Romanian Journal of Rhinology, Vol. 1, No. 2, April - June 2011

LITERATURE REVIEW

# Decision for surgical approach in malignancies of the sinuses and skull base

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## INTRODUCTION

The literature of carcinoma of the sinonasal tract is difficult to interpret because of the low incidence, the wide variety of treatment, and the absence of a uniform staging system.

These malignancies are rare and heterogeneous diseases of the head and neck, representing 3% of all head and neck malignancies and 0.1 – 1% of all malignancies. The cases are reported in all races and the mean age at diagnosis is in sixth decade.

History and symptoms are non-specific, while the unilaterally symptoms could represent the first suggestion for a tumor.

The etiology of such types of malignancies is related to environmental exposures (e.g. adenocarcinoma due to wood dust or leather dust)[1]. The type of wood is a significant factor, with African mahogany being the most dangerous. Squamous cell carcinoma is related to aflatoxin, chromium, asbestos, nickel, mustard gas or polycyclic hydrocarbons. Nickel increases the risk of developing sinonasal squamos cell carcinoma 250 times.

80% of sinonasal tumors involve the maxillary sinus. Isolated sinonasal involvement, according to the literature[1] cohorts, is as it follows: maxillary sinus 25%, ethmoid 5 - 25%.

The nasal cavities are much more involved than the sphenoid or frontal sinuses. 70 – 90% of the cases display invasion through at least one wall of the presenting sinus.

Sinonasal malignancies tend to spread by local invasion. In general, these carcinomas tend to fill the sinus cavity before eroding its bony walls. Periosteum, perichondrium and dura seem to act as a temporary barrier and resist tumor expansion to some extent. Lymphatic spread to regional lymph nodes becomes apparent in 25-35% of patients with the submandibular and jugulodigastric nodes being the most frequently involved.

Depending on tumor extension – surgical, radio therapeutic or chemotherapeutic measures are appropriate in order to obtain good results in terms of survival rates and disease free survival rates.

As most patients have advanced disease at the time of presentation, surgery runs the risk of raising hopes unrealistically and of increasing morbidity. We will try to define according to the literature some criteria regarding the indications for surgical approach.

## DECISION FOR SURGERY

There should be usually a choice between treatment for cure or palliation. For those patients who are considered curable, most centers recommend a combined radiosurgical treatment.

Surgical approach could be external, endoscopic endonasal or combined. Endonasal surgery could also be divided in extracranial, extradural, extended intracranial and extradural or combined extra and intradural resection.

Another important factor in recommending the surgical approach is the surgical team skills, in order to prevent or manage complications as intraorbital hematoma, lachrymal pathways, CSF leaks, major bleeding.

The key principle of the surgical procedure is considered by many authors the concept of choosing the best pathway to the pathology. Depending on the localization and extension of the tumor to the skull base or intracranial, the best pathway to the pathology is shown in Figure 1.

The most important question is if we do have significant prognostic factors in deciding surgery for the sinonasal and skull base malignancies. Reviewing the literature, we can easily observe that these factors vary among studies because there are reported studies with a small number of patients, there are different pathologies, and the data differ in terms of surgical technique and overall management.

Anyway, we can speak about **major predictors of recurrence**, such as: tumor grade, orbital, sphenoid sinus or transdural involvement. Clival and nasopharyngeal

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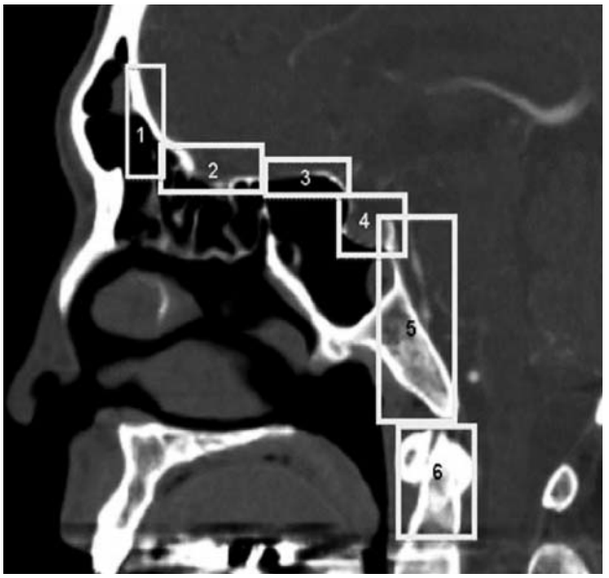


