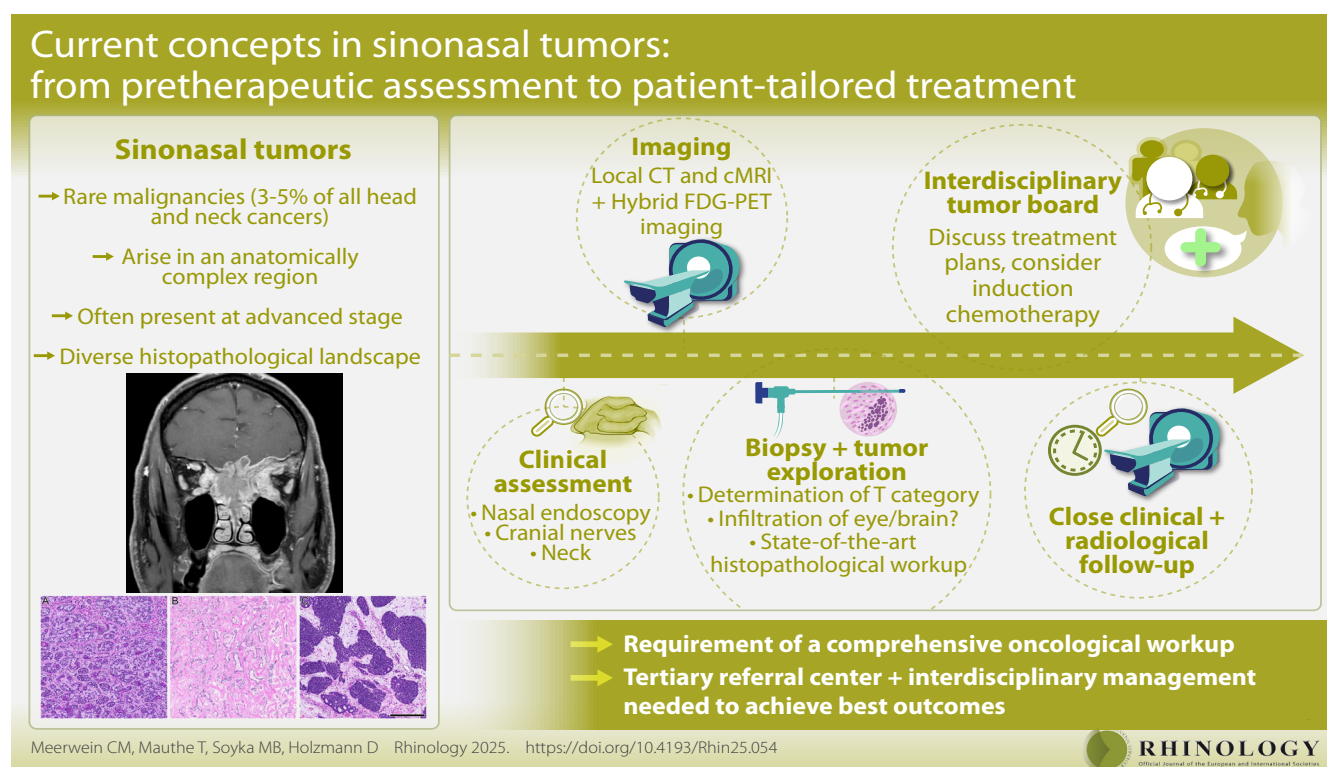


Current concepts in sinonasal tumors: from pretherapeutic assessment to patient-tailored treatment

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Abstract

Background: Managing sinonasal malignancies requires a thorough oncological assessment and interdisciplinary collaboration. Patients often present at an advanced tumor stage with a delay in diagnosis. With the recent advancements in imaging techniques along with the growth in molecular testing knowledge, the landscape of these tumors has become increasingly diverse. The pretreatment assessment must include information gathered from radiological and pathological evaluations, as well as intraoperative exploration of the tumors. Only a comprehensive approach allows a personalized treatment plan.

