Aspiration in Chemoradiated Patients With Head and Neck Cancer

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Objective: To review the incidence of aspiration after chemoradiation therapy in patients with head and neck cancer (HNC).

Design: Retrospective review.

Setting: Academic institution.

Patients: One hundred thirty patients with advanced HNC underwent chemoradiation therapy at our institution between 1998 and 2002 as part of a larger, multi-institutional, prospective study of induction chemotherapy followed by chemoradiation therapy; the 118 patients (91%) for whom oropharyngeal motility (OPM) study data were available are discussed in this article.

Main Outcome Measures: Incidence of trace (≤ 5% of swallowed bolus) and frank (>5%) aspiration (deep laryngeal or tracheal penetration) as determined by pretreatment and posttreatment OPM studies and correlation of the findings with the patients’ reported symptoms.

Results: Eighty-one patients (69%) underwent at least 1 OPM study demonstrating aspiration within the first year after chemoradiation therapy, with 30 (25%) demonstrating frank aspiration. Of the patients who aspirated, 61 (75%) reported no symptoms of coughing or choking (80% of trace and 67% of frank aspirators). The patients with cancer of the larynx and hypopharynx were more likely to be aspirators (P =.007 and P =.004, respectively). Of the 62 patients with available pretreatment OPM data, 33 (53%) demonstrated aspiration at baseline.

Conclusions: Aspiration is highly prevalent among patients with advanced HNC at baseline and is worse in the posttreatment period after chemoradiation therapy. The majority of these patients report no symptoms. All patients with advanced HNC should undergo instrumental swallow assessment, even in the absence of symptoms, to detect subclinical aspiration and to institute therapeutic maneuvers and swallow precautions as well as to determine the safety of oral feeding.

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Oral intake of food serves important nutritional functions for patients with head and neck cancer (HNC) and greatly improves their quality of life. For many patients undergoing organ preservation therapy, oral intake is a difficult task and can carry the risk of aspiration. The incidence of aspiration in patients with HNC who have undergone chemoradiation therapy is considered high, especially in the pretreatment period, but data are still emerging about the severity of aspiration and its relationship to the primary tumor site. Also, these patients may lack sufficient laryngeal sensation to detect aspiration. The incidence of subclinical, or “silent,” aspiration may be much higher than that of clinical aspiration.

Oropharyngeal motility (OPM) studies performed with videofluoroscopic observation of the swallowing reflex represent a highly sensitive tool for the detection of aspiration. We reviewed the OPM study data at our institution to determine the incidence of clinical and subclinical aspiration before and after chemoradiation therapy in a group of patients with HNC.

Methods

Patients with advanced HNC who underwent chemoradiation therapy from November 1998 to August 2002 at the University of Chicago, Chicago, Illinois, were identified as part of a prospective, multi-institutional clinical trial of induction chemotherapy followed by chemoradiation therapy. The results of this trial (including all participating centers) are described in detail elsewhere. Briefly, the 3-part protocol (A, B, and C) consisted of induction carboplatin-paclitaxel followed by 5 cycles of concomitant hydroxyurea-fluorouracil-paclitaxel and radia-
HNC at the University of Chicago were to be referred for OPM lobectomy and tracheostomy. The radiation dose was reduced sequentially for groups A, B, and C, and the induction chemotherapy (total dose, 72-75 Gy). The radiation dose was reduced sequentially for groups A, B, and C, and the induction chemotherapy schedule was altered for group C during this trial.

As part of the prospective study protocol, all patients with HNC at the University of Chicago were to be referred for OPM studies before and on completing chemoradiation therapy. The OPM technique at our institution has been described elsewhere. It is essentially a modified barium swallow during which patients are given different consistencies of radiopaque liquids and solids and monitored during swallowing via fluoroscopy (Figure 1). Parameters such as the presence of aspiration, the amount and type of material aspirated, and the patient’s response to aspiration are analyzed and documented. If an abnormality is detected, therapeutic maneuvers are instituted at that time. Any improvement in swallowing function as a result of therapy is also documented, and formal recommendations are made as to the safety of oral feeding and any needed precautionary measures.

