Orbital Exenteration: One Size Does Not Fit All

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• PURPOSE: To evaluate the clinical indications for orbital exenteration in a tertiary referral center and to compare clinicopathologic correlation and cosmetic outcome with previously reported data.

• DESIGN: Retrospective, nonrandomized, consecutive case series.

• METHODS: Review of Electronic Medical Record system, Orbital Clinic, Jules Stein Eye Institute, between January 1999 and December 2003. MAIN OUTCOME MEASURES: Surgery type, clear margins histologically, survival, and wearing an eye patch.

• RESULTS: Thirty-four patients (mean age 67 years) underwent orbital exenteration; mean follow-up 1.2 ± 1.5 years (6 months to 6 years). Diagnosis included orbital, ocular, and adnexal malignancies, with squamous and basal cell carcinoma being the most common. Twenty-one patients (62%) underwent total or extended orbital exenteration, and 13 patients (38%) underwent subtotal exenteration including tissue reconstruction. Clear surgical margins were obtained in 23 cases (68%), whereas positive margins were left in 11 cases (32%). Many of the patients preferred an eye patch to cover the surgical region regardless of surgical reconstruction. Only 4 patients (11.8%) who underwent subtotal exenteration with orbital prosthesis did not use a patch. During follow-up period 3 patients expired, only 1 of which was tumor-related.

• CONCLUSIONS: Clinical indications for orbital exenteration remain similar over the last four decades with a higher prevalence of squamous cell carcinoma in our institute. Orbital exenteration is considered curative in cases of basal or squamous cell carcinoma but not in cases of malignant infiltrative processes such as adenoid cystic carcinoma of the lacrimal gland. Patients are likely to wear an eye patch regardless of any attempt at surgical reconstruction. (Am J Ophthalmol 2005;139:11-17.

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ORBITAL EXENTERATION IS A DISFIGURING SURgery. The surgery is performed mostly for orbital malignancies in an attempt to achieve cure with tumor free margins. It is also performed in painful or life-threatening orbital inflammations and infections. Malignancies of the ocular adnexa are the most prevalent causes of orbital exenteration include squamous cell carcinoma, sebaceous cell carcinoma, and basal cell carcinoma. Other less common tumors include conjunctival malignant melanoma, adenoid cystic carcinoma of the lacrimal gland, and uveal melanoma with extrascleral extension.[1,2] The role of orbital exenteration in increasing survival in these cases is unclear, because most of the studies are retrospective in nature. One is reluctant to defer surgery, even when there is only a small chance of cure.

In our institute we try to tailor the extent of resected tissue to each case. When a surgical cure can be achieved, a more extended surgery is performed. However, in cases where there is extra-orbital or deep orbital apex involvement or evidence of metastatic disease, a more conservative approach may be taken to ease pain or to simplify nursing care.

The surgical site may be left to granulate by secondary intention or could be covered with a split-thickness skin graft.[3,4] Secondary intention granulation tissue usually results in a shallower orbit[4] with slightly prolonged healing compared with split-thickness skin graft.

Depending on the tissue remaining there are several methods of orbital reconstruction. Common techniques include muscle flaps,[5–8] free flaps and tissue transfer,[9,10] orbital fat,[11] bone flaps, autologous bone or Osseo-integration,[12–14] and periosteal flaps.[15] In many cases, despite efforts to perform large surgical reconstruction, patients prefer to wear a black eye patch.

Recently, we published a series of 25 orbital exenterations performed in our center.[16] This series comprised 13 patients with more extensive disease who underwent total exenteration. The remaining 12 patients underwent sub-

FIGURE 1. A 78-year-old patient with a history of four previous conjunctival resections for squamous cell carcinoma of the conjunctiva. MRI scan demonstrates an enhancing lesion in the anterior lateral orbit on the left side (upper images). Exenteration may result in cure. The patient underwent total exenteration with split thickness skin graft. Pathologic report showed negative margins. Lower image showing deep socket 1 year post-exenteration surgery.

total exenteration. The latter group had shown better functional and esthetic results.

