ISSN: 2643-3907

Qahtan and Mohammed. Res Rep Oral Maxillofac Surg 2023, 7:070
DOI: 10.23937/2643-3907/1710070
Volume 7 | Issue 1
Open Access

Research Reports in Oral and Maxillofacial Surgery

SYSTEMIC REVIEW

Sensory Recovery of Free Flaps Used in Reconstruction of Tongue after Resection of Squamous Cell Carcinoma: What Factors Could Influence the Process?

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Abstract

Background: Reconstruction of defects after resection of tongue squamous cell carcinoma (TSCC) becomes an insurmountable thing that aims to improve the life quality of patients. Recently, reconstruction procedure not only aims to restore function and bulk of tongue, but also to restore the sensation modalities that increase efficacy of the neo-tongue. Sensory recovery of neo-tongue remains a very difficult topic that influenced by multiple factors that could delay or diminish sensory recovery process. Until now, no agreement about these factors and their effects, therefore this systematic review was performed to find out factors that could have an impact on sensory recovery of neo-tongue.

Methods: A search in five databases (PubMed, science direct, web of science, Cochrane library, Ovid) was released. All articles that related to sensory recovery of neo-tongue were identified.

Results: (22) articles were included in our systematic review, in which 310 flaps of different types were performed, where the most performed flaps in the reviewed articles were anterolateral free flap (ALTF) and radial forearm free flaps (RFF). Different degrees of Sensory recovery were reported in association with different types of flaps used in reconstruction; innervated ALTF and RFF flaps were associated with the greatest degree of sensory recovery. Reci-pient nerve also reported to have clear influence on the degree of sensory recovery; lingual nerve and inferior alveo-lar nerve have superiority over other recipient nerves. Patient-related factors (age, gender, and smocking habit), ad-juvant therapies (radiotherapy/chemotherapy), size of resection, and follow-up period all are factors that still a matter of converser.

Keywords

Tongue reconstruction, Sensory recovery, Free flaps, Reinnervation

Introduction

Tongue squamous cell carcinoma is the most common cancer diagnosed in oral cavity presented about 25-40% of all oral carcinomas [1,2]. It has the worst prognosis of all oral squamous cell carcinoma (OSCC) types, with increased prevalence. Most cases occur on the lateral border of the tongue, and rarely occurs on the tongue dorsum [2]. Surgery remains the first choice of treatment for tongue cancer [3], followed by adjuvant radiation or chemotherapy plus radiation [known as chemoradiation or CRT) depending on the disease stage [3]. However, despite advances in surgery and adjuvant therapies, the mortality rate of tongue cancer has not improved in the past 40 years [4]. In the past, closing ablative defects as well as avoiding catastrophic complications were the only goals of oral cavity reconstruction [4]. Current goal of reconstruction for glossectomy deformities is to maximize post-operative function, [5] focusing on restoration of tongue volume, sensation, and mobility [4]. Although there is no universal agreement concerning the best method to be used, reconstruction of tongue should be performed immediately especially when the defect is large [6].

Functional outcomes are widely differing from one

Citation: Qahtan A, Mohammed E (2023) Sensory Recovery of Free Flaps Used in Reconstruction of Tongue after Resection of Squamous Cell Carcinoma: What Factors Could Influence the Process?. Res Rep Oral Maxillofac Surg 7:070. doi.org/10.23937/2643-3907/1710070

Accepted: April 24, 2023; **Published:** April 26, 2023

reconstruction method to another, and this subject remains an area of controversy within literature with unsolved questions about the ideal reconstruction option. Restoring of sensation modalities in flaps that transferred to intraoral area after resection of tumors is critical for tongue function, which is very important for improvement of patient's life quality [7]. Normal sensation of the tongue is of crucial importance for oral functions, [8] specifically important because tasting food depends on touch and thermal perceptions [7]. Some articles have reported successful sensory recovery in free flaps used for tongue reconstruction [6,9].

