Oral Oncology 69 (2017) 68–73

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

The feasibility of contralateral lower neck sparing intensity modulation radiated therapy for nasopharyngeal carcinoma patients with unilateral cervical lymph node involvement

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ARTICLE INFO

Article history:
Received 18 December 2016
Accepted 18 March 2017
Available online 17 April 2017

Keywords:
Head and neck cancer
Nasopharyngeal carcinoma
Unilateral cervical lymph node metastasis
Elective neck prophylactic irradiation
Magnetic resonance imaging
Intensity modulation radiated therapy
Treatment outcome

ABSTRACT

Objectives: To investigate the feasibility of contralateral lower neck sparing intensity modulation radiated therapy (IMRT) for nasopharyngeal carcinoma patients (NPC) with unilateral cervical lymph node metastasis.

Materials and methods: Retrospective review of 546 patients with unilateral cervical lymph node metastasis treated between November 2009 and February 2012 at one institution. All patients were staged using magnetic resonance imaging and received radical IMRT. Patients were classified into two groups: the inferior border of the negative neck irradiation field only covered Levels III to Va in Group 1; the inferior border covered entire neck down to Levels IV to Vb in Group 2.

Results: Median follow-up was 49.9 months (range, 1.3–69.2 months). Four-year overall survival (OS:89.3% vs. 88.9%, P = 0.91), disease-free survival (DFS:81.7% vs. 81.0%, P = 0.91), distant metastasis-free survival (DMFS:88.2% vs. 87.9%, P = 0.95), local relapse-free survival (LRFS:96.7% vs. 94.7%, P = 0.70) and nodal relapse-free survival (NRFS: 96.1% vs. 95.9%, P = 0.94) were not significantly different between Group 1 and Group 2. Twenty-two patients developed cervical lymph node relapse; of whom 20/22 (91.0%) developed unilateral relapse within pretreatment positive neck. Only one patient developed out-of-field relapse, though this patient also relapsed within the neck irradiation field (Level II). No clinicopathological feature tested had significant prognostic value for NRFS in multivariate analysis.

Conclusions: In the IMRT and MRI era, contralateral lower neck sparing IMRT seems to be feasible for NPC patients with unilateral cervical lymph node metastasis.

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Introduction

Nasopharyngeal carcinoma (NPC) is a malignant tumor type with a reported yearly incidence of 30–80 per 100,000 in southern China [1]. The nasopharynx contains a well-developed lymphatic network, and NPC has a higher incidence of cervical lymph node (LN) metastasis compared to other head and neck cancers [2]. Radiotherapy is the mainstay treatment for non-disseminated NPC. Currently, most protocols recommended by various research bodies, such as the Radiation Therapy Oncology Group, require routine prophylactic irradiation of the retropharyngeal area, Levels II–V and supraclavicular LN areas, regardless of nodal status [3–5]. It was reported that 19.1% NPC patients experienced clinical hypothyroidism after radiotherapy [6].

The pattern of cervical LN metastasis in NPC follows an orderly manner [2,7–9]. The retropharyngeal lymph nodes (RLNs) and Level II LNs are most commonly involved, followed by the Level III and Level V LNs, Level IV LNs, and supraclavicular fossa (SCF) LNs [9,10]. LN skipping metastasis is rare, with an incidence of only 0.5–7.9% [2,7,9]. Recent research confirmed patients without neck LN metastases rarely experience neck failure after elective prophylactic irradiation of bilateral Levels II, III and VA, and most of the thyroid gland was out of radiation field [11,12]. Furthermore, our previous study showed LN metastases of usually spread from higher-level to ipsilateral lower-level LNs [9]. It is reasonable to

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http://dx.doi.org/10.1016/j.oraloncology.2017.03.010
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investigate the feasibility of contralateral lower neck sparing IMRT in NPC patients with unilateral cervical lymph node metastasis.

Therefore, in this study, we compared the outcomes of patients with unilateral LN metastasis who received lower-neck-sparing irradiation or comprehensive irradiation of the negative neck. The aim of this research was to provide further data on the volume of the neck node levels that should be irradiated in patients with NPC with unilateral LN metastasis and improve the quality of life.