The purpose of this study is to determine the clinical indications for orbital exenteration in a tertiary referral center and to compare the clinicopathologic correlation and cosmetic outcome with previously published data.

PATIENTS AND METHODS

ALL EXENTERATION CASES WERE PERFORMED AT THE JULES Stein Eye Institute between January 1, 1999, and December 31, 2003. Data included preoperative diagnosis, tumor type, location, and previous treatment. Also included was type of surgery, tissue reconstruction, complications, pathologic report, and patient rehabilitation. The study complied with the policies of the local institute review board.

FIGURE 2. CT scan of orbits (upper image). A 64-year-old female showing squamous cell carcinoma anterior lateral orbit, encroaching the globe laterally. Cure may be possible with subtotal exenteration. Lower image showing the patient 4 years after subtotal exenteration sparing medial conjunctiva and eyelids with implant right orbit for squamous cell carcinoma. Patient is using ocular prosthesis.

Exenteration was classified as total when all orbital contents including the globe and periorbita were removed. Cases that included excision of adjacent bone were defined as extended exenteration. Total or extended exenterations were performed in cases when complete excision of the tumor with free margins was possible in an attempt to achieve cure (Figure 1). Subtotal exenteration was defined as a partial removal of orbital tissue with sacrifice of the eye. An eyelid-sparing procedure was preferred, with the exception of cases where eyelid was needed for tumor-free surgical margins (Figure 2 and Figure 3).

In cases of malignant tumors with positive margins, adjuvant therapy, usually in the form of orbital radiation was given. When possible, a wide excision with orbital and bone biopsies was performed to remove any evidence of malignant tissue. In cases of distant metastasis at the time of diagnosis or direct involvement of the brain or cavern-

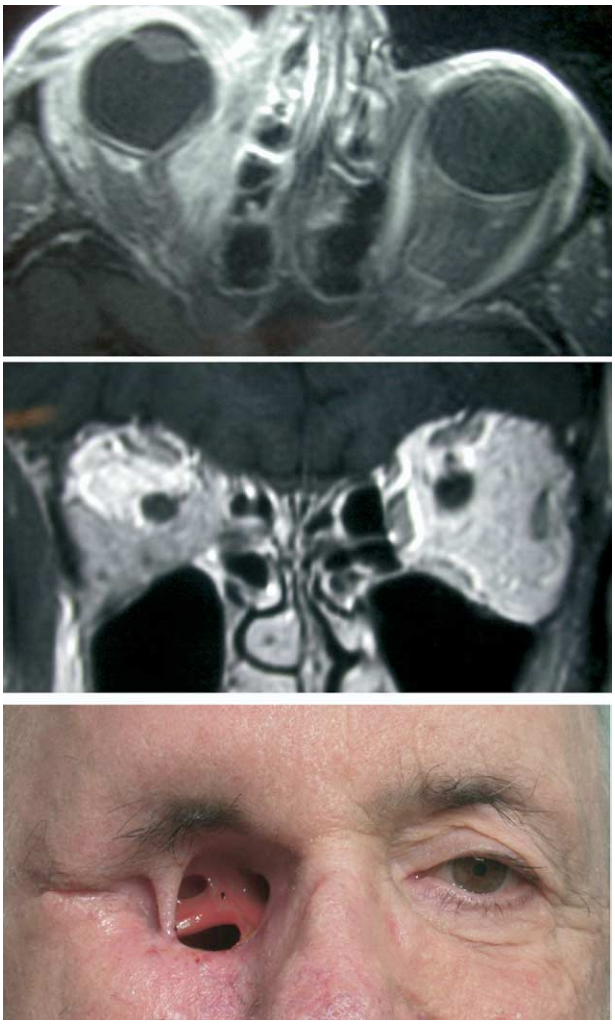

FIGURE 3. MRI scan of the orbits showing extensive medial basal cell carcinoma. Surgical cure is not expected. The patient underwent subtotal exenteration, with positive margins. Eyelid skin was spared, although this broke down over time leaving a lateral strand of skin.

ous sinus, a more palliative surgery was performed. All surgeries were performed by the authors.

