

## Sequential Evaluation of Swallowing Function During Chemoradiotherapy for Head and Neck Cancer

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### ABSTRACT

**Background** Many studies have addressed chronic dysphagia resulting from chemoradiotherapy for head and neck cancer (HNC) because of its severity, but changes in the swallowing function during chemoradiotherapy has been rarely reported. This study aimed to elucidate the changes in the swallowing function during chemoradiotherapy for HNC.

**Methods** From April 2018 to July 2020, 20 patients who underwent definitive or postoperative chemoradiotherapy at our hospital for head and neck squamous cell carcinoma were evaluated by flexible endoscopy with the Hyodo scoring system for swallowing, the Penetration–Aspiration Scale (PAS), and the Functional Outcomes Swallowing Scale (FOSS).

**Results** Assessments at the start of treatment, at 40 Gy, and at the end of treatment yielded these mean values: Hyodo score—0.39, 1.22, and 2.56; PAS—1.00, 1.05, and 1.5; FOSS—0.2, 0.55, and 1.1, respectively. The Dunn multiple comparison test was used for analysis to determine significance ( $P < 0.05$ ). The Hyodo score and FOSS were significantly increased at the end of treatment versus initial evaluation; however, score was maintained at a tolerable level for oral intake. PAS did not show a significant increase.

**Conclusion** In conclusion, changes in the swallowing function during chemoradiotherapy for HNC were mild, and swallowing function was maintained at a tolerable level for oral intake.

**Key words** head and neck cancer; radiotherapy; swallowing function

Chemoradiotherapy is a standard treatment for patients with locally advanced head and neck squamous cell carcinoma (HNSCC). Patients typically experience several acute adverse events during treatment, such as mucositis, dermatitis, and dysphagia. Chemoradiotherapy also induces several chronic adverse events, such as dry mouth caused by salivary gland dysfunction, cardiovascular events, secondary cancers, and dysphagia, all of which negatively affect the patient's quality of life.<sup>1,2</sup> Several reports have addressed chronic dysphagia in this population because of its life-threatening severity<sup>1, 3–5</sup>; however, changes in the swallowing function during chemoradiotherapy has been rarely reported.<sup>6,7</sup>

Lazarus et al. reported small number of cases evaluated by videofluorographic swallowing examination (VESE) before and after treatment to assess dysphagia during radiotherapy for HNSCC.<sup>6</sup> The findings demonstrated reduced posterior tongue base movement toward the posterior pharyngeal wall, and reduced laryngeal elevation during the swallowing. However, no information was provided for objective scoring regarding swallowing and for actual oral intake. Few studies have addressed changes in the swallowing function during chemoradiotherapy for HNSCC; however, the effectiveness of flexible endoscopic evaluation of swallowing (FEES) with the Hyodo scoring system was reported to predict aspiration.<sup>8,9</sup> This study performed FEES and VESE at the start of treatment, at 40 Gy, and the end of treatment to elucidate the changes in the swallowing function during chemoradiotherapy for HNSCC.

### MATERIALS AND METHODS

#### Patients and Examinations

From April 2018 to July 2020, patients who underwent definitive or postoperative chemoradiotherapy at the authors' hospital for HNSCC were evaluated with FEES with the Hyodo scoring system, VESE with the Penetration–Aspiration Scale (PAS), and the Functional Outcomes Swallowing Scale (FOSS) at the start of treatment, at 40 Gy, and at the end of treatment.

The Hyodo scoring method is the 4-point scale used to score the results of the flexible endoscopic procedure to evaluate the feasibility of oral intake. This method comprises the following four evaluation points:

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Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events; FEES, flexible endoscopic evaluation of swallowing; FOSS, Functional Outcomes Swallowing Scale; HNC, head and neck cancer; HNSCC, head and neck squamous cell carcinoma; IDDSI, International Dysphagia Diet Standardization Initiative