Methodology: This narrative review synthesizes current evidence, encompassing pretherapeutic evaluations and the development of individualized treatment protocols.

Results: Multimodal treatment strategies, including surgical resection, radiotherapy (RT), chemotherapy, and immunotherapy (for sinonasal mucosal melanoma) need to be tailored based on tumor histology, stage, and patient-specific factors. Endoscopic surgical approaches demonstrated oncologic outcomes comparable to traditional open techniques, with reduced perioperative morbidity. Neoadjuvant therapies facilitated improved local control and organ preservation in advanced-stage tumors.

Conclusion: Ongoing advancements in imaging, surgical interventions, as well as (neo-)adjuvant therapies have significantly improved the prognostic landscape of sinonasal malignancies. A multidisciplinary, personalized treatment approach remains pivotal in optimizing patient outcomes.

Key words: sinonasal neoplasms, multimodal therapy, endoscopic surgical procedures, radiotherapy, immunotherapy

Epidemiology and risk factors

Sinonasal malignancies represent 3–5% of all head and neck cancers, with a relatively stable incidence over time of approximately 0.6 cases per 100,000 population per year and a male-to-female ratio of 1.8:1.0^(1,2). The most common histological entities are sinonasal squamous cell carcinoma (SCC), sinonasal adenocarcinoma, sinonasal mucosal melanoma (SMM), and olfactory neuroblastoma (ONB). Less common types include sinonasal undifferentiated carcinoma (SNUC), adenoid cystic carcinoma (ACC), sinonasal neuroendocrine carcinoma, *Switch/sucrose non-fermentable (SWI/SNF)*-deficient carcinoma, and others^(1,3). While sinonasal SCC is typically the most frequent entity reported in studies from the United States, European series traditionally report higher incidence rates of sinonasal adenocarcinoma and SMM^(1,2,4). Particularly for SMM of the nasal cavity, an unexplained increase among white women aged 55 to 84 is observed⁽⁵⁾. The most frequent primary tumor sites are the nasal cavity along with its adjacent ethmoidal cells and the maxillary sinus, while tumors originating from the frontal sinus or sphenoid sinus are relatively rare^(1,6). Different risk factors contribute to the development of sinonasal cancer, depending on the histological entity. For sinonasal adenocarcinoma, particularly the intestinal-type sinonasal adenocarcinoma (ITAC) subgroup, previous studies revealed a strong predominance of male gender (male-to-female ratio, 21:1), mainly due to occupational exposure to known carcinogens such as wood dust and leather dust (relative risk, 29.4)^(7,8). Other known airway carcinogens, such as asbestos, nickel/chrome, or formaldehyde, were not confirmed to play a role in the pathogenesis of ITAC^(7,9,10). Non-intestinal-type sinonasal adenocarcinomas (Non-ITAC) are non-salivary adenocarcinomas found in the sinonasal tract, which do not exhibit either intestinal-type phenotypes or characteristics of salivary gland neoplasia. There are no known risk factors, and both males and females are equally affected⁽¹¹⁾. Unlike in SCC of the upper aerodigestive tract, the evidence for tobacco as a risk factor for sinonasal SCC is weak and outdated, and alcohol consumption has not been shown to promote the disease⁽¹²⁾. However, stronger evidence exists for occupational exposure to chrome, asbestos, arsenic, or welding fumes^(13,14). The role of active human papillomavirus (HPV) in the pathogenesis of sinonasal SCC is controversial, and a potential causative role has not been proven so far^(12,15). However, in analogy to mucosal oropharyngeal SCC, recent evidence suggests a survival benefit for patients with HPV-positive sinonasal SCC⁽¹⁶⁾. A small proportion of sinonasal SCCs develop from sinonasal inverted papilloma (SNIP) and represents a distinct entity. A recently published exploratory study has identified serum squamous cell carcinoma antigen and cytokeratin fragment antigen 21-1 as serum markers for the diagnosis of SNIP and SNIP with malignant transformation⁽¹⁷⁾. In our institutional series, both the incidence of synchronous (2%) and metachronous (0%) transformation

