Chirurgia (2011) 106: 219-225
Nr. 2, Martie - Aprilie

Craniofacial resection for malignant tumors of the paranasal sinuses

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Rezumat

Rezecția craniofacială în tumori maligne ale sinusurilor paranazale

Obiective: A descrie experiența acumulată cu rezecția craniofacială practicată în tumori ale rinobazei şi a identifica factori predictivi pentru supraviețuire.
Material şi Metode: Între 1996 şi 2008, 64 de pacienți consecutivi cu tumori sinusale cu atingerea rinobazei au suferit rezecție craniofacială. Au fost analizați mai mulți parametri pentru a identifica factori predictivi pentru supraviețuire prelungită: vârsta, sexul, tipul histopatologic de tumoră, invazia durei mater, invazia orbitei, statusul marginilor de rezecție, radioterapia adjuvantă, aplicată pre- sau postoperator. Supraviețuirea actuarială a fost calculată prin metoda Kaplan-Meier iar diferența dintre grupuri a fost stabilită prin testul log-rank. Factori identificați în analiza univariată au fost introduşi apoi în modelul Cocs pentru a stabili factori de prognostic pentru supraviețuire.
Rezultate: Supraviețuirea actuarilă la 5 ani a fost de 47% pentru tot lotul de pacienți. Cea mai ridicată supraviețuire a afost pentru pacienți cu estezioneuroblastom iar cea mai scăzută pentru cei cu melanom. Invazia durală şi invazia orbitei sunt factori de pronostic negativ pentru supraviețuire.
Concluzie: Supraviețuirea bună şi morbiditatea minimă asociată rezecției craniofaciale o impun drept procedură de elecție în tumorile rinosinusale cu extensie la nivelul fosei cerebrale anterioare.

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Cuvinte cheie: rezecția craniofacială, tumori, sinusuri paranazale, supraviețuire, factori prognostici

Abstract

Objective: To review the experience with craniofacial resection for malignant tumors of the anterior skull base and analyze prognostic factors for survival.
Material and Methods: Between 1996 and 2008, 64 consecutive patients with malignant tumors of the anterior skull base underwent craniofacial resection. Different parameters were analyzed to study their relationship with survival: age, sex, pathology, orbital involvement, dural involvement, status of the surgical margins, adjuvant radiotherapy, and whether the treatment was done before or after surgery. Survival analysis was carried out with the Kaplan-Meier product limit method and comparison between groups was performed by the log-rank test. Factors identified in the univariate analysis were then entered in the multivariate analysis using the Cox regression model in order to identify predictive factors of survival.
Results: For the entire group survival rates were 47% at 5 years. The highest survival was observed in patients with estesioneuroblastoma and the lowest in melanoma cases. Dural involvement and orbital clearance are predictors of poor survival.
Conclusion: The improved survival and minimal morbidity associated with craniofacial resection make it the approach of choice for anterior skull base tumors.

Key words: craniofacial resection, tumors, paranasal sinuses, survival, prognostic facors

Introduction

The oncologic problems presented by sinonasal malignant tumors have been recognized for many decades and led to pioneers such as Ketcham et al. (1) and Terz et al. (2) developing a combined intracranial and nasal approach. The initial report of Ketcham et al. (1) fostered the development of surgical techniques that evolved into the current practice of anterior skull base surgery. The craniofacial approach has become the accepted surgical approach for tumors which have breached the anterior cranial fossa, although technical details may vary from center to center. Improvements in surgical techniques were paralleled by advances in the fields of central nervous system imaging, anesthesia, and techniques of reconstruction, chemotherapy and radiotherapy.

The aim of this paper is to present our 12-year experience with anterior craniofacial resection, considering actuarial survival for the entire cohort and for individual pathologies where appropriate. It was also our purpose to determine prognostic factors which may have implications for future patient management.

Materials and Methods

All consecutive patients who had undergone craniofacial resection between 1996 and 2008 at the Department of Neurosurgery of the University of Medicine and Pharmacy Cluj-Napoca were included. The surgical team was composed from an otolaryngologist, a neurosurgeon and a maxillofacial surgeon.

