

A single centre's experience of 23 cases of total rhinectomy for the treatment of nasal vestibule squamous cell carcinoma.

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Abstract

Objectives: This study aims to analyse the management outcomes of total rhinectomy (TR) for nasal squamous cell carcinomas (SCCs) involving the vestibule, and to identify prognostic factors for disease recurrence. **Design:** A retrospective single centre study was conducted between September 2003 and February 2021 including all patients who underwent a TR for a SCC involving the nasal vestibule. **Results:** 23 patients were included in the study. Tumours originated from the septum (n=12), vestibule (n=8) or skin (n=3). Six TR (26.1%) were salvage procedures, after primary radiotherapy or nose-preserving rhinectomy. Seven patients had a concurrent neck dissection and 17 patients (73.9%) received adjuvant treatment (14 patients had radiotherapy and 3 had chemoradiotherapy). After a median follow-up of 32 months, six patients (26.1%) presented with tumour recurrence. Three patients (13%) had nodal-only recurrence. The estimated 5-year overall survival, disease-free survival and disease-specific survival was 67.5%, 66.3% and 80.7% respectively. Positive excision margins were a predictive factor for tumour recurrence after TR (p=0.0401). **Conclusions:** For nasal vestibule SCCs not amenable to limited surgical resection, TR along with adjuvant radiotherapy provide good oncological outcomes and should be considered the main treatment option.

Introduction

Squamous cell carcinoma (SCC) of the nasal vestibule is a rare malignancy (1,2). Risk factors for nasal carcinomas include male gender, smoking and exposure to organic solvents (3). Human Papilloma Virus infection has been identified in a significant proportion of tumours, although its prognostic impact remains unclear (4,5). Nasal vestibule malignancies can present with non-specific symptoms, sometimes masquerading as a dermatosis (6) and leading to a delay in diagnosis.

Due to the heterogeneity of published series, the level of evidence regarding the management of nasal SCC remains low. There is a lack of consensus for the treatment of both the primary tumour and the clinically N0 neck. While most authors recommend upfront surgery (rhinectomy) even for early stage tumours (2,7–9), interstitial brachytherapy and radiotherapy seem to be acceptable non-surgical alternatives (2,10,11). However, for locally advanced tumours, surgery in the form of Total Rhinectomy (TR) remains the mainstay of treatment (12,13). For the nodal management of cN0 vestibule SCCs, authors have recommended several strategies including surveillance, elective neck dissection and prophylactic radiotherapy (7,13).

The staging of nasal tumours is also controversial with three main tumour classifications being used i.e. Wang's classification, 8th edition of AJCC staging system for tumours of the nasal cavity and ethmoid sinus, and the AJCC staging system for nonmelanoma skin cancer of head and neck region (see table 1) (14,15). Wang's classification is specifically designed for vestibule tumours, and therefore may better represent the natural evolution of tumours at this anatomical subsite (15,16). Indeed, the local extension pathways and

the specific lymphatic drainage of nasal cavity malignancies justify using a specific classification system to infer disease management (17,18).

The need for clear excisional margins alongside the anatomical and cosmetic constraints make indications for partial rhinectomies rare. Furthermore, they require a challenging surgical reconstruction (16) whereas prosthetic reconstruction after TR brings satisfactory cosmetic outcomes (19). However, the psychological impact of TR can be significant and therefore must not be underestimated (19).

The aim of this retrospective single centre study was to analyse the outcomes of TR for the treatment of nasal vestibule SCCs and to identify risk factors for disease recurrence.

Material and methods

A retrospective case series was conducted in a regional tertiary centre for management of head and neck malignancies. All patients undergoing TR for a SCC of the nasal vestibule between September 2003 and February 2021 were included. Patients with a follow-up shorter than three months were excluded. Patients undergoing TR for nasal malignancies other than SCC were also excluded (as outlined in figure 1). This study was registered with the local research and development department as a quality improvement project (reference number 10343). The methodology was in accordance with the Process 2020 Guideline (<http://www.processguideline.com/>).

Due to the absence of clear-cut recommendations or guidelines, the regional multidisciplinary team proposed upfront surgery (partial or total rhinectomy) whenever feasible. For clinically N0 (cN0) necks, the multidisciplinary team generally recommended an elective neck dissection for very advanced tumours only. Adjuvant radiotherapy was indicated for positive or close margins or advanced T stage. Prophylactic irradiation of the neck for N0 disease was not considered. Concurrent chemotherapy was considered if tumour was locally advanced (T4) or in the presence of nodal metastasis with extracapsular extension.

Patient charts were reviewed retrospectively to identify the following information; gender, age, comorbidities, risk factors, tumour staging, histological findings, type of surgery and reconstruction, complications, adjuvant therapy and follow-up. The main endpoints were Overall Survival (OS), Disease-Free Survival (DFS), Disease-Specific Survival (DSS), and the prognostic factors for recurrence.

