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Postoperative intensity-modulated radiotherapy following surgery for oral cavity squamous cell carcinoma: Patterns of failure

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SUMMARY

Objectives: To review outcomes and analyze the patterns of locoregional recurrence of oral cavity squamous cell carcinoma (OCSCC) treated with surgery and postoperative intensity-modulated radiation therapy (IMRT).

Materials and methods: All patients with Stage I-IVB OCSCC treated with surgery and postoperative IMRT ± concurrent chemotherapy between 2005 and 2010 were evaluated. Patient survival and tumor outcomes were prospectively recorded. Outcome measures were 2 year overall survival (OS), local control (LC), regional control (RC) and distant control (DC). Locoregional recurrences were spatially localized in relation to dosimetric plans.

Results: A total of 180 consecutive patients with median follow-up of 34 months were identified. Disease subsites were oral tongue (46%), floor of mouth (23%), alveolus and hard palate (12%), buccal (9%), retromolar trigone (5%), and lip (4%). The 2 year rates of OS, LC, RC, locoregional control (LRC), and DC were 65%, 87%, 83%, 78% and 83%, respectively. The 2-year estimated rates of LRC for larger subsites were: oral tongue (72%), floor of mouth (84%). Of the 180 patients, 38 (21%) had locoregional failure (LRF). Most LRFs were in-field (26, 68%) with 7 marginal and 5 out-of-field. Marginal/out-of-field failures occurred in the contralateral neck in N2b patients, at high level II/skull base, and in intentionally spared regions (near parotid) of pathologically involved necks.

Conclusions: Nearly a third (12/38) of LR recurrences were marginal or out-of-field following postoperative IMRT for OCSCC. Postoperative IMRT following gross total surgical resection requires careful and comprehensive target volume delineation, and larger volumes may be needed than the primary RT setting.

Introduction

Locoregional control (LRC) of locally advanced oral cavity squamous cell carcinoma (OCSCC) is poor compared with other head-and-neck sites. This is despite a combined modality approach involving surgery and postoperative radiotherapy and limited improvements resulting from the addition of concurrent chemotherapy in high risk subsets.[1,2] Over the past decade, intensity-modulated radiotherapy (IMRT) has largely replaced traditional field-based radiation in large part relating to the ability to tailor the dose distribution to avoid normal tissues such as the parotid glands. However, with the ability to target or avoid specific structures, increasing use of a more selective neck irradiation approach requires evaluation to assess the competing goals of reduced toxicity vs risk of marginal recurrences.[3,4] These concerns have recently been highlighted in a number of case reports showing unexpected patterns of failure following postoperative IMRT.[5–7] As guidelines for postoperative target delineation differ, in particular with OCSCC, the true impact of IMRT on patterns of failure is unclear.

To inform this question, we report the largest outcome series to date for postoperative IMRT in OCSCC. Additionally, we analyzed the spatial relationship of locoregional recurrences with the

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treated dose distributions to determine the frequency and location of marginal or out-of-field recurrences.

Methods and materials

Patients

This study was approved by the institutional Research Ethics Board. Between January 2005 and January 2010, all consecutive patients with initial presentation of non-metastatic OCSCC treated with gross total surgical resection and postoperative IMRT were included in the analysis. Patients with a prior history of a head and neck malignancy were excluded. Patients with persistent disease or who developed recurrence prior to initiation of adjuvant treatment were excluded.

Management

Curative resection was completed in all patients with or without neck dissection according to the assessment of the treating surgeon and institutional guidelines. Patients were treated in the supine position on a custom-made head support with an S-frame immobilization mask and daily image-guidance. Mouth bites were used at the radiation oncologist's discretion, either to separate the jaw or to protect non-target tissues or alternatively to bolus tissues. Acquisition of the planning CT scans with 2.5 mm slices and intravenous contrast was completed in the treatment position, and the planning CT dataset was transferred to the treatment planning system (Pinnacle, Philips Medical Systems).

The median radiation dose prescribed to the postoperative bed was 60 Gy (2 Gy/fraction). The postoperative bed and dissected neck routinely received (at least) 60 Gy in 30 fractions, and any low risk (i.e. undissected) neck sites received (at least) 54 Gy in 30 fractions. If high risk sites were present (i.e. microscopically involved margins or pathological node(s) with extracapsular extension [ECE]), these sites received 66 Gy in 33 fractions while the remaining postoperative bed and dissected neck received 60 Gy in 33 fractions and low risk neck sites received 56 Gy in 33 fractions.

