Submandibular Gland Transfer for Prevention of Xerostomia After Radiation Therapy

Swallowing Outcomes

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Objective: To assess swallowing outcomes in patients with oropharyngeal carcinoma in relation to the Seikaly-Jha procedure for submandibular gland transfer (SJP). The SJP has recently been described as beneficial in the prevention of xerostomia induced by radiation therapy in patients with head and neck cancer.

Design: Inception cohort.

Setting: University-affiliated primary care center.

Patients: A phase 2 clinical trial was conducted from February 1, 1999, through February 28, 2002, to evaluate SJP in patients with head and neck cancer. During that period, a consecutive sample of 51 patients who underwent surgical resection and reconstruction with a radial forearm free flap for oropharyngeal carcinoma were referred for functional assessment of swallowing after completion of adjuvant radiation therapy. At 6 months after surgery, swallowing assessments for 24 patients were available.

Intervention: The cohort of 24 patients included 13 who had preservation of 1 submandibular gland (SJP group) and 11 who did not (control group).

Main Outcome Measures: Quantitative and qualitative aspects of swallowing were obtained to determine whether patients in the SJP group performed more optimally than those in the control group.

Results: Baseline and stimulated salivary flow rates were significantly different between groups. Patients in the SJP group were able to move the bolus through the oral cavity and into the pharynx faster than those in the control group. In addition, patients in the SJP group swallowed less often per bolus than patients in the control group. The complete swallowing sequence was twice as long in controls.

Conclusions: The SJP for submandibular gland transfer appears to be beneficial in promoting more time-efficient swallowing behaviors. This efficiency has implications for the overall well-being and nutritional status of patients with head and neck cancer.


Xerostomia is a condition in which the function of the salivary glands has been altered such that the oral cavity lacks saliva, resulting in subjective complaints of dry mouth. Xerostomia resulting from cancer treatment has a devastating impact on quality of life. Individuals diagnosed as having cancer of the head and neck are overwhelmed by the notion of treatment potentially involving surgery, radiation therapy, and chemotherapy. The common experience of the patients is that surviving these therapies is the primary morbid challenge to regaining quality of life. However, the common clinical experience is that where xerostomia occurs, this condition becomes a primary threat to regaining quality of life. Saliva is important for lubrication, and therefore comfort, of the mouth and oral pharynx, but is also necessary for modulation of microbial organisms in the mouth, remineralization of teeth, maintenance of the mucosal immune system, and preparation of a bolus of food during mastication. When salivary function is compromised, the resulting sequelae include oral discomfort, mucositis, periodontal disease, dental caries, loss of teeth, fissures of the tongue, decreased taste acuity, inability to wear dentures if needed, and difficulty with mastication and deglutition. The development of xerostomia in survivors of head and neck cancer, therefore, is of serious consequence to their nutritional status and their overall quality of life. Because of the location of primary tumors of the head and neck, the major sali-
vary glands are often in the field of the postoperative radiation therapy.\textsuperscript{1,10,11} For this reason, the potential for development of xerostomia in this patient population is very real. Salivary dysfunction develops immediately when the major salivary glands are in the radiation field, and such dysfunction is permanent with little chance for recovery.\textsuperscript{10,12} The prevalence of xerostomia in patients with head and neck cancer after radiation therapy, whether that therapy is the primary or secondary treatment, has been reported to vary from 94% to 100%.\textsuperscript{13-15}

Treatment for xerostomia can be supportive or preventive. Supportive care for xerostomia includes the use of saliva substitutes and moistening agents. Saliva substitutes duplicate the properties of normal saliva and provide relief for approximately 40% of patients who use them.\textsuperscript{16} However, they are costly and provide only temporary relief.\textsuperscript{1} Moistening agents include chewing gum, candy, and sips of water. Again, these provide only temporary relief of xerostomia. Furthermore, the constant intake of water during the course of a day is associated with polyuria, often resulting in nocturnal wakefulness. The use of candies is associated with increased dental caries and mucosal damage stemming from pressure against the soft tissues of the mouth when sucking on the candy.\textsuperscript{1}

