## Abstract:

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**Design, setting, participants**

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**Main outcome measure**

The main outcome measure was the incidence of metastatic disease.

**Results**

54 of the 82 cases identified underwent a neck dissection. Nodal metastases were detected in 10 cases of carcinomas ex-pleomorphic adenoma (high grade, invasive), 2 salivary duct carcinomas, 1 adenocarcinoma not otherwise specified (NOS) (high grade), 1 adenoid cystic carcinoma and 1 acinic cell carcinoma (high grade). No metastases were found in cases of acinic cell carcinoma (low grade), mucoepidermoid carcinoma (low grade), epithelial-myoepithelial carcinoma and non-invasive carcinoma ex-pleomorphic adenoma.

**Conclusions**

The findings of this study support the use of routine neck dissection in treating carcinoma ex-pleomorphic adenoma (high grade, invasive), salivary duct carcinoma, adenocarcinoma NOS (high grade), adenoid cystic carcinoma and acinic cell carcinoma (high grade).
The utility of neck dissection in managing carcinomas of the parotid gland.

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Conflict of Interest Statement

The authors have no conflicts of interest
The utility of neck dissection in managing carcinomas of the parotid gland

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Keywords: Parotid, carcinoma, neck, dissection, lymph, node, prognosis

Introduction

Salivary gland carcinoma is a rare disease and cases arise within any of the three major glands or the minor glands. The parotid gland remains the most common site for newly diagnosed major salivary gland cancer within the population of England and its incidence has
risen from 0.4 to 0.6 per 100,000 persons between 1994 to 2013. This rarity combined with the varied entities, behaviour types and location within in minor glands as well as major glands, has limited the construction of an evidence base to support treatment modalities. Study of the United States National Cancer Data Base 1998-2012 showed the presence of lymph node metastases to be associated with high T stage and high grade of malignancy. Higher grade and the presence of metastatic disease were associated with worse prognosis. This finding is supported by other US studies. Data from UK populations is limited. The aim of this study was to determine the frequency with which neck dissection is undertaken for parotid carcinoma within a London hospital and to validate the use of neck dissection by determining the incidence of cervical lymph node metastasis.

**Materials and Methods**

Ethical consideration: This is a retrospective validation study for the use of neck dissection in management of parotid carcinoma. There were no interventions made on human or animal subjects. To validate the use of neck dissection in treating carcinoma of the parotid gland, the Guy’s and St Thomas’ Hospital, Oral and Head and Neck pathology database was searched for patients who underwent primary resection of parotid carcinoma within the Head and Neck Unit between 1992 and 2014. Pathological data was retrieved from text reports. Further, clinical information was retrieved from the Trust’s electronic patient record system. One case was excluded as it was not possible to determine the T stage. Intra- and peri-parotid lymph nodes were included with level II. Statistical analysis was by Welch’s t-test using GraphPad Prism software. Mucoepidermoid carcinomas were graded according to the system published by Brandwein *et al.* Staging was according to UICC 7th edition. Patients were discussed at head and neck oncology multi disciplinary team meeting from 2007.
Results

*Histological types of parotid carcinoma and patient demographics.*

The patient group comprised 82 persons, 42 women and 40 men. Ages ranged from 10 to 84 years with a median value of 57 years.

The five most frequent histological types of primary parotid carcinoma were high grade invasive carcinoma ex-pleomorphic adenoma (16), low grade acinic cell carcinoma (14), low grade mucoepidermoid carcinoma (8), adenoid cystic carcinoma (7) and non-invasive (intracapsular) carcinoma ex-pleomorphic adenoma (6). Less common pathology types (5 or less cases) included high grade acinic cell, high grade adenocarcinoma, basal cell adenocarcinoma, invasive low grade carcinoma ex-pleomorphic adenoma, carcinosarcoma ex-pleomorphic adenoma, low grade cystadenocarcinoma, epithelial/myoepithelial, low grade salivary carcinoma NOS, intermediate and high grade mucoepidermoid, low grade myoepithelial, high grade salivary duct carcinoma, low grade secretory carcinoma.

*Treatment modalities*

Fifty four cases underwent a neck dissection and 28 cases did not. In one of the cases that did not receive a neck dissection, a record of the preoperative diagnosis was not available.

