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ORIGINAL ARTICLE

Simultaneous evaluation of symptoms, swallowing functions, and patient-reported swallowing difficulties and their correlations with ingestion status during definitive chemoradiotherapy for oropharyngeal and hypopharyngeal cancer

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Abstract

Purpose To clarify the correlations among symptoms, swallowing functions, and ingestion status and to validate a method of swallowing evaluation during chemoradiotherapy (CRT) for head and neck cancer.

Methods Oropharyngeal and hypopharyngeal cancer patients who were to receive definitive CRT as initial treatment were included in this prospective, single-center, observational study. The Functional Oral Intake Scale (FOIS) for ingestion status and grades of symptoms (dryness, dysgeusia, mucositis, and the analgesic ladder); the Yale Pharyngeal Residue Severity Rating Scale on fiberoptic endoscopic evaluation of swallowing (FEES) and the Penetration-Aspiration Scale (PAS) on videofluoroscopic (VF) evaluation for swallowing functions; and the 10-item Eating Assessment Tool (EAT-10) questionnaire were assessed at 5 time points unless the participant refused. The FEES and VF evaluation findings at each point were also compared.

Results There were 38 participants. Dysgeusia, mucositis, and pain grade, as well as the FOIS score, were the worst at 70 Gy and then improved after treatment. The improvements of pharyngeal residue and the PAS after treatment were limited. The EAT-10 and the pain ladder were highly correlated with the FOIS changes at many time points. The VF evaluation rate dropped after 40 Gy, whereas the FEES rate remained high. There were good correlations between pharyngeal residue and the PAS at 0 Gy, 70 Gy, and 3 months.

Conclusion The EAT-10 and pain reflected the FOIS score changes well, while two swallowing evaluations did not. To avoid aspiration, VF evaluation may not be necessary during CRT because of high correlations with pharyngeal residue on FEES.

Keywords Swallowing difficulties · Swallowing evaluation · Ingestion status · Chemoradiotherapy · Head and neck cancer

Introduction

Definitive chemoradiotherapy (CRT) for head and neck cancer (HNC) patients causes high rates of ingestion/swallowing dysfunction due to treatment-induced toxicities including mucositis, xerostomia, trismus, and dysgeusia [1, 2]. Some patients need nutritional support during their treatments, which includes adjustment of the amount or texture of the diet, nutritional supplementation by nasogastric tube or gastrostomy, and counseling with a dietitian. There have been some efforts to reduce these ingestion/swallowing dysfunctions by sparing anatomic structures important to swallowing using intensity-modulated radiation therapy (IMRT) [3], by introducing swallowing exercises [4–7], and by maintaining appropriate nutritional status based on dietary requirements [8].

Dysphagia and aspiration are common complications during and after definitive CRT. According to the meta-analysis, the frequency of deglutition disorders was highest (less than 6 months post treatment), except for pharyngeal residue, which increased from 6 to 12 months post treatment [9]. Major abnormalities on videofluoroscopic (VF) evaluation include reduced elevation of the larynx, weakness of posterior motion of the tongue base, reduced laryngeal closure, and

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prolonged pharyngeal transit time, contributing to a high rate of penetration and aspiration [1]. Of course, VF evaluation is the gold standard to evaluate swallowing functions, but it is sometimes high risk for head and neck cancer patients who are undergoing or have just undergone radiotherapy. On the other hand, fiberoptic endoscopic evaluation of swallowing (FEES) is a safer, more efficient, and sensitive method than VF evaluation for evaluating swallowing. However, it cannot evaluate the dynamics of the pharyngeal wall and larynx, and it only results in whiteout [10, 11]. Kelly et al. [12] insisted that FEES and VF evaluation are not interchangeable for use in rating some parameters of disordered swallowing. Both evaluations are important, but the appropriate timing or choice of evaluations is still unclear [13]. Recent studies showed late dysphagia long after CRT due to other causes, partly related to neuromuscular fibrosis and radiation-induced edema (because of collagen deposition and degradation) [14, 15] and progressive neuropathy [16].

Symptoms caused by radiotherapy such as xerostomia and mucosal sensitivity are related to oral energy or protein intake [17]. There were some reports in which objective swallowing functions were correlated to subjective symptoms and quality of life [18, 19] and, similarly, in which dysphagia affected quality of life after treatment [20]. To prevent swallowing disorders, radiation modifications are recommended, which include salivary gland sparing to avoid xerostomia and swallowing-related muscle sparing [21, 22]. Swallowing exercises are also reported to be important to avoid dysphagia around chemoradiotherapy [5]. However, there are no recommendations about swallowing evaluation during and after treatment, including the methods, time points, and intervals.

The aim of this study was to analyze the correlations among ingestion status, symptoms, swallowing functions, and patient-related swallowing difficulties around the therapeutic period and to validate the feasibility of the evaluation of swallowing functions.

