Title Page

1.Title

Influence of tongue perception alterations on oral and maxillofacial functions of patients with malignant/premalignant tongue tumors

2.A short running title

Tongue perception of tongue cancer patients

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Title: Influence of tongue perception alterations on oral and maxillofacial functions of patients with malignant/premalignant tongue tumors

Abstract

Aim: This study evaluated the association between pre- and postoperative changes in tongue perception and oral and maxillofacial functions in patients with tongue tumors.

Methods: A total of 19 patients with malignant/premalignant tongue tumors were included in this study. Patients were classified into two groups: the closure group, which included patients who underwent partial tongue resection and primary suture, and the flap group, which included patients who underwent less than hemiglossectomy and reconstruction with a radial forearm free flap. Tongue perception was assessed using an electrical stimulator. Perceptual thresholds for the apex, margin, and dorsum of the tongue on the nontumor and tumor sides were evaluated. Tongue movement, tongue pressure, water drinking test, gummy jelly chewing strength, and bite strength were evaluated for oral and maxillofacial function. Each parameter was examined pre- and postoperatively (1, 3, 6, and 12 months).

Results: Patients with large tongue cancer had decreased bilateral tongue perception before surgery. In the flap group, postoperative perception of the tongue on the nontumor side and chewing and bite strengths tended to improve over time compared with preoperative perception and chewing and bite strengths.

Conclusion: In the flap group, changes in tongue perception on the nontumor side may influence chewing function.

KEY WORDS: Tongue cancer, Tongue perception, Oral and maxillofacial function, Pre- and postoperative evaluation.

1 INTRODUCTION

Treatment for tongue cancer mainly involves surgery. However, tongue resection affects postoperative oral and maxillofacial functions, such as swallowing, chewing and speech. In particular, patients who have undergone flap reconstruction after tongue cancer resection experience a significant decrease in oral and maxillofacial functions[1–8]. Tongue resection has been reported to decrease the tongue pressure[4]. Moreover, resection of more than half of the tongue root and the lingual or hypoglossal nerves has been reported to decrease swallowing function[1-3,8]. Resection of the tongue apex and simultaneously the tongue and floor of the mouth has been reported to reduce speech function[1,5,7]. Furthermore, resection of the lingual and hypoglossal nerves and the tongue hemiglossectomy section, including the floor of the mouth, has been reported to reduce chewing function[3,6,7].

In their evaluation of tongue perception in patients with tongue cancer, Mochizuki et al.[9] assessed tactile, warm, cold, and painful sensations after tongue cancer resection and reported that warmth and pain sensations had not recovered in approximately 82% of patients even 1 year after hemiglossectomy and reconstruction with a radial forearm free flap. Nin et al.[10] evaluated tongue perception in 107 healthy individuals using an electrical stimulator that assessed cold/temperature perception, mainly pain perception, and reported that tongue perception thresholds increased with age. Maeda et al.[11] evaluated the tongue apex perception in healthy individuals and patients with lingualgia using three methods: monofilament baroreceptor, discriminator, and electrical stimulation. They reported that the electrostimulation perception test provided more precise perception than other tests[11]. However, no studies have evaluated tongue perception using an electrical stimulator in patients with tongue tumors. Therefore, in this study, tongue perception in patients with tongue tumors was evaluated using an electrical stimulator.

Regarding the association between tongue perception and oral and maxillofacial functions, Reilly et al.[12] evaluated changes in tongue perception and chewing strength before surgery and 5 years after surgery in patients with tongue or oral floor cancer and reported an association between tongue perception and chewing strength. However, no studies have examined the relationship between tongue perception using an electrical stimulator and oral and maxillofacial functions in patients with tongue cancer before surgery and compared it with those after surgery.

Therefore, this study evaluated objective tongue perception by using an electrical stimulator, pre- and postoperative oral and maxillofacial functions in patients with malignant/premalignant tongue tumors, preoperative tongue perception, postoperative tongue perception changes over time compared with preoperative tongue perception, and the association between pre- and postoperative changes in tongue perception and oral and maxillofacial functions.

