Conservation surgery in the management of T1 and T2 oropharyngeal squamous cell carcinoma: the Birmingham UK experience

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The aim of this paper was to evaluate our experience using conservation surgery in the management of T1 and T2 oropharyngeal squamous cell carcinoma. Eighteen patients underwent conservation surgery between 1993 and 2000 and were analysed retrospectively. The mean age was 54 years and the male to female ratio was 8:1. There were 14 tonsil and 4 tongue base tumours and 83% of cases presented with neck nodes, thereby classifying them as having advanced disease (stages 2–4). All patients received postoperative radiotherapy. All patients were followed up to December 2001. The median follow-up time was 3.8 years (minimum was 1.5 years). The 2-year and 5-year survival rates were 100% and 92% respectively. Approximately 66% of patients returned the EORTC and GHQ/12 quality-of-life questionnaires. Of these, seventy-five percent had a high healthy level of general functioning in accordance with the EORTC general health section. These results show that conservation surgery techniques are effective in the treatment of T1 and T2 oropharyngeal squamous carcinoma associated with significant metastatic neck disease. The techniques are well tolerated, produce minimal functional deficit and do not have a negative impact on the patients quality of life in either the immediate postoperative period or up to 4 years post-treatment.

Keywords squamous cell carcinoma oropharynx conservation surgery quality of life

Squamous carcinoma of the oropharynx is uncommon. It represents 10–15% of all head and neck tumours,1 constitutes 0.3–0.5% of all registered malignancies2 and has an incidence in the UK population of approximately 6–8 per million.2,3 The condition is more common in males with a sex ratio of approximately 4:1, and is usually associated with the sixth to seventh decades of life.2–4 It appears that the number of cases diagnosed is on the increase as well as the incidence in the fourth to fifth decades of life.2 In our institution, a tertiary referral centre covering an overall population of approximately 2 million, we would expect to see approximately 12–15 new patients per year presenting with this condition.

The main associated aetiological factors are smoking and alcohol consumption, the effects of which are cumulative.5 Enhanced expression of the human papilloma virus has been observed, specifically in cases of squamous carcinoma of the tonsil, perhaps implicating it in its aetiology.6,7

The commonest subsites involved are the lateral wall (i.e. the tonsil, 50%) with the tongue base (35%), soft palate (10%) and the posterior pharyngeal wall (5%) making up the rest.2,3 Lymphatic spread is common affecting up to 50% of patients at presentation and, unfortunately, as many patients present at an advanced stage, early disease is frequently asymptomatic.
The most common presenting feature in tonsil malignancy is that of tonsil asymmetry which may be associated with vague soreness in the throat. Otalgia may also be a presenting symptom. Soft palate tumours sometimes present early due both to ease of accessibility and a rich nervous innervation, while base of tongue and posterior pharyngeal wall tumours can be characteristically silent. A significant number of cases are also uncovered during the investigation for an occult primary when patients present with metastatic neck disease. The discovery of cystic squamous cell carcinoma in the neck is highly suggestive of tonsil carcinoma, there being only nine cases in the literature which fulfilled the minimum criteria established by Hayes Martin in 1950 to diagnose a branchial cyst carcinoma.

Conventional curative treatment options for oropharyngeal squamous cell carcinoma can be divided into surgical, radiotherapeutic or combined modality treatment, and cure rates differ depending upon the disease site and stage. Early disease can be treated with either radiotherapy or surgery and, historically, radical surgery has been used for advanced disease (usually with postoperative radiotherapy) with inevitable morbidity, reduction in quality of life and even mortality. The best achievable cure rates for stage I and II disease (tonsil and tongue base) are approximately 70–90% and for more advanced disease (stage III and IV) 40–60%.

Recently, there have been reports describing the use of conservation surgery (surgery to remove all the tumour but with the aim to preserve structure and function) in oropharyngeal carcinoma. The aim of this paper is to present our experience in the treatment of patients presenting with primary oropharyngeal squamous cell carcinomas measuring less than 4 cm in their maximum dimension (compatible with a primary tumour stage of T2 or less), who had resectable neck disease and who were treated with conservation surgery and postoperative radiotherapy.

**Patients and methods**

This was a retrospective analysis of 18 patients who presented with either a T1 or T2 oropharyngeal squamous carcinoma to the University Hospital Birmingham and who underwent conservation surgery over a 7-year period between 1993 and 2000. The censor date for analysis was December 2001. Patients were considered for conservation surgery regardless of coexisting neck disease as long as the primary tumour was resectable. The patient details are shown in Table 1.