Methods and materials

This was a prospective, single-center, observational study. Inclusion criteria were adult, oropharyngeal or hypopharyngeal cancer patients, who started receiving definitive chemoradiotherapy as initial treatment between July 2014 (after approval from the ethics committee) and December 2016 at our institute and who signed the consent form. Patients were excluded if they had a previous head and neck cancer history, simultaneous multiple primary cancers, severe chronic heart failure, respiratory failure, uncontrollable infectious diseases, and autoimmune diseases. The participants were assessed at 5 time points: pretreatment (0 Gy), during treatment (40 Gy), posttreatment (70 Gy), and 1 month and 3 months after treatment. The types of assessments and outcomes were defined as follows: Ingestion status was assessed using the Functional Oral Intake Scale (FOIS). Grades of symptoms were assessed by Common Terminology Criteria for Adverse Events (CTCAE) grades, using CTCAE version 4.0 for oral dryness and dysgeusia and version 3.0 for pharyngeal mucositis. The World Health Organization (WHO) analgesic ladder was used for pain. Swallowing dysfunctions were evaluated using the Yale Pharyngeal Residue Severity Rating Scale on FEES and the Penetration-Aspiration Scale (PAS) on VF evaluation. Finally, patient-reported swallowing difficulties were assessed using the 10-item Eating Assessment Tool (EAT-10).

The FOIS was used as an indicator of ingestion status. The FOIS is a clinician-rated scale that contains a 7-grade numerical rating to determine patients' oral intake status. A FOIS score of 1 means nil by mouth, and a FOIS score of 7 means no restrictions of oral diet. The FOIS score is obtained from medical records or interviews. Simultaneously, two types of swallowing function assessments were performed: the Yale Pharyngeal Residue Severity Rating Scale on FEES to evaluate pharyngeal residue and the PAS on VF evaluation to evaluate penetration and/or aspiration. FEES is a simple and useful swallowing test, but the moment of pharyngeal constriction is seen as whiteout, so VF evaluation was performed on the same day. For FEES, the Yale Pharyngeal Residue Severity Rating Scale was used [23]. The Yale Pharyngeal Residue Severity Rating Scale is a standardized, anatomically defined, image-based assessment of post-swallow pharyngeal residue. It is divided into two locations (the vallecula and the pyriform sinus), and each of them has a 5-grade assessment of the amount of residue. For VF evaluation, the PAS, which best reflects penetration or aspiration, was used [24]. This scale has 8 grades; a score of 0 means "material does not enter the airway", and a score of 8 means "material enters the airway, passes below the vocal folds, and no effort is made to eject." For FEES, participants in the sitting position underwent transnasal endoscopic examinations without nasal anesthetic spray. First, the appearance of the pharynx or larynx was checked, and then whether there were impairments in sensation or movement during swallowing without water was evaluated. If there was no sign of aspiration of saliva or saliva pooling in the larynx, 5 cm^3 of colored water was placed in the mouth of the participant, and then pharyngeal residue after swallowing was checked and rated by the Yale Pharyngeal Residue Severity Rating Scale. If the participant aspirated obviously and it was hard to pump out, the water was vacuumed, and the evaluation was finished. Only when it was confirmed that it would be safe to continue was the next examination performed with the participant's consent. For VF evaluation, the rater injected 3 cm^3 of 40% (w/v) barium sulfate into the mouth of the participant in the sitting position. Then, the participant was observed during swallowing to determine whether there was penetration or aspiration, rated by the PAS.

Participants could refuse any of the evaluations if they felt nausea or fatigue or if they were uncomfortable. Every evaluation was recorded, and all evaluations were discussed on the same day after the examination to obtain inter-rater agreement. Symptoms were also assessed by these raters at the same time. CTCAE grade v3.0 was used for pharyngeal mucositis, which provides a simple indication of the severity of radiation mucositis [25]. Oral dryness and dysgeusia CTCAE grade v4.0 describe patients' symptoms directly [25]. As an assessment of the degree of pain, medical records were checked for use of analgesics and classified according to the WHO analgesic ladder [26]. In the analgesic ladder, step 1 needs non-opioid analgesics, step 2 needs weak opioids, and step 3 needs strong opioids. For patient-reported swallowing difficulty, the EAT-10, which contains 10 questions about different aspects of the uncomfortableness of eating, was used [27]. For each question, participants answered with a score of 0–4, and the total score (range 0–40) was analyzed.

The amount and pattern of changes in each outcome were assessed around the time of CRT, and which outcomes were changing between 2 points in correlation with FOIS score changes was also assessed. In addition, the rate at which each swallowing examination was performed was evaluated at each point.

