavity and/or paranasal sinuses were treated at the Na-

tional University Hospital, Rigshospitalet, Copenhagen. All case histories with the diagnosis of nose or paranasal sinus neoplasm were retrieved. A total of 77 men and 44 women with a median age of 64 years (range 16–90) was included. The median follow-up time was 21 months (range 3–124). In 59 cases (49%), the tumor originated from the nasal cavity, in 35 cases (31%) from the maxillary sinuses, in 8 cases (7%) from the ethmoid sinuses, in one case from the frontal sinus and in one case from the sphenoidal sinus. In 14 cases the primary site of origin could not be established due to advanced local growth. Of the tumors assumed to have originated from the nasal cavity, the maxillary sinus was involved in 31 cases. The maxillary sinuses were involved in 87 cases (72%) either as the primary or the secondary tumor site. Thirty-one carcinomas of the maxillary sinus were staged according to the UICC, TNM Classification, most of them retrospectively on the basis of CT scans and descriptions of physical findings. The TN staging of the maxillary cases is shown in Table 1.

The distribution of histopathology by site is shown in Table 2. The most common pathologic diagnoses were squamous cell carcinoma (n = 52), adenocarcinoma (n = 14), malignant melanomas (n = 11), undifferentiated carcinomas (n = 11) and non-Hodgkin's lymphomas

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Table 1

Stage grouping of 31 maxillary sinus carcinomas according to UICC

Stage		T1	T2	T3	T4
II	N0	0	5	6	14
III	N1	0	1	0	4
IV	N2	0	0	0	1
	N3	0	0	0	0
	Total	0	6	6	19

(n = 9). Included under 'other' is one case of basal cell carcinoma located in the nasal cavity and maxillary sinus at presentation. Twenty-five patients (21%) had regional lymph node metastases, 9 (7%) were present at time of diagnosis. Six patients had metastases in the neck, 4 squamous cell carcinomas from the maxillary sinuses, one patient squamous cell carcinoma from an undetermined site (nose or maxillary sinus) and one undifferentiated carcinoma from the nose. Further regional lymph node metastases were found in 2 cases of melanoma and one case of non-Hodgkin's lymphoma. Five patients developed regional lymph node metastases within the first year of admission while 11 patients developed regional metastases at one year or later after admission.

Distant metastases developed in 13 patients (11%), the distribution showed 12 patients with metastases to the lung, 4 to bone, 3 to the liver and one to the brain. Five patients had developed metastases at more than one site.

Therapy

In choosing RT as the primary therapy modality, consideration was taken to general condition, age, expected postoperative basic abilities, tumor involvement, etc. This accounts for a selection of older patients with extensive tumor involvement in the group treated with this modality. Sixty-five patients were treated with RT to the primary site and five of these were treated with surgery shortly after RT. Nine cases with regional lymph node metastases on admission received RT in the regional lymph nodes as well. Patients receiving primary RT with curative intention were

treated to a total dose of 64–66 Gy, one fraction per day (F/D) and 5 fractions per week (F/W) with 2 or 3 angled wedged fields. Melanoma cases received a total of 52 Gy, 4 Gy/fraction and 2 F/W. Cases with regional lymph node metastases received 40–64 Gy on opposing fields with 2 Gy/fraction and 5 F/W.

Thirty-nine cases were treated with combined-modality therapy, consisting of surgery followed by radiotherapy within 8 weeks, whereas 11 patients were treated with surgery alone. Postoperative RT was recommended for cases with larger tumors, often with involvement of two or more sites or questionable radicality at the time of surgery (close/positive margins). The surgical treatment of tumors of the nasal cavity and the ethmoid sinuses involved extirpation through lateral or superior rhinotomy. Maxillary tumors were resected by the Caldwell-Luc approach and tumors with extension to the orbital contents required exenteration. Advanced cases were treated with maxillectomy, high, low, partial or total. There was a tendency for an increasing number of patients to be treated with primary surgery towards the end of the period.

Six patients received chemotherapy (CHT), all with non-Hodgkin's lymphoma. Table 3 shows the therapy related to histology. In cases of adenocarcinoma and melanoma, the majority of cases were treated with primary surgery and for all other groups primary RT was preferred.

Cases with primary location in the maxillary or ethmoidal sinuses were more frequently treated with primary surgery than tumors from other locations. Statistical analysis was performed using X²-test, Cox's regression analysis and Kaplan-Meier analysis.

