Improvement of a Delayed Swallowing Reflex with Treatment in Advanced Head and Neck Cancer Patients

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Abstract

Background The latency of the swallowing reflex is an important factor causing dysphagia in head and neck cancer patients. Although there are many reports comparing swallowing function before and after treatment, few studies have focused on the latency of the swallowing reflex. The aim of this retrospective study was to clarify the changes in the latency of the swallowing reflex before and after treatment.

Methods The latency of the swallowing reflex was quantified using the time from the injection of 1 ml of distilled water into the pharynx through a nasal catheter to the onset of swallowing.

Results The latency time of the swallowing reflex was significantly decreased 3 months after treatment compared to before treatment. Significant reduction was also observed in patients with pharyngeal cancer who underwent chemoradiation therapy.

Conclusions This retrospective study showed that a delayed swallowing reflex improved with treatment in advanced head and neck cancer patients.

1. Background

Advanced head and neck cancer and its treatment cause swallowing disorders that reduce patients' quality of life and decrease survival (1, 2). A delayed swallowing reflex is one of the most important factors causing dysphagia, such as reduced tongue base retraction, reduced laryngeal elevation, and cricopharyngeal dysfunction (3, 4). Both a delayed swallowing reflex and reduced elevation of the larynx are reported to be independent risk factors for aspiration pneumonia in head and neck cancer patients (5). The treatment, including both surgery and chemoradiation, for head and neck cancer is known to cause a delayed swallowing reflex (6, 7). Whereas direct invasion of tumor to the pharynx causes a delayed swallowing reflex, the disappearance of tumor with treatment can improve swallowing function (8, 9). Although there are many reports comparing swallowing function before and after treatment, few studies have focused on the latency of the swallowing reflex (10, 11). Thus, a retrospective study of patients with advanced head and neck cancer was conducted to clarify the changes of the latency of the swallowing reflex from before to after treatment.

2. Methods

2.1. Patient selection

This retrospective study was performed in accordance with the Helsinki Declaration and approved by The Institutional Review Board of Tohoku University Hospital (Number 2014-1-274). All patients who received treatment, including surgery and radiation therapy with or without chemotherapy, for advanced head and neck cancer and whose latency of the swallowing reflex was assessed both before and 3 months after treatment at the Department of Otolaryngology-Head and Neck Surgery of Tohoku University Hospital

between April 2014 and March 2019 were included. Patients who underwent total laryngectomy at the same time or had early clinical stage II or under were excluded.

2.2. Assessment of the latency of the swallowing reflex

Individual latency time of the swallowing reflex was assessed before and 3 months after treatment. The swallowing reflex was induced by a bolus injection of 1 ml of distilled water into the pharynx through an 8-Fr nasal catheter. The latency of the swallowing reflex was quantified using the time from the injection to the onset of swallowing, and the average of 3 measurements was used in the analysis (12). Patients with a latency time over 3 seconds were defined as having a delayed swallowing reflex in this study (13).

2.3. Statistical analysis

Differences were evaluated for significance using the paired t-test or the chi-squared test. Values are presented as means $\pm$ SD.

3. Results

A total of 53 patients (37 men and 16 women) were enrolled in this study, with an age range of 18–82 (median 65) years. The characteristics of the patients are shown in Table 1. There were 28 patients with oral cancers and 25 with pharyngeal cancers, including 17 oropharyngeal and 8 hypopharyngeal cancers. Forty-four patients were clinical stage IV, and 9 patients were stage III. Twenty-three patients underwent surgery, 22 patients received chemoradiation, 6 patients received both surgery and chemoradiation, and the other 2 patients received radiation without chemotherapy.

To evaluate whether the treatment of head and neck cancer changes the swallowing reflex, the latency time of the swallowing reflex was compared before and 3 months after treatment. The latency time of the swallowing reflex was significantly decreased at 3 months after treatment (1.91 ± 0.61 seconds) compared to before treatment (2.57 ± 1.73 seconds, $p = 0.012$, Fig. 1A). The ratio of patients with a delayed swallowing reflex was also significantly decreased at 3 months after treatment (3/53, 5.6%) compared to before treatment (13/53, 24.5%, $p = 0.0066$, Fig. 1B).