A direct telephone survey was performed by one of the authors (D.F.) at the end of the follow-up time (April 2004) to ascertain survival, esthetic, and functional results of the surgery. Patients were asked about postoperative course since the last office visit and the use of an eye patch vs ocular prosthesis.

Statistical analysis performed included the χ^2 nonparametric test to examine the likelihood of wearing an eye patch after surgery (total vs subtotal exenteration), to calculate the chance of death when positive margins were found on pathologic report, and to compare data from the current study to our previous report regarding orbital exenteration. The Kaplan-Meier survival analysis was used to calculate cumulative survival after orbital exenteration.

TABLE 1. Preoperative Diagnoses of 34 Patients Who Underwent Orbital Exenteration at the Jules Stein Eye Institute, 1999 to 2003

	Number of Patients (%)
Squamous cell carcinoma (SCC)	9 (26.5%)
Basal cell carcinoma (BCC)	6 (17.6%)
Mixed BCC/SCC	1 (2.9%)
Melanoma conj/eyelid/orbit	5 (14.7%)
Choroidal melanoma with extra scleral extension	4 (11.8%)
Sebaceous cell carcinoma/lid/orbit	3 (8.8%)
Adenoid cystic carcinoma/lacrimal gland	2 (5.9%)
Osteosarcoma	1 (2.9%)
Benign mixed tumor/lacrimal gland	1 (2.9%)
Adenocarcinoma	1 (2.9%)
Zygomecetes/mucormycosis	1 (2.9%)

Statistical analysis was carried out with Microsoft Excel XP and SPSS programs.

RESULTS

THIRTY-FOUR PATIENTS (10 MALES, 24 FEMALES, MEAN AGE 67 ± 14 [37 to 93] years) underwent orbital exenteration. Mean follow-up time was 1.2 ± 1.5 years [range 6 months to 6 years]. Preoperative diagnoses are summarized in Table 1. Most cases were categorized as orbital, ocular, and adnexal malignancy, with squamous and basal cell carcinoma being the most common (nearly 50%).

Summarized in Table 2 are modes of surgical intervention; nearly two thirds of the cases were total or extended exenterations, and one third was subtotal with some

TABLE 2. Type of Orbital Exenteration Performed in 34 Patients at the Jules Stein Eye Institute, 1999 to 2003

	Number of Patients (%)
Subtotal/lid-sparing	6 (17.6%)
Subtotal/myocutaneous flap	5 (14.7%)
Subtotal/HA implant	2 (5.9%)
Total	3 (8.8%)
Total/split thickness skin graft	9 (26%)
Total/dermis-fat graft	2 (5.9%)
Extended/maxillectomy/ethmoidectomy/ zygomatic bone	7 (20.6%)

HA = Hydroxyapetite.

Exenteration was classified as total when all orbital contents including the globe and periorbita were removed. Subtotal exenteration was defined as a partial removal of orbital tissue with sacrifice of the eye.

TABLE 3. Postoperative Complications in 34 Patients Who Underwent Orbital Exenteration at the Jules Stein Eye Institute, 1999 to 2003

	Number of Patients (%)
Fistula/sinus	2 (5.9%)
Infection/bacterial/fungal	1 (2.9%)
Orbital abscess	1 (2.9%)
Tissue necrosis/eschar formation	2 (5.9%)
Non-healing ulcer	1 (2.9%)
HA implant exposure	1 (2.9%)

HA = Hydroxyapetite.

attempt of tissue reconstruction. Mean preoperative visual acuity was 20/70 [range 20/20 to NLP].

A pathologic report was obtained in all cases; clear margin tumor and soft tissue excision was obtained in 23 cases (68%), whereas positive margins were obtained in 11 cases (32%). In cases with adenoid cystic carcinoma of the lacrimal gland, adenocarcinoma, and osteosarcoma margins were not cleared histologically. In cases of positive margins, usually no attempt was made to extend surgical margin, and adjuvant therapy in the form of orbital radiation was added when deemed medically necessary. One case (78-year-old male) who underwent subtotal orbital exenteration for basal cell carcinoma with positive margins later underwent total exenteration in an attempt to achieve surgical cure.

