Current Concepts in the Management of Oral Cancer

Abstract: For patients diagnosed with oral cancer, treatment may involve surgery or radiotherapy alone, or a combination of the two. Where radiotherapy is the sole modality, the addition of chemotherapy may be beneficial, particularly with advanced tumours. If the treatment is surgery, this may involve extensive microsurgical reconstruction. Follow up of treated patients should be rigorous and, ideally, quality of life should be measured.

Clinical Relevance: Ideally, the cancer patient’s routine dental treatment should be undertaken in a primary care setting. Knowledge of current treatment modalities will enable the dental team to be aware of dental problems that might arise as a consequence of cancer treatment, and co-ordinate their care of the cancer patient with the hospital team.

Pre-operative assessment

All patients suspected of having OSCC should be referred to, and be seen by, a senior oral and maxillofacial surgeon within two weeks of referral, in accordance with government guidelines. As the referring practitioner should have done, a full history should be taken from the patient and this will include his/her smoking and drinking habits. The patient’s oral cavity should be thoroughly examined as should the patient’s neck. Unless the patient’s diagnosis is clear and not a cancer, an incisional biopsy should be carried out under local anaesthetic. This should be done urgently, unless the biopsy is to distinguish between benign pathologies such as frictional keratosis or geographic tongue. Examination under general anaesthesia to carry out the biopsy and evaluate the extent of the tumour is indicated if:

■ The tumour is inaccessible, for example in the posterior part of the tongue;
■ The tumour is visible but its extent is difficult to ascertain, especially as this may be uncomfortable for the patient;
■ If the patient has presented with a lump in the neck, without any apparent cause, including a visible tumour in the mouth. In this instance, Positron Emission Tomography (PET) scanning can be useful to locate the primary tumour (Figure 1).

In some units, all patients that have presented with OSCC, regardless of the site, have panaendoscopy, which is a laryngoscopic, pharyngoscopic and oesophagoscopic examination of the upper aerodigestive tract, to detect coexistent (synchronous) tumours. However, the yield is poor and this should be reserved for patients whose symptoms suggest a second primary tumour.

Once the diagnosis of OSCC is clear (usually when confirmed by histology), the patient should be informed as soon as possible, with counselling made available. Further investigations should then be carried out. These should be MRI or CT scanning to image the tumour within the oral cavity and neck. MRI gives better soft tissue definition and better trabecular bone imaging, though a CT scan can sometimes be helpful in determining cortical bone invasion by the tumour. A CT scan of the chest should also be carried out to check for metastases or a second primary tumour of the lung.

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Figure 2. Levels of cervical lymph nodes. Level 1 = submandibular nodes; Level 2 = jugulodigastric nodes; Level 3 = superior jugulo-omohyoid; Level 4 = inferior jugulo-omohyoid and Level 5 = posterior triangle nodes.

Figure 3. Access to the posterior tongue and oropharynx with a mandibulotomy lip-splitting incision.

When this ‘work up’ has been completed, the patient should be seen on a multidisciplinary clinic, consisting of surgeons, clinical oncologist, pathologists and radiologists. Every patient diagnosed with OSCC should be seen by a clinical oncologist, even if it is not thought that radiotherapy will be necessary. The oral and maxillofacial team will almost certainly have the expertise to remove any oral tumour, deemed resectable, surgically and carry out the appropriate reconstruction. Dental assessment is particularly important in those patients who may require radiotherapy. An orthopantomogram is essential, with periapical radiographs for those teeth where more detail is required. The patient’s imminent treatment precludes a long course of restorative treatment and any teeth that may be periapically or seriously peridontally involved should be removed.

Patients should be seen pre-operatively by a speech and language therapist and dietician. All patients undergoing treatment will have at least a temporary inability to masticate and swallow. Usually, this will be less than a month and can be managed with the use of a nasogastric tube. If this period is likely to be longer, a gastrostomy tube can be placed through the abdominal wall, either with endoscopic or radiological visualization.

Treatment

All treatment decisions are based on the size, nodal status and metastatic status of the patient’s tumour, as well as any coexistent medical conditions and the patient’s social circumstances. These should be taken at a multidisciplinary meeting, but of course, ultimately, the patient will decide on the advice provided by the team.

