



Value of anatomic site, histology and clinicopathological parameters for prediction of lymph node metastasis and overall survival in head and neck melanomas



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ABSTRACT

Introduction: Head and neck melanoma comprises a group of aggressive tumours with varying clinical courses. This analysis was performed to find anatomic and clinicopathological parameters predictive for lymph node metastasis and overall survival.

Material and methods: Data and outcome of 246 patients with a malignant melanoma in the head and neck region were retrospectively analyzed for predictive parameters.

Results: Lentigo maligna melanoma ($n = 115$) was the most frequent histology, followed by superficial spreading ($n = 63$) and nodular melanoma ($n = 52$). More than half of the melanomas ($n = 138$) were in the face. Tumours of the face and anterior scalp metastasized to lymph nodes of the neck and parotid gland, whereas tumours of the posterior scalp and neck also metastasized to the nuchal region. Advanced Clark level, presence of tumour ulceration and younger age were the strongest predictors of lymph node metastasis in multivariate regression analysis ($p < 0.05$), but anatomic site, histological subtype and tumour thickness were also associated with lymph node metastasis. Lymph node metastases, distant metastases, ulceration, nodular subtype and non-facial site of origin were the strongest negative prognostic parameters for disease-specific overall survival ($p < 0.05$). In contrast, the width of resection margin (<1 cm vs. $1-2$ cm vs. >2 cm) did not correlate with tumour recurrence and overall survival ($p > 0.05$).

Conclusion: Histological subtype diagnosis, anatomic site of origin as well as the established factors tumour thickness, ulceration and depth of invasion are prognostic indicators of cervical lymph node metastasis and overall survival. A resection margin of at least 1 cm seems sufficient in head and neck melanoma. The status of sentinel lymph node biopsy and neck dissection has to be proven within the next years.

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1. Introduction

Malignant melanoma of the skin is a rare but often aggressive cancer. Primary melanomas arising in the head neck region are reported to have a worse prognosis than those originating elsewhere (Callender et al., 2011; Thorn et al., 1989). Some prognostic

factors, such as age, sex, Breslow tumour depth, Clark level, regional lymph and distant metastases have been reported in the literature (Balch et al., 1978; Huvos et al., 1974). The prognostic importance of tumour localization in the head neck area is not quite clear.

As mentioned above cervical lymph node metastases and distant metastases are a major negative predictor for long-term survival. Sentinel lymph node biopsy represents a staging procedure which should identify patients at risk of occult neck node metastases. However sentinel lymph node biopsy might be especially challenging in the head neck region due to the course of cranial nerves and variable lymphatic drainage patterns (Willis and

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Ridge, 2007). The extent of a neck dissection might be unclear as pre-surgical prediction of involved neck node levels is difficult for certain primary melanoma sites (Uren et al., 2003).

Complete surgical excision of a localized cutaneous melanoma is a key parameter for survival of the patient. Traditionally wide resection margins of more than 4 cm have been performed for melanoma. However, more recently resection margins have been reduced as studies have shown that smaller margins do not reduce overall survival (Gillgren et al., 2011; Kaufmann, 2000; Thomas et al., 2004).

2. Material and methods

2.1. Patients and therapy

The retrospective study comprises 246 patients with a malignant melanoma of the head and neck region who were treated between 1998 and 2011 at the departments of dermatology, otorhinolaryngology and oral and maxillofacial surgery of the University Hospital of Regensburg. Clinical data were obtained from the charts, the hospital data base system SAP® (Systemanalyse und Programmentwicklung) and the tumour registries.

Table 1 presents the subtypes and primary localization of the tumours. 7 tumours were mucosal melanomas (3 palate, 2 lip and 2 maxillary sinus). Final histological diagnosis was established after excision of the complete primary melanoma. Small lesions suspicious for melanoma were initially totally excised with small excision margins. For larger lesions or when the tumour was localized in critical facial areas, an incisional biopsy was performed prior to radical excision of the melanoma.

The study cohort comprised 102 male and 144 female patients with a mean age of 66.7 (range 25–96) years. 241 Patients had local tumour resections, in 29 cases accompanied by a single neck dissection. In 31 cases tumour resection was combined with a neck dissection and a partial or total parotidectomy. For defect reconstruction primary closure, skin graft and adjacent tissue transfer were the most common procedures. In most cases defect reconstruction was performed in a second procedure after certainty of tumour-free resection margins.

