

Research Article

Impacts of Oral Reconstruction on Patients with Tongue Squamous Cell Carcinoma

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Background: The application of reconstruction techniques in head and neck surgery has become the “workhorse” of head and neck surgeons; however, whether reconstruction is appropriate for all head and neck cancer patients remains as a critical issue. To address this question, this study analyzed the impacts of surgical treatment with immediate reconstruction and postoperative radiotherapy on the survival and functional outcomes of patients with different stages of tongue squamous cell carcinoma (TSCC).

Materials and methods: We collected the clinical data of 184 patients with different stages of TSCC. Sixty-eight patients were immediately reconstructed with a variety of flaps. Thirty-three patients underwent postoperative radiotherapy. The recurrence rate, survival time and functional outcomes, such as speech intelligibility and swallowing capacity, were evaluated and compared.

Results: Reconstruction contributed to a reduced recurrence rate and improved overall survival in the patients with T3/T4 TSCC; but did not significantly affect the recurrence rate or overall survival in T1/T2 TSCC patients. Reconstruction is profitable for postoperative speech intelligibility and swallowing capacity in the patients with T3/T4 TSCC, but not significantly in the patients with T1/T2 TSCC.

Conclusions: Surgical resection with immediate reconstruction resulted in improved oncological outcomes and oral function in the patients with T3/T4 TSCC.

Keywords: tongue squamous cell carcinoma, reconstruction, recurrence rate, overall survival, function.

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Introduction

Squamous cell carcinoma consists of more than 95% of all oral malignant neoplasm, and tongue squamous cell carcinoma (TSCC) is one of the most common types of oral malignant neoplasm [1, 2]. The clustered association of TSCC with relatively old men is gradually being replaced by an association with clusters of young men [3]. Surgical resection remains the primary modality of treatment for the patients with TSCC. Although the 5-year survival rate has been slightly improved with the introduction of new treatments, such as concurrent

chemo-radiotherapy, monoclonal antibody targeting epidermal growth factor receptor (EGFR) combined with chemotherapy or radiotherapy [4, 5], TSCC is still associated with poor prognosis due to the high incidence of local and regional recurrence [6, 7].

Extensive resection is critical to achieve a safe surgical margin for patients with advanced TSCC, and it is likely to cause serious functional and cosmetic deficits. Since reconstructive surgery emerged, several studies have demonstrated the reliability and promising outcomes for head and neck defects reconstructed with a variety of flaps [8-10]. However, reconstruction is a complex surgical

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procedure because of the high risk of vascular crisis and donor site morbidity. Additionally, whether reconstruction contributes to improved life quality and overall survival

Table 1. Clinicopathological features of the 184 TSCC patients.

Variable	No. of Patients (%)
Age (years)	
≤ 53	94 (51.1)
> 53	90 (48.9)
Gender	
Male	112 (60.9.1)
Female	72 (39.1)
T stage	
T1	71 (38.6)
T2	78 (42.4)
T3	22 (12.0)
T4	13 (7.1)
Lymph node metastasis (N)	
N0	112 (60.9)
N1	37 (20.1)
N2	35 (19.0)
Stage	
I	56 (30.4)
II	49 (26.6)
III	38 (20.7)
IV	41 (22.3)
Pathological grade	
I	132 (71.7)
II	41 (22.3)
III	11 (6.0)

Table 2. Surgical treatment for the 184 TSCC patients

Variable	No. of Patients (%)
Neck dissection	175 (95.1)
Ipsilateral RND	13 (7.4)
Ipsilateral MRND	20 (11.4)
Ipsilateral SND	139 (79.4)
Ipsilateral RND and contralateral SND	1 (0.6)
Ipsilateral SND and contralateral SND	2 (1.1)
Flap	68 (37.0)
Anterolateral thigh flap (ALTF)	46 (67.6)
Radial forearm flap (RFF)	17 (25.0)
Pectoralis major myocutaneous flap (PMMF)	3 (4.4)
Rectus abdominis flap (RAF)	1 (1.5)
Latissimus dorsi flap (LDF)	1 (1.5)

Abbreviations:RND, radical neck dissection;MRND, modified radical neck dissection;SND,selective neck dissection (usually supraomohyoid neck dissection).

rate in the patients with TSCCremains as a controversial issue [11, 12], and very few researchers have studied on

this topic. For this reason, the aim of this study was to analyze more recent data on disease control, survival and functional outcomes in patients with TSCC treated with reconstruction, to make clear the impacts of immediate reconstruction using a variety of flaps in patients with different T stages of TSCC, and to identify which groups of TSCC patients are suitable for reconstruction.

