

# Sinonasal adenocarcinoma: clinical outcomes and predictive factors

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**Abstract.** A retrospective study of 39 patients treated for sinonasal adenocarcinoma between 1995 and 2010 was performed. Epidemiological, clinical, histological, and therapeutic aspects of this series of patients were analyzed statistically and their impact in terms of overall and disease-free survival established using the Kaplan–Meier method. A search for prognostic factors was made using a log-rank test. The male to female sex ratio was 6.8 to 1. The average age at diagnosis was 65.7 years (range 40.2–85.6 years). An occupational risk factor (wood dust, leather) was found for 19 patients (48.7%). The median patient follow-up was 51.9 months (range 8–180 months). Tumours were classified as T1 in 20.5%, T2 in 25.6%, T3 in 23.1%, and T4 in 30.8% of cases. Disease-free survival rates at 1, 5, and 10 years were 87.9%, 44.8%, and 39.2%, respectively; overall survival rates were 86.1%, 72.2%, and 50.3%, respectively. Overall survival was correlated with tumour status (TNM, American Joint Committee on Cancer) ( $P = 0.004$ ). Surgery followed by radiotherapy improved overall survival ( $P = 0.012$ ) and disease-free survival ( $P = 0.028$ ) when compared to other treatment modalities. When compared to surgery alone, surgery followed by radiotherapy improved disease-free survival regardless of tumour stage ( $P = 0.049$ ).

Key words: sinus carcinoma; surgery; radiotherapy.

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Sinonasal adenocarcinomas (SADC) are rare tumours, even though they represent 35% to 75% of all sinonasal cancers.<sup>1,2</sup> They are associated with well-described occupational risk factors.<sup>1–4</sup>

Many multi-centre studies have been published aimed at improving the statistical results for these rare tumours.<sup>1–5</sup> While this strategy has helped improve the significance of the results obtained, it also runs the risk of blurring certain characteristics related to local specificities.

The aim of this study was to perform a statistical analysis of the epidemiological, clinical, histological, and therapeutic aspects of a series of patients with SADC and to determine their impact in terms of overall and disease-free survival.

## Materials and methods

This was a retrospective study of 39 consecutive patients treated for SADC at the Department of Otolaryngology – Head

and Neck Surgery, Aix-Marseille University, between July 1995 and July 2010. Epidemiological (age, sex), clinical (tumour side, tumour staging), radiological (tumour staging, involvement of key structures), and histological features, as well as treatment modalities and patient outcomes, were studied. To ensure the homogeneity of the series, the 2009 American Joint Committee on Cancer (AJCC) TNM classification was applied retrospectively to all patients.<sup>6</sup> The database was

created using FileMaker Pro (version 5; FileMaker, Inc., Santa Clara, CA, USA). Only patients treated at the authors' institution were included in this study.

Overall and disease-free survival rates were established using the Kaplan-Meier method. A search for prognostic factors was performed using the log-rank test. Multivariate analysis of all significant factors was performed by Cox proportional hazards model. All statistical tests were conducted using SPSS version 17.0 software (SPSS Inc., Chicago, IL, USA).

## Results

The study sample comprised five female (12.8%) and 34 male (87.2%) patients. Their average age at diagnosis was 65.7 years (range 40.2–85.6 years). The tumour was on the right side in 12 cases (30.8%), on the left in 13 cases (33.3%), and on the midline in 14 cases (35.9%). An occupational risk factor was found for 19 patients (48.7%): one patient had worked in the leather industry and 18 were woodworkers. The duration of wood dust exposure was reported in 14 cases; the mean duration of wood dust exposure was 21.8 years (range 4–38 years). No information was available on the degree of wood dust exposure. The mean duration of follow-up in this series was 51.9 months (range 8–180 months).

### Clinical presentation

Clinical data were adequate for all 39 patients (100%). Initial symptoms were unilateral in 82.1% of cases, the most frequent being nasal obstruction (71.9%) and epistaxis (53.1%). Other symptoms included rhinorrhoea (15.6%), eye symptoms (9.4%), pain (9.4%), skin damage (9.4%), and neurological signs (6.2%).

### Location, extension, and TNM staging

Radiological investigations included a sinus computed tomography (CT) scan for local staging and a neck and thorax CT scan for regional and remote staging in all cases. Sinus magnetic resonance imaging (MRI) completed this assessment in 37 patients (94.9%). Image analysis was used to study the primary tumour sites and their modes of propagation, and to define the TNM stage.<sup>6</sup> In all cases, tumour locations were the nasal cavity and the ethmoid sinus.

