

# Change of Swallowing in Patients With Head and Neck Cancer After Concurrent Chemoradiotherapy

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**Objective** To evaluate the functional characteristics of swallowing and to analyze the parameters of dysphagia in head and neck cancer patients after concurrent chemoradiotherapy (CCRT).

**Methods** The medical records of 32 patients with head and neck cancer who were referred for a videofluoroscopic swallowing study from January 2012 to May 2015 were retrospectively reviewed. The patients were allocated by duration after starting CCRT into early phase (<1 month after radiation therapy) and late phase (>1 month after radiation therapy) groups. We measured the modified penetration aspiration scale (MPAS) and American Speech-Language-Hearing Association National Outcome Measurement System swallowing scale (ASHA-NOMS). The oral transit time (OTT), pharyngeal delay time (PDT), and pharyngeal transit time (PTT) were recorded to assess the swallowing physiology.

**Results** Among 32 cases, 18 cases (56%) were of the early phase. In both groups, the most common tumor site was the hypopharynx (43.75%) with a histologic type of squamous cell carcinoma (75%). PTT was significantly longer in the late phase ( $p=0.03$ ). With all types of boluses, except for soup, both phases showed a statistically significant difference in MPAS results. The mean ASHA-NOMS level for the early phase was  $5.83\pm 0.78$  and that for the late phase was  $3.79\pm 1.80$ , with statistical significance ( $p=0.01$ ). The PTT and ASHA-NOMS level showed a statistically significant correlation (correlation coefficient =  $-0.52$ ,  $p=0.02$ ). However, it showed no relationship with the MPAS results.

**Conclusion** The results of our study suggest that in the late phase that after CCRT, the OTT, PDT, and PTT were longer than in the early phase and the PTT prolongation was statistically significant. Therefore, swallowing therapy targeting the pharyngeal phase is recommended after CCRT.

**Keywords** Deglutition disorders, Head and neck neoplasms, Chemoradiotherapy

Received February 22, 2016; Accepted June 13, 2016

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### INTRODUCTION

Head and neck cancer includes tumors involving the oral cavity, pharynx, and larynx, which are anatomical sites associated with the swallowing function. The main treatments for head and neck cancer patients (HNCs) include surgery, radiation therapy, chemotherapy or a combination of these [1,2]. Adjuvant radiotherapy after surgery or exclusive radiotherapy, with or without concurrent chemotherapy, is a valuable treatment option in many patients with head and neck cancer [3,4].

The advantage of undertaking radiation therapy is that it can preserve the muscle, nerve, bone and blood vessels. However, one of the common complications of radiotherapy is dysphagia, which alters the quality of life of patients [5]. Radiation-induced dysphagia is responsible for a change in the type of diet and a prolongation of the meal times, which participate in anorexia and malnutrition [6,7]. Also, severe dysphagia can lead to aspiration, and among HNCs, the incidence of aspiration is estimated to be 36%–94% while the incidence of silent aspiration due to a decrease in the cough reflex is 22%–67% [8–10].

Radiation therapy is well known to induce fibrosis and neuropathy, which ultimately impair the swallowing mechanism and thus increase the risk of dysphagia [11–13]. Some researchers have reported that after radiation therapy, the penetration and aspiration exhibited a statistically significant increase [14–16]. Videofluoroscopic analysis of the swallowing process after radiation therapy has revealed a decrease in pharyngeal peristalsis, defective posterior inversion of the base of the tongue, incomplete closure of the larynx, decreased inversion of the epiglottis, and delayed opening of the upper esophageal sphincter [10,17,18]. Murphy reported that these complications begin to show from 4 to 5 weeks after radiation-based therapy [19]. Due to mucositis, edema of the soft tissues, copious mucous production, xerostomia, and tissue swelling, patients begin to develop acute dysphagia. Later, fibrosis, lymphedema, and damage to neural structures occur, leading to the late effects of dysphagia [19].

However, to the best of our knowledge, these studies have only analyzed the results of the videofluoroscopic swallowing study (VFSS) in a quality active manner and have described the characteristics of impairment, so it is difficult to compare the swallowing function using mea-

surable objective factors. Therefore, the aim of this study is to compare functional data after concurrent chemoradiotherapy (CCRT) and to analyze the change in swallowing function with respect to quantitative physiologic data.