Next, in order to examine the difference among the sites of head and neck cancer, the 53 patients were divided into those with cancers of the oral cavity ($n = 28$) and the pharynx ($n = 25$), which was further subdivided into oropharynx ($n = 17$) and hypopharynx ($n = 8$). Whereas there was no significant difference between before and 3 months after treatment in patients with the cancers of the oral cavity (2.24 ± 1.27 to 2.01 ± 0.71 seconds, $p = 0.36$), a significant reduction of the latency time of the swallowing reflex was observed in patients with the cancers of the pharynx (2.89 ± 2.11 to 1.80 ± 0.46 seconds, $p = 0.017$, Fig. 2A). No significant latency time reduction of the swallowing reflex was observed in patients with cancers of the oropharynx (3.02 ± 2.48 to 1.85 ± 0.52 seconds, $p = 0.073$), but it was observed in those with cancers of the hypopharynx (2.61 ± 1.01 to 1.88 ± 0.23 seconds, $p = 0.047$, Fig. 2A). On the other hand, the ratio of patients with a delayed swallowing reflex was not significantly changed in patients with cancers of the oral cavity (6/28, 21.4% to 3/28, 10.7%, $p = 0.27$), whereas significant reduction was

observed in patients with the cancers of the pharynx (7/25, 28.0% to 0/28, 0%, $p = 0.0043$, Fig. 2B). Significant reduction of the ratio of patients with a delayed swallowing reflex was observed in patients with cancers of the oropharynx (4/17, 23.0% to 0/17, 0%, $p = 0.033$), but no significant reduction was observed in those with cancers of the hypopharynx (3 / 8, 37.5% to 0 / 8, 0%, $p = 0.054$, Fig. 2B).

Next, in order to examine the difference among treatments, the patients were divided into those treated with surgery ($n = 23$) and those treated with chemoradiation ($n = 22$). Patients who underwent both surgery and chemoradiation ($n = 6$) and those who underwent radiation without chemotherapy ($n = 2$) were excluded because of their small numbers. Whereas there was no significant difference between before and 3 months after treatment in the patients who underwent surgery (2.08 ± 0.93 to 2.10 ± 0.72 seconds, $p = 0.88$), significant reduction of the latency time of the swallowing reflex was observed in the patients who underwent chemoradiation (2.80 ± 1.83 to 1.76 ± 0.45 seconds, $p = 0.036$, Fig. 3A). On the other hand, the ratio of patients with a delayed swallowing reflex was not significantly changed in the patients who underwent surgery (4/23, 17.3% to 3/23, 13.0%, $p = 0.68$), whereas significant reduction was observed in the patients who underwent chemoradiation (5/22, 22.7% to 0/22, 0%, $p = 0.017$, Fig. 3B).

4. Discussion

This study demonstrated that a delayed swallowing reflex improved after treatment in advanced head and neck cancer patients. A delayed swallowing reflex is known to be an independent risk factor for aspiration pneumonia in head and neck cancer patients (5). Both invasion of the tumor into the pharynx and cancer treatment including surgery and chemoradiation are known to cause a delayed swallowing reflex due to decreased pharyngeal sensation (6–8). Although there are many reports comparing swallowing function, such as laryngeal elevation or penetration-aspiration, before and after treatment, few studies have focused on the latency of the swallowing reflex. To the best of our knowledge, this is the first report showing significant improvement in the delayed swallowing reflex after treatment in head and neck cancer patients. Despite an increased rate of dysphagia in patients after treatment due to reduced tongue base retraction, reduced laryngeal elevation, cricopharyngeal dysfunction, and so on, some patients reported improved swallowing function (14, 15). In addition to disappearance of tumor, the improvement of a delayed swallowing reflex shown in the present study may contribute to recovery from dysphagia in such cases. In the present study, improvement of a delayed swallowing reflex was observed only in patients with pharyngeal cancer or who received chemoradiation. Because most patients (22 of 25 patients) with pharyngeal cancer received chemoradiation, the difference between the two groups is considered to be small in the present study. Since chemoradiation for pharyngeal cancer causes various sensory disorders with mucositis, such as pharyngeal pain, xerostomia, and dysgeusia, the improvement of a delayed swallowing reflex shown in the present study may have some relationship with pharyngeal hypersensitivity following radiation pharyngitis (16, 17). On the other hand, no improvement of the swallowing reflex was observed in patients with oral cancer or those who underwent surgery in the present study. Because the swallowing reflex was induced by injection of water into the pharynx in the present study, oral cancer without direct invasion into the pharynx or surgery without manipulation of the pharynx was thought to have little effect on the swallowing reflex.