2 MATERIALS AND METHODS

2.1 Patients

A total of 19 patients with malignant/premalignant tongue tumors were included in this study. Details of the patients are shown in **Table 1**. Of the 19 patients, 10 were male and 9 were female patients, an average age of 61.7 years (range, 34–89 years). The patients were classified into the closure group, who underwent tongue partial resection and primary suture, and the flap group, who underwent less than hemiglossectomy and reconstruction with radial forearm free flap. Tumor resection and reconstruction were performed by each one surgeon familiar with the technique, respectively. In reconstructive surgery, the flap was sutured to the tongue using absorbable thread so as not to interfere with tongue movements (**Figure 1**). No tooth extraction was performed in any of the patients, and no change in the number of teeth was observed between the pre- and postoperative periods.

The closure and flap groups included 10 and 9 patients, respectively. None of the groups received preoperative radiation therapy, Of the 9 patients in the flap group, 4 received preoperative chemotherapy. Furthermore, both groups did not receive postoperative chemotherapy or radiation therapy. Regarding the extent of tongue resection, 8 of 9 patients in the flap group underwent partial tongue resection and 1 underwent hemiglossectomy. Of 10 patients, 7 were in the closure group and all patients in the flap group underwent the oral floor resection.

Moreover, in the closure group, the lingual nerve present on the tumor side was preserved in all patients, whereas in the flap group, the lingual nerve present on the tumor side was severed in 8 of 9 patients. However, the lingual nerve on the nontumor side was preserved in all patients. Additionally, 3 patients in the closure group and 1 patient in the flap group had histopathological evidence of nerve invasion on the tumor side.

Furthermore, 2, 8, 7, and 2 patients had preoperative classification of leukoplakia and T1, T2, and T3 for tongue cancer, respectively.
In both groups, no patient had a history of cerebrovascular disease, central nervous system disorders, treatment for head and neck cancer, glossodynia, or lingual nerve palsy. Diabetes mellitus and hypertension was prevalent in 1 and 7 patients, respectively.

2.2 Evaluation of tongue perception

Figure 2 shows the evaluation sites of tongue perception in patients with tongue tumors. A total of 6 evaluation sites (1, 2, and 3 for the tongue apex, tongue margin, and tongue dorsum on the nontumor side and 1′, 2′, and 3′ for the tongue apex, tongue margin, and tongue dorsum on the tumor side, respectively) were evaluated. During the preoperative period, the site near the tumor side was evaluated so as to avoid the tumor. In the postoperative period, points replaced by the flap were measured as the flap, and points that were not replaced by the flap were measured as the residual tongue. An electrical stimulator (STG 4002R, Multi Channel Systems, Germany) was used for evaluation. A counterplate was fixed to the patient's left wrist, and a 2-mm-diameter in diameter spherical probe was placed to the tongue surface lightly. Stimulation time was 0.2 ms, and tongue stimulation was started at 200 μmA and was increased every 100 μmA. The value that the patient could recognize was set as the upper threshold. The upper threshold was measured thrice, and the average value was used as the tongue perception threshold. The tongue perception threshold scores were set. Considering the changes over time, perception noted at <500 μmA, 500 to <1000 μmA, 1000 to <1500 μmA, 1500 to <2000 μmA, 2000 to <2500 μmA, and 2500 to <3000 μmA, was scored 5, 4, 3, 2, and 1 point, respectively. If no perception was observed at >3000 μmA, the score considered 0. Evaluations were performed preoperatively and at 1, 3, 6, and 12 months postoperatively.

