MANAGEMENT OF THE ORBIT IN MALIGNANT SINONASAL TUMORS

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Abstract: Malignant ethmoid and maxillary sinus tumors frequently involve the orbit. Orbital involvement is an important prognostic predictor of recurrence-free, disease-specific, and overall survival. Most authors agree that orbital preservation as opposed to orbital exenteration or clearance does not result in significant differences in local recurrence or actuarial survival. The eye can be safely preserved in most patients with ethmoid or maxillary sinus cancer invading the orbital wall, including malignancies that invade the orbital soft tissues with penetration through the periorbita provided that they can be completely dissected away from the orbital fat. Malposition of the globe and nonfunctional eyes frequently result when patients have not had adequate rigid reconstruction of the orbital floor, particularly if they have received postoperative radiotherapy. This underscores the importance of such reconstruction. Isolated defects following orbital exenteration may be reconstructed with a temporalis muscle flap. Microvascular free-tissue transfer is the best option for repair of defects following orbital exenteration and total maxillectomy, although an obturator still has a role in selected patients. © 2007 Wiley Periodicals, Inc. Head Neck 30: 242–250, 2008

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Malignant sinonasal tumors usually present as advanced disease because early diagnosis is difficult. Surgical extirpation remains the mainstay of treatment, but its relative therapeutic value compared with alternative treatments is controversial.1 Before the 1970s, the classic surgical
treatment for sinonasal cancers in close proximity to the orbit involved radical excision with orbital clearance or exenteration. Since the introduction of orbital preservation surgery more than 30 years ago, the indications and need for removal of orbital structures have diminished. Nonetheless, despite several reports claiming the effectiveness of various treatment strategies, the issue remains controversial. The 2 main points of contention are the oncological safety of orbital preservation and the functional outcome in preserved eyes. The goal of the present review is to critically appraise the functional outcome and oncological safety of orbital preservation in malignant sinonasal tumors.

PROGNOSIS BY HISTOPATHOLOGY
Tumor histology plays an important independent role in patient outcome, irrespective of orbital invasion. However, the histological diversity and rarity of individual tumor types in this region confound accurate statistical analysis. Every form of malignant histopathology can be encountered in the nose and sinuses, each with a distinct natural history and range of behavior, with malignant melanoma having the worst outcome, whereas esthesioneuroblastoma and chondrosarcoma have the best prognosis. However, for most tumor types, recurrence may happen many years later, rendering conventional 5-year actuarial survival meaningless in terms of cure. On the other hand, patients with the 2 most common histologic types, adenocarcinoma and squamous cell carcinoma, have an intermediate survival rate, patients with adenocarcinoma having a better disease-specific survival and recurrence-free survival than those with squamous cell carcinoma. Therefore, in addition to extent, the histologic findings of the primary tumor must be considered when selecting therapy.

ORBITAL INVOLVEMENT RATE IN SINonasal Tumors
The incidence of orbital invasion by malignancies of the sinonasal tract varies with the site of origin, histology, and aggressiveness of the particular tumor. Visual symptoms, including unilateral epiphora, proptosis, and diplopia, occur in 50% of patients with malignant sinonasal tumors and obviously relate to the site of disease with 62% of ethmoidal as opposed to 46% of nasal tumors producing orbital problems. Some tumors such as chondrosarcoma can result in bilateral blindness because of their propensity for skull base infiltration. Tumors may invade the orbit via preformed pathways, via neurovascular structures, or by direct extension through bone. Tumor extension into the orbit occurs particularly in ethmoid tumors, because of the thin lamina papyracea separating the 2 structures. Invasion of the orbital wall is present in 66% to 82% of the patients with ethmoidal malignancy, with involvement of the orbital periosteum in 30% to 50% of patients. Orbital invasion (bone erosion/invasion) occurs in 60% to 80% of maxillary sinus malignancies. The periorbitum is a barrier against invasion, but once the tumor has transgressed this robust periosteum it gains access to a space that lacks barriers to check local tumor spread. The lack of a clear definition as to what constitutes orbital invasion has been a source of confusion when reporting outcome of patients undergoing orbital preservation versus clearance or exenteration. It has become increasingly evident that the surgeon should determine the exact extent of tumor penetration into the orbital tissues more precisely. An important distinction should be made between erosion of the bony orbital wall, involvement of the perisoteum, and deeper penetration to involve the orbital soft tissues.