The type of flaps used in reconstruction of tongue defect is the most common factor influences the degree of restored sensation. Free flaps such as anterolateral thigh flap (ALTF), radial forearm flap (RFF), jejunal flaps etc. promote complex reconstruction of oral cavity with good structural results, but with comparatively less sensory recovery [10]. Free flaps could be further divided into innervated (sensate) and non-innervated (non-sensate) flaps. Beside the type of flap, so many literatures described other factors that could have an impact on sensory recovery of flaps used in reconstruction of defects after resection of squamous cell carcinomas. One previous systematic review [11] about the effect of sensation recovery on improving functional benefits after tongue reconstruction discussed briefly some of these factors. The goal of the present review is to find out factors that could have an impaction on sensation recovery after tongue reconstruction.

Methods

The following databases (Embase, Medline, Web of Science, PubMed, Cochrane, and Google Scholar) were used to search for these key words (tongue reconstruction, sensory recovery, free flaps, and innervation). A combination of searching criteria was used to identify all articles concerning sensory recovery of flaps used in tongue reconstructions.

The criteria for eligibility:

- Original articles studying patients as well as systematic reviews that studying sensory recovery.
- Only studies written in English, no other languages, were included.
- Tongue reconstructions included within the study, at least one of the study groups consisted of it.
- Tongue reconstructions flaps were free flaps, or at least compared to one type of free flaps.

All articles references were manually searched to check for any differences or different ideas. Other important studies related to sensory recovery using free flaps were added to prepare for this review.

Results

This review identified (756) articles. (734) articles were excluded because they were not suitable with our inclusion criteria. Only (24) articles were suitable with inclusion criteria [5,7-10,12-31].

The total number of flaps that have been performed in reviewed articles was 310 flaps, 137 were innervated flaps, and 173 were non-innervated flaps. Of which 73 are ALTF, 181 RFF, 15 JFF, 8 NLIS, and 15 RAF, the remaining were less than 10 flaps each. In the present study we focused on free flaps more than pedicled flaps, however we include the pedicled flaps as much as possible.

Age of patients in reviewed articles ranged between 27-79 years. Defect size was highly varied and ranged from 19 cm^2 to 142 cm^2. The gender of patients in the reviewed papers has been reported in 263 patients; include 185 male patients, and 78 female patients.

Importance of sensory recovery after reconstruction of tongue

Restoration of sensation in the flap transferred for purpose of reconstruction of intraoral defects is important for tongue function after resection of intraoral tumors. Therefore, sensory recovery is very important for improving the quality of life for patients [7]. It becomes unaccepted to provide basic reconstruction for resulted defect without restoration of sensory function [12]. Cicconetti, et al. stated that absence of sensory stimulation in the anterior of the tongue my leads to food retention and drooling after reconstruction of defects on this area, Whereas Dysphagia and aspiration are the most common problems that occurred after reconstruction of posterior tongue [10]. However, sensory return could improve functions and dietary variety as well as reduce cough and adaptive maneuvers [4].

Factors that influence sensory recovery of tongue

So many literatures described different factors that could influence the outcomes of innervation of flaps used in tongue reconstruction. Some of these factors related to tongue defects resulted after resection of tongue squamous cell carcinoma, others are related to flap type, adjuvant therapies, recipient nerve, and follow-up period.

Factors most commonly reported at studies are:

1. Type of flap used in reconstruction, either innervated or non-innervated (ALTF, RFFF, NLIS, etc.) [7-10,12-17].
2. Patient related factors (age, gender, smocking status) [8,9,13,18-20].
3. Preoperative or postoperative radiotherapy and chemotherapy [8,12,21].

4. Recipient nerve [7,10].
5. Location of resection in the tongue [12,13], and size of flap [21].
6. Follow-up period [5,12,13,15,22,23].

Type of flap used in reconstruction

Seven articles reported about the sensory recovery of tongue after reconstruction with radial forearm free flaps (RFFF) (Table 1 and Table 2) [7,8,14,21,24-26]. However, three articles particularly studied anterolateral Thigh free flap (ALTFF) [12,27,28]. Another six studies compared flaps of different types [8,10,13,22,29,30] (Table 3).

