ORIGINAL ARTICLE

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ENDOSCOPIC ENDONASAL RESECTION OF ADVANCED STAGE T3/T4 SINONASAL MALIGNANCIES INVOLVING SKULL BASE: MONOCENTRIC SINGLE-SURGEON STUDY (2020-2024)

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Abstract. Objective: *This study aims to evaluate the outcomes of endoscopic endonasal resection in patients with advanced-stage T3/T4 sinonasal malignancies involving the skull base, analyzing surgical efficacy, challenges, and implications for future clinical practice.* ***Materials and Methods:*** *A retrospective analysis was conducted on a monocentric single-surgeon cohort of 16 patients (mean age 60.7 ± 10.5 years) diagnosed with T3/T4 sinonasal malignancies affecting subsites of the skull-base region between 2020 and 2024. All the patients underwent primary radical endoscopic endonasal resection at the Department of ENT, Head & Neck Surgery, University Hospital "Tsaritsa Ioanna – ISUL", Medical University – Sofia, followed by adjuvant radiotherapy.* ***Results:*** *The cohort consisted of predominantly male patients (56.25%), with squamous cell carcinoma being the most common histological type (81.25%). Outcomes indicated a recurrence-free survival rate of 81.3% at a median follow-up of 30 months. Intraoperative findings revealed complexities in distinguishable tumor invasion, especially concerning critical anatomical structures, necessitating meticulous surgical techniques.* ***Conclusions:*** *Endoscopic endonasal resection demonstrates potential efficacy in managing advanced sinonasal malignancies, with a favorable recurrence-free survival rate underscoring its role as a viable surgical option. The study emphasizes the importance of individualized treatment strategies and the need for multidisciplinary collaboration to optimize patient care in this challenging clinical scenario.*

Key words: *skull base endoscopic surgery, squamous cell carcinoma, internal carotid artery, dura mater, recurrence-free survival*

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INTRODUCTION

Sinonasal malignancies are a rare heterogeneous group of head and neck neoplasms, with an incidence of approximately 0.5 per 100,000 persons per year [1]. This rarity is accompanied by a wide array of histopathological types, including, but not limited to, squamous cell carcinoma, adenocarcinoma, and sinonasal undifferentiated carcinoma. The diversity of the sinonasal tract, which encompasses multiple tissue types and cellular origins, contributes to the complex histological landscape of these malignancies. Consequently, this results in a varied molecular background, which influences both the behavior of these tumors and their response to therapeutic interventions.

Over the past few decades, advancements in endoscopic surgical techniques have ushered in a new era for the management of sinonasal tumors. The rise of minimally invasive approaches has not only enhanced surgical precision but also improved patient recovery times and minimized complications. Coupled with the emergence of new adjuvant therapies – such as targeted therapies and immunotherapy – there has been a gradual increase in survival rates among patients diagnosed with sinonasal malignancies. The literature reflects this trend, indicating stable outcomes and significant improvements in the disease management paradigms [2].

However, the complex and intricate anatomy of the skull base presents a distinct set of surgical and oncological challenges for each individual patient. Variability in tumor location, extent of invasion, and proximity to critical neurovascular structures necessitates a highly individualized approach to treatment [3]. Therefore, both surgical and adjuvant therapies must be custom-tailored according to the specificities of each case, taking into consideration factors such as tumor size, histological subtype, and the patient's overall health status.

Moreover, there is a pressing need for multidisciplinary collaboration in the management of these challenging cases. Oncologists, neurosurgeons, otolaryngologists, and radiologists must work together to construct a comprehensive treatment plan that addresses the multifaceted aspects of sinonasal malignancies [4]. This integrative approach not only aims to maximize the therapeutic efficacy but also seeks to optimize the quality of life for patients as they navigate their treatment journey.

In this context, our study aims to explore the outcomes of endoscopic endonasal resection for advanced-stage T3/T4 sinonasal malignancies involving the skull base. By analyzing a monocentric cohort treated by a single surgeon from 2020 to 2024, we endeavor to provide insights into the effectiveness of this surgical approach, the associated challenges, and the implications for future clinical practice.