The term “orbital exenteration” is normally applied to complete removal of the contents of the orbit, including the eyelids. This is rarely required for most sinonasal tumors. “Orbital clearance” is a procedure in which the globe, muscles, fat, and periorbita are removed, while the lids, and usually the palpebral conjunctiva, are preserved. The 2 obviously require different types of reconstruction. After exenteration, a large cavity remains open to the nasal, oral, and pharyngeal cavities. It is necessary to fill this cavity with muscle bulk, as by transfer of temporalis muscle, with or without skin grafting, or with a revascularized free flap. If the lids are preserved, and the patient survives subsequent treatment, an obturator is usually sufficient to provide bulk. To avoid repetition of the cumbersome expression “exenteration/clearance,” the term “clearance” will be used throughout this text, unless exenteration is specifically referred to, as this accounts for the majority of cases, and the prognostic statistics apply equally.

Iannetti et al identified 3 stages of orbital invasion: grade I, erosion or destruction of the medial orbital wall (see Figure 1); grade II, extraconal invasion of the periorbital fat (see Figure 2); grade III, invasion of the medial rectus muscle, optic nerve, ocular bulb, or the skin.
overlying the eyelid (see Figure 3). They propose that only grade III orbital invasion warrants orbital clearance or exenteration. Even with the most accurate imaging combining fine-detail CT and MRI, frozen section confirmation is required at the time of surgery to determine whether tumor has transgressed the orbital periosteum (Figure 2B).12

**IMPACT OF ORBITAL INVOLVEMENT ON SURVIVAL**

Orbital involvement is associated with a significant reduction in survival both in ethmoid and maxillary sinus tumors. In a review of 100 patients with ethmoid tumors involving the anterior skull base, multivariate analysis revealed that involvement of orbital soft tissue was an independent factor significantly influencing survival. Survival, however, was not affected when invasion was limited to orbital periosteum.4 Ganly et al,3 in a multi-institutional study of 334 patients who underwent craniofacial resection of the anterior skull base for ethmoid tumors, reported that lack of involvement of the orbital contents was a predictor of recurrence-free, disease-specific, and overall survival. In this study, disease-specific survival with orbital involvement was 41% compared to 75% without orbital involvement. Other reports have shown that orbital involvement significantly affects survival, particularly if the apex is involved,13,14 and that it is not improved by orbital clearance. It is noteworthy that tumor grade and orbital invasion were the only significant independent variables adversely affecting survival in McCaffrey et al’s series.15 It is not surprising, therefore, that many authors have reported poorer survival in those patients requiring orbital clearance compared with those who did not.5

In a series of 259 sinonasal malignancies undergoing craniofacial resection,16 no orbital involvement was present in 187 patients, 53 underwent orbital clearance at the time of primary surgery and 50 underwent resection of orbital periosteum with preservation of the eye. Five of these individuals subsequently underwent orbital clearance between 5 months and 4 years later. A multivariate analysis identified brain involvement, type of malignancy, and orbital involvement as the 3 most significant prognostic factors but did not show that the decision to resect periosteum alone adversely affected outcome.

**FIGURE 1.** Grade I of orbital invasion with erosion of the medial orbital wall.

**FIGURE 2.** (A) Grade II of orbital invasion showing an extracranial invasion of the periorbita in a chondrosarcoma. (B) This patient illustrates the need of an intraoperative exploration to confirm in some instances the depth of the invasion. Despite the appearance, both eye bulbs were pushed by the tumor with limited involvement of the periorbita.
With some exceptions, most authors also found orbital invasion to have a deleterious impact on the outcome of maxillary sinus tumors. In a review of 57 patients who underwent maxillectomy, multivariate analysis confirmed that skull base and orbital involvement were the only factors significantly associated with disease-specific survival. Involvement of the orbit was associated with a 5-year survival of only 17%, as opposed to 49% when there was no invasion. On the other hand, no survival benefit was achieved by orbital clearance: only 11% of patients with orbital involvement remained alive after 5 years despite complete extirpation of orbital contents. Orbital invasion also was an independent prognostic factor in a series of 95 tumors of the maxillary sinus, and T4 tumors with orbital invasion had a worse prognosis than other T4 tumors. Nevertheless, agreement has not been reached on the degree of orbital invasion that is oncologically safe when sparing orbital contents. Different indications for orbital clearance have been proposed based on involvement of periorbita, orbital fat, extraocular muscles, or orbital apex. Thus, a selection bias exists in all of these studies because the tumors in more advanced stages (ie, orbital apex invasion) with expected worse outcomes were treated with orbital clearance, whereas those with more favorable orbital extension were treated with more conservative approaches.