2.3 Oral and maxillofacial functions

Figure 3 shows the assessment of the oral and maxillofacial functions. Oral and maxillofacial functions were evaluated for three items: tongue, swallowing, and chewing. Tongue function was assessed based on tongue movements and tongue pressure. Tongue movements were evaluated using forward, lateral, and elevation movement items (total 7 points)[8]. Tongue pressure was

measured three times at the center of the tongue dorsum using a digital tongue pressure measuring instrument (JMS Tongue Pressure Measuring Instrument; JMS, Hiroshima, Japan), and the average value was used as tongue pressure (kPa) [13-15]. Swallowing function was assessed using the modified water swallowing test[16,17]. Furthermore, 3 mL of cold water was sprayed on the patient's oral floor using a syringe, and swallowing dynamics were evaluated during two repetitive swallows (total 5 points). Chewing function was evaluated by chewing and bite strengths.

For chewing strength evaluation, square gummy jellies measuring 18.5 × 21.4 × 10.8 mm (Soshaku-noryoku sokuteiyou gummy jelly; UHA Mikakuto, Osaka, Japan) were chewed 30 times, and the size of the bite fragments was evaluated using a score sheet (total 9 points)[13,14,18]. Bite strength was measured using a pressure- sensitive film for bite force measurement (Dental Prescale II, GC, Tokyo, Japan) for actual values (N)[13,14,19]. In patients who used dentures, chewing and bite strengths were measured with dentures under the same preoperative and postoperative conditions. These evaluations were performed preoperatively and at 1, 3, 6, and 12 months postoperatively. With regard to the longitudinal evaluation criteria, each function was evaluated by assessing postoperative change as improvement (+), no change (0), or decrease (−) based on the preoperative standard. Preoperative and postoperative tongue pressure measurements were compared. A postoperative percent change of >+10% was considered an improvement (+), <10% was considered no change (0), and >−10% was considered a decline (−).

2.4 Association between changes in tongue perception and oral and maxillofacial functions

Cases were defined as improvement (++) if tongue perception and oral and maxillofacial function improved 12 months postoperatively compared with preoperatively. Cases were defined as recovered to preoperative level (+) and improvement in the broadest sense if tongue perception and oral and maxillofacial function declined 1 month postoperatively and improved to preoperative level 12 months postoperatively. Cases were defined as the absence of improvement (−) if tongue perception and oral and maxillofacial function decreased 12 months postoperatively compared with preoperatively.

3 RESULTS

3.1 Preoperative tongue perception score

Table 2 shows the preoperative tongue perception scores of the patients. The leukoplakia group showed no difference in bilateral tongue perception; bilateral perceptions in the apex, margin, and dorsum of the tongue were good (score 5). Compared with the leukoplakia group, the T1 group had a lower perception score on the tumor side, and 1,2, and 3 of the 8 patients had no perception on the tongue apex, tongue margin, and tongue dorsum, respectively. In the T2 and T3 groups, as the tongue tumors grew, tongue perception on the nontumor side also tended to decrease, and 3 of 9 patients had a bilateral absence of perception.

3.2 Changes over time in preoperative and postoperative tongue perception scores

Changes in tongue perception scores in the closure group over time are shown in **Figure 4**. Based on the preoperative standard, + indicates improvement, 0 indicates no change, and − indicates a decrease postoperatively. On the nontumor side, 5 (50.0%), 3 (30.0%), 4 (40.0%), and 4 (40.0%) of 10 patients had decreased tongue apex perception at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative perception **(Figure 4-1)**. Moreover, 5 (55.6 %), 5 (55.6%), 5 (55.6%), and 2 (22.2%) of the 9 patients had decreased tongue margin perception at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative perception **(Figure 4-2)**. In addition, 3 (30.0 %), 3 (33.0%), 2 (20.0%), and 1 (10.0%) of the 10 patients had decreased tongue dorsum perception at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative perception **(Figure 4-3)**.

On the tumor side, 5 (50.0%), 4 (40.0%), 4 (40.0%), and 4 (40.0%) of the 10 patients had decreased tongue apex perception at 1, 3, 6, and 12 months, respectively, compared with preoperative perception **(Figure 4-1')**. Moreover, 8 (88.9 %), 8 (88.9%), 5 (55.6%), and 3 (33.3%) of the 9 patients had decreased tongue margin at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative perception **(Figure 4-2')**. In addition, 4 (40.0 %), 4 (40.0%), 5 (40.0%), and 2 (20.0%) of the 10 patients had decreased tongue dorsum at 1, 3, 6, and 12 months, respectively, compared with preoperative perception **(Figure 4-3')**.