**Table 1. Flexible endoscopic evaluation of swallowing with the Hyodo scoring method**

FEES with Hyodo scoring method
(1) The salivary pooling degree at the vallecula and piriform sinuses
0: No pooling
1: Pooling at the only vallecular
2: Pooling in vallecula and piriform sinuses and no penetration into larynx
3: Pooling in vallecula and piriform sinuses and penetration into larynx
(2) The glottal closure reflex induced by touching the epiglottis or arytenoid with the endoscope
0: Marked reflex by one touching
1: Slow and/or weak reflex by one touching
2: Reflex by two or three touching
3: No reflex despite three touching
(3) The location of the bolus at the swallowing reflex initiation assessed by “white-out” timing
0: Pharyngeal
1: Vallecula
2: Piriform sinuses
3: No swallowing
(4) The extent of pharyngeal clearance after blue-dyed water is swallowed
0: No residue
1: Pharyngeal residues remain, but are absent after swallowing is attempted two or three times
2: Pharyngeal residues remain, but do not penetration into larynx
3: Pharyngeal residues remain and penetration into larynx

**Table 2. Videofluorographic swallowing examination with the Penetration–Aspiration Scale**

Penetration Aspiration Scale
1. Material does not enter the airway
2. Material enters the airway, remains above the vocal folds, and is ejected from the airway
3. Material enters the airway, remains above the vocal folds, and is not ejected from the airway
4. Material enters the airway, contacts the vocal folds, and is ejected from the airway
5. Material enters the airway, contacts the vocal folds, and is not ejected from the airway
6. Material enters the airway, passes below the vocal folds and is ejected into the larynx or out of the airway
7. Material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort
8. Material enters the airway, passes below the vocal folds, and no effort is made to eject

(1) salivary pooling at the vallecula and piriform sinus; (2) glottal closure reflex induction by touching the epiglottis or arytenoid with the endoscope; (3) location of the bolus at a timing of swallowing reflex initiation; and (4) pharyngeal clearance after swallowing (Table 1). These four parameters are scored with a range of 0–3 on a 4-point scale, and the final score is calculated as the sum of each score in the four parameters. All patients underwent FEES examination with the Hyodo scoring method that was obtained by the transnasal flexible

endoscopic view with the patient swallowing 3 mL colored water while in an upright seated position.

The Penetration–Aspiration Scale (PAS) is an 8-point scale to evaluate the depth and response to airway invasion, which has been widely used as the method to score the results of VESE (Table 2). The PAS scale score is determined while a 5 mL barium swallow is administered to the patient in upright seated position.

FOSS categorizes swallowing function into 6 stages: stage 0, normal function and asymptomatic; stage

1, normal function with episodic or daily symptoms of dysphagia; stage 2, compensated abnormal function manifested by significant dietary modifications or prolonged mealtimes but without weight loss or aspiration; stage 3, decompensated abnormal function with weight loss of < 10% of body weight over 6 months caused by dysphagia or daily cough, gagging, or aspiration during meals; stage 4, severely decompensated abnormal function with weight loss of > 10% of body weight over 6 months caused by dysphagia or severe aspiration with bronchopulmonary complications; and stage 5, nonoral feeding for all nutrition.

In addition, patients were evaluated with the patient's diet for each point using Complete International Dysphagia Diet Standardization Initiative (IDDSI) Framework Detailed Definition 2.0, 2019.<sup>10</sup>

### Treatment

All patients underwent concurrent chemoradiotherapy for HNSCC. Cisplatin was administered every three weeks at a dose of 100 mg/m<sup>2</sup> for three cycles concurrently with radiotherapy. Radiotherapy was performed 5 days/week, and all patients received intensity-modulated radiotherapy. The planned total dose to macroscopic disease (tumor/involved lymph nodes), and high-risk area because of positive margin for transoral surgery was set to 66 Gy (2 Gy/day, 33 fractions). All patients performed prophylactic swallowing exercise such as range of motion for lips, tongue, and larynx, Mendelsohn maneuver, and supraglottic swallowing during the treatment.

### Analysis

Statistical analyses were conducted using GraphPad Prism 9 (GraphPad Software, San Diego, CA). The objective changes in the Hyodo score, PAS, and FOSS were compared by using the Dunn multiple comparison test. For all analyses,  $P < 0.05$  was considered statistically significant.

### Ethical declaration

The protocol of the investigation has been approved by the institutional review board of our university (No. 19A101). This study was conducted in accordance with the Declaration of Helsinki (adopted by the World Medical Association General Assembly in Helsinki in 1964, including subsequent revisions) and "Ethical Guidelines for Medical and Health Research Involving Human Subjects" (December 2014, Ministry of Education, Culture, Sports, Science and Technology, Japan).<sup>11</sup> In accordance with the "Ethical Guidelines for Medical and Health Research Involving Human

Subjects," informed consent for participation was obtained by providing study-related information on the home page and at our outpatient department.