Patients and Methods

Clinical data

Patients with TSCC initially treated between January 1, 2005 and April 13, 2010 were recruited in this review. The patients included in this study met the following criteria: (1) histologically proven, untreated resectable primary TSCC; (2) an absence of confounding variables (second primary tumor, prior history of other cancers). Patients with distant metastasis were excluded. Finally, a total number of 184 patients met the inclusion criteria and were enrolled into this study. Follow-up ended on April 30, 2012.

The patients included 112 males and 72 females with an age range of 20 to 81 years (mean, 52.5 years). The TNM classification and staging were based on the 7th International Union Against Cancer (UICC) staging criteria (2010). The patients' detailed characteristics are summarized in Table 1. All of the 184 patients underwent surgical resection with or without neck dissection. Sixty-eight of the patients underwent simultaneous reconstruction of intraoral defects and the rest 116 patients did not. Seventeen of the 71 (23.9%) patients with T1 TSCC, 26/78 (33.3%) patients with T2 TSCC, 18/22 (81.8%) patients with T3 TSCC and 7/13 (53.8%) patients with T4 TSCC underwent reconstruction. In this study, 175 patients underwent neck dissection, including ipsilateral neck dissection in 172 patients and bilateral neck dissection in 3 patients.

The standard indications for postoperative irradiation were applied, including one or more of the following pathologic findings (risk factors): T3/T4 stage; N2/N3 stage; pathologic lymph nodes of level IV/V; close margins (< 5 mm); perineural invasion or vascular space invasion. Sixty-four of the 184 patients met the indications for postoperative irradiation. Because of the limited financial resources or some other reasons, only 33 of these 64 patients underwent postoperative radiotherapy. The radiotherapy dosage ranged from 50 Gy to 76 Gy. Twenty-three of the 33 patients were still alive at the last

follow-up, and the 23 patients received postoperative radiotherapy with a dose range of 50 Gy to 66 Gy (detailed data are presented in Table 2).

Postoperative evaluation of oral function

All survived patients received a postoperative speech and swallowing evaluation using the method described by Yanai [9]. In short, speech intelligibility was estimated by a speech therapist who graded the patients after a conversation as: 5, no sound errors and speech can be easily understood; 4, speech is occasionally misunderstood; 3, speech is understood only when the context of the text is known to the listener; 2, speech is occasionally understood; and 1, speech is completely unintelligible. Speech intelligibility was then classified as good (scores 5–4), acceptable (score 3) or poor (scores 1–2). Swallowing capacity was evaluated using the MTF classification based on the method of food intake (M), the time required for food intake (T) and the consistency of food (F) [13]. The method of food intake (M) was classified and scored as: M5, swallowing is unlimited (5 points); M4, capacity for swallowing anything, but occasional aspiration (4 points); M3, capacity to swallow anything prepared in a suitable

form (3 points); M2, capacity to swallow small portions of food, but stomach tube is the main means of ingestion (2 points); and M1, capacity to swallow nothing and stomach tube is the only method of ingestion (1 point). The time required for food intake (T) was assessed according to the average time required to eat a daily meal (irrespective of its nature and consistency) as: T5, food intake time is not significantly different before and after therapy. (5 points); T4, food intake time is prolonged by 0 to 10 min (4 points); T3, food intake time is prolonged by 10 to 20 min (3 points); T2, food intake time is prolonged by 20 to 30 min (2 points); and T1, food intake time is prolonged by more than 30 min or is impossible (1 point). The consistency of food that a patient was able to ingest (F) was classified as: F5, capacity to ingest any food (5 points); F4, capacity to ingest soft, chewable food (4 points); F3, capacity to ingest gruel (3 points); F2, capacity to ingest viscous fluids (2 points); and F1, capacity to ingest only non-viscous fluids (1 point). Finally, the M, T and F scores were added and swallowing capacity was classified as good (scores 13–15), acceptable (scores 9–12) or poor (scores ≤ 8) according to the sum MTF value.