Written, informed consent was obtained from all individual participants included in the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of the Tohoku University School of Medicine (number 2014-1-274).

Friedman's test was used for repeatedly measured ordinal scales, and Holm's method was used for multiple comparisons. Spearman's rank correlation test was used to clarify correlations between the FOIS score and the other variables. A p value < 0.05 was considered significant, and all tests were two-tailed. All statistical analyses were performed with the statistical program R for Windows (http://cran.r-project.org).

Results

Patients' characteristics

A total of 38 patients (31 men and 7 women) were enrolled in this study, with an age range of 44–81 years (median 68 years). Their baseline characteristics are shown in Table 1. There were 22 patients with oropharyngeal cancers and 16 with hypopharyngeal cancers. In all cases, the tumor was pathologically diagnosed as squamous cell carcinoma. The most frequent clinical stage was stage IVa. Most patients received CRT with a high-dose cisplatin regimen (80–100 mg/m^2 body surface area (BSA) of cisplatin infusion triweekly), except for patients who had renal disorders. Two patients received induction chemotherapy before CRT. The regimen was a combination of cisplatin (70 mg/m^2 BSA), docetaxel (60 mg/m^2 BSA), and 5-fluorouracil (700 mg/m^2 BSA). For radiation therapy, 24 patients received 3-dimensional radiotherapy (3D-RT), and 12 patients received IMRT. Thirty-seven patients underwent prophylactic gastrostomy before treatment started, and only one patient could not undergo gastrostomy because of anatomical factors. There were no patients who underwent gastrostomy on demand.

Table 1 Demographics and clinical characteristics of the patients

Characteristics	Values
Sex (male), *n* (%)	31 (81.6)
Age in years, median (range)	68 (46–81)
Primary location, *n* (%)	
Oropharynx	22 (57.9)
Hypopharynx	16 (42.1)
Clinical stage, *n* (%)	
Stage II	5 (13.2)
Stage III	2 (5.3)
Stage IVa	27 (71.1)
Stage IVb	4 (10.5)
Treatment, *n* (%)	
Chemoradiotherapy	32 (84.2)
Radiotherapy	4 (10.5)
IC-CRT	2 (5.3)
Radiotherapy, *n* (%)	
3D-RT	26 (68.4)
IMRT	12 (31.6)
Gastrostomy, *n* (%)	
Prophylactic	37 (97.4)
Reactive	0 (0)
None	1 (2.6)
Observation period in months, median (range)	21.1 (3.3–44.9)

IC-CRT induction chemotherapy followed by chemoradiotherapy, *3D-RT* 3-dimensional radiotherapy, *IMRT* intensity-modulated radiation therapy

Changes in ingestion status

At the time of pretreatment, all patients (100%) ate almost normal food (FOIS score 6 or 7). FOIS scores decreased significantly during the radiation therapy ($p < 0.001$) and reached the lowest score at the end of radiation therapy (70 Gy). Although the score improved after treatment, with a significant change between post 1 month and 3 months, there was still a significant difference from the score at 0 Gy ($p < 0.001$)

(Fig. 1a). At post 3 months, 25 patients (65.8%) ate almost normal food (FOIS score 6 or 7). There were no significant changes by primary tumor site (Fig. 1b) at any time point.

Changes in swallowing functions

The Yale Pharyngeal Residue Severity Rating Scale shows the degree of pharyngeal residue of the vallecula and pyriform sinus independently. Pharyngeal residue of both the vallecula and the pyriform sinus increased but showed no significant changes, as shown in Fig. 2. At 0 Gy, the pharyngeal residue of the vallecula was high in some oropharyngeal cancer cases, while the residue at the pyriform sinus was high in some hypopharyngeal cancer cases. However, there was no significant difference in both sites of the Pharyngeal Residue Scale by the tumor primary site. The PAS shows the degree of penetration into the larynx and aspiration, and it showed almost the same changes as the Yale Pharyngeal Residue Severity Rating Scale, with no significant difference between during and after treatment; recoveries of these scales after treatment were limited.

Changes in grades of symptoms

The results are shown in Fig. 3. Oral dryness and dysgeusia grades were significantly worse during radiation therapy compared with that baseline. Dryness grade worsened at posttreatment and even at 3 months after treatment. On the other hand, dysgeusia showed a significant difference between 0 Gy and post 3 months ($p < 0.05$). Mucositis grade was also significantly worse during treatment compared with that at 0 Gy ($p < 0.001$), and after treatment, it improved to nearly its original level. The change in analgesic use was similar to that of mucositis grade: it worsened during treatment and improved to its original level after treatment.

Changes in patient-reported swallowing difficulty

The EAT-10 score reflects the changes in subjective symptoms and feelings or attitudes for eating. Although there was a large variance among the EAT-10 scores at pretreatment, they worsened significantly through treatment ($p < 0.001$). The scores decreased partly after treatment, but the changes were not significant, and the variances were still large.

