Comparison of Treatment Outcomes Between Total and Near Total Glossectomy with Larynx Preservation and Flap Reconstruction: A Single Institution Experience with 23 Patients

Objective: The purpose of this study was to evaluate the functional and oncological outcomes of total glossectomy with laryngeal preservation (TGLP) compared to near-total glossectomy with laryngeal preservation (nTGLP).

Methods: In this retrospective study, the data of 23 patients who underwent either TGLP or nTGLP between January 2010 and December 2020 in a tertiary university hospital were analyzed. The data including demographic findings, tumor stage, extent of surgery and technique, method of reconstruction, complications, overall survival (OS) and recurrence-free survival (RFS), and tracheostomy and gastric tube dependence during follow-up were assessed.

Results: Of the 23 eligible patients, 15 had undergone nTGLP (Group 1) and 8 had undergone TGLP (Group 2). Tracheostomy dependence and gastric tube dependence rates at the sixth month were 3/19 (15.7%) and 12/19 (63.1%), respectively, with no significant differences between the two groups. OS and RFS at one year were 47.6% and 27.8%, respectively, for the study population. OS rate showed significance with nodal positivity and extranodal extension (p=0.004 for both) only, but not within patient groups (p=0.734).

Conclusion: Both TGLP and nTGLP are feasible treatment options in patients with advanced tongue cancer with no differences in terms of functional and oncological results. Survival rates are still not satisfactory, and recurrences are high despite appropriate treatments. Proper selection of patients who are highly motivated and willing for long-term postoperative rehabilitation is essential.

Keywords: Cancer of tongue, glossectomy, laryngectomy, surgery, survival, tracheostomy
Introduction

Total glossectomy (TG) or near-total glossectomy (nTG) and postoperative radiotherapy (RT) or chemoradiotherapy (CRT) are widely accepted as the treatments of choice in patients with massive infiltrating malignant tongue lesions (1-4). However, some drawbacks still remain for the extensive resection of the oral tongue, such as high morbidity, poor oral intake, aspiration problems, challenges in reconstruction, low speech intelligibility, tracheostomy dependence and overall reduced quality of life despite improved survival. Since the extent of the surgery involves either the whole or half of the tongue base, there is a high risk of aspiration in these patients. Total laryngectomy (TL) combined with TG is suggested in conventional teaching to overcome aspiration problems. With the emergence of successful reconstruction techniques with flaps, some studies have reported promising functional results by preserving the larynx (1, 5-7). They suggested that total glossectomy with laryngeal preservation (TGLP) provided better speech intelligibility and maintained swallowing ability (6-11).

Another issue is the high mortality rates, hence unsatisfactory survival rates, either because of locoregional recurrence or distant metastasis, despite radical surgical treatment combined with RT or CRT protocols. The oncologic outcomes and survival rates were found to be similar with or without TL combined with TG but were still low (12). To achieve better functional results, preservation of one functional unit of the tongue base, namely nTG (Type IVb) may be considered (13). However, some concerns such as surgical safety margin and recurrence-free survival can arise with Type IVb glossectomy instead of TG (Type V).

In this study, we aimed to assess and compare the functional and survival outcomes in patients who underwent TGLP or near-total glossectomy with laryngeal preservation (nTGLP).

Methods

This retrospective study was planned, and ethics approval was granted by the local ethics committee (Approval no. 2021-1/28). The study was conducted at the department of otolaryngology and head & neck surgery of a tertiary university hospital with patients who underwent TGLP or nTGLP with simultaneous bilateral neck dissection. Clinicopathological data of 27 patients diagnosed with an advanced stage malignant tongue lesion and who had TG or nTG between January 2010 and December 2020 were reviewed. Among these patients, four who had TL combined with primary surgery due to tumor extension beyond the base of the tongue and with distant metastasis were excluded. Thus, the data of 23 eligible patients included in the study population were retrieved from patient files. Data on demographic characteristics, pathological tumor stage, extent and technique of surgery, method of reconstruction, adjuvant treatment, complications, follow-up, survival, tracheostomy status and oral intake were recorded. All patients were evaluated by complete otolaryngological examination with endoscope, preoperative computed tomography (CT) and magnetic resonance imaging (MRI) of the primary site and neck, and positron emission tomography/CT for the presence of any distant metastasis.

