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Contemporary clinical and treatment perspectives, and survival analysis of paranasal sinuses and nasal cavity malignancies

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Abstract

Background Paranasal sinus and nasal cavity malignancies are rare and histologically diverse, often presenting with delayed diagnosis. Understanding their demographic, clinicopathological, and therapeutic characteristics is critical for optimizing outcomes. This retrospective cohort study aimed to evaluate the characteristics of paranasal sinus and nasal cavity malignancies. Patient data were analyzed in terms of histopathology, demographics, clinical presentation, tumor characteristics, treatment modalities, and 5-year survival outcomes, with additional subgroup analyses performed according to tumor location.

Results A total of 119 patients (male 58.8%, female 41.2%) were included. 51.1% were smokers, and 43.9% were non-office workers. In terms of presentation, 40.4% reported nasal symptoms as their primary concern, whereas symptoms related to the oral cavity accounted for 22.0% while facial symptoms made up 11.0% of the reported symptoms. The mean duration of diagnosis was 5.2 months. Tumor types included squamous cell carcinoma (40.3%), sarcomas (16.8%), minor salivary gland tumors (14.3%), hematolymphoid tumors (11.8%), neuroectodermal tumors (8.4%), non-squamous cell carcinomas (6.7%), and metastases (1.7%). Most (55.5%) underwent transfacial procedures, while 21.0% were treated endoscopically. Neck lymph nodes were detected in 19 (16.0%) and 16 (13.5%) underwent neck dissection. The rate of adjuvant treatment was 54.7%, and 15.5% of the patients received primary chemoradiotherapy or chemotherapy. The 5-year overall survival (OS) rate was 48.9%, the disease-free survival (DFS) rate was 42.4%, and the disease-specific survival (DSS) rate was 66.3% for all.

Conclusion By thoroughly evaluating patient and tumor factors, it is possible to obtain similar or even improved survival outcomes within specific tumor groups.

Keywords Paranasal sinus cancer, Nasal cavity cancer, Clinical outcomes, Epidemiology, Survival analysis, Cancer outcomes

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Background

Malignant neoplasms affecting the nasal cavity (NC) and paranasal sinus (PNS) are infrequently observed but often disregarded tumors, characterized by a notable prevalence of delayed diagnosis and treatment. They exhibit distinct etiological characteristics compared to other head and neck tumors. Individuals employed in industrial settings and exposed to inhaled gases or particles, such as wood dust, nickel, and aflatoxin may develop various types of tumors [1]. Notably, both surgical and non-surgical treatments necessitate a comprehensive assessment of functional consequences in addition to adhering to oncological principles.

In the current study, the diagnostic procedures, symptoms, duration of symptom identification, demographic information, etiologically significant factors, histopathological records, applied therapeutic method, and postoperative monitoring procedures, and their impact on survival rates were retrospectively reviewed.

Methods

This retrospective cohort study included patients diagnosed with PNS and NC malignancies who presented to a single tertiary referral center between 1996 and 2023. The necessary patient data were analyzed retrospectively, and patients were excluded whose data was unavailable or incomplete. Patients with a histopathologically confirmed PNS or NC malignancy consecutively evaluated at our institution during the study period with accessible clinical data were included. Conversely, patients with inaccessible clinical data, missing or incomplete follow-up information, those lost to follow-up, or those who declined to participate were excluded.

Patient characteristics including age and gender distribution, smoking habits, whether they had any history of other malignancy, the time of onset of their complaints, and primary tumor location were collected. Patients were categorized into three separate groups based on age: 18 years old and younger, between 19 and 59 years old, and 60 years old and older. To examine the potential occupational etiological risk factors, patients were divided into two groups: office workers and non-office workers. To ensure a comprehensive understanding of each patient's condition, complete ENT physical examination information, preoperative imaging results, surgery notes, and pathology reports were collected and then patients were staged using the American Joint Committee on Cancer (AJCC) (8th edition) system [2]. In addition, patients were sourced and grouped based on their histopathological type according to the classification provided by the World Health Organization (WHO) [3].

Table 1 Enumeration of patients segregated according to age groups and gender

Gender - Age	≤ 18	19–59	≥ 60	Total
Female	7 (5.9%)	24 (20.2%)	18 (15.1%)	49 (41.2%)
Male	2 (1.7%)	36 (30.3%)	32 (26.9%)	70 (58.8%)
Total	9 (7.6%)	60 (50.4%)	50 (42.0%)	119 (100.0%)

In this study the different surgical treatment methods employed, including neck dissections and reconstruction techniques were investigated. This included whether tracheotomy was necessary and the use of radiotherapy and chemotherapy in primary, adjuvant, or neoadjuvant setup was evaluated. The decision to perform neck dissection was made based on imaging methods, clinical examinations, location and stage of the disease, and histopathology. Positive preoperative cervical lymphadenopathy was the main indication for the neck dissection. The rates of recurrence, neck lymph node metastasis, and distant metastasis, as well as the surgical and non-surgical treatments administered during follow-up during follow-up were considered.