All patients underwent a full otolaryngological assessment in addition to clinical assessment of the primary lesion. CT or MRI imaging was performed in all patients to ensure accurate staging of both the primary site and neck. All tumours were staged using the current TNM classification which did not change during the study period. Direct endoscopy preceded the definitive procedure. Conservation surgery for tonsillar carcinoma consisted of a transoral extended radical tonsillectomy (Fig.1). A Boyle Davis gag was inserted and the primary tumour assessed. Tonsillectomy was carried out along with a cuff of pharyngeal musculature and the excision extended to include parts of the soft palate, lateral pharyngeal wall or tongue base as appropriate. This was facilitated by moving the gag to facilitate access so that tumour excision could be done under direct vision using cutting diathermy. Haemostasis was controlled in the conventional way. Surgery for tongue base lesions consisted of either a transoral excision or an external approach using a lateral pharyngotomy and excision of the ipsilateral hyoid. Local resection of the primary tumour under direct vision was then carried out with cutting diathermy, the latter being covered with an elective tracheostomy. Patients undergoing conservation surgery all received prophylactic antibiotic therapy. Regional metastases were treated either by modified radical or classical radical neck dissection (Table 1). One patient had a selective neck dissection.

All patients received postoperative radiotherapy both to the primary site and the neck. This was commenced 6–8 weeks following surgery and the following protocol was used. Postoperative irradiation was delivered to the neck to a dose of 49.5 Gy in 18 daily fractions, a further 5.5 Gy in two daily fractions to the primary site using 6–8 Mv Photons. Of the 18 patients treated, seven took part in the UKHAN 1 trial, of whom three received radical radiotherapy alone and four received radical radiotherapy plus simultaneous methotrexate 100 mg/m² with folinic acid rescue given on days 1–14 of the radiation.

Following completion of radiotherapy patients were reviewed in outpatients every month to six weeks for the first year, and then two monthly for the second year. After two years, follow-up has been six monthly. To assess the impact of these treatment options on the quality of life, patients have been contacted (with ethical approval) by mail and asked to complete both the EORTC and GHQ quality-of-life questionnaires.

**Results**

Eighteen patients with oropharyngeal squamous carcinoma were recruited into the study with a mean age of 54 years (range 42–70 years) and a male:female ratio of 8:1. When divided into subsites, there were 14 tonsil and 4 base of tongue tumours. Seven patients presented with T1 tumours and 10 with T2 disease. Ten patients had an operative procedure prior to referral (Table 1). Eighty three per cent of cases (15/18) presented with concomitant neck disease, thereby classifying these patients as having stage 2–4 (i.e. advanced disease), despite all presenting with early primary disease. With a median follow-up time of 3.8 years (minimum 1.5 years),
<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age at presentation (years)</th>
<th>Date of presentation</th>
<th>Sex</th>
<th>Previous history</th>
<th>Primary site</th>
<th>TNM stage</th>
<th>Overall stage</th>
<th>Surgical procedure</th>
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<tr>
<td>1</td>
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<td>August 1995</td>
<td>M</td>
<td>Tonsillectomy and neck node biopsy</td>
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<td>TXN3</td>
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<td>2</td>
<td>53</td>
<td>February 1998</td>
<td>M</td>
<td>Neck node biopsy</td>
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<td>T2N2C</td>
<td>Stage 4</td>
<td>Completion tonsillectomy + right RND</td>
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<td>3</td>
<td>60</td>
<td>June 1998</td>
<td>M</td>
<td>Node biopsy</td>
<td>Tongue base</td>
<td>T2N2C</td>
<td>Stage 4</td>
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<td>June 2000</td>
<td>M</td>
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<td>T1N2</td>
<td>Stage 4</td>
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<td>T2N1</td>
<td>Stage 3</td>
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<td>Stage 1</td>
<td>Tonsillectomy Nil</td>
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<td>Stage 4</td>
<td>– RND</td>
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<tr>
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<td>TXN0</td>
<td>–</td>
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<td>Stage 4</td>
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<td>T3N2B</td>
<td>Stage 4</td>
<td>Tonsillectomy MRND (type 1)</td>
</tr>
</tbody>
</table>

All patients received postoperative radiotherapy to the primary site and neck.

* Included in UKHAN-1 trial.

† Radiotherapy alone.

‡ Chemoradiation.

§ Died 2.5 years following initial treatment due to a second chest primary.
the 2 year and 5 year survival rates were 100% and 92% respectively (Fig. 2). The one patient who died succumbed to a second chest primary 2.5 years following initial treatment.