RESULTS

Local control

The 5-year local control of the total material was 48% (product-limit method) and there was no significant difference in local control between the different tumors. Looking at treatment modality of maxillary carcinomas by stage, there was no apparent difference as to the local control, but the material is too small to allow for statistical

Table 2

Histopathology by topographical site, all tumors

	NC	MS	ES	FS	SS	Not established
Squamous cell carcinoma	18	23	4	1	1	5
Undifferentiated carcinoma	7	2	1			1
Adenocarcinoma	9	3	1			1
Non Hodgkin lymphoma	2	5	0			2
Melanoma	10	0	1			
Other	13	5	3			3
Total	59	38	8	1	1	14

NC = nasal cavity, MS = maxillary sinus, ES = ethmoid, sinus, FS = frontal sinus, SS = sphenoid sinus

Table 3
Therapy by histology, all tumors

	SCC N = 52	UC N = 11	AC N = 14	MM N = 11	Other N = 33	All N = 121
RT	34	9	6	3	8	60
RT + S	1	1	0	0	3	5
S	4	0	1	4	2	11
S + RT	13	1	7	4	13	38
CHT	0	0	0	0	2	2
CHT + RT(+S)	0	0	0	0	5	5

SCC = squamous cell carcinoma, UC = undifferentiated carcinoma, AC = adenocarcinoma, MM = malignant melanoma, S = surgery, RT = radiotherapy, CHT = chemotherapy

analysis. Including secondary treatment (<1 year) and treatment of relapse cases (>1 year) the local control for T2 tumors was 2/6, 4/6 for T3N0-N1 tumors and 6/16 for T4N0-N1 tumors. Including secondary and relapse treatment for all tumors the local control was 50% (61/121).

Regional control

The 5-year regional control of the total material was 74% (product-limit method). Regional control was achieved in 6 of 9 patients with regional node metastasis at admission. They were all treated by RT and 5 of them had complete remission whereas one was treated with neck dissection because of recurrence. Five patients developed regional lymph node metastasis within the first year of admission and 3 were controlled, one by RT and 2 by neck dissection. Eleven patients developed regional metastases 1 year or later after admission; 6 cases were controlled by neck dissection. Three of these patients had melanomas, 2 had undifferentiated carcinomas and one had squamous cell carcinoma.

Distant metastases

On account of the small numbers within the subgroups statistical analysis was not possible.

Survival

The crude 5-year survival was 35% and the disease-specific survival 45% (Fig. 1). In the group of squamous cell carcinoma there was significantly lower 5-year survival for cases with regional metastases at time of admission ($p < 0.01$) or regional metastases developed within the first year ($p < 0.01$) (Fig. 2). Similarly patients with well-differentiated squamous carcinoma did significantly better than those with poorly differentiated tumors ($p < 0.05$). The 5-year survival for patients with squamous cell carcinomas was 29%, for primary location in the maxillary sinus 25% and in the nasal cavity 39%. Patients with adenocarcinoma had a 5-year survival of 45%, while that for patients with melanoma was 53%. For patients with undifferentiated carcinoma and adenoicycstic carcinoma the 5-year survival

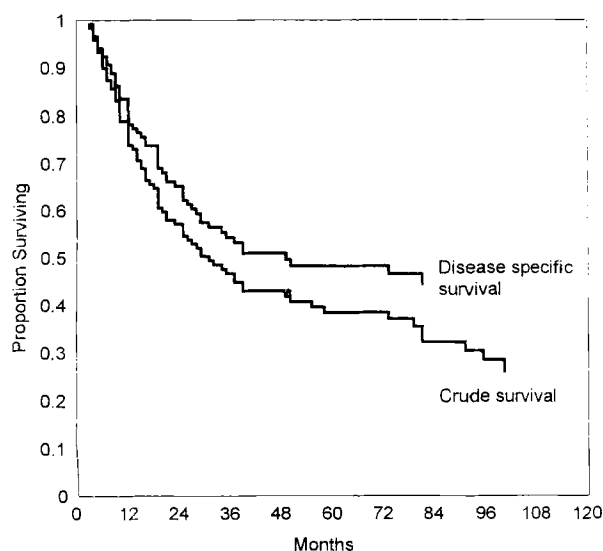


Fig. 1. Crude and disease specific survival.

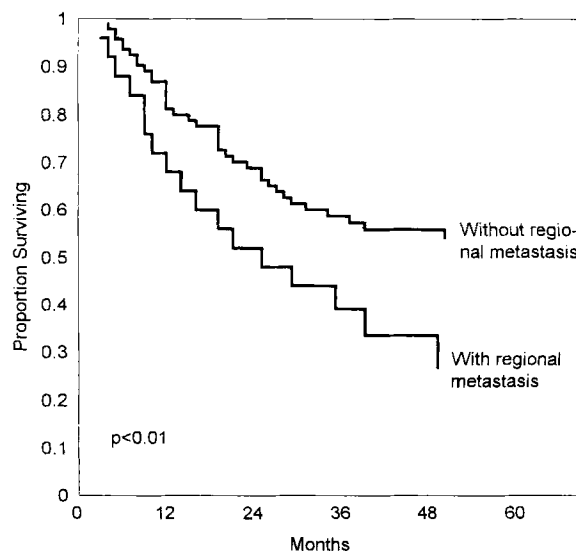


Fig. 2. With and without regional metastasis.

was 31% and 100% respectively. Survival rates could not be analysed for the other histological groups due to the small number of cases.