The survival rates associated with various factors, such as tumor location, histopathological type, tumor stage was also investigated. To obtain a comprehensive understanding of the overall survival rates, disease-free survival rates, and disease-specific survival rates, these rates were calculated and compared. Patients who experienced an event (death, recurrence, or metastasis) at any point during follow-up were included in the survival analyses regardless of follow-up duration. Patients without an event who had not yet reached five years of follow-up were excluded from the survival analyses due to indeterminate outcome status at the time of data collection. The cases of carcinomas were compared with other tumor types, as were epithelial tumors with other tumor types, and the outcomes of stage 1, 2 and 3 cases were compared to stage 4 cases separately and independently.

All statistical analyses were performed using SPSS, version 29.0 (IBM Corp., Armonk, NY, USA). Kolmogorov-Smirnov and the Shapiro-Wilk tests were used to assess the assumption of normality. Continuous variables are presented as median and interquartile range (IQR). Categorical variables are summarized as counts and percentages. Kaplan-Meier analysis with Log-Rank test was used for the survival analysis. Bonferroni correction was applied to adjust for multiple comparisons. A p-value < 0.05 was considered statistically significant.

Results

This investigation included a total of 119 individuals (Table 1). The cohort mean age was 54.3 years. The youngest patient was only four months old, while the oldest patient was 86 years of age.

Analysis of etiological risk factors

Among the 94 patients who disclosed details of smoking habits, 46 (48.9%) were identified as individuals who

had never engaged in smoking, while 48 (51.1%) had a smoking history, with an average yearly consumption of 30 packs (ranging from 2 to 90 packs). Of the 82 patients who provided information regarding their occupation, 46 (56.1%) were classified as office workers, and the remaining 36 (43.9%) were classified as non-office workers. The non-office worker category included industrial factory workers, although no individuals employed in the wood/furniture industry were encountered. The rates of smoking, along with the proportions of office and non-office workers, stratified according to tumor subtypes, are presented in Table 2. It was observed that in the group with carcinomas (both squamous cell carcinoma and non-squamous cell carcinomas), the smoking rate was above the value for the whole cohort at 67.5%. On the other hand, within the group of non-carcinoma tumors, the smoking rate was 37.3%. Notably, a significantly higher prevalence of smoking was observed within the group diagnosed with carcinomas ($p = 0.004$). Only two individuals (4.2%) had a history of inverted papilloma.

Analysis of symptoms

Of 119 patients, because of missing data, 109 (91.6%) were evaluated for symptom information, and 99 (83.2%) were evaluated for the time from symptom to diagnosis. In the patient population, 44 (40.4%) experienced nasal symptoms alone, such as nasal congestion, runny nose, and nosebleeds. Additionally, 24 patients (22.0%) manifested exclusively oral symptoms, including masses, wounds, and bleeding in the mouth. Furthermore, 12 patients (11.0%) presented with facial symptoms only, such as swelling, numbness, and skin lesions. In terms of eye-related symptoms, two patients (1.8%) had epiphora, exophthalmus, and diplopia. One patient (0.9%) presented with headache only, while one other patient (0.9%) displayed only referred symptoms, including otalgia and sore throat. There were 21 (19.3%) who displayed symptoms involving multiple areas. Lastly, three patients (2.8%) were incidentally diagnosed through radiological imaging.

When symptom frequency was assessed, nasal symptoms were the most prevalent (40.4%), with symptoms associated with the oral cavity being the second most prevalent (22.0%), followed by facial symptoms at 11.0%. The average length of time between the onset of complaints and diagnosis was 5.2 months. The fastest diagnosis was less than one month, while the longest diagnosis time was 60 months. Among the patients, 81 (81.8%) received their diagnosis within the first six months, 13 (13.1%) between six and 12 months, and 5 (5.1%) after 12 months.

Table 2 the distribution of patients based on histopathological tumor type, along with age, F/M ratio, smoking use, and office/non-office work rates

Malignancy types	Number (Percent)	Age	Female / Male	Smoking rate	Non-office worker rate
Squamous Cell Carcinomas and variants	48 (%40.3)	60.5 (43–86)	10/38	68.6%	56.5%
non-SCC carcinomas	8 (%6.7)	48,1 (26–69)	5/3	75.0%	17.1%
Minor salivary gland	17 (%14.3)	56,1 (15–78)	13/4	27.3%	21.4%
Sarcomas	20 (%16.8)	38,8 (0–75)	10/10	23.5%	18.8%
Hematolymphoid	14 (%11.8)	57.1 (30–84)	8/6	55.6%	50.0%
Neuroectodermal	10 (%8.4)	52.1 (11–76)	2/8	60.0%	42.9%
Metastasis	2 (% 1.7)	51.5 (51–52)	1/1	-	-
Whole malignancies	119	54.3 (0–86)	49/70	%51.1	43.9%

*Percentages for the non-SCC carcinoma group ($n = 8$) should be interpreted with caution given the small subgroup size

Histopathological analysis

The histopathological distribution is provided in Table 2. Forty-eight (40.3%) patients were diagnosed with squamous cell carcinomas and its variants. Amongst these, 4 (8.3%) had poorly differentiated carcinoma, 2 (4.1%) had basosquamous carcinoma, 2 (4.1%) had Schneiderian carcinoma, 1 (2%) had verrucous carcinoma, and the remaining 39 (81.2%) had squamous cell carcinoma. In the non-squamous cell carcinoma group, there were 8 (6.7%) patients. Of these, 1 (12.5%) had ameloblastic carcinoma and 7 (87.5%) had adenocarcinoma.