**Figure 1** Lateral CT scan showing the best way to plan the surgical approach according to the localization of the disease.

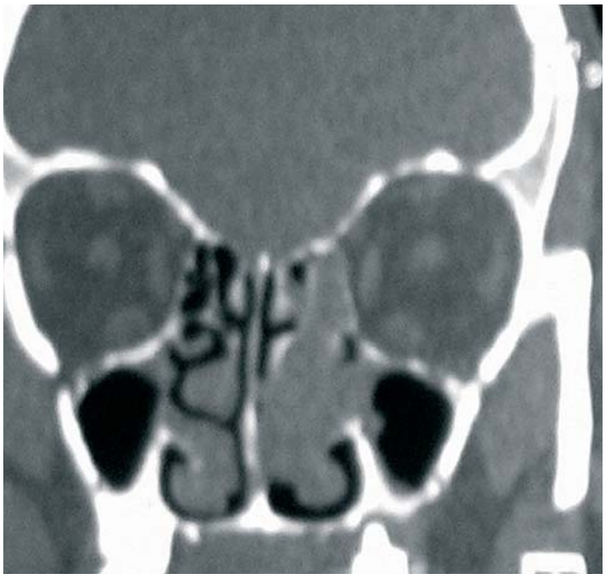

**Figure 2** Squamos cell carcinoma – endoscopic resection then chemoradiation

involvement is usually not a limiting factor.

There are some **critical structures** - the brain and dura seem to be the most important, while the aim of the surgery should be to obtain a good cleavage plain between the tumor and the frontal lobe.

**The principal limiting factor** is the presence of the tumor in the cavernous sinus and infratemporal fossa (pterygoid plates). The **most serious situation,** described by a lot of surgeons, is the infiltration into the wall of the ICA at the skull base (cavernous sinus).

According to McCaffrey et al[2], in a group of 54 patients with malignant anterior cranial fossa tumors, they found out that only the tumor grade and orbital involvement were independent variables associated with decreased survival.

Distant metastasis always indicate a bad prognosis and, by definition, these patients are incurable. Involvement of the facial skin is not a contraindication to treatment, because the involved area is excised and then repaired with rotation or free flaps.

In terms of external vs endoscopic approach, the outcomes after endoscopic procedures are **at least equal** to standard external approaches (excellent functional terms and significantly better overall QoL)[3]. But there are a lot of limitations due to the anatomical spread of the tumor. Of course that multidisciplinary teams with special skills and training could make endoscopic surgery beeing rather radical (bone and even dura of the anterior skull base can be resected as can the periorbit, and all structures reconstructed in the same session). This is, anyway, the exception that proves the rule according to which endoscopic surgery should be reserved for special selected cases, for well trained teams after a correct and realistic examination of the patient history, imaging, endoscopy and histhopathologic features.

One study compared the outcome of traditional craniofacial resection (tCFR) with endoscopic or endoscopic-assisted resection in 25 patients with anterior skull base malignancies[4]. Both groups had similar tumor extent as determined by anatomical subsite involvement. There was no statistical difference in survival or recurrence between the 2 groups. Similarly, there was no statistically significant difference in operative time, blood loss, hospital or ICU stay, although the trend favored the endoscopic group.