In 21 of the cases that did not undergo neck dissection, the preoperative fine needle aspiration cytology result was equivocal or incorrectly benign. For the other cases that did not receive neck dissection, the preoperative diagnosis was acinic cell carcinoma in two cases, mucoepidermoid carcinoma in three cases and carcinoma ex-pleomorphic adenoma in one case. Forty three of the 54 cases that underwent neck dissection had a pre-operative diagnosis of carcinoma. Seven cases had a pre-operative diagnosis that was suspicious of malignancy and 1 case had a pre-operative diagnosis of benign pleomorphic adenoma but with an associated enlarged lymph node that although benign on fine needle aspiration cytology was excised as part of a neck dissection limited to level II. A pre-operative diagnosis could not be located for 3 cases that underwent neck dissection.
Nineteen cases did not receive radiotherapy. In 6 cases information was not available relating to provision of radiotherapy for reasons including continued care at other centres. In 1 case the patient had undergone radiotherapy for a separate tonsil squamous cell carcinoma (diagnosed 8 months previously). All cases that did not receive radiotherapy were N0 and T1, 2 or 3 low grade carcinomas. In one T2N0 non invasive carcinoma ex-pleomorphic adenoma, tumour was present at the margin. However, this area of the tumour was composed of a histologically benign pleomorphic adenoma element. In a T3N0 secretory carcinoma, the margin status could not be determined. In all other cases, carcinoma was excised by 0.1 to 1mm. No perineural invasion or lymphovascular spread was recorded in the cases that did no received radiotherapy.

Outcome of neck dissection

Histological types, T stage and patient demographics

For patients that underwent neck dissection, the final staging is given in table 1. Lymph node metastases arose from 10 out of 14 carcinoma ex-pleomorphic adenomas (invasive, high grade), the only case of carcinosarcoma ex-pleomorphic adenoma and 2 of 4 salivary duct carcinomas. Lymph node metastases occurred in 1 of 2 cases of high grade acinic cell carcinoma, 1 of 6 adenoid cystic carcinomas and 1 of 3 high grade adenocarcinomas NOS (table 1).

Combining all histological types for cases that underwent a neck dissection, the carcinomas with and without lymph node metastases did not differ significantly for age or T stage (p>0.05).

Examining invasive high grade carcinoma ex-pleomorphic adenomas only, all cases without lymph node metastases were T2. Cases showing metastases were T2, T3 or T4a. Univariate analysis showed a higher T stage was significantly associated with lymph node metastases (p=0.007). There was no significant difference in patient age between cases with metastases and those without (p>0.05). Case numbers for other histological types of carcinoma were insufficient to allow univariate or multivariate analysis.
Site and number of lymph node metastases

The neck dissections included level I in 22 cases, level II in 52 cases, level III in 33 cases, level IV in 20 cases and level V in 11 cases (for 2 neck dissection patients there was insufficient information regarding levels). All cases with lymph node metastases showed involved nodes within level II. Metastases were present at levels I, II, III, IV and V in 3, 16, 2, 2 and 1 of neck dissection cases respectively.

With the exception of three cases, the recorded involved levels were anatomically sequential. Two of these exceptions showed involved lymph nodes at level II and IV. The other exception showed involved lymph nodes at level II and V.

In cases with lymph node metastases, the number of involved lymph nodes ranged from 1-34 with mean and median values of 6.0 and 3.5 respectively. All but one case had 11 or fewer involved lymph nodes. This highly metastatic carcinoma produced metastases in 34 lymph nodes. The patient was a male in this 6th decade and the tumour was a high grade T4aN2b carcinoma ex-pleomorphic adenoma.

Frequency of occult lymph node metastases

Eight of the 16 patients showing lymph node metastases were preoperatively diagnosed as having nodal disease. Metastases were occult in 8 patients all of whom received some form of preoperative imaging. In all but one case there was a record of a preoperative CT and this patient had undergone an MRI and ultrasound examination.