In all cases, we performed surgery using lip-splitting median mandibulotomy approach combined with apron flap incision. The extent of dissection was determined according to accurate evaluation and analysis of preoperative CT and MRI images. We removed all anatomical compartments of the tongue and the floor of the mouth involved with tumor according to the imaging and clinical findings intraoperatively. A nTG (Type IVb) was used if the lesion exceeded the border of the hemi-lingual area of origin infiltrating the ipsilateral base of the tongue and the contralateral genioglossus muscle (13). Thus, one functional unit of the tongue base on one side could be spared (Figure 1). In cases where massive infiltrating tongue lesions bilaterally involved extrinsic genioglossus, hyoglossus, styloglossus and tongue base with impairment of the mobility of the tongue, then TG (Type V) was preferred (13). This involved removal of the entire tongue with the intrinsic and extrinsic muscles and the floor of the mouth above the hyoid bone (Figure 2). Simultaneous bilateral modified radical neck dissection, including levels from I to V, was performed in all cases. The reconstruction of the defect was performed immediately after tumor removal and frozen section examination confirmed negative tumor margins. Oral cavity reconstruction was performed by either free or pedicled myocutaneous flap. Tracheostomy cannula and nasogastric tube were placed in all patients.

Surgical margin positivity was accepted as the tumor being adjacent to the surgical margin or closer than five mm in histopathological examinations. Postoperative follow-up for functional outcomes was carried out by flexible endoscopic examination for both swallowing and airway edema. Patients who had satisfactory swallowing function without aspiration began oral feeding. Tracheostomy tube decannulation was performed when airway edema resolved, and flaps were secured in place. Functional assessment of oral intake and airway was made at the 6th month of surgery (9). Oncological outcomes such as overall survival (OS), disease-free survival (DFS) and local disease control were also recorded during the follow-up, and all prognostic variables were compared between the TGLP and nTGLP groups.

Statistical Analysis

The findings of the presented study were analyzed with the SPSS 23.0 software package (IBM SPSS® Statistics 23.0, Armonk, N.Y., USA). The results were analyzed with 95%
Figure 1. (a) Intraoperative; (b) specimen; and (c) postoperative photographs of a patient who underwent Type IVb glossectomy.

Figure 2. (a) Intraoperative; (b) specimen; and (c) postoperative endoscopic photographs of a patient who underwent Type V glossectomy.
confidence intervals, and $p<0.05$ was considered statistically significant. Chi-square test was used to determine the predictors of categorical variables listed in Table 1. The Mann–Whitney U test was used to analyze continuous variables. OS and DFS rates were estimated, and survival distributions were analyzed with the Kaplan–Meier analysis with log-rank test.

Results

Patients' Profiles and Surgical Characteristics

The study population included 16 men and 7 women with a mean age at diagnosis of 52.87 years (range: 28 to 77). Eight patients underwent salvage surgery due to recurrence of oral cavity cancer following primary surgical treatment. The distribution of 23 patients regarding the operation technique was nTGLP in 15 patients (Group 1) and TGLP in 8 patients (Group 2). Squamous cell carcinoma was the histopathological diagnosis in all cases. Primary tumor site was the oral tongue in 16, the base of tongue in one and the floor of mouth in six cases. Segmental (n=4) or marginal mandibulectomy (n=5) was required in nine patients, and in four patients, resection included supraglottic structures; two had partial epiglottectomy, one had epiglottectomy with hyoid bone resection and another had supraglottic laryngectomy. We used pectoralis major myocutaneous flap in 15, radial forearm free flap in two, anterolateral thigh free flap in five and deltopectoral flap in one patient for defect reconstruction. Reexploration and reanastomosis were performed in one patient due to flap compromise. Revision reconstructive surgery was performed in four patients due to flap failure. Mandibular reconstruction plate was exposed in two patients, and orocutaneous fistula, which was treated conservatively, occurred in six patients. All patients underwent bilateral neck dissection except two who had neck dissection in their previous surgery with no sign of metastatic lymph node in imaging studies (Table 1).