All available OPM records through November 2004 were collected. Aspiration, which was defined as deep laryngeal penetration to the level of the vocal cords or beyond, into the trachea, was quantified as a percentage of the swallowed bolus during the OPM procedure. For the purposes of our study, aspiration of 5% or less of the swallowed bolus was considered trace, and greater than 5% was considered frank. Data were extracted and combined with the preexisting prospective spreadsheet (Microsoft Excel; Microsoft Corp, Redmond, Washington) to create the database used in this study.

Clinical characteristics and treatment outcomes were compared between tumor site groups and between patients with and without a tracheostomy using the Fisher exact test. A Wilcoxon rank sum or Kruskal-Wallis test was used when the clinical or outcome variable was ordinal (eg, none, trace, and frank aspiration). Spearman rank correlation coefficients assessed the association between 2 ordinal variables. A 2-sided P value of less than .05 was considered statistically significant. Analyses were performed using a commercially available statistical computer software program (Stata Version 9; Stata Corp, College Station, Texas). This retrospective study was approved by the University of Chicago’s institutional review board as an adjunct to the preexisting prospective chemoradiation study protocol.

One hundred thirty patients were identified. Pretreatment OPM data were available for 62 patients (48%) (Table). An additional 34 patients (26%) underwent their planned baseline OPM study during induction chemotherapy and were not included in further analysis because of the possibly confounding effect of this treatment on swallowing function. Thirty-two of the remaining 34 patients without true baseline OPM studies were enrolled consecutively in the clinical chemoradiation trial between January and October 2001, during which time no patients were scheduled to undergo baseline OPM studies. The remaining 2 patients did not complete OPM studies as scheduled.

Fifty-three percent (n=33) of the patients demonstrated aspiration at baseline (39%, n=24 trace, and 15%, n=9 frank). Almost half (46%) of the patients with aspiration had laryngeal primary tumors; 8 (33%) of the trace aspirators and 7 (78%) of the frank aspirators. Viewed another way, 79% (n=13) of the 19 patients with laryngeal cancer demonstrated aspiration at baseline. Regarding other sites, 71% (5 of 7) of the patients with oropharyngeal cancer, 44% (8 of 18) of those with oropharyngeal cancer, and 23% (3 of 13) of those with cancer of the oral cavity demonstrated aspiration at baseline (Figure 2). Baseline aspiration increased with increasing T stage: T1, 3 (33%); T2, 4 (40%); T3, 6 (54%);
and T4, 20 (66%). This trend was significant ($P = .04$).
Nodal status and age were not associated with aspiration ($P = .71$ and $P = .31$, respectively). Importantly, only 11 (33%) of baseline aspirators reported symptoms of coughing or choking: 8 (33%) of trace aspirators and 3 (33%) of frank aspirators.

In the first year after treatment, 118 patients (91%) underwent OPM studies (Table). Three of these patients underwent salvage surgery on their primary tumor during this period. Excluding the OPM studies that were conducted after salvage surgery, a total of 240 OPM studies for the 118 patients were analyzed. Eighty-one (69%) of the 118 patients had at least 1 OPM study that demonstrated aspiration during this period. Fifty-one patients (43%) showed trace aspiration (Figure 3), and 30 (25%) showed frank aspiration (Figure 4). Most of the 81 patients (86%) aspirated liquids only, although some did aspirate paste (14%).