Table 3. Influence of clinicopathological characteristics on recurrence and survival in TSCC.

Variable	Observation	Recurrence	<i>P</i>	Survival	<i>P</i>
T stage			0.001		0.018
T1	71	14		60	
T2	78	37		50	
T3	22	7		16	
T4	13	8		7	
Lymph node metastasis (N)			<0.001		<0.001
N0	112	27		97	
N1	37	17		21	
N2	35	22		15	
Pathological stage			<0.001		<0.001
I	56	7		51	
II	49	19		39	
III	38	15		24	
IV	41	25		19	
Grade			0.017		0.002
I	132	39		105	
II	41	21		22	
III	11	6		6	

Statistical Analysis

Statistical analysis was performed using Statistical

Program for Social Sciences (SPSS) PASW Statistics for Windows version 18.0 (SPSS Inc., USA). The influence of clinicopathological characteristics and treatment strategy on recurrence and survival rates were assessed using Chi-square test. The Kaplan–Meier method was used to plot survival and disease-free interval curves, and log-rank method was used for comparisons between groups. *P* values were subject to a global significance at the level of 0.05.

Results

Relationship between clinicopathological characteristics and prognosis in TSCC.

Recurrence was significantly associated with N-stage ($P < 0.001$), T-stage ($P = 0.001$), pathological stage ($P < 0.001$)

Reconstruction for tongue squamous cell carcinoma and tumor grade ($P = 0.017$) in patients with TSCC. N-stage ($P < 0.001$), T-stage ($P = 0.018$), pathological stage ($P < 0.001$) and tumor grade ($P = 0.002$) were also significantly associated with overall survival (Table 3). A lower loco-regional recurrence rate ($P = 0.015$) and higher overall survival rate ($P = 0.001$) were observed in T3/T4 TSCC patients who received immediate reconstruction, compared to T3/T4 patients who did not undergo immediate reconstruction (Fig 1). However, immediate reconstruction did not significantly affect the recurrence rate ($P = 0.513$) or overall survival in T1/T2 TSCC patients ($P = 0.354$; Fig 2), detailed data is presented in Table 4. The recurrence rate ($P = 0.397$) and overall survival rate ($P = 0.150$) were not significantly different in TSCC patients who received preoperative chemotherapy and those who did not.

