Predictors of Long Term Prognosis of Dysphagia in Tonsil Cancer Patients

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Objective: To evaluate the factors affecting long-term prognosis for dysphagia in tonsil cancer patients, after treatment.

Method: This was a retrospective study of subjects who underwent a videofluoroscopic swallowing study (VFSS) following treatment for stage 3 or 4 tonsil cancer. Data including sex, age, cancer characteristics, and methods of cancer treatment were collected. To evaluate the swallowing-related outcome, we collected data including findings regarding the last VFSS, method of feeding, and history of aspiration pneumonia requiring in-patient care. We evaluated the correlation between these data and the characteristics of cancer and treatment methods.

Result: Among 32 subjects included in this study, eight had aspiration or penetration confirmed by the last VFSS. There were no significant differences in swallowing-related factors according to the presence of aspiration or penetration in the last VFSS. Patients who underwent curative tonsillectomy retained more residues on the last VFSS than those who did not.

Conclusion: Among subjects with tonsil cancer, history of curative tonsillectomy was correlated with more pharyngeal residue. However, other cancer- or treatment-related factors did not affect the outcome of swallowing. (JKDS 2018;8:35-40)

Keywords: Videofluoroscopic swallowing study (VFSS), Deglutition disorders, Tonsillar neoplasms, Prognosis

INTRODUCTION

Dysphagia after treatment for locally advanced head and neck cancer can negatively affect the quality of life1. Cancer itself and the sequelae of treatment can alter physiologic function during swallowing, with incorrect motion of the supraglottic larynx, epiglottis, and vestibule, changes in the prevertebral space, and other neuromuscular dysfunctions2.

Previous studies reported that increasing age, primary site, and the use of concurrent chemotherapy were associated with development of long-term dysphagia in head and neck cancer patients3. In another study, sex, the extent of tumor resection, and lymph node metastasis affected swallowing in tongue cancer patients4.

However, there are few studies on the long-term outcome of dysphagia, especially with regard to
specific types of cancer. Previous studies have been unable to predict the outcome of dysphagia, because head and neck cancer includes several cancer subtypes with different anatomical lesions, and can bring about dysphagia in different ways.

Tonsil cancer is one of the most common types of oropharyngeal cancer. Because of its anatomic location, resection of the tonsil sometimes requires sacrifice of the soft palate, base of the tongue, tonsillar bed, uvula, and pharyngeal wall, and can cause peristaltic dysfunction due to anatomic abnormalities. However, there has been no published report about factors associated with swallowing outcome in tonsil cancer.

The aim of this study was to investigate the factors affecting long-term prognosis of dysphagia in patients with tonsil cancer after treatment.

MATERIALS AND METHODS

1. Participants

This study was performed retrospectively through medical record review. Patients who had tonsil cancer (American Joint Committee on Cancer [AJCC] stage III or IV) and underwent a videofluoroscopic swallowing study (VFSS) at least 8 months after completion of treatment at our hospital were enrolled. Patients who had recurrence or a dual primary head and neck malignancy, metastasis from cancers of other origin (e.g., lymphoma, melanoma), or other oropharyngeal or neurologic disease that could influence swallowing function were excluded.

We identified sex, age, side of tumor, and duration from completion of treatment to the date of the last VFSS.

We also collected data including cancer characteristics (AJCC stage) and the method of treatment, such as curative tonsillectomy, chemotherapy, intensity-modulated radiation therapy (IMRT), and lymph node dissection. We categorized patients who underwent radical tonsillectomy, including free-margin and/or surrounding structure resection for therapeutic purposes, not only biopsy, as the tonsillectomy group.

2. Outcomes

We defined the presence of aspiration or penetration when the subject was 1) percutaneous endoscopic gastrostomy (PEG) tube-dependent at the last follow-up visit; 2) confirmed with penetration or aspiration on the last VFSS; or 3) clinical diagnosis of aspiration pneumonia requiring in-patient treatment. Aspiration pneumonia was defined as culture-proven bacterial pneumonia, with radiographic evidence of infiltrate, either with recurrent episodes or in the setting of patient-reported dysphagia.

