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Original Article

Postoperative (Chemo)Radiotherapy for Oral Cavity Squamous Cell Carcinomas: Outcomes and Patterns of Failure

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Abstract

Aims: To determine outcomes after adjuvant radiotherapy for squamous cell carcinoma of the oral cavity and to correlate locoregional recurrence patterns with radiotherapy target volumes.

Materials and methods: All patients receiving adjuvant radiotherapy ± chemotherapy after surgery with curative intent for oral cavity squamous cell carcinoma between 2007 and 2012 were retrospectively analysed. Locoregional recurrences were reconstructed on the planning computed tomography scan by both deformable image co-registration and by visual assessment. Recurrences were categorised as in-field, marginal or out-of-field if >95%, 20–95%, and <20% of the recurrence volume was encompassed by 95% of the prescription isodose, respectively.

Results: In total, 106 patients with a median follow-up of 42 months were included. Oral cavity subsites included oral tongue (54%) and floor of mouth (32%). Thirty (28%) patients received concurrent chemotherapy. Fifty-five (52%) patients received bilateral neck radiotherapy. Two year overall, disease-free, local disease-free, regional disease-free and distant metastases-free survival were 72, 83, 92, 89, 94%, respectively. On multivariate analysis, extracapsular nodal spread was the only factor significantly associated with inferior overall survival. Fourteen (13%) patients have experienced locoregional failure. Of the eight local recurrences at the primary tumour site, four, three and one were classified as in-field, marginal and out-of-field, respectively. Of 10 regional recurrences, one, one and eight were in-field, marginal and out-of-field. There were 7/21 (33%) contralateral regional recurrences in patients with pN2a/b disease who did not receive contralateral neck irradiation; there were 0/21 (0%) and 0/9 (0%) contralateral regional recurrences in patients with pN0 or pN1 disease, respectively, who did not receive contralateral neck irradiation.

Conclusion: Marginal recurrences highlight the need for generous target volume delineation. Based upon rates of contralateral regional recurrences, a comprehensive approach to target volume selection should be advised for tumour subsites with bilateral lymphatic drainage in the presence of pN2a/b disease.

Key words: Chemotherapy; deformable image registration; oral cavity cancer; radiotherapy; recurrence

Introduction

The standard approach to the treatment of oral cavity cancers is surgical resection ± reconstruction with adjuvant radiotherapy for early stage disease in the presence of high risk features or for locally advanced disease [1]. Adjuvant radiotherapy improves local control [2,3] and overall survival for lymph node-positive patients [4]. Adjuvant chemoradiotherapy with concurrent cisplatin has been shown to provide a significant survival advantage in the presence of close/positive margins and/or extracapsular lymph node spread [5,6]. However, limited locoregional control remains a key issue in the management of oral cavity carcinomas [7,8]. Salvage outcomes for patients who develop locoregional recurrence after adjuvant radiotherapy are poor [9].

Appropriate target selection is a key issue in the adjuvant management of oral cavity carcinoma [7] with a balance required between minimising the risk of marginal or out-of-field recurrences versus toxicity. These decisions are generally based upon patient, tumour and surgical factors,

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and include decisions as to whether to treat the primary site, and comprehensive or selective nodal irradiation in the ipsilateral or bilateral neck. Previous reports have highlighted the risks of inappropriate highly selective target selection, with the potential for out-of-field recurrences [7]. The introduction of intensity-modulated radiotherapy (IMRT) has enhanced the ability to selectively spare tissues, but steep dose gradients may increase the risk of edge recurrences, with some reports of marginal treatment failures after postoperative IMRT [8,10].

The purpose of this study was to evaluate our institutional outcomes after adjuvant treatment of oral cavity carcinomas and patterns of recurrence in relation to dosimetry.

Materials and Methods

Study Population

This retrospective study was carried out using patient records, radiotherapy treatment plans and diagnostic imaging on all consecutive patients with non-metastatic squamous cell carcinoma of the oral cavity treated with surgery and postoperative radiotherapy between January 2007 and December 2012. Patients with persistent disease or recurrence before starting adjuvant radiotherapy were excluded; we do not carry out routine postoperative diagnostic imaging and detection of persistent or recurrent disease was based upon symptomatic presentation, clinical examination or findings detected on planning computed tomography scans. Patients with a previous history of head and neck cancer were also excluded.

Treatment Approach

Surgery

Patients underwent surgery with curative intent ± unilateral or bilateral neck dissections according to the input from the multidisciplinary team meetings before surgery. In general, unilateral neck dissections were carried out for disease that was considered lateralised based upon clinical and radiological assessment and bilateral neck dissections were considered for primary disease approaching or crossing midline.

Radiotherapy treatment planning

Patients in the initial era of the study period were treated with a conformal non-IMRT technique. From 2010 IMRT was gradually introduced. Patients were treated supine with a five-point thermoplastic mask. Planning computed tomography scans were acquired with 2–5 mm slices; intravenous computed tomography contrast and a 2 mm computed tomography slice thickness were routinely used for patients treated with IMRT. The planning computed tomography data set was transferred to the treatment planning system (Masterplan®, Elekta, Xio®, Elekta and from 2010 Monaco®, Elekta). Standard doses were 60 Gy in 30 fractions over 6 weeks with a higher dose of 66 Gy in 33 fractions over 6.5 weeks prescribed with the presence of high risk features (extracapsular lymph node spread and/or very close; typically <1–2 mm or positive margins); other dose schedules were occasionally used at the clinician's discretion.

Target volume selection was carried out using preoperative imaging, surgical and pathological findings. Decisions on the treatment of the primary site, ipsilateral neck and bilateral neck were made by the clinician based upon patient and tumour factors, including comorbidity, disease subsite and laterality, imaging, surgical and pathological findings.

Conformal Radiotherapy

For patients who were to be treated using a lateral parallel opposed pair, a planning target volume was directly defined using virtual simulation. For conventionally fractionated treatment schedules (2 Gy per fraction) a maximum dose of 48 Gy to the spinal cord and 54 Gy to the brainstem were accepted. Radiotherapy was delivered with 6 MV photons ± posterior electron fields. Treatment was commonly planned using a two-phase technique of lateral opposed pair of multiple field-in-fields, with the posterior border moved anterior to the spinal cord before reaching spinal cord tolerance and matched posterior electron fields used to treat nodal areas overlying the cord. A 6 MV photon anterior neck field was matched geometrically to the lateral opposed photon fields. Treatment was planned to provide adequate coverage of the primary target and lymph nodes at risk according to ICRU-62 guidelines [11].

Intensity-modulated Radiotherapy

A primary tumour clinical target volume (CTV60-66) was created to include the tumour bed and adjacent surgical changes, modified to anatomical boundaries to exclude air and/or bone without evidence of invasion. Lymph node target volumes were outlined following published postoperative guidelines [12]. Dissected lymph node levels were included within a CTV60-66. Undissected lymph node levels were included in a CTV54-60. The planning target volume was created by auto-expansion of the CTV by 4 mm. Organ at risk constraints were spinal canal maximum 48 Gy, brainstem maximum 54 Gy, larynx mean <45 Gy (excluding parts of the larynx within the planning target volume), contralateral parotid mean <26 Gy. Treatment was delivered with a 5–7 angle step and shoot IMRT technique.

Concurrent Chemotherapy

Patients <70 years old with high risk features of positive margins or ≤2 mm or extracapsular spread were considered for concurrent chemotherapy. Standard concurrent chemotherapy was cisplatin 100 mg/m^2 days 1 and 29. Carboplatin AUC 4 was substituted for cisplatin if creatinine clearance was <55 ml/min.

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