ALTF flaps

Three articles reported the sensation recovery in tongue reconstruction using ALTF flaps [12,27,28]. A total of 47 patient undergone tongue reconstructions using this type of flap, of which 32 flaps are innervated and 15 flaps are non-innervated (Table 2).

Sensate ALT flaps: One study [27] reported full recovery of temperature perception, pain perception, and two-point discrimination that occurs in 13 sensate ALT flaps [27]. The same study compared sensation modalities on the tip of native tongue with sensation on the tip of the neo-tongue preoperatively (in the donor site) as well as postoperatively (after reconstruction). The result was satisfactory sensory recovery of neo-tongue postoperatively, Even if neo-tongue pressure thresholds measurements after reconstruction were found to be significantly reduced compared with the native tongue [27].

Sensate versus non-sensate ALT flap: Two articles [12,28] compared innervated and non-innervated ALT flaps with 34 flaps, of which 19 non-innervated flaps and 15 innervated flaps. In addition, Yu, et al. reported that the sensory recovery of the sensate ALT flaps is much greater than that of non-sensate ALT flaps [12]. These two studies revealed that sensation modalities such as two-point discrimination, pain perception, and temperature differentiation restored in almost all innervated ALT flaps, while they are absent in almost all non-innervated flaps [12,28].

RFF flaps

Seven articles have reported about sensory recovery in patients undergone tongue reconstruction by using RFF flaps. In these articles 120 RFF flaps had been examined, of which (92) are innervated and 28 are non-innervated.

Sensate RFF: Four studies [9,21,24,25] specifically studied the sensate RFF flaps either in compared to contralateral side or to healthy controls, all authors found that sensation in all sensate RFF flaps is inferior to that of contralateral side or that of healthy control. Santamaria, et al. [21] showed that only two points discrimination has a comparable value between reconstructed tongue and contralateral, whereas

Table 1: Flaps included in reviewed studies.

Type of flap	RFFF\no. of studies	ALTFF\no. of studies	Jejunal\no. of studies	Fibula flaps\no. of studies	RA\no. of studies	G.O\no. of studies	P.M\no. of studies	NLIS\no. of studies
Innervated	**92** (in 7 studies)	**40** (in 4 studies)	-	-	**5** (in 1 study)	-	-	**8** (in 1 study)
Non-innervated	**89** (in 8 studies)	**33** (in 4 studies)	**15** (in 2 studies)	**9** (in 1 study)	**10** (in 1 study)	**6** (in 1 study)	**3** (in 1 study)	

Table 2: Anterolateral thigh flaps.

Study name	Number of Cases	Types of flap	Results
Longo, et al. [27]	13 case	All are *sensate* ALT Flaps. With different size of Resection	Hot/cold and pain perception, as well as 2-point discrimination were observed to be fully restored in innervated flaps reconstruction.
Yu, et al. [28]	13 flaps	Eight *sensate* ALT flaps Five non-sensate ALTF	Sensate versus non-sensate: Two-point discrimination (5/8 vs. 0/5). Pain perception (8/8 vs. 0/5). temperature differentiation (5/6 vs. 0/5)
Yu, et al. [12]	21 flaps	11 *sensate* ALT flaps 10 *non-sensate* ALT flaps	Innervated flaps were superior in two-point discrimination 9/ 11 versus 0/10 (mean 2.6 ± 0.9 mm). perception (11/11 vs. 0/10), and temperature Differentiation (11/11 vs. 1/10).

Table 3: Radial forearm free flaps.