VFSS was performed using the dysphagia diet of our hospital: 80 g of dysphagia diet I (soup), II (chopped fruits), or III (steamed eggs) was mixed with 10 g of barium sulfate (Solotop Suspension 140; Teajoon Pharm, Seoul, Korea). Thin fluid was a 35%/v low-concentration liquid diet containing 300 ml of normal saline mixed with 140 g/100 ml of barium sulfate. Thick fluid was a 70%/v high-concentration liquid diet. VFSS was performed on a lateral view by using digitized fluoroscopy (IRF-850-150; Philips Healthcare, Best, The Netherlands) and images were recorded in real time after administration of each 5 ml of fluid material. Abnormalities in the swallowing process were evaluated in detail by using the recorded images. Patients were observed during the oral, pharyngeal, and esophageal phases of swallowing. Aspiration was defined as a bolus passing through the vocal cords. Penetration was defined when a bolus entered the glottis and moved as far as the vestibule above the true vocal folds.

We also identified residue in the pyriform sinus and/or vallecular pouch through VFSS. We evaluated the amount of residue at the vallecular pouch (none: <10%, small: 10-50%, large: >50%) and at the pyriform sinus. We classified the patients into 2 groups: with or without residue, with either small or large volume.

3. Statistical analysis

All data were analyzed using SPSS ver. 18.0 for Windows (SPSS Inc., Chicago, IL, USA). The Mann-Whitney U test and chi-square test were used to
compare characteristics in patients with dysphagia and normal subjects and in patients with or without residue on VFSS. Univariate logistic regression analysis was used to evaluate risk factors for residue on VFSS. Results were considered statistically significant if the P-value was <0.05.

RESULTS

A total of 32 patients were initially included in this study, their mean age was 52.9±9.3 years and there were 30 men and 2 women. Five patients had AJCC stage III and 27 had stage IV cancer.

The shortest duration from completion of treatment to the last VFSS was 8 months, and mean duration was 20.2±9.0 months. On VFSS, 7 patients showed aspiration and/or penetration, 18 had residue in the vallecular pouch, and 13 had residue in the pyriform sinus after swallowing.(Table 1) Three patients were diagnosed with clinical aspiration pneumonia, and no patient was dependent on tube feeding. Finally, there were 8 patients in the aspiration/penetration group and 18 in the residue group.

The baseline characteristics of patients with regard to the presence of aspiration/penetration are shown in Table 2. There were no significant differences in age, gender, side of tumor, follow-up duration, tumor stage, nodal stage, or overall AJCC stage.

The characteristics of treatment in aspiration/penetration patients and normal subjects are shown in Table 3. There were no significant differences in treatment methods between groups.

When we sorted the subjects into residue and non-residue groups according to the findings on VFSS, we found that the rate of curative tonsillectomy differed between the 2 groups.(Table 4) Univariate logistic regression analysis revealed that the incidence of residue on VFSS was 18.33 times higher in patients who underwent curative tonsillectomy than in those who did not (hazard ratio [HR], 18.33; 95% confidence interval [CI], 3.01-108.65).(Table 5)

Table 1. VFSS findings of study patients.

| Patients (n=32) |        |
|----------------|--------|
| Clinical aspiration pneumonia | 3 (9.4%) |
| Dependent on tube feeding       | 0      |
| VFSS                          |        |
| Aspiration or penetration      | 7 (21.9%) |
| Vallecular pouch residue       | 18 (56.3%) |
| Pyriform sinus residue         | 13 (40.6%) |

The values are numbers.

Table 2. Comparison of aspiration/penetration patients and normal patients according to the patients’ characteristics.

|                | Aspiration/Penetration (+) (n=8) | Aspiration/Penetration (-) (n=24) | P-value |
|----------------|----------------------------------|-----------------------------------|---------|
| Age (year)     | 52.0±10.3                        | 53.8±9.3                          | 0.420   |
| Gender (male : female) | 7:1                              | 23:1                              | 0.399   |
| Side (right : left)    | 4:4                              | 14:10                             | 0.681   |
| Follow up duration (months) | 23.1±8.8 | 19.0±5.9                          | 0.542   |
| Tumor stage       |                                  |                                   |         |
| 1-2              | 6 (75.0%)                         | 17 (70.8%)                        | 0.820   |
| 3-4              | 2 (25.0%)                         | 7 (29.2%)                         |         |
| Nodal stage       |                                  |                                   |         |
| 0                | 0                                | 0                                 | 0.557   |
| 1-3              | 8 (100.0%)                        | 1 (4.2%)                          |         |
| AJCC stage       |                                  |                                   |         |
| III              | 0                                | 5 (20.8%)                         | 0.160   |
| IV               | 8 (100.0%)                        | 19 (79.2%)                        |         |

The values are number or mean±SD.