Target volume delineation was completed by the radiation oncologist. Surgical and pathological findings, direct input from the head-and-neck surgeon, and radiologist's interpretation of postoperative imaging were utilized as necessary. Nodal CTV targets based on axial CT images were contoured as previously described.[3,8,9] Our institution employs standardized target and normal tissue nomenclature to facilitate communication and streamline planning, workflow, and quality assurance. Target volumes are reviewed in the head-and-neck radiotherapy quality assurance rounds.

Follow-up and analysis of failure

Patient survival and tumor outcomes were prospectively recorded in the Princess Margaret Hospital Head and Neck Cancer Anthology of Outcomes.[10] Patients were seen in a multidisciplinary clinic environment with a full head and neck examination 4–6 weeks following completion of treatment, every 3 months for the initial 2 years, every 6 months for 3 years, and then yearly as necessary. Follow-up imaging was arranged 8–12 weeks following completion of treatment (baseline) and upon clinical suspicion of recurrence.

Dosimetric assessment of locoregional recurrent disease

The radiologic imaging of recurrence was co-registered with the treatment planning CT dataset. The recurrent tumor volume (V_{rec}) was delineated on the diagnostic CT or MR scans by a single radiation oncologist and verified by a specialist head-and-neck cancer radiologist. The radiation dose received by V_{rec} was determined using dose-volume histograms. Recurrences were classified as "in-field" when $\geqslant$95% of V_{rec} was within the 95% isodose of the intended treatment dose, "marginal" if 20% to <95% of V_{rec} occurred within the 95% isodose, and "out-of-field" if <20% of V_{rec} occurred within the 95% isodose. The mean, minimum and maximum dose received by V_{rec} were obtained.[8]

Statistical analysis

The outcome measures were overall survival, local control and regional control at 2 years calculated by the Kaplan–Meier method from the date of surgery. For analysis of local/regional (ie. neck nodes) control, patients without LRF were censored at the last disease assessment date or the date of death. Univariate and multivariate analysis were carried out using the log-rank test and the Cox proportional hazard model, respectively. Statistical analysis was performed using SAS v9 (Cary, NC, USA).

Results

Patients

A total of 180 patients met our inclusion criteria. Median age was 61 years (range: 21–84 years). Patient and disease characteristics are detailed in Table 1. The median follow-up was 34 months (range: 6–70 months).

Surgical treatment

Of the 180 patients, 168 (93%) patients underwent neck dissection (103 unilateral and 65 bilateral). Of the 12 patients not having a neck dissection, 3 had T1 disease (tongue, buccal, retromolar) and 9 had T2 disease [tongue (4), lower lip (2), floor of mouth, buccal, lower alveolus].

Radiation therapy

The majority of patients were treated with bilateral neck irradiation (117, 65%) with 45 (25%) treated with unilateral neck irradiation and 18 (10%) treated with primary site radiotherapy only. The target volumes selected for the subsites are detailed in Table 2. Most patients with oral tongue and floor of mouth tumors were treated with bilateral neck irradiation with <7% treated with primary site irradiation only. The specific neck nodal regions selected for irradiation, and the proportion of comprehensive or selective neck irradiation are given in Table 3. Of 162 patients treated with ipsilateral neck radiotherapy, the superior extent of the neck target was the retropharyngeal nodes to C1 or base of skull in 90 (56%), high level II in 49 (30%), level II below the level of the posterior belly of the digastric in 22 (14%) and selective IA-B in 1 (0.6%). Of the 117 patients treated with contralateral neck radiotherapy, the superior extent was the retropharyngeal nodes in 20 (17%), high level II in 31 (26%), low level II (superior border positioned where posterior belly of the digastric muscles crosses the jugular vein) in 63 (54%) and selective IA-B in 3 (3%).

Concurrent chemotherapy

Concurrent cisplatin was given in 47 (26%) patients with high risk features (positive margin or ECE). Of the 47 patients, 85%, 5%, and 10% were given cisplatin 100 mg/m^2 every 3 weeks, 75 mg/m^2 every 3 weeks, and 40 mg/m^2 weekly, respectively. In patients treated every 3 weeks, 8% received one cycle, 70% received