Sino-nasal Cancer in Denmark 1982–1991

A Nationwide Survey

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Cancer of the nasal cavity and paranasal sinuses is a rare disease. The many different histologies and sites make the management of this disease a challenge. The current report from the Danish Society for Head and Neck Oncology comprises a joint analysis of five retrospective series covering the entire country, with 315 patients seen in the 10-year period from 1 January 1982 to 31 December 1991. Tumour sites were nasal cavity (n = 156), maxillary sinus (n = 139), ethmoid sinus (n = 14), sphenoid sinus (n = 5) and frontal sinus (one case). The most common histologies included squamous cell carcinoma (126 cases), adenocarcinoma (41 cases), malignant melanoma (38 cases) and malignant lymphoma (34 cases). A total of 284 patients (90%) received treatment with curative intent; most of these patients were treated with radiotherapy, either alone (120 patients) or in combination with surgery (111 patients). There was no significant difference between the five centres in disease specific survival and overall survival. The results showed that histology, localization and nodal involvement were significant prognostic factors for locoregional control and survival. Patients with squamous cell carcinoma had a significantly poorer prognosis compared with patients with adenocarcinoma. However, a Cox multivariate analysis revealed that this was likely the result of tumour localization, as most adenocarcinomas were in the nasal cavity. The experience from this data collection has inspired the Danish Society for Head and Neck Oncology to arrange common data registration of several other clinical head and neck series. In the future, the Society plans to expand this activity further.

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Cancer in the nasal cavity and paranasal sinuses is a rare disease. The many different histologies and sites are a challenge in the management of this disease. The treatment approach is often multidisciplinary, and also requires optimal imaging for staging and follow-up. The Danish Society for Head and Neck Oncology is a multidisciplinary forum for medical personnel specializing in head and neck oncology. At the annual meeting of the society in 1996 the main topic was sino-nasal cancer. Several oncology centres in Denmark, represented by the co-authors of this paper, each presented their local experience with these relatively rare disease, and the results from these institutional series have been published (1–3). The Society encouraged the authors to pool their data and also include the remaining two centres in order to have a nationwide material. The current report is the common analysis of these five series.

MATERIAL AND METHODS

The initial data recording was done in three different database formats and time periods (Fig. 1). The Finsen Centre recorded 121 patients from 1982 to 1992, Odense University Hospital (VSK) 115 patients from 1978 to 1993, Aarhus (GH), Herlev (KW), and Aalborg (CR) used identical databases to record 275, 53 and 67 patients, respectively, in different periods from 1963 to 1995. A total of 631 patients were recorded. The data presented here represent the common denominator of the parameters recorded in the three databases for the 315 patients seen in the 10-year period from 1 January 1982 to 31 December 1991.

The age range of these 315 patients was 10 to 94 years, median age 66 years. The patient group included 116 females and 199 males. The occupational status of the patients was not specified in detail, but there were 27 carpenters (9%).

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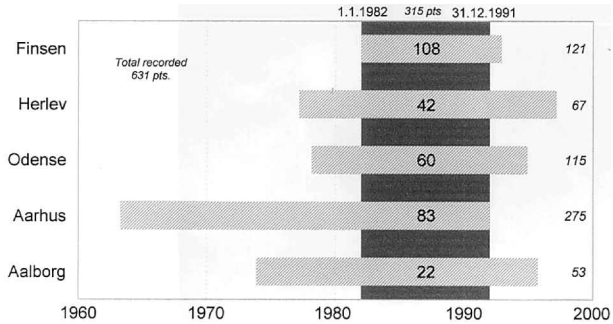

Fig. 1. Inclusion period and number of patients with sino-nasal cancer recorded in the five oncology centres in Denmark.

The origin of the primary tumour was determined by clinical examination, sinoscopy and various imaging procedures, mostly CT scan. Half of the patients (n = 156) had tumours originating in the nasal cavity (Table 1). The other major site was the maxillary sinus (n = 139; 44%). Ethmoid cancer occurred in 14 cases (4%). Even more rare were tumours sited in the sphenoid sinus (n = 5) and frontal sinus (one case).

The histologies of the primary tumours are presented in Table 2. Squamous cell carcinoma was by far the most common type, with 126 cases (40%). Adenocarcinoma constituted 41 cases (13%), and malignant melanoma and malignant lymphoma were almost as common with 38 and 34 cases, respectively. Adenoid cystic carcinoma, undifferentiated carcinoma, aesthesioneuroblastoma (olfactory neuroblastoma), soft-tissue sarcoma were all very rare histologies. No specific pathology review was done for this study.