*P<0.05 by Mann-Whitney U test and Chi square test.

AJCC: American joint committee on cancer.
**Table 3.** Comparison of aspiration/penetration patients and normal patients according to the treatment.

|                        | Aspiration/Penetration (+) (n=8) | Aspiration/Penetration (-) (n=24) | P-value |
|------------------------|----------------------------------|-----------------------------------|---------|
| Chemotherapy           |                                  |                                   |         |
| Yes                    | 7 (87.5%)                        | 18 (75.0%)                        | 0.660   |
| No                     | 1 (12.5%)                        | 6 (25.0%)                         |         |
| IMRT                   |                                  |                                   |         |
| Yes                    | 5 (62.5%)                        | 17 (70.8%)                        | 0.611   |
| No                     | 3 (37.5%)                        | 7 (29.2%)                         |         |
| Radiation dose (cGy)   | 6625.0±450.0                     | 6431.0±509.2                      | 0.262   |
| Tonsillectomy          |                                  |                                   |         |
| Yes                    | 5 (62.5%)                        | 13 (54.2%)                        | 0.681   |
| No                     | 3 (37.5%)                        | 11 (45.8%)                        |         |
| Reconstruction         |                                  |                                   |         |
| Yes                    | 2 (25.0%)                        | 5 (20.8%)                         | 0.805   |
| No                     | 6 (75.0%)                        | 19 (79.2%)                        |         |
| Lymph node dissection  |                                  |                                   |         |
| Yes                    | 5 (62.5%)                        | 18 (75.0%)                        | 0.496   |
| No                     | 3 (37.5%)                        | 6 (25.0%)                         |         |

The values are number or mean±SD.

*P*<0.05 by Mann-Whitney U test and Chi square test.

IMRT: intensity-modulated radiation therapy.

**Table 4.** Comparison of patients who remained residue on VFSS and normal patients.

|                        | Residue (+) (n=18) | Residue (-) (n=14) | P-value |
|------------------------|--------------------|--------------------|---------|
| Age (year)             | 52.9±9.3           | 53.6±10.0          | 0.420   |
| AJCC stage             |                    |                    |         |
| III                    | 2 (11.1%)          | 3 (21.4%)          | 0.425   |
| IV                     | 16 (88.9%)         | 11 (78.6%)         |         |
| Chemotherapy           |                    |                    |         |
| Yes                    | 12 (66.7%)         | 13 (92.9%)         | 0.075   |
| No                     | 4 (33.3%)          | 1 (7.1%)           |         |
| Radiation dose (cGy)   | 6625.0±450.0       | 6431.0±509.2       | 0.188   |
| Tonsillectomy          |                    |                    |         |
| Yes                    | 15 (83.3%)         | 5 (21.4%)          | <0.001* |
| No                     | 3 (16.7%)          | 11 (78.6%)         |         |
| Reconstruction         |                    |                    |         |
| Yes                    | 5 (27.8%)          | 2 (14.3%)          | 0.360   |
| No                     | 13 (72.2%)         | 12 (85.7%)         |         |

The values are number or mean±SD.

*P*<0.05 by Mann-Whitney U test and Chi square test.

AJCC: American joint committee on cancer.

**DISCUSSION**

Survival in head and neck cancer patients is increasing due to advances in treatment. Swallowing disorders after completion of treatment have, therefore, become an important problem, not only for quality of life but also for survival. Therefore, predicting risk factors for dysphagia in head and neck cancer patients and providing management for possible swallowing problems are important. This is the first report about predictors of long-term prognosis for dysphagia in tonsil cancer patients. Generally the long-term prognosis for dysphagia in tonsil cancer patients was favorable, in that there were no patients dependent on tube feeding, and only 8 (25%) showed aspiration/penetration after treatment in our study. Caudell et al. reported that the 1- and 2-year rate of PEG tube-dependence was 24.6% and 14.2% in head and neck cancer, respectively. Nguyen et al. reported that 5 of 55 head and neck cancer patients died from pneumonia, and 25 (45%) developed severe dysphagia requiring prolonged tube feedings for more than 3 months (22 patients) or repeated dilations (3 patients), during a median follow-up of 17 months (range 6-48 months). Patients with tonsil cancer who underwent curative
Table 5. Comparison of Chemotherapy and Tonsillectomy in patients who remained residue on VFSS and normal patients.