The impact of orbital invasion on survival related to tumor histology has been separately studied and reported. In a limited series of 26 patients with orbital invasion who underwent simultaneous combined therapy with preservation of orbital contents, Nishino et al reported a 5-year overall survival rate of 74% for patients with squamous cell carcinoma, and 40% for patients with disease other than squamous cell carcinoma. The difference was statistically significant. Imola and Schramm analyzed oncologic outcomes according to 3 histological subgroups (squamous cell carcinoma, adenomatous carcinomas, and undifferentiated carcinoma). None of these subgroups demonstrated a significant difference between patients managed by orbital preservation and those treated by orbital clearance. For 2 histological subgroups (squamous cell carcinoma and adenomatous carcinomas), local recurrence occurred with somewhat greater frequency in patients undergoing orbital clearance versus those managed by orbital preservation, although there was no statistical difference between any of the subgroups.

**IMPACT OF ORBITAL CLEARANCE ON LOCAL RECURRENCE RATE**

Early reports called for orbital clearance in all cases with bony orbital invasion. In a retrospective review of 111 patients with maxillary sinus tumors who had invasion of the orbital floor, it was reported that when clearance was performed, the 5-year survival rate was 27.3% and the rate of recurrence within the orbit was 12.5%. In patients with preservation of the orbital contents,
the corresponding rates were 34.8% and 8.6%, respectively, with no significant differences between these groups. Several authors have advocated an eye-sparing approach in the treatment of sinonasal tumors with periorbital involvement based on similar oncologic results with the less radical procedures, while others report a reduced local control rate after orbital preservation.

Carrau et al compared the survival of patients presenting with invasion of the bony orbit without soft tissue invasion in which the orbital content was spared, with patients presenting with invasion of the orbital bones and soft tissues whose treatment included orbital clearance. At 3-year follow-up, 52% of the patients whose orbits were cleared were alive without evidence of disease, compared with 59% whose orbital contents were preserved. Similarly, the difference in rate of local recurrence (29% vs 22%) was not statistically significant.

Imola and Schramm analyzed 66 patients who underwent surgical treatment for sinonasal malignancy encroaching on the orbit in which orbital preservation was performed in all patients with tumor extension up to and including resectable periorbital involvement. Within the orbital preservation group as a whole, local recurrence occurred in 30%, compared with 33% in patients treated by orbital clearance. Eye-sparing surgery was associated with local recurrence at the original site of orbital involvement in only 7.8% of cases. This strategy has been supported by long-term results and is summarized in Figure 4.

In a review of 53 patients with squamous cell carcinoma of the maxillary antrum, clearance was performed in 25 patients for disease invading the orbit with gross involvement of periorbita, whereas the other 28 patients with disease that either did not fully invade through bone into the orbit or invaded the orbit without gross periorbital involvement were treated by orbital preservation. Again, the results demonstrate no significant difference in local recurrence or actuarial survival between the orbital preservation and orbital clearance groups.

Nazar et al reported orbital recurrence in 13% of patients with orbital preservation, while 15% of patients who underwent clearance recurred in the orbit, showing that preservation of the orbit does not adversely affect outcome.

Finally, a meta-analysis of disease-free survival and local recurrence in 170 patients with orbital invasion by squamous cell carcinoma revealed that patients in whom the orbital contents were preserved had 5-year survival and local recurrence rates of 41% and 20%, versus 37% and 36% when orbital clearance was undertaken. These results do not demonstrate any significant difference in local control or actuarial survival. However, it should be noted that these studies were retrospective and that patients who underwent orbital clearance generally had more advanced orbital involvement, a selection bias not corrected by prospective matching and randomization.

The rationale for orbital preservation has been supported by histological studies of maxillectomy with orbital clearance. These have demonstrated that, in most specimens, invasion of the orbit is limited to the periorbita. On the basis of these findings, it may be surmised that these tumors could be completely resected by total maxillectomy with limited removal of the periorbital tissue. Clinicoanatomic studies have clearly demonstrated the presence of a thin, distinct fascial layer that surrounds the periocular fat and separates it from the periorbita.

**IMPACT OF CONSERVATIVE THERAPIES ON SURVIVAL**

Itami et al analyzed local control in patients who underwent less aggressive piecemeal debulking followed by conventional fractionated radiation therapy. Local recurrence-free survival at 5 years was 59%. Orbital clearance was performed in only 1 patient. For patients with macroscopic...
residual disease, >58 Gy administered with conventional fractionation appeared to be necessary to improve local control.

