Rev. Otorrinolaringol. Cir. Cabeza Cuello 2025; 85: 95-104
doi: 10.4067/S0718-48162025000100549 REVIEW ARTICLE

Comparison of functional outcomes of radial forearm and anterolateral thigh free flaps after hemiglossectomy in patients with tongue cancer: a systematic review and meta-analysis

Comparación de resultados funcionales posteriores a reconstrucción utilizando colgajos libres radial antebraquial y anterolateral de muslo en pacientes con cáncer de lengua sometidos a hemiglosectomía: revisión sistemática y meta-análisis

Luis Sepúlveda A.[1,2], Gonzalo Peralta J.[3], Vanessa Ampuero E.[1,2], Francisca Fernández A.[2]

Abstract

Introduction: One of the surgical challenges of tongue cancer its functional reconstruction. The radial forearm free flap (RFFF) is usually used in minor resections such as partial glossectomies, and the anterolateral thigh free flap (ALTFF) in subtotal and total glossectomies. In hemiglossectomy, there is controversy because there is no rigorous review that considers functional results. **Objectives:** To compare functional outcomes among patients receiving RFFF or ALTFF for tongue reconstruction after hemiglossectomies. **Material and Methods:** A comprehensive search was conducted in PubMed, EMBASE, and CENTRAL databases from inception until August 2023. This rigorous approach ensured that all relevant studies were included. Primary outcomes included speech and swallowing after hemiglossectomies reconstruction with RFFF or ALTFF, providing a comprehensive overview of the functional outcomes. **Results:** Our analysis included six studies meeting the criteria and involved 148 RFFF and 94 ALTFF patients. The key finding was the significantly better speech results in the RFFF group (SMD: 0.30; 95% CI [0.03, 0.56], p-value = 0.0301). However, there were no significant differences in swallowing outcomes, which warrants further investigation. **Conclusion:** Our findings indicate that the RFFF is associated with better speech results than the ALTFF for hemiglossectomies reconstruction. However, it's important to note that the RFFF also carries a higher risk of donor site complications. Therefore, when choosing the flap for reconstruction, the preferences of the surgeon and the patient should be considered, and the potential complications should be carefully considered.
Keywords: Glossectomy, Tongue Cancer, Speech Intelligibility, Swallowing Disorders, Microsurgical Free Flaps.

Resumen

Introducción: *Uno de los retos quirúrgicos del cáncer de lengua es su reconstrucción funcional. El colgajo libre radial antebraquial (RFFF, por sus siglas en inglés) se suele utilizar en resecciones menores, como las glosectomías parciales, y el colgajo anterolateral del muslo (ALTFF, por sus siglas en inglés) en las glosectomías subtotales y totales. En la hemiglosectomía, existe controversia porque no existe una revisión rigurosa que considere los resultados funcionales* ***Objetivos:*** *Comparar los resultados funcionales entre los pacientes que recibieron RFFF o ALTFF para la reconstrucción de la lengua posterior a una hemiglosectomía.* ***Materiales y Métodos:*** *Se realizó una búsqueda exhaustiva en las bases de datos PubMed, EMBASE y CENTRAL desde su inicio hasta agosto de 2023. Los resultados primarios incluyeron el habla y la deglución después de la reconstrucción posterior a una hemiglosectomía*

[1]Departamento de Otorrinolaringología, Universidad de Valparaíso, Valparaíso, Chile.
[2]Servicio de Otorrinolaringología, Hospital Carlos Van Burén, Valparaíso, Chile.
[3]Servicio de Salud Arica, Subdirección de Gestión Asistencial, Arica, Chile.

The authors declare no conflicts of interest.

Received 05 June 2024.
Accepted 02 March 2025.

Corresponding author:
Luis Sepúlveda A.
Calle del Sol 85, depto. 94, Concón, Valparaíso, Chile.
Email: luis.sepulvedaag@postgrado.uv.cl

ISSN 0718-4816 versión en línea - ISSN 0716-4084 versión impresa

utilizando RFFF o ALTFF, lo que proporcionó una visión general completa de los resultados funcionales. ***Resultados:*** *Nuestro análisis, que incluyó 6 estudios que cumplieron con los criterios, involucró a 148 pacientes con RFFF y 94 pacientes con ALTFF. El hallazgo clave fueron los resultados del habla significativamente mejores en el grupo RFFF (DME: 0,30; IC del 95% [0,03, 0,56], valor p = 0,0301). Sin embargo, no hubo diferencias significativas en los resultados de la deglución, un resultado que justifica una mayor investigación.* ***Conclusión:*** *Nuestros hallazgos indican que el RFFF se asocia con mejores resultados del habla que el ALTF para la reconstrucción con hemiglosectomía. Sin embargo, es importante tener en cuenta que el RFFF también conlleva un mayor riesgo de complicaciones en el sitio donante. Por lo tanto, a la hora de elegir el colgajo para la reconstrucción, se deben tener en cuenta las preferencias del cirujano y del paciente, y se deben considerar cuidadosamente las posibles complicaciones.*