Complications occurred in 23.5% of the cases and are summarized in Table 3; in most cases therapy included local antibiotics or surgical excision.

At the end of the follow-up period, most patients chose to wear an eye patch to cover the wound regardless of any attempt of surgical reconstruction. Only four patients (11.8%) who underwent subtotal exenteration with orbital prosthesis did not wear a patch. One patient who underwent flap reconstruction did not wear a patch. Two additional patients underwent dermis fat graft and one HA (hydroxyapetite) orbital implant surgery. Patients who underwent subtotal exenteration were more likely not to use an eye patch ($P = .012$, χ^2). During follow-up period, three patients expired; two were diagnosed with squamous cell carcinoma (SCC) and one with osteosarcoma, the only tumor-related death. Positive surgical margins were confirmed in one of these SCC patients ($P = .034$, χ^2). Cumulative survival plot is shown in Figure 4.

DISCUSSION

ORBITAL EXENTERATION, ALTHOUGH HIGHLY DISFIGURING surgery, may provide cure in cases of local invasive tumors such as basal and squamous cell carcinoma. When all involved tissue and bone is removed and no positive margins remain,[1] there is a low recurrence rate of 7% to 10% and low tumor-related death. Other tumors such as malignant melanoma, sarcomas, and adenoid cystic carcinoma of the lacrimal gland carry a poorer prognosis. This may be because of undiagnosed distant micro-metastasis present before the time of surgery.

We have achieved local control with tumor-free margins in more than 50% of the cases and had only one case of tumor-related death. It is likely that with longer follow-up the survival analysis would have been different; we can estimate that patients with adenoid cystic carcinoma of the lacrimal gland or patients with positive margins may change the survival outcome with longer follow-up.

Squamous cell carcinoma was the most prevalent in our series. This is slightly different than the series described by Rathbun and associates.[1] In contrast they found 30% of the cases (14/48) to be basal cell carcinoma, and only 12.5% (6/48) to be Squamous cell carcinoma. This may represent a trend toward early diagnosis and treatment of basal cell carcinoma, most likely because of a high index of suspicion at early stages. Additionally, the introduction of Mohs' micrographic surgery[17] could also be cause for the lower incidence of basal cell carcinoma found in our study. Squamous cell carcinoma remains a more severe problem, and more extensive surgery is likely because of perineural invasion.[18,19]

Several investigators have attempted to minimize deforming effect of the surgery by using eyelid-sparing technique, emphasizing the rapid healing and more acceptable cosmetic results. Shields and associates report that eyelid-sparing technique can be used in most of the cases of malignant tumors and in more than half of the cases originating in the eyelids.[20] We managed 25% of the cases with eyelid-sparing exenteration. The rehabilitation following eyelid-sparing exenteration is usually a black patch.

Several investigators,[21] along with previous work from our institute,[16] reported a more conservative surgery with an attempt of globe and vision preservation in selected cases of orbital and ocular adnexa malignancies. We prefer using an individualized approach with maximal tissue-preserving technique whenever possible. However, one must take into consideration the biological behavior of the tumor. In cases of highly malignant infiltrative tumors such as adenoid cystic carcinoma of the lacrimal gland or conjunctival malignant melanoma, which are potentially surgically cureable, we prefer a wider surgical margin and additional separate intraorbital map biopsies after removing the tumor en-block. If surgical cure is not possible, then limited debulking is performed.

Controversy remains regarding the appropriate extension of local resection in patients with these tumors, and there is only limited data[1,22–25] that surgery can provide cure for these types of orbital malignancies. New treatment modalities such as adjuvant chemotherapy and plaque radiotherapy may improve the surgical cure rates for these aggressive neoplasms.[26,27] Orbital exenteration may be