The minor salivary gland cancers group contained 17 (14.3%) patients. Within this group, 12 (70.6%) had adenoid cystic carcinoma, 3 (17.6%) had mucoepidermoid carcinoma, 1 (5.9%) had oncocytic carcinoma, and 1 (5.9%) had salivary gland clear cell carcinoma.

There were 14 patients (11.8%) with hematolymphoid tumors, with 3 (21.5%) being in the solitary plasmacytoma group and 11 (78.5%) in the lymphoma group. Synonasal plasmacytomas made up 2.5% of all sinonasal malignancies. Lymphomas accounted for 9% of all sinonasal malignancies, with 54.5% being diffuse large B-cell lymphoma, 36.5% being NK/T cell lymphoma, and 9% being maltoma subtype.

The sarcoma group consisted of 20 patients (16.8%). Within this group, 4 (20.0%) had rhabdomyosarcoma, 2 (10.0%) had malignant fibrous histiocytoma, 1 (5.0%) had epithelioid hemangioendothelioma, 3 (15.0%) had hemangiopericytoma, 1 (5.0%) had osteoblastic osteosarcoma, 3 (15.0%) had chondrosarcoma, 1 (5.0%) had teratosarcoma, 1 (5.0%) had pleomorphic sarcoma/dedifferentiated chondrosarcoma, 1 (5.0%) had

synovial sarcoma, and 3 (15.0%) had unclassified soft tissue sarcoma.

The neuroectodermal tumors group consisted of 10 patients (8.4%). Among them, 4 (40.0%) had olfactory neuroblastoma, 5 (50.0%) had mucosal malignant melanoma, and 1 (10.0%) had Ewing sarcoma.

In terms of secondary malignancies, 17 (14.3%) patients had an additional malignancy. Among these, eight had a secondary malignancy in the head and neck area, two had lung carcinoma, one had renal cell carcinoma and prostate carcinoma, two had gastrointestinal malignancy, one had a hematolymphoid tumor, two had breast carcinoma, and one had pineoblastoma.

There were two cases of metastatic disease (1.7%), one breast and one lung carcinoma.

Analysis of primary location

The maxillary sinus was the most common primary location, and there were 69 (58.0%) patients in this group. There were 48 (40.3%) patients in the NC and ethmoid sinus combined group. And, 2 (1.7%) patients in the frontal, but none in the sphenoid sinus.

In the squamous cell carcinoma and variants group, it was found that 2 (4.1%) tumors were located in the frontal sinus, 18 (37.5%) in the ethmoid sinus and NC complex, and 28 (58.3%) in the maxillary sinus. In the group of hematolymphoid tumors, two of the plasmacytomas originated in the NC and one in the maxillary sinus. In addition, 36.4% of the lymphomas were located in the maxillary sinus, while 63.6% were found in the NC. Among the cases of malignant melanoma, three were found in the maxillary sinus and two in the NC. Furthermore, one instance of Ewing's sarcoma was localized in the NC. Lastly, when evaluating the primary tumor location in the minor salivary gland group, 1 (5.9%) of the patients had tumor localization in the NC, whereas the remaining 16 (94.1%) had localization in the maxillary sinus.

Analysis of surgical approaches

The surgical interventions were: 28 cases (23.5%) undergoing biopsy procedures only; 25 cases (21.0%) of endoscopic surgery; and 66 cases (55.5%) of external approach conducted through transfacial incisions. Among the surgeries, 10 patients (8.4%) underwent endoscopic medial maxillectomy (with simultaneous pterygopalatine fossa surgery in 1 patient), while 17 patients (14%) underwent infrastructure maxillectomy, 3 patients (2.5%) underwent suprastructure maxillectomy, 13 patients (10.9%) underwent subtotal maxillectomy, 22 patients (18.4%) underwent total maxillectomy (with simultaneous orbital exenteration in 5 patients), 9 patients (7.6%) underwent primary excision of lesions, and 2 patients (1.7%) underwent anterior cranial resections.

Tracheotomy was performed for 12 (10.1%) patients to ensure the safety of the airway in 1 out of 17 patients who underwent infrastructure maxillectomy, 4 out of 13 patients who underwent subtotal maxillectomy, and 7 out of 22 patients who underwent total maxillectomy. None of the patients who underwent endoscopic procedures, biopsies, or suprastructure maxillectomy required tracheotomy. Reconstruction procedures were carried out in 43 (36.1%) of 119 patients, while those who underwent endoscopic sinus surgery and biopsy were left to undergo secondary recovery. The employed reconstruction techniques included Split-Thickness Skin Graft (STSG) in 11 patients, full thickness skin graft (FTSG) in 1 patient, free fibula flap in 4 patients, radial forearm in 1 patient, 13 local flaps, 3 titanium patches, and 3 Medpor® (Porex Surgical, Newman, GA, USA), as well as 2 free bones.