Study name	Number of cases	Types of flap	Results
Santamaria, et al. [21]	28 case	All sensate RFF With different recipient nerve	Light-touch, Pain sensation, and Hot and cold perception were clearly decreased in the reconstructed side. Only two-point discrimination was comparable with collateral side
Kuriakose, et al. [24]	17 case	All sensate RFF	2-point discrimination (moving and static) as well as pressure sensitivity were reported to be greater in innervated than on the site opposite to donor site. Values were almost equal to those of normal tongue.
Loewen, et al. [25]	16 case	8 sensate RFF 8 control	There were significant differences with healthy control in light touch, temperature sensation, and two-point discrimination (20-50% correct response of reconstructed flaps compared to 60-90% correct response from control)
L.Zhu, et al. [9]	40 cases	20 sensate RFF 20 control	Light mechanical stimuli (MDT) were observed in 20 patients of 20 patients. A thermal painful stimuli (CPT, HPT) within degree limits of (0 °C, 52 °C) was not detected in 0 of 20 patients.
Boyd, et al. [14]	28 flaps	8 sensate RFF 10 non-sensate RFF 10 historical controls (PM flaps)	Percentage of presence of sensation modality (sensate versus non-sensate), Sharp/dull discrimination was 75% versus 10%. Hot and cold perception: 100% (both) versus 50% (hot) and 40% (cold). Two-point discrimination: 14.25 g/mm^2 versus 27 g/mm^2.
Biglioli, et al. [26]	16 flaps	Seven sensate RFF Nine non-sensate RFF	Perception of tactile stimuli was slightly better in the sensate group (average 83%) compared to non-sensate group (71%). Sharp/ dull discrimination and cold perceptions were higher (average of 85%) compared with non-sensate (average 50%)
Katou, et al. [7]	13 flaps	Four sensate RFF Nine non-sensate RFF	(Sensate vs. nonsensate) sharp/dull discrimination (4/4 versus 4/9 patients). Hot/cold discrimination presented in (4/4 versus 2/9).

Table 4: Comparison between different types of flaps.

Study name	Number of flaps	Type of flaps	Result
Shindo, et al. [29]	18 cases	9 non-sensate fasciocutaneous RF flaps 9 non-sensate osteocutaneous fibula Flaps	No return of sensibility in the 2 cases of total glosse. However, Sensibility was reported in all five patients undergoing partial lesions.
Close, et al. [22]	12 cases	8 non-sensate fasciocut- aneous (4 RF, 4 ALT). 4 non-sensate pedicled musculocutaneous (1 LD, 3PM)	10 out of 12 patients restored sensibility ability after 6 months. Of 8 FCFF, 6 restored Sharp/dull discrimination, 8 restored Touch sensation, and 5 restored Two-point discrimination. Of 4 MCF, 2 restored Sharp/dull sensation, 2 restored Touch sensation, and only one restored Two-point discrimination.
Sabesan, et al. [13]	39 cases	23 non-sensate FC RFF 6 non-sensate gastro-omental free flaps 10 non-sensate jejunal	Comparison between three types of flap reported that RF flaps have the most superior measures of all modalities of sensation, and jejunal almost have the lowest one.
Kimata, et al. [30]	27 cases	Eight sensate ALT flaps, Six non-sensate ALT flaps, Five sensate RA flaps 10 non-sensate RA flaps	Sensate versus non-sensate flaps: Sensibility of light touch (87.5% vs. 30%). Hot/cold discrimination (87.5% vs. 0%). two-point discrimination (7/8 patients vs. 1/6 patients). innervated ALT flaps were able to detect pressures as low as (6.62g vs. 184.7g).

L.ZHU, et al. [8]	52 cases	16 non-sensate RFFF 8 non-sensate ALTF 8 Nasolabial Island Flap 20 control	RFFFs and NLIFs were significantly less sensitive than ALTFFs for WDT. For HPT, ALTFs were better than RFFs. For MDT, RFFFs showed significantly lower sensory recovery than ALTFFs and NLIFs. NLIFs were the best regarded to MPT, followed by ALTFs, while RFFs were the last.
Cicconetti, et al. [10]	14 cases	9 non-sensate RFFF 5 non-sensate jejunal F	Recovery of sensation was better in patients with free radial forearm flaps (6(9/ than in patients with jejunal free flaps (5/0). This difference was statistically significant (p50.005)

other sensation modalities (temperature recognition, light touch sensation, and pain perception) were all inferior compared to contralateral side [21]. One study compared the sensory recovery on sensate RFF flaps to both residual normal tongue and contralateral donor site [24]. Kuriakose, et al. showed that RFF flaps could restore sensory fidelity better than that of native RFF contralateral donor site, but closely approached that of normal tongue [24]. In contrast, Loewen, et al. [25] no significant difference was found between patients and controls, even though reconstructed tongues show slightly poorer responses abilities compared to controls [25]. L Zhu, et al. [9] showed significantly lower sensitivity for all parameters in the patient group compared to that of those in controls within cut of 9 months and 18 months, except for DD, in which rapid recovery was detected [9].