A breach of the key structures was evident in several cases, such as the skull

base in 11 patients (29.7%), orbit in eight (21.6%), dura mater in six (16.2%), brain in three (8.1%), sphenoid bone in three (8.1%), skin in three (8.1%), and maxillary sinus in one patient (2.7%).

The tumour was classified as T1 in eight cases (20.5%), T2 in 10 cases (25.6%), T3 in nine cases (23.1%), and T4 in 12 cases (30.8% of cases). The 12 tumours classified as T4 were divided into eight T4a (67%) and four T4b (33%). One patient (2.6%) was N+ at the time of initial diagnosis (staging T3N2c). One patient had metastatic pulmonary and liver lesions at the time of initial diagnosis (staging T4bN0M1).

### Histological data

Of the 39 cases of histologically proven SADC, the exact subtype was noted in 25 (64.1%). According to the Barnes classification,<sup>7,8</sup> the SADC was an intestinal type adenocarcinoma (ITAC) in 15 cases (60%), among which three cases were papillary ITAC (20% of the ITAC and 12% of the 25 SADC), five were tubular ITAC (33.3% of the ITAC and 20% of the 25 SADC), and seven were mucinous ITAC (46.7% of the ITAC and 28% of the 25 SADC). The SADC was a low-grade non-intestinal type adenocarcinoma (NITAC) in seven cases (28%) and high-grade NITAC in three cases (12%).

## Treatment

Five types of initial treatment were used: surgery alone in 10 cases (25.6%); surgery followed by radiotherapy in 20 cases (51.3%); concurrent chemoradiotherapy in six cases (15.4%), chemotherapy in one case (2.6%) (patient staged T4b presenting with carcinomatous meningitis), and supportive care in two cases (5.1%).

Thirty patients (76.9%) underwent surgery. The surgical approach was craniofacial in 11 cases, transfacial in six cases, degloving in six cases, and endoscopic in seven cases. The quality of excision margins was identified in all 30 cases (100%). All patients showed clear margins on final histological analysis.

Chemotherapy was performed using platinum salts with fluorouracil when the patient had no contraindication. Radiotherapy was performed using an unfractionated protocol. Doses delivered to the tumour site were 45 Gy or 50 Gy in the case of adjuvant (postoperative) radiotherapy and 70 Gy in the case of chemoradiotherapy.

### Recurrence and survival

The disease-free survival rates at 1, 5, and 10 years were 87.9%, 44.8%, and 39.2%, respectively (Fig. 1). The overall survival rates at 1, 5, and 10 years were 86.1%, 72.2%, and 50.3%, respectively (Fig. 2).

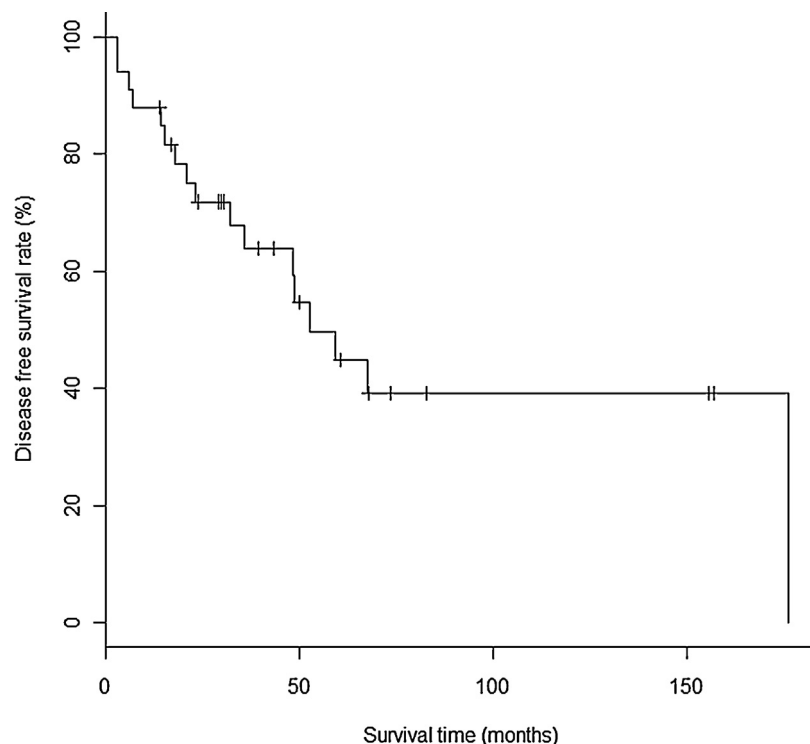


Fig. 1. Disease-free survival of sinonasal adenocarcinoma patients.

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