Neck approach analysis

Nineteen patients (16.0%) exhibited positive lymphadenopathy in radiological or clinical examination of the neck. Among these, neck dissection was not performed in three because of distant metastases in two, and one who was treated with primary chemoradiotherapy. The remaining 16 patients (13.5%) underwent neck dissection, and of these, eight (50.0%) had pathologically tumor-positive lymph nodes. Prophylactic neck dissection was not performed in any patients. Out of the 80 patients who did not undergo prophylactic neck dissection and underwent a 60-month follow-up, three patients (3.7%) experienced recurrences in the neck lymph nodes.

Analysis of non-surgical primary or additional treatments

The adequate treatment data was available for 102 (85.7%) patients. Among them, 28 (27.4%) individuals did not receive any adjuvant treatment. Following the surgical procedure, 56 (54.9%) patients were subjected to adjuvant therapies, which included 39 (38.2%) who underwent radiation therapy (RT), 16 (15.7%) who underwent chemoradiation therapy (CRT), and 1 (1.0%) patient who underwent chemotherapy (CT).

Eight (7.8%) patients were given primary chemoradiation therapy, of whom two had rhabdomyosarcoma, one had NK/T cell lymphoma, and three had squamous cell carcinoma or its variants arising from T4b or metastasis. The remaining two patients had a signet ring cell carcinoma and an adenoid cystic carcinoma. Eight (7.8%) patients received primary chemotherapy, of whom six had lymphoma, one had embryonal rhabdomyosarcoma, and one had malignant fibrous histiocytoma with distant metastases. Lastly, neoadjuvant therapy was administered to two (1.9%) patients diagnosed with plasmacytoma and osteosarcoma.

Table 3 TNM Staging of the patients

	TNM				Stage			
	T1	**T2**	**T3**	**T4**	**1**	**2**	**3**	**4**
SCC (total = 43)	5 (11.6%)	4 (9.3%)	14 (32.15%)	13(30.2%) T4a, 7(16.3%) T4b	5 (11.6%)	4 (9.3%)	14 (32.6%)	13 (30.2%) 4a, 6 (14.0%) 4b, 1 (2.3%) 4c
	5 (11.26%) N+, 1 (2.3%) M+							
Non-SCC (total = 8)	-	4 (50%)	2 (25%)	1 (12.5%) T4a, 1 (12.5%) T4b	-	4(50%)	2 (25%)	1 (12.5%) 4b, 1 (12.5%) 4c
	1 (12.5%) had both N + and M+							
Salivary gland (total = 17)	1 (5.9%)	4 (23.5%)	5 (29.4%)	6 (35.3%) had T4a, 1 (5.9%) had T4b	1 (5.9%)	3 (17.7%)	6 (35.3%)	4 (23.5%) 4a, 1 (5.9%) 4b
	2 (11.8%) N+, none M+							
Sarcomas (total = 20)	7 (35.0%)	1 (5.0%)	9 (45.0%)	3 (15.0%)				
	1 (5.0%) N + and M+							
Lymphoma (total = 11)	9 (81.8%) stage 1e, 2 (18.2%) stage 2							
Olfactory neuroblastoma (total = 4)	Neuroendocrine Tumor Modified Kadish Staging [4] and Hyams Grade [5], 1 case was classified as Stage A grade 1 (25%), 1 case as Stage C grade 3 (25%), and 2 cases as Stage D grade 4 (50%) [4, 5].							
Melanoma	all T4a (100%)							

Table 4 Distribution of all patients included in the survival analysis categorized by tumor type and survival data will be rates

	Number (Percent)	OS	DFS	DSS
Whole malignancies	92 (100.0%)	48,9%	42.4%	66,3%
Epithelial tumors	57 (62.0%)	50.9%	42.1%	73.7%
Non-epithelial tumors	35 (38.0%)	45.7%	42.9%	54.3%
Carcinomas	44 (47,8%)	44.5%	38.6%	72.7%
Non-Carcinomas	48 (52,2%)	52.1%	45.8%	60.4%
SCC and variants	38 (41.3%)	42,1%	34.2%	73,7%
Non-SCC carcinomas	6 (6.5%)	66,7%	66,7%	66,7%
Minor salivary gland	13 (14.1%)	%69,2	53.8%	76,9%
Adenoid cystic carcinoma	8 (61.5%)	62.5%	37.5%	75.0%
Sarcomas	14 (15.2%)	42,9%	35.7%	50,0%
Hematolymphoid	13 (14.1%)	53,8%	53.8%	61,5%
Lymphomas	10 (10.9)	45.5%	45.5%	54.5%
Neuroectodermal	8 (8.7%)	37,5%	25.0%	50,0%

Analyses of TNM staging (Table 3)

When carcinomas and salivary gland tumors were collectively analyzed as epithelial tumors, it was evident that the majority, accounting for 73.5%, fell into the advanced stages of T3 and T4.