Pre-surgically, all patients were staged by full-body computed tomography and sonography of the neck, in some cases magnetic resonance tomography or positron emission tomography–computed tomography (PET–CT) was added. Neck dissection ($n = 60$) was performed when pre-surgical imaging was suspicious for lymph node metastasis (therapeutic neck dissection) or in cases with advanced tumour thickness and increased Clark level, although staging did not show any suspicious lymph nodes (elective neck dissection). Technically, neck dissection was mainly carried out as a selective neck dissection or a modified radical neck dissection. Radical neck dissection was only performed in two cases. Patients with tumours localized in the face, the anterior scalp or the ear received a neck dissection of at least levels I–IV, in cases

with nodal involvement level I–V were removed. In patients with posterior primaries level I was often preserved, whereas lymph nodes of the nuchal area were dissected.

Sentinel lymph node biopsy (lymphoscintigraphy with ^{99m}Tc -Nanocoll) has been introduced at our clinic recently, but, case numbers are still low and this technique was therefore not evaluated in the present study.

27 out of 235 patients with positive resection margins (R1, R2) of the primary tumour, desmoplastic melanomas or advanced lymph node metastasis (N2, N3) received adjuvant radiotherapy with a mean dose of 53.8 Gy (range 30–70). 48 out of 233 patients presented with a tumour stage of IIB or higher received adjuvant interferon therapy (3×3 IE per week).

All patients were staged according to UICC TNM criteria of 2009 (7th edition) (Sobin et al., 2009). Pathological TNM-stage was decisive. When pathological classification was not available (e.g. distant metastases, no neck dissection performed), clinical TNM-classification, e.g. cN0 or cM0 was used.

The mean follow-up period of all patients was 4.5 years (range 0.3–16.3) and was measured from date of histopathological diagnosis until death or end of follow-up. Both overall survival (OS) and disease-specific survival (DSS) were recorded. Moreover, recurrence-free survival (RFS) was documented from date of histological diagnosis until date of recurrence.

2.2. Statistics

Data were analyzed with SPSS for Windows, version 20.0 (SPSS, IBM, Ehningen, Germany). Relationships between parameters were examined using the Pearson's chi-square test ($p < 0.05$) and the Fisher's exact probability test ($p < 0.05$) for dichotomised variables. Univariate survival curves were calculated with the Kaplan–Meier method, distributions were compared by means of the log-rank test. Cox proportional hazards model (enter method) was used in multivariate analyses. Multivariate logistic regression analysis was conducted (enter method) to determine the effect of predictor variables on regional lymph node and distant metastases.

3. Results

56.1% of the melanomas (138/246) were diagnosed in the facial skin (see Table 1), in detail 83 (60.1%) in the cheek region, 31 (22.5%) in the frontal area, 16 (11.6%) on the nose, 5 (3.6%) in the lid area and 3 melanomas elsewhere. Lentigo maligna melanoma was the most frequent histology ($n = 115$, 46.7%), followed by superficial spreading melanoma ($n = 63$, 25.6%), nodular melanoma ($n = 52$, 21.1%), desmoplastic melanoma ($n = 8$, 3.3%), mucosal melanoma ($n = 7$, 2.8%) and one malignant spitzoid naevus ($n = 1$, 0.4%). Lentigo maligna melanoma was predominantly (83.5%) found in the facial area, whereas superficial spreading and nodular melanoma were more often (69.8% and 65.4% respectively) detected in other head and neck regions ($p < 0.001$).

Table 1
Histological subtype and localization of melanoma.

Subtype ($n = 246$)	Anatomic site					Total
	Face	Scalp	Ear	Neck	Mucosa	
Lentigo maligna	96 (83.5%)	11 (9.6%)	7 (6.1%)	1 (0.9%)		115 (46.7%)
Superficial spreading	19 (30.2%)	19 (30.2%)	15 (23.8%)	10 (15.9%)		63 (25.6%)
Nodular	18 (34.6%)	14 (26.9%)	13 (25.0%)	7 (13.5%)		52 (21.1%)
Desmoplastic	5 (62.5%)	2 (25.0%)	1 (12.5%)			8 (3.3%)
Malignant spitz				1 (100%)		1 (0.4%)
Mucosal					7 (100%)	7 (2.8%)
Total	138 (56.1%)	46 (18.7%)	36 (14.6%)	19 (7.7%)	7 (2.8%)	246

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