Patients with laryngeal and hypopharyngeal cancers showed higher incidences of aspiration (3 [11%] and 0 [0%], no aspiration; 15 [56%] and 4 [44%], trace aspiration; and 9 [33%] and 5 [56%], frank aspiration) than those with other cancers (33 [41%], 32 [39%], and 16 [20%], respectively). These differences were statistically significant ($P = .007$ for laryngeal cancer and $P = .004$ for hypopharyngeal cancer; Figure 5). There was no significant difference by primary site in regard to aspiration of liquids vs paste ($P = .22$). Aspiration was not affected by age ($P = .21$), T stage ($P = .84$), nodal status ($P = .65$), or study group (A, B, or C; $P = .15$).
Of the 81 patients who had aspiration, 61 (75%) reported no symptoms of coughing or choking (80% of trace and 67% of frank aspirators). There was no statistically significant difference between patients with and without laryngeal or hypopharyngeal cancer in regard to their reported symptoms (P = .65). In 71 of the aspirating patients, the depth of aspiration was specified. In 47 (66%) of these patients, the aspiration visualized on the OPM study was limited to the level of the vocal cords, with no detectable penetration into the trachea. The remaining 24 patients (34%) had penetration into the trachea (Figure 4), which was more common in the frank aspirators (16 [62%] with tracheal penetration) than in the trace aspirators (8 [18%] with tracheal penetration; P < .001). Among the tracheal aspirators, the primary sites were as follows: unknown (n = 1 [4%]), oral cavity (n = 1 [4%]), oropharynx (n = 11 [46%]), larynx (n = 8 [33%]), and hypopharynx (n = 3 [13%]).

Fifty-two patients (44%) underwent planned neck dissections for pretreatment N2 or N3 nodal disease between 3 and 28 weeks after completion of chemoradiation therapy (median, 10 weeks). A posttreatment biopsy was performed during the same procedure unless the patient had an unknown primary site. Thirty-nine patients underwent an OPM study both before and after their neck dissection, allowing comparison. Twenty-three (59%) aspirated before neck dissection, and 22 (96%) of those 23 patients aspirated after neck dissection. Of the remaining 16 patients who did not aspirate before neck dissection, 11 (69%) aspirated after neck dissection. Before neck dissection, 16 patients (41%) had no aspiration, 19 (49%) had trace aspiration, and 4 (10%) had frank aspiration, compared with 6 (15%), 21 (54%), and 12 (31%), respectively, after neck dissection (P = .003).

Seventeen patients had a tracheostomy at the time of at least 1 of their OPM studies. All 17 patients underwent tracheotomy before treatment: 16 for acute upper airway obstruction at our institution and 1 for unclear reasons at an outside hospital. Twelve (71%) of the 17 patients had laryngeal cancer, representing 44% of the 27 patients with laryngeal cancer compared with the remaining 5 patients, representing only 6% of the patients with nonlaryngeal cancer (P < .001). Also, of the 17 patients with a tracheostomy, 3 (18%) had no aspiration, 9 (53%) had trace aspiration, and 5 (29%) had frank aspiration, compared with 33 (33%), 43 (42%), and 25 (29%), respectively, of the patients without a tracheostomy (P = .29). Among all patients who aspirated, there was no statistically significant difference between patients with or without a tracheostomy and reported symptoms (P > .99).

During the OPM procedure, a patient’s sensitivity to aspiration was noted (eg, coughing, gagging, or repeated swallowing with clearing of the aspirated material). This information was available for 69 (85%) of the 81 aspirators. Overall, 58% had good sensitivity, 35% had diminished sensitivity, and 7% had poor sensitivity. Sensitivity was not correlated with tracheotomy status (P = .78) but was correlated with primary site; oral cavity primary sites had better sensitivity than other sites, with 86%, 14%, and 0% of cases demonstrating good, fair, and poor sensitivity, respectively, compared with 51%, 40%, and 9%, respectively, for all other sites (P = .02).

Therapeutic maneuvers are taught to patients who show signs of swallowing abnormalities during the OPM study. Of the 73 patients who aspirated and for whom data on therapy outcomes were available, 51 (70%) showed a good response to therapy, with complete or near resolution of aspiration with appropriate maneuvers (eg, chin tuck, head turn, or double swallow). Therapy was much more effective for patients with trace aspiration (82% with good response) than for those with frank aspiration (50% with good response, P = .002). Also, patients with oral cavity primary sites had much better success with therapy (93% with good response) than patients with other primary sites (64% with good response, P = .03). Of the 33 patients who aspirated during their pretreatment OPM procedure, 14 (42%) showed a good response to therapy; all of these patients were trace aspirators.

