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Oncological outcome and prognostic factors in malignant parotid tumours

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ABSTRACT

Objective: To evaluate the oncological outcome of malignant parotid tumours and identify the prognostic factors for survival.
Study design: Retrospective study.
Methods: One hundred and forty-one patients with primary epithelial carcinoma of the parotid gland were examined. The overall survival (OS) and disease specific survival (DSS) rates were calculated. The DSS was evaluated according to different parameters.
Results: The 5- and 10-year OS rates were 72.3% and 58.4%. The 5- and 10-year DSS rate was 75% and 71%, respectively. The univariate analysis showed that the pathological staging, clinical and pathological tumour and nodal status, surgical procedure and histological subtype significantly influenced the DSS ($P \leq 0.05$). The 5- and 10-year loco-regional control rates were 82.1% and 78%. The multivariate analysis showed that the pathological nodal status and the pathological staging influenced the DSS. It further demonstrated that the clinical tumour status and the histological subtype were the most important preoperative prognostic factors.
Conclusion: The pathological nodal status, the pathological staging, the clinical tumour status and the histological subtype are the most important factors influencing survival in malignant parotid tumours.

1. Introduction

Parotid malignant neoplasms represent 0.3% of all human cancers (Bron et al., 2003) and 1–3% of all head and neck malignancies (Lima et al., 2005). The low incidence of malignant parotid tumours and the heterogeneity of the histological types are the main problems emerging when evaluating the oncologic outcome and assessing the impact of different prognostic factors (Mommaerts et al., 2012; Lukšić et al., 2012). Furthermore, different factors that do not facilitate the analysis of the results thus rendering it particularly challenging include: surgical procedures on primary tumour and regional nodes, the use of adjuvant therapy, the small number of cases treated in each institution and the different natural history of the multitude of histological subtypes.

Surgery is the primary treatment for almost all parotid malignancies, particularly regarding small tumours carrying better prognosis. More advanced diseases may require the use of adjuvant therapy due to the size or aggressiveness of the tumour (Armstrong et al., 1990; North et al., 1990; Garden et al., 1997; Terhaard et al., 2005 and Mendenhall et al., 2005). The aim of the present study was to evaluate the disease specific survival rate of malignant parotid tumours and to identify the prognostic factors for survival, influenced by disease management.

2. Materials and methods

From January 1997 to December 2009, 141 consecutive patients diagnosed with primary epithelial carcinoma of the parotid gland were treated at our Institution. The clinical records of all cases were retrospectively reviewed and reclassified where necessary, using the 2005 WHO histological classification for salivary gland tumours (Barnes et al., 2005) and TNM staging system (7th Edition 2009) (Sobin et al., 2009). All histology slides underwent independent review by two pathologists who reached a consensus on the diagnosis.

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Variables related to patient (age, gender), tumour (size, localization, preoperative facial palsy), clinical and pathological classification of tumour (cT, pT), lymph nodes (cN, pN), final histology, lymph node extracapsular spread (ECS), pathological stage and treatment (type of surgery, adjuvant radiotherapy (RT)) were evaluated and collected.

The study was approved by the local ethics committee. All patients were previously discussed in the Head Neck Disease Management Team of the Institution and unanimous consensus on the treatment was reached.

All patients underwent ultrasonography of the parotid and neck region combined with fine-needle aspiration cytology of parotid neoplasms and suspected lymph nodes before surgery. Further examination was performed on suspected deep lobe involvement, infiltration of the surrounding tissues and lymph node metastasis.

Surgery on the parotid gland consisted mainly of: superficial parotidectomy (excision of the gland superficial to the facial nerve), total parotidectomy, completion parotidectomy (operation following a previous parotidectomy less than total), or extended total parotidectomy (operation including the removal of the entire parotid gland, with sacrifice of the facial nerve and the resection en bloc of the adjacent structures affected by neoplastic infiltration). Surgical treatment on the neck consisted mainly of: selective neck dissection (ND) (levels I–III) (Robbins et al., 1991), in case of high grade or ≥T3 stage tumours without evidence of nodal metastases, modified radical ND (levels I–V) (Robbins et al., 1991) for clinical lymph node metastasis (diameter ≤3 cm) or in case of positive subdigastric lymph node frozen section performed during surgery, or radical ND (levels I–V) for nodal metastasis >3 cm or nodal infiltration to adjacent structures.