### MATERIALS AND METHODS

#### Subjects

We retrospectively reviewed the medical records of patients with head and neck cancer who had been referred from January 2012 to May 2015 for a VFSS. The inclusion criteria included those who (1) were diagnosed with head and neck cancer; (2) had undergone concurrent chemoradiotherapy; (3) were first referred for examination; (4) had full medical records; and (5) did not participate in swallowing therapy before VFSS. The exclusion criteria included (1) non-primary cancer; (2) recurrent cancer; and (3) insufficient medical records. A total of 86 patients were evaluated during the study period, and 54 patients were excluded according to the above criteria. Thus, the records of 32 patients were analyzed. All patients were allocated by duration after starting CCRT into an early phase (<1 month after radiation therapy) or late phase (>1 month after radiation therapy) group. The clinical characteristics consisted of patient (age, gender), cancer (TNM stage, date of diagnosis, histological type, location of cancer), and radiation therapy (date, dose) characteristics (Table 1). For the analysis, we compared the clinical characteristics, modified penetration aspiration scale (MPAS), the American Speech-Language-Hearing Association National Outcome Measurement System (ASHA-NOMS) level and swallowing physiologic data of both groups.

#### Methods

All patients underwent VFSS that were performed and recorded simultaneously (FLEXAVISION; Shimadzu Corp., Kyoto, Japan). Patients were seated upright on the fluoroscopy chair or wheelchair, and any patient who could not control his or her head independently used a reclined wheelchair. Then, each subject was asked to swallow 5 types of boluses: Yoplait, soup, 2.5 mL liquid, 5 mL liquid, and rice. During the entire test period, the sessions were simultaneously recorded as video files at 30 frames per second (INFINITT PACS video). The image was viewed in the lateral plane, which included the lips

anteriorly to vertebrae posteriorly, and the soft palate superiorly to the sixth cervical vertebra inferiorly [20] (Fig. 1). Testing was discontinued if patients showed dyspnea, decrease in saturation, or unstable vital signs. A physiatrist with more than 5 years of experience performing swallowing studies analyzed the results after VFSS had been finished.

**Table 1.** Demographic and clinical characteristics

Characteristic	Early phase	Late phase
Age (yr)	65.50±11.66 (33-86)	59.86±7.34 (45-68)
Sex		
Female	2 (11.11)	2 (14.29)
Male	16 (88.89)	12 (85.71)
Site		
Oral cavity	3 (16.67)	3 (21.43)
Nasopharynx	2 (11.11)	3 (21.43)
Oropharynx	0 (0)	3 (21.43)
Hypopharynx	10 (55.56)	4 (28.57)
Larynx	3 (16.67)	1 (7.14)
Histology		
Squamous	15 (83.33)	9 (64.29)
Non-keratizing	2 (11.11)	2 (14.29)
Atypical	0 (0)	1 (7.14)
Other	1 (5.56)	2 (14.29)
Dose of radiation (cGy)	5,651.78±2,139.92 (1,350-6,900)	5,823.33±1,837.98 (1,440-6,750)

Values are presented as median±standard deviation (minimum-maximum) or number (%).

*Swallowing physiology*

After VFSS was finished, a physiatrist reviewed the recorded video file without knowing to which group each case had been allocated. The physiatrist counted the number of frames and divided it by 30, and then data was collected as time (seconds) taken during each phase of swallowing [7].

(1) The oral transit time (OTT) was defined as the length of time it takes the bolus to move through the oral cavity from the first frame showing backward movement of the food until the bolus head or tail passes a landmark in the posterior oral cavity.

(2) The pharyngeal transit time (PTT) was defined as the time it takes the bolus to move through the pharynx from the point at which the bolus head passes the back of the tongue or the ramus of the mandible until the bolus tail passes through the cricopharyngeal region, located behind the cricoid cartilage, approximately 1 cm below the true vocal folds.

(3) The pharyngeal delay time (PDT) is a component of the PTT, defined as the time from the bolus head arrival at the point where the shadow of the lower edge of the mandible crosses the tongue base until the pharyngeal swallow is triggered.

*Functional measurement of swallow*

After the VFSS, the results were assessed by obtaining the MPAS and ASHA-NOMS swallowing tests. The MPAS consists of a 5-point scale, ranging from 1 to 5 as follows: 1, material does not enter the airway; 2, material enters the airway, remains above the vocal folds; 3, material enters the airway, contacts the vocal folds; 4, material enters the airway, passes below the vocal folds and effort is



**Fig. 1.** Videofluoroscopic swallowing study lateral plane view. Each image included the lips anteriorly to the vertebrae posteriorly, and the soft palate superiorly to the 6th cervical vertebra inferiorly.

made to eject; 5, material enters the airway, passes below the vocal folds and no effort is made to eject. The ASHA-NOMS scales are listed in Table 2 [21].