Tumor extension was assessed by means of CT scan and MRI. As suggested by Shah et al. (3) contraindications for craniofacial resection were represented by involvement of the only seeing eye, optic chiasm or massive brain involvement, invasion of the clivus, sella or pituitary by the malignant tumor, involvement of the cavernous sinus or the internal carotid artery. Twenty patients had received previous radiotherapy and presented with recurrent or persistent disease and underwent salvage surgery. The rest of 44 patient received planned postoperative radiation therapy.

The surgical technique has been extensively described in the literature (3-5) and is briefly outlined: the intracranial portion of the procedure is performed initially using a bicoronal scalp incision. In elevating the frontal scalp, a galeal-pericranial flap is created for the purpose of skull base reconstruction *(Fig. 1)*. When necessary, dura mater or limited portions of the frontal lobes were resected and the resulting dural defect was repaired with a fascial or pericranial graft. When dura is uninvolved, extradural dissection is performed with division of the olfactory roots at the cribriform plate and closure of the dural sleeves of the olfactory roots. Appropriate cuts are made in the cribriform plate, fovea ethmoidalis, jugum sphenoidale and orbital roof depending on the extent of the tumor. The facial exposure is obtained through a lateral rhinotomy or Weber-Fergusson incision depending on the extent of resection *(Fig. 2)*. The specimen incorporated the lateral nasal wall, septum, ethmoid in continuity with the bony anterior cranial fossa *(Fig. 3)*. If tumor was adjacent to the orbital periosteum, this was resected and the orbital contents were preserved. If tumor transgressed the periosteum, orbital clearance was undertaken *(Fig. 4)*. Larger resections included the maxilla, orbital contents and infratemporal fossa *(Fig. 5, Fig. 6)*. All tissue removed was submitted to detailed histopathology with the intent of identifying dural or orbital involvement. Reconstruction of the skull base is begun with watertight closure of the dural defect. The frontal sinus is cranialized with resection of its posterior wall. The galeal-pericranial flap is used to separate the intracranial contents from the sinuses. The flap is sutured in place by anchoring it to the periphery of bony defect *(Fig. 7)*. Extensive defects of the skull base and of the orbital roof were reconstructed by means of titanium mesh *(Fig. 8)*. Dental obturators were required following the procedure in 12 patients. Assessment of surgical margins was

Figure 1. *The galeal-pericranial flap*

Figure 2. *The Weber-Fergusson incision*

Figure 3. *Patient after ethmoidectomy and total maxillectomy*

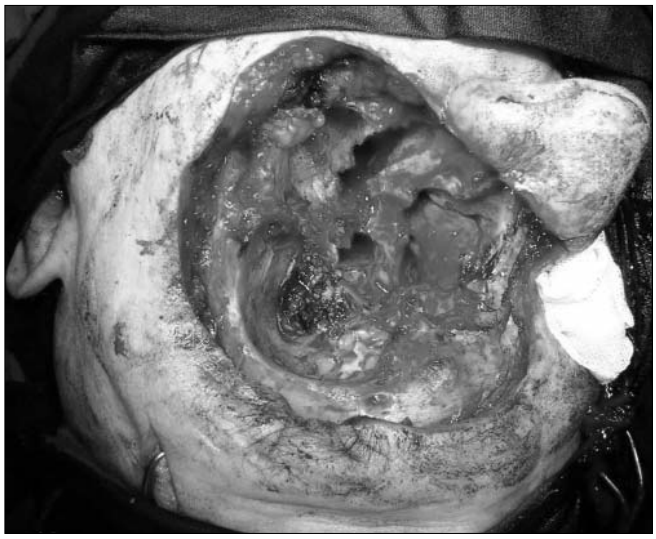

Figure 4. *Patient after medial maxillectomy, ethmoidectomy and orbital exenteration*

