
SITE OF DISEASE AND TREATMENT PROTOCOL AS CORRELATES OF SWALLOWING FUNCTION IN PATIENTS WITH HEAD AND NECK CANCER TREATED WITH CHEMORADIATION

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Abstract: *Background.* The relationship between type of chemoradiation treatment, site of disease, and swallowing function has not been sufficiently examined in patients with head and neck cancer treated primarily with chemoradiation.

Methods. Fifty-three patients with advanced-stage head and neck cancer were evaluated before and 3 months after chemoradiation treatment to define their swallowing disorders and characterize their swallowing physiology by site of lesion and chemoradiation protocol. One hundred forty normal subjects were also studied.

Results. The most common disorders at baseline and 3 months after treatment were reduced tongue base retraction, reduced tongue strength, and slowed or delayed laryngeal

vestibule closure. Frequency of functional swallow did not differ significantly across disease sites after treatment, although frequency of disorders was different at various sites of lesion. The effects of the chemotherapy protocols were small.

Conclusions. The site of the lesion affects the frequency of occurrence of specific swallow disorders, whereas chemoradiation protocols have minimal effect on oropharyngeal swallow function. © 2005 Wiley Periodicals, Inc. *Head Neck* 28: 64–73, 2006

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Over the past 10 years, a number of investigators have noted significant negative effects of chemoradiation on oropharyngeal swallow. Investigators have examined oropharyngeal swallow in patients with head and neck cancer undergoing or

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having completed external beam irradiation to define swallowing physiology in these populations and thereby to define possible rehabilitation strategies.¹⁻⁶ These most frequently noted effects have been described as delay in triggering the pharyngeal swallow, reduced laryngeal elevation, and reduced tongue base retraction.⁷ Xerostomia also has been well-documented in patients treated with radiotherapy with or without chemotherapy.^{2,8-10} Generally, investigators have studied patients who received individual chemoradiation protocols^{11,12} or patients with a specific site of disease.¹³ Few studies have examined differences in oropharyngeal swallow as a result of the site of the patient's tumor (ie, larynx, hypopharynx, nasopharynx, oropharynx, and unknown primary tumor). Pauloski et al^{14,15} reported varying rates of patient-reported complaints of dysphagia across sites of disease, with patients with tumors of the oral cavity showing higher pretreatment rates of complaint, whereas patients with pharyngeal tumors showing the highest rates of complaint when posttreatment evaluations were included. Few comparisons have been made of the effects of various chemoradiation protocols on swallow. Newman et al¹⁶ compared temporal swallowing measures between intraarterial cisplatin with radiation (RADPLAT) with other protocols of systemic chemoradiation treatment and observed lower rates of aspiration with RADPLAT. This article examines differences in swallowing disorders and swallowing physiology across five sites of disease and across four chemoradiation protocols in a group of 53 patients with head and neck cancer.

PATIENTS AND METHODS

Patients. Patients for the study were 53 individuals with advanced head and neck cancer accrued sequentially from participating institutions between 1996 and 2001. Subjects received a full-course of radiotherapy and chemotherapy to areas in the upper aerodigestive tract, including nasopharynx, oral pharynx, hypopharynx, and larynx. No patient had prior surgery. Each patient received a standard radiation dose of between 6700 and 7275 rad without intensity-modulated radiotherapy (IMRT; see Table 2). Each subject received a videofluoroscopic examination of oropharyngeal swallow at two time points: before tumor treatment and at 3 months after completion of tumor treatment. In addition, at each time

point, a questionnaire was completed on the presence of gastric or jejunostomy tubes and the nature of oral intake, including the intake of various food consistencies. All subjects were disease free at the time of follow-up and completed both evaluation points. All procedures were approved by the Institutional Review Board and the Human Subjects Committee of all participating institutions.

Site of Disease. Patients had cancer of the nasopharynx ($n = 3$), oropharynx ($n = 22$), larynx ($n = 14$), or hypopharynx ($n = 4$), or of unknown location ($n = 10$).

Treatment Protocols. The 53 patients received one of four treatment protocols: (1) TFHX, taxol infusion: 13 subjects who received hydroxyurea, 5-fluorouracil, and paclitaxel infusion administered continuously over 1 week¹⁷; (2) TFHX, taxol bolus: 16 subjects who received hydroxyurea, 5-fluorouracil, and paclitaxel 1-hour bolus¹⁸; (3) TFHX, bolus, induction: 15 subjects who received induction chemotherapy with carboplatin and paclitaxel followed by concurrent chemoradiation with hydroxyurea, 5-fluorouracil, and paclitaxel 1-hour bolus¹⁹; and (4) RADPLAT: nine subjects who received supradose intraarterial cisplatin with parenteral sodium thiosulfate for neutralization and conventional external-beam irradiation.²⁰