**Statistical analysis**

All of the baseline demographic and clinical data between two groups were analyzed using a Pearson chi-square test for categorical variables and an independent t-test for continuous variables. The differences were considered to be statistically significant at  $p < 0.05$ , and the

**Table 2.** The American Speech-Language-Hearing Association National Outcome Measurement System (ASHA-NOMS) swallowing scale

Level	Description
1	Individual is not able to swallow anything safely by mouth. All nutrition and hydration is received through non-oral means.
2	Individual is not able to swallow safely by mouth for nutrition and hydration, but may take some consistency with consistent maximal cues in therapy only. Alternative method of feeding is required.
3	Alternative method of feeding required as individual takes less than 50% of nutrition and hydration by mouth, and/or swallowing is safe with consistent use of moderate cues to use compensatory strategies and/or requires maximum diet restrictions.
4	Swallowing is safe but usually requires moderate cues to use compensatory strategies, and/or individual has moderate diet restrictions and/or still requires tube feedings and/or oral supplements.
5	Swallow is safe with minimal diet restrictions and/or occasionally requires minimal cueing to use compensatory strategies. May occasionally self cue. All nutrition and hydration needs are met by mouth at mealtime.
6	Swallowing is safe and individual eats and drinks independently and may rarely require minimal cueing. Usually self cues when difficulty occurs. May need to avoid specific food items (e.g., popcorn and nuts), or requires additional time (due to dysphagia).
7	Individual's ability to eat independently is not limited by swallow function. Swallowing would be safe and efficient for all consistencies. Compensatory strategies are effectively used when needed.

Pearson correlation tests were used to determine whether the functional parameters were statistically correlated with the swallowing physiology. All statistical analyses were performed using the SPSS ver. 22.0 software (IBM Company, Armonk, NY, USA).

**RESULTS**

**Demographics and clinical characteristics**

A total of 32 medical records were reviewed. 18 patients were determined to belong to the early phase and 14 patients to the late phase. In the early status group, the average age was  $65.50 \pm 11.66$  years with 16 males and 2 females in the population and an average period after radiation therapy of  $8 \pm 8.73$  days. In late status group, the average age was  $59.86 \pm 7.34$  years with 12 males and 2 females in the population and an average period after radiation therapy of  $153 \pm 132.66$  days. In both phases, the most common tumor site was the hypopharynx (43.75%). Histologically the most common type was squamous cell carcinoma (75%). The baseline demographic information is described in Table 1, and there were no statistically significant differences between both groups for all demographic and clinical parameters ( $p > 0.05$ ).

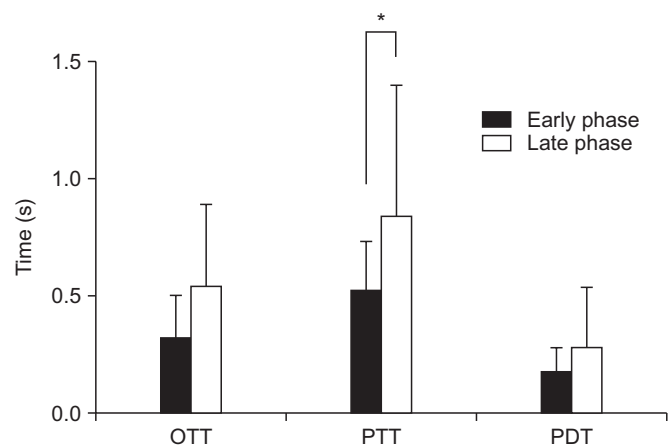
**Swallowing physiology**

(1) Oral transit time: The mean OTT for the early phase was  $1.47 \pm 0.70$  seconds and for the late phase was  $1.53 \pm 0.35$  seconds. Although there was no statistically significant difference ( $p = 0.76$ ), the late phase had a tendency for a longer OTT.