Follow up

Cases that did receive radiotherapy

Fifty-nine cases received radiotherapy for the treatment of the parotid carcinoma. In one case a patient received radiotherapy for a separate head and neck primary carcinoma. In 5 cases it could not be determined from the data available whether radiotherapy was provided. Among the 59 cases in which radiotherapy was provided, there were 13 deaths. Nine of these deaths were the result of the parotid carcinoma and all of these patients received neck
dissections (details are provided in the neck dissection section). One death was from an unrelated cause and for two deaths a record of the cause could not be found (these patients did receive a neck dissection and these deaths are included in that section). There was one death of a patient who had received post-operative radiotherapy but not a neck dissection (details are provided in the no neck dissection section), the cause of this death could not be determined. One patient who received post-operative radiotherapy for a pT4bN0 high grade acinic cell carcinoma developed pulmonary metastases (this patient did receive a neck dissection and this morbidity is included in that section). There was no further morbidity or mortality. Follow up time for this group ranged from 0.23-142.1 months with mean and median values of 44.1 and 30.1 months, respectively.

**Cases that did not receive radiotherapy**

Among the 19 cases that did not receive radiotherapy, follow up data was available for all but one case. There was one death from an unrelated lung adenocarcinoma (this patient did receive a neck dissection and this death is also included in that section). Follow up time range from 1.2-70.2 months with mean and median values of 32.1 and 30.1 months, respectively. There were no recurrences, metastases or disease specific deaths.

**Cases that did not receive a neck dissection**

Among the 28 cases that did not receive a neck dissection, follow up ranged from 1.4-145.6 months with mean and median values of 41.7 and 31.2 months, respectively. Four cases had no follow information available. There was one death for which neither a record of the cause nor any follow up information could be found. This was a male in the 9th decade of life. The tumour was an epithelial-myoepithelial carcinoma (T2N0) and the patient had received post-operative radiotherapy. There was one recurrence at the primary site relating to a pT2N0 mucoepidermoid carcinoma (low grade). This tumour was incompletely excised initially and was operated on again and completely excised 12.5 months after the primary surgery. No metastases or disease specific deaths were recorded.
Cases that underwent a neck dissection

Among the 54 cases that underwent a neck dissection, three cases had no follow up information. Among cases with follow up information, the length was 0.8-167.0 months with mean and median values of 40.7 and 29.6 months respectively.

There were 13 recorded deaths. One death was due to a lung adenocarcinoma in a patient who had not received radiotherapy for the parotid carcinoma. The remaining deaths were in cases where post-operative radiotherapy had been provided for the parotid carcinoma these included: One death from an unrelated cause; two deaths for which a record of the cause could not be found; nine deaths deemed to be related to the parotid carcinoma (table 1), although biopsy confirmation of metastases and spread was not available. These nine deaths, all related to high grade carcinoma with the exception of a pT3N0 low grade but invasive carcinoma ex-pleomorphic adenoma. Six of the nine disease related deaths had shown lymph node metastases. The disease specific deaths occurred after 5.9-79.1 months of follow up. Further morbidity without mortality was limited to one case of pulmonary metastases from a pT4bN0 high grade acinic cell carcinoma.

The Kaplan–Meier overall survival of high grade parotid carcinomas that underwent a neck dissection is shown in figure 1. The median survival was 2.11 years. The 5-year survival fell between 11 and 22%. The 10 year estimated survival was between 0 and 11%.

Discussion

Key findings and comparison with other studies;

Combining histological grades, the three most common histological types of carcinoma in this cohort were carcinoma ex-pleomorphic adenoma and acinic cell carcinoma followed by mucoepidermoid carcinoma. Other studies from the UK and US have found mucoepidermoid carcinoma to be the most common histological type of epithelial malignancy.²,⁶ The occurrence of cervical lymph node metastases in 50% or more of invasive high grade carcinoma ex-pleomorphic adenoma and salivary duct carcinoma is consistent with previous series²,⁷,⁸ and would therefore support a neck dissection for these histological types. The
single case of carcinosarcoma ex-pleomorphic adenoma in this series also showed lymph node metastases. Although data is limited for this rare entity, it is acknowledged to show aggressive behaviour.\textsuperscript{9} One of the two cases of high grade acinic cell carcinoma presented here showed lymph node metastases. This is in keeping with previously reported series of this entity that showed lymph node metastases in 40-49\% of cases.\textsuperscript{2,10} Adenocarcinoma NOS (high grade) cases in this series showed lymph node metastases in 33\% of cases. Previous series have found a slightly higher incidence ranging from 45-65\%.\textsuperscript{2,3} Seventeen percent of adenoid cystic carcinomas presented here showed lymph node metastases and this is also in keeping with previous reports.\textsuperscript{2,11} It is acknowledged that distant rather than lymph node metastases are more typical of adenoid cystic carcinoma.\textsuperscript{11,12}