Swallow Evaluation. Collection and reduction of videofluoroscopic swallowing data followed procedures described in Logemann et al.²¹ Each subject completed two swallows each of 3 mL and 10 mL of "watery" liquid barium and 3 mL of pudding barium during videofluorography in the lateral view. Videofluorographic studies were recorded on either three-quarters or one-half inch videotape, with timing information encoded onto each frame to facilitate later frame-by-frame, slow motion examination to identify and define any possible swallowing disorders. Each subject's videofluorographic study was first analyzed in slow motion to define any swallowing disorders, that is, visible swallowing abnormalities in bolus flow or structural movements displayed on each swallow. The presence or absence of each of the following 21 swallowing disorders was noted for each swallow: (1) reduced lip closure (causes drooling), (2) tongue thrust (reduces tongue control), (3) reduced tongue control/shaping (reduces chewing ability), (4) reduced vertical tongue

movement (reduces chewing ability, slows oral transit time), (5) reduced manipulation and propulsion of the bolus (reduced anteroposterior [AP] tongue movement) (slows oral transit time), (6) reduced tongue stabilization (slows oral transit time, increases residue), (7) reduced tongue lateralization (reduces chewing ability), (8) reduced tongue strength (increases oral residue), (9) oral apraxia (oral initiation delay), (10) delayed pharyngeal swallow (up to 30-second delay) (increases aspiration risk), (11) absent pharyngeal swallow, (12) reduced velopharyngeal closure (causes nasal reflux), (13) reduced tongue base retraction (causes vallecular residue), (14) slowed/delayed laryngeal vestibule closure (can cause aspiration), (15) incomplete laryngeal vestibule closure (can cause penetration), (16) reduced laryngeal elevation (causes residue at top of airway), (17) reduced glottic closure (can cause aspiration), (18) unilateral pharyngeal weakness (causes residue on one side of pharynx), (19) bilateral pharyngeal weakness, (20) reduced cricopharyngeal opening (causes residue in pyriform sinuses), and (21) visible cricopharyngeal bar (can cause residue in pyriform sinuses). Each swallow was also categorized as functional (no aspiration and minimal residue) or nonfunctional (aspiration and/or moderate to severe residue).

The videotape of the videofluorographic study of oropharyngeal swallow was then analyzed in slow motion and frame by frame to determine 15 temporal measures of oropharyngeal swallow and five observations of residual food remaining in the oral cavity and pharynx after the swallow. Of the 14 temporal measures, 13 were measures of bolus movement, namely (in seconds): (1) oral transit time; (2) pharyngeal transit time; (3) pharyngeal delay (time from the bolus head reaching the point where the lower edge of the mandible crosses the tongue base until the first laryngeal elevation in the swallow is seen), whereas eight were measures of structural movement; (4–6) base of tongue contact at three levels of the posterior pharyngeal wall (PPW) (mid C2, inferior C2 and superior C3); (7) velopharyngeal closure; (8) laryngeal closure; (9) cricopharyngeal opening; (10) laryngeal elevation; and (11) hyoid elevation. There were also two coordination measures (in seconds): (12) onset of base of tongue posterior movement relative to the first contact with the PPW at the level opposite the anterior inferior corner of the second cervical vertebra and (13) time from first airway closure to first cricopharyngeal opening. In addition to these temporal

measures, (14) the onset of swallow measured the time from clinician command to swallow to the first backward movement of the bolus.

The following six observations were also made from the swallow studies: the number of attempts to swallow each bolus; approximate percent oral residue after the first swallow on a bolus; approximate percent pharyngeal residue after the first swallow on a bolus; and approximate percent aspirated before, during, or after the first swallow of a bolus.

Oropharyngeal swallow efficiency (OPSE)²² was calculated from the swallowing measures and observations. OPSE, defined as the approximate percent of the bolus swallowed into the esophagus divided by oropharyngeal transit time, is a global measure that describes the interaction of speed of movement of the bolus and the safety and efficiency of the mechanism in clearing material from the oropharynx.

Ten percent of all videofluoroscopic measures and observations were repeated by two raters who were each identically trained with more than 5 years experience in the interpretation of videofluoroscopic studies. Average interobserver and intraobserver reliability as determined by Pearson correlation coefficients were .93 and .99, respectively.

Controls. Controls were individuals without cancer who were recruited through advertisements to be participants in ongoing studies of swallowing evaluations. They had no swallow complaints and no prior history of otolaryngologic or neurologic disorder. They were on no medications known to affect swallowing. Controls received one videofluorographic swallowing evaluation for which the 15 temporal measures of oropharyngeal swallow and five observations of residual food remaining in the oral cavity and pharynx after the swallow were obtained. Swallowing disorders were not assessed in controls.

Statistical Analyses. The main goal of the statistical analyses was to determine whether there were differences in swallowing function, as measured 3 months after treatment, across disease site or across treatment protocol. Because the comparison groups are observational and not randomized, adjustment was made for baseline differences in swallowing function and extent of disease. For the swallowing disorders and the temporal measures, these analyses were done using generalized estimating equation (GEE)

analysis.²³ This method allowed for the use of swallow as the unit of analysis, where multiple swallows at multiple bolus types were observed for each person at each time point. For each dependent variable analyzed, the GEE model included the factors of bolus type (3 mL liquid, 10 mL liquid, 3 mL paste), clinical stage (IV or not IV), T classification (4 or not 4), and the baseline value of that variable averaged over the multiple swallows of each bolus type. Adjusted analyses are presented when models converged. Models did not converge for lower frequency swallowing disorders, and these were compared using unadjusted analyses. Baseline characteristics were compared among groups using either GEE analysis or the Fisher exact test.

RESULTS

Data are presented first for all subjects regardless of site of disease or treatment protocol, then by site of disease, and, finally, by treatment protocol. There were 53 patients in the study, 41 men and 12 women, diagnosed with squamous cell cancers of the head and neck in one of five locations: nasopharynx ($n = 3$), oropharynx ($n = 22$), larynx ($n = 14$), hypopharynx ($n = 4$), and of unknown location ($n = 10$). Ages ranged from 38 to 78 years (mean, 57 years; median, 56 years). Most subjects had T3 ($n = 16$) or T4 tumors ($n = 19$), whereas 11 had T2 disease, and two had T1 disease. Five patients had unknown primary tumors. Forty-one of the patients were white, 11 were black, and one was Hispanic.