MATERIALS AND METHODS

Study Design and Treatment Protocols

A total of sixteen patients (mean age at diagnosis 60.7 ± 10.5 years) with pathologically verified primary sinonasal malignancies were analyzed in the current study. The main inclusion criteria were: 1) advanced stage T3/T4 sinonasal malignancy and 2) invasion of the skull base structures. The enrolled cohort is a single-surgeon consecutive series. The diagnosis was made based on current standards. All the patients were admitted and surgically treated at the Department of ENT, Head & Neck Surgery, Medical University – Sofia, during the period 2020-2024, as they underwent primary radical endoscopic endonasal tumor resection. All the patients, excluding one, underwent postoperative radiotherapy, according to the protocol.

Statistical Analysis

SPSS software v.23.0 for Windows (IBM SPSS, NY, USA) and GraphPad Prism software were used for data analysis. The Kolmogorov–Smirnov test for normality and the Wilcoxon test were used as appropriate. Spearman's correlation test was used to analyze the relationship between two continuous variables. Statistical significance was defined as a two-tailed p-value <0.05.

RESULTS

Clinicopathological Characteristics of the Studied Cohort

This study encompassed a cohort of 16 patients who underwent endoscopic surgery for sinonasal malignancies affecting the skull base. The mean age of patients in this cohort was 60.7 years ± 10.5, with ages ranging from 41 to 78 years (Table 1). This indicates that the population encompasses middle-aged and older adults, which is consistent with the typical age range for sinonasal malignancies. In terms of sex distribution, there were 9 men (56.25%) and 7 women (43.75%), suggesting a slight male predominance among the patients in this group.

Tumor staging according to the pT classification revealed that 6 patients (37.5%) presented with pT3 tumors, while a more advanced stage, pT4a and pT4b, was observed in 10 patients (62.5%) (Fig. 1).

In our analysis of histopathological findings, squamous cell carcinoma was the predominant type observed, accounting for 81.25% (13 cases) of the total samples examined. This was followed by adenoid cystic carcinoma, which comprised 12.5% (2 cases) of the findings. Rhabdomyosarcoma was the least represented, with only 6.25% (1 case) of the total diagnoses.

Table 1. Clinicopathological characteristics of the patients enrolled in the study

Characteristics	Number of patients	Percentage
Age	60.7 ± 10.5 (mean), 41-78	N/A
Gender	9 males, 7 females	56,25% vs 43,74%
T-stage		
pT3	6	37,5%
pT4a & pT4b	10	62,5%
Primary site		
Sphenoid	5	31,25%
Ethmoid	9	56,25%
Frontal	2	12,5%
Histopahology		
Squamous cell carcinoma	13	81,25%
Adenoid cystic carcinoma	2	12,5%
Rhabdomyosarcoma	1	6,25%
Margins		
	R0	85%
	R1	25%
Radiotherapy (postop)		
Postoperative radiotherapy	14	87,5%
None	2	12,5%
Ophthalmological symptoms		
Dyplopia	4	25%
Vision reduction/loss	2	12,5%
Invasion of specific skull base subsites		
Erosion/Invasion of the internal carotid artery canal	3	18,75%
Erosion/Invasion of the cavernous sinus	2	12,5%
Erosion/Invasion (including minimal) of the dura	10	62,5%
Erosion/Invasion of the optic nerve/chiasma	4	25%

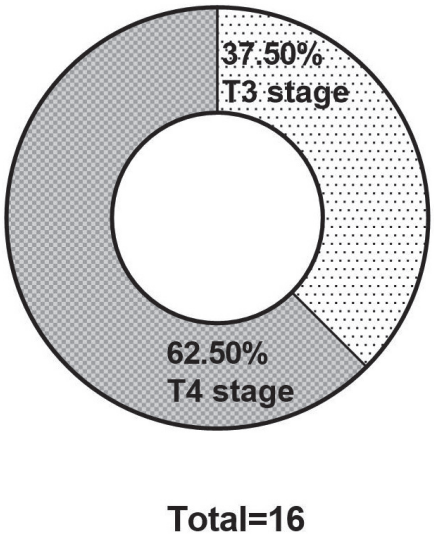


Fig. 1. T-stage distribution among the cohort of patients enrolled in the study

The primary sites of the sinonasal malignancies were predominantly located in the ethmoid region, with 9 patients (56.25%) having tumors originating there. The sphenoid sinus was involved in 5 patients (31.25%), while only 2 patients (12.5%) had tumors originating from the frontal sinus. Erosion or invasion of critical skull base subsites was assessed, revealing that 10 patients (62.5%) had some degree of invasion of the dura mater. Additionally, 3 patients (18.75%) showed erosion/invasion of the internal carotid artery canal, while 2 patients (12.5%) were found to have invasion of the cavernous sinus. Furthermore, 4 patients (25%) exhibited erosion/invasion of the optic nerve or chiasma. In those cases, tumor tissue was invading the adjacent tissue of the optic nerve/cavernous sinus/carotid but no macroscopic invasion was evident after denuding those. R-status was marked as R1 (positive) in cases where the closest layer of tissue adjacent to vital structures was pathohistologically positive. R1-status correlated with higher levels of recurrence as expected (chi-square, $p<0.05$).