Sensate versus non-sensate RFFF: Three articles compared sensory recovery between sensate and non-sensate RFF [7,14,26]. The superiority of sensate flaps over non-sensate flaps was reported by all authors (Table 3) [11]. Additionally, katou, et al. [7] showed that earlier recovery occurs in sensate RFF flaps (13 months) than non-sensate RFF flaps (25.4 months) [7]. No significant difference was found when two points discrimination and temperature discrimination was compared between flap and contralateral site [14].

Comparison between different types of flaps

Six studies, [8,22,30] compared sensory recovery between different types of flap such as anterolateral thigh (ALT), radial forearm (RFF), rectus abdominus (RA), nasal labial island (NLIF), gastro omental (GO), jejunal (JF), and latissimus dorsi LD (Table 4).

ALT and RA flaps: Kimata, et al. [30] compared innervated and non-innervated anterolateral thigh flaps (ALTF) with innervated and non-innervated rectus abdominis (RA) [30]. Generally, recovery of sensory in innervated ALT flaps has superiority over non-innervated ALT flaps and innervated RA flaps. However, sensate RA flaps were found to be better than non-sensate RA flaps in most sensation modalities except for hot and cold perception no significant difference was found [11].

ALT, RFF, and NLIF: One study [8] compared between healing of sensation in non-sensate ALT flaps, non-sensate RFFF, and NLIF flaps. This study found significant differences for a number of sensation modalities between RFFF, ALTFF, and NLIF after surgery. ALTFF was better than RFFF and NLIF in hot perceptions. However, NLIF and ALTFF were better than RFFF in mechanical perceptions with slight superiority of NLIF over ALTFF. No significant differences between the measurements of different flaps were shown for cold perceptions and two point's discrimination (static, dynamic, and direction) [8].

ALT, RFF, LD, and PM: Close, et al. [22] compared between non-sensate ALTFF and other non-sensate flaps such as RFF, latissimus dorsi (LD), and pectoralis major (PM) [22]. This study reveals that of 4 patients with non-sensate ALT flaps, 4 restored touch perception, 3 restored sharp/dull, and 2 restored two-point discrimination and temperature perception. Of Four RFFF patients, 4 restored touch, 3 restored sharp /dull and two points discrimination, and only one restored temperature perception. Recovery of touch, sharp/dull, and two points discrimination was reported only on one of 3 patients with non-sensate PM flap. In one patient with non-sensate LD flap all modalities except temperature were recovered [22].

RFF and FIBULA flap: One study used RFF flaps and fibula flaps to restore defects in oral cavity [29], of which seven flaps used for reconstruction of tongue. Two cases with total glossectomies and five partial glossectomies were reconstructed in this study. No sensation recovery was detected in both total glossectomies, whereas in all partial glossectomies sensory recovery was detected even partially.

RFF, GO, and JF: sensory recovery in 23 non-innervated radial forearm flaps were compared to 5 non-innervated jejunal and 6 non-sensate gastro-omental free flaps by Sabesan, et al. and they have found better sensory recovery in the radial forearm flaps group than in the other two groups [13].

RFFF and JF: Cicconetti, et al. [10] showed that better sensory recovery after reconstruction of tongue defects with radial forearm free flaps than with jejunal free flaps [10].