A retrospective clinical staging was hindered by the lack of a generally accepted T-classification for tumours in this region. Some of the centres used AJC/UICC and Lederman systems (1), whereas other centres used 'home-made' recording systems based on involvement of, for example, orbit or skin (2, 3). All the centres recorded the presence or absence of metastatic disease in their patients. A total of 30 patients (10%) had lymph node involvement and 7 patients (2%) had distant metastases at time of presentation.

A recording of the applied treatment modalities was made at all the centres (Fig. 2). A total of 284 patients (90%) received treatment with curative intent, while the remaining 31 patients received palliative treatment or no

Table 1

Localization of primary tumour

Site	No. of patients	Percent
Maxillary sinus	139	44
Nasal cavity	156	50
Ethmoid sinus	14	4
Sphenoid or frontal sinus	6	2

Table 2

The histological classification of the 315 patients with sino-nasal cancer in Denmark 1982–1991

Histology	No. of patients	Percent
Squamous cell carcinoma	126	40
Adenocarcinoma	41	13
Malignant melanoma	38	12
Lymphoma	34	11
Adenoid cystic carcinoma	21	7
Undifferentiated carcinoma	23	7
Esthesioneuroblastoma	13	4
Sarcoma	14	4
Other	5	2

treatment at all. Most of the patients were treated with radiotherapy, either alone (120 patients) or in combination with surgery (116 patients). Chemotherapy was combined with radiotherapy for malignant lymphoma, but none of the patients received chemotherapy alone. Surgery was the only treatment in 21 patients. Radiotherapy was delivered by linear accelerator (4–6 MV) or cobalt-60 in 2 Gy per fraction and 5 fractions per week. Radiation dose and chemotherapy schedules were too inconsistently recorded to allow detailed analysis.

All patients were followed regularly at the oncology centres for a period of five years after treatment. Recurrent disease was verified by biopsies. For the present analysis, all patient charts were reviewed and the disease and survival status was updated as of June 1, 1997. Endpoints for the present study were locoregional tumour control (combined control in both primary (T) and nodal (N) site), disease-specific survival (only deaths from or with the actual cancer were counted) and overall survival (death from any cause). All time estimates began at the first date of the initial consultation at the oncology centre. The data were analysed using the SPSS for Windows version 8.0 statistical software. Tumour response and survival data were analysed actuarially using the Kaplan-Meier method. The statistical difference between various prognostic

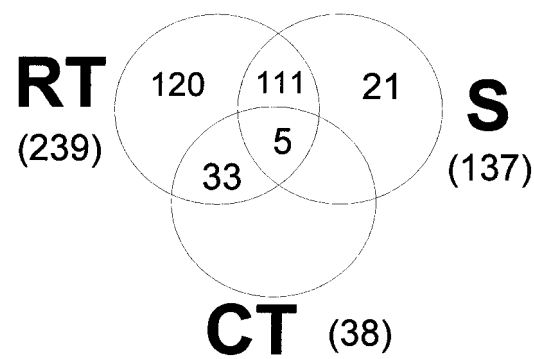

Fig. 2. The initial treatment modalities applied. A total of 284 patients were treated with radical intent and 31 patients received palliative or no treatment. RT = radiotherapy; S = surgery; CT = chemotherapy.

parameters was tested using a log-rank test, and a test for trend was used when applicable. A significance level of 5% (two-sided) was used for all tests. Data are represented as 5-year actuarial estimate ± standard error, unless otherwise stated. The independent significance of parameters was tested in a Cox proportional hazard model. Parameters were included in the model using the enter method and statistical analysis was performed using likelihood ratio. The time for evaluation of locoregional control and disease-specific survival was five years after the initial visit, since patients were only followed routinely at the oncology centre for this time period.

