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Changes in Nasal Patency of Nasopharyngeal Carcinoma Patients after Concurrent Chemoradiotherapy as Evaluated Using Acoustic Rhinometry

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ABSTRACT

Objective: Concurrent chemoradiotherapy (CCRT) is currently the gold standard of treatment for locoregionally advanced nasopharyngeal carcinoma (NPC). However, the impact of CCRT on nasal patency is equivocal. The purpose of this study was to investigate the changes in nasal patency of patients with NPC after CCRT.

Methodology: Fifteen patients with NPC were enrolled in the study. The nasal patency of the patients was quantified with the minimum cross-sectional area of the nasal cavity (MCA), measured using acoustic rhinometry. We recorded the MCA and body weight (BW) of the patients with NPC at two time points: prior to initiation of CCRT (pre-CCRT) and 6 months after initiation of CCRT (post-CCRT). The pre- and post-CCRT MCA measurements were analyzed and compared using a paired *t*-test. The correlation between the patients' post-CCRT BW loss and MCA change was assessed using Spearman's rank correlation analysis.

Result: The mean MCA was 0.75 and 0.65 cm^2 pre and post CCRT, respectively. The post-CCRT MCA was significantly smaller than the pre-CCRT MCA (P=0.001). A negative correlation between post-CCRT BW loss and MCA change was observed (ρ=-0.431, P=0.017).

Conclusion: This study demonstrated (1) that the nasal patency of patients with NPC was significantly smaller after they underwent CCRT, and (2) that patients with NPC who had low post-CCRT BW loss experienced a prominent decrease in nasal patency.

Keywords: Acoustic rhinometry; Concurrent chemoradiotherapy; Nasopharyngeal carcinoma; Nasal patency

Introduction:

Concurrent chemoradiotherapy (CCRT) is currently the gold standard of treatment for locoregionally advanced nasopharyngeal carcinoma (NPC)[1]. The common late toxicities of CCRT in head and neck cancer, such as neuropathy, hearing loss, dysphagia, xerostomia, neck fibrosis, and osteoradionecrosis, are widely known, and their influences on quality of life have been reported[2,3]. However, the impacts of CCRT on nasal patency have remained unclear. Further investigation is necessary to elucidate the optimal clinical practices regarding CCRT. Therefore, we conducted this study to examine changes in the nasal patency of patients with NPC after CCRT.

Materials and Methods:

Patients:

In this prospective study, we enrolled 15 newly diagnosed locoregionally advanced NPC patients who had undergone complete CCRT and at least 6 months of follow-up care between September 2013 and March 2015. All the patients had no previous history of chronic nasal disease or nasal operations.

CCRT regimen:

The CCRT regimen for the patients comprised cisplatin (30 mg/m^2 on day 1 every week) and radiotherapy (2 Gy on days 1-5 every week). The accumulated radiation dose to the primary tumor was 70 Gy. The accumulated radiation dose was 63 Gy to the entire nasopharynx, posterior third of the maxillary sinus, posterior ethmoid sinus, sphenoid sinus, bilateral level Ib-V cervical lymph nodes, parapharynx, and retropharynx. The accumulated radiation dose was 56 Gy to the bilateral supraclavicular fossa.

Measurements:

The nasal patency of the patients was quantified with the minimum cross-sectional area of the nasal cavity (MCA). We measured the patients' MCA by using acoustic rhinometry at two time points: prior to the initiation of CCRT (pre-CCRT) and 6 months after initiation of CCRT (post-CCRT). The time point for post-CCRT measurement was based on evaluation of late toxicities of CCRT. Measurements were obtained using Otopront-Acoustic rhinometry-2.32 (Otopront Medizintechnik, Germany).

The patients had no drug administered in the week before the measurement, and had exhibited no upper respiratory infection in the previous month. If these circumstances existed, measurement was delayed. Nasal endoscopy was performed in advance to rule out nasal crusting, mass recurrence, choanal atresia or other anatomical variants that may impact the nasal airway. Measurements were performed in a quiet examination room with a temperature of 25°C and humidity of 50%. The patients sat quietly in the examination room for 20 minutes before the measurement, during which they remained sitting upright. The patients cleansed their nasal discharge, if any, immediately prior to measurement.

The patients' body weight (BW) was recorded pre and post CCRT.

Statistical analysis:

(1) The pre- and post-CCRT MCAs were calculated using a SPSS paired *t*-test program for planned comparison.

(2) Post-CCRT BW loss was calculated by ([post-CCRT BW] – [pre-CCRT BW])/ (pre-CCRT BW). Post-CCRT MCA change was calculated by ([post-CCRT MCA] – [pre-CCRT MCA])/ (pre-CCRT MCA). The correlation between post-CCRT BW loss and MCA changes was assessed using SPSS Spearman's rank correlation program.

Results:

Patient characteristics:

Fifteen patients with NPC were enrolled in the study, of whom 13 were male and 2 were female. The patients' ages ranged from 33 to 71 years, with a mean age of 46.5 years. The median follow-up time of post-CCRT MCA was 6.5 months. In the study population, 9 patients were stage II, 3 were stage III, 1 was stage IVA, and 2 were stage IVB (American Joint Committee on Cancer TNM staging system, 7th edition). Their characteristics are shown in (Table 1).