Patient related factors

Factors such as age, sex, habits, and health status

are the most common patient-related factors reported to influence sensory recovery of tongue reconstruction flaps. Studies about these factors reported very contrast results, and no agreement about the extent of effect of this factor on the sensory recovery process. Three studies have reported a tendency for better sensory recovery of the flaps occurring in younger patients [18-20], and in non-smokers [19]. In contrast, Vriens, et al., Santamaria, et al., Sabesan, et al., and Close, et al. reported no definite association between the sensory return and age, or tobacco use or smoking [13,15,21,22], or gender [8,13,15]. Even though, males may have higher score of OHIP-VII (handicap) than females [8]. One study reveals that different psychological factors could easily affect the results of sensibility tests [7].

Pre- and post- operative radiotherapy and chemotherapy

Controversial results have been produced for probable effects of post-operative radiotherapy on sensory recovery of the flaps by many previous studies [8]. Many authors reported reduced, delayed, or failed sensory recovery in radiated patients [18,21,22,31]. Close, et al. and Santamaria, et al. found radiated patients to have lower sensory recovery for light touch, hot/cold, and pinprick pain perceptions [21,22]. In contrast to the previous studies, no significant correlation was founded by Yu, et al., L Zhu, et al., Sabesan, et al., and Chena, et al. between post-operative radiotherapy and recovery of sensation in free flaps used in reconstruction of the tongue, they found that true only with a long follow-up [5,8,12,13]**.** However primary radiation treatment may causes intrinsic tongue and pharyngeal injuries that cause effects on sensory recovery and outcomes of reconstruction compared to adjuvant radiotherapy [5].

Only a few studies have mentioned the effect of post-operative chemotherapy on the sensory recovery of the flaps [9]. L Zhu, et al**.** showed that patient received post-operative chemotherapy were found to be less sensitive in terms of the WDT than the patients that did not receive postoperative chemotherapy [8,9]. Galiè, et al. and Massarelli, et al. reported no significant differences were found in sensory recovery of patients who underwent adjuvant radio-chemotherapy [6,23].

Recipient nerve

Six studies reported the impact of recipient nerve on sensory recovery level of flaps. Most studies agree that for innervated flaps the greatest recovery occurs when recipient nerve is the lingual nerve or inferior alveolar nerve. The use of sensate flaps considered to be more favorable if nerves existed at the recipient site is suitable [7]. Nerves that could act as recipients are lingual nerve, inferior alveolar nerve, antebarchial nerve, hypoglossal nerve, great auricular nerve, and cervical plexus, with superiority of lingual and inferior alveolar nerves over all others [7]. Santamaria, et al. and Yu, et al. reported the superiority of lingual and inferior alveolar nerves upon others such as cervical plexus, hypoglossal, and posterior auricular nerves [12,21]. Kuriakose, et al. documented that by microsurgical anastomosis of lingual nerve to lateral antebrachial cutaneous nerve, sensation of radial forearm free flap becomes almost like normal part of the tongue [24]. Urken, et al. reported decreased discrimination ability in case of nerve anastomosis with great auricular nerve [10,17].

Follow up period

The impact follow-up time on sensory recovery has been reported in many studies but still an area of controversy. Many studies reported improvement of sensory recovery in flaps after longer follow up period, while it was decreased in shorter follow up periods [5,12,23]. Zhu, et al. [9] reported the presence of significantly improved somatosensory function at 18 M compared to that at 9 M [9]. In contrast to the previous studies, three studies found that the somatosensory function of the flap was not significantly correlated with the follow-up time [13,15,22] after six months [22].

Size and location of resection and reconstruction

Remnant of the native residual tongue after resection of cancer was found to strongly influence the entity of functional impairment [23]. Kimata, et al. thought that postoperative function depends on the size of resection [30]. Oral cavity glossectomy defects limited to less than half of the tongue can often be sufficiently managed by secondary or primary types of closure that resulted in good recovery, while larger size glossectomies, require more extensive reconstructive [5]. Large and thick non-sensate flaps may have worse sensory recovery than small and thin flaps when used for large defects [12]. Shindo, et al. stated that reconstruction of large defect or total glossectomy will result in a few remaining nerve fibers sprouting into the flap from the edges, thus a complete reinnervation will not be expected [29]. In contrast, Santamaria, et al., Close, et al., Sabesan, et al., and vriens, et al. all reported no significant relation between sensory recovery and flap size [15,21,22].

