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Reirradiation with IMRT for recurrent head and neck cancer: A single-institutional report on disease control, survival, and toxicity

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ABSTRACT

Aim: To study and explores the feasibility and efficacy of re-irradiation (Re-RT) for locally recurrent head and neck cancer (HNC) and second primary (SP) malignancies.

Background: The most common form of treatment failure after radiotherapy (RT) for HNC is loco-regional recurrence (LRR), and around 20–50% of patients develop LRR. Re-irradiation (Re-RT) has been the primary standard of care in the last decade for unresectable locally recurrent/SP HNC.

Materials and methods: It was a retrospective analysis in which we reviewed the medical records of 51 consecutive patients who had received Re-RT to the head and neck region at our institute between 2006 and 2015.

Results: Forty-eight patients were included for assessment of acute and late toxicities, response evaluation at 3 months post Re-RT, and analyses of locoregional control (LRC) and overall survival (OS). The median LRC was 11.2 months, and at 2 and 5 years the LRC rates were 41% and 21.2%, respectively. A multivariate analysis revealed two factors: initial surgical resection performed prior to Re-RT, and achievement of CR at 3 months after completion of Re-RT to be significantly associated with a better median LRC. The median OS was 28.2 months, and at 1, 2, and 5 years, OS were 71.1%, 55.9% and 18%, respectively. A multivariate analysis revealed initial surgical resection performed prior to Re-RT, and achievement of CR at 3 months post completion of Re-RT being only two factors significantly associated with a better median OS. Acute toxicity reports showed that no patients developed grade 5 toxicity, and 2 patients developed grade 4 acute toxicities.

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Conclusion: Re-RT for the treatment of recurrent/SP head and neck tumors is feasible and effective, with acceptable toxicity. However, appropriate patient selection criteria are highly important in determining survival and treatment outcomes.

1. Background

The most common form of treatment failure after radiotherapy (RT) for head and neck cancers (HNC) is locoregional recurrence (LRR), and around 20–50% of patients develop LRR.[1–3] Those who survive are also at risk of developing a second primary (SP) malignancy. The risk of SP varies from 3 to 5% per year.[4,5] An added complication for LRR and SP malignancy is the fact that salvage therapy often yields poor results. Despite advancements in surgery, survival rates for locally recurrent/SP are low, with 40–60% of cancer-related deaths being due to LRR.[6,7] Moreover, recurrent disease is only resectable in 15–20% of patients. The remaining patients require management with either palliative chemotherapy or supportive care.

Reirradiation (Re-RT) has been the primary standard of care in the last decade for unresectable locally recurrent/SP HNC. The main reasons for this include the availability and increasing use of newer RT techniques, such as intensity modulated radiotherapy (IMRT), "renewed confidence" of physicians in delivering a second course of RT with radical intent, and the information available about factors which can be used for appropriate patient selection for Re-RT. Moreover, Re-RT has replaced chemotherapy and supportive care as the treatment of choice for unresectable locally recurrent/SP HNC.

One of the challenges of Re-RT is the fact that patients have previously received a high dose of irradiation. Therefore, the probabilities of late toxicities are increased, especially in instances where Re-RT is delivered in a short time interval after the first course of RT, or in the event that surgical resection has been performed for the first primary or locally recurrent/SP HNC. Growing evidence favoring the role of Re-RT for unresectable locally recurrent/SP HNC and postoperative Re-RT in patients with high risk features following salvage surgery has been presented in the last decade.

We reviewed our 10 years of experience in using IMRT for Re-RT for locally recurrent/SP HNC, and explored the long-term treatment outcomes, toxicity, and factors that affect the treatment outcomes.

2. Materials and methods

2.1. *Pretreatment work up*

The institutional ethics board approved this retrospective study. We reviewed the medical records of 51 consecutive patients who had received Re-RT to the head and neck region at our institute between 2006 and 2015. The first course of RT was performed either at our centre or elsewhere.

The patient selection criteria were stringent for this study. The inclusion criteria were:

1. Patients for whom the first course of RT technique type (either conventional or IMRT) and total delivered target dose were available
2. Patients who did not develop severe toxicity as a result of prior radiation
3. First and recurrent/SP malignancy were squamous cell carcinomas
4. Re-RT using IMRT only
5. Retreated sites included oral cavity, oropharynx, larynx and hypopharynx only (nasopharynx, paranasal sinus, salivary gland, thyroid, skin and metastasis of unknown origin were excluded)
6. Eastern Cooperative Oncology Group (ECOG) performance status $\leq$2 at the time of Re-RT
7. Intent of Re-RT being curative, with or without concurrent chemotherapy
8. Minimum time period between completion of the first course of RT and the commencement of Re-RT was 1-year

Patients who had received neoadjuvant chemotherapy were excluded from our analyses.

Tumors were classified as SP when they originated more than 2 cm away from the original tumor site or when patients had been in complete remission for at least 24 months.

Pretreatment assessment included clinical examination, endoscopy with biopsy under anesthesia, locoregional imaging with magnetic resonance imaging (MRI), and metastatic screening using chest radiography and upper abdominal ultrasound. Thirty-six (70%) patients underwent positron emission tomography-computed tomography (PET-CT). Dental prophylaxis was done for all patients prior to the commencement of Re-RT. Assisted feeding (nasogastric tube or percutaneous endoscopic gastrostomy) was provided for 23 (45%) patients before the commencement of Re-RT.

2.2. *Treatment strategy*

All patients were assessed by a Multidisciplinary Tumor Board and evaluated for surgical resection. Two patients who were treated with intra-operative brachytherapy and 1 patient treated with electron beam radiotherapy were excluded. Thus, 48 patients were included for assessment of acute and late toxicities, response evaluation at 3 months post Re-RT, and analyses of locoregional control (LRC) and survival. Thirty-six of the 48 patients had unresectable/inoperable disease, and underwent definitive Re-RT. The remaining 12 patients underwent adjuvant Re-RT in view of the presence of features such as pT3/pT4, positive resection margin, and nodal