There were 140 controls in the study, 47 men and 93 women. Controls were selected so that ages also ranged from 38 to 78 years (mean, 56 years; median, 53 years). A maximum of 804 swallows was observed over the three bolus types, 3 mL and 10 mL liquid and 3 mL pudding. No controls had gastrostomy or jejunostomy for nutrition and all were taking 100% of their nutrition orally.

Swallow Disorders. At baseline, before treatment, eight patients (15%) had gastrostomy or jejunostomy for nutrition. Three patients (6%) were taking 50% or less of their nutrition orally. Four patients (8%) were aspirating before tumor treatment began. The 53 subjects contributed 351 swallows to the analysis. Eighty-five percent of the swallows were functional swallows. The swallow disorders of varying severity occurred in the following frequencies (percent of swallows in decreasing order): reduced tongue base retraction

(50%), reduced tongue strength (39%), slowed/delayed laryngeal vestibule closure (19%), reduced tongue control/shaping (17%), delayed pharyngeal swallow (up to 30-second delay) (15%), reduced laryngeal elevation (13%), reduced manipulation and propulsion of the bolus (reduced AP tongue movement) (12%), reduced lateral/anterior tongue stabilization (7%), bilateral pharyngeal weakness, movement (6%), reduced vertical tongue movement (5%), reduced cricopharyngeal opening (3%), visible cricopharyngeal bar (2%), and unilateral pharyngeal weakness (2%). No swallows exhibited the following disorders: reduced tongue lateralization, incomplete laryngeal vestibule closure, reduced velopharyngeal closure, reduced glottic closure, reduced lip closure, tongue thrust, oral apraxia (oral initiation delay), or absent pharyngeal swallow.

Three months after treatment, 21 patients (40%) had gastrostomy or jejunostomy for nutrition. Twelve patients (23%) were taking 50% or less of their nutrition orally, and 12 patients (23%) were aspirating, all increases over baseline. The 53 patients contributed 310 swallows to the analysis. Sixty-five percent of the swallows were functional swallows. The most frequently occurring disorders were reduced tongue base retraction (89%), reduced tongue strength (51%), and slowed/delayed laryngeal vestibule closure (31%). The following disorders occurred in less than 5% of the swallows: reduced lateral/anterior tongue stabilization (5%), incomplete laryngeal vestibule closure (5%), reduced velopharyngeal closure (4%), reduced vertical tongue movement (3%), and reduced glottic closure (1%). No swallows exhibited the following disorders: reduced lip closure, tongue thrust, reduced tongue lateralization, oral apraxia (oral initiation delay), absent pharyngeal swallow, and unilateral pharyngeal weakness.

Temporal Measures and Observations. Table 1 summarizes the 25th, 50th, and 75th percentiles for the distribution of the 15 temporal measures of oropharyngeal swallow and for observations of residue, aspiration, and OPSE. These summaries are given for the patients at baseline, the patients at 3 months after treatment, and the controls. By comparing the percentiles in the controls with the patients at baseline, it may be seen that several parameters were slightly lower in controls. These were onset of oral swallow, durations of cricopharyngeal opening, laryngeal elevation, and hyoid elevation and residues. Oropharyngeal swallow efficiency was higher in controls. Other

Table 1. Percentiles (25th, 50th, 75th) of the distributions of temporal measures for patients at baseline, patients at 3 months, and controls. *n* = number of swallows.