Changes in tongue perception scores in the flap group over time are shown in **Figure 5**. On the nontumor side, 3 (33.3%), 2 (22.2%), 1 (11.1%), and 1 (11.1%)

of the 9 patients had decreased tongue apex perception at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative perception **(Figure 5-1)**. Moreover, 4 (50.0 %), 2 (25.0%), 1 (12.5%), and 1 (12.5%) of the 8 patients had decreased tongue margin perception at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative perception **(Figure 5-2)**. In addition, 3 (33.3 %), 3 (33.3%), 2 (22.2%), and 0 (0.0%) of the 9 patients had decreased tongue dorsum perception at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative perception **(Figure 5-3)**.
On tumor side, 5 (55.6%), 4 (44.4%), 5 (55.6%), and 4 (44.4%) of the 9 patients had decreased tongue apex perception at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative perception **(Figure 5-1')**. Moreover, 3 (37.5 %), 3 (37.5%), 3 (37.5%), and 2 (25.0%) of the 8 patients had decreased tongue margin perception at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative perception **(Figure 5-2')**. In addition, 4 (44.4 % of all cases), 4 (44.4%), 4 (44.4%), and 2 (22.2%) of the 9 patients had decreased tongue dorsum perception at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative perception **(Figure 5-3')**.

Therefore, compared with preoperative perception, the closure group tended to have improved postoperative the perception of the tongue dorsum on the nontumor side. Compared with preoperative perception, the flap group tended to have improved postoperative perception of the entire tongue on the nontumor side.

3.3 Changes over time in preoperative and postoperative oral and maxillofacial functions

Changes in tongue movements over time are shown in **Figure 6-a, a'**. Based on the preoperative standard, + indicates improvement, 0 indicates no change, and − indicates a decrease, postoperatively. In the closure group, 9 (90.0 %), 8 (80.0%), 9 (90.0%), and 10 (100.0%) of the 10 patients had no changes in tongue movements at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative data **(Figure 6-a)**. In the flap group, 9 (100.0 % of all cases), 8 (88.9%), 6 (66.7%), and 8 (88.9%) of the 9 patients had decreased tongue movements at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative data **(Figure 6-a')**. Therefore, tongue movements did not change pre- and postoperatively in the closure group, whereas they decreased postoperatively in the flap group.

Changes in tongue pressure over time are shown in **Figure 6-b, b'**. In the closure group, the tongue pressure in 5 (50.0 %), 4(40.0%), 2(20.0%), and 5 (50.0%) of the 10 patients did not change at postoperative 1, 3, 6, and 12 months, respectively, compared with preoperative data **(Figure 6-b)**. In the flap group, the tongue pressure decreased at postoperative 1, 3, 6, and 12 months in 7 (77.8 %), 8 (88.9%), 8 (88.9%), and 8 (88.9%) of the 9 patients, respectively, compared with preoperative data **(Figure 6-b')**. Therefore, the tongue pressure did not change pre- and postoperatively in the closure group, whereas it decreased postoperatively in the flap group.

Changes in the water swallowing test over time are shown in **Figure 6-c, c'**. In the closure group, the swallowing test scores did not change at postoperative 1, 3, 6, and 12 months in 10 (100.0 % of all cases), 10 (100.0%), 10 (100.0%), and 10 (100.0%) of the 10 cases, respectively, compared with preoperative data **(Figure 6-c)**. In the flap group, the swallowing test did not change at postoperative 1, 3, 6, and 12 months in 8(88.9 %), 8 (88.9%), 7 (77.8%), and 7 (77.8%) of the 9 patients, respectively, compared with preoperative data **(Figure 6-c')**. Therefore, the water swallowing test did not change pre- and postoperatively in the closure and flap groups.

