




## ORIGINAL RESEARCH

# Free-flap volume correlates with body mass index in patients with tongue squamous cell carcinoma

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## Abstract

**Objectives:** This study aimed to investigate the relationship between postoperative reconstructed tongue flap volume (RTFV) and body mass index (BMI) and identify factors affecting the flap volume in patients with tongue squamous cell carcinoma.

**Methods:** Thirty-two patients were evaluated for RTFV from computed tomography images and BMI. The first and second evaluations were done at 6 months and 1.5 years after surgery respectively. RTFV rate changes and BMI differences from the first and second evaluations were calculated. The correlation between RTFV rate change and BMI difference was assessed using Spearman's rank correlation coefficient. Multiple regression analysis evaluated the relationship between the flap volume rate change and age, sex, flap type, and BMI difference to identify influencing factors.

**Results:** The flap volume rate change and BMI difference correlated significantly ( $r = .594$ ,  $p < .05$ ). BMI difference and flap type were independent factors that affected reconstructed flap volume rate change in multiple regression analysis ( $p < .05$ ).

**Conclusion:** The flap volume of patients with tongue squamous cell carcinoma correlates with the BMI change in the chronic phase. Patients after tongue reconstruction need to be well nourished to maintain BMI and thus postoperative tongue volume to maintain the quality of life.

**Level of Evidence:** Level 3.

## KEYWORDS

body mass index, flap volume changes, reconstructive surgery, tongue squamous cell carcinoma

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## 1 | INTRODUCTION

Tongue squamous cell carcinoma (TSCC) is the most common oral cancer with a high occult cervical lymph node metastasis rate.<sup>1</sup> Resection and reconstruction surgery and concurrent chemoradiotherapy treatment are typically recommended for advanced TSCC.<sup>2</sup> Since the reconstructed tongue has no mobility, tongue volume plays an important role in maintaining patient's swallowing and articulation functions and therefore, quality of life (QOL).<sup>3</sup>

The extent of tongue resection depends on the degree of cancer progression. When the excision area is wide, a flap is transplanted to compensate for the lost tongue function and volume. Several flaps have been developed to reproduce the volume loss of the tongue.<sup>4</sup> These can broadly be divided into pedicle and free flaps.<sup>5</sup> Free flaps are widely used for tongue reconstruction owing to fewer complications at the donor site and better function than pedicle flaps.<sup>6</sup> Free flaps include forearm, rectus abdominis, and anterolateral thigh flaps. Forearm flaps are often transplanted when the tongue excision area is <50%.<sup>7</sup> If it exceeds this, fat-rich rectus abdominis flaps or anterolateral thigh flaps are used.<sup>8,9</sup> The part lost by resection is compensated by the flap. However, if the flap volume is insufficient, the patient will have reduced oral function and lose weight.<sup>10</sup> This can also trigger postoperative dysphagia.

Approximately 6 months postsurgery, reconstructed tongue flap volume (RTFV) decreased mainly due to edema reduction and muscle atrophy.<sup>11</sup> If the RTFV decrease progresses and dysphagia or dysarthria occurs, it would be necessary to compensate for the decrease in flap volume, such as by using a palatal augmentation prosthesis.<sup>12</sup> However, it is crucial to prevent RTFV decrease.

While the flap muscle continues to atrophy, fat increases, depending on the patient's condition, and high fat-to-muscle ratio flaps can show an increased volume of the entire flap after a period.<sup>13</sup> Therefore, we hypothesized that the patient's nutritional status affects RTFV. Further, when reconstructed tongue shape is depressed, patients lose weight, leading to dysphagia, and dysarthria.<sup>10</sup> RTFV decrease primarily results from muscle atrophy.<sup>11</sup> RTFV decreases significantly when the muscle volumes are  $\geq 40\%$  of the flap and the flap fat positively correlates with patient's disease-free state.<sup>13</sup> Postoperative radiotherapy is a risk factor for RTFV loss<sup>14</sup> or has no effect on RTFV change.<sup>11,13</sup> Preoperative triglyceride and albumin levels correlate with RTFV.<sup>15</sup> Flap type affects RTFV,<sup>16</sup> its shrinkage percentage,<sup>10-16</sup> and RTFV atrophy continues for 6 months postoperatively.<sup>14</sup> No report has clarified whether RTFV changes in the chronic phase are reversible and factors affecting the changes. We hypothesized that a correlation exists between RTFV and postoperative nutritional status. Additionally, RTFV of fat-rich type flaps is more affected by nutritional status. Once insight is gained regarding reversible RTFV change and its effectors, the importance of postoperative nutritional management can be emphasized to patients and information on maintaining their RTFV can be provided to maintain oral functions and QOL.