Pre-CCRT MCA *vs.* post-CCRT MCA

The pre- and post-CCRT MCA of the patients are shown in (Table 2). The mean pre- and post-CCRT MCAs were 0.75 and 0.65 cm^2, respectively. Paired *t*-test results revealed that the post-CCRT MCAs were significantly smaller than the pre-CCRT MCAs (P=0.001). This result suggested that the nasal patency of patients with NPC was significantly smaller after undergoing CCRT than it was before undergoing CCRT.

Correlation between post-CCRT BW loss and MCA changes

We observed a negative correlation between post-CCRT BW loss and MCA changes by using Spearman's rank correlation analysis (ρ=-0.431, *P*=0.017). This result suggested that patients with NPC who had low post-CCRT BW loss experienced a prominent decrease in nasal patency.

Discussion:

Acoustic rhinometry is a rapid, objective, painless, noninvasive, and well-established method for assessing nasal airway obstruction. Acoustic rhinometry has been used to examine patients in many different aspects of rhinology[4-6]. Thus, acoustic rhinometry was applied in this study for evaluating nasal patency by estimating MCA. The MCA is the narrowest portion of the nasal cavity, and if this area collapses the patient experiences significant symptoms of nasal obstruction[7].

The post-CCRT MCA of patients with NPC is correlated to the thickness of mucosa near the nasal valve, which is mostly determined by regional blood flow and radiation-induced mucositis. Popovic et al. observed a decrease of regional blood flow in patients with head and neck cancer and chemoradiotherapy-induced injury[8]. A decrease of regional blood flow attenuates the congestion of nasal mucosa and thus leads to an increase of nasal patency. Conversely, radiation-induced mucositis is a frequent toxicity in

Case	Gender	Age	Pre-CCRT BW	Post-CCRT BW	TNM stage
1	M	43	75	74	T1N1M0 stage II
2	M	33	71	61	T4N1M0 stage IVA
3	M	38	65	56	T1N1M0 stage II
4	M	33	84	68	T1N1M0 stage II
5	M	35	85	51	T3N3aM0 stage IVB
6	M	54	87	74	T1N1M0 stage II
7	F	50	68	58	T2N2M0 stage III
8	M	41	73	69	T1N1M0 stage II
9	M	54	82	72	T1N1M0 stage II
10	F	54	60	51	T1N1M0 stage II
11	M	33	79	67	T1N3bM0 stage IVB
12	M	54	63	59	T1N1M0 stage II
13	M	71	70	60	T1N1M0 stage II
14	M	58	73	65	T3N1M0 stage III
15	M	46	86	74	T1N2M0 stage III

Pre-CCRT BW: body weight (kg) measured before CCRT.
Post-CCRT BW: body weight (kg) measured 6 months after initiation of CCRT.

Table 1: Patient characteristics.

Case	Pre-CCRT MCA R	Pre-CCRT MCA L	Post-CCRT MCA R	Post-CCRT MCA L
1	0.5	1.3	0.4	0.8
2	1.2	0.5	0.8	0.4
3	1.1	0.4	1.2	0.6
4	0.8	0.9	0.7	0.7
5	0.7	1.5	0.9	1.2
6	0.5	0.2	0.6	0.4
7	0.7	0.8	0.8	0.8
8	0.7	1.1	0.6	0.8
9	1.1	1.3	0.6	0.3
10	0.3	0.6	0.6	0.6
11	0.6	0.9	0.9	1.0
12	0.6	0.2	0.4	0.2
13	0.9	1.0	0.5	0.7
14	0.6	0.5	0.8	0.4
15	0.3	0.6	0.5	0.4

Pre-CCRT MCA: minimum cross-sectional area (cm^2) of nasal cavity measured before CCRT.
Post-CCRT MCA: minimum cross-sectional area (cm^2) of nasal cavity measured 6 months after initiation of CCRT.
R: right nasal cavity, L: left nasal cavity

Table 2: Pre- and post-CCRT MCA of patients.

patients with head and neck cancer who undergo chemoradiotherapy, and it increases mucosal perfusion[9-11]. In other words, radiation-induced mucositis leads to enhanced congestion of nasal mucosa and decreased nasal patency. In addition, radiation-induced mucositis ultimately evolves into a fibrotic change characterized by increased collagen deposition and scarring[12]. To summarize, the chemoradiotherapy-induced decrease of regional blood flow and radiation-induced mucositis influence nasal patency reciprocally.

We determined that the nasal patency of patients with NPC was significantly smaller after they underwent CCRT than it was before they underwent CCRT. On the basis of this result, we speculate that radiation-induced mucositis had a greater impact on the nasal patency of patients with NPC compared with the chemoradiotherapy-induced decrease of regional blood flow. These results indicate the importance of changes in nasal patency and the subsequent impact on quality of life being considered in a clinical setting when treating post-CCRT patients with NPC.

To our knowledge, this is the first study to examine the nasal patency of patients with NPC after CCRT. However, our study has some limitations, including the small number of patients and their uneven distribution across NPC stages. Future studies should involve the long-term follow-up of patients. Subjective data in the form of either nose obstruction symptom evaluation (NOSE) questionnaire or a visual analog scale (VAS) would be helpful to correlate the symptomatic effect of the observed nasal airway narrowing. The cause and effect between BW loss and changes in nasal patency of post-CCRT patients with NPC also requires further exploration.

Conclusion:

This study demonstrated that

(1) The nasal patency of patients with NPC was significantly smaller after undergoing CCRT than it was before undergoing CCRT, and

(2) That patients with NPC who had low post-CCRT BW loss experienced a prominent decrease in nasal patency.

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