When pretreatment and posttreatment OPM study findings were compared, we found that 17 (59%) of the 29 baseline nonaspirators went on to aspirate in the first year after treatment. Eighty-eight percent of the 33 baseline aspirators continued to aspirate after treatment, resulting in 29 patients who aspirated both before and after treatment. Thirteen (45%) of the 29 patients had a good response to therapy before treatment and 17 (59%) had a good response after treatment. The 4 most com-
mon sites—oral cavity, oropharynx, larynx, and hypopharynx—were all associated with increased incidences of aspiration after treatment, and for all sites but the larynx, the incidence of frank aspiration increased as well (Figure 6). The pretreatment association between T stage and aspiration was not present after treatment (P = .32).

**COMMENT**

Preservation of functional organs remains the great challenge of chemoradiation therapy protocols. Airway protection is one of the most important, and most assailed, functions in need of preservation. Patients want to eat, and those who can overcome mucositis, trismus, disordered swallowing reflexes, dysphagia, and stricture formation may ignore symptoms of aspiration. However, aspiration can result in pneumonia, with significant morbidity and mortality, and can further debilitate patients with HNC.

The present study demonstrated a very high rate of aspiration in patients with advanced-stage HNC both before (53%) and in the first year after (69%) chemoradiation therapy. This posttreatment incidence was slightly higher than that reported in another recent study involving 63 patients conducted by Nguyen and colleagues using similar methods. That series demonstrated a 59% incidence of aspiration as well as a 9% mortality rate related to the aspiration but did not analyze aspiration by primary site.

Aspiration is a multifactorial, anatomically defined event. Lack of adequate shunting of the food bolus around the larynx, pharyngeal stasis, poor hypopharyngeal transit, loss of supraglottic sensation and food clearing, and inadequate glottic sensation and closure all play a role, with the final 2 factors ultimately permitting food entry into the lower respiratory tract. Before treatment, tumor burden would be expected to cause more site-specific swallowing dysfunction, a theory that is supported by the higher representation of larynx cancer in the baseline aspiration group and by recent data from Logemann and colleagues demonstrating that the primary tumor site correlates with specific swallowing dysfunctions. The degree of tumor burden (T stage) also negatively affected airway protection at baseline. The field effects of chemotherapy and radiation therapy resulting in diffuse functional perturbations, and the reduction in tumor burden, may be responsible for the more even distribution of aspiration among sites in the posttreatment period, even though the larynx still remains one of the sites with a higher incidence of aspiration.

A hypopharyngeal primary site was also associated with a higher incidence of aspiration before and after treatment. Functional derangement at that level may lead to pharyngeal stasis and reduced laryngeal elevation, predisposing to ultimate aspiration. Also, irradiation of the hypopharynx may have a greater affect on the nearby larynx than irradiation of other sites. Along similar lines, it was not surprising that patients with oral cavity primary sites had better sensitivity to aspiration and better response to therapy. The absence of tumor in the larynx and pharynx may prevent tumor-associated anatomical changes in those areas, as well as spare those areas the majority of radiation. Furthermore, proximal swallowing dysfunction may be more amenable to therapy. Further research is needed on this topic. Although cases involving oral cavity tumors appear to have better sensitivity, it should be noted that patients with oral cavity cancer still had a 47% incidence of aspiration in our series and oral feeding is not an a priori safe option for them.

The response to therapy did improve slightly after chemoradiation therapy (59% vs 45%, with a good response after treatment vs before treatment, respectively), although the absolute number of patients with pretreatment and posttreatment data is small. It may be that the reduction in tumor burden makes some patients’ upper digestive tracts more amenable to swallowing maneuvers. Future work on larger numbers of patients may better characterize the relationship between chemoradiation therapy and swallowing therapy.