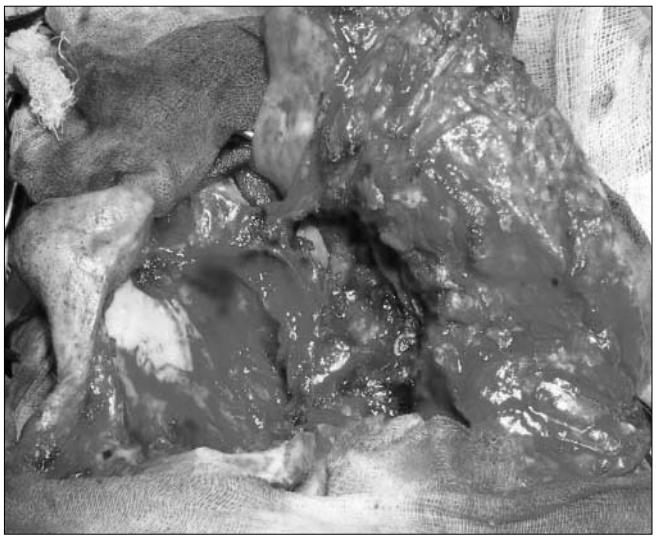

Figure 5. *Extensive resection comprising the maxilla, orbital contents and infratemporal fossa*

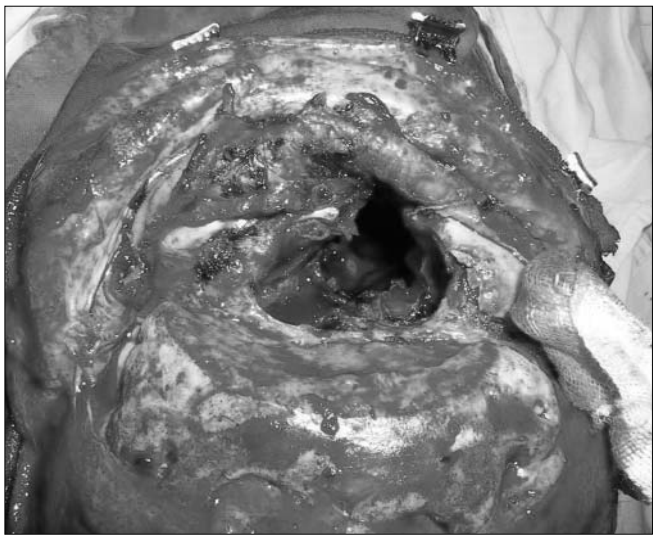

Figure 6. *Defect of the anterior skull base after craniofacial resection*

based on final histopathological investigation.

Following the surgical procedure, clinical follow-up and imaging were performed for all patients at regular intervals. Patients not seen in the year before the conclusion of the study were contacted by telephone. Survival analysis was carried out with the Kaplan-Meier product limit method and comparison between groups was performed by the log-rank test. The variables included age, sex, pathology, orbital involvement, dural involvement, status of the surgical margins, adjuvant radiotherapy, and whether the treatment was done before or after surgery. Factors identified in the univariate analysis were then entered in the multivariate analysis using the Cox regression model in order to identify predictive factors of survival. A $p<0.05$ value was the level of significance selected.

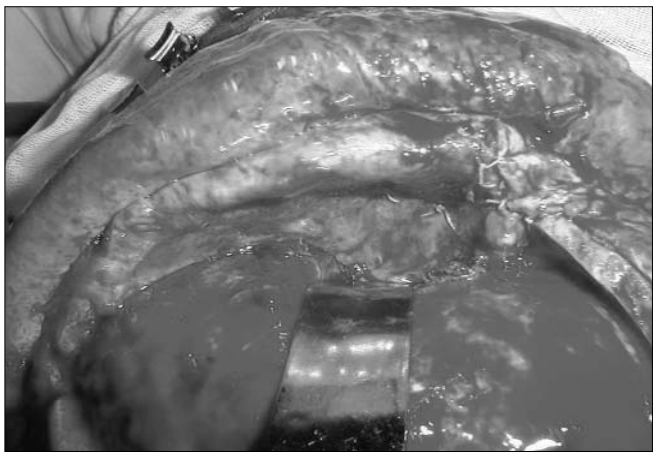

Figure 7. *The galeal-pericranial flap used to separate the intracranial contents from the sinuses*