The present study has several limitations. First, this retrospective study did not consider oral food intake or swallowing function other than the latency of the swallowing reflex. As with many other reports, despite the improvement of the delayed swallowing reflex, oral food intake of the patients in this study did not improve after treatment (data not shown). This is thought to be because oral food intake is affected by many factors other than the latency of the swallowing reflex, such as prophylactic nutrition tube placement, xerostomia, and dysgeusia (18). Second, the latency of the swallowing reflex was measured at only one point, 3 months after treatment, in the present study. Although pharyngeal mucositis and pain have ceased at this point, hypersensitivity of the pharynx can exist and affect the results. Third, this study had a small sample size, so that small numbers of pharyngeal cancer patients underwent surgery. Surgery of the tongue base, which is well known to cause dysphagia, could have affected the results of this study (19). Despite these limitations, this study provides valuable information about the latency of the swallowing reflex before and after treatment in head and neck cancer patients. The result will be helpful for better management of patients with swallowing disorders.

5. Conclusion

This retrospective study showed that a delayed swallowing reflex improved after treatment in advanced head and neck cancer patients.

Declarations

Ethics approval and consent to participate

This study was performed in accordance with the Helsinki Declaration and approved by The Institutional Review Board of Tohoku University Hospital (Number 2014-1-274).

Consent for publication

All patients have signed the Informed consent for publication.

Availability of data and material

The datasets during and/or analyzed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

AO designed the study and wrote initial draft of the manuscript. KK designed the study, assisted in the preparation of the manuscript. TO and AN contributed analysis and interpretation of data. RI and YK have contributed to data collection and interpretation, and critically reviewed the manuscript. All authors approved the final version of the manuscript, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References

- [1] Chen AY, Frankowski R, Bishop-Leone J et al. The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer: the M. D. Anderson dysphagia inventory. *Arch Otolaryngol Head Neck Surg*. 2001; 127 (7): 870-876.
- [2] Shune SE, Karnell LH, Karnell MP, Van Daele DJ, Funk GF. Association between severity of dysphagia and survival in patients with head and neck cancer. *Head Neck*. 2012; 34 (6): 776-784.
- [3] Van der Molen L, van Rossum MA, Burkhead LM, Smeele LE, Hilgers FJ. Functional outcomes and rehabilitation strategies in patients treated with chemoradiotherapy for advanced head and neck cancer: a systematic review. *Eur Arch Otorhinolaryngol*. 2009; 266 (6): 889-900.
- [4] Manikantan K, Khode S, Sayed SI et al. Dysphagia in head and neck cancer. *Cancer Treat Rev*. 2009; 35 (8): 724-732.
- [5] Jung SJ, Kim DY, Joo SY. Risk factors associated with aspiration in patients with head and neck cancer. *Ann Rehabil Med*. 2011; 35 (6): 781-790.
- [6] Eisbruch A, Lyden T, Bradford CR et al. Objective assessment of swallowing dysfunction and aspiration after radiation concurrent with chemotherapy for head-and-neck cancer. *Int J Radiat Oncol Biol Phys*. 2002; 53: 23-28.
- [7] Stenson KM, MacCracken E, List M et al. Swallowing function in patients with head and neck cancer prior to treatment. *Arch Otolaryngol Head Neck Surg*. 2000; 126 (3): 371-377.
- [8] Pauloski BR, Rademaker AW, Logemann JA et al. Pretreatment swallowing function in patients with head and neck cancer. *Head Neck*. 2000; 22 (5): 474-482.
- [9] Hutcheson KA, Lewin JS. Functional outcomes after chemoradiotherapy of laryngeal and pharyngeal cancers. *Curr Oncol Rep*. 2012; 14 (2): 158-165.