Palabras clave: *Glosectomía, Cáncer de lengua, Inteligibilidad del Habla, Trastornos de Deglución, Colgajos Quirúrgicos.*

Introduction

The oral cavity is one of the most common cancers in the Head and Neck region. In 2020, it was estimated that there were 377,713 new cases of oral cavity cancer worldwide, with the tongue being the most common site[1]. The standard treatment in this type of tumor is surgical resection of the primary lesion (glossectomy), cervical lymph node dissection and radiotherapy, chemotherapy, or both as adjuvant therapy, depending on the histological report. In general, a partial glossectomy involves the resection of less than one-third of the tongue, hemiglossectomy consists of the resection of one-third to half of the tongue, subtotal glossectomy requires resection of half to three-fourths of the tongue, and total glossectomy involves resection of the entire tongue.

After tumor resection, primary reconstruction of the defect is essential to minimize morbidity. Restoring its form and function will be necessary since the tongue plays a vital role in speech and swallowing. Patients with early disease (T1, T2, and N0) generally have good outcomes, and the 5-year survival rates range from 75% to 89%[2-4]. The treatment includes wide excision with primary closure or wide excision with reconstruction. Oncological margins of 1.5 to 2 cm are recommended for squamous cell carcinomas; even small cancers can lead to relatively large surgical defects. Using a free flap for reconstruction achieved a large free margin, relatively lower recurrence, and good survival rates[5]. On the other hand, it presents better results regarding intelligibility, swallowing, and life quality[6-9].

Free flap reconstruction of an intraoral defect was first introduced in 1983 with the radial forearm free flap (RFFF)[10], subsequently expanding to various free flaps and surgical techniques to optimize postoperative function. But until today, the radial forearm flap is still the most popular one[11-16]. The radial free flap offers a surface area between 9x12 cm or greater if necessary[17]. The main advantages of this flap are: the vessels have a diameter similar to that of the cervical vessels, making an anastomosis easier to perform; it has a long pedicle; constant anatomy; it can be elevated simultaneously while performing oral ablation; has a potential for reinnervation through coaptation of the lateral antebrachial nerve with the lingual or inferior alveolar nerve; the flap is thin and foldable, allowing better manipulation when shaping the tongue, even raising it with additional adipose tissue to give greater volume; and the volume provided will be sufficient, avoiding difficulties during breathing or speech in the initial postoperative period[18-22].

On the other hand, the most significant disadvantage described in this type of flap is related to the high morbidity of the donor site. Forearm deformities resulting from loss of soft tissue, delayed healing, need for skin grafts to close the donor site, visible scars, changes in sensitivity, edema in the hand, and altered wrist mobility are the most frequently reported complications. In this sense, the literature reports 19-53% of partial skin graft loss at the donor site, 13-33% of flexor tendon exposure, and 16-100% of patients complaining of reduced grip strength[23]. Some of these problems, and particularly the need

for a skin graft to close the primary site, have been solved by introducing new methods, such as the use of tissue expanders or new designs to elevate the flap, such as suprafascial dissection and V-Y fasciocutaneous advancement based on the ulnar artery. However, this is possible in defects smaller than 6 x 4 cm, which is insufficient in many large tumors[24]. For this reason, alternative methods began to appear in the search for less donor site morbidity and, thus, the appearance of the anterolateral thigh flap.

The anterolateral thigh free flap (ALTFF), originally described by Song in 1984[25], is currently considered an alternative to the radial flap in head and neck reconstruction[26]. It provides a thin, pliable skin to replace the defect in the tongue after resection, where it not only acts as a bulge but allows the remaining tongue to have some degree of mobility. However, its anatomy is less consistent, sometimes leading to a more difficult harvest. Furthermore, its pedicle is typically shorter than RFFF ones[6]. Designing the skin flap more distally (closer to the knee) can increase the harvested pedicle length. This flap provides a large territory of skin and shows great versatility. Where it can be elevated as a flap as thin as the radial one, or in a case requiring bulkier tissue or multiple components are necessary, it is raised as a musculocutaneous flap combined with the vastus lateralis or tensor fascia lata muscle. With minimal compromise at the donor site[27], marginal necrosis of the inset ALTFF is the most common flap-specific complication, but total flap failure is rare.