was low, whereas other authors reported higher rates, concluding that approximately 15% of all sinonasal SCC cases are either synchronously or metachronously associated with SNIPs^(12,18,19). There exist two systematic reviews and meta-analyses, which have both shown that SNIP-associated SCCs reveal a better prognosis than de-novo SCCs^(20,21). Interestingly, there seems to be an association between HPV-infection and malignant transformation of SNIPs to SNIP-associated SCCs⁽²²⁾. Sinonasal mucosal melanomas (SMM), which comprise 1.3% of all melanomas, typically manifest a molecular fingerprint different from that of cutaneous melanoma⁽²³⁾. It is a highly aggressive entity with a 5-year overall survival (OS) between 24–26.1% and a disease-specific survival (DSS) of around 29.5%^(24,25). Its pathogenesis does not depend on ultraviolet light exposure but rather on the migration of melanocytes into ectodermal tissue⁽²⁶⁾. From a molecular point of view, BRAF mutation is usually absent, and the pathogenesis of SMM is driven by various other driver mutations such as NRAS, KIT, and KRAS^(23,27,28). Kimura et al. additionally reported on Tripartite motif-containing 27 (TRIM27), a biomarker for several malignant tumors⁽²⁹⁾. They found that high TRIM27 expression in SMM is associated with advanced T classification, poor prognosis, and distant metastasis (DM)⁽²⁹⁾.

Pretherapeutic assessment

The past medical history including exposure to potential carcinogens needs to be complemented by a thorough nasal endoscopy of the nasal cavity including the postnasal space. Owing to the growth pattern of sinonasal malignancies, being characterized by locally aggressive expansion and a close relationship to pivotal neurovascular structures, patients often present at an advanced T category, showing involvement of the orbit, bony or dural skull base, brain or perineural spread⁽⁴⁾. Therefore, the evaluation must also take into account the cranial nerve status. Furthermore, assessment of the neck, including palpation, ultrasonography, and ultrasonography-guided fine-needle aspiration of suspicious lymph nodes (LN), is paramount. Cross-sectional imaging with computed tomography (CT) and magnetic resonance imaging (MRI) is then used for not only distinguishing benign from malignant lesions but also for defining tumor size and extent of involvement of adjacent compartments. CT or cone-beam CT, as a first-line imaging modality addresses bony alterations (e.g., erosions), is useful for identifying calcifying or ossifying elements (e.g., osteoma), and provides a bony roadmap for surgery⁽³⁰⁾. It is supplemented with MRI, which may delineate the tumor from surrounding tissue (e.g., mucosal retention and reactive polyps) and identify perineural spread, bone marrow infiltration, or metastases. Hypointense areas of the tumor on T2 may guide biopsy to obtain representative material⁽³¹⁾. However, even state-of-the-art cross-sectional imaging modalities may fail to correctly identify orbital or skull base infiltration, and false-positive or false-negative findings must be

Table 1. Outline of the main primary sinonasal malignancies in a concise and systematic manner.