Correlation between FOIS score changes and other outcomes in each period

Spearman's rank correlation tests were performed for all time points to determine which outcomes changed similarly to the FOIS score changes. Table 2 shows which outcomes had correlations in their changes with the FOIS score changes and when the correlations existed. Both swallowing functions had no correlations with FOIS score changes. Mucositis grade change had a correlation with FOIS changes from 0 to 40 Gy and from 40 Gy to post 3 months. Changes in dryness grade or dysgeusia grade also had no significant correlations with FOIS score changes. Changes in the WHO pain ladder were

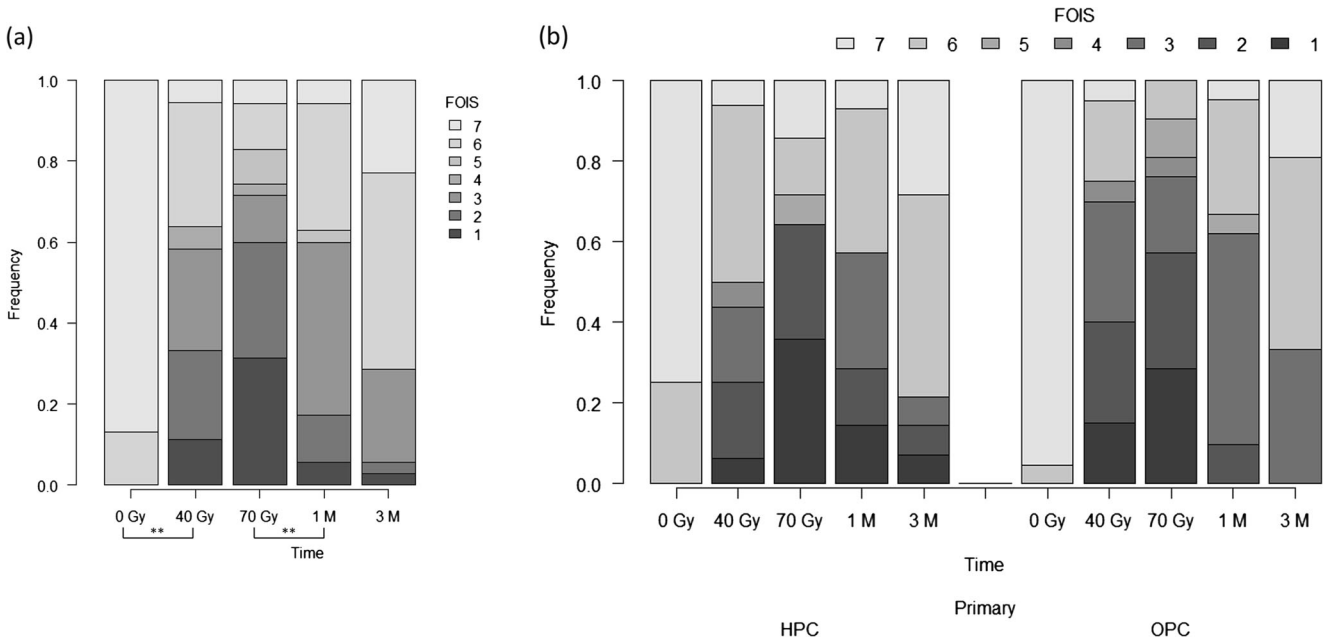


Fig. 1 Changes in Functional Oral Intake Scale (FOIS) scores reflecting ingestion status. **a** Overall change in FOIS scores. **b** changes in FOIS scores by primary tumor site. FOIS shows a significant change during and after chemoradiotherapy (CRT) ($p < 0.001$). There is also a significant difference between pretreatment and after 6 months. There are no significant changes either by radiation method or by primary tumor site. HPC, hypopharyngeal cancer; OPC, oropharyngeal cancer. $^{**}p < 0.001$