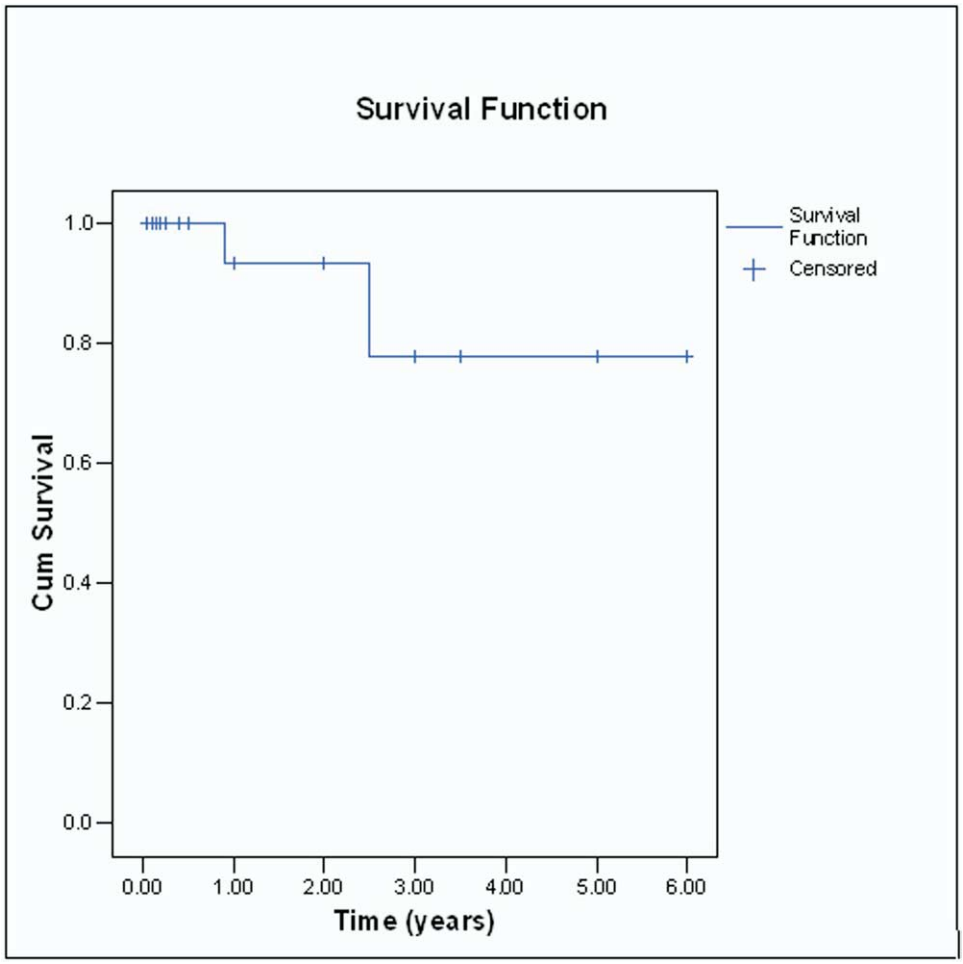

FIGURE 4. Cumulative survival plot for 34 patients who underwent orbital exenteration in the Jules Stein Eye Institute, 1999 to 2003.

more characterized as a procedure that achieves local tumor control, and in cases of adenoid cystic carcinoma there is evidence that radical surgery does not necessarily lead to improved disease-free survival.[24,28,29]

When analyzing findings from our previous report,[16] we noticed an increase in the total number of exenterations performed over a shorter period of time. In our earlier work,[16] there were 25 cases in 17 years, whereas in this work 34 patients are included in only 5 years. We do not think, however, that this represents an actual increase in extenteration rate but instead a change in the referral pattern to our orbital clinic. In the past years, additional surgeons joined our clinic, and we have been using a new electronic medical record that enables a more accurate and thorough data collection and analysis. We also participate in the ear, nose, and throat, and maxillofacial tumor board and believe that this, as well, increased the total number of exenteration cases referred. An accurate estimate of the incidence of orbital exenteration can only be evaluated by a larger national or multicenter study. We also notice a higher rate of SCC, 10 patients (29.4%)in the current study vs 6 patients (25%) with SCC in our previous report. This difference is not statistically significant ($P = .6$, χ^2). Finally, there has been a shift toward total and extended exenteration, but this was not statistically significant. In the current study 21 patients (62%) underwent total exenteration whereas in our previous study 13 patients (52%) underwent total or extended exenteration ($P = .45$, χ^2).