Nishino et al21 examined the oncologic and functional outcomes of multimodality therapy for patients with advanced malignant maxillary sinus tumors that invaded the orbit. All patients underwent simultaneous combined therapy consisting of conservative surgery through a sublabial incision, radiotherapy, and regional chemotherapy. The 5-year overall survival and local control rates were 68% and 66%, respectively. Local control rates were significantly worse in patients with disease involving the orbital apex, as well as in patients with disease other than squamous cell carcinoma. All patients retained their orbital contents, and 73% demonstrated adequate ocular function, despite orbital involvement.

Jansen et al30 studied the contribution of combined radiotherapy and debulking on local control and survival in paranasal sinus tumors of different histologic types. Five-year local control and overall survival with combined treatment were 65% and 60% respectively, compared to 47% and 9% with radiotherapy alone, but the groups were not strictly comparable as patients with more advanced disease tended to choose radiotherapy alone. Cox-regression analysis showed that clinical orbital and orbital wall invasion, among other findings, were parameters significantly associated with poor local control.

**EYE FUNCTION IN CONSERVATIVE PROCEDURES**

Imola and Schramm22 reported functional results in patients in whom the orbit had been preserved. Overall eye function was reported as functional without impairment in 54%, functional with impairment in 37%, and nonfunctional in 9%. The most common abnormality was globe malposition in 63% of patients and was associated with lack of adequate rigid reconstruction of the complete orbital floor or multisegmental orbital defects, with persistent diplopia in 9% of patients. Radiation therapy increased the risk of ocular complications, in particular optic atrophy, cataracts, excessive dryness, and ectropion. Stern et al27 reported that only 17% of patients, who had the orbital floor resected without an attempt to reconstruct the orbital floor, retained significant function in that eye. On the other hand, patients who had an intact bony orbital floor and when radiation fields did not include the eye had minimal problems.

Eye function is thus strongly influenced by the position of the resected orbital segment, with abnormal eye function in patients undergoing total maxillectomy without reconstruction of the orbital periosteum and bony floor. However, eye function in patients subjected to total ethmoidectomy or resection of the lateral wall is almost always normal.31 It follows that large defects resulting from complete orbital floor resection or resections involving 2 or more orbital walls and large portions of orbital periosteum should undergo reconstruction.

**RECONSTRUCTION OF THE ORBITAL FLOOR**

Repairing lost orbital support decreases the risk of globe malposition, diplopia, and disturbance of extraocular muscle function, as well as lid malposition and ectropion resulting in exposure keratitis.22 Minimal bony resection such as isolated orbital wall (lateral or medial) or small orbital floor defects do not require any kind of reconstruction. Resection of medial orbital periosteum can be repaired with split skin or fascia lata with minimal morbidity.16 This can equally be undertaken endoscopically as these approaches are increasingly undertaken in selected cases of sinonasal malignancy.32

Larger defects in the orbital floor can be repaired using a thick fascial sling tightly secured to the margins of the bony defect. With subtotal or total floor defects (>75% surface area) and multisegmental defects (orbital floor and 1 or more walls), some form of rigid reconstruction is advisable. Furthermore, it is important to reconstruct extensive orbital defects primarily because established secondary defects are difficult to repair.

Primary reconstruction of total maxillectomy defects with preservation of orbital contents remains a complex problem without a perfect solution. In addition to conventional prosthetic obturators, a number of techniques have been introduced to support the orbital floor following maxillectomy without orbital clearance. These methods include skin graft or a temporalis muscle sling, the sheath of the upper portion of the rectus abdominis muscle or other related procedures, but they have also resulted in complications, such as enophthalmos, diplopia, and facial deformity. Reconstruction following total maxillectomy with preservation of the orbital contents should provide support to the orbital contents, reconstruct the palatal surface, and achieve facial symmetry and a good aesthetic result. Nonvascularized bone grafts or a titanium or synthetic (polyethylene or
polypropylene) mesh, in conjunction with a soft-tissue free or pedicled muscle flap, can be used to reconstruct the orbital floor. Split ribs, split calvaria and iliac crest grafts, or even vascularized calvarial bone flaps, radial forearm osteocutaneous flaps, or coronoid-temporalis pedicled rotation flaps have been used for reconstruction of the orbital floor combined with a myocutaneous rectus abdominis free flap for soft-tissue reconstruction and resurfacing of the palatal mucosa and the skin of the cheek when it has been resected. In addition to the rectus abdominis flap, other free flap reconstructive options for patients with total maxillectomy defects that have been used include the latissimus dorsi, and scapular and anterolateral thigh, and free fibula flaps. To achieve better functional results, Kakibuchi et al presented a sophisticated reconstructive procedure for complex maxillary defects using the latissimus dorsi-scapular rib osseomusculocutaneous flap. The hard palate was reconstructed with a vascularized scapular angle, whereas the infraorbital rim was reconstructed with vascularized rib. A bone graft, replacing the zygomatic buttress, was added between the infraorbital rim and the hard palate, and the latissimus dorsi muscle flap, which was supported by a skeletal framework, obliterated the remaining cavities around the bone grafts, thus reconstructing both the oral side of the hard palate and the lateral wall of the nasal cavity. Triana et al reported 51 reconstructions of partial and total maxillectomy defects with only 1 complete and 2 partial flap failures, whereas Cordeiro and Santamaria had a free-flap survival of 100% with only a partial flap necrosis in 1 of 55 cases.