Epithelial sinonasal malignancies	
De-novo SCC	– Keratinizing and non-keratinizing – Subtypes: adenosquamous, spindle cell, basaloid, papillary, verrucous – HPV-associated SCC (mainly non-keratinizing)
SCC ex inverted papilloma	– better prognosis compared to de-novo SCC
Non-salivary type adenocarcinoma	– Intestinal Type Adenocarcinoma (ITAC): • Kleinsasser/Schroeder classification: papillary-tubular, alveolar goblet cell, signet-ring cell, transitional • Signet-ring cell exhibits worst prognosis – Non-Intestinal Type (Non-ITAC): • low-grade vs. high-grade
Sinonasal undifferentiated carcinoma (SNUC)	– Displays oncogenic IDH2 or IDH1 mutations in 80% of cases
NUT carcinoma	– Formerly known as NUT-midline carcinoma
Neuroendocrine carcinoma	– Large cell vs. small cell
Olfactory carcinoma	– Differentiated by epithelial characteristics
SWI/SNF-complex deficient carcinoma	– Defined by loss of SMARCB1/INI-1
HPV-multiphenotypic carcinoma	– MYB-NFIB gene fusion usually absent (in contrast to sinonasal adenoidcystic carcinoma)
Non-epithelial sinonasal malignancies	
Olfactory neuroblastoma (ONB)	– Grading: Hyams 1 – Hyams 4
Sinonasal mucosal melanoma (SMM)	– by definition at least T3 category
Hematolymphoid tumors	– i. a. Extramedullary plasmacytoma, Extramedullary myeloid sarcoma
Mesenchymal tumors	– i. a. Biphenotypic sinonasal sarcoma, Mesenchymal chondrosarcoma, Rhabdomyosarcoma, Undifferentiated small round cell sarcomas, Desmoplastic small round cell tumor
Salivary gland-derived malignancies	
Sinonasal adenoid cystic carcinoma	– Szanto classification: tubular-cribriform, tubular-trabecular, solid growth pattern – Solid variant linked to aggressive behavior and poor outcome
Mucoepidermoid carcinoma	
Salivary-type adenocarcinoma	

HPV = Human Papillomavirus; IDH 1/2 = isocitrate dehydrogenase 1/2; INI-1 = integrase interactor 1; NUT = Nuclear Protein in Testis; SCC = Squamous cell carcinoma; SMARCB1 = SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily B member 1; SWI/SNF = Switch/Sucrose Non-Fermentable Complex.

considered. Well-known pitfalls of these modalities include (a) the discrimination of bony pressure erosion and infiltration and (b) the discrimination of reactive dural enhancement and infiltration by the tumor⁽³²⁾. For the medial orbital wall (MOW), MRI and CT both tend to overestimate the tumor extension. Often, only an intraoperative exploration can determine the true extent of infiltration. For the anterior skull base (ASB), the rates of false-positive and false-negative imaging findings are comparably high, and the frequency of intraoperative biopsies to clarify the extent of infiltration is increased (compared with MOW). CT is typically challenging to interpret for tumors adjacent to the cribriform plate, where pressure erosion often cannot reliably be distinguished from tumor infiltration of this particularly thin bone⁽³³⁾. MRI-based prognosticators of dural involvement are dural thickening of ≥ 5 mm, nodular dural thickening, or brain parenchyma invasion⁽³³⁻³⁵⁾. During the last decades, ¹⁸F-fluorodeoxy-D-glucose (FDG) positron emission tomography (PET)/CT

(FDG-PET/CT) has emerged as an alternative imaging modality for the initial staging of sinonasal tumors, providing information on the metabolic activity and local extent of the primary tumor and on the presence of regional and DM. While various studies have investigated the diagnostic accuracy of FDG-PET/CT in the staging and restaging of SCC of the upper aerodigestive tract, only a few studies have addressed its usefulness for the initial staging of sinonasal tumors^(35,36). However, while FDG-PET/CT might hence replace CT for initial staging, it is not a suitable replacement for MRI. With the advent of FDG-PET/MRI, a new hybrid imaging modality for oncological staging, particularly for tumors in the head and neck region, became available⁽³⁷⁾. FDG-PET/MRI can simultaneously address the need for high soft tissue contrast in the paranasal sinuses and skull base while allowing for whole-body staging, including the skull base and brain⁽³⁷⁾.