Therefore, this study aimed to investigate the correlation between RTFV and nutritional status in patients with TSCC.

Additionally, the relationship between RTFV change and age, sex, flap type, and nutritional status was examined.

## 2 | MATERIALS AND METHODS

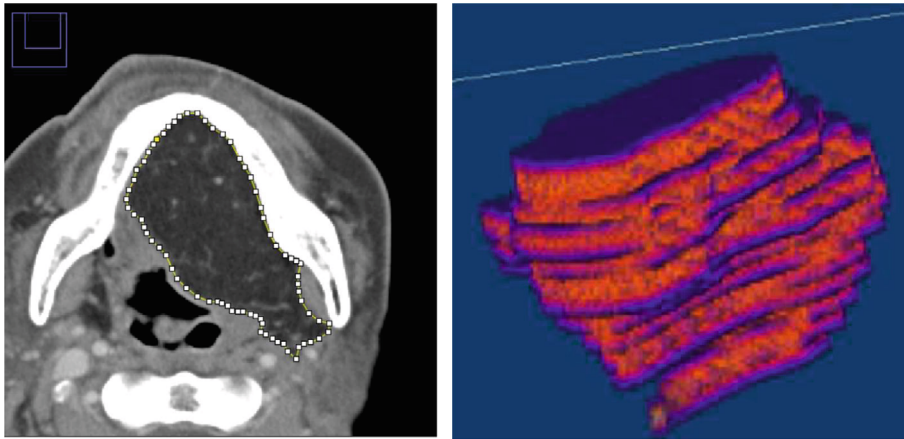
The study protocol conformed to the principles outlined in the World Medical Association Declaration of Helsinki and was approved by the Dental Research Ethics Committee of Tokyo Medical and Dental University (approval number: D2020-068-01). Informed consent was obtained in the form of opt-out by using posters. Patients who declined to participate were excluded. In addition, this study followed the reporting guidelines of the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) Statement and the Reporting of studies Conducted using Observational Routinely collected Data (RECORD) Statement.<sup>17</sup>

### 2.1 | Participants

We retrospectively analyzed patients who underwent tongue reconstruction owing to TSCC and who had been requested to undergo swallowing function examination at the Department of Dysphagia Rehabilitation at Tokyo Medical and Dental University Dental Hospital (Tokyo, Japan) between 2015 and 2021. Patients were enrolled if they had available computed tomography (CT) scans, obtained at 6 months and 1.5 years postoperatively as part of oral cancer treatment. Those who had many metal artifacts caused by dental materials in the scans that were difficult to analyze were excluded. We collected data on the sex, age, height, weight, presence, or absence of chemoradiotherapy treatment and types of surgery, and flap from patient records.

### 2.2 | Flap volume measurement

Postoperative CT images (slice width, 3 mm) were used to evaluate the RTFV. CT was performed using a Somatom Sensation 64 scanner (Siemens Healthineers, Erlangen, Germany). Imaging data were stored in a DICOM file, imported to a personal computer, and opened in Image J software (version 1.53; National Institutes of Health, Bethesda, MD). The reconstructed flap area of each axial CT image was manually traced according to the boundary of gray values and reference of the surgery record (Figure 1). The scaling of the image was automatically corrected after opening the DICOM data and the area of each traced part was calculated by using the "Measure" function in ImageJ. Volume was calculated by integrating the area of each slice multiplied by the slice thickness. The volumetric analyses were performed by two investigators (a dental college graduate with 4 years of experience, and a radiation specialist with 21 years of experience). Intraclass correlation coefficients (ICCs) were calculated for measurements of the RTFV. Intrarater and interrater reliability were assessed. Both ICCs exceeded 0.7, showing high reliability (ICC [1] = 0.99, ICC [1, 2] = 0.93).



**FIGURE 1** Computed tomography sections of a tongue and a three-dimensional reconstructed tongue image.

### 2.3 | Assessment of patient's nutritional status

We used body mass index (BMI) to assess the patient's nutritional status. BMI is a global index of the nutritional status,<sup>18</sup> noninvasive, and a simple indicator for patients to understand their nutritional status. Within 1 month preoperative BMI and BMI at the same time of CT examination were calculated from patients' height and weight, which were collected from patient records.