Some authors have suggested that the bulkiness of an ALTFF leads to less mobility of the neotongue[28], obtaining better functional results with the RFFF[29]. In a direct comparison of tongue defects reconstructed with RFFF versus ALTFF, however, de Vicente et al. found no significant differences in postoperative speech intelligibility, tongue mobility, or deglutition. They concluded that because the ALTFF has less donor morbidity, it is a superior choice to the RFFF for tongue reconstruction[23]. Of note, a confounding factor in this study is that ALTFF is typically a much larger flap than RFFF. ALTFF is generally only used for larger glossectomy defects (usually larger than half of the tongue). Therefore, the RFFF is traditionally used in minor resections such as partial glossectomies, as a thinner and more flexible flap, and the ALTFF in cases of advanced tumors requiring subtotal and total glossectomies. However, in the case of hemiglossectomies, there is some controversy about it[30].

A rigorous review considering functional results has not been performed to determine the selection between these reconstructive options, specifically in the case of hemiglossectomies. Thus, we conducted a systematic review and meta-analysis to evaluate the current literature on speech and swallowing after hemiglossectomies and reconstruction with RFFF or ALTFF.

Material and Methods

This systematic review adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[31-32]. We searched PubMed, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL) from inception until August 30th, 2023, using a combination of the following keywords: (hemiglossectomy[Title/Abstract] OR glossectomy[Title/Abstract] OR tongue resection[Title/Abstract]) AND (radial forearm[Title/Abstract] OR radial artery[Title/Abstract]) AND (anterolateral thigh[Title/Abstract] OR femoral artery[Title/Abstract]). We used Rayyan for the screening process[33]. After removing duplicates, two independent reviewers perform a title and abstract screening. We selected potentially relevant studies that were retrieved and assessed in the full text against the eligibility criteria by two independent reviewers. We also screened reference lists of the papers chosen for other potentially valuable articles we may have missed in the initial search.

We used the following criteria to select papers for meta-analysis: This review considers studies that include patients with tongue cancer over 18 years old and undergoing anterolateral thigh or radial forearm free flap reconstruction after hemiglossectomies. If the study does not mention the type of surgery that was performed, those patients T2 and T3 according to the staging AJCC 8th edition[34] will be included. The study's primary outcome includes speech

and swallowing. Donor site morbidity, flap failure, other postoperative complications, and operation time are significant but not critical outcomes for this study. This review considers experimental and quasi-experimental study designs, including randomized control studies, non-randomized controlled trials, before and after studies, and interrupted time-series studies. Because of the lack of experimental and quasi-experimental studies, prospective and retrospective cohort studies and case-control studies were included. Studies were excluded if they were not published in English or Spanish, were unavailable in full text, or did not report our primary outcomes (**Figure 1**).

After completing the search, 6 studies[23,29,30,35-37] met the defined criteria, and we extracted their data. Information was collected by two reviewers independently. For conflicting evaluations, an agreement was reached after a discussion.

Data collection

We collected the following data: year of publication, first author, country of origin, number of cases according to RFFF and ALTF, Follow-up time, percentage of female patients, age, tumor stage, tumor size, concomitant radiotherapy, if ALTFF was made thinner, and primary and secondary outcomes. We extracted data from the included articles' text, tables, and figures. Our primary outcomes were speech and swallowing. Our secondary outcomes were operative time, donor site, flap failure, and other postoperative complications.