| | Patients, baseline | | | Patients, 3 mo | | | Controls | | | | | |
|---|--------------------|--|--|----------------|----------|--|----------|--|----------|--|--|--|
| | <i>n</i> | 25 th , 50 th , 75 th | | | <i>n</i> | 25 th , 50 th , 75 th | | | <i>n</i> | 25 th , 50 th , 75 th | | |
| Oral onset of swallow (s) | 286 | -1.34, -0.87, -0.52 | | | 263 | -1.55, -0.92, -0.57 | | | 219 | -1.75, -1.22, -.80 | | |
| Duration of oral transit time (s) | 347 | 0.22, 0.31, 0.47 | | | 306 | 0.23, 0.33, 0.55 | | | 801 | 0.22, 0.31, 0.44 | | |
| Duration of pharyngeal transit time (s) | 345 | 0.65, 0.72, 0.84 | | | 302 | 0.65, 0.76, 0.90 | | | 799 | 0.58, 0.70, 0.83 | | |
| Duration of pharyngeal delay (s) | 346 | -0.18, -0.12, -0.03 | | | 306 | -0.17, -0.10, -0.01 | | | 802 | -.20, -0.12, 0.00 | | |
| Duration of tongue base contact to PPW at level of mid-C2 (s) | 345 | 0.28, 0.35, 0.46 | | | 307 | 0.28, 0.40, 0.50 | | | 378 | 0.30, 0.37, 0.45 | | |
| Duration of tongue base contact to PPW at level of inferior C2 (s) | 347 | 0.23, 0.30, .040 | | | 307 | 0.19, 0.32, 0.47 | | | 372 | 0.24, 0.30, 0.37 | | |
| Duration of tongue base contact to PPW at level of superior C3 (s) | 347 | 0.19, 0.26, 0.37 | | | 306 | 0.18, 0.29, 0.42 | | | 354 | 0.20, 0.24, 0.31 | | |
| Duration of velopharyngeal closure (s) | 339 | 0.47, 0.57, 0.71 | | | 299 | 0.56, 0.68, 0.90 | | | 788 | 0.53, 0.65, 0.85 | | |
| Duration of laryngeal closure (s) | 339 | 0.37, 0.46, 0.57 | | | 305 | 0.43, 0.52, 0.65 | | | 800 | 0.40, 0.50, 0.63 | | |
| Duration of cricopharyngeal opening (s) | 347 | 0.45, 0.53, 0.60 | | | 303 | 0.47, 0.54, 0.62 | | | 799 | 0.42, 0.50, 0.58 | | |
| Duration of laryngeal elevation (s) | 347 | 0.95, 1.08, 1.28 | | | 306 | 0.94, 1.09, 1.31 | | | 802 | 0.92, 1.03, 1.22 | | |
| Duration of hyoid elevation (s) | 349 | 0.94, 1.08, 1.23 | | | 307 | 0.93, 1.08, 1.27 | | | 803 | 0.91, 1.03, 1.19 | | |
| Onset base of tongue to posterior pharyngeal wall (s) | 345 | 0.10, 0.13, 0.17 | | | 282 | 0.10, 0.15, 0.20 | | | 376 | 0.08, 0.11, 0.15 | | |
| Time from first airway closure to first cricopharyngeal opening (s) | 347 | -0.04, 0.01, 0.07 | | | 305 | -0.04, 0.02, 0.07 | | | 375 | -0.08, -0.03, 0.01 | | |
| Oral residue (% of bolus) | 349 | 1, 2, 5 | | | 303 | 1, 4, 6 | | | 803 | 0, 0, 1 | | |
| Pharyngeal residue (% of bolus) | 350 | 2, 3, 7 | | | 307 | 4, 6, 12 | | | 804 | 0, 0, 2 | | |
| Aspiration (% of bolus aspirated) | 351 | 0, 0, 0 | | | 307 | 0, 0, 0 | | | 804 | 0, 0, 0 | | |
| Oropharyngeal swallow efficiency (%/s) | 343 | 64, 85, 100 | | | 297 | 49, 72, 94 | | | 797 | 74, 94, 114 | | |
| Number of attempts to swallow 1 st bolus | 348 | 1, 1, 2 | | | 303 | 1, 2, 2 | | | 804 | 1, 1, 1 | | |

Abbreviations: *n*, number of swallows; PPW, posterior pharyngeal wall.

measures such as oral and pharyngeal transit times showed similar percentiles in controls compared with patients at baseline. By comparing the percentiles in the patients at 3 months with the patients at baseline, it may be seen that several parameters were higher in the patients at 3 months. These were durations of velopharyngeal and laryngeal closure and residues. Oropharyngeal swallow efficiency was lower in patients at 3 months. Other measures showed similar percentiles in patients over time.

Differences by Site of Disease. Table 2 shows the pretreatment distribution of patients and their characteristics by site of disease. Patients with disease at the five sites differed significantly on radiation therapy dose, in that those with an unknown primary tumor received the lowest average radiation dose (6705), whereas those with lesions in the hypopharynx received the highest dose (7275). Those with lesions in the hypopharynx or larynx were most frequently aspirating before treatment.

Table 2. Patient characteristics by site of disease before chemoradiation treatment.

| | Nasopharynx | Oropharynx | Larynx | Hypopharynx | Unknown primary | <i>p</i> value |
|---------------------|-------------|------------|--------|-------------|-----------------|----------------|
| Number of patients | 3 | 22 | 14 | 4 | 10 | |
| Mean age, y | 55.5 | 58.9 | 56.6 | 57.9 | 54.4 | 0.81 |
| Mean dose, cGy | 7033 | 7224 | 7120 | 7275 | 6705 | 0.05* |
| Mean % oral intake | 100 | 98 | 95 | 100 | 90 | 0.80 |
| % Male | 33 | 82 | 78 | 75 | 80 | 0.46 |
| % Stage 4 | 100 | 82 | 79 | 100 | 100 | 0.42 |
| % T4 | 67 | 27 | 29 | 50 | 50 | 0.48 |
| % G-tubes | 0 | 9 | 28 | 25 | 10 | 0.41 |
| % Oral intake ≤ 50% | 0 | 4 | 7 | 0 | 10 | 0.86 |
| % Aspirating | 0 | 0 | 14 | 50 | 0 | 0.02* |

**p* ≤ .05.

Table 3. Percent (SE) of swallows with swallow disorders and functional swallow by site of disease 3 months after chemoradiation treatment.

| | Nasopharynx | Oropharynx | Larynx | Hypopharynx | Unknown primary | <i>p</i> value |
|---|-------------|------------|--------|-------------|-----------------|----------------|
| Number of swallows | 12 | 124 | 77 | 20 | 77 | |
| Reduced tongue base retraction | 51 (6) | 94 (1) | 96 (1) | 74 (9) | 83 (9) | .01*† |
| Reduced tongue strength | 23 (5) | 77 (2) | 50 (3) | 30 (6) | 33 (40) | .03*† |
| Slowed/delayed vestibule closure | 42 (8) | 37 (3) | 6 (1) | 31 (5) | 33 (5) | .12‡ |
| Reduced tongue control/shaping | 50 (14) | 25 (4) | 21 (5) | 0 | 18 (4) | <.01* |
| Reduced anteroposterior tongue movement | 17 (11) | 20 (4) | 29 (5) | 0 | 18 (4) | .04* |
| Delayed pharyngeal swallow | 17 (11) | 26 (4) | 35 (5) | 0 | 3 (2) | <.01* |
| Reduced laryngeal elevation | 0 | 4 (2) | 27 (5) | 10 (7) | 26 (5) | <.01*‡ |
| Reduced cricopharyngeal opening | 0 | 4 (2) | 17 (4) | 5 (5) | 18 (4) | <.01*‡ |
| Visible cricopharyngeal bar | 0 | 7 (2) | 0 | 0 | 29 (5) | <.01*‡ |
| Bilateral pharyngeal weakness | 0 | 7 (2) | 14 (4) | 0 | 14 (4) | .09 |
| Functional swallow | 66 (4) | 61 (1) | 62 (2) | 42 (5) | 75 (5) | .78‡ |

**p* < .05.

†Analyses adjusted for bolus type, baseline value, and stage of disease.