Sabesan, et al. and Santamaria, et al. reported that the anterior tongue showed significantly better recovery [13,21]. Patients with lesions in anterior tongue areas presented slightly better outcomes than those with subtotal tongue resection group; however, statistical significance could not be found [27].

Contralateral Side of the Tongue

The contralateral side of the tongue is the most used as a healthy control in sensory recovery; so many studies compare their results of reconstructed side to those of the contralateral side of the tongue. However, some recent studies showed that sensation of contralateral side itself might be influenced by

resection and reconstruction procedures. One study showed that not only treated (resected) side, but also the contralateral side (preserved) of the tongue showed sensory loss after tongue reconstruction surgery [8]. In addition, there were significant differences between contralateral sensation of reconstructed tongue and healthy controls, indicating significant somatosensory impairment at the contralateral side of the flap [5,8].

Discussion

The search was released in five databases that mean it covers so many research and articles available about the selected subject. Manual selected of articles as well as inclusion and exclusion criteria makes this systematic review with reasonable grade of strength. However, the number of articles reviewed and the number of flaps or sample sizes examined are relatively small that makes this review highly depended. Some articles that discuss sensory recovery were also added for preparation of this review as resources of information included within this review, and this may be causes some exclusion criteria. Tongue squamous cell carcinoma is one of the most common oral cancers, which has the worst prognosis among other oral cancers. The proper method for treating this cancer is still by surgical resection or surgical resection associated with adjuvant treatment (radiotherapy or chemotherapy). The reconstruction method will be selected according to the size of defect that formed after resection of cancer. For small defects primary or secondary closure may be sufficient, however for bigger defects (partial, subtotal, and total glossectomies) reconstruction by using free flaps taken from other site (donor site) becomes urgent and should be done immediately in the time of resection. Restoring bulk, function, and sensation of tongue are the most important goals in recent literature about tongue reconstruction. Recently, sensory recovery of neo-tongue has gained a great importance, as it plays critical role in improving mastication, deglutition, and even speaking. However, Sensation in neotongue could also prevent the repeated biting, inspiration, and burning of neo-tongue.

Many factors could have an influential effect on the ability of sensory recovery within flaps involved as reconstructed material of tongue. Here we did our review paper in order to know what are the factors and what are the evidences about their effects. In the present review paper, reviewed articles contain RFF flaps (181), followed by ALTF flaps (73), then jejunal flaps (15), RAF (15), and the remaining flaps (less than 10 for each). Different degree of sensation was restored in different types of flaps, of course controversial is always present and no two articles gave the same results or conclusions. However, articles that compared innervated with non-innervated flaps [7,12,14,26,28,30] revealed that innervated flaps have obvious superiority over non-innervated flaps. In addition, the superiority in sensory recovery ability of innervated (RF) flaps has been proved to be similar in innervation architecture to normal skin, while the opposite were founded in non-sensate RF flaps [11]. Sensibility of non-innervated flaps has been confirmed either, although the resulted sensibility was fairly reasonable and not as that of innervated flaps. On the other hand, articles that compared different types of flaps (ALTFF, RFF, RAF, GOF, JF. etc.) to each other have found different degree of sensation has been restored within these flaps [8,10,13,22,29,30]. Kimata, et al. reported the sensory healing in innervated ALTF flaps are better than non-innervated ALTF flaps and innervated RA flaps. Close, et al. [22] compared between non-sensate ALTF flaps and RFF flaps with other flaps showed that best results was gained with non- sensate ALTF and non-sensate RFF flaps, and the sensory modalities were almost equally regained in these two flaps. The results of these two studies were repeated over the rest of comparison studies. On another face of comparison, fasciocutaneous flaps were compared to musculocutaneous flaps where the first flaps got better results, this result may be due to thickness differences between these two types [22].