As a general rule, those OSCC less than 2 cm (T1) are usually best treated by surgery only. This may be carried out with a laser and, more recently, by sensitizing the tumour to UV light with a photodynamic sensitizing agent (PDT), which may offer superior results in terms of oral function after tumour excision. Those tumours 2–4 cm (T2) are usually treated by surgery. However, OSCC in the lateral border of the tongue can often be treated using a combination of external beam radiotherapy (40 Gray) and the insertion of radioactive iridium implants for a week (25–30 Gray). Often, patients with T2 OSCC will have an elective neck dissection. Particular indications for this are thick tumours, as those greater than 5 mm in depth will have a 50% chance of having microscopic metastases, even if it cannot be detected with clinical assessment and imaging. Over the past decade, emphasis has been placed on clearing the inferior jugulo-omohyoid lymph nodes (level IV) (Figure 2) in clinically node negative necks where, in 12% of cases, the tumour ‘skips’ the higher levels to involve this microscopically.

Often, the patient may be best reconstructed with a free vascularized soft tissue flap that will require access to the neck vessels for anastomoses and, at the same time, an elective neck dissection can be carried out. A prospective controlled randomized trial to determine if performing an elective neck confers patients with a survival advantage will hopefully soon be underway in the UK. Tumours greater than 4 cm (T3), and tumours involving deeper structures such as extrinsic tongue muscle (T4), will usually be treated by surgery and reconstruction followed by radiotherapy. Access to posterior tongue tumours and oropharyngeal tumours is best obtained by a lip-split and mandibulotomy procedure (Figure 3). However, large tonsillar tumours can often be treated with radiotherapy alone, and T4 tumours of the posterior tongue and oropharynx may often be best treated by combined chemo-radiotherapy. Currently, cisplatin, 5 fluorouracil and methotrexate are the commonest chemotherapeutic agents used in isolation or in combination to treat OSCC. Although the prognosis is not good for these large tumours, surgery probably offers no better survival for this group, which is around 20% at five years, and may well be far more debilitating in terms of speech and swallowing. Cisplatin also seems to have some benefit when added to radiotherapy that is used in conjunction with surgery. Although side-effects, such as nausea with chemotherapy, can be treated well with anti-emetic drugs, the side-effects of combined chemo- and radiotherapy can be severe. These can affect all systems of the body and ultimately be fatal. Therefore, when the patient is deemed unfit for surgery, these treatments are not an alternative or ‘easier options’.

Neck dissection

Patients with OSCC presenting with lymph nodes detected either by palpation or imaging are assumed to have regional metastatic spread and, even if the primary tumour is treated with radiotherapy, will have some type of neck dissection to remove the cervical lymph nodes. There has been a trend over the past...
two decades to adopt a more conservative approach to neck dissection. Classic radical neck dissection, involving sacrifice of the internal jugular vein, sternomastoid muscle and accessory nerve, is only indicated if the tumour is likely to have invaded these structures. Whilst removing lymph nodes from all triangles and levels of the neck, any of these structures can be preserved providing this does not compromise the integrity of the tumour clearance. As the incidence of metastases to the posterior triangle is so low, at 5%, there is a trend towards even more conservative neck dissections, omitting this triangle, and there is evidence that this does not influence recurrence.

Treatment for tumours involving bone

Tumours that involve bone (T4) are only likely to be cured using surgery. The amount of bone required to resect the tumour safely will depend on the degree of bone invasion. This can be determined fairly accurately by the use of an MRI scan (Figure 4) supplemented with plain radiography and, if neither of these investigations is diagnostic, a bone scan (Figure 4). At operation, the presence of bony invasion can be assessed by stripping the periosteum. This technique is used in conjunction with the pre-operative investigations to determine the extent of bony invasion. Recent work has shown that, although in edentulous patients 50% of bony invasion occurs via the occlusal surface, bony invasion in dentate patients occurs almost entirely at the point of junction between attached and unattached mucosa. At least 1 cm of normal uninvaded bone should be removed from around the tumour. Contrary to earlier belief, SCC does not travel along the inferior alveolar nerve to involve the neurovascular bundle outside the extent of cancellous bone invasion. In the mandible, therefore, if the invasion is small or only affects the periosteum, it may be possible to resect a margin of bone, leaving the lower border intact (marginal resection). The soft tissues can be closed primarily or by using a flap. If this is not possible, a segment of bone will have to be removed and, ideally, replaced by a bone graft and, as post-operative radiotherapy is almost always a possibility, this should be vascularized by recipient vessels in the neck, also comprising covering soft tissue, constituting a composite flap. Bony resection in the maxilla, no matter how small, will almost always perforate the nasal or maxillary cavity. Small defects can sometimes be closed by local soft tissue flaps. Most, however, will require either obturation with a prosthesis or, ideally, reconstruction with a vascularized bone graft.