### RESULTS

This study evaluated 20 HNSCC cases for changes in the swallowing function during chemoradiotherapy (Table 3). Mean patient age was 64.5 years, and most patients (17 of 20) were male. All patients had good performance status, and the Eastern Cooperative Oncology Group Performance Status (ECOG PS) score was 0 for all patients. Primary tumor sites were 1 in the nasopharynx, 2 in oropharynx, 11 in hypopharynx, 3 in larynx, 2 in maxillary sinus, 1 in the cervical lymph nodes as metastasis from an occult primary tumor. Clinical stages were 4 patients in stage II, 6 in stage III, and 10 in stage IV. Median irradiation dose was 66 Gy with 33 fractions, and all patients received intensity-modulated radiotherapy. Two patients received chemoradiotherapy in the postoperative setting because of positive margins with transoral surgery for oropharyngeal cancer. The other 18 patients received chemoradiotherapy in the definitive setting. All patients completed concurrent chemoradiotherapy without treatment interruption or delay. No patients had tracheostomy at the start of treatment; and three patients had unilateral vocal cord paralysis at the initial diagnosis. No patients had a history of aspiration pneumoniae. No patients had cognitive dysfunction or impaired consciousness during chemoradiotherapy.

Figure 1 shows the sequential changes of FEES assessed by the Hyodo score. The score was 0.39 at the initial evaluation, 1.22 at 40 Gy, and 2.56 at the end of treatment. The bar charts show means  $\pm$  standard error of the mean (s.e.m.). The Hyodo score at the end of treatment was significantly increased compared with the initial evaluation score on the Dunn multiple comparison test ( $P < 0.05$ ). No significant difference was observed in the mean score between the initial evaluation and 40 Gy and between 40 Gy and the end of treatment.

In sub-item, the mean of the salivary pooling degree at the vallecula and piriform sinuses was 0.22 at the initial evaluation, 0.5 at 40 Gy, and 1.0 at the end of treatment. Compared with the initial evaluation score on the Dunn multiple comparison test ( $P < 0.05$ ), the salivary pooling degree was significantly higher at the end of the treatment.

The other mean values for each point are as follows: glottal closure reflex induction by touching the epiglottis or arytenoid with the endoscope—0, 0.06, and 0.56; location of the bolus at a timing of swallowing reflex initiation—0.17, 0.39, and 0.5; pharyngeal clearance

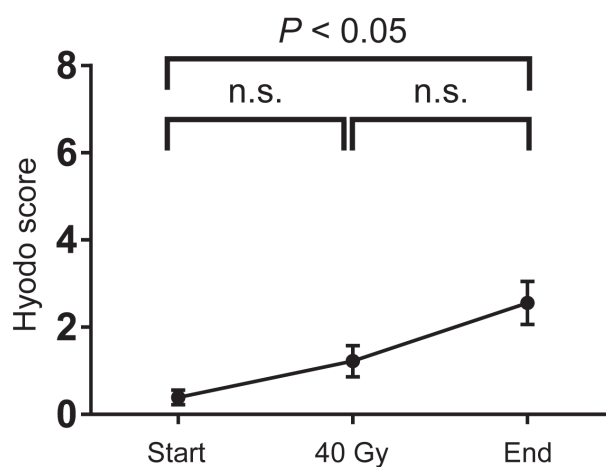
**Table 3. Patient characteristics (n = 20)**

Characteristics	n	%
Age (years)	66.5 (45–75)	
Sex		
Male	17	85
Female	3	15
Performance status		
0	20	100
1–4	0	0
Primary site		
Hypopharynx	11	55
Oropharynx	2	10
Larynx	3	15
Nasopharynx	1	5
Maxillary sinus	2	10
Occult primary	1	5
Stage		
II	4	20
III	6	30
IV	10	50
RT dose (Gy)	66	
IMRT	20	100
Tracheostomy		
No	20	100
Yes	0	0
Vocal cord paralysis		
No	3	15
Yes	17	85
Previous treatment		
No	2	10
Surgery	2	10
Chemotherapy	15	75