Traditionally, the presence of a tracheotomy tube was thought to put patients at increased risk for aspiration. Data have emerged to the contrary in tracheotomized postsurgical patients with HNC and in unselected patients who have been tracheotomized for other diagnoses. By
evaluating swallowing function with and without the tube in place, these studies show that the tracheotomy tube does not in itself result in an increased risk of aspiration. The present study builds on this concept by further demonstrating that even the presence of a tracheostoma does not affect aspiration status in patients with HNC who have undergone chemoradiation therapy, as there was no statistically significant difference between patients with and without tracheostomies (P = .29). This conclusion is best limited to patients with laryngeal cancer at this time, given the disproportionate number of tracheotomized patients with laryngeal cancer in this study.

Whereas the presence of a tracheostoma did not have a significant adverse effect, those patients for whom preoperative and postoperative neck dissection data were available did have a significantly increased incidence of aspiration after surgery. This finding is consistent with recent long-term data correlating posttreatment neck dissection with swallowing dysfunction, as evidenced by increased gastrostomy tube dependence. Edema, pain, scarring, and nerve injury due to surgical manipulation are all potential culprits in the pathogenesis of swallowing dysfunction. As evidence mounts to implicate neck dissection in long-term morbidity, alternatives to planned neck dissections, such as screening with positron emission tomography, may become more attractive.

Three-fourths of the patients who aspirated reported no symptoms of aspiration, which is perhaps the most significant and troubling finding of this study and highlights the importance of routine swallowing assessment in patients with head and neck cancer. History alone cannot rule out aspiration in the post–chemoradiation therapy period (or even at baseline). It may be that aspiration risk follows a predictable posttreatment course and that the need for swallowing assessment diminishes over time; however, it is known that swallowing dysfunction may still be present even 1 year after chemoradiation therapy. Further research on the course of aspiration and the need for prolonged swallow assessment follow-up is warranted.

Even though most patients who aspirated lacked symptoms, a considerable percentage presented to their OPD procedure with overt symptoms of aspiration, many of them with continued oral intake. Continued oral intake, even with symptoms of aspiration, indicates either a lack of understanding about the signs and dangers of aspiration or an unyielding desire to eat. In the former, the clinician’s role is education, before the initiation of oral feeding. In the latter, the therapy instituted during the OPD procedure can provide a safer strategy for eating.

This study uses a broad definition of aspiration, including both deep laryngeal (to the level of the vocal cords) and deep tracheal penetration. While a distinction can and should be made between these 2 levels of airway penetration, food entry to either level represents a considerable perturbation of airway protective mechanisms. Videofluoroscopy of normal individuals showed that transient, superficial laryngeal penetration occurred in more than 50% of the 92 subjects tested, but none of these normal subjects showed penetration to the level of the vocal cords. Lower airway protection during deep laryngeal penetration events is reliant only on the apposition of the vocal cords, which may not be an effective barrier. Indeed, tracheal penetration occurred in subsequent swallows in 85% of deep laryngeal penetrators when prolonged monitoring was used.

Our study was limited in part by its retrospective nature as well as by a lack of consistent time points for the pretreatment and posttreatment OPD studies. Owing to scheduling difficulties with multiple appointments and many patients having to travel great distances, the OPD data were sporadic in the first year and the intervals between studies varied greatly. It is possible that the mucositis and edema that occur in the first 1 to 3 months after treatment cause transient aspiration, which resolves with a reduction in inflammation of the oropharyngeal mucosa. Alternatively, delayed posttreatment fibrosis may result in more durable aspiration that worsens over time. These theories could not be tested with this data set. Also, we did not examine the long-term swallowing outcomes, which may or may not show an ultimate benefit of chemoradiation therapy on swallowing function compared with baseline.

In conclusion, aspiration is highly prevalent among patients with advanced HNC at baseline and is worse in the posttreatment period after chemoradiation therapy. The vast majority of these patients will report no symptoms. Laryngeal and hypopharyngeal primary sites were significantly correlated with increased incidence of aspiration (P = .007 and P = .004, respectively). All patients with advanced HNC should undergo instrumental swallow assessment, even in the absence of symptoms, to detect subclinical aspiration and to institute therapeutic maneuvers and swallow precautions, as well as to determine the safety of oral feeding. Future trials of organ preservation therapy should include swallow assessment as part of their outcome measures.

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