Ophthalmological symptoms were noted in this cohort, with 4 patients (25%) experiencing diplopia and 2 patients (12.5%) reporting vision reduction or loss. These symptoms may indicate the involvement of adjacent structures due to the tumor or its treatment.

Postoperatively, the majority of patients (14, or 87.5%) received adjuvant radiotherapy, underscoring the importance of comprehensive treatment strategies in managing sinonasal malignancies. Only 2 patients (12.5%) did not receive postoperative radiotherapy.

Recurrence-free Survival of the Studied Cohort

In our cohort, the evaluation of survival outcomes reveals a recurrence-free survival rate of 81.3%, underscoring the potential efficacy of endoscopic endonasal resection in managing advanced-stage T3/T4 sinonasal malignancies (Fig. 2). With a median follow-up period of 30 months, these findings illustrate that a significant proportion of patients experience prolonged disease-free intervals following surgical intervention. This level of recurrence-free survival is particularly noteworthy given the aggressive nature of T3/T4 tumors and highlights the critical role of meticulous surgical technique and comprehensive postoperative care in this patient population. Moreover, these results suggest that endoscopic endonasal approaches might provide a viable alternative to more invasive surgical strategies, contributing to favorable long-term outcomes.

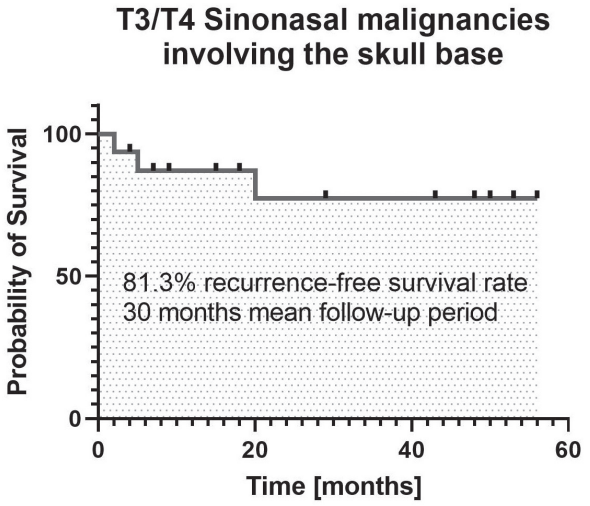


Fig. 2. Kaplan–Maier recurrence-free survival curve, mean follow-up period of 30 months