‡Unadjusted differences present at baseline.

Three months after treatment, the 310 swallows distributed across sites of disease as follows: nasopharynx (*n* = 12), oropharynx (*n* = 124), larynx (*n* = 77), hypopharynx (*n* = 20), and un-

known primary tumor (*n* = 77). The frequency of occurrence of swallowing disorders by site of disease is shown in Table 3. Tumors of the nasopharynx had the highest frequency of reduced

Table 4. Mean (SEM) duration of temporal measures and frequencies of observations of swallowing by site of disease 3 months after chemoradiation treatment.

| | Nasopharynx | Oropharynx | Larynx | Hypopharynx | Unknown primary | <i>p</i> value |
|---|-------------|-------------|-------------|-------------|-----------------|----------------|
| Number of swallows | 12 | 124 | 77 | 20 | 77 | |
| Oral onset of swallow (s) | -2.05 (.42) | -1.39 (.21) | -1.08 (.25) | -1.55 (.35) | -1.09 (.25) | .22 |
| Duration of oral transit time (s) | 0.02 (.29) | 0.55 (.11) | 0.30 (.20) | 0.58 (.23) | 0.50 (.17) | .32 |
| Duration of pharyngeal transit time (s) | 0.81 (.09) | 0.87 (.04) | 0.91 (.05) | 0.79 (.09) | 0.80 (.06) | .43 |
| Duration of pharyngeal delay (s) | 0.07 (.08) | -0.04 (.04) | -0.06 (.05) | -0.17 (.10) | 0.02 (.05) | .31 |
| Duration of tongue base contact to PPW at level of mid-C2 (s) | 0.44 (.15) | 0.38 (.06) | 0.42 (.08) | 0.40 (.12) | 0.51 (.09) | .85 |
| Duration of tongue base contact to PPW at level of inferior C2 (s) | 0.32 (.14) | 0.30 (.06) | 0.28 (.08) | 0.33 (.13) | 0.38 (.09) | .96 |
| Duration of tongue base contact to PPW at level of superior C3 (s) | 0.27 (.14) | 0.32 (.05) | 0.25 (.08) | 0.19 (.12) | 0.37 (.09) | .67 |
| Duration of velopharyngeal closure (s) | 0.58 (.19) | 0.74 (.07) | 0.83 (.10) | 0.91 (.14) | 0.81 (.10) | .51 |
| Duration of laryngeal closure (s) | 0.46 (.15) | 0.63 (.06) | 0.54 (.09) | 0.66 (.13) | 0.57 (.10) | .75 |
| Duration of cricopharyngeal opening (s) | 0.53 (.04) | 0.59 (.02) | 0.61 (.03) | 0.59 (.04) | 0.52 (.03) | .14 |
| Duration of laryngeal elevation (s) | 1.04 (.18) | 1.24 (.08) | 1.29 (.11) | 1.28 (.16) | 1.13 (.12) | .68 |
| Duration of hyoid elevation (s) | 1.04 (.19) | 1.24 (.08) | 1.25 (.11) | 1.19 (.16) | 1.16 (.12) | .87 |
| Onset base of tongue to posterior pharyngeal wall (s) | 0.11 (.03) | 0.16 (.01) | 0.16 (.02) | 0.18 (.03) | 0.18 (.02) | .22 |
| Time from first airway closure to first cricopharyngeal opening (s) | 0.02 (.11) | -0.02 (.04) | 0.05 (.06) | 0.03 (.08) | 0.06 (.06) | .66 |
| Oral residue (% of bolus) | 2.9 (4.5) | 9.0 (0.2) | 7.3 (2.3) | 5.6 (3.3) | 1.6 (2.5) | .21 |
| Pharyngeal residue (% of bolus) | 8.7 (4.6) | 13.4 (2.1) | 13.4 (2.7) | 11.5 (5.0) | 10.9 (3.0) | .85 |
| Aspiration (% of bolus aspirated) | 0.00 (.18) | 0.12 (.08) | 0.06 (.11) | 0.43 (.20) | 0.26 (.12) | .35 |
| Oropharyngeal swallow efficiency (%/s) | 90 (9) | 67 (4) | 65 (5) | 69 (9) | 87 (6) | .03* |
| Number of attempts to swallow 1 st bolus | 1.8 (.5) | 2.1 (.2) | 2.4 (.3) | 2.6 (.4) | 1.8 (.3) | .44 |
| % of patients with G-tubes | 0 | 36 | 50 | 75 | 30 | .32 |
| % of patients with oral intake ≤ 50% | 0 | 32 | 21 | 25 | 10 | .68 |
| % of patients aspirating | 33 | 18 | 7 | 50 | 40 | .15 |

Abbreviation: PPW, posterior pharyngeal wall.