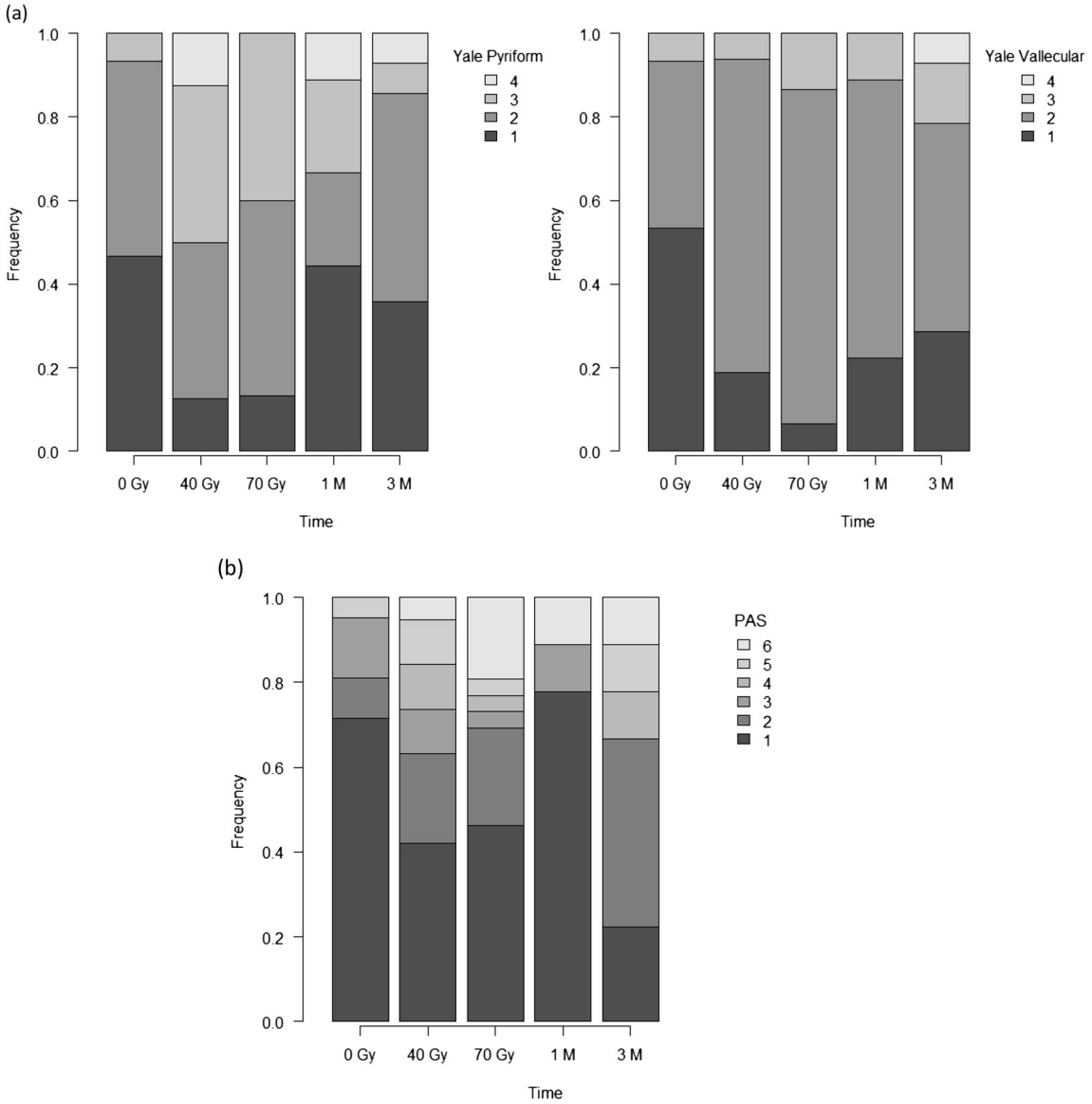


Fig. 2 Changes in swallowing evaluations. **a** The Yale Pharyngeal Residue Severity Rating Scale (pyriform sinus and vallecula). **b** Penetration-Aspiration Scale (PAS). There are no significant changes, but both the Yale Pharyngeal Residue Severity Rating Scale and the PAS show deterioration during treatment and recovery after treatment. The PAS seems to be worse at 3 months. PAS Penetration-Aspiration Scale, CTCAE Common Terminology Criteria of Adverse Events