An important part of patient's rehabilitation is reconstruction of the exenterated orbit.[3,5–9,11,13,15] Talking with the patient before surgery and understanding the patient's desire to go through numerous stages of complex orbital reconstruction or to simply wear a patch is important. Subtotal exenteration with preservation of orbital tissue volume, eyelids, or conjunctiva may facilitate the use of orbital and ocular prosthesis and improve esthetic and functional results. In our study patients who underwent subtotal exenteration or had an orbital implant were less likely to wear an eye patch, but even in this subgroup, more patients wore an eye patch than did not. Patients should be informed that the likelihood of using an eye

patch is high even in cases of subtotal exenteration. In total or extended exenteration, our data support not attempting orbital reconstruction.

The complication rate was 25% (Table 3) and included local infection, fistula formation, one case of implant exposure, and one case of nonhealing ulcer. In general, these could be treated with medical management or a local excision. Interestingly, Yassur and associates report the efficacy of becaplermin gel (recombinant human platelet-derived growth factor) for the treatment of chronic orbital ulcer after exenteration.[30]

Pitfalls of our study stem from its retrospective design; however, given the small number of exenteration surgeries performed, a prospective study would be difficult to establish. Some of our patients have follow-up time of only 6 months, which is short in terms of local recurrence or disease-free survival. However, analysis of preoperative diagnosis, pathologic evaluation, and functional and esthetic results was possible.

Orbital exenteration may be successful in curing locally spreading tumors such as basal and squamous cell carcinoma. The success of the surgery depends on obtaining tumor-free margins at the time of surgery if performed before distant metastasis. In cases of tumor positive margins, other treatment modalities such as radiation or chemotherapy may play a roll in prolonging survival. Esthetic reconstruction of the exenterated orbit is complicated but may be associated with good cosmetic results. It is more likely to be successful in cases of subtotal exenteration. We consider the best functional and cosmetic outcome by the ability to wear a prosthetic device, the absence of a patch, and the lack of postoperative complications such as sino-orbital fistula. The risk of local control or metastasis with subtotal exenteration is controversial, and it is important to individualize treatment decisions based on the biology of the tumor, anatomic location, potential tissue planes to achieve adequate margins, and on the patient's goals for rehabilitation. We recommend subtotal exenteration in cases where tumor-free margins can be obtained, especially with globe preservation, or when distant metastasis exists at the time of diagnosis. A randomized controlled study is needed to establish the role of subtotal exenteration compared with total or extensive surgery in these cases.

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REPORTING VISUAL ACUITIES

The AJO encourages authors to report the visual acuity in the manuscript using the same nomenclature that was used in gathering the data provided they were recorded in one of the methods listed here. This table of equivalent visual acuities is provided to the readers as an aid to interpret visual acuity findings in familiar units.

Table of Equivalent Visual Acuity Measurements

Snellen Visual Acuities				
4 Meters	6 Meters	20 feet	Decimal Fraction	LogMar
4/40	6/60	20/200	0.10	+1.0
4/32	6/48	20/160	0.125	+0.9
4/25	6/38	20/125	0.16	+0.8
4/20	6/30	20/100	0.20	+0.7
4/16	6/24	20/80	0.25	+0.6
4/12.6	6/20	20/63	0.32	+0.5
4/10	6/15	20/50	0.40	+0.4
4/8	6/12	20/40	0.50	+0.3
4/6.3	6/10	20/32	0.63	+0.2
4/5	6/7.5	20/25	0.80	+0.1
4/4	6/6	20/20	1.00	0.0
4/3.2	6/5	20/16	1.25	−0.1
4/2.5	6/3.75	20/12.5	1.60	−0.3
4/2	6/3	20/10	2.00	−0.3

From Ferris FL III, Kassoff A, Bresnick GH, Bailey I. New visual acuity charts for clinical research. Am J Ophthalmol 1982;94:91–96.

Biosketch

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