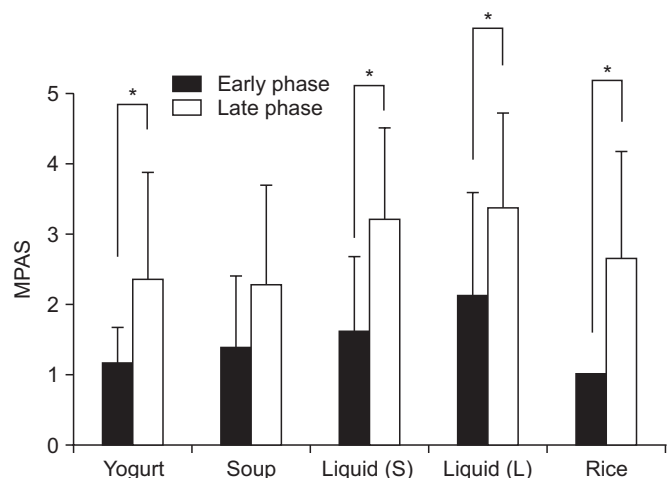
(2) Pharyngeal transit time: The mean PTT for the early phase was  $1.52 \pm 0.21$  seconds and for the late phase was  $1.83 \pm 0.56$  seconds. The PTT was longer in late phase with statistical significance ( $p = 0.03$ ).

(3) Pharyngeal delay time: The mean PDT for the early phase was  $1.17 \pm 0.11$  seconds and for the late phase was  $1.28 \pm 0.25$  seconds. Although there was no statistically significant difference ( $p = 0.10$ ), the late phase had a tendency for a longer PDT.

A quantitative analysis of the swallowing physiology showed that the HNCs exhibited a significant delay in the pharyngeal transit time after the CCRT during the late phase (Fig. 2).



**Fig. 2.** Quantitative data of the swallowing physiology. People in the late status group showed a tendency for longer oral transit time (OTT) and pharyngeal delay time (PDT) than those in the early status group. Pharyngeal transit time (PTT) was statistically longer in the late status group (\*p<0.05).



**Fig. 3.** Modified penetration aspiration scale (MPAS) for 5 different boluses between 2 phases. In all type of boluses, except soup, both groups showed a statistically significant difference in the MPAS results. That is, the late phase MPAS results were higher than those of the early phase.

**Functional measurement of swallow**

In early phase, no patient showed penetration or aspiration. However, in the late phase, 6 (42.8%) patients showed penetration or aspiration.

The mean MPAS of Yogurt was 1.17 for the early phase and 2.36 for the late phase (p=0.014). The MPAS of soup for the early and late phase were 1.39 and 2.29 (p=0.06), respectively. The MPAS of liquid (2.5 mL) were 1.61 and 3.21 (p=0.01), respectively. In all types of boluses, except

**Table 3.** Relationship between functional factors and PTT in late phase

	Pearson correlation coefficient	p-value
MPAS		
Yogurt	0.146	0.42
Soup	0.316	0.07
Liquid 2.5 mL	0.220	0.22
Liquid 5 mL	0.112	0.54
Rice	0.331	0.06
ASHA-NOMS	-0.524	0.002*

PTT, pharyngeal transit time; MPAS, modified penetration aspiration scale; ASHA-NOMS, American Speech-Language-Hearing Association National Outcome Measurement.

\*p<0.05.

for soup, both groups showed a statistically significant difference in MPAS results, that is, the results of the late-phase MPAS were higher than those for the early phase (Fig. 3).

The mean ASHA-NOMS level for the early phase was 5.83±0.78 and for the late phase was 3.79±1.80, with a statistically significant difference (p=0.01).

**Relationship between functional factors and PTT in late phase**

Pearson correlation tests were used to determine whether the MPAS of each bolus or ASHA-NOMS level were statistically correlated with PTT, which was statistically delayed in the late phase. The correlation coefficient showed a statistically significant correlation with ASHA-NOMS level (correlation coefficient=-0.52, p=0.02) (Table 3). However, it showed no relationship with MPAS for each of the boluses.

**DISCUSSION**

In this study, we quantitatively investigated the change in swallowing after CCRT for HNCpPs. In the early phase, all patients did not show any aspiration. However, 6 people (42.86%) showed aspiration or penetration in the late phase. For the swallowing physiology, people in the late phase showed a tendency for a longer OTT and PDT than in the early phase. The PTT showed a significant delay in the late phase.

