The Journal of Laryngology & Otology (2011), ***125***, *837–840*.

doi:10.1017/S0022215111001095

MAIN ARTICLE

Is it oncologically safe to leave the ipsilateral submandibular gland during neck dissection for head and neck squamous cell carcinoma?

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Abstract

Aim: To investigate the incidence of metastasis to the submandibular gland in patients with head and neck squamous cell carcinoma.

Methods: We retrospectively evaluated histological reports of neck dissections for upper respiratory tract carcinoma (performed 2002–2009), recording: primary tumour site, tumour–node–metastasis stage, level Ib involvement, previous radiotherapy, perineural invasion, lymphovascular invasion, extracapsular spread, and the presence of malignant disease in the submandibular gland.

Results: We evaluated 107 cases. The most common primary site was the oral cavity (49 per cent) followed by the supraglottis (21 per cent), glottis (14 per cent), oropharynx (9 per cent) and hypopharynx (6 per cent). Forty-eight per cent of patients had advanced local disease, with 21 per cent at tumour stage 3 and 27 per cent at tumour stage 4. Fifty-six per cent had cervical lymph node metastasis, and 8 per cent received pre-operative radiotherapy. Forty-eight per cent had perineural invasion, 46 per cent lymphovascular spread, 27 per cent extracapsular spread and 8 per cent level Ib metastasis. Only one patient had submandibular gland involvement, due to direct spread (a case with prior radiotherapy and macroscopic submandibular gland involvement evident peri-operatively).

Conclusion: Submandibular gland metastasis from head and neck primary squamous cell carcinoma is extremely rare. Preservation of the ipsilateral submandibular gland during neck dissection is oncologically safe, except in patients with prior surgery or radiotherapy, or a primary tumour in close relation to the gland.

Key words: Submandibular Gland; Neoplasm Metastasis; Pathology; Xerostomia; Salivary Gland

Introduction

The first radical neck dissection was performed by Crile in 1906. At that time, it was standard practice to perform a radical neck dissection in cases of primary head and neck squamous cell carcinoma (SCC), but this was associated with fairly high morbidity. Over the years, more conservative yet oncologically safe options have evolved, such as the modified radical and selective neck dissections.[1–3]

Given the tendency of SCC to metastasise to the neck, a therapeutic or prophylactic neck dissection is a common intervention. It is standard practice for this to include the submandibular gland when level Ib is taken, although anatomically it is debatable whether the submandibular gland contains lymph vessels or nodes.[4,5]

Saliva has many important functions. It has significant antimicrobial properties and thus plays an important role in preventing dental caries; it facilitates the lubrication and irrigation of food; it contributes toward taste and speech; and it protects the upper aerodigestive tract mucous membranes and remineralises tooth enamel.

Approximately 600 ml of saliva is produced daily, most of which is derived from the paired submandibular and parotid glands. The parotid gland contributes 50 per cent of stimulated saliva but only 21 per cent of unstimulated saliva. The submandibular gland, however, contributes 72 per cent of unstimulated saliva; the minor salivary glands contribute the remainder. Stimulated saliva is secreted for short periods daily with mastication. For most of the day, unstimulated saliva is continuously being secreted, and this is vital for the functions listed above. The submandibular gland plays a pivotal role in maintaining this continuous supply of unstimulated saliva.

Removal of one or both submandibular glands is associated with a decrease in total saliva production.[6]

Accepted for publication 22 December 2010 First published online 2 June 2011

It is the lack of unstimulated saliva that results in the subjective feeling of xerostomia.[7] Xerostomia can significantly impair patients' quality of life.

Radiotherapy to the head and neck is frequently used to control local disease, either primarily or post-operatively. However, its use is associated with significant morbidity, including xerostomia as a result of injury to both major and minor salivary glands. Radiotherapy-induced xerostomia was first described in 1911 by the French radiobiologist Jean Bergonie.[8] Salivary gland tissue is exceptionally sensitive to external beam radiation: it has been reported that as little as 35 Gy results in permanent salivary dysfunction.[8] Studies have shown that the contralateral submandibular gland can be preserved and transferred into the submental space to reduce radiation-induced xerostomia.[7,8]

With the trend in surgery towards organ preservation, we wished to investigate the possibility of preserving the ipsilateral submandibular gland during neck dissection.

Methods

We retrospectively reviewed the histological reports of patients treated over a seven year period (2002–2009) at Tygerberg Academic Hospital, South Africa. We included all patients who had undergone neck dissection for primary SCC of the head and neck.