Survival analyses

Of the 119 patients, 92 (77.3%) were included in the survival analyses — either because they experienced a survival event (death, recurrence, or metastasis) at any point during follow-up, or because they completed the full five-year follow-up period without an event (Table 4; Fig. 1). The remaining 27 patients (22.7%) had not yet reached five years of follow-up and had not experienced an event; their outcome status was therefore indeterminate, and they were excluded from the survival analyses. Among the 92 patients included in the survival analyses, the median follow-up time was 54 months (range: 1–60 months). Among the 46 patients who developed recurrence, the median time to recurrence was 9.5 months (range: 1–55 months). Among patients without distant metastasis at initial diagnosis, distant metastasis subsequently developed in 12 patients, with a median time to distant metastasis of 25.5 months (range: 1–43 months).

When the most common variant squamous cell carcinoma and variants group compared with the remaining groups, no statistically significant difference was found in survival rates for OS, DFS, and DSS (For OS, the Bonferroni-adjusted p-values were 1.000, 0.590, 1.000, 1.000, and 1.000; for DFS, the Bonferroni-adjusted p-values were all 1.000; and for DSS, the Bonferroni-adjusted p-values were 1.000, 1.000, 0.875, 1.000, and 1.000).

Malignancies were also analyzed in two different subgroups: epithelial (scc and non-scc + minor salivary gland) and non-epithelial (hematolymphoid, NE, sarcomas). For epithelial tumors ($n = 57$, 62.0%), OS was 50.9%, DFS 42.1%, and DSS 73.7% of the cases. For non-epithelial tumors ($n = 35$, 38.0%), OS was 45.7%, DFS 42.9%, and DSS 54.3% of the cases. Although OS and DSS data showed better proportions in epithelial tumors, no significant difference was observed for OS, DFS, and DSS ($p > 0.05$ for all three).

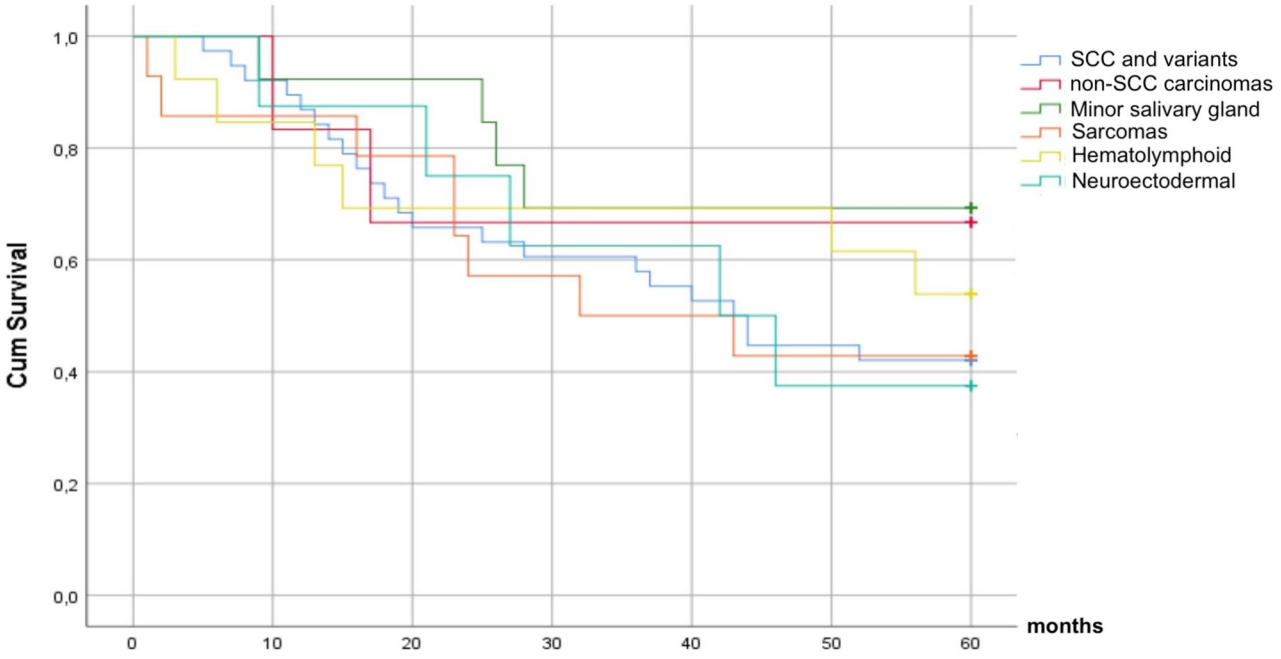


Fig. 1 Overall survival curves of tumors based on histopathological types

Table 5 Stage-dependent survival rates of epithelial tumors

Epithelial Tumors	Number	OS	DFS	DSS
Stage 1	6	%66,7	%66.7	%100
Stage 2	10	%80	%60.0	%90
Stage 3	17	%58,8	%52.9	%88,2
Stage 1,2,3	33	%66,7	%57.6	%90,39
Stage 4	24	%29,2	%20.8	%50
Whole Epithelial Tumors	57	%50,9	%42.1	%73,7

When evaluating the group of epithelial tumors according to their stages (Table 5), there was no statistical difference between Stage 1,2,3 in terms of OS, but Stage 4 was significantly worse than the others ($p = 0.002$). In terms of DFS, there were no statistical differences between stages 1, 2 and 3, but stage 4 was again significantly worse than the other three ($p = 0.002$). This pattern was repeated for DSS, with no difference between stages 1, 2 and 3 but stage 4 being again significantly poorer ($p < 0.001$).