Recently, the preservation of the swallowing function



has been reported to be important as an oncologic cure for head and neck cancer treatment [22]. Radiotherapy and chemoradiotherapy offer high rates of locoregional control with good potential for functional organ preservation. However, the radiosensitized effect of chemotherapy is known to possibly lead to acute toxicity and late complications [23]. An inflammatory reaction and the production of reactive oxygen species after CCRT can cause dysphasia [24,25], and patients show acute dysphagia within 4 to 5 weeks of starting therapy. As the acute effects are resolved, late effects including fibrosis, lymphedema, and damage to neural structures remain manifested [26].

Many studies have reported changes in swallowing function after chemoradiotherapy. Kotz et al. [18] followed 12 patients with stage III or IV squamous cell carcinoma of the head and neck cancer and showed that swallowing dysfunction is a common side effect of chemoradiation. However, the study was conducted with a small sample size, and the VFSS results were only analyzed in a qualitative manner. Katherine found late dysphagia after a radiotherapy-based treatment of head and neck cancer [22]. They analyzed 29 patients who were previously treated with radiotherapy, but they only analyzed the MPAS results. Nguyen et al. [14] retrospectively reviewed the Modified Barium Swallow in 63 patients who underwent concurrent chemoradiotherapy for head and neck cancer. However, they only categorized patients on a scale from 1 to 7, lacking a description of the phase of swallowing that had been impaired.

In this study, we tried to quantitatively determine the change in swallowing function after CCRT using physiologic and functional data. Dysphagia was more prevalent in late phase after CCRT than in the early phase. This is consistent with observations from previous studies [18,22]. Regarding swallowing physiology, most patients with dysphagia showed a problem in the pharyngeal phase. We evaluated a quantitative comparison between the early phase and late phase after CCRT, not just comparing the qualitative characteristics. Our study showed that late phase PTT was significantly longer than for the early phase.

We also evaluated the functional measurement. In all types of boluses, except for soup, both groups showed a statistically significant difference in MPAS results. The risk of aspiration or penetration is known to vary accord-

ing to the various types of food consistencies [27]. Soup has a low risk of aspiration or penetration, so it showed no significant difference between both groups.

Until now, CCRT is reported to induce dysphagia, but by just using ASHA-NOMS and MPAS, it is hard to know in which phase of swallowing the patient has a problem. A quantitative analysis of the swallowing physiology indicates that the HNCs after CCRT have a problem mainly in the pharyngeal phase. Therefore, this can imply that when doing swallowing therapy, exercises and maneuvers targeting the pharyngeal phase will be more effective than others. Furthermore, a follow-up evaluation of PTT after rehabilitation is recommended.

PTT showed no relationship with MPAS, but it was correlated with the ASHA-NOMS level. This may be explained by reviewing the swallowing process for which each dysphagia scale focuses on. MPAS is a scale that evaluates aspiration or penetration, and it focuses on whether there is penetration into the airway. However, the pharyngeal transit time, which showed statistical significance in this study, focuses on the bolus passage to the pharynx rather than the airway. The ASHA-NOMS level evaluates the overall bolus passage through the airway and the pharynx and allows for a decision for the further feeding route (oral or non-oral). Therefore, this may explain the relationship between the PTT and ASHA-NOMS level. Still, it seems that using only one of the scales (MPAS, ASHA-NOMS, swallowing physiology) is limited in being able to fully evaluate the swallowing of the patient. In summary, a comprehensive assessment is needed before planning the treatment maneuver.

The limitations of this study include its retrospective nature, absence of data regarding quality of life, and lack of long-term follow-up. In addition, our study did not compare the same patient in the early phase and late phase, but rather compared each of the cases of different phases. This can limit selection bias, and a future study comparing the swallowing physiology in the same patient at different times is needed. Finally, our study sample size was somewhat small.

In conclusion, the result of our study suggests that as more time passed after CCRT, the patient showed a delay in OTT, PDT, PTT, and this delay was statistically significant in PTT. Therefore, CCRT induced dysphagia mainly affects the pharyngeal phase during swallowing physiology, and swallowing therapy focusing on the pharyngeal

phase is recommended. Additional prospective studies with long-term follow-up of same patients are needed to assess the change in swallowing in HNCPs after CCRT. Also, the change in function following rehabilitative management is needed to clarify the effect of rehabilitation training for the swallowing function.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

## ACKNOWLEDGMENTS

This study was supported by a grant from the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (2015R1C1A1A01055923), Korean Health Technology R&D Project (HI10C2020, HI3C1990), Ministry of Health & Welfare.

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