All surgical specimens, including the primary tumour and neck dissection specimens, were submitted to the department of anatomical pathology for histopathological assessment. The first step was to measure the dimensions of the sternocleidomastoid muscle and the internal jugular vein, and to describe their involvement by tumour. Next, the pathologist dissected and divided the submandibular gland, sternocleidomastoid muscle and internal jugular vein, and separated the fat containing nodes into five levels: Ia and Ib (submental and submandibular), IIa and IIb, III, IV, and Va and Vb. The presence of tumour in soft tissues, submandibular gland and muscle was evaluated and the number of lymph nodes in each level noted. If tumour tissue was present, the size of the metastases and the presence of extracapsular spread was documented. Finally, tissue sections of all lymph nodes, the submandibular gland, the sternocleidomastoid muscle and the internal jugular vein were submitted for microscopy.

Aside from submandibular gland involvement, we also evaluated the following parameters: primary tumour site, tumour–node–metastasis (TNM) stage, level Ib nodal involvement, pre-operative radiotherapy, perineural invasion and lymphovascular spread.

Results

A total of 107 patients were evaluated.

The oral cavity was the most common tumour site involved, accounting for 49 per cent of patients, followed by the supraglottis (21 per cent), glottis (14 per cent), oropharynx (9 per cent) and hypopharynx (6 per cent) (Table I).

Table II shows the distribution of T stages in our series. The most common stage was T_2 (36 per cent), followed by T_4 (27 per cent). Forty-eight per cent of our patients had advanced tumours (i.e. either T_3 or T_4).

Table III shows the distribution of (histologically determined) N stages. Forty-six per cent of our patients were staged as N_0, 34 per cent as N_2 and 4 per cent as N_3. Eight per cent of patients had metastasis to level Ib. Eight per cent had received previous radiotherapy.

Table IV shows prognostic histological parameters. Forty-eight per cent of patients had perineural invasion, 27 per cent had extracapsular spread and 46 per cent had lymphovascular spread.

Of the 107 patients evaluated, only one had evidence of submandibular gland metastasis. This patient's primary tumour was a T_3 oral cavity SCC involving the buccal mucosa. However, this patient had undergone previous radiotherapy, and it was clinically apparent during surgery that the submandibular gland was involved by direct spread.

Discussion

The risk of malignant spread to the submandibular gland can occur via three routes: haematogenous, lymphatic and direct extension. Anatomically, the submandibular gland contains a poorly developed lymphovascular framework.

DiNardo has reviewed the literature on the lymphatic anatomy of the submandibular region.[4] This author also performed cadaver dissections and undertook prospective clinical and radiological evaluation of metastasis to the submandibular region, in cases of oral cavity SCC. Six lymphatic groups were described, namely: preglandular, prevascular, retrovascular, retroglandular,

TABLE I
PRIMARY SITES

Primary site	Cases (*n* (%))
Oral cavity	52 (49)
Oropharynx	10 (9)
Supraglottis	22 (21)
Glottis	15 (14)
Hypopharynx	7 (6)

TABLE II
TUMOUR STAGE

Stage	Cases (*n* (%))
T_1	18 (16)
T_2	39 (36)
T_3	22 (21)
T_4	28 (27)

T = tumour stage

https://doi.org/10.1017/S0022215111001095 Published online by Cambridge University Press

TABLE III
NODE STAGE

Stage	Cases (*n* (%))
N_0	49 (46)
N_1	17 (16)
N_2	36 (34)
N_3	5 (4)

N = node stage

intraglandular and deep submandibular. The cadaver dissections and clinical specimens revealed no intraglandular nodes. The most common nodes involved by metastasis were the perivascular groups (pre and retrovascular nodes). In addition, the six lymphatic groups were not consistently found in all the cadaver dissections. The presence of intraglandular nodes has been doubted by many authors, and DiNardo's research supports this.[4,6,9,10]

Haematogenous spread to the submandibular gland is more likely to occur from primaries outside the head and neck region, in sites such as the breast, genitourinary system and lung.[1,11] Metastasis from head and neck primary malignancies to salivary glands is an extremely rare phenomenon; however, should this occur, spread to the parotid gland is more likely since it has a better lymphovascular supply.[11] Spiegel and colleagues' review concluded that submandibular gland metastasis occurred only via direct spread, and not via lymphovascular spread.[8]

The submandibular gland is usually removed during traditional radical neck dissection. Resection of either one or both submandibular glands will result in reduced salivary outflow and may cause xerostomia. In Jacob and colleagues' study, a third of patients undergoing neck dissection with concomitant removal of the submandibular gland experienced xerostomia, and had an increased incidence of dental caries, compared with control groups.[6] These authors also found: (1) a statistically significant decrease in unstimulated saliva secretion in patients undergoing unilateral submandibular gland resection, compared with a control (non-cancer) group; and (2) decreased salivary flow rates, both unstimulated and stimulated, in patients undergoing bilateral submandibular gland resection, compared with unilateral resection (the difference was however only statistically significant for stimulated saliva).