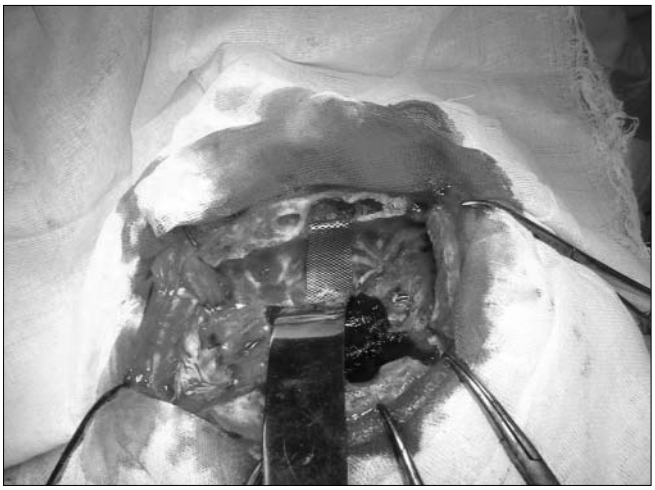

Figure 8. *Defect of the skull base reconstructed by means of titanium mesh*

Results

During the time period mentioned 64 patients underwent craniofacial resection. The cohort was composed of 42 men (65%) and 22 women (35%), their age ranged from 20 to 75 years, with a median age of 47 years. The most common tumor histology was squamous cell carcinoma (n=20), followed by adenocarcinoma (n=-14), adenoid cystic carcinoma (n=8), with a variety of tumors being present (see *Table 1*). Disease arose in the ethmoid sinuses in the majority of cases, though many other areas were affected *(Table 2)*. In some cases, the extent at presentation precluded accurate determination of site of origin.

The follow-up period ranged from 12 months to 90 months. When all cases are considered, 33 are alive and well, 28 dead of disease, 2 dead of intercurrent disease and 1 lost to follow-up. The overall actuarial survival for the whole group of patients was 47% at 5 years. *Table 3* also shows actuarial survival for individual histology types while the Kaplan–Meier survival curves for various histology types are displayed in *Fig. 9*. The small number of cases with each histological diagnosis precludes formal statistical comparison between these groups (p=NS, log-rank test). Orbital contents preservation was accomplished in 52 patients, while 12 cases underwent orbital clearance at the time of craniofacial resection. Kaplan-Meier survival curves are depicted in *Fig. 10* and an improved survival is statistically significant associated with eye preservation (p=0.03, log-rank test). With regard to intracranial involvement, after detailed assessment, 51 patients had no evidence of spread into the dura and 13 cases had dural involvement which was resected. Survival is worse in patients presenting with dural involvement as compared to patients without dural invasion (see *Fig. 11*, p=0.04 log-rank test). The effect on survival of delivering radiotherapy before and after craniofacial resection was compared and showed no statistical difference. Although there is a trend for better survival in patients with negative margins, the difference did not reach statistical significance (*Fig. 12*, p=0.5 log-rank test).

Table 1. *Histological diagnosis of 64 patients undergoing craniofacial resection*

Diagnosis	No cases
Squamous cell carcinoma	20
Adenocarcinoma	14
Adenoid cystic carcinoma	8
Esthesioneuroblastoma	7
Chondrosarcoma	6
Mucosal melanoma	4
Others (osteogenic sarcoma, hemangiopericytoma, mucoepidermoid carcinoma, spindle cell sarcoma)	5

Table 2. *Site of disease*

Site	No
Ethmoid	26
Nasal cavity	11
Orbitoethmoid	10
Frontoethmoid	9
Antroethmoid	8

Table 3. *Actuarial survival for whole group and individual histologies*

Histology	5 yr (%)	No
Overall	47	64
Esthesioneuroblastoma	62	7
Chondrosarcoma	55	6
Adenocarcinoma	42	14
Squamous cell carcinoma	36	20
Adenoid cystic carcinoma	25	8
Others	55	5
Melanoma	0	4

The Cox analysis identified two factors which significantly affect both outcome and survival of the patient: orbital and dural involvement.

Postoperative complications included: death in two cases (one due to pneumonia and the other due to intracranial sepsis), major local sepsis (n=6 cases), delayed return of neurological function (n=5 cases), meningitis (n=4 cases), with a number of patients suffering more than one complication.