Intraoperative Specificities

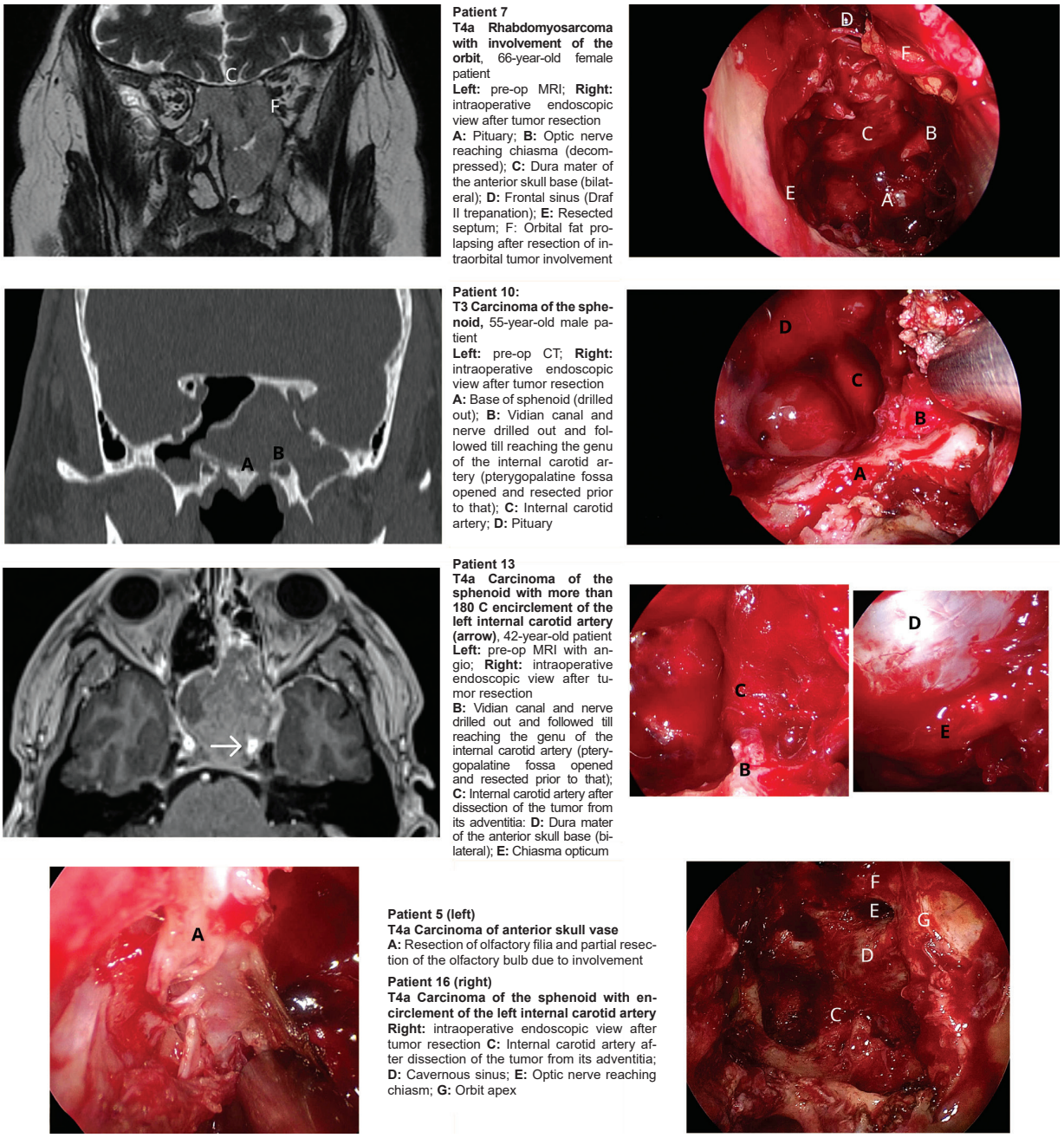
Most of the sinonasal malignancies (especially in the advanced stage), when evaluated with MRI/CT modalities, seem to invade/erode a great number of subsites, which are neighboring the tumor mass. In contrast, intraoperatively, an experienced surgeon would recognize that only part of those structures would be invaded in reality, and the rest are only in contact with the tumor mass. Exactly this specific characteristic should be very precisely evaluated during surgery - after the primary debulking of the tumor mass, attention should be devoted to these precise locations, and resection/drilling of those should be performed meticulously. An example is the drilled-out floor of the sphenoid reaching almost the first genu of the internal carotid artery (ICA) (Fig. 3, patient 10, A to C).

Certain areas of the skull base require highest level of attention and surgical precision since possible complications could be dire [5]. Maybe the most significant anatomical structure to be respected is the internal carotid artery. Cases, where erosion and especially encapsulation of the artery from the tumor tissue are evident, should be classified as very high-risk. An example of such case is the patient 13 illustrated in Figure 3 – encirclement of the ICA of more than 180 degrees is evident. Intraoperative finding suggested not only erosion of the bony canal but also of the soft tissues around the artery. That necessitated meticulous dissection of the adventitia of the ICA which always carries a high possibility of laceration despite using even the most precautious surgical technique. Blunt techniques and precise dissection with fine grasping forceps with four-hand technique were used. Covering the denuded internal carotid with a Hadad flap was not possible due to resection of the feeding branches, but no post-radiotherapy complications occurred.

Microscopic dural involvement and the indications for its resection is a topic with no definitive answer in the literature. Firstly, it is genuinely not a straightforward process to assess with certainty the chances of a microscopic invasion of the dura. On the other hand, it has been found that overzealous dural resection leads to a very high percentage of postoperative complications with no evidence of significant survival gains. In Figure 3, the intraoperative snapshots of patients 7 and 13 illustrate large areas of denuded dura with no visible infiltration.