In an attempt to preserve the submandibular gland and prevent xerostomia, Spiegel *et al.* have successfully transplanted and replanted the submandibular gland in a rabbit model, and have suggested that this could be attempted in humans as the risk of metastasis to the submandibular gland is virtually zero.

In 2000, Seikhaly and Jha successfully pioneered the oncologically safe technique of contralateral submandibular gland transfer into the submental space, in order to reduce radiation-induced xerostomia.[7] A total of 60 patients underwent submandibular gland transfer, and these patients had lower scores for xerostomia (as assessed using the Washington quality of life questionnaire).

Radiation-induced xerostomia can also be reduced with intensity-modulated radiotherapy. Saarilahti *et al.* have demonstrated the preservation of contralateral submandibular gland function using intensity-modulated radiotherapy, with no associated increase in locoregional recurrence.[12] Unstimulated salivary flow rates and xerostomia scores were significantly better in the intensity-modulated radiotherapy group.

Our findings support the results of the above-mentioned studies. In our patients, the most common primary site was the oral cavity (49 per cent). Despite the fact that the first echelon nodes for the oral cavity are at level Ia (submental) and Ib (submandibular), only 8 per cent of our cases had positive nodes at level Ib. Forty-eight per cent of our cases had advanced local disease (i.e. T_3 or T_4), and 54 per cent had nodal metastases. A significant proportion of our series also had perineural invasion (48 per cent), extracapsular spread (27 per cent) and lymphovascular spread (46 per cent). Despite the advanced local disease and poor prognostic histological factors mentioned, only one of our cases had submandibular gland involvement, which was via direct spread.

- **In therapeutic or prophylactic neck dissection, it is routine practice to remove the submandibular gland**
- **This study investigated submandibular gland metastasis in patients with head and neck squamous cell carcinoma (SCC)**
- **Of 107 patients, only one developed submandibular gland disease (with evident macroscopic changes), due to direct spread; this patient had received prior radiotherapy**
- **Since submandibular gland metastasis from head and neck primary SCC is rare, submandibular gland preservation during neck dissection is oncologically safe, except in cases with prior surgery or radiotherapy, or primary tumour close to the gland**

Therefore, one must ask the question, why not preserve the ipsilateral submandibular gland? Studies have proven that salivary output is significantly reduced with the removal of one submandibular gland, resulting

TABLE IV
PROGNOSTIC HISTOLOGICAL PARAMETERS

Parameter	Cases (*n* (%))
Perineural invasion	51 (48)
Extracapsular spread	29 (27)
Lymphovascular spread	49 (46)

in xerostomia. The surgical transfer pioneered by Jha *et al.* has demonstrated the viability of functional preservation of the submandibular gland, and has shown this to be oncologically safe. With improved radiotherapy techniques (e.g. intensity-modulated radiotherapy), exocrine glandular function can also be preserved. Bearing in mind these factors, and the fact that submandibular gland metastasis is very rare, preservation of the ipsilateral submandibular gland should be considered, in order to reduce xerostomia without compromising oncological safety. Radiation-induced xerostomia could also be minimised through either surgical transfer of the spared ipsilateral submandibular gland or intensity-modulated radiotherapy.

Conclusion

Submandibular gland metastasis from head and neck SCC is extremely rare; any neoplastic involvement of the gland usually occurs via direct spread. A review of the literature indicates that the submandibular gland contains no intraglandular lymph nodes and has a poor periglandular lymphatic supply. Preservation of contralateral submandibular gland function, via surgery or intensity-modulated radiotherapy, has been proven to be oncologically safe. Therefore, we suggest that it is safe to preserve the ipsilateral submandibular gland as well, in the majority of patients receiving neck dissections. The exceptions to this are patients who have received previous radiotherapy or surgery to the neck, as this may alter the predictability of lymphatic drainage, and those in whom the primary tumour lies close to the submandibular gland.

Acknowledgements

We acknowledge Dr Eric Post for initiating this project.

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Dr A K Ebrahim takes responsibility for the integrity of the content of the paper
Competing interests: None declared