|                | Residue (+) (n=18) | Residue (−) (n=14) | P-value | HR (95% CI) |
|----------------|--------------------|--------------------|---------|-------------|
| Chemotherapy   |                    |                    |         |             |
| Yes            | 12 (66.7%)         | 13 (92.9%)         | 0.481   |             |
| No             | 4 (33.3%)          | 1 (7.1%)           |         |             |
| Tonsillectomy  |                    |                    |         |             |
| Yes            | 15 (83.3%)         | 3 (21.4%)          | 0.001*  | 18.33 (3.01-108.65) |
| No             | 3 (16.7%)          | 11 (78.6%)         |         |             |

HR: hazard ratio, CI: confidence interval.
*P < 0.05 by univariate logistic regression analysis.

tonsillectomy showed more post-swallow residue than subjects who did not. It is widely known that post-swallow residue constitutes a risk for delayed aspiration. We presumed that this was because the structures contributing to swallowing function, including not only the tonsil bed but also the base of the tongue, pharyngeal wall, and soft palate, were usually damaged after curative tonsillectomy. The base of the tongue seals the oral cavity and pushes food into the oropharynx, and the pharyngeal wall elevates and shortens the pharynx, contributing to peristalsis and bolus transport. The soft palate moves superiorly and posteriorly to close off the nasopharynx.

Son et al. reported that male gender, extensive tumor resection, a higher nodal stage, and more extensive lymph node dissection were major risk factors for aspiration in tongue cancer patients. Caudell et al. reported that increasing age, primary site, and the use of concurrent chemotherapy were significantly associated with development of long-term dysphagia in head and neck cancer patients.

However, in our study, we could not find any correlative factors that led to dysphagia in tonsil cancer. We surmised that this was because the general prognosis for dysphagia in tonsil cancer was more favorable than in other head and neck cancers.

In contrast to the tongue and pharynx, which are directly involved in the swallowing process, the tonsil itself contributes little to swallowing function, therefore, the stage of cancer might be less important in causing dysphagia than in other head and neck cancers. Moreover, since there is no consensus on whether surgery should be performed before combined chemotherapy or radiation therapy in stage 3 or 4 tonsil cancer, the preference of the surgeon, tumor size, and location can affect the treatment method; thus, the stage of cancer contributes less to the development of dysphagia.

Curative tonsillectomy results in anatomical and physiological changes in the swallowing structures. The surgery sacrifices pharyngeal muscles that aid in peristalsis in most cases and can lead to residue in the vallecular pouch and/or pyriform sinuses, as seen in our study.

Although previous studies reported a correlation between radiation therapy and dysphagia, none was observed in our study. This might be because the mean interval from completion of treatment to the date of VFSS was too short to demonstrate the effect of radiation. A previous study reported that radiotherapy could induce late normal tissue effects in long-term (>5-year) head and neck cancer survivors, and cause severe dysphagia as a late complication of radiotherapy. Therefore, several years of follow-up may be required to identify the effect of radiation on dysphagia.

The strength of this study was that we only investigated tonsil cancer, not other types of head and neck cancer. Previous studies included all types of head and neck cancer, and the locations, stages, and...
treatment methods were heterogeneous. This heterogeneity made it difficult to interpret the results. Moreover, about two-thirds of the patients in our study underwent pretreatment VFSS, and normal findings were identified in all patients. Considering that underlying swallowing problems are sometimes found in patients with head and neck cancer before treatment, we were able to exclude patients with pretreatment disorders.

The main limitation of this study was the relatively small numbers of subjects. Second, this study did not enroll all patients with tonsil cancer, but those who were referred to the rehabilitation clinic for VFSS, which might introduce a selection bias.

Among subjects with tonsil cancer, history of curative tonsillectomy was correlated with increased pharyngeal residue which is usually known to increase aspiration risk. However, other cancer- or treatment-related factors did not affect the outcome of swallowing.

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