In the non-squamous cell carcinomas group, the survival rates for OS, DFS, and DSS were 80.0% for adenocarcinomas. Unfortunately, the only patient diagnosed with ameloblastic carcinoma was lost due to his disease in the seventeenth month.

Out of the salivary gland cases that could be analyzed for survival, 8 (61.5%) were adenoid cystic carcinoma, 3 (23.1%) were mucoepidermoid carcinoma, 1 (7.7%) was oncocytic carcinoma, and 1 (7.7%) was clear cell solid salivary gland carcinoma. During the 60-month follow-up of ADCCs, no neck lymph node metastasis was detected. In the postoperative period, distant metastasis to the lung and bone, as well as local recurrence, were detected in two patients. Perineural invasion was observed in five patients, and lymphovascular invasion was detected in three patients. The 5-year survival rates of patients diagnosed with synonasal adenoid cystic carcinoma were 62.5% OS, 37.5% DFS, and 75.0% DSS.

A comparison was also made between carcinomas (scc and non-scc) and other tumors with survival rates of 44.5%, 38.6%, and 72.7%, respectively, for OS, DFS and DSS for carcinomas, and 52.1%, 45.8%, and 60.4% for non-carcinoma tumors. No significant difference was found between these groups ($p > 0.05$).

Among the four patients evaluated in the neuroectodermal tumor group with olfactory neuroblastoma, three were lost due to disease (OS, DFS, and DSS 25.0%). Of the three patients with relapsed malignant melanoma, one was alive, one was lost to disease, and one was lost due to non-disease (OS 33.3%, DFS 0.0%, DSS 66.7%). A patient diagnosed with Ewing Sarcoma/PNET remained relapse-free in the fifth year.

Patients diagnosed with lymphoma had survival rates of OS 45.5%, DFS 45.5%, and, DSS 54.5%.

Among the sarcoma cases, two patients diagnosed with chondrosarcoma and osteosarcoma were followed for 60 months without relapse. Of the four patients in the rhabdomyosarcoma group, two (50%) did not relapse, while two relapsed and died due to the disease. In our sarcoma cases included in the survival analysis, 5 (35.7%) developed distant metastases.

Two patients diagnosed with metastasis from primary to PNS, primary breast and lung, were lost within 5 years due to their disease.

Table 6 Survival rates by location

Localization	Number (Percent)	OS	DFS	DSS
Paranasal sinuses	59 (64.1%)	%44,1	%37.3	%61.0
Nasal cavity	33 (35.9%)	%57,6	%51.5	%75,8
All cases	92 (100.0%)	%48,9	%42.4	%66,3

All patients were divided into NC and PNSes according to their co-localization, and these two groups were compared in terms of survival rates (Table 6). NC Tumors tended to have a better prognosis compared to PNS Tumors, but there was no statistically significant difference between the two groups for OS, DSS or DFS (all $p > 0.05$).

Discussion

PNS and NC malignancies, which are relatively less common in the head and neck, constitute a unique category of tumors due to their variety and diverse symptoms. Unfortunately, misdiagnoses and delay rates are still high. These tumors typically manifest in individuals over the age of 50 to 60, with a male-to-female ratio of approximately 2:1 [6]. However, in the present study, we observed that the incidence of these tumors was most prevalent between the ages of 19 and 59, with an average age of 54.2 among our cases. The occurrence of these tumors at a younger age compared to other head and neck tumors, particularly between the ages of 19 and 59, can be attributed to the relatively higher prevalence of various tumor types other than squamous cell carcinoma (SCC) in this region. Moreover, these tumors seem to be relatively more common in younger individuals.

PNS and NC tumors are relatively more common among workers in the furniture, nickel, leather, and aluminum industries, where exposure to toxic inhalants is prevalent [7]. Conversely, smoking and alcohol consumption appear to have relatively less influence on the occurrence of these tumors. In the present study, smoking was observed more frequently, particularly in the group of carcinomas, compared to non-carcinoma tumors (67.5% vs. 37.3%). In the current city, the overall prevalence of active smokers was showed as 32.3%, and ex-smokers as 21.5% [8]. It may be assumed that smoking causes carcinomas more often. Interestingly, office workers in our study were generally not exposed to toxic inhalants, whereas those working outside the office had relatively higher exposure to such substances. Although there were industrial factory workers in the non-office worker group, no individuals employed in the wood or furniture sectors were identified as a risk factor, particularly concerning adenocarcinomas. However, in cases of squamous cell carcinoma and its variants, it was observed that approximately two-thirds of the patients were tobacco smokers and non-office workers. This suggests that patients who smoke and work outdoors with greater exposure to environmental factors and potential toxic inhalants may have a higher likelihood of developing squamous cell carcinoma.