Should the deep temporal artery not have been damaged during tumor resection, a temporalis muscle transposition is a suitable and less time-consuming procedure than microvascular flaps, the drawback being a higher flap necrosis rate and an unsightly temporal fossa defect. Reconstruction of the floor of the orbit generally allows for adequate functional vision with ectropion being the most common undesirable result. However, it should be remembered that once in place, these complex reconstructions prevent inspection of the surgical cavity and make interpretation of follow-up imaging more difficult.

**RECONSTRUCTION OF EXENTERATION AND CLEARANCE DEFECTS**

General indications for orbital clearance include involvement of the orbital apex, irresectable full-thickness invasion through periorbita into retrobulbar fat, extension into the extraocular eye muscles and invasion of the bulbar conjunctiva or sclera. Complete exenteration is undertaken when the eyelids are involved beyond reasonable hope for reconstruction. When the eyelids are preserved, as is often the case, and orbital clearance is undertaken, the lids, or palpebral conjunctiva, may be sutured together, allowing them to sink back to line the socket, and no further reconstruction is required other than fashioning an orbital prosthesis.

In ethmoid tumors, isolated defects following orbital exenteration can be reconstructed with a temporalis muscle flap. The entire temporalis muscle may be used by creating a large window of about $3 \times 2$ cm in the lateral wall of the orbit with a burr, without resecting the lateral orbital rim. The muscle, pedicled on its insertion on the coronoid process, is passed through the opening made in the lateral orbital wall. This is a good alternative to the other commonly performed methods of orbital reconstruction because of its completion in 1 operative stage, short operative time, and minimal donor site morbidity. A split skin graft can be applied. To enhance the useful volume of the flap, a reverse temporalis muscle flap based on the superficial temporal vessels has been proposed. However, the temporalis muscle flap is not large enough to cover more extensive defects resulting from both orbital exenteration and total maxillectomy.

Maxillectomy defects become more complex when critical structures such as the orbit, globe, and cranial base are resected, and reconstruction with distant tissue becomes essential. Rectus abdominis microvascular free-tissue transfer for repair of orbital exenteration or clearance defects with or without total maxillectomy is a safe and reliable alternative to the use of the temporalis muscle pedicled flap. It provides a larger volume of well-vascularized tissue and greater placement flexibility, and the long vascular pedicle facilitates the use of multiple donor vessels within the head and neck, which is an advantage in previously irradiated patients. The flap allows reliable obturation of the oral maxillectomy defect. Pryor et al reported a successful outcome in 92% of 13 patients in whom the rectus abdominis free flap was used following orbital exenteration. Other microvascular free flaps have been used under these circumstances, including the scapular, latissimus dorsi, and combination of latissimus dorsi and scapular flaps, as well as the anterolateral...
thigh flap, even achieving orbital restoration with prosthetics. Microvascular free flap reconstruction provides an expeditious and immediate means of reconstruction of surgical defects, where soft tissue replacement and lining in multiple areas are required.

Orbital prostheses can be applied to the socket once healing has occurred. Ideally, these can be secured with osteo-integration, which can be done primarily at the time of the resection or as a secondary procedure. It is worth noting that integration is slower around the orbital rim than elsewhere in the facial skeleton and may be further hampered by radiotherapy.

CONCLUSIONS
Sparing the soft tissues of the orbit when the peri-orbital area has been not been deeply transgressed by tumor generally does not appear to adversely affect cure or local control. However, due to the small number of reports with adequate data, a large multi-institutional study to address the issue of orbital preservation in malignant sinonasal tumors is warranted.

Rigid orbital reconstruction is essential for large defects resulting from total orbital floor resection or resections involving 2 or more orbital walls, to prevent displacement and dysfunction of the eye.

REFERENCES