One modality of preventive care for xerostomia is the Setkaly-Jha procedure for submandibular gland transfer (SJP). One submandibular salivary gland is transferred into the submental space, using retrograde flow through the facial vessels. An incision is made from the mastoid process to the mentum. A flap is elevated, and the submandibular gland is released from surrounding structures and then repositioned in the submental space under the anterior belly of the digastric muscle. The submental and sublingual space is then shielded during postoperative radiation therapy, thereby protecting and preserving the transferred submandibular and sublingual salivary glands. If any facial, preglandular, or submental nodes are found to be involved with metastatic cancer, the gland transfer is abandoned and the gland is resected. The surgical procedure is described as requiring no special surgical skills and adds approximately 45 minutes to the total surgical time.\textsuperscript{10} It is a relatively inexpensive treatment modality, with recent reports demonstrating efficacious results in the prevention of xerostomia after radiation therapy.\textsuperscript{10,17-19} Statistically significant differences in salivary flow between patients who have received the SJP and a group of control subjects have been demonstrated. The SJP prevented xerostomia in 83% of patients undergoing that treatment, whereas all of those in the control group experienced severe xerostomia.\textsuperscript{19} Previous publications provide a more detailed description of the surgical procedure.\textsuperscript{10,17-19}

Unlike well-documented evidence describing the impact of xerostomia in the development of mucositis, periodontal disease, and dental caries,\textsuperscript{1,20} the impact on the development of swallowing disorders in patients with head and neck cancer has only recently been described.\textsuperscript{7,9} In 2 related reports,\textsuperscript{7,9} a reduction in saliva weight after chemoradiation therapy was related to patient report of poorer swallowing outcomes. There was no relationship found in either report between saliva weight and objective assessment of swallowing function, which included temporal measures of swallowing events. In contrast, another report involving patients with head and neck cancer\textsuperscript{a} found that patients with xerostomia took longer to masticate a dry bolus and were left with greater oral and pharyngeal residues than a group of healthy controls. These reports appear to provide conflicting information regarding the effect of xerostomia on objective measures of swallowing function. However, the effect of xerostomia was being compared differently, with one set of reports using salivary weight to understand the effect of xerostomia on swallowing.\textsuperscript{7,9} and the other report using a group of healthy controls for comparison with patients with xerostomia.\textsuperscript{8} Regardless, evidence is emerging that supports what has been largely anecdotal evidence of swallowing problems related to xerostomia.

From previous salivary flow studies, it has been demonstrated that the SJP has yielded beneficial results in preventing xerostomia in patients undergoing radiation therapy of the head and neck region.\textsuperscript{10,17-19} The objectives of the present study were to explore the benefits of the SJP beyond previously reported salivary flow rates.\textsuperscript{10} Specifically, we compared measures of swallowing outcomes obtained via videofluoroscopy after adjuvant radiation therapy between a group of patients who received the SJP and a group of controls (ie, patients who did not receive the SJP owing to oncological reasons).

### METHODS

A phase 2 clinical trial was conducted from February 1, 1999, through February 28, 2002, to evaluate the SJP for submandibular gland transfer in patients with head and neck cancer. The trial was approved by the internal review board and the human ethics committee of the University of Alberta (Edmonton), and informed consent was obtained from each patient. During that period, 31 patients who underwent surgical resection and reconstruction with a radial forearm free flap for oropharyngeal carcinoma were referred for functional assessment of swallowing after completion of adjuvant radiation therapy (ie, at least 6 months after surgery). Of those patients, 8 died before a post–radiation therapy assessment could occur, 8 were lost to follow-up, 4 did not receive conventional adjuvant postoperative radiation therapy (ie, they received intensity-modulated radiation therapy), 4 had a history of previous surgery or radiation therapy for head and neck cancer, and 3 underwent videofluoroscopic swallow studies in which the image was too dark for proper analysis. Thus, for the current study, 24 patients underwent assessment for swallowing ability via videofluoroscopy.

All patients underwent surgical resection of an oropharyngeal tumor and reconstruction with a radial forearm free flap, followed by a standard course of conventional radiation therapy. All patients were treated by a single medical rehabilitation team. The anatomical areas involved in oropharyngeal resections included the soft palate, lateral pharyngeal wall, tonsil, and base of tongue (BOT). No individual was included who had involvement of the oral tongue, maxilla, nasopharynx, or larynx. Data were available for 4 women (17%) and 20 men (83%) who ranged in age from 33 to 75 years (mean age, 57 years). Of the 24 patients, 13 underwent the SJP for submandibular gland transfer (SJP group) and the remaining 11 did not (control group). All patients received 50 to 70 Gy of radiation in 2 Gy per fraction, with treatment once a day, 5 times a week, during the course of 6 weeks. Radiation therapy was started 4 to 6 weeks after

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surgery. In those patients who underwent the SJP, shielding covered more than 80% to 90% of the transferred submandibular salivary gland. The posterior border shielding always remained anterior to the hyoid bone. Disease areas or potential sites of spread were not shielded. Primary target volume included the major salivary glands (parotid and the nontransferred submandibular salivary glands) and had greater than 50 Gy of radiation delivered to that volume via external beam.