One patient suffered a significant surgical complication when the pharynx was entered during a staged neck dissection following extended tonsillectomy. This was repaired and resolved on conservative treatment with nasogastric feeding and intravenous antibiotics.

Sixty-six per cent (12) of the 20 patients in this study returned the EORTC and GHQ-12 quality-of-life questionnaires (QOL-Q). Of these, 10 were smokers and 12 drank alcohol. Of the patient population who returned the QOL-Q in this study, it was reported that indeed 75% had a high/healthy level of general functioning in accordance with the EORTC general health section. However, regarding the EORTC specific head and neck symptoms section, it seems that some patients were still experiencing a high (100%) problem level in the following key areas. Twenty-five per cent of patients had problems regarding mouth opening, 50% had problems with a dry mouth, 42% had problems with sticky saliva, 25% remained on supplements, 33% had significant weight loss and a further 33% remained on analgesia.

There were three patients (25%) in this study who persistently scored badly in both global health EORTC section and in EORTC specific head and neck symptoms. Two of these exhibited significant signs of reduced mental health and, therefore, a higher probability of developing or having developed a psychiatric disorder (general health (GHQ-12) section), and two of these patients were also observed to have financial difficulties. They were identified to be the only patients apart from one other to have smoked around their surgery and who continue to smoke now. Most patients in this study drank alcohol around their surgery time and continue to drink now.

Discussion

Oropharyngeal squamous carcinoma is a relatively uncommon head and neck tumour with crude overall 5-year survival rates of between 40 and 50%. Treatment options have included radiotherapy, surgery alone or combined modality treatment usually involving surgery followed by radiotherapy. Surgery for oropharyngeal malignancy has historically involved major ablative surgery which is often associated with significant morbidity and indeed mortality, and is usually reserved for more advanced disease.

Radiotherapy has been used as a primary treatment alone and also in conjunction with surgery. Radiotherapy would be expected to give at least a 70% 5-year survival rate in T1 and T2, N0 tumours of the lateral wall but, unfortunately, squamous cell carcinoma at this site does not often present in this way. Either the tumours are occult or, if they are obvious and either T1 or T2, they are usually associated with cervical lymph node metastases. Radiotherapy for T3 or T4 tumours is less effective and at best can achieve 30–40% 5-year survival rates. Many authors have suggested that, if there are nodal metastases, then radiotherapy has no place to play in initial management and surgery should be the primary modality, which is usually followed by postoperative irradiation. However, a recent publication has shown that small oropharyngeal tumours with limited neck disease (nodes measuring less than 2 cm) can be treated safely by external beam radiotherapy. For small T1 and T2 lateral wall tumours in the absence of cervical lymphadenopathy, external radical beam radiothera-
apy can safely be given. For tongue base tumours, these usually present late so that radiotherapy alone has historically been of little value. However, if they are detected early, they can be treated with external radical beam radiotherapy with 5-year survival rates approaching 80%.18,21

For the not uncommon scenario of a small primary oropharyngeal carcinoma with bulky neck metastases, preservation of function is possible using radiotherapy to the primary site and then treating the neck with surgery and postoperative radiotherapy.22,23 An alternative approach in advanced (stage III and stage IV) tongue base tumours is to use chemoradiation. This technique avoids radical surgery (which is often futile) and early reports of some long-term survivors are encouraging.24 However, the results of controlled trials are awaited.

Overall, radiotherapy treatment 5-year survival rates have been reported from 85% in stage I oropharyngeal disease to as low as 30% for stage IV disease.17–20 A recent study at the Memorial Sloan Kettering Cancer Centre21 has reported their long-term results of primary radiotherapy with or without neck dissection for squamous cell carcinoma of the tongue base for 68 patients treated over the period 1981 through to 1995. External beam radiotherapy was delivered to the primary site and neck with an additional electron-beam boost to areas of nodal involvement. In addition an Iridium-192 implant brachytherapy boost (20–30 Gy) was given to the base of tongue about 3 weeks later under the same anaesthetic used for a discontinuous neck dissection. Actuarial 5- and 10-year local control rates were 98% and 89%, with overall survival at this time being 86% and 52% respectively. However, this treatment was not without significant complications and side-effects (which included severe xerostomia and osteoradionecrosis) which occurred in 16% of cases in this study. Other studies have reported similar treatment protocols using an interstitial Iodine-125 brachytherapy boost as an alternative to Iridium-192. In one study of 20 patients,25 the 5-year actuarial overall survival rate was 72% with the authors reporting good functional outcomes in 90% of patients. In another study,26 other sites of the oropharynx were included and the authors claimed several advantages compared to iridium-192 with similar rates of tumour control and late complications.