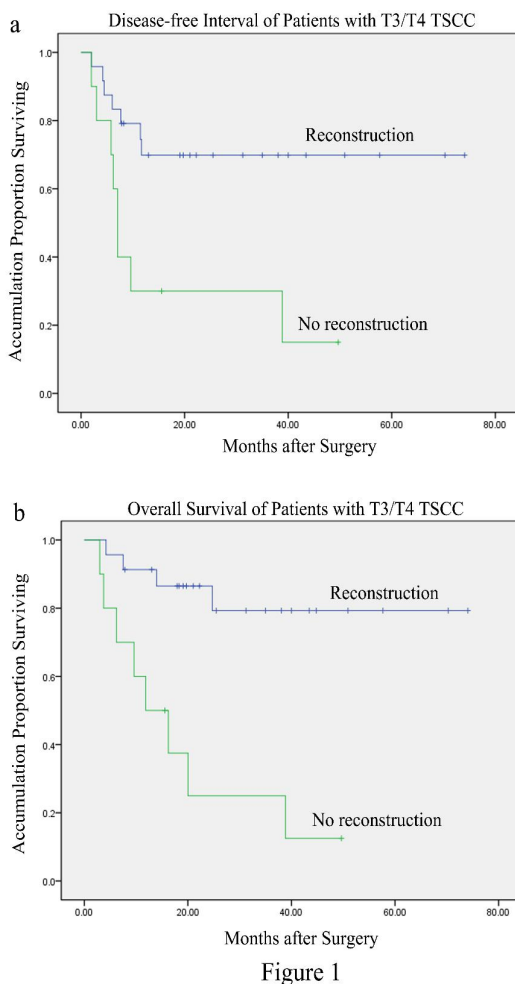


Figure 1. Disease-free interval (1a; $P=0.015$) and overall survival (1b; $P=0.001$) of T3/T4 TSCC patients after surgical treatment with ($n =17$) and without reconstruction ($n = 18$).

Effect of reconstruction on functional outcomes in stage

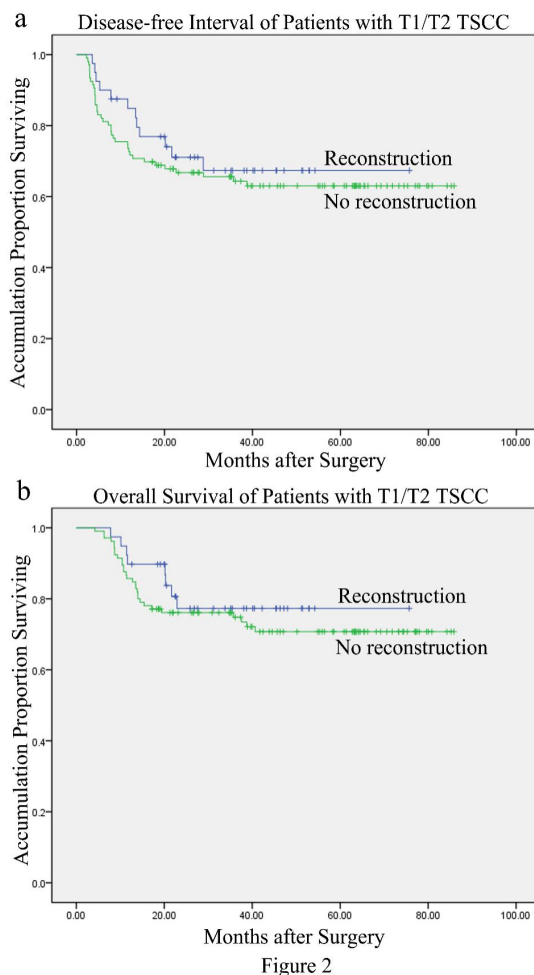


Figure 2. Disease-free interval (2a; $P=0.513$) and overall survival (2b; $P=0.354$) of T1/T2 TSCC patients after surgical treatment with ($n = 43$) and without reconstruction ($n = 106$).

T1/T2 TSCC patients.

Speech Intelligibility: There was no significant difference in speech intelligibility between the reconstruction group and the group without reconstruction ($P = 0.309$; Table 5).

Swallowing Capacity: The surviving patients underwent postoperative swallowing capacity evaluation using the MTF method. None of the surviving patients was stomach tube dependent during the functional survey. There was no significant improvement in patients who received reconstruction, compared to patients who did not undergo reconstruction ($P = 0.746$; Table 5).

Effect of reconstruction on functional outcomes in stage

T3/T4 TSCC patients.

Speech Intelligibility: Nineteen of the 21 (90.5%) patients in the T3/T4 reconstruction group achieved good speech intelligibility; one patient achieved good speech intelligibility and another achieved acceptable speech intelligibility in the group of T3/T4 patients who did not receive reconstruction. As only two patients from the advanced T3/T4 group without reconstruction survived, we did not pursue further statistical analysis. However, the speech intelligibility outcome of these T3/T4 patients after reconstruction was satisfactory (Table 5).

Table 4. Influence of reconstruction on recurrence and survival in TSCC patients at different T stages.