Biopsy; exploration of the tumor

An adequate and representative biopsy of the tumor is a fundamental step of every pretherapeutic assessment. The role of in-office biopsies vs. biopsies under general anesthesia is widely debated, and recommendations are mainly based on expert opinions. While several studies have shown that in-office biopsies in patients with sinonasal lesions can be safe, another study showed that biopsy volume significantly affects the reliability of the diagnosis⁽³⁸⁾. Additionally, biopsy under local anesthesia bears the risk of a non-representative tissue sample. It also may cause bleeding in well-vascularized lesions, which requires further treatment and causes significant patient discomfort. However, also under optimal biopsy conditions, the rarity of these neoplasms and the broad range of histological subtypes can lead to substantial discrepancies in the interpretation of biopsy results among pathologists, which underlines the importance of tertiary referral centers for the treatment of these patients⁽³⁹⁾. For instance, there is a substantial difference between the rather inaccurate histologic diagnosis of a “poorly-differentiated carcinoma” and a lesion, which can be categorized as SNUC or Switch/Sucrose Non-Fermentable Complex (SWI/SNF)-complex-deficient carcinoma. Table 1 outlines the main entities in a concise and systematic manner. In addition, and most importantly, a biopsy under general anesthesia allows for a thorough exploration of the tumor to assess its epicenter and relationship to adjacent structures, such as the medial orbital wall and bony or dural skull base. The extent of the tumor can be visualized and demonstrated during interdisciplinary tumor board discussions using an anatomical diagram, which enhances the understanding of the exact tumor extension and determination of T category⁽⁴⁰⁾. Knowledge of orbital and skull base infiltration is of utmost importance for sinonasal tumor staging, as it ultimately defines the T category and hence serves as a strong predictor of the 5-year DSS^(41,42).

Risk stratification

Based on the pretherapeutic assessment, which incorporates both the clinical and radiological characteristics of the lesion and the information obtained by biopsy and tumor exploration, tumors should be staged following the Union for International Cancer Control or the eighth edition of the American Joint Committee on Cancer staging manual before treatment⁽⁴³⁾. Concerning primary tumor staging, tumors of the maxillary sinus must be distinguished from tumors of the nasal cavity and ethmoid sinus⁽⁴³⁾. For both tumor localizations, an infiltration of the orbital floor, medial orbital wall, or cribriform plate renders the tumor category T3, whereas, for instance, a dural or brain parenchyma infiltration signifies T4b category⁽⁴³⁾. All SMMs qualify for a T3 category at least⁽⁴³⁾. The incidence rate of LN metastases at initial diagnosis is typically only 5–12.2%⁽⁴⁴⁾. Ipsilateral and contralateral levels I and II and the retropharyngeal area are

nodal basins at risk and must be carefully evaluated during staging⁽⁴⁵⁾. While there is broad consensus on the need to treat a positive neck, no general recommendation regarding elective neck management has been established. Decisions should be made on an individual basis within an interdisciplinary tumor board, considering the initial T category, tumor histology, tumor grading and clinical characteristics (e.g.⁽¹¹⁾). In general, elective neck treatment can be considered for patients with locally advanced tumors, especially in aggressive histological subtypes with a high propensity for lymphatic metastasis (e.g., Hyams grade III/IV for ONB, poorly differentiated SCC, advanced SCC of the maxillary sinus, SNUC)^(11,46). Distant metastases are present in approximately 4% of cases and can be reliably assessed with whole-body hybrid PET imaging, providing excellent sensitivity and specificity⁽⁴⁷⁾. Orbital infiltration, especially when involving the orbital apex, is well known to negatively impact both the OS and recurrence-free survival (RFS)^(48,49). Depending on the extent of the infiltration, the 5-year OS may decrease from 55–65% to 20–30%⁽⁵⁰⁾. Accordingly, as various series have shown, dural or brain involvement is associated with poor outcome^(4,41,42).