Patients underwent assessment for swallowing after the completion of radiation therapy. Time elapsed from the surgery date to the swallowing assessment reported herein ranged from 155 to 398 days, with an average across patients of 220 days. Preoperatively, degree of resection, and days since surgery were entered as covariates in the analysis. The data were analyzed via a 1-way multivariate analysis of covariance with fixed effects on the between-subjects factor. The between-subjects factor was group and had 2 levels (SJP and control). An independent-samples t test was used to determine differences between baseline and stimulated flow rates. Approximately 20% of the data were reanalyzed to establish interobserver reliability. Intraclass correlation coefficients (average of raters) revealed a value of 0.96, with the upper and lower bounds of a 95% confidence interval at 0.98 and 0.92, respectively.

**DATA COLLECTION**

At the 6-month postoperative assessment time, saliva from the anterior floor of the mouth was collected at least 1 hour after the most recent meal, between 9:30 AM and 12:30 PM, and was calculated as collected volume/collection time. An appliance consisting of a micropipette holder fitted with a latex dropper bulb was used to collect the baseline and stimulated saliva samples. Baseline saliva samples were collected first, followed by a 3-minute rest interval. Then, stimulated saliva samples were collected after administration of a 6% citric acid solution to the posterior dorsal surface of the tongue. The details of this procedure are described more thoroughly elsewhere.

A modified barium swallow procedure was completed in the presence of a radiologist within the radiology department of the hospital. Two consistencies of food were administered, including approximately 10 mL of pudding mixed with paste barium (barium sulfate cream [Esobar]; Therapex, Montreal, Quebec) in a 3:1 ratio presented as a calibrated bolus on a teaspoon, and a quarter of a digestive cookie covered with barium paste. Two trials of each consistency were consumed and recorded on a videofluoroscopic study. Based on the methods of previous studies of swallowing, each swallow study was analyzed in frame-by-frame slow motion using the Digital Swallowing Workstation (Model 7200; Kay Elemetrics Corp, Lincoln Park, NJ) for the following timing events: oral transit duration, pharyngeal transit duration, oral containment duration, oropharyngeal transit duration, cricopharyngeal open duration, and sequence duration. We recorded the number of swallows per each bolus consistency. In addition, we observed any occurrences of laryngeal penetration or pulmonary aspiration during the swallow study and rated them on the Penetration-Aspiration Scale. Observers also rated the degree of residue remaining in the oral cavity after all swallows in a sequence of swallows on 1 bolus. A rating of 1 was assigned in instances where there was no or very mild oral residue. A rating of 2 was assigned in instances where there was considerable residue in the mouth, which was estimated to be no more than 25% of the original bolus. A rating of 3 was assigned in instances where there was approximately 25% or more of the original bolus remaining in the mouth. Finally, we judged the degree of pharyngeal residue at the end of each swallowing sequence. A rating of 1 was assigned in instances where there was no or very mild pharyngeal residue. A rating of 2 was assigned in instances where there was considerable residue in the pharynx that did not threaten the airway. A rating of 3 was assigned in instances where there was considerable residue in the pharynx that appeared to threaten the airway.

**STATISTICAL ANALYSIS**

All statistical analyses were performed using SPSS (version 11.5 [2002]; SPSS Inc, Chicago, Ill). Preliminary statistical analyses showed that patient age and percentage of the BOT resected were significantly correlated with several of the dependent variables. Therefore, age and percentage of BOT resected were entered as covariates in the analysis. The data were analyzed via a 1-way multivariate analysis of covariance with fixed effects on the between-subjects factor. The between-subjects factor was group and had 2 levels (SJP and control). An independent-samples t test was used to determine differences between baseline and stimulated flow rates. Approximately 20% of the data were reanalyzed to establish interobserver reliability. Intraclass correlation coefficients (average of raters) revealed a value of 0.96, with the upper and lower bounds of a 95% confidence interval at 0.98 and 0.92, respectively.