Results of Histopathological Examinations

T stage was reported as T4 in all patients according to the 8th edition of the AJCC. Metastatic lymph nodes were found in 16 (76%) 16/21 patients, with extracapsular invasion in 13 patients. Nodal stages of the study population were as follows: N0 (n=5), N1 (n=2), N2b (n=3), N2c (n=5), N3 (n=4) and N3b (n=2). Surgical margin positivity in permanent pathologic examination was reported in three cases. Mean tumor dimension was found 59.30 mm (15-150 mm), while mean depth of invasion was 28.09 mm (8-50 mm). There was mandibular invasion in three patients and hyoid bone invasion in one patient. All patients were diagnosed with squamous cell carcinoma and tumors were well-/moderately differentiated (n=17) and poorly differentiated (n=6), respectively (Table 1).

| Table 1. Clinical, surgical, and histopathological characteristics of patients in general and with respect to the type of glossectomy |
|---------------------------------------------------------------|
|                                | Total  | Group 1 | Group 2 | p-value |
| Age (years)                  |        |         |         |         |
| Min-max                      | 28–77  | 28–77   | 30–58   | 0.047*  |
| Mean                         | 52.87  | 57.33   | 43.00   |         |
| Median                       | 55     | 57      | 43      |         |
| SD                           | 14.763 | 14.509  | 11.880  |         |
| Gender                       |        |         |         |         |
| Female                       | 7 (30.4%) | 3 (20.0%) | 4 (50.0%) | 0.182** |
| Male                         | 16 (69.6%) | 12 (80.0%) | 4 (50.0%) |         |
| Follow-up time (month)       |        |         |         |         |
| Min-max                      | 3–108  | 3–46    | 3–108   | 0.506*  |
| Mean                         | 21.48  | 16.53   | 30.75   |         |
| Median                       | 11     | 11      | 8.5     |         |
| SD                           | 27.799 | 12.755  | 44.190  |         |
| Primary/salvage surgery      |        |         |         |         |
| Primary                      | 15 (65.2%) | 10 (66.7%) | 5 (62.5%) | 1.000** |
| Salvage                      | 8 (34.8%) | 5 (33.3%) | 3 (37.5%) |         |
| Tumor localization           |        |         |         |         |
| Tongue                       | 16 (69.6%) | 11 (73.3%) | 5 (62.5%) | 0.443***|
| Floor of mouth               | 6 (26.1%) | 4 (26.7%) | 2 (25.0%) |         |
| Tongue base                  | 1 (4.3%)  | 0 (0.0%)  | 1 (12.5%) |         |
| Supraglottic laryngectomy    |        |         |         |         |
| No                           | 19 (82.6%) | 14 (93.3%) | 5 (62.5%) | 0.103** |
| Yes                          | 4 (17.4%)  | 1 (6.7%)   | 3 (37.5%) |         |
| Mandibulectomy               |        |         |         |         |
| No                           | 14 (60.9%) | 8 (53.3%)  | 6 (75.0%) |         |
| Marginal                     | 5 (21.7%)  | 3 (20.0%)  | 2 (25.0%) | 0.396***|
| Segmental                    | 4 (17.4%)  | 4 (26.7%)  | 0 (00.0%) |         |
| Neck dissection              |        |         |         |         |
| No                           | 2 (8.7%)   | 1 (6.7%)   | 1 (12.5%) | 1.000** |
| Yes                          | 21 (91.3%) | 14 (93.3%) | 7 (87.5%) |         |
| Tumor size                   |        |         |         |         |
| Min-max                      | 15–150  | 15–70   | 50–150  | 0.000*  |
| Mean                         | 59.30   | 44.13   | 87.75   |         |
| Median                       | 52      | 45      | 80      |         |
| SD                           | 30.598  | 15.090  | 32.697  |         |
| Depth of invasion            |        |         |         |         |
| Min-max                      | 8–50   | 8–42    | 20–50   | 0.008*  |
| Mean                         | 28.09  | 23.07   | 37.50   |         |
| Median                       | 26     | 20      | 40      |         |
| SD                           | 11.874 | 9.316   | 10.690  |         |
| Differentiation              |        |         |         |         |
| Well-moderately              | 17 (73.9%) | 11 (73.3%) | 6 (75.0%) | 1.000** |
| Poorly                       | 6 (26.1%)  | 4 (26.7%)  | 2 (25.0%) |         |
One patient died due to early postoperative complications after the third month of operation. Mean follow-up duration was 21.5 months (range: 3 to 108) and for patients still alive was 51.8 months. All patients, except one, had adjuvant RT, chemotherapy, or CRT. There were locoregional recurrences in nine patients during follow-up and another five patients were diagnosed with metastatic lung cancer. Functional outcomes were assessed at the sixth month after surgery and three (15.7%) patients among the 19 who survived more than six months were tracheostomy dependent. An adequate swallowing function and good/acceptable oral intake were obtained in seven patients. OS rate was 50.0% for Type IVb and 42.9% for Type V glossectomy at one year. Disease-specific survival rates were 16.7% and 50.0% for Type IVb and Type V at one year, respectively. The comparison of functional outcomes and mortality rates between TGLP and nTG groups did not reveal any difference (Table 2). The extent of surgery and other clinical variables did not show any relation with survival rates, but we found significance for nodal positivity and extranodal extension with survival in the results of Kaplan-Meier analysis (Tables 3, 4, and Figures 3, 4).