Treatment options

For head and neck cancer in general, and for sinonasal tumors in particular, most institutions aim to initiate treatment within 4–6 weeks after diagnosis. Achieving this goal is fundamental, as patients often present at an advanced stage, owing to long-time unnoticed tumor growth, which often causes alarming symptoms at an advanced stage⁽⁵¹⁾. Based on the clinical, radiological, and endoscopic workup, a treatment recommendation is made by a multidisciplinary head and neck tumor board, which is composed of skull base surgeons, maxillofacial surgeons, reconstructive surgeons, radiation oncologists, medical oncologists, pathologists, radiologists, and nuclear medicine physicians. Besides patient-specific factors, such as age or Eastern Cooperative of Oncology Group performance (ECOG) status, curative treatment protocols depend both on locoregional tumor extension (T and N categories) and the histological entity (including grading and other factors identified from histopathological analysis). In general, curative treatment plans consist of surgery, RT, chemotherapy, and immunotherapy (for SMM), whereas these modalities can be used alone or in combination and as part of neoadjuvant, definitive, or adjuvant protocols. Historically, surgical tumor resection (potentially followed by postoperative RT) represented the gold standard for the treatment of sinonasal malignancies⁽⁴¹⁾. Application of this paradigm in curatively intended treatment protocols for sinonasal SCC, ONB, most adenocarcinomas, and ACC is still beyond controversy^(12,41,52,53). Neoadjuvant chemotherapy for locally advanced sinonasal SCC was reported to improve tumor control and increase the rate of orbital preservation^(12,48,54–56). Despite all efforts to preserve the organ, certain conditions are

typically considered indications for orbital exenteration. These include tumor extension into the extraocular muscles, significant invasion of retrobulbar fat, involvement of the eye bulb and optic nerve, invasion of the bulbar conjunctiva or sclera, and extensive eyelid involvement ⁽⁴⁸⁾. It is important to note that orbital preservation does not appear to impact survival or local control. Additionally, infiltration of the orbital apex typically renders a patient incurable, regardless of the treatment protocol. ⁽⁴⁸⁾. Neoadjuvant chemotherapy using cisplatin, 5-fluorouracil, and leucovorin may provide high response rates and long-term control for some patients with advanced intestinal-type adenocarcinoma, particularly those whose tumors have a functional p53 protein ⁽⁵⁷⁾. For SNUC, belonging to the spectrum of neuroendocrine tumors and sharing overlapping features with neuroendocrine carcinoma and ONB, recent data indicated that induction chemotherapy for bioselection followed by definitive chemoradiation provided the best outcome ⁽¹¹⁾. For patients with advanced high-grade ONB tumors, combined treatment protocols consisting of surgical tumor resection and adjuvant RT may even be complemented with neoadjuvant chemotherapy, and surgery as single-modality treatment may be sufficient for patients with small, low-grade tumors if negative surgical margins are obtained ^(52,58–60). With regard to SMM, the best local control can be achieved through surgical tumor removal followed by adjuvant RT. However, immunotherapy has changed the approach to managing SMM in both curative and non-curative contexts, potentially leading to remarkable treatment responses and significant progression-free survival ^(5,27,61). Neoadjuvant checkpoint inhibition for resectable SMM followed by surgery and RT has been shown to be feasible, with an overall response of 47% and a 2-year OS rate of 64% ⁽⁶²⁾. Ongoing clinical trials, e.g. the PRISM (Preoperative Radiotherapy & Immunotherapy for Sinonasal Melanoma study, NCT05546827) are currently exploring the role and timing of checkpoint inhibitors along with RT and surgery.

Since its first implementation in the 1960s, open craniofacial resection has remained the standard technique for surgical resection of sinonasal tumors for decades, although it was associated with substantial perioperative mortality (0–13%) and high incidence rates of major complications (35–63%) ^(63,64). In recent decades, advanced transnasal endoscopic techniques and newly developed transnasal corridors have replaced open techniques in a significant number of cases, resulting in a paradigm shift. ^(41,65,66). Even in patients with stage 4 sinonasal malignancies and skull base involvement, the expanded endoscopic approaches were associated with lower mortality and non-inferiority in terms of outcome ⁽⁶⁷⁾. However, endoscopic skull base surgery follows a paradigm seen with many novel surgical strategies: by pushing the limits of traditional corridors there is a substantial risk for CSF leak and therefore a growing recognition of a need