Reconstruction	Tumor stage (T1, T2)					Tumor stage (T3, T4)				
	Observation (cases)	Recurrence (cases)	<i>P</i>	Survival	<i>P</i>	Observation (cases)	Recurrence (cases)	<i>P</i>	Survival	<i>P</i>
Yes	43	13	0.513	34	0.354	25	7	0.015	21	0.001
No	106	38		76		10	8		2	

Swallowing Capacity: After reconstruction, 15/21 (71.4%) of the T3/T4 patients acquired good swallowing capacity and 6/21 (28.6%) achieved acceptable swallowing capacity. None of the surviving patients was stomach tube dependent during the functional survey. One surviving patient who did not undergo reconstruction achieved good

swallowing capacity and another achieved acceptable swallowing capacity. Due to the small number of surviving patients in the group without reconstruction (two patients), we did not pursue further statistical analysis. However, the swallowing capacity outcome of the T3/T4 patients who underwent reconstruction was satisfactory (Table 5).

Table 5. Influence of flap reconstruction on speech intelligibility and swallowing capacity in TSCC patients at different T stages.

Oral function	Evaluation	Tumor stage (T1, T2)			Tumor stage (T3, T4)	
		Flap reconstruction (cases)	No flap reconstruction (cases)	<i>P</i>	Flap reconstruction (cases)	No flap reconstruction (cases)
Speech intelligibility	Good	33	76	0.309	19	1
	Acceptable	1	0		2	1
	Poor	0	0		0	0
Swallowing capacity	Good	28	66	0.746	15	1
	Acceptable	6	10		6	1
	Poor	0	0		0	0

Discussion

Reconstruction has been used in the surgical treatment of head and neck cancer for more than five decades, and it has recently become more popular; however, many patients

with TSCC still do not achieve the desired results. This study suggests that reconstruction should be applied in selected patients with TSCC.

Controversy of which group of patients with TSCC are appropriate for flap reconstruction always exists. Some

clinicians suggest that since the patients with advanced TSCC have a high recurrence rate [14, 15], the benefits of reconstruction are very limited. In contrast, others have advocated that larger defects should be reconstructed when there is a functional or aesthetic loss of structure in the oral cavity after tumor ablation [16-18]. Additionally, immediate reconstruction has been reported to significantly influence the survival of patients with advanced TSCC (T3/T4) [11, 12, 19]. Advanced cancer has always been associated with high recurrence rate, and insufficient surgical margin is the major reason for local recurrence [20, 21]. Extensive resection is necessary in patients with advanced TSCC in order to obtain a safe surgical margin. In this study, we investigated the impacts of reconstruction in patients with different T stage of TSCC, and found that proper reconstruction could enable the head and neck surgeons to perform radical resection of advanced primary tumors (T3/T4). All T3/T4 patients who received reconstruction completed surgical resection (a clinical margin of excision of at least 10 mm). Comparing with T3/T4 TSCC patients who did not receive reconstruction, T3/T4 patients who received reconstruction significantly improved overall survival and lowered rate of recurrence. Probably, because the T1/T2 patients have sufficient surgical margins and sutured directly, in the study, reconstruction did not significantly affect the overall survival and rate of recurrence in the patients with early stage TSCC (T1/T2).

Patients with advanced TSCC have bad functional outcomes after tumor ablation. Malone et al [22] reported that patients with stage III and IV squamous cell carcinoma of the tongue base showed worse results of Normalcy of Diet and Understandability of Speech, compared to patients with early-stage cancer. Zelefsky et al. [23] demonstrated that these subjective functional scores deteriorated with increasing T stage in patients with advanced stage oral cavity and oropharyngeal carcinoma. Reconstruction of oral resections rehabilitated the functions in acceptable levels, improving quality of life in these patients [10, 24]. In most literatures, only the postoperative function of patients who received reconstruction was evaluated. In this study, speech and swallowing function of all patients was evaluated, and there was a comparison between patients who received reconstruction and patients who did not undergo reconstruction. Additionally, postoperative function of patients was analyzed in different

T stage. The results suggested that surgical resection combined with reconstruction tended to offer satisfactory speech and swallowing function in advanced patients, while the speech and swallowing functional outcomes were less satisfactory in T3/T4 TSCC patients who did not receive reconstruction. In contrast to the advanced TSCC patients, immediate reconstruction after tumor ablation had no significant effect on speech and swallowing function in early-stage TSCC (T1/T2) patients. Additionally, reconstruction increased the risk of medical complications, including the wound to heal by secondary intention, split-thickness skin or dermal grafting and so on.