### 2.4 | Assessment of the relationship between RTFV and BMI

Since postoperative edema reduction and muscle atrophy of the flap continue up to 6 months after surgery,<sup>14</sup> the first evaluation of RTFV was done 6 months postoperatively and was set as a baseline. The second evaluation of RTFV was done 1.5 years after surgery. By using RTFV of the first and second evaluations, the rate change was calculated as follows:

$$\text{RTFV rate change} = \frac{\text{RTFV}_{2\text{nd}} - \text{RTFV}_{1\text{st}}}{\text{RTFV}_{1\text{st}}} \quad (1)$$

where  $\text{RTFV}_{2\text{nd}}$  is the RTFV of the second evaluation and  $\text{RTFV}_{1\text{st}}$  is the RTFV of the first evaluation. To assess the relationship between postoperative RTFV and BMI, we verified the correlation of the RTFV rate change and difference of the BMI at the same time of the RTFV evaluation which was calculated as follows:

$$\text{BMI difference} = \text{BMI}_{2\text{nd}} - \text{BMI}_{1\text{st}} \text{ [kg/m}^2\text{]} \quad (2)$$

where  $\text{BMI}_{2\text{nd}}$  is the BMI at the same time of RTFV second evaluation,  $\text{BMI}_{1\text{st}}$  is the BMI at the same time of RTFV first evaluation.

Patients were divided into those with increased RTFV and those with decreased RTFV, and we examined whether there was a difference in preoperative BMI between the groups.

**TABLE 1** Patient characteristics.

Characteristics	n = 32 (%)
Sex	
Male	16 (50.0)
Female	16 (50.0)
Age (years)	
Mean	52.7
Range	22–73
Type of surgery	
Subtotal glossectomy	17 (53.1)
Hemiglossectomy	15 (46.9)
Type of flap	
Rectus abdominis musculoperitoneal flap	8 (25.0)
Anterolateral thigh flap	15 (46.9)
Free radial forearm flap	9 (28.1)
Preoperative body mass index	
<18.5	4 (12.5)
18.5–25.0	23 (71.9)
≥25.0	5 (15.6)
Postoperative oral irradiation	
Yes	7 (21.9)
No	25 (78.1)

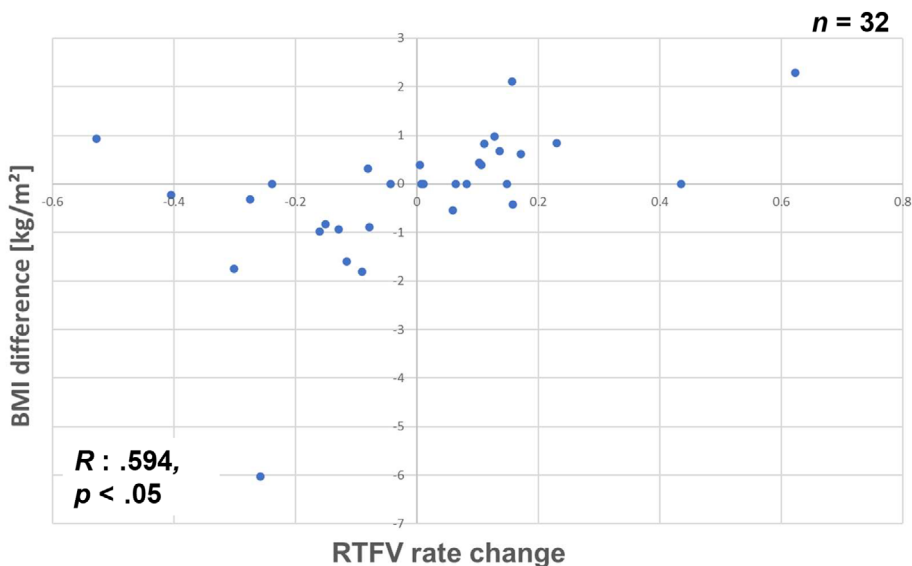
### 2.5 | Statistical analysis

The relationship between RTFV rate change and BMI difference was evaluated using Spearman's rank correlation coefficient. In addition, multiple regression analysis was performed with RTFV rate change as the dependent variable, and age, sex, type of flap (rectus abdominis muscle flap, anterolateral thigh flap, or forearm flap), and the BMI difference as independent variables. We also examined the differences in preoperative BMI between groups with increased and decreased RTFVs using the Student's *t*-test. The differences in RTFV rate change between those who had or had not undergone postoperative

**TABLE 2** Patient's BMI and RTFV preoperation, 6 months postoperation (first evaluation), and 1.5 years postoperation (second evaluation).

	n = 32		
	Preoperative	Postoperative first evaluation	Postoperative second evaluation
<b>BMI</b>			
Average (kg/m <sup>2</sup> )	22.0 ± 3.53	21.1 ± 3.07	20.9 ± 3.30
Range (kg/m <sup>2</sup> )	16.3–33.8	15.9–31.5	15.3–31.3
<b>RTFV</b>			
Average (cm <sup>3</sup> )	–	19.2 ± 17.0	20.0 ± 20.2
Range (cm <sup>3</sup> )	–	2.51–70.0	1.19–100.5

Abbreviations: BMI, body mass index; RTFV, reconstructed tongue flap volume.