to develop systematic strategies in terms of repair ⁽⁶⁸⁾. In certain patients with substantial anterior or lateral involvement of the frontal sinus, dural infiltration over the orbital roof, or brain parenchymal involvement, a combination of endoscopic endonasal and open subcranial approaches may be more suitable than a purely endoscopic attempt ⁽⁶⁹⁾. The same can be true for resections resulting in a large high-flow CSF leak, where the reconstruction via a combined approach (endoscopic, open) can be more successful. Traditionally, the goal of oncological surgery was to achieve an en-bloc resection with clear surgical margins and to avoid spillage of tumor cells ⁽⁷⁰⁾. Owing to the complex anatomy surrounding the operation field in skull base surgery, with proximity to vital healthy structures (e.g., optic nerve), such is often difficult to achieve with transnasal endoscopic techniques. Instead, tumors are resected with a “piecemeal” technique, disassembling the lesions with a view of the borderline between the normal and infiltrated portions of the nasal mucosa ⁽⁶⁹⁾. This approach is safe and effective, achieving equivalent results compared to open techniques, with less morbidity and decreased hospital stay duration ^(65,69,71,72). The recent introduction of intraoperative surgical navigation has been shown to contribute to achieve negative margins, especially if endoscopic and open techniques are combined ^(73,74). As it was shown in patients undergoing unilateral cranial resection for ONB, unilateral preservation of the olfactory apparatus in combination with smell training can lead to partial postoperative olfactory function ⁽⁷⁵⁾. RT can be delivered either as photon therapy in intensity-modulated technique (IMRT) or as an intensity-modulated particle therapy (IMPT; e.g., protons) ⁽⁷⁶⁾. Depending on the treatment protocol, RT is mainly administered as a definitive or adjuvant therapy, and concomitant chemotherapy can be given. The role of neoadjuvant RT, mostly in combination with CT (neoadjuvant chemoradiotherapy), in the treatment of locally advanced sinonasal malignancies was investigated in previous studies to increase the chance of organ preservation in definitive treatment ^(77–80). As for neoadjuvant chemotherapy, this therapeutic approach should be further evaluated in the context of prospective studies, with organ preservation as an endpoint ⁽¹²⁾. The indication for adjuvant RT depends on tumor histology (radiosensitivity), tumor grade, T category, presence of perineural spread or lymphovascular invasion, N category, and surgical margins. IMRT is suitable for complex, irregularly shaped target lesions adjacent to critical organs at risk ⁽⁸¹⁾. On the other hand, IMPT offers the additional advantage of creating a sharp dose gradient (“Bragg peak”), enhanced radiobiological effectiveness, and relative independence of tissue oxygenation ^(12,82,83). Owing to these benefits of IMPT, it has been established as an important treatment option for tumors in complex anatomical districts such as the skull base to maximally reduce the toxicity to critical adjacent structures (e.g., optic system, brain stem) ⁽¹²⁾. Regardless of the chosen RT technique, prompt coordination between the

times of surgical treatment and RT initiation is of utmost importance ⁽¹²⁾. Ideally, RT plans and dose gradients are established in close cooperation between surgeons and radiation oncologists. Recently, a consensual segmentation atlas based on important structures in CT scans was published, aiming to limit morbidity and optimize outcomes ⁽⁸⁴⁾. Furthermore, a recent study demonstrated that surgery-to-radiation intervals in patients with sinonasal cancer should be kept within 61 days to avoid worse outcomes ⁽⁸⁵⁾. When it comes to quality of life, Maggiore et al. recently reported that IMRT does have the greatest impact on quality of life in endoscopically treated patients. Therefore, continuous supportive care should be offered to these patients ⁽⁸⁶⁾.