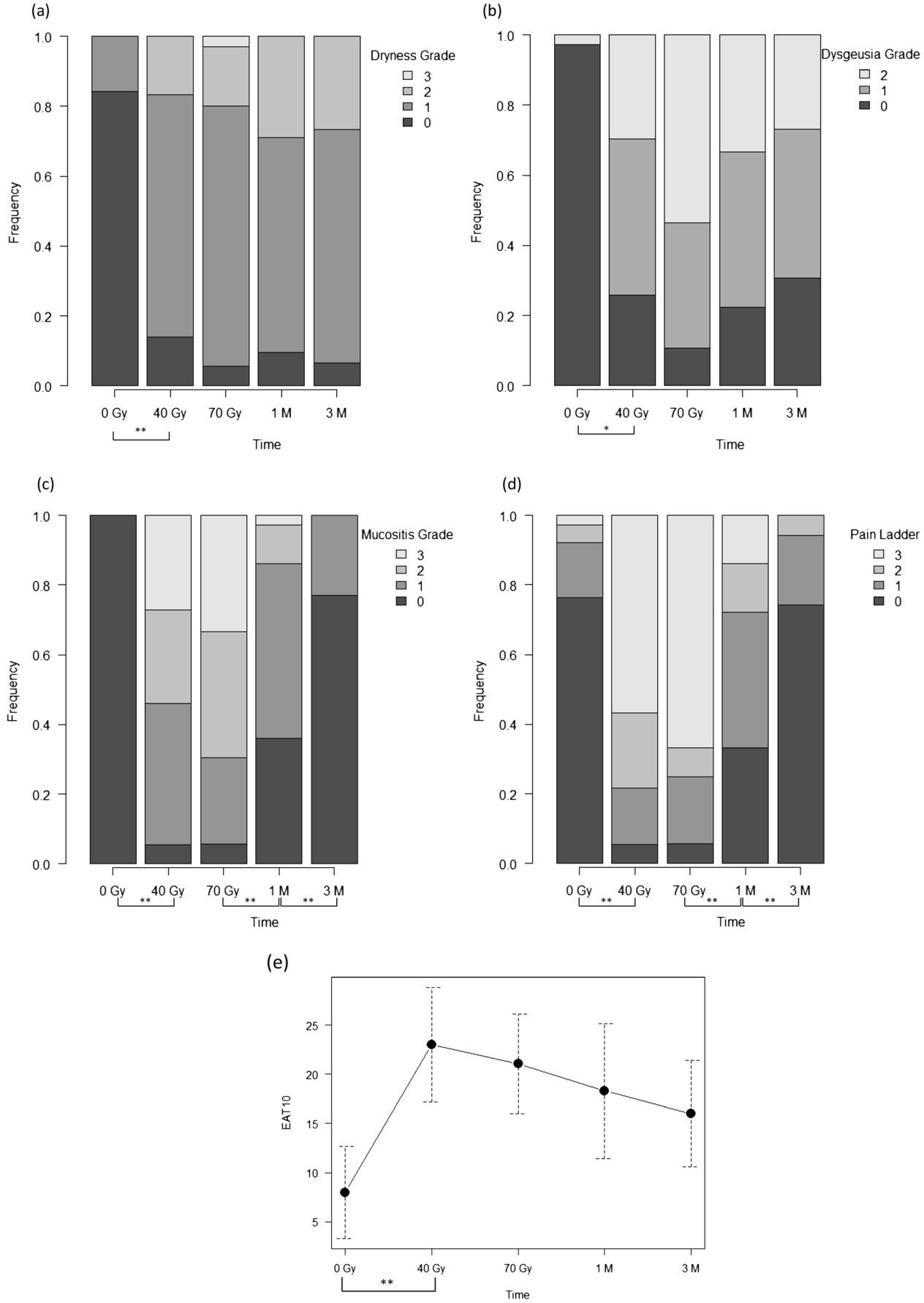
correlated with FOIS score changes during treatment. In addition, EAT-10 changes had significant and good correlations with FOIS score changes both during and after treatment. These results suggest that pain and swallowing difficulty were the factors affecting ingestion status directly and strongly.

Examination rate at each point

Table 3 shows the rate of swallowing examinations performed at each time point. Because participants could refuse any of the evaluations due to nausea, fatigue, or feeling uncomfortable, the rate of both examinations decreased after treatment. The rate of VF evaluation reached a minimum of 71% at 40 Gy and remained low thereafter, in contrast to the high and constant rate of VE; surprisingly, it was almost 100% throughout the treatment period.

Correlations between the PAS (VF evaluation) and the Yale Pharyngeal Residue Severity Rating Scale (FEES) at each point

Table 3 also shows the correlations between the PAS and the Yale Pharyngeal Residue Severity Rating Scale at each time point. There were good correlations between these two scales, in both residue in the vallecula and residue in the pyriform


(a)
Dryness Grade
3
2
1
0
Frequency
1.0
0.8
0.6
0.4
0.2
0.0
0 Gy
40 Gy
70 Gy
1 M
3 M
**
Time
(b)
Dysgeusia Grade
2
1
0
Frequency
1.0
0.8
0.6
0.4
0.2
0.0
0 Gy
40 Gy
70 Gy
1 M
3 M
*
Time
(c)
Mucositis Grade
3
2
1
0
Frequency
1.0
0.8
0.6
0.4
0.2
0.0
0 Gy
40 Gy
70 Gy
1 M
3 M
**
**
**
Time
(d)
Pain Ladder
3
2
1
0
Frequency
1.0
0.8
0.6
0.4
0.2
0.0
0 Gy
40 Gy
70 Gy
1 M
3 M
**
**
**
Time
(e)
EAT10
25
20
15
10
5
0 Gy
40 Gy
70 Gy
1 M
3 M
**
Time