**FIGURE 2** Relation between reconstructed tongue flap volume (RTFV) rate change and body mass index (BMI) difference.

radiotherapy, and with or without a low preoperative BMI ( $<18.5 \text{ kg/m}^2$ )<sup>18</sup> were also examined using the Student's *t*-test.

Statistical analysis was performed using SPSS software (version 27.0; IBM, Armonk, NY). The *p*-values  $< .05$  were considered statistically significant.

### 3 | RESULTS

#### 3.1 | Relationship between RTFV and BMI

Eighty-one patients with TSCC underwent tongue reconstruction and requested swallowing function examination at the Department of Dysphagia Rehabilitation at Tokyo Medical and Dental University Medical Hospital (Tokyo, Japan) between 2015 and 2021. However, due to difficulty of RTFV calculation by dental metal artifacts and lack of patient's weight data, we examined 32 of 81 patients as summarized in Table 1. The mean values of BMI and RTFV at the measurement timepoints are given in Table 2. RTFV increased in 18 and decreased in 14 patients, with no significant difference in preoperative BMI between these groups ( $p = .811$ ). Additionally, no

difference was found in RTFV rate changes in groups defined by postoperative radiotherapy ( $p = .132$ ) or low preoperative BMI ( $p = .306$ ).

The relationship between RTFV rate change and BMI difference is shown in Figure 2. A significant positive correlation was found between the RTFV rate change and the BMI difference ( $r = .594$ ,  $p < .05$ ). Multiple regression analysis was performed with the RTFV rate change as the dependent variable and age, sex, flap type, and BMI difference as the independent variables. The overall regression was statistically significant ( $p = .005$ ,  $R^2 = .453$ ). Among the independent variables, BMI difference ( $p = .001$ ) and flap type ( $p = .012$ ) were found to be significant explanatory factors for RTFV rate change (Table 3).

### 4 | DISCUSSION

We found a correlation between RTFV and BMI. In addition, multiple regression analysis showed that BMI and flap type significantly affected postoperative RTFV, while there was no difference in preoperative BMI and postoperative radiotherapy.

	n = 32			
	$\beta$	p-Value	95% CI	VIF
BMI difference (%)	.562	.001	0.039–0.143	1.145
Age (years)	-.107	.523	-0.007 to 0.004	1.299
Sex	-.016	.926	-0.164 to 0.150	1.249
Flap type				
Rectus abdominis musculoperitoneal flap	Reference			
Anterolateral thigh flap	-.206	.377	-0.307 to 0.120	2.489
Free radical forearm flap	-.544	.012	-0.501 to -0.068	1.917

Note:  $R^2 = .453, p = .005$ .

Abbreviations: 95% CI, 95% confidence interval; BMI, body mass index; RTFV, reconstructed tongue flap volume; VIF, variance inflation factor;  $\beta$ , standardized coefficient.

**TABLE 3** Multiple regression analysis of RTFV rate change.

#### 4.1 | Relationship between RTFV and BMI

The aggregated data of the RTFV was measured three-dimensionally using CT. It is possible to measure flap volumes, which have complicated shapes, more accurately by using three-dimensional measurements than using two-dimensional measurements. In a study of the anterolateral thigh flap, shrinkage was found to occur within 6 months after surgery, at which time the residual volume was 69.0% of that determined at 1 month postoperatively.<sup>14</sup> Additionally, analysis of RTFV changes by magnetic resonance imaging showed that fat will increase in free flaps between 6 months and 1 year after surgery.<sup>11</sup> Therefore, we calculated and compared the flap volume using CT images performed 6 months after the operation as a baseline with the CT examination performed 1.5 years after surgery.