The surgical margin is under the direct control of surgeons and has been demonstrated a strong correlation with survival rates [21, 25]. Owing to the advancements of reconstruction, more extensive resections are now available than before. Additionally, T3/T4 TSCC patients who received reconstruction achieve satisfactory speech and swallowing function. Considering the patient's survival and quality of life, reconstruction is a good choice for patients with advanced TSCC (T3/T4); however, for this circumstance, using a free flap or pedicle flap to reconstruct the oral defect might cause adversities to the patients with early TSCC. So it is still controversial whether to apply a flap reconstruction for the patient with early TSCC, and the decision to perform reconstruction should be made cautiously in patients with early TSCC (T1/T2).

The overall success rate of reconstruction in this study was 97.2%, which is similar to other studies [26, 27]. Flap vascular crisis occurred in six patients due to phlebothrombosis; four of these were successfully salvaged. One patient had total flap necrosis, and as the patient refused repeat reconstruction, the tongue defect was closed directly after the necrotic flap was removed. The other patient had partial flap necrosis. The most commonly observed donor-site morbidity was a broad scar; therefore, to decrease the impact of donor site scarring we suggest the Anterolateral thigh flap (ALTF) is the ideal soft tissue flap for intraoral defect reconstruction, as it has a number of advantages, including enough volume, a flexible shape, secret donor site and long vessel pedicle [10, 28, 29]. Even though many other flaps are available, we usually apply radial forearm flap (RFF) and pectoralis major myocutaneous flap (PMMF) as backup flaps, in case the ALTF fails in vascular crisis.

Compared to patients who did not have the standard risk factors for radiotherapy, the rate of local or regional relapse was significantly higher in patients with one or more risk factor, such as T3/T4 stage, N2/N3 stage, pathologic level IV/V lymph nodes, close margins (< 5 mm), perineural invasion or vascular space invasion. Postoperative radiotherapy is efficient to control local or regional relapse, and it has been previously recommended in patients with one or more risk factors [14, 15, 30-34]. In this study, our results are consistent with previous studies. Postoperative radiotherapy has been reported to negatively influence the functional speech and swallowing outcome in patients with TSCC [17, 35, 36]. While some authors have reported that postoperative radiotherapy at 20 to 40 Gy did not prevent the continued recovery of tongue function with respect to speech, the majority of patients recovered gradually and could still achieve an acceptable functional status and quality of life [9, 23, 37-39]. Schultze-Mosgauet al. [40] reported that irradiation at a dose of 40–50 Gy and chemotherapy at a median interval of 1.5 months prior to surgery did not lead to significant histological changes in the recipient vessels. In this study, the impact of postoperative radiation was estimated from two aspects—survival and function. Postoperative radiation improved loco-regional control and overall survival in patients with the risk factors. Speech intelligibility and swallowing capacity were classified as good, acceptable or poor according to the scores. Most patients who underwent postoperative radiation got a low score in the same level, but speech and swallowing capacity was still satisfactory. Postoperative radiation at a dose 50 Gy to 66 Gy partly interfered the life quality for these patients, but the results showed no statistical significance compared to patients who did not undergo postoperative radiotherapy.

In conclusion, it is important to choose the appropriate patients for reconstruction. In this study, immediate oral reconstruction is recommended for advanced TSCC patients. For patients with early TSCC, reconstruction should be reserved and used selectively, but reconstruction can be considered when there is functional or esthetic loss of the oral cavity. Speech and swallowing functional outcomes are not significantly influenced by postoperative radiotherapy in patients receiving a dose 50 Gy to 66 Gy. A moderate dose of postoperative radiotherapy is recommended for patients with the common/standard risk factors.

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Conflict of Interest

The authors have no conflicts of interest to declare.

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