Discussion

The rarity of paranasal sinus malignant tumors makes it complicated to accrue numerically large series with long-term follow-up. This combined with the histological diversity of the area renders meaningful statistics difficult.

In the pre-craniofacial era, the 5-year results of 23% to 38% for malignant tumors of the nasal sinuses were usual (6). Management consisted in extended maxillectomy, often with orbital clearance and radiotherapy (6). By comparison, patients undergoing craniofacial resection achieve better

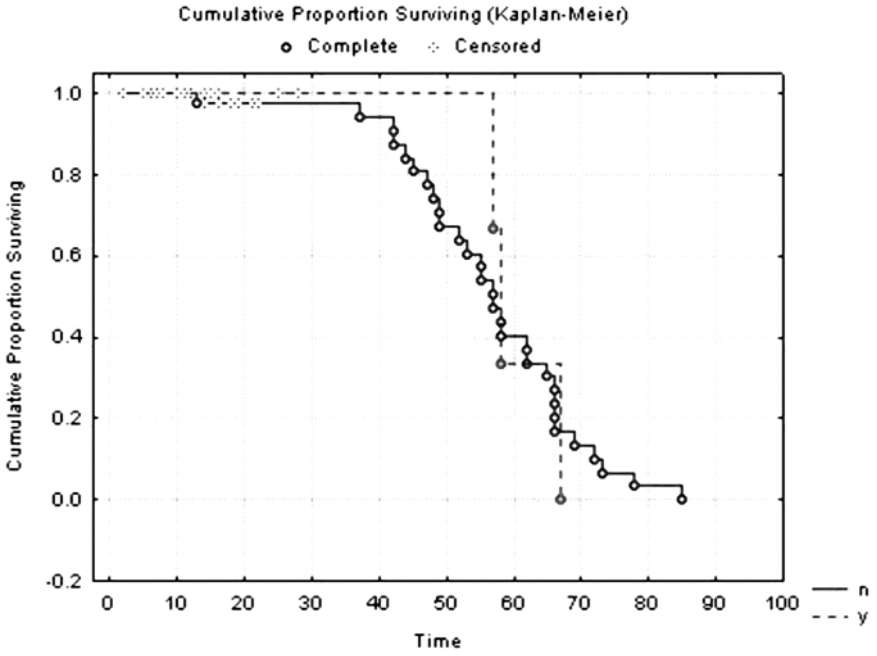

Figure 9. *Kaplan-Meier survival curves comparing individual histologies*

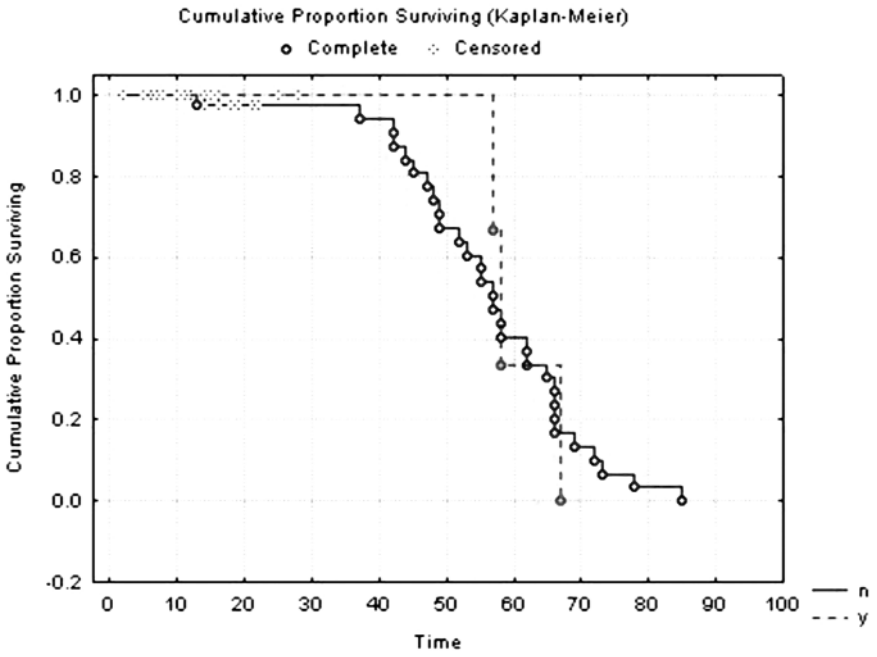

Figure 10. *Kaplan-Meier survival curves comparing patients with no orbital involvement with cases with orbital invasion*

outcomes. In our series, the 5-year survival is 47%, which compares favorably with other reported series: 58% Shah et al. (3), 69% Jackson et al. (5), 44% Lund et al (7), 74% Janecka et al (4).

