Mortality following exenteration for malignant tumours of the orbit

I Rahman, A Maino, A E Cook, B Leatherbarrow

Background: Orbital exenteration is a rare, but disfiguring procedure reserved for the treatment of locally invasive malignancy or potentially life threatening orbital neoplasms, when less destructive techniques are inadequate. The authors report their experience and analyses of 64 cases of orbital exenteration performed over a 13 year period, looking specifically at key factors affecting mortality associated with such a destructive surgical procedure.

Methods: Records were reviewed retrospectively of all patients who had undergone exenteration of the orbit from 1 January 1991 to 1 April 2004 inclusive, at the Manchester Royal Eye Hospital. In all cases of deceased individuals, the cause of death was determined by liaison with the general practitioner and local health authority. Duplicate death certificates were requested for all deceased patients from the Registrar for Births, Deaths, and Marriages, Southport, UK. Kaplan-Meier analysis was used to estimate survival following exenteration.

Results: Overall, 1 year survival post-exenteration was high at 93%. After 3 years this had fallen to 67%, followed by 57% after 5 years, and 37% at 10 years. 13 patients died as a direct result of the orbital tumour. A further nine died of unrelated medical conditions, and two patients succumbed to malignant processes originating elsewhere in the body. There was no difference in survival rate at 3 years (p = 0.59) and 5 years (p = 0.454) between those with clear resection margins and those without.

Conclusion: In this study it was found that there was an overall mortality rate of 38% over 12 years. The presence of clear surgical margins, although reassuring for the surgeon, should not be regarded as an indication of cure. However, an overall 1 year survival of 93% and a 10 year survival of 37% are reassuring in that a proportion of individuals achieve surgical cure following exenteration. 38% of patients died as a result of other medical causes over the 12 year follow up.

METHOD
Theatre records were reviewed retrospectively via a computerised database to identify all patients who had undergone exenteration of the orbit from 1 January 1991 to 1 April 2004 inclusive, at Manchester Royal Eye Hospital. Patients surgical records were analysed and the following data recorded: age, sex, histological diagnosis, histological margins, the presence of recurrence or metastasis, and long term outcomes.

The cause of death was determined by liaison with the general practitioner and local health authority for those who had died. Duplicate death certificates were requested for all patients from the Registrar for Births, Deaths, and Marriages, Southport, UK.

Kaplan-Meier analysis was used to estimate survival following exenteration. Categorical variables were compared using contingency tables (Fisher’s exact test). Prism statistical software was used throughout the study (GraphPad Software Inc, San Diego, CA, USA, Version 4.0).

RESULTS
A total of 64 orbits of 64 patients were identified from the database as having undergone orbital exenteration for malignant disease; 38 were females and 36 males. An equal distribution of 32 right and left eyes was noted. The age at exenteration ranged from 4–93 years (mean 70 years).

In the cohort of 64 patients, 14 different tumours were encountered. These are highlighted in table 1.

The eyelids were the most common sites of tumour origin, accounting for 38 of the 64 exenterated patients. Malignant disease originating in the orbit and lacrimal gland (18), globe and conjunctiva (five), and three cases of unknown origin accounted for the remaining 26 cases.

Of the 64 orbits, 35 required a total orbital exenteration and a further a 21 subtotal exenteration (three with lid sparing procedures). In nine cases the procedure was not clearly documented. Morbidity/complications have been presented in a previous paper.

Survival and long term follow up
Follow up and subsequent course of the malignant disease to the time of writing was available in all 64 cases. Follow up to discharge ranged from 2–69 months (average: 19 months). Overall, 1 year survival post-exenteration was high, at 93%. After 3 years this had fallen to 67%, followed by 57% after 5 years, and 37% at 10 years (fig 1). Table 2 outlines the details of the 24 patients who died during the period of study.

Thirteen patients died as a direct result of the orbital tumour. A further nine died of unrelated medical conditions, and two patients succumbed to malignant processes originating elsewhere in the body. A further two cases have metastatic disease.

Abbreviations: BCC, basal cell carcinoma; SCC, squamous cell carcinoma

O rbital exenteration is a rare, but disfiguring procedure reserved for the treatment of locally invasive or potentially lives threatening orbital neoplasms, when less destructive techniques are inadequate. Several large studies have described their experience with orbital exenteration. However, few have reported on long term survival.
neither comfortable nor comforting. For the patient, exenteration represents a final attempt at cure of a potentially lethal process. For the surgeon, exenteration is both a radical and disfiguring procedure. For the patient, the thought of sacrificing a prominent part of the face is neither comfortable nor comforting.

**DISCUSSION**

Exenteration of the orbit is both a radical and disfiguring procedure. For the surgeon, exenteration represents a final attempt at cure of a potentially lethal process. For the patient, the thought of sacrificing a prominent part of the face is neither comfortable nor comforting.