Adjuvant RT was considered for high grade tumours, facial nerve invasion, extraparenchymal extension, close or positive resection margins, tumour size ≥4 cm, lymph node metastasis (Barnes et al., 2005 and Walvekar et al., 2011), in accordance with the NCCN guidelines for Head and Neck Cancers (Pfister et al., 2000).

Chemotherapy was used in association with RT in the few cases of massive nodal involvement.

Patients who underwent previous incomplete surgical procedures without clear margins and without clinical evidence of persistent disease, were considered according to their initial operative staging and pathology report. The statistical analysis considered the completion parotidectomy as a total parotidectomy because of the complete removal of the parotid gland.

Statistical analysis of the clinical and pathological tumour status was performed by grouping T1 with T2 cases, and T3 with T4 cases in order to avoid dispersing data. Similarly, the group of patients with clinical or pathological lymph node metastases (N1-3) were considered as a single group (cN1-3 or pN1-3) and compared to cN0 or pN0 cases. To prevent dispersal of data the number, size, and neck level were not analysed.

For all patients, the 5- and 10-year rates for overall survival (OS), disease specific survival (DSS), local control and distant metastasis-free were calculated. The DSS rate according to each of the variables was analysed. The variables evaluated were: age (≥50 vs. <50 years); gender (male vs. female), facial palsy (yes vs. no), cT (cT1-2 vs. cT3-4), cN (cN0 vs. cN1-3), pT (pT1-2 vs. pT3-4), pN (pN0 vs. pN1-3), lymph node ECS (yes vs. no), pathological stage group (I–II vs. III–IV), type of surgery (extended vs. superficial parotidectomy; total vs. superficial parotidectomy), histology (high vs. low grade), extraparenchymal extension (present vs. absent), adjuvant RT (yes vs. no). The DSS of two groups were compared including different histological subtypes of parotid carcinoma depending on their biological behaviour: low grade (acinic cell carcinoma, low grade mucoepidermoid carcinoma, basal cell adenocarcinoma, low grade adenocarcinoma and carcinoma ex pleomorphic adenoma) and high grade (lymphoepithelial carcinoma, high grade mucoepidermoid carcinoma, adenoid cystic carcinoma, undifferentiated carcinoma, ductal carcinoma, squamous cell carcinoma, salivary duct carcinoma and high grade adenocarcinoma) malignancies (Matsuba et al., 1985; Gallo et al., 1997 and Magnano et al., 1999). Patients with intra-parotid secondary metastases from cutaneous or mucosal malignancies and lymphoma were excluded from the study.

The univariate analysis revealed the difference between the DSS of the different variables. All the variables considered significant in the univariate analysis were performed in the multivariate analysis. The statistical analysis was carried out using SPSS version 17.0 statistical software. The survival curves were calculated by a Kaplan–Meier method and compared to the Log Rank Test. The univariate and multivariate analyses were developed by the Cox multiple regression model. The cut-off *P*-value was set at 0.05. Results of the multivariate analysis are reported as a hazard ratio (HR) with a 95% confidence interval (CI).

3. Results

The study group was composed of 141 patients: 75 male and 66 female. The median age was 62 years (range 9–89 years). The

Table 1
Demographic, clinical, histological characteristics and treatment of 141 patients. (c: clinical; p: pathological; T: tumour stage; N: lymph node stage, ECS: extracapsular spread).

	n.	%
Gender		
Male	75	53.2
Female	66	46.8
Localization		
Superficial lobe	93	65.9
Deep lobe	19	13.5
Superficial lobe + deep lobe	23	16.3
Parapharyngeal space	6	4.3
Size		
≤2 cm	50	35.5
2–3.9 cm	64	45.4
4–5.9 cm	22	15.6
≥6 cm	5	3.5
Preoperative facial palsy		
No	124	87.9
Yes	17	12.1
cT		
1	46	32.6
2	50	35.5
3	18	12.8
4	27	19.1
cN		
0	113	80.1
1–3	28	19.9
pT		
1	53	37.6
2	44	31.2
3	17	12.1
4	27	19.1
pN		
0	35	24.8
1–3	34	24.1
None	72	51.1
Lymph node ECS		
Yes	11	7.8
No	23	16.3
Stage grouping		
I	36	25.5
II	39	27.7
III	13	9.2
IVa	51	36.9
IVb	1	0.7
Total patients	**141**	**100**