Regarding the resection type in sinonasal malignancies, there are no published data suggesting that *en bloc resection* is better than *piecemeal*, with the stated goal of complete tumor removal. There are experienced surgical teams that prefer in the majority of their series the endoscopic procedures. In a 10-year retrospective analysis *Nicolai et al*[5] evaluated 184 patients with nasoethmoidal malignancies possibly involving the adjacent skull base. From these patients, 134 were treated with an exclusive endoscopic approach, while 50 were treated with a cranioendoscopic approach.

Despite these encouraging results, many surgeons are doubtful about using endoscopy for sinonasal malignancies. All these authors support *en bloc* surgery using open procedures.

*Paolo Castelnuovo et al.*[6] established the major ex-

clusion criteria for the endoscopic cranio facial resection as it follows:

1. Tumors involving the lacrimal tract,
2. Tumor infiltration of the hard palate,
3. Tumors that involve the posterior wall of the sphenoid sinus,

Tumor invasion of all but the medial wall of the maxillary sinus.

Surgical planning should include the assessment of bony and soft tissue structures to be included for en bloc resection. Approach must provide adequate exposure, while preserving function and cosmetic integrity are advocated whenever possible. Repair should include planned prosthetics or free tissue transfer when necessary (e.g. lower maxilla – fibula oseocutaneous, orbitozygomatic support – scapula osteocutaneous, iliac crest osteomyocutaneous flap for additional bone/bulk).

Despite these advanced rehabilitation procedures, care should be taken in order to avoid ***"covering recurrent disease"!***

Tumor volume was related to the oncologic status of surgical margins, with high volume tumors nearly twice as likely to have positive margins. Furthermore, margin status appears to be prognostically relevant. Series from worldwide literature are reporting interesting results depending on the surgical margins status and of course the histhologic type of the malignancy. Both of these parameters should be considered prognostic factors.

Series of surgical patients with adenoid cystic carcinoma revealed that 63.3% had positive microscopic margins despite aggressive surgery, including maxillectomy, orbital exenteration and craniofacial resection. The authors found some factors leading to positive margins including skull base and major nerves proximity, and the tumor's tendency to spread perineurally. Howard and Lund[7] reported histologic evidence of an embolic pattern of perineural spread in paranasal sinus adenoid cystic carcinoma.

Series of other studies[8] state that clear margins might correlate with better local control but not with better survival!

There are different staging systems in use, except the TNM which is divided for maxillary, ethmoid sinus or nasal cavity. Kadish[9] staging system with Morita's modification is also very useful for the treatment decision.

**Stage Characteristic**

- **A.** Limited to nasal cavity
- **B.** Involving nasal cavity and sinuses
- **C.** Extension beyond nasal and paranasal sinuses cavities
- **D.** Tumor with metastasis to cervical nodes or distant sites

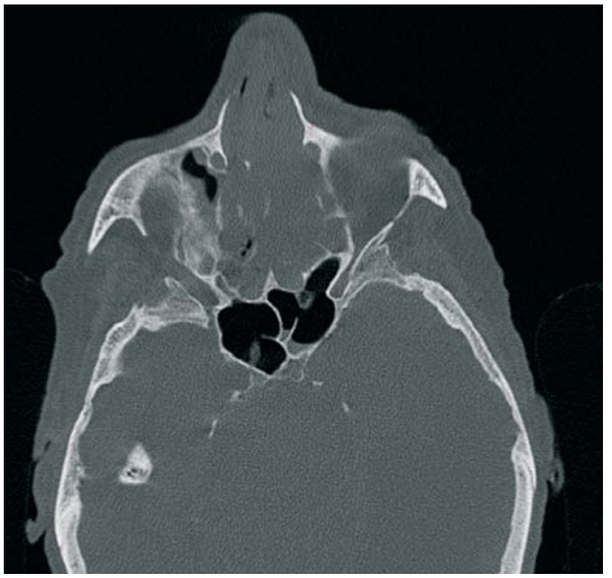

**Figure 3** Adenoid cystic carcinoma, intestinal type; endoscopic resection followed by chemoradiation

Defining the role of and indications for adjunctive therapy in anterior skull base malignancies has been a frustrating task. Standardized, evidence-based adjunctive therapy protocols are lacking. Also, advances in radiation planning, delivery and dosing are not reflected in current literature of skull base tumors. Nonetheless, patients in most studies do receive some form of adjunctive therapy, typically neoadjuvant or adjuvant radiotherapy, sometimes combined with chemotherapy.