In the present study, nasal symptoms were the most common, followed by oral and dental symptoms, and then facial symptoms. Notably, the second most frequent presenting symptom group in this study included patients presenting with symptoms solely related to the oral cavity and teeth. This suggests that nasal symptoms may not always be apparent, either due to their coexistence with other long-standing nasal symptoms or because they are habitual and have been chronically overlooked.

Squamous cell carcinoma emerged as the most common tumor type in the present study, with sarcomas being the second most common type, and minor salivary gland tumors being third most common. Although the proportion of tumor types, excepting squamous cell carcinoma were relatively similar, it is clear that non-squamous cell carcinoma tumors are common in the region. Specifically, in the case of sinonasal adenocarcinomas, previous studies have reported a prevalence rate ranging from 10% to 20%, designating it as the second most common tumor group [9,10]. However, the rate in the present study was only 6.1%. This discrepancy can be attributed to various factors, such as sectoral differences within the region and the decreased presence of the wood and leather sector. The overall survival rate observed in the present study (48.9%) falls within the range reported in major published series, albeit toward the lower end. Dulguerov et al. reported a 5-year survival rate of 40% among 220 patients with nasal and paranasal sinus carcinoma, noting substantial variation by histology and tumor stage [6]. A population-based SEER database analysis by Turner and Reh demonstrated an improvement in 5-year survival from 49.6% to 66.7% between 1973 and 2001 [9]. This temporal trend toward better outcomes at the population level is not fully reflected in our single-center cohort [9].

Primary methodological and clinical factors may account for this discrepancy. First, our cohort encompasses a broader histological spectrum than carcinoma-only series. Second, a substantial proportion of our patients presented at an advanced stage (73.5% T3/T4 in epithelial tumors). Third, limiting our survival analysis to patients with confirmed outcomes may preclude direct comparison with registry-based population data that benefit from more complete follow-up. These differences in cohort composition, staging distribution, and methodology complicate direct comparisons and warrant consideration when interpreting our findings.

Broader regional, temporal, and treatment-related variations may further explain differences between our survival outcomes and those reported elsewhere. Regional etiological factors—such as varying occupational

exposures (e.g., wood dust, leather processing, and industrial carcinogens), regulatory workplace health measures, and lifestyle habits like smoking and alcohol consumption—significantly influence incidence, histological distribution, and prognosis. Furthermore, recent domestic improvements in healthcare access, diagnostic nasal endoscopy, and specialist awareness have likely altered the stage distribution and case mix relative to older or geographically distinct cohorts. Finally, advances in multidisciplinary management—including refined surgical techniques, modern radiotherapy planning, and evolving systemic therapies—have improved outcomes in recently treated patients. Collectively, these interacting factors highlight why caution is needed when generalizing our results to other clinical settings.

Furthermore, the implementation of improved protective measures and increased awareness might have contributed to a decline in the occurrence of these tumors. Interestingly, no significant difference was observed when evaluating these patients based on their occupation as office workers or otherwise.

In the present study, neuroectodermal tumors mainly consisted of malignant melanoma and olfactory neuroblastoma, and survival rates were relatively low at only 25%, which is lower than expected. This can be attributed to the fact that the majority of cases were advanced, the surgical margin positivity was relatively high on endoscopic surgeries, and there were two pathological neck metastases in this group. While gender differences are generally not expected in malignant melanoma, it is noteworthy that all patients in our study were male, which is a different finding, although the numbers in this group were small [11].

Hematolymphoid tumors, although ranking third in frequency in some studies in the sinonasal tract, occurred at a rate of 11.8% and were the fourth most frequent in our study [12]. We observed lymphomas more often in the NC and ethmoid complex, contrary to some studies that reported these malignancies to be more common in the maxillary sinus [13].

Sarcomas, which account for 7% of tumors of the head and neck region, are primarily localized to the sinonasal region [14]. These tumors can also occur at relatively younger ages. In our study, one in three of our patients with sarcomas were under 18 years of age, resulting in an average age of 38.8 years in this group which was significantly lower than the other tumor groups. Unlike other regions, distant metastases were detected at a rate of approximately 3 to 1 in patients with sarcoma who completed the 5-year follow-up period, indicating a higher occurrence of distant recurrences.

For minor salivary gland tumors, our analysis revealed that adenoid cystic carcinomas constituted approximately 70% of the cases, whereas mucoepidermoid carcinomas, which are comparatively uncommon, accounted for about 18% of the cases but this was only three patients. Notably, the survival rates were found to be more favorable for mucoepidermoid carcinomas in comparison to adenoid cystic carcinomas. However, it is important to consider that this discrepancy can be attributed to the uneven distribution of cases and the fact that all mucoepidermoid carcinomas were detected in their early stages, rather than implying a more promising prognosis.