RESULTS

The results of the actuarial analysis of different prognostic parameters are presented in Table 3. A significant difference between centres was found for locoregional tumour control, with the 5-year values ranging from 64% to 35% ($p = 0.006$). However, this difference in the recording of the initial treatment results did not affect the final out-

Table 3

Five-year actuarial probability for a) locoregional control, b) cause-specific survival (death from cancer in question) and c) overall survival for the 315 patients with sino-nasal cancer in Denmark, 1982–1991. The parameters were tested using a Kaplan–Meier analysis and differences between groups were tested for significance using a two-sided log-rank test (5% significance level)

Parameter	No. of patients	Locoregional tumour control (%) ± s.e.; p-value	Cause-specific survival (%) ± s.e.; p-value	Overall survival (%) ± s.e.; p-value
Overall	315	41 ± 3		35 ± 3
Cener				
Finsen	108	35 ± 5	45 ± 5	37 ± 5
Herlev	42	46 ± 9	48 ± 8	32 ± 8
Odense	60	64 ± 8	37 ± 6	33 ± 6
Aarhus	83	35 ± 7	42 ± 6	36 ± 5
Aalborg	22	47 ± 11	36 ± 10	32 ± 10
		0.006	0.85	0.73
Age				
10–65 years	154	42 ± 4	49 ± 4	44 ± 4
66+ years	161	41 ± 5	35 ± 3	26 ± 3
		0.99	0.05	0.0003
Gender				
Female	116	40 ± 6	40 ± 5	34 ± 4
Male	199	43 ± 4	44 ± 4	36 ± 3
		0.99	0.92	0.89
Period				
1982–1986	152	45 ± 5	44 ± 5	36 ± 4
1987–1991	163	40 ± 5	41 ± 4	35 ± 4
		0.57	0.71	0.91
Histology				
Squamous cell carcinoma	126	40 ± 5	36 ± 5	29 ± 4
Adenocarcinoma	41	52 ± 9	53 ± 8	44 ± 8
Malignant melanoma	38	14 ± 8	20 ± 7	13 ± 5
Lymphoma	34	68 ± 9	61 ± 9	56 ± 9
Adenoid cystic carcinoma	21	51 ± 12	74 ± 10	67 ± 10
Esthesioneuroblast.	13	58 ± 17	62 ± 13	62 ± 13
Sarcoma	14	43 ± 14	43 ± 13	43 ± 13
Undifferentiated carcinoma	23	0 ± 0	10 ± 6	9 ± 6
		0.0008	0.0000	0.0000
Localization				
Maxillary sinus	139	39 ± 5	32 ± 4	27 ± 4
Nasal cavity	156	43 ± 5	49 ± 4	40 ± 4
Other	20	56 ± 13	56 ± 12	53 ± 11
		0.32	0.007	0.028
Nodal involvement				
N0	285	43 ± 3	45 ± 3	38 ± 3
N+	30	12 ± 11	10 ± 6	7 ± 5
		0.033	0.0000	0.0000

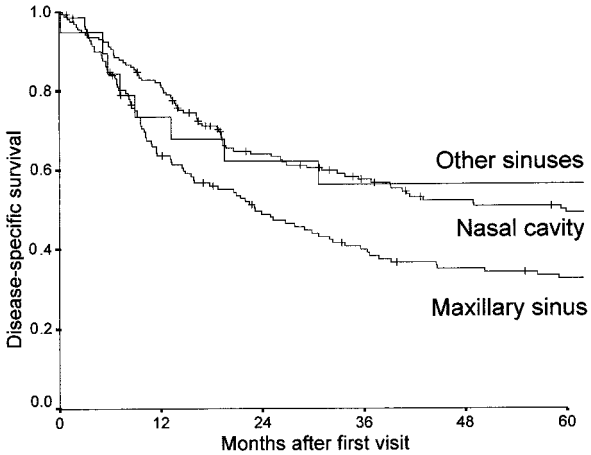

Fig. 3. Disease-specific survival of the 315 patients with sino-nasal cancer as a function of primary tumour localization.

come: very similar disease-specific survival and overall survival rates were obtained at the five centres; the 5-year estimates were around 40% and 35%, respectively (p = 0.85 and 0.73).

Patient age naturally had an influence on the survival rate, whereas it did not impact on the probability of locoregional control. Patient gender and treatment period (first or second part of the study period) did not influence the outcome. Much more important was histology: the best 5-year prognosis was seen in patients with rare histologies such as lymphoma, adenoid cystic carcinoma and aesthesioneuroblastoma. Patients with adenocarcinoma had an intermediate prognosis of around 50% for 5-year locoregional control and survival rate. The worst prognosis was for squamous cell carcinoma, malignant melanoma and undifferentiated carcinoma, with less than 40% 5-year locoregional control and survival rates. None of the patients with undifferentiated carcinoma obtained locoregional control, and the 5-year survival was only 9%.

Localization was also important (Table 3). Patients with tumours originating in the maxillary sinus had a significantly poorer disease-specific survival than those with tumours in the nasal cavity or other sinuses (Fig. 3). The latter group was, however, very small. Interestingly, localization influenced the locoregional control rate to a lesser extent than disease-specific survival.