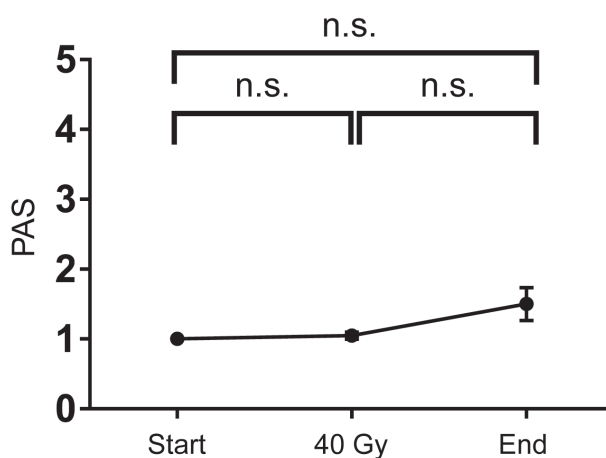
IMRT, intensity modulated radiation therapy; RT, radiation therapy.

after swallowing—0, 0.28, and 0.5, respectively. These scores did not significantly increase throughout the treatment.

Figure 2 shows the mean of PAS score for each point as follows: 1.00 at initial evaluation, 1.05 at 40 Gy, and 1.5 at the end of treatment. The bar charts show means  $\pm$  standard error of the mean (s.e.m.). No significant difference in the mean score was observed between three data points on the Dunn multiple comparison test. Thus, the PAS score did not significantly increase throughout the treatment.



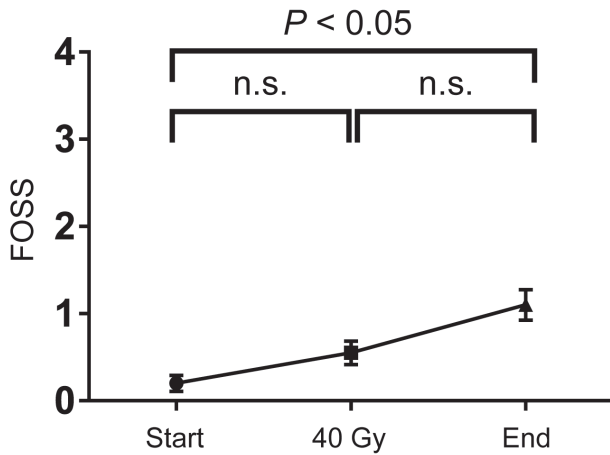
**Fig. 1.** Sequential changes on flexible endoscopic evaluation of swallowing with the Hyodo scoring method. The bar charts show means  $\pm$  standard error of the mean (s.e.m.). Statistical analysis was performed using the Dunn multiple comparison test. n.s., not significant.



**Fig. 2.** Sequential changes on the videofluorographic swallowing examination with the Penetration–Aspiration Scale (PAS). The bar charts show means  $\pm$  standard error of the mean (s.e.m.). Statistical analysis was performed using the Dunn multiple comparison test. n.s., not significant.

Figure 3 shows the sequential changes of FOSS. The score was 0.2 at the initial evaluation, 0.55 at 40 Gy, and 1.1 at the end of treatment. The bar charts show means  $\pm$  standard error of the mean (s.e.m.). The FOSS at the end of treatment was significantly increased compared with the initial evaluation score on the Dunn multiple comparison test ( $P < 0.05$ ). No significant difference was observed in the mean score between the initial evaluation and 40 Gy and between 40 Gy and the end of treatment.

Table 4 shows the form of the patient's diet at



**Fig. 3.** Sequential changes on the Functional Outcome Swallowing Scale (FOSS). The bar charts show means  $\pm$  standard error of the mean (s.e.m.). Statistical analysis was performed using the Dunn multiple comparison test. n.s., not significant.

each point. At the start of treatment, all patients had a Level 7 regular oral diet. At 40 Gy, 3 patients required modification of the diet form. At the end of treatment, 12 (60%) patients had maintained a Level 7 regular diet, 1 (5%) patient was at Level 7 easy to chew, 2 (10%) patients were at Level 6, and 1 (5%) patient was receiving enteral nutrition transorally. In total, 16 (80%) patients continued oral diet intake and 4 (20%) patients required enteral nutrition using nasogastric tube at the end of treatment.