Two low grade and two intermediate grade mucoepidermoid carcinomas were included within the neck dissection cohort and demonstrated no metastases. All three cases of epithelial-myoepithelial carcinoma and all 3 cases of non invasive carcinoma ex-pleomorphic adenoma demonstrated no metastases where a neck dissection was performed. Within the cohort that did not receive neck dissection were 3 cases of non invasive carcinoma ex-pleomorphic adenoma, 3 cases of epithelial-myoepithelial carcinoma and 2 cases of low grade mucoepidermoid carcinoma. On follow up this cohort showed no cases of recurrence, metastases or related mortalities. Other low grade carcinomas were present within the cohort but in numbers that were too low for useful inferences to be drawn.

The indolent behaviour described for non invasive carcinoma ex-pleomorphic adenoma is consistent with previous studies and reviews.\textsuperscript{7,13-15} The described behaviour of mucoepidermoid carcinoma and epithelial-myoepithelial carcinoma is also consistent with previous studies. In an American cohort including more than 20,000 patients, the incidence of lymph node metastases among cases of epithelial-myoepithelial carcinoma was 6.4\%.\textsuperscript{2} In this cohort the overall incidence of lymph node metastases for mucoepidermoid carcinomas was 20.2\%. High histological grade and high T stage were found to be predictive of lymph node metastases. De Brito Santos \textit{et al.}\textsuperscript{16} described a risk 11.1\% and 16.7\% for low and intermediate grade mucoepidermoid carcinoma, respectively. Lau \textit{et al.}\textsuperscript{17} describe rate of
metastases as 0%, and 10% for low and intermediate grade mucoepidermoid carcinoma, respectively, within a clinically N0 cohort. The presented data, although limited, therefore support previous series demonstrating a low incidence of metastases from non invasive carcinoma ex-pleomorphic adenoma, epithelial-myoepithelial carcinoma and low grade mucoepidermoid carcinoma.

Limitations of study

It is acknowledged that refining surgical treatment based on histological type and grade requires accurate preoperative diagnosis by cytology or histology that may not always be possible. The primary limitation of this study is the size of the total cohort together with variable numbers of each histological type of carcinoma that were included. The study is further limited by the variation in the neck levels included in neck dissection and the number of lymph nodes yielded. The study is also limited by the variation and in some cases limited follow up time. This is especially pertinent in the context of the known propensity for salivary carcinomas to show delayed local recurrence and metastasis, sometimes more than 30 years after the initial presentation. The variable behaviour of salivary gland carcinomas and the complex interactions of stage, grade and patient factors emphasize the importance of preoperative imaging, biopsy and multidisciplinary team discussion in their management including consideration of reconstruction.

Clinical applicability of the study.

This paper summarises the 22-year experience of treating primary parotid carcinoma in a tertiary centre, providing data from the one of the largest UK cohorts. The findings here are in keeping with previous findings and in this context support the use of neck dissection when treating carcinoma ex-pleomorphic adenoma (high grade, invasive), salivary duct carcinoma, and adenocarcinoma NOS (high grade), adenoid cystic carcinoma and acinic cell carcinoma.
The data from this study concerning lower grade carcinomas is more limited and requires further evaluation in a multicentre setting.

**Conflict of Interest**

No conflict of interest

**Ethics statement/confirmation of patient permission**

Retrospective study using anonymised patient data approved by Audit department of the hospital. Patient permission not applicable- no identifying information included

**References**


Table and Figure Legends

**Table 1** Pathological staging of parotid carcinomas for which a neck dissection was undertaken

Ca: carcinoma, PA: Pleomorphic adenoma

Each † indicates one death related to the parotid carcinoma

**Figure 1** Kaplan–Meier graphs for overall survival of high grade parotid carcinoma that received a neck dissection
Table 1 Pathological staging of parotid carcinomas for which a neck dissection was undertaken

Ca: carcinoma, PA: Pleomorphic adenoma

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Figure 1 Kaplan–Meier graphs for overall survival of high grade parotid carcinoma that received a neck dissection