Depending on the type and extent of the tumor, surgical, radiotherapeutic or chemotherapeutic measures are appropriate. In surgery, the main goal is complete removal of the tumor, the free margins, successful management of the complications and the aesthetic rehabilitation if extended resections were necessary. Different protocols are recommended by different centers[10]. Correct indications regarding the treatment should take in account the fact that there is no data in the literature showing statistically significant difference in the series in **overall survival rates** between patients who were treated with surgery plus adjuvant radiotherapy and those treated with surgery alone. The issue as to whether radiation is more effective before or after surgery remains controversial. Effectiveness of preoperative radiation is similar to that of postoperative radiation. Type of malignancy (e.g.-adenoid cystic carcinoma is considered to be a radiosensitive but not radio curable tumor) seems to be one of the most important decisional factors in choosing the treatment planning.

According to Chen et al[11], in a retrospective five decades study regarding the radiotherapy results and

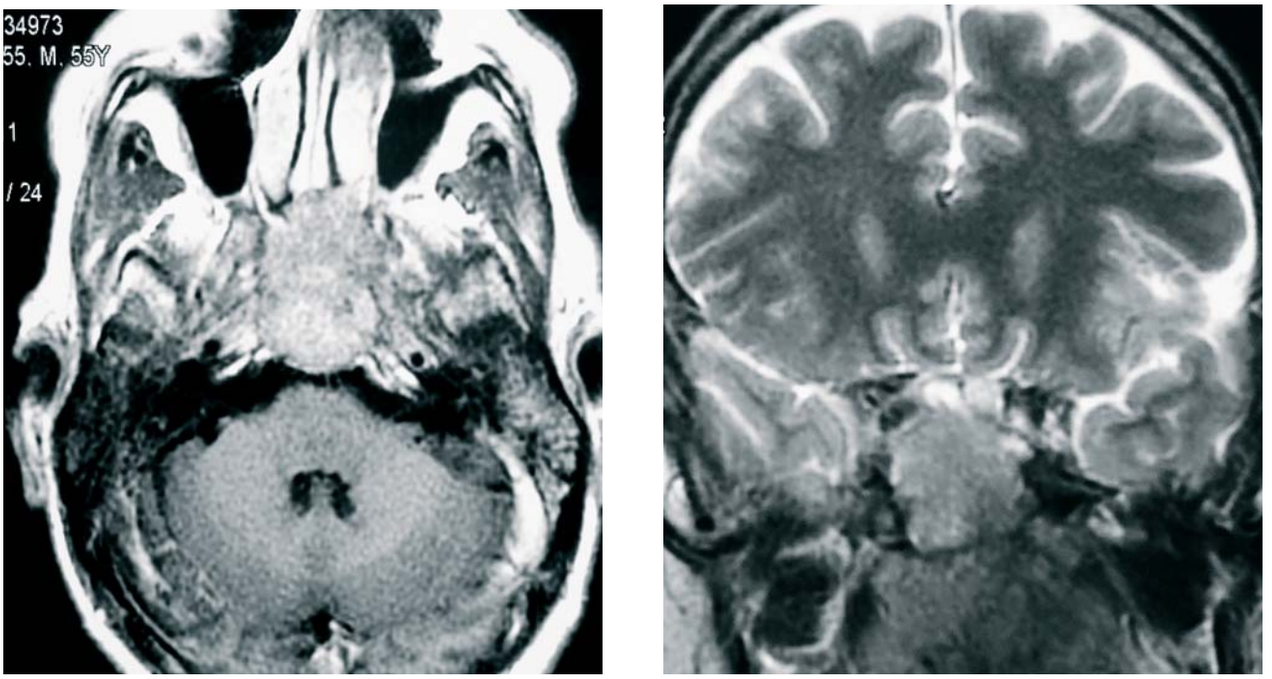


**Figure 4** Squamos cell carcinoma of the skull base and rhinopharynx, suitable for combined treatment radio and chemotherapy

outcomes, no improvements in disease control or overall survival for patients treated over time were registered. On the other hand, the incidence of complications has significantly declined and an improved therapeutic ratio for patients with carcinomas of the paranasal sinuses and nasal cavity were reported.