**p* < .05.

Table 5. Patient characteristics (mean and percent) by treatment protocol before chemoradiation treatment.

| | TFHX, Taxol infusion | TFHX, taxol bolus | TFHX, bolus, induction | RADPLAT | <i>p</i> value |
|---------------------|----------------------|-------------------|------------------------|---------|----------------|
| Number of patients | 13 | 16 | 15 | 9 | |
| Mean age, y | 57.4 | 58.2 | 56.1 | 56.6 | .95 |
| Mean dose, cGy | 7071 | 7162 | 7063 | 7042 | .92 |
| Mean % oral intake | 100 | 96 | 81 | 100 | .04* |
| % Male | 92 | 56 | 87 | 78 | .09 |
| % Stage 4 | 92 | 81 | 100 | 67 | .10 |
| % T4 | 46 | 19 | 40 | 44 | .39 |
| % G-tubes | 15 | 25 | 0 | 22 | .24 |
| % Oral intake ≤ 50% | 8 | 0 | 0 | 22 | .06 |
| % Aspirating | 8 | 13 | 0 | 11 | .58 |

**p* < .05.

oral tongue control. Tumors of the oropharynx exhibited a high frequency of reduced tongue base retraction and reduced tongue strength. Tumors of the larynx had the highest frequency of reduced tongue base retraction, reduced AP tongue movement, delayed pharyngeal swallow, reduced laryngeal elevation, and reduced cricopharyngeal opening. Tumors of unknown origin had among the highest frequency of reduced laryngeal elevation, reduced cricopharyngeal opening, and visible cricopharyngeal bar. The occurrence of a functional swallow did not differ significantly across disease sites.

Table 4 gives the mean duration of the temporal measures for patients in each of the disease sites. Only OPSE was significantly different by site of disease, with the lowest OPSE (greater dysfunction) in patients with tumors at the oropharyngeal, laryngeal, and hypopharyngeal sites. For the oropharyngeal, laryngeal, and

hypopharyngeal sites, OPSE was slightly below the normal range.

Differences by Treatment Protocol. Patient pretreatment characteristics by protocol are shown in Table 5. Only mean percent oral intake was significantly different between treatments, with patients receiving taxol TFHX bolus induction exhibiting the lowest percent oral intake.

Three months after treatment, the 310 swallows distributed across treatment protocols as follows: TFHX, taxol infusion (*n* = 70); TFHX taxol, bolus (*n* = 98); TFHX, bolus, induction (*n* = 69); and RADPLAT (*n* = 73). The frequency of occurrence of swallowing disorders by treatment protocol is shown in Table 6. The TFHX, taxol infusion protocol exhibited the highest frequency of visible cricopharyngeal bar. The TFHX taxol, bolus, and RADPLAT protocols had the highest level of delayed pharyngeal swallow. The TFHX,

Table 6. Percent (SE) of swallows with swallow disorders and functional swallow by treatment protocol 3 months after chemoradiation treatment.

| | TFHX, taxol infusion | TFHX, taxol bolus | TFHX, bolus, induction | RADPLAT | <i>p</i> value |
|----------------------------------|----------------------|-------------------|------------------------|---------|----------------|
| Number of swallows | 70 | 98 | 69 | 73 | |
| Reduced TB retraction | 84 (4) | 82 (3) | 95 (1) | 98 (1) | .44* |
| Reduced tongue strength | 67 (3) | 55 (3) | 70 (2) | 51 (4) | .20* |
| Slowed/delayed vestibule closure | 35 (3) | 23 (3) | 30 (3) | 13 (2) | .07* |
| Reduced tongue control | 27 (2) | 28 (3) | 32 (3) | 6 (1) | .21* |
| Reduced AP tongue movement | 20 (3) | 25 (3) | 22 (3) | 12 (2) | .59* |
| Delayed pharyngeal swallow | 11 (4) | 27 (4) | 13 (4) | 27 (5) | .01† |
| Reduced laryngeal elevation | 40 (4) | 9 (1) | 42 (3) | 13 (2) | .12* |
| Reduced cricopharyngeal opening | 7 (3) | 5 (2) | 30 (6) | 3 (2) | <.01†† |
| Visible cricopharyngeal bar | 30 (5) | 7 (3) | 4 (2) | 0 | <.01†† |
| Bilateral pharyngeal weakness | 11 (4) | 4 (2) | 16 (4) | 10 (4) | .06‡ |
| Functional swallow | 57 (3) | 74 (1) | 59 (2) | 73 (3) | .10* |

Abbreviations: TB, tongue base; AP, anteroposterior.

*Analyses adjusted for bolus type, baseline value, and stage of disease.

†*p* ≤ .05.

‡Unadjusted differences present at baseline.

Table 7. Mean duration (SEM) of temporal measures of swallowing by treatment protocol 3 months after chemoradiation treatment. (PPW = posterior pharyngeal wall).