Changes in chewing strength over time are shown in **Figure 6-d, d'**. In the closure group, the chewing strength improved at postoperative 1, 3, 6, and 12 months in 1 (10.0 %), 3 (30.0%), 4 (40.0%), and 5 (50.0%) of the10 patients, respectively, compared with preoperative data **(Figure 6-d)**. In the flap group, chewing strength improved at postoperative 1, 3, 6, and 12 months in 1 (11.1 %), 3 (33.3%), 4 (44.4%), and 5 (55.6%) of the 9 patients, respectively, compared with preoperative data **(Figure 6-d')**. Therefore, chewing strength tended to improve over time postoperatively in the closure and flap groups.

Changes in bite strength over time are shown in **Figure 6-e, e'**. In the closure group, the bite strength improved at postoperative 1, 3, 6, and 12 months in 4 (40.0 %), 6 (60.0%), 5 (50.0%), and 5 (50.0%) of the 10 patients, whereas bite strength decreased at postoperative 1, 3, 6, and 12 months in 5 (50.0 %), 4 (40.0%), 5 (50.0%), and 5 (50.0%) of the 10 patients, respectively, compared with preoperative data **(Figure 6-e)**. In the flap group, bite strength improved at

postoperative 1, 3, 6, and 12 months in 3 (33.3 %), 4 (44.4%), 5 (55.6%), and 6 (66.7%) of the 9 patients, respectively, compared with preoperative data **(Figure 6-e')**. Therefore, bite strength tended to improve over time postoperatively in the flap group.

3.4 Association between changes in tongue perception and chewing function

In the flap group, postoperative perception of the entire tongue on the nontumor side and chewing and bite strengths tended to improve over time compared with preoperative perception and chewing and bite strengths. Therefore, the association between changes in tongue perception on the nontumor side and chewing function was evaluated in the flap group.

Table 3 shows the association between changes in tongue perception on the nontumor side and chewing function (chewing and bite strength) at 12 months postoperatively compared with preoperative tongue perception and chewing function in each patient in the flap group. Changes in tongue perception on the nontumor side and chewing strength, and changes in tongue perception and bite strength were consistent in 6 of 9 patients (more than half of the patients).

4 DISCUSSION

4.1 Preoperative decrease in tongue perception in patients with tongue cancer

In this study, patients with tongue cancer tended to have decreased tongue perception on the tumor and the nontumor sides as the cancer progressed. Patients with tongue cancer often experience chronic and mechanical pain around the tumor, which interferes with eating, drinking, and speaking, which reduces quality of life[20]. Caroline et al.[21] evaluated the static tactile and capsaicin sensitivity test on the nontumor and tumor sides preoperatively in 11 patients with tongue cancer and reported that in the static tactile test, 7 of 11 patients experienced pain on the tumor side than nontumor side. They determined that the tumor side had increased sensitivity to mechanical and chemical pain. Koyama et al.[22] reported that rats implanted with SCC cells on the tongue had a significantly reduced escape reflex threshold in mechanical stimulation. In contrast, the tongue perception on the tumor side in patients with tongue cancer was reduced in this study, a result different from those of Caroline et al.[21] and Koyama et al.[22] Tongue perception evaluated using an electrical stimulator was mainly based on tongue pain and accessory

cold/warmth sensation; however, the nerve fibers that are stimulated remains unclear[10]. Sensory receptors on the tongue include Aβ fibers that transmit tactile and pressure sensations, Aδ fibers that transmit cold sensations, and C fibers that transmit warmth and dull pain sensations. However, only Aδ and C fibers were evaluated in this study. In future, the inclusion of a tactile test (Aβ fibers) would be necessary to elucidate the cause of decreased tongue perception.

4.2 Association between preoperative and postoperative changes in tongue perception and oral and maxillofacial function over time.

In this study, patients who underwent less than hemiglossectomy and reconstruction with a radial forearm free flap (the flap group) tended to have improved postoperative perception of the entire tongue on the nontumor side compared with preoperative perception. With regard to oral and maxillofacial functions, postoperative chewing and bite strength tended to improve over time compared with the preoperative function in the flap group. Therefore, we evaluated the association between pre- and postoperative changes in tongue perception on the nontumor side and chewing function (chewing strength and bite strength) in the flap group. Changes in tongue perception on the nontumor side and chewing function were consistent in more than half of the patients.

