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Original Research Article

Reirradiation for patients with recurrence head and neck squamous cell carcinoma: A single-institution comparative study

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ABSTRACT

Background and objective: In the last decade, the number of publications that report on the use of external beam radiotherapy and high-dose-rate brachytherapy (HDR-BRT) in the treatment of recurrent head and neck cancer has increased, but no studies compare external beam radiotherapy and HDR-BRT. The aim of this study was to evaluate and to compare the efficacy and toxicity of the three-dimensional conformal radiotherapy (3D-CRT) and HDR-BRT in the treatment of recurrent head and neck cancer.

Material and methods: A total of 64 patients with head and neck cancer recurrence were randomly assigned at a 1:1 ratio to receive either 3D-CRT (50 Gy/25 fractions) in the control group or HDR-BRT (30 Gy/12 fraction) in the experimental group.

Results: The overall survival rate of patients treated with HDR-BRT at 1 and 2-years was 74% and 67%, respectively, compare to 3D-CRT group – 51% and 32%, respectively ($P = 0.002$). Local control at 1- and 2-years in patients who received HDR-BRT was 77% and 63% compare with 47% and 25%, respectively, for the patients who received the 3D-CRT ($P < 0.001$). Most patients developed mild to moderate acute mucositis and dermatitis. In the 3D-CRT group, severe late toxicity was determined in 11 patients (35.5%), and in the HDR-BRT group, in 1 patient (3.1%) ($P = 0.001$). There was no grade 5 toxicity.

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Conclusions: Following our results, we concluded that HDR-BRT is a more effective and safer treatment approach for head and neck cancer recurrences than 3D-CRT.

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1. Introduction

Despite advances in multidisciplinary treatment for head and neck cancer after radical treatment, approximately 20–50% of patients are diagnosed with locoregional recurrence during the first two years [1–4]. The main treatment for recurrent disease is surgery, but it is possible only for 15–30% patients, and the five-year overall survival rate is 16–36% [1–3,5–9]. The possibilities for reirradiation with external beam radiotherapy (EBRT) are limited by normal tissue complications [7,10–13]; in cases of high-dose-rate brachytherapy (HDR-BRT), a high total dose can be delivered directly to the tumour and rapid dose fall-off above planning target volume (PTV) allows for sparing of normal tissue [6,12–14]. The results of retrospective studies presented in the literature, using repeated three-dimensional radiotherapy (3D-CRT) for head and neck cancer recurrence, according to a 2-year overall survival (OS), local control (LC) and toxicity, are poor: OS was 15.2–42%, LC – 24–50%; the rate of grade 3 and 4 late toxicity was 1.4–47%, the rate of grade 5 (lethal) late toxicity was 2–16.5% [10,15–17]. The results of several phase II and retrospective studies related to the use of the HDR-BRT for treatment of head-neck cancer patients are published so far; fractionation regimes are being actively discussed. In these studies, 3–4 Gy fractions up to 30–40 Gy total dose are administered to treat the head and neck cancer recurrence most often, and 2-year OS rate was 19–63%, LC – 67–71%; rate of toxicity grade 3 and 4 was 8–22.2% [6,12,13,18]. There are discussions available regarding the possibility to reduce the rate and grade of late toxicity through the use of less than 3 Gy per fraction in HDR-BRT group while increasing the total number of fractions. Although the number of publications, presenting the results of repeated 3D-CRT and results of HDR-BR when treating the head and neck cancer recurrence, increased recently, the research comparing the effectiveness and safety of treatment using the three-dimensional radiotherapy and high-dose-rate brachytherapy have been not accomplished yet so far.

The aim of this study was to evaluate and to compare the efficacy and toxicity of the 3D-CRT and HDR-BRT in the treatment of recurrent head and neck cancer.

2. Material and methods

From October 1, 2008, to February 11, 2011, a prospective single-institution study was conducted in the Hospital of Lithuanian University of Health Sciences Kaunas Clinics. Sixty-four patients with head and neck relapse were randomly assigned in a 1:1 ratio to receive either 3D-CRT (50 Gy/25 fractions) in the control group or hypofractionated HDR-BRT

(30 Gy/12 fractions) in the experimental group. Randomisation was performed using a computer program. One patient in the control group after randomisation was removed from analysis due to myocardial infarction. The permission to conduct this clinical study was obtained from the Kaunas Regional Biomedical Research Committee (No. BE-2-15).

2.1. Patients

Before reirradiation, all patients were evaluated for eligibility and the following selection criteria were applied: (1) histologically confirmed head and neck squamous cell cancer relapse; (2) locoregional relapse identified in an area that had been irradiated during previous radiotherapy using a total dose of ≥ 50 Gy; (3) Karnofsky Performance Score ≥ 80 ; (4) no distant metastases; and (5) no late grade 3 and 4 toxicity after the primary radiotherapy. The patients' characteristics are presented in Table 1.

2.2. Three-dimensional conformal radiotherapy methodology used to treat the control group patients

For patients' immobilisation, thermoplastic masks with five fixation points were used. A computed tomography (CT) scan from the base of the skull, including the neck, with 3-mm slices was used for three-dimensional (3D) treatment planning. The gross tumour volume (GTV – the volume of tumour, identified by clinical and radiological tests) was defined in the 3D planning system “Eclipse”. The clinical tumour volume (CTV) was obtained by adding 5-mm margins along all directions around the GTV. To generate the PTV, a 3–5 mm isotropic margin was added to the CTV. Organs at risk (OAR) (e.g., spinal cord, mandible, carotid artery) were delineated. The total dose was calculated at the isocenter, so that the PTV would be covered by $\geq 95\%$ of the prescribed dose, and the maximum dose level would not exceed 107% of the prescribed dose. This also ensured that the cumulative dose for the spinal cord would not exceed 50 Gy. During this study, the total dose of 50 Gy per 25 fractions was prescribed to all of the patients by administering 2-Gy single fractions (Fig. 1).

2.3. High-dose-rate brachytherapy methodology used to treat the patients from the experimental group

When treating patients with recurrent locoregional head and neck cancer, the principles of the Paris system are applied [19]. The loop technique was used to treat the local recurrences of the oral cavity and oropharyngeal tumours. The closed-end tube technique was used most often after the disease relapse had been diagnosed at the regional lymph nodes of the neck, at the sites of localised salivary gland cancer recurrence, or at the

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