## DISCUSSION

This study characterized to elucidate the changes in the swallowing function during chemoradiotherapy for HNSCC with objective scoring methods: FEES with the Hyodo scoring system, VESE with the PAS score, and FOSS. Chiba et al. reported that a Hyodo score  $> 6$  was the independent predictive factor for aspiration.<sup>8,9</sup> In the present study, the Hyodo score at the end of treatment was 2.56, which was significantly increased compared with the score at initial evaluation. However, swallowing function was maintained at the tolerable level for oral intake at the end of treatment, with or without modification of the diet form. The mean value of FOSS at the end of treatment was 1.1, which was significantly increased. However, FOSS at the end of treatment was also maintained at tolerable level for oral intake without weight loss or aspiration. PAS was not significantly increased throughout the treatment, which supports the characterization of the dysphagia during chemoradiotherapy for HNSCC as not very severe, and the swallowing function was maintained at the tolerable level for oral intake. Swallowing function evaluated

**Table 4.** Diet form during chemoradiotherapy

Diet form	Start	40 Gy	End
Level 7 Regular	20	17	12
Level 7 Easy to chew	0	2	1
Level 6 Soft & bite-sized	0	1	2
Level 3 Liquidised	0	0	1
Enteral nutrition (Nasogastric tube)	0	0	4

by FEES could become worse than that by VFSE as described previously, and VESE is thought to be a gold standard technique to evaluate swallowing function.<sup>12,13</sup> The difference might have caused the dissociation of results between VESE and FEES.

Several studies reported that prophylactic swallowing exercises before and during chemoradiotherapy were useful to prevent a swallowing dysfunction for patients with HNSCC after completing therapy.<sup>14-17</sup> The range of motion exercise of the lips, jaw, tongue, and larynx is a frequent procedure in prophylactic swallowing exercises and aims to improve the movement of the targeted structure and prevent the fibrosis induced by radiotherapy.<sup>12,13</sup> The Mendelsohn maneuver enhances the opening of the upper aerodigestive sphincter and improves pharyngeal clearance by prolongation laryngeal elevation during swallowing.<sup>12,13</sup> In our hospital, all patients who were treated with chemoradiotherapy for HNSCC received prophylactic swallowing exercise during the treatment, which may have been effective to maintain the swallowing function at the tolerable level for oral intake during chemoradiotherapy.

The results of this study showed that swallowing function was able to be maintained at the tolerable level for oral intake. In contrary the authors' overall experience with patients with HNSCC who underwent chemoradiotherapy has been that these patients could not continue oral intake during chemoradiotherapy, especially at the end of treatment. This study also evaluated actual oral intake and diet form using the Complete IDDSI Detailed Definitions 2.0, 2019 for each point (initial evaluation, at 40 Gy, and at end of treatment). Most patients (80%) could continue oral intake with or without diet form modification through the end of treatment; however (20%) could not continue oral intake despite maintaining their FEES, VESE, and FOSS scores. Oral intake is not affected only by swallowing function, but also by the pain, nausea, dysgeusia, and fatigue that result from chemotherapy and radiotherapy.<sup>18</sup> Thus, it is critical to manage these symptoms to enable patients to continue the oral intake during chemoradiotherapy.

The radiation dose for cricopharyngeal muscle and

cervical esophagus has been shown to be relevant for dysphagia during radiotherapy.<sup>7</sup> In this study,  $\geq$  Grade 3 dysphagia according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 was defined as dysphagia; however, dysphagia in CTCAE version 4.0 is not only influenced by swallowing function but also by oral intake status. As discussed, oral intake is not affected only by swallowing function; therefore, dysphagia in CTCAE version 4.0 may not accurately reflect the pure swallowing function. In the present study, 11 patients with hypopharyngeal cancer were included, and therefore the radiation dose for cricopharyngeal muscle and cervical esophagus may be relatively higher than that for patients with other types of HNSCC; however, results showed that deterioration of swallowing function were not severe. Despite the thought that pure swallowing function may be maintained during chemoradiotherapy, the pain, nausea, dysgeusia, and fatigue caused by chemotherapy and radiotherapy mainly results in a negative effect for maintaining the oral intake.

This study elucidated that deterioration of swallowing function during chemoradiotherapy for HNC is not severe based on the objective scoring methods using the Hyodo score, PAS, and FOSS. Swallowing function was maintained at a tolerable level for oral intake at the end of treatment, although a minority of patients could not continue oral intake. Oral intake is affected not only by swallowing function but also by the pain, nausea, dysgeusia, and fatigue that result from chemotherapy and radiotherapy. Therefore, all of these symptoms should be managed to ensure that oral intake can be maintained.

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