As expected, while stage 1, 2, and 3 tumors showed better survival rates, stage 4 tumors have significantly worse outcomes. Surgical treatments were effective for stages 1 to 3, leading to higher survival rates. However, in a significant proportion of stage 4 cases, the lack of surgical treatment leads to poorer outcome. In the present study, epithelial tumors tended to show better survival rates compared to non-epithelial tumors, but the difference was not significant. Therefore, with a multidisciplinary evaluation and appropriate treatment, it is possible to achieve similar survival rates in non-epithelial tumors, as in classic epithelial tumors.

In the current study, we evaluated the patients for the necessity of neck dissection depending on clinical and radiological findings, location and stage of the disease, and histopathology. We didn't encounter any patient who requires prophylactic neck dissection. Thus, we did not perform any prophylactic neck dissection, and the neck recurrence rate for these patients was as low as 3.7%. Furthermore, pathological N positivity was observed in more than half of the patients who were clinically or radiologically evaluated as positive and performed neck dissection.

When considering the limitations of our study, it is important to note that information regarding the profession, workplace, and potential exposure to toxic inhalants in the patients' residential areas was not readily available. Moreover, the fact that patients were employed in diverse industrial sectors and the relatively small number of patients per tumor groups hindered statistical analysis. Although the total number of patients was adequate for a general study of PNS and NC tumors, it was not possible to compare and statistically analyze additional parameters, such as the various locations of histopathological subtypes. Furthermore, the presence of distinct tumor types, even within the same group, exhibited varying degrees of malignancy, different staging criteria, and the absence of standardized or easily applicable staging systems for certain tumor types, which further limited the scope of comparisons in the study.

Combining stage groups across distinct staging systems (e.g., Ann Arbor for lymphomas, Kadish-Hyams for olfactory neuroblastoma, and AJCC TNM for carcinomas) into a 'Stage 1–3 vs. Stage 4' comparison is a

methodological simplification. While reporting survival separately within individual stages and histological subtypes partially mitigates this issue, heterogeneity in staging criteria requires cautious interpretation of the pooled data.

Small sample sizes in several histological subgroups further restrict statistical power and limit the generalizability of subgroup-specific findings; results for groups with fewer than 10 patients must be interpreted with particular caution. Additionally, incomplete exposure histories hindered our evaluation of how environmental and occupational factors affect tumor distribution and clinical behavior. Given that exposures can alter both disease aggressiveness and histological subtype, unmeasured confounding may have affected our survival analyses. Future multicenter studies with complete exposure data are required to clarify these subgroup-specific and exposure-related dynamics.

The histopathological diversity of tumors of the PNS and NC are high, and some of these tumors are exceedingly rare. This scarcity of cases presents a unique challenge in terms of diagnosing and treating patients afflicted with such tumors. Our study aimed to shed light on the distribution of patients in relation to demographic, histopathological, symptomatic, and etiological risk factors. In addition, we sought to provide valuable insights that can aid in predicting the prognosis for cases that may be encountered in the future. The aim of using survival analyses was to contribute to the field by uncovering unexpected findings that could potentially enhance our understanding of tumors in this particular region. Moreover, these tumors should be treated and monitored with the most up-to-date information and a comprehensive, multidisciplinary approach in order to ensure optimal patient outcomes.

Conclusions

Although outcomes vary considerably by histology and stage at presentation, our findings suggest that survival rates comparable to or exceeding historical benchmarks are achievable across most tumor types. Such outcomes depend on several key factors: prompt referral for nasal endoscopy in patients with persistent unilateral sinonasal symptoms to facilitate early diagnosis, accurate histological subtyping using disease-specific staging systems, individualized multidisciplinary treatment planning tailored to tumor extent, and diligent long-term surveillance given the risk of late recurrence. Prospective, multicenter studies employing standardized staging and follow-up protocols are required to validate these findings and define optimal management strategies for each histological subgroup.

Abbreviations

AJCC	American joint committee on cancer
CRT	Chemoradiotherapy
CT	Chemotherapy
DFS	Disease-free survival
DSS	Disease-specific survival
ENT	Ear, Nose, and Throat
FTSG	Full-thickness skin graft
IQR	Interquartile range
NC	Nasal cavity
OS	Overall survival
PNS	Paranasal sinuses
RT	Radiotherapy
SCC	Squamous cell carcinoma
STSG	Split-thickness skin graft
WHO	World health organization

Author contributions

E.E., H.M.D., and A.A.E. performed the data collection, conception, and drafting. B.Y.B. and S.B. performed the data collection, analysis of data, and review. M.O. and A.Y. performed the conception, design, drafting, and critically review. All the authors approved the final manuscript.

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Data availability

The datasets generated and/or analysed during the current study are not publicly available due to patient privacy and institutional restrictions but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki and relevant institutional ethical guidelines. The study protocol was reviewed and approved by the Kocaeli University Ethics Committee (approval number: KU-GOKAEK-2020/13.14-2020/13.14). The requirement for informed consent was waived by the Kocaeli University Ethics Committee due to the retrospective nature of the study.

Competing interests

The authors declare no competing interests.

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