Nodal involvement was a rare but important negative prognostic factor. The 30 patients with positive nodes had significantly poorer neck control (32% vs. 87%), locoregional control (12% vs. 43%) and disease-specific survival (10% vs. 45%, Fig. 4). The importance of this parameter was further confirmed in the Cox multivariate analysis (Table 4). Here only patients with squamous cell or adenocarcinoma in the nasal cavity or maxillary sinus were included. The analysis showed that nodal involvement and localization were independent prognostic parameters, whereas histology and age did not influence the risk of death from sino-nasal cancer.

DISCUSSION

The current survey is the first result of a strategy encouraged and sponsored by the Danish Society for Head and Neck Oncology to merge institutional experience into national surveys. The idea was first fostered after the initial data collection, so these are the compiled results from several different database formats and variables.

At the time of initiation of the study, one of the main concerns was the possible 'geographical' difference between the five centres. Although there was a significant difference between centres in terms of locoregional control, this did not affect the final outcome: very similar disease-specific survival and overall survival rates were obtained at the five centres. One explanation may be a difference in the recording of treatment schedules between centres. A common treatment policy has been to use radiotherapy followed by surgery for residual disease at 6–8 weeks. Since this is a planned combined approach, any residual disease at this time point should perhaps not be considered as a local failure, and accordingly, at least some of the centres have not recorded this as such.

Elective neck treatment has generally not been advocated in this type of head and neck cancer. The data from the current series seem to justify this policy. Initial nodal involvement was uncommon, and N0 patients rarely had neck recurrences (5-year neck control 87%). Similar results have been found in several other series (1, 4–6).

The results have shown that, of the recorded parameters, only histology, localization and nodal involvement were significant prognostic factors for locoregional control and survival. Undifferentiated carcinoma and malignant melanoma had the poorest prognosis, which is well known from other studies (1, 2, 7). By far, the most common histology was squamous cell carcinoma. Patients with this tumour type had a significantly poorer prognosis com-

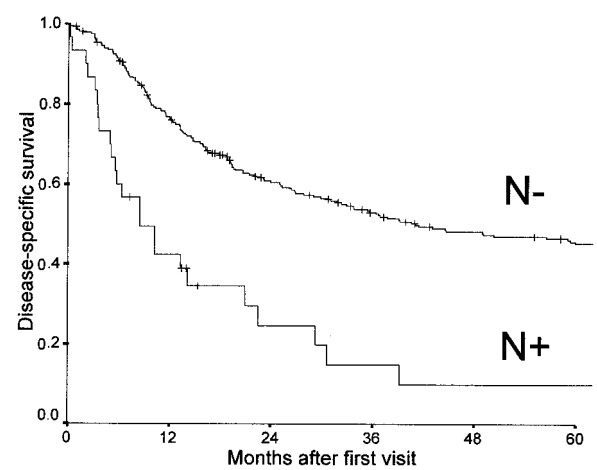

Fig. 4. Disease-specific survival of the 315 patients with sino-nasal cancer as a function of primary nodal involvement. N− = no initial nodal involvement (n = 285); N+ = positive nodes at presentation (n = 30).

Table 4

Cox multivariate analysis of prognostic factors for death from cancer in question in 167 patients with squamous cell carcinoma or adenocarcinoma in the nasal cavity or maxillary sinus (91 events)

Parameter	Significance	RR	(95% confidence limits)
N+ vs. N0	0.0009	3.1	(1.6–6.0)
Maxillary sinus vs. nasal cavity	0.00001	2.6	(1.6–4.0)
Squamous cell vs. adenocarcinoma	0.45	n.e.	
Age ($\pm$ 66 years)	0.19	n.e.	

pared with that of the other large group, adenocarcinoma. However, the Cox analysis demonstrated that this apparent effect was more the result of tumour localisation, where 'nasal cavity tumour' conferred a much better chance of disease-specific survival. Probably tumours in the nasal cavity are diagnosed at an earlier stage, but unfortunately this could not be included in the Cox analysis as it was not recorded consistently between centres.

The experience from this data collection has inspired the Danish Society for Head and Neck Oncology to arrange common data registration of several other clinical head and neck series, such as the management of cervical lymph node metastases from unknown primary tumour (8) and surgical complications after salvage laryngectomy in irradiated patients. Here, an important advantage over the current series has been that the recording was done using a common database format, which has made data merging and analysis considerably easier. In the future, the Society plans to expand this activity further.

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