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Cytology and histology have limited added value in prognostic models for salivary gland carcinomas

Marc P. van der Schroeff [a,*], Chris H.J. Terhaard [b], Marjan H. Wieringa [a], Frank R. Datema [a], Robert J. Baatenburg de Jong [a]

[a] Department of Otorhinolaryngology, Head and Neck Surgery, Erasmus Medical Center, Rotterdam, The Netherlands
[b] Department of Radiation Oncology, University Medical Center Utrecht, Utrecht, The Netherlands

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SUMMARY

Univariate analyses on malignant salivary gland tumors report a strong relation of histological subtypes and prognosis. However, multivariate analyses with sufficient patients and reflecting the broad spectrum of putative prognostic factors are rare.

In order to study the prognostic value of cytology and histology in salivary carcinoma we performed multivariate analyses on 666 newly diagnosed patients.

In multivariate analyses sex, tumor size, N- and M-staging, localization, comorbidity, skin involvement and pain were independent predictors of survival. Histology was an independent prognostic factor, mainly because acinic cell carcinoma acted differently from the other histological subtypes. However, a simple prognostic model without cytology and/or histology has similar predictive power compared to more elaborate models.

The added prognostic value of cytology and/or histology factors in salivary carcinoma is limited, largely due to the combined prognostic value of other prognostic factors such as tumor size, N- and M-classification and comorbidity.

Introduction

Malignant salivary gland tumors are rare (1–3% of all head and neck cancers), histological and biological diverse neoplasm's. Reportedly, this diverse group of tumors has variable outcomes with respect to different measures of survival, such as disease free survival and overall survival. Probably because of its rarity, there are no published prospective studies available. In general, its insidious clinical course necessitates studies with long follow up. Known important prognostic risk factors are stage[1–7] and positive cervical lymph nodes.[4,7–12]

The histopathological diversity of malignant salivary gland tumors and its relation to prognosis has been subject to relatively few retrospective studies. Van der Poorten et al.[11] and Carrillo et al.[13] investigated the prognostic value of various possible prognostic factors in parotid tumors including histopathology in prognostic models on disease free survival, and in both studies histopathology did not seem to be relevant as it was not incorporated in the final models.

The aim of this study is to perform multivariate analyses on a broad range of putative prognostic factors available, and to look at the prognostic value of cytology and histology in particular. We constructed prognostic models based on relevant prognostic factors to aid the clinician in decision making and counseling. We used overall survival as prognostic endpoint, because this, in our view, represents the most relevant entity at the time of diagnosis and initial treatment for individual patients.

Patients and methods

Based on a dataset of the Dutch Head and Neck Cooperative Group (NWHHT) concerning salivary gland cancer general results,[14] the role of radiotherapy,[15] and the importance of facial nerve palsy in parotid cancer[16] have already been published.

We performed an update of the database of the NWHHT concerning salivary gland cancer from all subsites, including the variable comorbidity, and including the results of all eight tertiary referral centers in The Netherlands. The database has been extended to 666 cases treated between 1985 and 1994. Median follow-up time of patients alive at the last follow-up is 125 months. Clinical characteristics and analysis of disease free survival have been reported recently.[17]

* Corresponding author. Address: Department of Otorhinolaryngology, Head and Neck Surgery, Erasmus Medical Center, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands. Tel.: +31 107033106; fax: +31 107033102.
E-mail address: m.vanderschroeff@erasmusmc.nl (M.P. van der Schroeff).

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Table 1
Multivariate analysis (cox proportional hazards model) in model A, B and C. Presented hazard ratios (HR) are used to build the prognostic models.