DISCUSSION

Rawal et al. made a very thorough review of results in sinonasal malignancies and their aggregate and pooled analysis of all the included studies showed a 2-year follow-up overall survival rate of 85.8-87.5% [6]. This combined meta-analysis includes data from patients with malignancies in all stages (T1-T4), overall, but not recurrence-free survival and all subsites of the nasal cavity and sinuses. A very well-built population-based Danish trial showed a 56% 5-year overall survival rate [7]. The largest study on endoscopically treated sinonasal malignancies – the MUSES (Multi-institutional collaborative Study on Endoscopically treated Sinonasal cancers) encapsulates 1360 patients and reports 3-year recurrence-free survival rates ranging between 68.2-74.4% [8]. In that respect, our results show the encouraging 81.3% recurrence-free survival rate with a mean follow-up period of 2 years and a half among a selection of patients only



Patient 7
T4a Rhabdomyosarcoma with involvement of the orbit, 66-year-old female patient
Left: pre-op MRI; **Right:** intraoperative endoscopic view after tumor resection
A: Pituary; **B:** Optic nerve reaching chiasma (decompressed); **C:** Dura mater of the anterior skull base (bilateral); **D:** Frontal sinus (Draf II trepanation); **E:** Resected septum; F: Orbital fat prolapsing after resection of intraorbital tumor involvement

Patient 10:
T3 Carcinoma of the sphenoid, 55-year-old male patient
Left: pre-op CT; **Right:** intraoperative endoscopic view after tumor resection
A: Base of sphenoid (drilled out); **B:** Vidian canal and nerve drilled out and followed till reaching the genu of the internal carotid artery (pterygopalatine fossa opened and resected prior to that); **C:** Internal carotid artery; **D:** Pituary

Patient 13
T4a Carcinoma of the sphenoid with more than 180 C encirclement of the left internal carotid artery (arrow), 42-year-old patient
Left: pre-op MRI with angio; **Right:** intraoperative endoscopic view after tumor resection
B: Vidian canal and nerve drilled out and followed till reaching the genu of the internal carotid artery (pterygopalatine fossa opened and resected prior to that); **C:** Internal carotid artery after dissection of the tumor from its adventitia: **D:** Dura mater of the anterior skull base (bilateral); **E:** Chiasma opticum

Patient 5 (left)
T4a Carcinoma of anterior skull vase
A: Resection of olfactory filia and partial resection of the olfactory bulb due to involvement

Patient 16 (right)
T4a Carcinoma of the sphenoid with encirclement of the left internal carotid artery
Right: intraoperative endoscopic view after tumor resection **C:** Internal carotid artery after dissection of the tumor from its adventitia; **D:** Cavernous sinus; **E:** Optic nerve reaching chiasm; **G:** Orbit apex

Fig. 3. A representative sample of patients from the studied cohort exhibited with illustrative Computed Tomography (CT) angiography /Magnetic Resonance (MR) angiography slice images and intraoperative endoscopic snapshots of the resected skull-base region

in advanced stage (T3/T4), in whom malignancies invade directly structures of the skull base.

An important aspect is the preoperative assessment in terms of operability, levels of intraoperative risks and approach vectors. This assessment should always be based on two pillars: 1) the extent of the tumor and its proximity/adjacency to vital structures of the skull base, 2) the preexisting anatomical circumstances, especially the degree of pneumatization of the sinuses. Variances of the latter characteristics are well described in a paper of Bechev K et al. [9]. Additionally, histology of the tumor could impact the selection of treatment strategies, since some malignant tumors could be also well suited for neo-adjuvant therapy [10] or benign lesions could mimic cancerous neoplasms [11].

Despite the rarity of those pathologies, possible shortcoming of our study is the small number of patients along with the lack of melanoma cases in the cohort.

CONCLUSIONS

Our study highlights the effectiveness of endoscopic endonasal resection for managing advanced-stage T3/T4 sinonasal malignancies involving the skull base. With an encouraging recurrence-free survival rate, the results indicate that this minimally invasive surgical approach can yield favorable long-term outcomes in Bulgarian population. While our findings are promising, the limitations inherent in the small cohort size and the absence of certain malignancy types indicate the need for further research to validate these results and refine treatment protocols in the management of sinonasal tumors. Future studies should aim to encompass larger, more diverse populations to establish more robust conclusions regarding best practices in the surgical management of sinonasal malignancies.

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Data Availability Statement: *Raw data were generated at the Medical University – Sofia. Derived data supporting the findings of this study are available from the corresponding author (TP) on request.*

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