**SALIVARY FLOW RATES**

Baseline and stimulated salivary flow rates were available for all patients in the SJP group and for a subgroup of controls. In the SJP group, mean baseline flow rate was 0.07 mL/min (range, 0.01-0.17 mL/min), whereas in the control group it was 0 mL/min. Mean stimulated salivary flow rate for the SJP group was 0.32 mL/min (range, 0.04-0.90 mL/min), whereas in the control group it was 0.07 mL/min (range, 0-0.21 mL/min). An independent-
samples t test showed that differences between the 2 groups were significant for the baseline \((P = .002)\) and stimulated \((P = .05)\) flow rates.

**SWALLOWING OUTCOMES**

**Pudding Bolus**

Means and SDs for all dependent variables are shown in Table 2. For the pudding bolus, 23 of 24 fluoroscopic studies were analyzed (12 SJP and 11 control). A study from 1 patient in the SJP group was not included because the image was not satisfactory for analysis. The results showed that, while controlling for age and percentage of BOT resected, there were significant between-group differences for the dependent variables oral containment duration (ie, the interval from the start of the sequence until the tail of the bolus passes the posterior border of the ramus of the mandible) and sequence duration (ie, the interval between the start and the end of the complete swallowing sequence). Individuals in the SJP group had significantly shorter oral containment duration (mean, 1.97 seconds) than those in the control group (mean, 4.13 seconds). In addition, overall swallowing sequence duration differed between the 2 groups. Individuals in the SJP group took a mean of 10.65

<table>
<thead>
<tr>
<th>Measure, Group</th>
<th>Control</th>
<th>SJP</th>
<th>Significance*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral transit duration, s</td>
<td>Mean (SD) 1.10 (1.08)</td>
<td>0.59 (0.38)</td>
<td>.19</td>
</tr>
<tr>
<td>Minimum</td>
<td>0.13</td>
<td>0.2</td>
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<tr>
<td>Maximum</td>
<td>3.85</td>
<td>1.2</td>
<td></td>
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<tr>
<td>Pharyngeal transit duration, s</td>
<td>Mean (SD) 2.25 (2.90)</td>
<td>1.22 (0.76)</td>
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</tr>
<tr>
<td>Minimum</td>
<td>0.58</td>
<td>0.4</td>
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</tr>
<tr>
<td>Maximum</td>
<td>10.61</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Oropharyngeal transit duration, s</td>
<td>Mean (SD) 3.35 (3.81)</td>
<td>1.81 (0.79)</td>
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</tr>
<tr>
<td>Minimum</td>
<td>0.83</td>
<td>0.93</td>
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<tr>
<td>Maximum</td>
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<td>3.2</td>
<td></td>
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<tr>
<td>Cricopharynx open duration, s</td>
<td>Mean (SD) 0.45 (0.22)</td>
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<tr>
<td>Maximum</td>
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<tr>
<td>Oral containment duration, s</td>
<td>Mean (SD) 4.13 (2.98)</td>
<td>1.97 (1.03)</td>
<td>.02</td>
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<tr>
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<tr>
<td>Maximum</td>
<td>11.25</td>
<td>3.89</td>
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</tr>
<tr>
<td>Sequence duration, s</td>
<td>Mean (SD) 20.99 (14.93)</td>
<td>10.65 (5.53)</td>
<td>.054</td>
</tr>
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<tr>
<td>Maximum</td>
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<td>23.52</td>
<td></td>
</tr>
<tr>
<td>No. of swallows</td>
<td>Mean (SD) 4.36 (3.96)</td>
<td>2.50 (1.57)</td>
<td>.18</td>
</tr>
<tr>
<td>Minimum</td>
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<td>1</td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
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<td>7</td>
<td></td>
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<tr>
<td>Penetration-Aspiration Scale level†</td>
<td>Mean (SD) 1.36 (0.50)</td>
<td>1.75 (1.76)</td>
<td>.57</td>
</tr>
<tr>
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<td>1</td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
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<td>7</td>
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<tr>
<td>Pharyngeal residue</td>
<td>Mean (SD) 1.64 (0.92)</td>
<td>1.50 (0.67)</td>
<td>.89</td>
</tr>
<tr>
<td>Minimum</td>
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<td>1</td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>3</td>
<td>3</td>
<td></td>
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<tr>
<td>Oral residue</td>
<td>Mean (SD) 1.18 (0.40)</td>
<td>1.17 (0.39)</td>
<td>.98</td>
</tr>
<tr>
<td>Minimum</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

(continued)

Abbreviation: SJP, Seikaly-Jha procedure for submandibular gland transfer.