	N (%)	Analysis A (model A)		Analysis B (model B)		Analysis C (model C)	
		HR	95% CI	HR	95% CI	HR	95% CI
Sex							
Female (referent)	323 (49%)						
Male	343 (51%)	1.4	1.2–1.7	1.4	1.2–1.7	1.4	1.2–1.6
Missing	0						
Age (continuous. mean 59 years)	666	1.0	1.0–1.0	1.0	1.0–1.0	1.0	1.0–1.0
Missing	0						
Tumor size							
<2 cm (referent)	134 (20%)						
2–4 cm	225 (34%)	1.1	0.8–1.4	1.1	0.8–1.4	1.1	0.7–1.4
4–6 cm	125 (19%)	1.2	0.8–1.5	1.2	0.8–1.5	1.2	0.9–1.6
>6 cm	73 (11%)	2.0	1.6–2.4	2.0	1.6–2.4	1.5	1.1–1.9
Missing	109 (16%)						
N-classification							
N0 (referent)	555 (83%)						
N1	31 (5%)	1.3	0.9–1.8	1.3	0.8–1.8	1.2	0.7–1.7
N2	59 (9%)	2.2	1.9–2.5	2.0	1.7–2.4	1.8	1.5–2.1
N3	7 (1%)	3.6	2.8–4.3	3.1	2.4–3.9	1.6	0.8–2.4
Missing	14 (2%)						
M-classification							
M0 (referent)	638 (96%)						
M1	25 (3%)	4.4	3.9–4.9	4.6	4.1–5.1	2.8	2.3–3.4
Missing	3 (1%)						
Localization							
Gl. parotis (referent)	372 (56%)						
Gl. submandibularis	86 (13%)	1.1	0.8–1.4	1.2	0.8–1.5	1.2	0.8–1.5
Accessory glands; mouth	175 (26%)	0.6	0.3–0.9	0.6	0.3–1.0	0.6	0.3–1.0
Accessory glands; other	33 (5%)	0.9	0.4–1.3	0.9	0.4–1.4	0.6	0.1–1.2
Missing	0						
ACE-27							
ACE-27 0 (referent)	394 (59%)						
ACE-27 1	119 (18%)	1.4	1.1–1.6	1.3	1.0–1.6	1.3	1.0–1.6
ACE-27 2	71 (11%)	1.6	1.3–1.9	1.7	1.3–2.0	1.7	1.4–2.0
ACE-27 3	29 (4%)	1.9	1.5–2.4	2.0	1.5–2.5	1.9	1.5–2.4
Missing	53 (8%)						
Skin involvement							
No (referent)	594 (89%)						
Yes	46 (7%)	1.7	1.4–2.1	1.7	1.3–2.1	1.5	1.2–1.9
Missing	26 (4%)						
Pain							
No (referent)	465 (70%)						
Yes	169 (25%)	1.7	1.5–1.9	1.8	1.5–2.0	1.8	1.5–2.0
Missing	32 (5%)						
Cytology							
Acinic cell ca. (referent)	27 (4%)						
Mucoepidermoid ca.	21 (3%)			1.0	0.4–1.6		
Adenoid cystic ca.	46 (7%)			0.9	0.4–1.4		
Adeno ca.	74 (11%)			1.3	0.8–1.8		
Squamous cell ca.	20 (3%)			1.0	0.4–1.6		
Undifferentiated	27 (4%)			1.1	0.5–1.6		
Other	68 (10%)			1.0	0.5–1.5		
Not malignant	39 (6%)			0.9	0.3–1.4		
Missing	344 (52%)						
Treatment							
Surgery (referent)	141 (21%)						
Surgery and radiotherapy	444 (67%)					1.1	0.8–1.5
Radiotherapy and/or chemotherapy	47 (7%)					3.1	2.6–3.6
No therapy	34 (5%)					3.4	2.9–4.0
Missing	0						
Histology							
Acinic cell ca. (referent)	91 (14%)						
Mucoepidermoid ca.	105 (16%)					2.1	1.6–2.6
Adenoid cystic ca.	181 (27%)					1.7	1.2–2.2
Adeno ca.	140 (21%)					2.5	2.0–3.0
Carcinoma ex-pleomorfic adenoma	55 (8%)					2.1	1.5–2.6
Squamous cell ca.	34 (5%)					2.4	1.8–3.0
Undifferentiated	44 (7%)					2.8	2.2–3.3
Missing	16 (2%)						