The other factor that should be considered when reconstruct tongue defects is that which recipient nerve. All articles showed the superiority of the lingual and inferior alveolar nerves over other flaps such as hypoglossal, cervical plexus, posterior auricular nerves. Lingual nerve and inferior alveolar nerve have been used in almost all reviewed article except for one article [21] that used other nerves beside to these two, however even these Articles agreed with superiority of lingual and inferior alveolar nerves. Whether lingual or inferior alveolar nerve was used, no difference in the cooptation technique (end to end, or end to side).

Patient related factors were reported to have an effect on sensation of neo-tongue; it was supposed that young patient have rapid ability to restore the sensation. Moreover, Vriens, et al., Santamaria, et al., Sabesan, et al., and Close, et al. found no significant association between the sensory recovery and age, or smoking [13,15,21,22], or gender [8,13,15]. More recently, L Zhu, et al. stated that although OHIP-VII (handicap) in males was higher than that on female, no significant relation between gender of patient and sensation healing after surgical reconstruction [9].

The effects of radiotherapy on flap sensation appear to be depended on whether it was preoperative radiotherapy or postoperative radiotherapy. Almost the same numbers of articles have reported contrasted results of radiotherapy effects, half of these articles reported delayed, decreased, or diminished sensory recovery after postoperative radiotherapy, and the other half reported no significant effect of postoperative radiotherapy on sensation [5,8,12,13,18,21,22,31]. Moreover, one study [5] found preoperative radiotherapy

could have effects on the tissues of oral and pharyngeal areas that could not be significantly restored with flaps [5]. Chemotherapy in turn could have an impact in sensation of the flaps as was stated by most recently studies [9] where they found lower sensation of WDT in patients undertaken postoperative chemotherapy than patients did not taken chemotherapy [9].

Method of tongue reconstruction selection is depended on the size and location of resected portion of the tongue, small lesions in the anterior area (mobile tongue) could be sufficiently restored with primary or secondary closures that resulted in good sensation ability. However larger lesions in this area should be reconstructed using either pedicled or free flaps, healing of sensation in this area was reported to be slightly higher than the posterior area, however no statistically significant relation was founded [27]. In contrast, no significant difference was founded between sensory recovery and the size of flap, [15,21,22] despite the sprouting theory of sensory recovery that state, "The important factor of sensory recovery is the sprouting grow of nerves from the remaining healthy tissues into the transferred flaps" [29]. According to this theory, the growth of nerves would be effected in the thicker and bigger flaps.

Long follow up time is critical for complete recovery of sensation; most authors suggested 6 months as the lower level of follow up time after reconstruction of the tongue. Improvement of sensory recovery in flaps after long follow-up period was obvious [5,12,23]. This may be due to adaptive ability of tongue with different sensations. In addition, three studies found no significantly correlated relation of sensory recovery with the follow-up time [13,15,22] after six months [22]. However, the Most recently released study of Zhu, et al. [9] reported the presence of significantly improvement in somatosensory function at 18 months follow up group compared to those of only followed up for 9 months, this result proved the effect of follow-up time on sensory recovery [9].

The contralateral side represented the most common control group to which all sensory measurements were compared in most studies related to sensory recovery. However, recent studies have shown the possibility of contralateral side sensibility to be affected after reconstruction of defected side in the tongue [8,9]. One study compared measurements from contralateral side with those of other healthy controls before resection then again after resection and reconstruction, and they found differences in preoperative measurement form those of postoperative [8]. This may suggest that, 2-point discrimination could be diminished on the intact tongue tissue, instead of recovery of 2-point discrimination on the reconstructed tongue [25]. However, No significant differences were found between the reconstructed and intact portions of the tongue for light touch [25].

Conclusion

Sensory recovery of reconstructed tongue is affected by many different factors. Type of used flap, and type of recipient nerve have been confirmed to be the most effective factors, whereas other factors such patient-related factors, adjuvant radiotherapy\chemotherapy, follow-up time, and size and location of resection (and so the flap) all still need more research to confirm or deny their influence.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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