◀ **Fig. 3** Changes in grades of symptoms and patient-reported swallowing difficulties. **a** Dryness Common Terminology Criteria for Adverse Events (CTCAE) grade. **b** Dysgeusia CTCAE grade. **c** Mucositis CTCAE grade. **d** Analgesia World Health Organization (WHO) ladder. **e** 10-item Eating Assessment Tool (EAT-10). Dryness and dysgeusia grade are significantly worse during the radiation and remain so long after treatment, whereas pain improves to its original level after the treatment. The EAT-10 score reflects these changes in subjective symptoms, which worsen through treatment and are partially prolonged after treatment. Error bars indicate 95% confidence intervals. *$p < 0.05$; **$p < 0.001$

sinus, at 0 Gy, 70 Gy, and post 3 months. There were no obvious differences between the sites of residue.

Discussion

This study showed that ingestion status was well correlated with pain and patient-reported swallowing difficulties in pharyngeal cancer patients who underwent CRT. Although it was novel to assess two swallowing evaluations simultaneously, the rate of VF evaluation decreased to about 70% during treatment, whereas the rate of FEES remained high. In addition, the PAS and the Yale Pharyngeal Residue Severity Rating Scale had good correlations during and after treatment, so that this simultaneous evaluation may not be necessary, which would avoid aspiration.

The FOIS was first reported by Crary et al. [28] as an appropriate tool for estimating and documenting changes in the functional eating abilities of stroke patients over time. A previous study reported that a low pretreatment FOIS score was related to enteral nutrition (EN) dependency and first attaining swallowing function after the surgery in advanced oral and oropharyngeal malignancies [29]. Messing et al. [30] compared HNC patients' swallowing functions including FOIS with or without prophylactic swallowing therapy in those undergoing CRT. This randomized trial suggested the importance of swallowing therapy for better oral intake at 3 months after CRT, but there was no significant difference [30]. There were some similar studies of FOIS scores around CRT for HNCs, and these reports showed similar changes in the FOIS as the present study [6, 31].

Some recent reports focused on patient-reported symptoms or dysphagia in CRT for HNC, because the toxic effect of CRT is underestimated by practitioner-reported compared with patient-reported evaluations [30]. For dysphagia, a prospective study showed that dryness was the main problem and was correlated to patient-reported dysphagia [32, 33]. Although Nevens et al. [34] observed a significant association between physician- and patient-scored dysphagia, pretreatment and posttreatment, the PAS did not show significant changes among three time points (baseline, 6 months, and 12 months). This is consistent with the results of the present study. The present study did not show significant changes in the PAS, but Hedström et al. [35] reported that severe dysphagia according to the PAS could be predicted by patient-reported symptoms.

To the best of our knowledge, this is the first study in which grades of symptoms, two types of swallowing evaluations (FEES and VF evaluations), and patient-reported swallowing difficulty were assessed simultaneously and frequently around the treatment period. In a similar but different previous study, FEES was reported to be feasible and useful for detecting changes in swallowing function, especially in pharyngeal residue, and implied that it was a valid alternative to VF evaluation for instrumental swallowing evaluation [36]. In terms of the associations between patients' symptoms and swallowing functions, Kirsh et al. [37] showed that worsened function after CRT was not correlated with patient-reported quality of life measures. Shapira-Galitz et al. [38] showed that the Yale Pharyngeal Residue Severity Rating Scale was correlated with the PAS in dysphagia patients including HNC patients, and

Table 2 Correlations between FOIS changes and other factors (Spearman's rank correlation rho)

	0–40 Gy	40–70 Gy	70 Gy to post 1 month	Post 1–3 months
FOIS vs Yale Pharyngeal Residue Severity Rating Scale of the vallecula	− 0.031 ($p = 0.85$)	0.19 ($p = 0.27$)	− 0.048 ($p = 0.79$)	0.14 ($p = 0.47$)
FOIS vs Yale Pharyngeal Residue Severity Rating Scale of the pyriform sinus	− 0.18 ($p = 0.29$)	0.071 ($p = 0.69$)	− 0.22 ($p = 0.21$)	− 0.37 ($p = 0.054$)
FOIS vs PAS	0.13 ($p = 0.53$)	0.0055 ($p = 0.81$)	− 0.13 ($p = 0.54$)	− 0.20 ($p = 0.40$)
FOIS vs mucositis grade	− 0.37 ($p = 0.026$)*	− 0.16 ($p = 0.38$)	0.057 ($p = 0.75$)	0.036 ($p = 0.84$)
FOIS vs dryness grade	0.098 ($p = 0.56$)	0.077 ($p = 0.66$)	− 0.068 ($p = 0.70$)	0.16 ($p = 0.38$)
FOIS vs dysgeusia grade	− 0.17 ($p = 0.33$)	0.17 ($p = 0.35$)	0.12 ($p = 0.51$)	− 0.089 ($p = 0.62$)
FOIS vs WHO analgesic ladder	− 0.37 ($p = 0.024$)*	− 0.44 ($p = 0.009$)**	− 0.20 ($p = 0.24$)	− 0.31 ($p = 0.072$)
FOIS vs EAT-10	− 0.53 ($p = 0.002$)**	− 0.19 ($p = 0.45$)	− 0.40 ($p = 0.098$)	− 0.56 ($p = 0.003$)**