Reconstruction

Soft tissue reconstruction is not always required for T2 tumours, which may be closed primarily. However, many of these tumours, and most T3 and T4 OSCC, will be optimally reconstructed with a free vascularized soft tissue flap. Unless a large amount of bulk is required, this will be forearm skin supplied by the radial artery and its vena comitantes and cephalic vein (radial forearm flap). Alternatively, thigh skin can be used, based around perforators of the lateral circumflex femoral artery (anterolateral thigh flap). This flap offers reduced donor site morbidity and it is becoming increasingly popular, particularly in the Far East. Where bulk is required,
such as after a total glossectomy, a flap of skin and portion of the rectus abdominus muscle can be used.

There are three main ‘composite flaps’ used in orofacial reconstruction, where both bone and soft tissue is required. The vascularized iliac crest graft pedicled on the deep circumflex iliac artery and its vena comitantes (DCIA) offers the best bone, excellent muscle but a rather bulky skin flap (Figures 5 and 6). The fibular flap, based on the peroneal vessels, offers less bone, no muscle but a versatile skin paddle. The scapular flap based on the subscapular vessels offers similar bone and soft tissue to the fibula, with the advantage of a very mobile skin paddle that is not tethered to the bone like the previous flaps. It offers the lowest co-morbidity to the patient in terms of function, as the other two flaps may affect gait. Unfortunately, it cannot be harvested at the same time as the resection, increasing the operating time by as much as three hours. Vascularized bone grafts, even after radiotherapy, offer an excellent platform on which to place dental implants, and all patients undergoing this type of reconstruction are likely to obtain immense benefits from implant-retained fixed (Figure 7) or removable prostheses.14

When considering a patient for free tissue transfer, coexistent disease should always be considered. Generally, only those patients who are either ASA 1 or 2 (therefore not having systemic disease that restricts their daily activity) are candidates for this technique. Age in itself is no bar to this type of surgery. Where the prognosis is extremely poor and surgery is to be carried out, complex reconstruction that might cause the patient to spend a long time in hospital should not be contemplated.

Pedicle flaps, such as the pectoralis major or nasolabial, and even primary closure may offer a less satisfactory functional result but will be quicker to do, cause less co-morbidity, and hence often be best overall for the patient. Even patients with hemimandibular defects do surprisingly well in terms of appearance, eating and speech without bony reconstruction. All patients requiring surgical resection may require a temporary tracheostomy to allow safe airway management. Patients with large tumours, particularly affecting the tongue and oropharynx, are highly likely to require this and the patients should be warned that they may well require this permanently.

Aspects of radiotherapy
Radiotherapy may have to be the only treatment for medically compromised patients, even though, in some instances, for example where there is bone involvement, the prognosis will be far worse without surgery. It should be borne in mind though that most radical radiotherapy is of 60 Gray spanning 6 weeks with 30 treatments or fractions. There is considerable co-morbidity in terms of mucosal damage and discomfort and this is compounded by the almost inevitable loss of salivary function. Radiotherapy is not necessarily a soft option! To reduce morbidity and optimize the effect of radiation to the tumour by giving the radiotherapy more frequently over a shorter time period has been tried without a definite benefit.

One of the more recent adaptations of radiotherapy technique is intensity modulated radiotherapy (IMRT), in which multiple-shaped radiation beams are modulated to produce highly conformal dose distributions. In conventional radiotherapy, the dose across a radiotherapy beam is uniform. In IMRT, this is modulated so that, for example, the dose in the midpoint of the beam is virtually zero, with a high dose either side. This allows treatment of a concave tumour with sparing of normal tissues within the concavity. This approach enables the delivery of increased doses to tumour tissue while limiting the dose delivered to normal structures, especially to the salivary glands, auditory and optic apparatus, spinal cord, and larynx. The use of IMRT in oropharyngeal cancers has been reported in a number of small studies in patients with locally advanced disease. In these studies, salivary function was improved and locoregional control was excellent, although the follow-up is too short to draw conclusions.17

Dental consequences of treatment
After radiotherapy, as a consequence of salivary gland damage, there will always be some degree of xerostomia. All patients who have undergone radiotherapy should be given fluoride mouthwash to reduce their increased caries risk. They may often be affected with a painful stomatitis which may be ulcerative, particularly if the patient is also having chemotherapy, which can produce a particularly florid oral ulceration. Chlorhexidine mouthwash should be prescribed to prevent secondary infection and proprietary brands such as Difflam may be useful in reducing discomfort. Cocaine mouthwash 2% is extremely effective at reducing discomfort, but has to be prescribed initially in a hospital, although subsequent prescriptions can be dispensed via the patient’s general medical practitioner.