Statistical analysis

Estimations of survival were calculated using the Kaplan-Meier method. Patients that developed disease recurrence (recurrence group) and those that did not (remission group) were compared using the Fisher's exact test for qualitative variables and the Mann-Whitney test for quantitative variables. A p-value < 0.05 was considered statistically significant. Statistical analysis was performed using GraphPad Prism version 8.4.2.

Results

Overall, 23 patients underwent TR for SCC of the nasal vestibule, of which 69.6% were males and 30.4% were females (gender ratio 2.29:1). The median age was 63 years (range 38 – 87). Twenty patients (87%) had a history of smoking, and alcohol abuse was noted in two patients (8.7%). Four patients (17.4%) were immunocompromised including two cases of haematological malignancy (multiple myeloma, chronic lymphocytic leukaemia) and two patients taking immune suppressant medication. The median time between the initial presentation of symptoms and surgery was 7 months (range 3 – 18). Pre-operative imaging for staging included MRI (100%), CT (86.4%) and/or PET-CT (4.5%). Clinical T staging using the Wang's classification and the AJCC classification for nasal cavity cancers (thus excluding the three primaries of cutaneous origin) are shown in Table 2. Six patients (26.1%) presented with symptoms of recurrent disease, either following radiotherapy (n=3) or nose-preserving surgery (n=3). The outlines of patients' presentation and treatment are shown in Figure 1.

Surgery was performed by ENT surgeons (73.9%) or maxillofacial surgeons (26.1%) and consisted of a TR, which was extended in six cases (26.1%) to the maxilla, the orbit or the ethmoid sinus. Seven patients

(30.4%) underwent a concurrent neck dissection, due to a clinical suspicion of nodal involvement (cN+) or an extensive tumour requiring free flap reconstruction in two cases (8.7%). All patients were offered prosthetic rehabilitation. Late complications included nasolacrimal duct obstruction (20%) and mucocele (5%). The psychological issues and abutment complications related to the prosthesis were not studied.

On histological analysis, all tumours involved the nasal vestibule and originated from either the septum (n=12), vestibule (n=8) or skin (n=3). The main pathological characteristics are presented in Table 2, alongside statistical comparisons between patients that developed disease recurrence (recurrence group) and those that did not (remission group). Notably, three SCCs from the remission group presented with adenosquamous features. Five patients (21.7%) required re-operation for further surgical excision in the month following the TR. Among the seven patients who underwent neck dissection, only one had a pathological nodal involvement, demonstrating extracapsular extension. Seventeen patients (73.9%) received adjuvant treatment, with 14 patients having radiotherapy and 3 having chemoradiotherapy.

After a median follow-up of 32 months (range 3 – 195), six patients (26.1%) presented with tumour recurrence. The median time to recurrence was 12 months (range 5 – 25). One recurrence at the primary site was treated via a salvage cranio-facial resection, the patient was alive and disease free 15 years after treatment. Three patients developed regional recurrence (13%) and were treated by salvage neck dissection, of which two were also given further radiotherapy treatment. One of these patients subsequently developed metastatic disease to the lung and died. Finally, there was one case of both local and regional recurrence (involving the retropharyngeal lymph nodes) and one case of local recurrence alongside metastatic disease involving the lung, pleura and bone. Both patients received palliative care and died during follow-up. Overall, seven patients (30.4%) died during the study period, because of the disease evolution in three cases (13%) or due to another malignancy in four cases (17.4%). The estimated 5-year OS, DFS and DSS was 67.5% [IC95: 41–84.1], 66.3% [IC95: 49.1–83.4] and 80.7% [IC95: 50.3–93.5] respectively (see figure 2).

Discussion

This study reports the oncological outcomes of TR in a series of locally-advanced nasal vestibule SCC. Unlike most series of TR within the literature (6,19–21), our cohort has the advantage of having a homogeneous tumour histology. The largest published series of total or subtotal rhinectomies dates back to 1988 and included 51 patients, with only 25 SCCs and mainly lesions originating from the skin (6). Yet the origin of the tumour is an additional confounding factor since it may influence the natural evolution and prognosis. Bouaoud *et al.* published the most conclusive study on this topic, with a series of TR for 35 locally advanced SCCs (13).

Prognostic factors

Our series identified positive excision margins as predictive factor for tumour recurrence after TR ($p=0.0401$). This reiterates the importance of complete tumour excision with sufficiently clear margins. In cases of involved margins, considerations should be made for further surgical resection and the use of adjuvant treatment. To our knowledge, only one similar study found statistically significant factors predictive for recurrence i.e., better local control and DSS in case of clear margins, and better regional control in cases of bilateral neck prophylactic treatment (13). On multivariate analysis, they also observed that R1 or R2 margins were associated with a poorer DFS, despite this not reaching statistical significance (13).