FOIS Functional Oral Intake Scale, *PAS* Penetration-Aspiration Scale, *WHO* World Health Organization, *EAT-10* 10-item Eating Assessment Tool

*$p < 0.05$; **$p < 0.01$

Table 3 Comparison of two swallowing evaluations

	0 Gy	40 Gy	70 Gy	Post 1 month	Post 3 months
Number of patients and rate of 2 swallowing evaluations at each point					
FEES	38 (100)	38 (100)	38 (100)	37 (97.4)	30 (78.9)
VF evaluation	38 (100)	27 (71.1)	33 (86.8)	30 (78.9)	29 (76.3)
Correlations between the PAS (VF evaluation) and the Yale Pharyngeal Residue Severity Rating Scale (FEES) at each point (Spearman's rank correlation rho)					
Yale Pharyngeal Residue Severity Rating Scale					
Vallecula	0.42 ($p = 0.0094$)**	0.093 ($p = 0.65$)	0.46 ($p = 0.011$)*	0.13 ($p = 0.52$)	0.46 ($p = 0.020$)*
Pyriform sinus	0.37 ($p = 0.023$)*	0.30 ($p = 0.14$)	0.52 ($p = 0.0032$)**	0.19 ($p = 0.36$)	0.57 ($p = 0.0031$)**

FEES fiberoptic endoscopic evaluation of swallowing, *VF* videofluoroscopic, *PAS* Penetration-Aspiration Scale

*$p < 0.05$; **$p < 0.01$

the present study may support their results, at least with respect to penetration and aspiration during and after CRT.

The present study suggested that ingestion status around CRT may reflect pain and patient-reported swallowing difficulties separately from the risk for aspiration and worsened swallowing function. However, the correlations among symptoms and patient-related outcomes require further consideration to understand the quality of life of CRT survivors, because patient-related outcomes were reported to be highly associated with each other [39]. Another implication of this study is that VF evaluation may not be necessary during CRT because of high correlations with pharyngeal residue on FEES. However, the VF evaluation study before treatment was very important, because there were good correlations between the PAS at 0 Gy and 70 Gy, with Spearman's rank correlation rho of 0.58 ($p < 0.001$). This shows that the risk of aspiration after treatment can be predicted by VF evaluation testing pretreatment. Therefore, further investigation is needed to establish the method of evaluating swallowing functions and ingestion status, taking into account patients' symptoms and quality of life in CRT survivors.

Some limitations in this study should be mentioned. First, there were missing data for swallowing evaluations, since participants could refuse any of the evaluations because of nausea, fatigue, or feeling uncomfortable. Thus, there might be selection bias in the participants who underwent swallowing evaluations. However, the rate of participants who were evaluated according to the protocol was one of the important considerations in this study. Second, all of the outcomes in this study were ordinal scales, in which the number of categories varied depending on the outcome. Because outcomes had only three or four categories of actual data, some of them might have changed more significantly if there were more categories. Finally, four grades of symptoms were defined, and one patient-reported questionnaire was used in this study, but there may be symptoms and questionnaires that are more important or more worth examining. Today, patient-related outcomes are becoming more important also in the area of HNC [40]; it may be necessary to plan a study with more patient-reported outcomes.

Conclusions

In conclusion, this prospective observational study showed that pain and patient-reported swallowing difficulties reflected the FOIS score change well during and after CRT for HNC, while two swallowing evaluations did not. VF evaluation may not be necessary during CRT because of the low rate of examination and high correlations with pharyngeal residue in FEES, which would avoid aspiration. Further investigation is needed to establish the means for evaluating swallowing functions, patients' symptoms, and quality of life in CRT survivors.

Authors' contributions Ryo Ishii, Kengo Kato, Ai Hirano, and Yukio Katori contributed to the conception and study design, data acquisition, analysis, and drafting of the manuscript. Takeshi Sato contributed to the data acquisition and analysis. Akira Ohkoshi and Takenori Ogawa contributed to the analysis and drafting of the manuscript. All authors revised the article critically and approved the final version for publication.

Data availability The authors have full control of all primary data and agree to allow the journal to review the data if requested.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of the Tohoku University School of Medicine (number 2014-1-274).

Consent to participate Written, informed consent was obtained from all individual participants in this study.

Consent to publication Not applicable

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