The muscle content in flaps decreases over time, but fat volumes can increase, depending on the patient's condition.<sup>13</sup> One Japanese patient with tongue cancer who underwent subtotal glossectomy showed an increase in the flap fat volume over time with weight gain.<sup>19</sup> This study measured the total flap volume of 32 patients and found that the postoperative BMI change correlated with RTFV. BMI is a global nutritional indicator for managing the patients' nutritional status and thus flap volume.<sup>18</sup>

#### 4.2 | Factors affecting RTFV change

No significant difference was found in preoperative BMI between those with increased and decreased RTFV, consistent with a previous study's findings.<sup>15</sup> The study also found correlation between RTFV change at 6 months postoperative and preoperative triglyceride levels. In addition, correlation between RTFV change at 1 year postoperatively and preoperative albumin levels was found. Within 6 months postoperatively, high preoperative triglyceride levels led to a smaller decrease in RTFV, suggesting that RTFV is influenced by the patient's fat percentage. After postoperative 1 year, high preoperative albumin levels led to smaller decrease in RTFV, which suggested that preoperative nutritional status affects RTFV.<sup>15</sup> BMI, triglyceride, and albumin are all nutritional indices. However, since preoperative BMI

more strongly correlates with triglyceride levels than with that of albumin,<sup>20</sup> and the half-life of albumin is about 20 days while that of triglyceride is under an hour, the assessment time for nutritional status differs.<sup>21</sup> However the number of patients with low preoperative BMI (BMI < 18.5 kg/m<sup>2</sup>) was only 12.5% of the sample size in this study, making the number too small to determine preoperative nutritional status influencing RTFV change.

Multiple regression analysis showed that the RTFV change was significantly associated with BMI change and flap type, whereas age and sex did not affect RTFV change. While age and sex do not affect the volume change, the flap type is associated with the flap volume change in head and neck reconstruction.<sup>16</sup> The study differed from the present study in terms of free flap (anterolateral thigh flap) and pedicled flap (pectoralis major myocutaneous flap). We only compared free flaps, namely rectus abdominis, anterolateral thigh, and forearm flaps. When we examined the correlation between RTFV rate change and BMI difference by flap type, we found a correlation between rectus abdominis flap ( $r = .783, p < .05$ ) and anterolateral thigh flap ( $r = .685, p < .05$ ), but not the forearm flap ( $r = .170, p = .663$ ; Figure S1). This result suggests that fat-rich flap types may have strong correlations with BMI.

There are reports of the association of postoperative radiotherapy with RTFV volume decrease<sup>14</sup> and reports that counters it.<sup>11,13</sup> However, herein, there was no difference in RTFV rate changes between the group that underwent postoperative radiotherapy and the nonexposed group. Irradiated flap volume decreases due to fibrosis, which mainly occurs for 6 months after treatment<sup>22</sup>; the measurement in this study was done after completion of radiotherapy and so no difference in side effect was found.

#### 4.3 | Importance of maintaining RTFV

Tongue volume plays an important role in swallowing and articulation function.<sup>23</sup> In patients with TSCC, these functions are diminished owing to restricted tongue movement after tongue reconstruction.<sup>24</sup> Considering the decreased volume of the reconstructed tongue after surgery, the tongue is generally reconstructed to be larger than the

excised tissue.<sup>23</sup> However, if the patient's BMI decreases, their tongue volume will decrease further, making oral ingestion and speaking difficult.<sup>10</sup> Therefore, it is necessary for patients to understand the importance of perioperative management to maintain their BMI and reconstructed tongue volume. BMI assessment only requires weight evaluation and does not require any invasive procedure, such as blood sampling. Thus, for understanding their nutritional status, BMI is a simple indicator for patients, making it easy for them to manage their nutritional status and thus their RTFV.

#### 4.4 | Study limitations

Herein, the number of patients with poor preoperative nutrition (BMI < 18.5 kg/m<sup>2</sup>, accounting for only 12.5% of the sample size) was likely too small to determine whether preoperative nutritional status influences the rate of change in RTFV. Additionally, this was a retrospective study; prospective studies are needed to determine whether the differences of preoperative nutritional status really exist, and to identify other factors associated with the RTFV.

## 5 | CONCLUSION

We showed that changes in the RTFV correlate with BMI, which is a simple indicator of nutritional status. After TSCC surgery, reconstructed tongue volume plays an important role in swallowing and speaking. Although tongue volume decreases due to edema reduction and muscle atrophy, the volume of the tongue can increase reversibly by increasing BMI. Therefore, it is important for the patient to be well nourished to avoid a decrease in BMI and thus postoperative tongue volume so that the QOL is maintained in patients with TSCC after reconstruction surgery.

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#### CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest.

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#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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