In our series, there was no correlation between the risk of tumour recurrence and the Wang classification ($p>0.9999$), clinical T stage ($p>0.9999$) and pathological T stage of 8th edition of AJCC for tumours of the nasal cavity ($p=0.2898$). Several other series of vestibule SCCs emphasised the absence of association between rates of recurrence and the Wang or AJCC classification (8,9). However, the population-based study by Agger *et al.* including 174 vestibule SCCs found a significant association between DSS and the Wang classification (2). Controversy remains regarding the accuracy of the current staging classifications available for vestibule SCCs (8), whilst further series may help to develop more appropriate and specific staging systems.

Primary tumour treatment

In the largest series of nasal vestibule SCCs published to this date, the 5-year DSS and OS was only 74% and 50%, reaffirming the need for an aggressive treatment strategy even for early-stage tumours (2). The authors of this series reported significantly higher 5-year locoregional control for Wang T1 tumours in case of surgery alone (94%) or surgery with adjuvant radiotherapy (87%) compared to radiotherapy alone (61%) (2). Indeed, many authors recommend upfront surgery regardless of the stage of the tumour (2,7–9), albeit the level of evidence remains limited.

Interstitial brachytherapy or even radiotherapy seem to be acceptable non-surgical alternatives for early-stage SCCs. In a systematic review by Tagliaferri *et al.*, the 5-year local control rate following brachytherapy ranged from 69 to 97%, with 79% of patients having good cosmetic outcomes despite the risk of soft tissue necrosis (10). The two largest series were published by the same team and concerned only Wang T1 and T2 tumours (22,23). Tumour size $<1.5\text{cm}$ resulted in a significantly better local and regional control, whilst tumour volume $[?]2.3\text{cm}^3$ was associated to a worse regional control (22,23). Radiotherapy alone or with a boost of brachytherapy seems to provide poorer local control rates, which remain acceptable for early-stage SCCs (2,11,24).

There is a clearer consensus regarding the management of locally-advanced nasal vestibule SCCs in the form of surgery alongside adjuvant radiotherapy (2,12,13). Several authors reported worse outcomes when treating Wang T2 and T3 tumours using radiotherapy alone compared to surgery with or without adjuvant radiotherapy (2,12).

Bouaoud *et al.* observed a significantly better DFS and OS in patients treated by adjuvant radiotherapy after TR for locally-advanced SCCs. They also proposed neo-adjuvant chemotherapy for fast-growing lesions, although there is no statistical evidence to support this claim (13).

Zaoui *et al.* recommended adjuvant radiotherapy only for advanced staged tumours. In their series of 26 vestibule SCCs treated by primary surgery, which included only 50% of patients having TR, only two patients received postoperative radiotherapy. Despite low rates of adjuvant radiotherapy the 5-year DFS was 86.7% (8). In a similar series of 30 vestibule SCCs, also including 50% of patients having TR, Koopman *et al.* achieved a 5-year DFS of 91.7%. Only seven patients in this series received adjuvant radiotherapy in instances of cartilage invasion, invasion of the upper lip or resection margins of 1mm or less from the tumour. They observed that poor tumour differentiation was significantly associated with poorer OS, but had no significant impact on DFS (9).

Neck management

In a systematic review of vestibule SCCs, the overall incidence of nodal disease varied from 4 to 40% between series (18). This heterogeneity explains the discrepancies noted between authors and their recommendations of surveillance, elective nodal dissection or prophylactic radiotherapy for the management of cN0 vestibule SCC (7,13). Scurry *et al.* published a meta-analysis of nasal cavity SCCs with and without prophylactic neck treatment, irrespective of the type of treatment of the primary tumour. They observed a 18.1% rate of regional recurrence, approaching the 20% cut-off, often cited as suggestive of consideration for elective nodal treatment (17). Other authors observed a significant association between tumour size or volume and regional control (22,23). In our series, the rate of regional recurrence was 13% despite the absence of prophylactic irradiation of the neck for N0 disease.

Some authors advocate neck dissection only for cases of suspected metastasis in early-stage lesions (7,9). Sentinel lymph node biopsy could be developed in this indication, to select patients requiring a neck dissection (25). Bouaouad *et al.* recommended treating lymph nodes systematically and bilaterally for locally-advanced tumours, either by neck dissection if cN+ or by RT if cN0, since they found better regional control when bilateral neck prophylactic treatment was performed (13). Treatment of the neck should at least include

levels I, II and III, however, metastasis to the pre-auricular, facial and retropharyngeal lymph nodes are possible and should be considered (13,18).

Limitations

Limitations of this study include its retrospective nature, however, utilising all available resources minimised the risk of missing data. Furthermore, due to the limited sample size of this study it was not possible to identify other prognostic factors affecting disease recurrence aside from positive excision margins.

Conclusion

For nasal vestibule SCCs not amenable to limited surgical resection, TR along with radiotherapy provide good oncological outcomes and should be considered the main treatment option. Larger studies, particularly in the form of prospective multi-centre studies, are warranted to consolidate the existing findings within the literature and to determine the best management for cN0 necks.

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