| | TFHX, taxol infusion | TFHX, taxol bolus | TFHX, bolus, induction | RADPLAT | <i>p</i> value |
|---|----------------------|-------------------|------------------------|-------------|----------------|
| Number of swallows | 70 | 98 | 69 | 73 | |
| Oral onset of swallow (s) | -1.25 (.20) | -1.35 (.21) | -1.43 (.35) | -1.14 (.23) | .81 |
| Duration of oral transit time (s) | 0.56 (.13) | 0.70 (.13) | 0.39 (.11) | 0.18 (.15) | .02* |
| Duration of pharyngeal transit time (s) | 0.76 (.04) | 0.93 (.05) | 0.85 (.04) | 0.88 (.05) | .04* |
| Duration of pharyngeal delay (s) | -0.06 (.05) | -0.05 (.05) | 0.01 (.04) | -0.05 (.06) | .58 |
| Duration of tongue base contact to PPW at level of mid-C2 (s) | 0.41 (.07) | 0.33 (.07) | 0.48 (.06) | 0.45 (.08) | .34 |
| Duration of tongue base contact to PPW at level of inferior C2 (s) | 0.41 (.07) | 0.24 (.07) | 0.33 (.06) | 0.28 (.08) | .34 |
| Duration of tongue base contact to PPW at level of superior C3 (s) | 0.39 (.06) | 0.15 (.06) | 0.37 (.05) | 0.27 (.07) | .02* |
| Duration of velopharyngeal closure (s) | 0.82 (.09) | 0.75 (.09) | 0.74 (.08) | 0.85 (.10) | .70 |
| Duration of laryngeal closure (s) | 0.58 (.08) | 0.47 (.08) | 0.72 (.07) | 0.54 (.08) | .13 |
| Duration of cricopharyngeal opening (s) | 0.54 (.02) | 0.58 (.02) | 0.59 (.02) | 0.56 (.03) | .30 |
| Duration of laryngeal elevation (s) | 1.18 (.10) | 1.16 (.10) | 1.27 (.08) | 1.22 (.11) | .79 |
| Duration of hyoid elevation (s) | 1.22 (.10) | 1.16 (.10) | 1.26 (.09) | 1.18 (.11) | .88 |
| Onset base of tongue to posterior pharyngeal wall (s) | 0.16 (.02) | 0.18 (.01) | 0.15 (.01) | 0.18 (.02) | .50 |
| Time from first airway closure to first cricopharyngeal opening (s) | 0.04 (.05) | 0.01 (.05) | -0.02 (.05) | 0.06 (.05) | .68 |
| Oral residue (% of bolus) | 5.6 (2.0) | 9.4 (2.0) | 5.5 (1.8) | 5.04 (2.38) | .29 |
| Pharyngeal residue (% of bolus) | 13.8 (2.4) | 13.5 (2.5) | 10.6 (2.2) | 13.5 (2.8) | .67 |
| Aspiration (% of bolus aspirated) | 0.34 (.09) | 0.17 (.10) | 0.09 (.09) | 0.00 | .04* |
| Oropharyngeal swallow efficiency (%/s) | 76 (5) | 66 (5) | 74 (4) | 78 (6) | .32 |
| Number of attempts to swallow 1 st bolus | 2.04 (.23) | 2.06 (.24) | 2.24 (.20) | 1.97 (.28) | .84 |
| % of patients with G-tubes | 46 | 50 | 20 | 44 | .33 |
| % of patients with oral intake ≤ 50% | 31 | 19 | 13 | 33 | .58 |
| % of patients aspirating | 54 | 19 | 13 | 0 | .02* |

Abbreviation: PPW, posterior pharyngeal wall.
**p* < .05.

bolus, induction protocol had the highest level of reduced cricopharyngeal opening.

Table 7 gives the mean duration of the temporal measures for patients in each of the disease sites. The RADPLAT treatment exhibited the lowest (most normal) duration of oral transit time and the lowest frequency of aspiration. Duration of tongue base contact to the posterior pharyngeal wall at the superior point of C3 was lowest in the TFHX taxol, bolus, protocol. Most differences across treatment protocols were small, and many differences were within the range expected in persons without head and neck cancer.

DISCUSSION

This article examined swallowing function before treatment and 3 months after treatment in patients with head and neck cancer who received chemoradiation treatment. A total of 310 swallows were studied in 53 patients diagnosed with squamous cell cancer in one of five locations: nasopharynx, oropharynx, larynx, hypopharynx,

and unknown location. Most patients (35 of the 53) had T3 or T4 disease. The study particularly examined effects of site of disease and chemoradiation protocol on swallow function.

Before treatment (baseline), although most swallows (85%) were functional (as shown in Table 1; ie, there was no aspiration and only mild residue left after the swallow), at least 50% of the swallows exhibited disorders, albeit mild. Most of these disorders occurred during the pharyngeal stage of swallow. Thus, the disease itself introduces some pharyngeal disorders, particularly disorders in tongue base, pharyngeal wall, and laryngeal entrance. This agrees with earlier work by Pauloski et al.¹⁴

Three months after treatment, the same disorders were observed as were seen before treatment but in higher frequencies and in greater severity, as evidenced by the larger percentage of patients with gastrostomy or jejunostomy at that time and the lesser percentage of functional swallows (65% at 3 months, 85% before treatment). These data emphasize that the tumor treatments

examined in the study do not create new disorders but rather increase the frequency, severity, and clinical manifestation of those disorders seen before treatment. The disorders observed in this article agree with earlier studies of swallow disorders after chemoradiation to the head and neck.^{2,4,7,10} The most frequent disorders observed affect pressure generation during swallow (reduced tongue base retraction and reduced tongue strength) and airway protection. Temporal data on patients at baseline and 3 months after treatment and controls find similar measurements between patients and controls at both time points.

Temporal measures of the oropharyngeal swallow by site of disease reveal the only significant difference to be oropharyngeal swallow efficiency. All differences were within normal limits. Effects by site of disease revealed significantly more frequent reduction in tongue base movement in patients with disease in the oropharynx and larynx. Because the tongue base lies between the oropharynx and larynx, it is likely that the tongue base is receiving the maximal radiation dose when these areas are radiated. There is some evidence^{2,4} that this may improve 6 months after treatment and continue to improve long term. It is also possible that the small differences we observed may increase over years after treatment. There is need for longer term follow-up of these patients to fully understand the long-term effects of treatment.