- [10] Patterson JM, McColl E, Carding PN, Hildreth AJ, Kelly C, Wilson JA. Swallowing in the first year after chemoradiotherapy for head and neck cancer: clinician- and patient-reported outcomes. *Head Neck*. 2014; 36 (3): 352-358.
- [11] Ohkoshi A, Ogawa T, Nakanome A et al. Predictors of chewing and swallowing disorders after surgery for locally advanced oral cancer with free flap reconstruction: A prospective, observational study. *Surg Oncol*. 2018; 39 (2): 77-81.
- [12] Ebihara T, Ebihara S, Watando A et al. Effects of menthol on the triggering of the swallowing reflex in elderly patients with dysphagia. *Br J Clin Pharmacol*. 2006; 62 (3): 369-371.
- [13] Ebihara T, Takahashi H, Ebihara S et al. Capsaicin troche for swallowing dysfunction in older people. *J Am Geriatr Soc*. 2005; 53: 824-828.
- [14] Langerman A, Maccracken E, Kasza K, Haraf DJ, Vokes EE, Stenson KM. Aspiration in chemoradiated patients with head and neck cancer. *Arch Otolaryngol Head Neck Surg*. 2007; 133 (12): 1289-1295.
- [15] Newman LA, Vieira F, Schwiezer V et al. Eating and weight changes following chemoradiation therapy for advanced head and neck cancer. *Arch Otolaryngol Head Neck Surg*. 1998; 124 (5): 589-592.
- [16] Hovan AJ, Williams PM, Stevenson-Moore P et al. A systematic review of dysgeusia induced by cancer therapies. *Support Care Cancer*. 2010; 18 (8): 1081-1087.
- [17] Logemann JA, Pauloski BR, Rademaker AW et al. Xerostomia: 12-month changes in saliva production and its relationship to perception and performance of swallow function, oral intake, and diet after chemoradiation. *Head Neck*. 2003; 25 (6): 432-437.
- [18] Ishii R, Kato K, Ogawa T et al. Poor oral intake causes enteral nutrition dependency after concomitant chemoradiotherapy for pharyngeal cancers. *Eur Arch Otorhinolaryngol*. 2018; 275 (6): 1607-1611.
- [19] Fujiki M, Sakuraba M, Miyamoto S, Hayashi R. Predictive factors of dysphagia after lateral and superior oropharyngeal reconstruction with free flap transfer. *Surg Oncol*. 2016; 113 (2): 240-243.

Table

Please see the supplementary files section to access the table.

Figures

Figure 1

Latency of the swallowing reflex before and 3 months after treatment. Asterisks indicate significant differences between before and after treatment. The error bars indicate standard deviation. A, Comparison of the latency time of the swallowing reflex before and 3 months after treatment (n=53, p<0.05, paired t-test). B, Comparison of the ratio of patients with a delayed swallowing reflex before and 3 months after treatment (p<0.01, chi-squared test). Time over 3 seconds was defined as a delayed swallowing reflex.

Figure 2

Latency of the swallowing reflex before and 3 months after treatment among the sites of head and neck cancer. Asterisks indicate significant differences between before and after treatment. The error bars indicate standard deviation. A, Comparison of the latency time of the swallowing reflex between before and 3 months after treatment in cancers of the oral cavity (n=28), pharynx (n=25, p<0.05, paired t-test), oropharynx (n=17), and hypopharynx (n=8, p<0.05, paired t-test). B, Comparison of the ratio of patients with a delayed swallowing reflex between before and 3 months after treatment in patients with cancers of the oral cavity, pharynx (p<0.01, chi-squared test), oropharynx (p<0.05, chi-squared test), and hypopharynx. Time over 3 seconds was defined as a delayed swallowing reflex.

Figure 3

Latency of the swallowing reflex before and 3 months after surgery or chemoradiation. Asterisks indicate significant differences between before and after treatment. The error bars indicate standard deviation. A, Comparison of the latency time of the swallowing reflex between before and 3 months after surgery (n=23) or chemoradiation (n=22, p<0.05, paired t-test). B, Comparison of the ratio of patients with a delayed swallowing reflex between before and 3 months after surgery or chemoradiation (p<0.05, chi-squared test). Time over 3 seconds was defined as a delayed swallowing reflex.

Supplementary Files

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