Patients treated with the combined modality of first surgery (S) and secondly radiotherapy (RT) or first RT and secondly S had a significantly better survival rate than did those treated with RT alone ($p = 0.01$). However, the latter group consisted of many patients who were considered to be unsuitable for primary surgery. Patients in their seventies, for some reason did significantly better than those in the other age groups. There was no significant difference in 5-year survival between sex, site of primary tumor, or T-stage (maxillary sinus carcinomas). Similarly, no significant difference was detected between patients with squamous cell carcinoma and those with adenocarcinoma.

In Cox's regression analysis of the total material, there was no significant difference in age, sex, differentiation or treatment modality. Local control had a positive prognostic significance ($p = 0.02$), while neck node metastasis ($p < 0.01$) and secondary involvement of the maxillary sinus ($p = 0.03$) correlated negatively with survival. In cases of squamous cell carcinomas in the maxillary sinus, neck node metastasis ($p < 0.01$) and undifferentiated carcinoma ($p = 0.02$) had negative prognostic significance, while local control had no significance.

DISCUSSION

The disease-specific 5-year survival of sinonasal cancer in Denmark has improved substantially during the last 4–5 decades, from 18% in 1945 to 47% in 1985 (3). The 5-year survival of 45% in this series seems to be at the same level. The histopathologic pattern is similar to findings in other series (4, 5) and the varied picture contributes to the complexity of deciding the best treatment modality for cancer of the upper jaw. The topographic distribution does not resemble two large series from the 1950s and 1960s, as cancer of the nasal cavity are almost 50% in the present series, compared with 20–30% in the older series (4, 5). In general, the distribution of the two subsites has changed from a predominance of maxillary sinus cancers during the 1940s and 1950s to a predominance of nasal cavity cancers in the 1970s and 1980s (6). Of 1 489 cases from 1943–1982, 52% were cancers of the nasal cavity, the remainder were located in the paranasal sinuses (3).

There was no significant difference in the number of patients treated with primary surgery or primary RT in the first half of the period compared with the last half of the period. The main treatment methods in this series were primary RT (60 cases) and a treatment modality of surgery followed by RT within 6–8 weeks (38 cases). This treatment modality is consistent with series from the 1960s and 1970s (7–9) while some series from the last decade advocate a combination treatment modality of surgery and RT

because of improvements in survival and local control (10, 11).

The combination treatment modality was reviewed as early as in the 1950s by Larsson et al. (12) who demonstrated a 5-year survival of 45%. The results in the present series do not on the basis of a regression analysis, support the superiority of the combined modality over a single modality of RT or S. The exact selection criteria for choosing a treatment modality are difficult to define in a retrospective study. This results in a selection bias as the distribution of patients in the treatment modality groups is not identical. In this series extensive consideration has been taken to age, advanced disease and function laesa, resulting in a preponderance towards allocation to RT for this subgroup of patients and this applies to most other series as well. Neck metastases are generally associated with poor local control and survival (10, 12–15), and the results of this series confirmed this finding. We found this to be the most important prognostic parameter for survival in the group of squamous cell carcinomas. Attempts have been made to treat patients with negative neck nodes with elective RT to the neck, but no survival benefit was noted (15). To investigate this, Stern et al. (10) described a regimen with systematic elective irradiation of the cervical lymph nodes during the course of postoperative RT for all patients with T3 and T4 maxillary sinus squamous cell carcinomas. The results though, remain to be published. In this series 2 patients received primary RT to clinically negative lymph nodes, one case resulted in regional control while the other case developed regional metastases. The role of chemotherapy in a multimodality therapy including RT and surgery was reported by Konno et al., (16) revealing a relative 5-year survival of 80% for squamous cell carcinomas and 72% for the total material, while another series had a 5-year actuarial survival of 53% (11). In the present material only patients with non-Hodgkin's lymphoma were treated with chemotherapy and no reliable statistical analysis of survival was possible, due to the few cases. The results in most studies favor combination treatment, at least in cases with more advanced disease (10, 13). Neck node metastases, in almost all series including the present, are associated with poor survival rates. Prospective studies on elective postoperative irradiation of the cervical lymph nodes and combination treatment of less advanced cases, may contribute to an improvement in locoregional control and survival. Because of the low incidence and great diversity of sino-nasal cancer, a multicenter design is desirable for further prospective studies.

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