Following radiotherapy, there is a lifetime risk of osteoradionecrosis of the jaws. Although the dental needs of these patients are best managed in a primary setting, extractions which may be unavoidable should be carried out in an oral and maxillofacial surgery unit. Simple single tooth extractions, especially where periodontally involved, can usually be carried out safely with a careful atraumatic technique, primary flap closure of the socket and postoperative antibiotics. Multiple or complex extractions should ideally be proceeded by, and followed up with, hyperbaric oxygen therapy. Although this is expensive and time consuming, osteoradionecrosis can be a devastating condition for patients. If this therapy is used it should be planned to account for all likely extractions, as it is not efficacious if used repeatedly.
Post-operative assessment

Following a surgical resection, the specimen will be examined both macro- and microscopically by the histopathologist. This will give crucial information regarding prognosis and the patient can be staged pathologically still utilizing the TNM system, with greater accuracy. Also, additional prognostic factors, such as extracapsular spread in the neck, are taken into account, to enable the planning of any further treatment. Most multidisciplinary teams will advise the patient to have postoperative radiotherapy to the neck:
- If two or more lymph nodes in the neck contain SCC confined within their capsule;
- If any lymph node contains SCC that has escaped the capsule (extracapsular spread).

Most multidisciplinary teams will also advise the patient to have postoperative radiotherapy to the primary site if:
- The tumour exists at the margin of the resection specimen (incomplete resection);
- The primary tumour was large (T3) or greater.

Controversy exists about the necessity of post-operative radiotherapy where the margins are clear but the tumour exists less than 5 mm from the resection margin. Many multidisciplinary teams consider this to be an indication for post-operative radiotherapy, but recently this view has been challenged, as it seems to be the size of the tumour and not the closeness of the resection margin that is linked to recurrence.18 The presence of the tumour infiltrating along nerves (perineural spread) or within blood vessels (intravascular spread) may sway the decision to give radiotherapy where the margin is close. The decision to prescribe radiotherapy should not always err on the side of radiotherapy if in doubt. Patients who have had both surgery and radiotherapy are less likely to be salvaged than those who had previously had surgery alone and, if the patient has a new primary tumour in the oral cavity in the future, radiotherapy cannot be repeated. This will ultimately determine survival. This issue is to be the subject of a prospective randomized controlled trial but, until this is completed and published, each case will be treated on its merits and the view of the local multidisciplinary team.

Follow up

Following completion of treatment, be it surgery or radiotherapy or both, all patients will be followed up for a minimum of 5 years, unless death intercedes. For the first post treatment year, patients are followed up monthly, bi-monthly for the second year, every three months for the third year and with an extra month’s interval for each additional year.

Normally, follow up will consist of clinical examination only, but for inaccessible tumours this will include examination with a flexible nasendoscope. MRI and CT scans are not used for routine follow up but only to clarify if there is a recurrence. PET scanning can also be used three months after treatment for the confirmation of recurrence. It is best utilized with other modes of investigation, such as MRI and CT.19 Of those tumours that recur, 67% do so in the first year after treatment and 90% within two years.20 Thereafter, recurrence is hence far less common and probably the result of a new tumour rather than the recurrence of an old one.

If a recurrence is detected and confirmed histologically, the patient will have to be fully investigated and treatment determined by the multidisciplinary team. Treatment will be surgery if the recurrence is deemed ‘resectable’, almost certainly with additional radiotherapy, if the area has not been previously irradiated. If the recurrence is not treatable, as much as possible should be done to palliate the patient’s condition, usually with analgesia, though this may even involve radiotherapy or chemotherapy or even surgery, and photodynamic therapy may also be useful here. The palliative care team will be involved and, ultimately, the patient may require hospice treatment.

Despite the advances in therapy, whilst the benefits to patients in terms of function and aesthetics are unclear, the improvement in survival, particularly in disadvantaged groups, is less clear.21 However, relatively small samples from individual units may show 5 year survival rates of as much as 87% for early disease presentation, with even 43% of those with advanced disease surviving for 5 years.22

It is paramount that any team treating OSCC audits its results. This does not simply entail examining outcomes, such as free tissue transfer success rate and rate of recurrence, but the outcome in terms of the patient’s quality of life, as can be assessed by the University of Washington Quality of Life Questionnaire (Table 1). Only by doing this can the current trends in the

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**Table 1.** Samples from the University of Washington Quality of Life Questionnaire with a scoring system out of 100.
management of OSCC be harnessed for the real benefit of patients.

References


Further reading