Differences in effects of chemotherapy treatment protocols on oropharyngeal swallow in this study were minimal, and most differences were well within the range of variability in normal swallow measures. One reason for these minimal differences may relate to the fact that these patients all had advanced disease, and the radiotherapy could not be limited in extent. Patients received conventional radiotherapy with large fields without IMRT. Many studies have examined effects of radiation and surgical treatment or the combination of the two on swallow function. However, very few studies have looked at chemoradiation effects. As new treatment protocols, including new chemoradiation protocols, are developed, swallow effects need to be examined.

REFERENCES

- David J, Paty E, Bachaud J, Vignaud J. Tongue necrosis after radiotherapy. Arterial disease after radiotherapy. *Rev Stomatol Chir Maxillofac* 1989;90:334–336.
- 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.
- Eisele DW, Koch DG, Tarazi AE, Jones B. Aspiration from delayed radiation fibrosis of the neck. *Dysphagia* 1991;6:120–122.
- Ekberg O, Nylander G. Pharyngeal dysfunction after treatment for pharyngeal cancer with surgery and radiotherapy. *Gastrointestinal Radiology* 1983;8:97–104.
- Puthawala A, Nisar Syed A, Eads D, Gillin L, Gates T. Limited external beam and interstitial 192-iridium irradiation in the treatment of carcinoma of the base of the tongue: a ten year experience. *Int J Radiat Oncol Biol Phys* 1988;14:839–848.
- Scott R, Gillespie B, Perez C, et al. Hyperthermia in combination with definitive radiation therapy: results of a phase I/II RTOG study. *Int J Radiat Oncol Biol Phys* 1988;15:711–716.
- Lazarus CL, Logemann JA, Pauloski BR, et al. Swallowing disorders in head and neck cancer patients treated with radiotherapy and adjuvant chemotherapy. *Laryngoscope* 1996;106:1157–1166.
- 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;25:432–437.
- Eisbruch A, TenHaken RK, Kim HM, Marsh LH, Ship JA. Dose, volume, and function relationships in parotid salivary glands following conformal and intensity-modulated irradiation of head and neck cancer. *Int J Radiat Oncol Biol Phys* 1999;45:577–587.
- Eisbruch A, Kim HM, Terrell JE, Marsh LH, Dawson LA, Ship JA. Xerostomia and its predictors following parotid-sparing irradiation of head and neck cancer. *Int J Radiat Oncol Biol Phys* 2001;50:695–704.
- Mittal BB, Kepka A, Mahadevan A, et al. Tissue/dose compensation to reduce toxicity from combined radiation and chemotherapy for advanced head and neck cancers. *Int J Cancer Radiat Oncol Invest* 2001;96(Suppl):61–70.
- Samant S, Kumar P, Wan J, et al. Concomitant radiation therapy and targeted cisplatin chemotherapy for the treatment of advanced pyriform sinus carcinoma: disease control and preservation of organ function. *Head Neck* 1999;21:595–601.
- Wu CH, Hsiao TY, Ko JY, Hsu MM. Dysphagia after radiotherapy: endoscopic examination of swallowing in patients with nasopharyngeal carcinoma. *Ann Otol Rhinol Laryngol* 2000;109:320–325.
- Pauloski BR, Rademaker AW, Logemann JA, et al. Pretreatment swallowing function in patients with head and neck cancer. *Head Neck* 1999;22:474–482.
- Pauloski BR, Rademaker AW, Logemann JA, et al. Swallow function and perception of dysphagia in patients with head and neck cancer. *Head Neck* 2001;24:555–565.
- Newman LA, Robbins KT, Logemann JA, et al. Swallowing and speech ability after treatment for head and neck cancer with targeted intraarterial versus intravenous characteristics. *Head Neck* 2002;24:68–77.
- Kies MS, Haraf DJ, Rosen F, et al. Concomitant infusional paclitaxel and fluorouracil, oral hydroxyurea and hyperfractionated radiation for locally advanced squamous cell head and neck cancer. *J Clin Oncol* 2001;19:1961–1969.
- Rosen FR, Haraf DJ, Kies MS, et al. Multicenter randomized phase II study of paclitaxel (1-hour infusion), fluorouracil, hydroxyurea, and concomitant twice daily radiation with or without erythropoietin for advanced head and neck cancer. *Clin Cancer Res* 2003;9:1689–1697.

19. Vokes EE, Stenson K, Rosen FR, et al. Weekly carboplatin and paclitaxel followed by concomitant paclitaxel, fluorouracil, and hydroxyurea chemoradiotherapy: curative and organ-preserving therapy for advanced head and neck cancer. *J Clin Oncol* 2003;21:320–326.
20. Robbins KT, Vicario D, Seagren S, et al. A targeted supradose cisplatin chemoradiation protocol for advanced head and neck cancer. *Am J Surg* 1994;168:419–422.
21. Logemann JA. Manual for the videofluorographic study of swallowing, 2nd ed. Austin, TX: Pro-Ed; 1993. p 170.
22. Rademaker AW, Pauloski BR, Logemann JA, Shanahan TK. Oropharyngeal swallow efficiency as a representative measure of swallowing function. *J Speech Hear Res* 1994;37:314–325.
23. Zeger SL, Liang K-Y, Albert PS. Models for longitudinal data: a generalized estimating equation approach. *Biometrics* 1988;44:1049–1060.