**Discussion**

In patients with locally advanced tongue cancer, total or near nTG is sometimes the only possible treatment option. Unfortunately, the survival rate of patients with advanced stage tongue cancer is still very low despite extended surgical resection with adjuvant RT or CRT treatment. The adverse consequences of this mutilating surgery, such as chronic aspiration, poor speech, airway problems and social isolation, can be viewed negatively by many patients. However, the recent development of reconstruction techniques with flaps and laryngeal preservation can provide good functional outcomes. While considering the safe margins of resection oncologically, we should also consider maximum preservation of tumor-free tissues. Thus, our institutional approach was mainly targeted to sparing at least one functional unit of the tongue base if possible. In the last decade, we performed TGLP in eight cases and were able to preserve one half of the tongue base in the other 15 cases.

The tumor size and spread mainly determine the extent of resection in the oral cavity. In our study population, as would be expected, we performed TG rather than nTG in significantly larger tumor sizes and invasion depths. However, we had some concerns, because as the extent of resection increases, oral tongue functions deteriorate inevitably. Mazarro et al. (1) conducted a study with 12 patients who had undergone TGLP and reported that five of seven (71%) patients alive at one year were PEG dependent due to chronic aspiration. The study also revealed that in all seven patients, tracheostomy cannula was removed. Navach et al. (10) suggested that with proper postoperative feeding rehabilitation, 70% of these...
patients could return to oral feeding. In the study by Keski-Säntti et al. (2), the authors evaluated the functional outcomes of 15 TGLP and 14 nTGLP patients at one year after surgery. They found that gastrostomy and tracheostomy tube dependence in all patients was 77% and 15%, respectively. However, the authors did not compare the outcomes between these two groups. In another study, Barry et al. (4) compared the oral intake outcomes of patients who had TGLP as first-line or salvage therapy and noted that the ability to eat soft food was 23/49 (47%) in the first-line group vs 25/60 (42%) in the salvage group with no significant difference. On the contrary, Rihani et al. (5) pointed out that sufficient oral intake without the need for a gastric tube was higher for primary surgery followed by postoperative RT compared with primary RT followed by surgical salvage: 56% vs 11% respectively. Overall, an important number of patients, 27/94 (29%) required prolonged gastrostomy tube in their study (5). Dziegielewski et al. (6) reported the gastrostomy tube dependency rate as 24% in a systematic review of the related literature. In another literature review, they concluded that gastric tube dependency after TGLP ranged from 30% to 44% and that tracheostomy tube removal was between 85% to 95% (11).