Follow-up and surveillance

The aim of regular examinations after primary treatment is 1) an early identification of tumor persistence or recurrence and 2) diagnosis and management of treatment-related complications. Limited data are available regarding the optimal timing and duration of follow-up. Establishing an international consensus on surveillance protocols, tailored to different tumor entities, would be highly valuable. An effective surveillance protocol should consider treatment characteristics and tumor histology. At our institution, we recommend clinical follow-up examinations every 6–8 weeks during the first year and every 3 months from the second year after treatment completion. Follow-up intervals may be extended after the second year. In general patients should be followed for 5–10 years. However, certain entities with known late regional or distant recurrences, or high risk of local failure, such as adenoid cystic carcinoma, ONB or adenocarcinoma, need to be monitored life-long ⁽⁸⁷⁾. Thus, the surveillance protocol needs to be nuanced based on histopathology and risk profile. The clinical examination consists of an assessment of treatment-associated symptoms (e.g., smell function, nasal crusting, tearing eye, nasal obstruction), nasal endoscopy (using rigid or flexible endoscopes), and a thorough examination of the neck (palpation, ultrasonography, ultrasonography-guided fine-needle aspiration of suspicious LNs). In order to monitor sinonasal quality of life and function of smell, quantitative measurements such as questionnaires or smell tests may be used. In order not to miss RT-induced hypopituitarism, the hypothalamo-pituitary axis needs to be monitored. Mainly due to treatment-related mucosal swelling, nasal endoscopy has been shown to have comparably low sensitivity (24%) in detecting tumor persistence/recurrence ⁽⁸⁸⁾. Hence, it must be complemented by cross-sectional imaging. Radiological follow-up usually consists of a regional baseline MRI, which is scheduled 3 months after completion of treatment and should include at least fat-suppressed T2-weighted pulse sequences, non-enhanced T1-weighted pulse sequences, and fat-suppressed contrast-enhanced T1-weighted, pulse sequences in different planes ⁽⁸⁹⁾. Aiming to achieve a high inter-patient and intra-patient comparability, this

protocol should remain unchanged, regardless of (A) the tumor entity, (B) the treatment algorithms, (C) the timing of the examination (pretherapeutic vs. posttherapeutic), and (D) the used scanner ⁽⁸⁹⁾. Depending on the risk constellation (tumor entity, particular histopathological features rendering the tumor more aggressive, advanced TNM staging, surgical margins), radiological assessment with regional MRI is complemented by whole-body hybrid PET imaging ^(37,47,90–92). To avoid false-positive results, the first hybrid PET imaging should be scheduled at the earliest 3 months after treatment completion, since the posttreatment sinonasal skull base is characterized by a prolonged period of hypermetabolism that endures beyond the period previously described for deep tissue sites of the head and neck ⁽⁹³⁾. Further whole-body hybrid PET examinations should then be scheduled at 6 months after treatment completion and thereafter depending on the risk constellation. In case of unclear endoscopic or radiological findings, a transnasal endoscopic biopsy under general anesthesia remains imperative.

Limitations of the narrative review

This narrative review has certain limitations due to its broad scope, covering a wide range of tumor entities. Consequently, it does not provide an in-depth discussion of novel treatment options or all aspects of histopathologic findings. Additionally, it is not intended to offer comprehensive coverage of specific topics, as is typically expected in systematic reviews.

Conclusion

Although rare, the evidence-based workup and treatment of sinonasal malignancies have evolved significantly in recent years. Advances in our understanding of various tumor subtypes are bringing us closer to personalized treatment strategies. Achieving the best outcomes not only requires a highly skilled team at a tertiary referral center, but also relies on multidisciplinary collaboration, including tumor board discussions to guide comprehensive care decisions.

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Authors' contributions

CMM: manuscript writing, conceptual lead. TM: manuscript writing, conceptual input; MBS: manuscript editing, conceptual input; DH: manuscript editing, conceptual lead.

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Conflicts of interest

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