Tumor histological diagnosis plays a major role in treatment outcome. Survival is the highest for patients with estesioneuroblastoma and chondrosarcoma, similar to other published series (3,7,8). The natural history and surgical pathology of esthesioneuroblastoma would suggest that it is a tumor for which craniofacial resection is the optimum approach. Levine et al. (8) found an actuarial survival of 90% at (5) years for these patients, and similar figures were reported by other authors: 78% at 5 years Eden et al. (9), 65% Lund et al (7). Chondrosarcoma has an ostensibly high actuarial survival rate, although some authors caution against its creeping characteristics across the skull base leading to repeated surgical procedures (7). Survival rates for patients with squamous cell carcinoma of the sinonasal tract and adenocarcinoma are comparable. Survival is poor for patients with adenoid cystic carcinoma and mucosal melanoma. The well known propensity for adenoid cystic tumors to spread insidiously along nerve sheaths and other structures makes microscopic tumor-free margin an unrealistic expectation, and

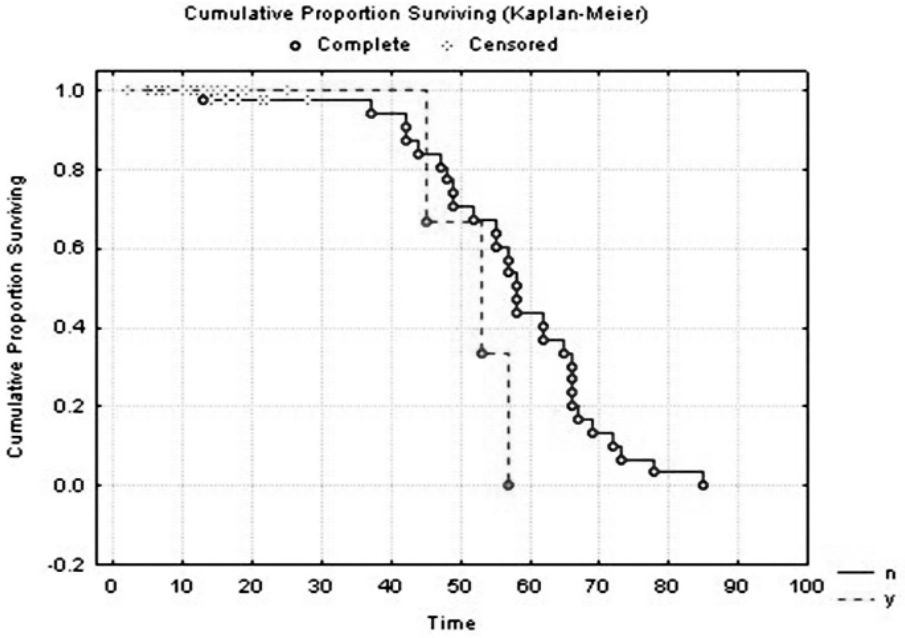

Figure 11. *Kaplan-Meier survival curves comparing patients with dural invasion with cases without dural involvement*