In a squamos cell carcinoma group[12], the five-years local control was 65% with combination of radiotherapy and debulking surgery, compared with 47% with radiotherapy alone, *but this difference was not statistically significant (p = 0.58)!!!*

However, combination treatment gave significantly better 5-year overall survival (OS) (60% vs. 9%; p = 0.001) and 5-year disease-free survival (DFS) (53% vs. 6%; p < 0. 0001).

Debulking surgery of paranasal sinus malignancies followed by high-dose radiotherapy to the involved sites was associated with better survival and (although not statistically significant) local control.

Other protocols describe the chemoradiation vs or together with surgery. For example, in Sakai et al.[13], the 5-year survival rates for series of more than 780 patients with malignancies of the paranasal sinuses and skull base (since 1957), who received 5000 cGy, continuous intrarterial 5-FU followed by

Caldwell-Luc type approaches, improved from 20% to 54%.

According to Nibu et al.[14], in case of patients with squamos cell carcinoma of the maxillary sinus, who received 3000 – 4000 cGy preoperatively, concomitant intra-arterial chemotherapy and again 3000 – 4000 cGy post-operatively, the 5-year survival rates were 86% in T3 patients and 67% in T4 cases.

Chemotherapy does not currently have a role in treatment of adenoid cystic carcinoma. Although no scientific studies specifically address neutron beam radiotherapy for adenoid cystic carcinoma of the sinonasal region, studies involving this hystologic type of cancer in other areas of the head and neck have shown improved local control rates over traditional radiation. No overall survival benefit has been shown in large series of patients worldwide. Recurrence is common, occurring in up to 55% of cases. Overall disease-specific 5-year survival rates were respectively 63% and 70% in the MD Anderson Cancer Center experience[15].-

Many retrospective series have reported better results with surgery followed by radiotherapy in resectable disease. New radiotherapeutic techniques have been recently evaluated in these tumors. Roa et al.[16], using postoperative three-dimensional conformal radiotherapy alone, achieved a 3-year local control and overall survival rates of 32%.

Padovani et al.[17], in 25 patients with local advanced maxillary or ethmoid sinus carcinoma treated with postoperative three-dimensional conformal radiotherapy, reported a 2-year overall survival of 47%. Duthoy *et al.*[18], in 39 patients treated with intensity-modulated photon radiotherapy in a postoperative setting, repor-

ted 4-year local control and survival rates of 68% and 59%, respectively.

Another important factor is the presence of metastasis in the cervical lymph nodes at the moment of diagnostic. An average of 20% that represent a relatively low incidence is reported in the literature. Neck dissection in paranasal sinuses cancer cases could be diagnostic and therapeutic.

According to Rinaldo et al., when cervical node disease is present, neck dissection is indicated. The type of dissection should be as aggressive as possible.

In some cases, individual consideration for radiating retropharyngeal and parapharyngeal lymph nodes is cited in the literature. Neck irradiation is another option.

## CONCLUSIONS

Most paranasal sinuses and skull base malignant tumors present at an advanced stage require aggressive multimodality therapy.

The treatment should be individualized according to prognostic factors, histology, imaging, surgical team's skills and complementary options like radiation therapy or chemotherapy.

We have to consider primary and secondary nodal metastasis in advanced disease and to include it in the therapeutic planning.

Treatment options are various, the team decision is mandatory and it has to be aware of comparative literature when determining evidence-based treatment plan.

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