In addition to consideration of radiotherapy to the primary site, evaluation of the neck in cases of oropharyngeal malignancy is crucial. A significant number of patients will present with neck node metastases as a primary feature and, even in the absence of apparent regional metastasis, caution must be exercised. In one recent study,27 elective neck dissection of the clinically N0 neck yielded pathological micrometastases in 30% of cases, indicating the need to treat the neck electively in this condition. Oropharyngeal squamous carcinoma predictably metastasizes to the lymph nodes in levels II, III and IV in the untreated neck as well as the retropharyngeal area. Therefore, elective dissection of these levels when a surgical option is chosen would seem appropriate.

In the N+ neck, the situation is more controversial. Some authors have alluded to the satisfactory control rates achieved by radiotherapy in the N1 neck in squamous carcinoma of the oropharynx, but for N2 disease radiotherapy is undoubtedly inferior to the surgical clearance achieved by neck dissection.28 As oropharyngeal squamous carcinoma commonly presents with advanced neck disease, the use of radiotherapy alone in treatment of the N+ neck is probably inadequate as a primary treatment modality.

Historically, surgical treatment by radical neck dissection as described by Hayes Martin29 remains the gold standard by which others may be judged in the control of regional metastasis. This procedure is, however, associated with significant morbidity, most notably as the result of the ‘shoulder syndrome’ arising from paralysis or resection of the spinal accessory nerve. The preservation of this nerve, when not involved in tumour, in the modified radical neck dissection (type I) attempts to obviate this morbidity without significantly impacting on long-term control and is the operation of choice wherever possible.

Surgical treatment of squamous oropharyngeal carcinoma has historically involved major surgery which has commonly, although not exclusively, been used for advanced stage III and IV disease, and involves appropriate access surgery, wide resection of the primary site with or without partial mandibular resection, neck dissection as appropriate, pedicled or free flap reconstruction with tracheostomy and postoperative radiotherapy. This is a prohibitive undertaking with significant morbidity, quality-of-life implications and indeed mortality,30 and usually involves prolonged hospital admission, access to ITU facilities and intense multidisciplinary input.

Common complications include bleeding and infection, wound breakdown and fistula formation. More specifically, patients report problems related to swallowing, speaking and facial disfigurement which still have a significant impact on the quality of life 6 to 12 months following surgery.31–34 Conservation surgery is a relatively new concept in Head and Neck surgery and has arisen out of a desire to reduce the functional impairment endured by patients as a result of major extirpative surgery whilst still attaining similar control rates to those achieved by more radical, mutilating surgery.35 It may be defined as a surgical procedure which removes all underlying tumour and which aims to effect the same cure as radical surgery but with preservation of both structure and function. It is usually combined with either radiotherapy or chemoradiation.35,36 Such surgical measures result in much less morbidity without necessarily affecting the long-term outcome.

When considering conservation surgery as a main therapeu tic modality, certain important issues need to be addressed. These relate to the tumour site, its size and its extent clinically, radiologically as well as at EUA. Patient factors are also
important with regards to age, general condition and informed consent and it is important to have the appropriate multi-disciplinary backup and surgical skills to carry out this sort of work.

It is crucial that the primary tumour must be deemed to be resectable and, obviously, the larger the primary lesion the greater the likelihood is of an extensive procedure being required to control the disease and the less likely conservation surgery will be successful. It is also important to discuss with the patient that some conservation procedures are more demanding in terms of recovery.\textsuperscript{36} Patients should also be aware that conservation surgery may not be the only option available to treat their specific tumour and that, in return for a superior functional outcome offered by conservation surgery, there may indeed be ‘trade-off’ in terms of outcome control.

Publications relating to this technique are notable by their absence. One study from Germany\textsuperscript{10} showed that, out of 117 patients (median age 56 years), 53 had tumours of the oropharynx which were treated with conservation surgery via an intraoral approach using the laser and staged discontinuous neck dissection. Within this group, there was a 42% recurrence rate and a 30% mortality. Three patients had postoperative bleeds following oropharyngeal resection and the survival rates at 3 years for stage I and II disease were 86%, 65% for stage III disease and for stage IV disease 21% (for oropharynx and oral cavity combined).