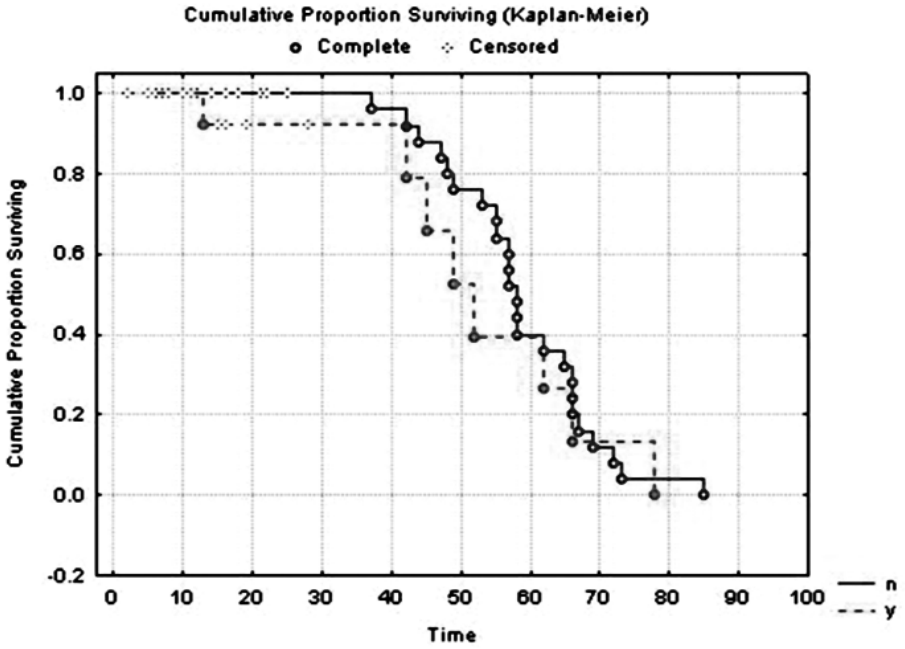

Figure 12. *Kaplan-Meier survival curves comparing patients with positive margins with patients with negative margins*

patients remain at high risk of developing disseminated disease. Mucosal melanoma has the lowest survival of all diagnoses in accordance with other published series (3,4).

A number of papers report dural invasion being a predictor of survival (3,7,10,11). In our cohort, dural invasion is statistically significant associated with decreased survival. Kraus et al. (10) noted long-term survival in 83% of patients with no dural involvement from ethmoid carcinoma and in 14% of cases with dural invasion undergoing craniofacial resection. Similar results were described by other authors (7,12). In contrast, Bohrer at al. (13), Richtsmeier et al. (14) and McCaffrey et al. (15) noted no difference in survival when comparing patients with and without dural involvement.

Orbital invasion also appears to be a significant factor influencing survival. In the current series, patients requiring orbital clearance had a statistical reduction in survival rates compared to those without orbital involvement. Ketcham et al. (1) reported 30% survival in patients with orbit preservation and 50% in those with orbital exenteration and concluded that the orbit should be resected if directly involved by tumor. By contrast, most authors have reported poorer figures in those patients requiring orbital clearance compared with those who

did not (3,4,7,10,12). Clearly, orbital resection becomes a necessity in patients with tumor invasion of the orbit. The reduced survival in patients requiring orbital clearance is a reflection of more advanced disease.

Interpretation of histological margins must be performed with care. After the craniofacial resection is complete, mucosa, soft tissue and bone is sampled from the periphery of the resected site and submitted for histopathologic evaluation. No attempt is made to perform additional resection even if positive margins are described. Microscopic invasion of the margins are addressed with postoperative radiation therapy. Because it is difficult to interpret margin status in a three dimensional, partially air-filled structure, it has been suggested that all patients should receive postoperative radiotherapy. The only patients who are not considered for postoperative radiation therapy are those who were previously treated with radiotherapy.

The role of craniofacial resection as a salvage procedure is a matter of controversy. In our series there was no difference in comparing survival rates in patients undergoing salvage surgery as compared with those undergoing primary treatment. Ketcham et al. (1) and Shah et al. (3) also noted similar survival between those groups. Conversely, Jackson et al. (5) and Janecka et al. (4) noted improved survival in the previously untreated group. Further studies, on large groups are required to solve this issue.

Conclusions

This series confirms that craniofacial resection offers acceptable long-term survival for patients with malignant tumors of the anterior skull base and where the extent of disease at presentation precludes cure, the operation offers excellent palliation. A major emphasis needs to be placed on the development of a standard methodology of reporting results in these patients to allow for meaningful comparison and to facilitate future development of multicenter trials.

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