Curtis et al. [23] reported that food mass formation by tongue sensation is essential for efficient chewing. Chewing requires normal rhythmic movement of the mandible and coordinated movements and sensations of the tongue and lips. In this study, the flap group showed improved food mass formation and chewing function because of improved tongue perception on the nontumor side.

Caroline et al.[24] reported that bite strength decreased 1 month after surgery but improved significantly 6 months postoperatively. In this study, bite strength improved over time postoperatively in the flap group. At 1 month postoperatively, occlusion was difficult in the flap group because of tongue pain and edema of the tongue and flap, which improved over time postoperatively, as did perception of the tongue over time. Therefore, the bite strength considerably improved postoperatively.

This study has several limitations. First, the study analyzed some patients who varied in age and sex. Therefore, more cases are required, and statistical analysis must be performed in future studies. Second, personal sensitivities vary among individuals. Thus, individual evaluations must be continued and analyzed. Third, surgical procedures vary. Tumor resection was limited to one surgeon, and reconstructive surgery was limited to one surgeon to unity the surgical procedures. Care should be taken so that the movement of the remaining tongue during flap reconstruction is hindered. Finally, the association between changes in tongue

perception and speech function was not evaluated in this study. A study on their association is ongoing, and the results will be reported in near future.

5. CONCLUSION

Patients who underwent less than hemiglossectomy and reconstruction with a radial forearm free flap (the flap group) tended to have improved postoperative perception of the entire tongue on the nontumor side and postoperative chewing function compared with preoperative perception and function. In the flap group, changes in tongue perception on the nontumor side may influence changes in chewing function.

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FIGURE Legends

FIGURE 1 Intraoperative and postoperative photographs of a case in the flap group.
a: Intraoperative findings, the flap was sutured to the tongue using absorbable thread so as not to interfere with tongue movements.
b: 1 year after surgery.

FIGURE 2 The evaluation sites of tongue perception in patients**.**
A total of six evaluation sites (1, 2, and 3 for the tongue apex, tongue margin, and tongue dorsum on the unaffected side and 1´, 2´, and 3´ for the tongue apex, tongue margin, and tongue dorsum on the affected side, respectively) were evaluated.

FIGURE 3 The assessment of oral and maxillofacial functions.
Oral and maxillofacial functions were evaluated for three items: tongue (tongue movement, tongue pressure), swallowing (the modified water swallowing test), and chewing (chewing and bite strengths).

FIGURE 4 Changes in tongue perception scores in the closure group over time.
Based on the preoperative standard, + indicates improvement, 0 indicates no change, − indicates a decrease, postoperatively. The closure group tended to have improved postoperative the perception of the tongue dorsum on the nontumor side, compared with preoperative perception.

FIGURE 5 Changes in tongue perception scores in the flap group over time.
Based on the preoperative standard, + indicates improvement, 0 indicates no change, − indicates a decrease, postoperatively. The flap group tended to have improved postoperative perception of the entire tongue on the nontumor side, compared with preoperative perception.

FIGURE 6 Changes in oral and maxillofacial functions over time.
Based on the preoperative standard, + indicates improvement, 0 indicates no change, − indicates a decrease, postoperatively. Tongue movements did not change pre- and postoperatively in the closure group, whereas they decreased postoperatively in the flap group (Fig.6-a, a'). Tongue pressure did not change pre- and postoperatively in the closure group, whereas it decreased

postoperatively in the flap group (Fig.6-b, b’). Water swallowing test did not change pre- and postoperatively in both the closure and the flap groups (Fig.6-c, c’). Chewing strength tended to improve over time postoperatively in the closure and flap groups (Fig.6-d, d’). Bite strength tended to improve over time postoperatively in the flap group (Fig.6-e, e’).