Some authors reported that even performing synchronous TL with TG does not prevent the risk of placement of a gastrostomy tube. Han et al. (7) found that 60% of patients who had total laryngoglossectomy (TGL) still required gastrostomy tube placement, but that this rate was 93% in those who had TGLP. They also reported that the eventual decannulation rate was 61%. Similarly, in another study, there was no difference (p>0.99) between feeding tube dependence rates in TGL and TGLP groups: 8/17 (47%) and 17/37

### Table 3. Results of overall survival analysis

| Glossectomy type | Total (n) | Death (n) | Death (%) | Survival mean (months) | Standard error | CI %95 lower | CI %95 upper | Log-rank test* | p-value |
|------------------|-----------|-----------|-----------|------------------------|---------------|--------------|--------------|----------------|---------|
| Type IVb         | 15        | 13        | 86.7%     | 17.933                 | 3.764         | 10.555       | 25.311       | 0.116          | 0.734   |
| Type V           | 8         | 5         | 62.5%     | 36.429                 | 17.133        | 2.848        | 70.010       |                |         |
| Overall          | 23        | 18        | 78.3%     | 26.602                 | 7.596         | 11.714       | 41.490       |                |         |
| Lymph node metastases |     |   |   |   |               |       |   |   |   |
| No               | 5         | 2         | 40.0%     | 72.000                 | 18.344        | 36.046       | 107.954      | 8.490          | 0.004   |
| Yes              | 16        | 14        | 87.5%     | 12.710                 | 2.408         | 7.991        | 17.429       |                |         |
| Overall          | 21        | 16        | 76.2%     | 28.572                 | 8.230         | 12.442       | 44.702       |                |         |
| Extranodal extension |     |   |   |   |               |       |   |   |   |
| No               | 8         | 4         | 50.0%     | 57.925                 | 16.757        | 25.082       | 90.768       | 8.300          | 0.004   |
| Yes              | 13        | 12        | 92.3%     | 11.333                 | 1.698         | 8.005        | 14.662       |                |         |
| Overall          | 21        | 16        | 76.2%     | 28.572                 | 8.230         | 12.442       | 44.702       |                |         |

*Chi-square value for Log-rank test, CI: Confidence interval

### Table 4. Results of recurrence free survival analysis

| Glossectomy type | Total (n) | Recurrence (n) | Recurrence (%) | Survival mean (months) | Standard error | CI %95 lower | CI %95 upper | Log-rank test* | p-value |
|------------------|-----------|----------------|---------------|------------------------|---------------|--------------|--------------|----------------|---------|
| Type IVb         | 15        | 11             | 73.7%         | 16.806                 | 4.903         | 7.196        | 26.415       | 1.215          | 0.270   |
| Type V           | 8         | 3              | 37.5%         | 66.175                 | 18.971        | 28.991       | 103.359      |                |         |
| Overall          | 23        | 14             | 60.9%         | 36.073                 | 10.980        | 14.553       | 57.593       |                |         |
| Lymph node metastases |     |   |   |   |               |       |   |   |   |
| No               | 5         | 2              | 40.0%         | 71.333                 | 19.552        | 33.012       | 109.655      | 4.961          | 0.026   |
| Yes              | 16        | 11             | 68.7%         | 13.006                 | 4.055         | 5.057        | 20.954       |                |         |
| Overall          | 21        | 13             | 61.9%         | 35.893                 | 11.163        | 14.014       | 57.772       |                |         |
| Extranodal extension |     |   |   |   |               |       |   |   |   |
| No               | 8         | 3              | 37.5%         | 64.190                 | 18.313        | 28.296       | 100.085      | 6.533          | 0.011   |
| Yes              | 13        | 10             | 76.9%         | 6.103                  | 0.977         | 4.187        | 8.018        |                |         |
| Overall          | 21        | 13             | 61.9%         | 35.893                 | 11.163        | 14.014       | 57.772       |                |         |

*Chi-square value for log-rank test, CI: Confidence interval
(45.9%), respectively (8). Sinclair et al. (12) revealed similar results in that although tube dependency (70%) was more common in TGLP patients, 30% of TGL patients were also tube dependent. In addition, 50% of TGLP cases were tracheostomy dependent too. The findings of our study are relevant to the previous literature in that about 63% of our patients were tube dependent at the 6th month of surgery but that this rate decreased to 50% at the end of one year follow-up. The tracheostomy removal rate was found to be 84%, which is similar to the literature.

To the best of our knowledge, the presented study is the first to evaluate and compare the functional results between TGLP and nTGLP in the literature. We concluded that there was no difference regarding adequate oral intake and tracheostomy removal rates between Type IVb and Type V glossectomy. None of our patients in the TGLP group was tracheostomy dependent compared to nTGLP (23.1%), but this did not reach significance. The rates of tube dependence were also similar for TGLP vs nTGLP: 50% vs. 69.2%, respectively. Based on our findings, we suggest that preserving one functional unit of the tongue base at one side does not have any additional functional benefit compared to total removal.