Ambrosch \textit{et al.}\textsuperscript{37} reported a series of 224 oropharyngeal carcinomas between August 1986 and June 1994 of which 48% originated from the tonsil or tonsillar region, 35% from the tongue base, 12% from the soft palate/uvula and 5% from the posterior pharyngeal wall. The treatment policy was to use primary surgery wherever possible and a surgical resection of the primary tumour was performed in most cases by transoral laser microsurgery. Elective and therapeutic neck dissections were performed preferably as unilateral or bilateral selective neck dissections and postoperative radiotherapy was directed at the primary site and both sides of the neck. Despite 50 patients (22%) having advanced local disease which was described as being unresectable, all patients were treated with curative intent. Sixty-three patients (28%) were treated exclusively by surgery, 42 (67%) of these receiving either a unilateral or bilateral neck dissection. One hundred and eleven patients (50%) underwent combined therapy of which 85 (77%) were treated with surgery and postoperative radiotherapy, 78 (70%) had a unilateral or bilateral neck dissection, 57 (67%) received adjunctive chemotherapy, and 26 (23%) who received combined therapy were given neoadjuvant chemotherapy prior to surgery and radiotherapy.

Using the UICC stage grouping, the distribution of patients was as follows: stage I disease (11) 5% of patients; stage II (15) 7%; stage III (47) 21%; and stage IV (151) 67%. At the end of follow-up, 70 patients (31%) with oropharyngeal carcinoma were alive with no evidence of disease, two (1%) were alive with tumour, 99 (44%) had died of tumour related causes, 53 (24%) had died of causes unrelated to their tumours. The overall survival according to UICC (1992) staging at 3 years overall survival was 75% for stage I and II disease, 58% for stage III disease and 30% for stage IV disease.

In this study, shows that we have achieved an overall disease-free survival of 94% over a mean follow-up period of 4 years 3 months. It is important to reiterate that, although the criteria for inclusion in the study was early primary disease as defined by joint AJCC-UICC (T1 and T2 stage), many patients (82%) had regional metastases at presentation and so had stage III and IV disease. Their disease was still controlled locally and regionally using conservation surgery together with postoperative radiotherapy. This avoided the more radical extirpative techniques and complications previously associated with such extensive disease.

In our series, one significant postoperative complication was observed. This occurred during a neck dissection for regional metastasis from a primary tonsillar tumour when the oropharynx was breached through the tonsillar fossa. This was repaired with an absorbable suture and resolved on conservative treatment with nasogastric feeding for 10 days and intravenous antibiotics. It is perhaps an argument for treatment of the primary tumour and the neck at the same sitting as extended tonsillectomy leaves the remaining pharyngeal wall relatively thin. Performing neck dissection at the same time avoids postoperative fibrosis and reduce this risk. All patients were noted to be eating and drinking normally prior to discharge from hospital with a mean postoperative hospital stay of 4.9 days.

We would, however, stress certain points when considering conservation surgery in the treatment of oropharyngeal malignancy to ensure success. It is crucial that the disease is resectable both locally and regionally, and, secondly, close liaison is required between the head and neck surgeon and oncologist. Thirdly, a well-structured follow-up strategy needs to be employed so that recurrences, should they occur, can be detected and treated early.

Seven patients in this study were entered into the UKHAN 1 Multicentre Randomized Trial,\textsuperscript{38} of whom three had radiotherapy alone and four had simultaneous chemoradiation. It is not possible to draw conclusions from these seven patients included in our study, however preliminary results from the UKHAN 1 Trial suggest that synchronous chemoradiation with methotrexate or a combination schedule using vincristine, bleomycin, methotrexate plus 5FU improves locoregional control for patients with squamous cell carcinoma of the head and neck.

Furthermore, when the long-term functional benefits were assessed by questionnaire using previously validated measures of assessment of quality of life in head and neck malignancy, it could be concluded from the small sample
of patients within this study that 75% of patients had a high/healthy level of general functioning following conservation surgery, but there are still a few patients who are experiencing a high problem level of specific head and neck symptoms. Also the results suggest that in order to reduce function and symptoms morbidity in this group of patients in the future, it may be necessary to investigate key persistent problem areas such as social behaviour, which would include continuation of smoking (as identified in this study), adequate pain control and psychosocial support.

In summary, our results show that conservation surgery techniques are effective in the treatment of T1 and T2 oropharyngeal squamous carcinoma associated with significant neck disease. They are well tolerated, produce minimal functional deficit and do not have a negative impact on the patient’s quality of life in the immediate postoperative period or up to 4 years post surgery.

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References


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