*Based on estimated marginal means (covariates appearing in the model were age and percentage of base of tongue resected) with adjustment for multiple comparisons via a Bonferroni correction.

†On this scale, level 1 indicates no penetration or aspiration; 2, penetration above the vocal folds but no residue; 3, penetration above the vocal folds with residue; 4, bolus contacting the vocal folds but no residue; 5, bolus contacting the vocal folds with residue; 6, bolus passing the glottis without subglottic residue; 7, bolus passing the glottis with subglottic residue and patient response; and 8, bolus passing the glottis with subglottic residue and no patient response.
seconds to swallow the pudding bolus, whereas those in the control group took 20.99 seconds.

**Cookie Bolus**

Means and SDs for all dependent variables are shown in Table 2. For the cookie bolus, 7 of 24 fluoroscopic studies were analyzed (5 SJP and 2 control patients). Seven studies were excluded from the analyses because the patients were given water to help propel the bolus into the pharynx before any swallow could be initiated (4 SJP and 3 control patients). Ten patients were not able to complete a cookie swallow owing to lack of dentition or diet restriction (4 SJP and 6 control patients). The results did not reveal any significant differences between groups.

Xerostomia is a devastating consequence of radiation therapy associated with head and neck cancer treatment. The sequelae of xerostomia have the potential to profoundly affect many aspects of quality of life in such patients. Recent surgical innovation, namely, the SJP for submandibular gland transfer, has provided hope in the battle against xerostomia in patients who have been treated for oropharyngeal cancer. Reports of this procedure suggest that it is successful in maintaining salivary flow in a high percentage of individuals receiving the treatment. For the patients in this study, significant differences in salivary flow rate existed between the 2 groups. Translation of the importance of the maintenance of saliva to functional outcomes after the SJP has not been described previously. The results of the present research show that the benefits of this procedure in maintaining saliva extend to swallowing outcomes.

With respect to the pudding bolus, patients in the SJP group were able to move the bolus through the oral cavity and into the pharynx faster than patients in the control group. Patients in the SJP group also were able to swallow the whole bolus in half the time of patients in the control group. In addition, inspection of the means shows that patients in the SJP group did not need to swallow as often per bolus as did patients in the control group. Although no significant differences in temporal measures were found for the cookie bolus, the means suggest that oral and oropharyngeal transit differences between groups may follow a similar pattern to that of the pudding bolus. Overall, patients who undergo the SJP appear to transport food through the mouth and into the pharynx more efficiently than do patients who do not undergo the procedure.

The findings from this study have significant clinical implications for the population of patients treated for head and neck cancer. Clinical anecdotes from these patients will often disclose that increased meal durations result in less food being consumed by them. This occurs for several reasons. First, their eating companions may finish their meals before them, and so patients may be reluctant to continue to eat for extended periods beyond their companions. Second, patients often report that their food cools off during lengthy eating times and becomes unappetizing, resulting in an unfinished meal. Finally, patients often report that they simply become tired after eating for extended periods of time. Because cachexia is often observed in individuals who have undergone treatment for head and neck cancer, increased meal duration is a clinical concern that must be addressed, especially in the xerostomic patient.

One limitation of the present study that must be addressed is the sample size that was available for analysis of swallowing related to the cookie bolus. Although power for the results obtained for the pudding bolus was moderate, that for the analysis of the cookie bolus was low. Future studies of solid boluses, with a greater and equal number of patients in each group, may allow for conclusions that could not be drawn from this study because of small subject numbers for that consistency of food.

Prevention of xerostomia in persons with head and neck cancer is of great significance to the maintenance of healthy oral structures, quality of life, and ability to eat. The SJP for submandibular gland transfer in patients with oropharyngeal cancer appears to be successful in maintaining salivary flow in a large number of patients. The procedure appears to be beneficial also in promoting more time-efficient swallowing behaviors. This efficiency has implications for a patient’s overall well-being and nutritional status.

**Conclusions**

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**References**


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