Survival rates and clinical variables that may have an impact on DFS are other important issues to consider in the management of advanced tongue cancers. Despite the appropriate treatment, the life expectancy is unfortunately still low in patients who have undergone TG. Navach et al. (10) found the actual five-year OS and DFS to be 54% and 47% respectively, and they reported that these rates decreased to 21% and 23% for patients who had TG as their second treatment. In another study, positive margins and rate of early recurrence were measured to be higher in patients who had preoperative RT (3). On the contrary, the study by Han et al. (7) reported no difference (p=0.45) regarding OS between primary treatment and salvage therapy, and one-year OS was 42% in the study population. In a study by Reiter and Harréus (9), three-year survival was found to be 57.1% but local disease control for patients with free resection margins reached 83.3% (10/12). Barry et al. (4) evaluated the prognostic risk factors in 109 patients who had undergone either first-line (n=49) or salvage (n=60) TGLP. They pointed out that shorter survival was significantly related to positive margins of resection (p=0.002) and tumor spread into the mandible (p=0.04), but not salvage surgery (p=0.09). Even so, 3-year and 5-year survival rates were higher in the first-line group compared to salvage surgery: 43% and 23% vs. 23% and 16%, respectively (4). However, tumor-free resection margins, pN class, extranodal extension and postoperative RT vs CRT did not reveal a significant relationship with OS in the study by Keski-Säntti et al. (2).

An interesting finding was reported by Mazarro et al. (1), that one-year OS in patients ≥50 years old was higher than in those <50 years old: 71.4% vs 40% with an overall OS of 58.3%.

In our study, the OS for one year was similar to the previous literature as 47.6%. In the analysis of our data, we found a significant relation between survival and positive lymph node and extranodal extension but not with other clinical variables such as primary vs salvage, tumor size, depth of invasion, bone invasion, differentiation, margin positivity, and lymphovascular and perineural invasion. It is known that the status of regional lymph nodes is an important prognostic factor for locoregional tumor control, and that extranodal extension is a major cause of death affecting survival. In addition, there was no significant survival difference between the TGLP and nTGLP groups, although Type V glossectomy showed better results at one year: 57.1% vs 50.0%.
Conclusion

In conclusion, although this retrospective study included a limited number of patients, we suggest that both TGLP (Type V) and nTGLP (Type IVb) are feasible treatment options in patients with advanced tongue cancer. However, survival rates are not satisfactory and locoregional and distant recurrences are still high despite appropriate surgical and adjuvant treatments. Thus, proper selection of patients who are highly motivated and willing for long-term postoperative rehabilitation and follow-up is essential. This is the first study to demonstrate that TGLP provides similar oncological and functional outcomes to nTGLP, despite the presence of higher tumor volume and extensive tissue removal.

Ethics Committee Approval: This retrospective study was planned and ethics approval was granted by the local ethics committee of Bursa Uludağ University (approval no. 2021-1/28).

Informed Consent: Informed consent was obtained from the patients/caregivers before the study was initiated.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: U.L.D., M.A., H.C.I., Concept: U.L.D., M.A., H.C.I., Design: U.L.D., M.A., Data Collection and/or Processing: M.A., H.C.I., Analysis and/or Interpretation: U.L.D., M.A., Literature Search: U.L.D., M.A., H.C.I., Writing: U.L.D.

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Main Points

- Survival rates are still low due to locoregional recurrence and metastasis in advanced stage tongue cancers. In our study, overall and recurrence-free one-year survival rates were 47.6% and 27.8%, respectively, in patients who underwent total or near total glossectomy with laryngeal preservation due to advanced stage tongue cancer.
- Statistical analysis showed that nodal positivity and extranodal extension were the only factors negatively affecting overall survival and recurrence-free survival.
- Functional and oncological outcomes of total and near-total glossectomy with laryngeal preservation are similar in patients with advanced stage tongue cancer.
- Near-total glossectomy does not have a positive effect on nasogastric and tracheostomy tube dependence compared with total glossectomy.

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