### Table 1 Histological diagnosis of patients undergoing exenteration

<table>
<thead>
<tr>
<th>Histological diagnosis</th>
<th>No of patients (total = 64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal cell carcinoma</td>
<td>28</td>
</tr>
<tr>
<td>Sebaceous cell carcinoma</td>
<td>9</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>6</td>
</tr>
<tr>
<td>Melanoma</td>
<td>2</td>
</tr>
<tr>
<td>Globe with extrascleral spread</td>
<td>8</td>
</tr>
<tr>
<td>Lids</td>
<td>1</td>
</tr>
<tr>
<td>Ethmoid sinuses</td>
<td>1</td>
</tr>
<tr>
<td>Adenocarcinoma (lacrimal gland)</td>
<td>1</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Liposarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Merkel cell</td>
<td>1</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1</td>
</tr>
<tr>
<td>Apocrine carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Secondary metastasis, gastrointestinal primary</td>
<td>1</td>
</tr>
<tr>
<td>Malignant schwannoma</td>
<td>1</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>1</td>
</tr>
</tbody>
</table>

BCC, basal cell carcinoma; SCC, squamous cell carcinoma.

In our series, 28 patients had BCCs. 36 patients, therefore, had what may be regarded as more highly metastatic orbital neoplasms. However, Kaplan-Meier curves for these two groups revealed no significance in overall 5 year survival. Many of the deaths of patients in the BCC group (seven of eight cases) were unrelated to the BCC, and then succumbed to other medical conditions. Conversely, in the non-BCC group, malignant tumours of the orbit accounted directly for 12 of 16 fatalities. Death as a result of ageing does not appear to be a significant contributing factor in the two groups, as the average age of death in the BCC group was 68 (range 50–91), compared to 65 (range 5–91). It can, therefore, be assumed that a similar prognosis maybe relevant in both groups at 5 years, regardless of the pathology.

Surgically clear margins are thought to be a key element in establishing surgical cure of a patient in any form of surgery for neoplasia. Our results confirm those reported by Mouriaux et al., in that tumour free margins have little effect on long term survival. This is somewhat surprising as the goal of tumour surgery relies largely on achieving clear margins. However, this apparent paradox confirms that many variables are involved in establishing cure. Clear excision margins may prevent local recurrence, but they do not prevent microscopic spread to lymph nodes or distant organs via the bloodstream.

Our study reveals that five of the 10 cases (50%) of malignant melanomas are dead as a result of metastatic disease. A further two have metastatic disease at present and three are free of tumour. However, nine cases had clear resection margins, suggesting early metastatic spread of the tumour. Pach et al. reviewed a series of 46 patients and found no benefit from exenteration compared to enucleation in long term survival. However, tumour size and ocular/orbital location were significant risk factors in survival. In a large study of 1607 cases, Starr and Zimmerman described a 5 year death rate of 66% in the presence of extrascleral metastasis.
extension. Rini et al. raised the issue of exenteration in orbitally invasive melanoma having a potentially detrimental effect in survival. Confirming this, Affeldt et al. and Kersten et al. reported a poor long term survival even with early exenteration. As such, exenteration in the context of orbital melanoma has been superseded by more conservative measures. Similarly, the role of orbital exenteration in the treatment of adenocystic carcinoma of the lacrimal gland remains unclear. However, in the face of poor alternatives, options are often limited. Wright et al. described 38 patients (of a series of 50) with malignant neoplasms of the lacrimal gland. Exenteration did not improve the survival or reduce the recurrence rate. However, with adjunctive radiotherapy and radical surgical resections survival tended to be longer. The poor prognosis of adenocystic carcinoma relates to early perineural spread. For cures to be effective, early spread of the tumour requires adjunctive therapy. Intra-arterial chemotherapy preoperatively has been postulated to be of benefit in this setting. This said, in our series, two patients have undergone exenteration for adenocystic carcinoma. Both had clear resection margins histologically, and both individuals are still alive 10 years and 12 years postoperatively. Only one of the two underwent adjunctive radiotherapy.

The method of wound closure is an important cosmetic concern, but secondary to total, aggressive tumour resection. The argument for spontaneous granulation of the defect centres on the possibility of early detection of recurrence and donor site morbidity. However, our study does not support this theory, as local recurrence rates are small at four of 64 cases, supporting Mohr and Esser’s observation of five of 74 cases with recurrence. Closure, therefore, may be planned preoperatively in discussion with patient concerns and likely prognosis of the condition.

**CONCLUSION**

Orbital exenteration should not be considered a curative procedure in most cases without adjunctive therapy. In cases of malignant melanoma and adenocystic carcinoma this should be thought of as palliative. However, the move towards more aggressive adjunctive therapy (chemotherapy and radiotherapy) may offer improved cure rates. Moreover, the presence of clear surgical margins, although reassuring for the surgeon, should not be regarded as an indication of cure.

In our study, we found a mortality rate of 38% over 12 years, of which 54% were associated with metastatic spread of the tumour. However, overall 1 year survival of 93%
and 10 year survival of 37% are reassuring as a proportion of individuals achieve cure following exenteration. Further, we confirm the favourable outcome associated with exenteration for BCC in this setting.

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