Materials and Methods

Patient characteristics

We retrospectively reviewed 1811 patients with newly-diagnosed, non-distant metastatic, histologically-proven NPC treated with IMRT between November 2009 and February 2012 at our institution. Written consent was waived, while oral consent from the patients was obtained via telephone and documented by telephone recording. All patients included had undergone routine pretreatment evaluations including a complete medical history, physical examination, and hematology and biochemistry profiles, as well as MRI of the neck and nasopharynx, chest radiography, abdominal sonography, and whole-body bone scans using single-photon emission computed tomography. Additionally, 29.2% (528/1811) of the patients received a (18)F-fluorodeoxyglucose (18F-FDG) positron emission tomography CT (PET/CT) examination. All patients were restaged according to the 7th edition of the UICC/AJCC staging system.

The incidence of unilateral cervical LN metastasis for the entire cohort was 40.1% (726/1811). Of these 726 patients, 180 (24.8%) patients were eliminated from this study as their treatment plans were incomplete due to loss of data (damage to hard disk). The remaining 546 patients with unilateral cervical LN metastasis were included in this study and their clinicopathological characteristics are summarized in Table 1.

Criteria for cervical LN metastasis

The criteria for LN metastasis included any visible LN in the median retropharyngeal group, or any node in the lateral retropharyngeal group with a minimum diameter $\geq$5 mm. Moreover, jugulodigastric LNs with a minimum diameter $\geq$11 mm, or cervical LNs in other regions with a minimum diameter $\geq$10 mm were considered malignant. A cluster of three LNs, on the basis of a shortest axial diameter of 8–10 mm, was also an imaging criterion for metastasis. In clinical practice, LNs of any size with necrosis or extracapsular spread were also defined as malignant [13–15].

Treatment methods

All patients were treated with IMRT. Patients were immobilized in the supine position with a thermoplastic mask. After administration of intravenous contrast material, 3 mm CT slices were acquired from the head to 2 cm below the sternoclavicular joint. Delineation of target volumes was in accordance with our institutional treatment protocol [16] and the International Commission on Radiation Units and Measurements reports 50 and 62. The prescribed doses were 66–72 Gy at 2.12–2.43 Gy/fraction to the planning target volume (PTV) of the primary gross tumor volume (GTVnx), 64–70 Gy/28–33 fractions to the PTV of the GTV of the involved LNs (GTVnd), 60–63 Gy/28–33 fractions to the PTV of the high-risk clinical target volume (CTV1) and 54–56 Gy/28–33 fractions to the PTV of the low-risk clinical target volume (CTV2).

Different clinicians determined the treatment areas. The neck irradiation field for the positive neck always included Levels II, III, IV and V. However, in patients with unilateral cervical LN metastasis, it is controversial whether it is necessary to include lower neck (Levels Vb and IV) in the prophylactic irradiation volume for the negative neck. The patients were classified into two groups according to the irradiation field for the negative neck: in Group 1, the inferior border of the negative neck irradiation field

Table 1
Clinicopathological characteristics of the 546 patients with NPC with unilateral cervical lymph node metastasis.

Characteristic	*n* (%)*	Group 1 *n* (%)*	Group 2 *n* (%)*	*P*-value
Sex				0.15
Male	409 (74.9%)	136 (72.0%)	273 (76.5%)	
Female	137 (25.1%)	53 (28.0%)	84 (23.5%)	
Age (years)				0.87
≤60	502 (91.9%)	173 (91.5%)	329 (92.2%)	
>60	44 (8.1%)	16 (8.5%)	28 (7.8%)	
Histological type				0.55
Keratinizing squamous cell carcinoma	2 (0.4%)	0 (0.0%)	2 (0.6%)	
Non-keratinizing carcinoma	544 (99.6%)	189 (100.0%)	355 (99.4%)	
Chemotherapy				0.14
No	34 (6.2%)	16 (8.5%)	18 (5.0%)	
Yes	512 (93.8%)	173 (91.5%)	339 (95.0%)	
T-category				0.09
T1	90 (16.5%)	34 (18.0%)	56 (5.7%)	
T2	80 (14.7%)	36 (19.0%)	44 (1.23%)	
T3	210 (38.5%)	62 (32.8%)	148 (41.5%)	
T4	166 (30.4%)	57 (30.2%)	109 (30.5%)	
N-category				0.58
N1	482 (88.3%)	170 (89.9%)	312 (87.4%)	
N3a	13 (2.4%)	3 (1.6%)	10 (2.8%)	
N3b	51 (9.3%)	16 (8.5%)	35 (9.8%)	
Stage-group				0.12
II	142 (26.0%)	59 (31.2%)	83 (23.2%)	
III	189 (34.6%)	59 (31.2%)	130 (36.2%)	
IV	215 (39.4%)	71 (37.6%)	144 (40.3%)	

* Values are *n* (% of column).

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