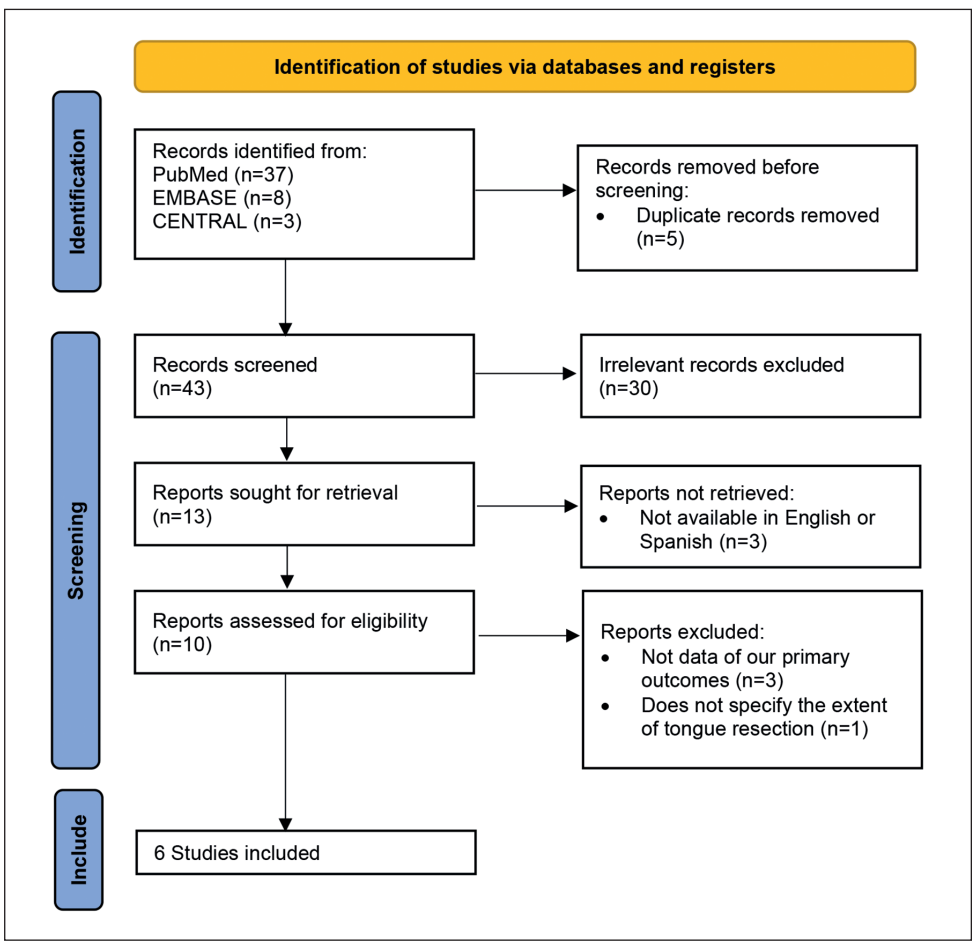

Figure 1. Flowchart of the literature search

Data analysis

We calculated standardized mean differences (SMD) and 95% confidence intervals (95% CI) to compare speech and swallowing outcomes. We used Cochran's Q and I2 statistics to assess heterogeneity. We considered heterogeneity low if I2 < 25%, moderate if 25% ≥ I2 < 75%, and high if I2 ≥ 75%. We combined the data using a fixed-effects or random-effects model if heterogeneity was low or moderate, respectively. We decided not to perform a meta-analysis if heterogeneity was high. We considered statistical significance if $p < 0.05$. We used R software and the meta library for data processing and analysis.

Risk of publication bias assessment

We assessed the risk of publication bias using funnel plots and Begg's and Egger's tests. We considered statistical significance if $p < 0.05$.

Results

Studies characteristics

We pooled a sample of 242 subjects, of which 80 were female (33.1%). Reconstruction after hemiglossectomies were performed with RFFF and ALTFF in 148 and 94 subjects, respectively.

Table 1 summarizes the characteristics of the studies included in the meta-analysis.

All of these studies were observational and retrospective in design. We excluded 11 patients from Cai et al. according to our inclusion criteria when the type of surgery was not specified. Speech and swallowing evaluation methods are described in **Table 2.**

Speech

We detected low heterogeneity between studies as of Cochran's Q = 6.26 for 5 degrees of freedom (p-value = 0.2820) and I2 = 20.1%. We found a statistically significant difference in favor of RFFF for speech (SMD: 0.30; 95% CI [0.03, 0.56], p-value = 0.0301). The results of the speech meta-analysis are shown in **Figure 2.**

The funnel plot and Begg's (p-value = 0.3476) and Egger's (p-value = 0.2615) tests are suggestive that there would be no significant publication bias.

Swallowing

We detected high heterogeneity between studies as of Cochran's Q = 31.57 for 5 degrees of freedom (p-value < 0.0001) and I2 = 84.2%. Given these results, we decided not to perform the swallowing meta-analysis.

Discussion

In a meta-analysis published in 2022 by Randanath et al.[38] comparing radial and anterolateral flaps in oral cavity defects, they found equivalent results regarding flap survival and oral function between the two flaps but less donor-site morbidity with the ALTFF. It also establishes that it is necessary to incorporate patient-specific factors into the decision. The reconstruction in each anatomical site and tumor stage will differ significantly when we have to decide the type of reconstruction to perform. In the case of lingual reconstruction, we consider that hemiglosectomy becomes an intermediate resection in terms of the percentage of volume resected. It needs to be clarified whether the greater volume provided by ALTFF during reconstruction would achieve better or inferior results than RFFF. In this sense, while some authors suggest that the bulkiness of the ALTFF would give Newspeak less mobility, others, on the other hand, establish that there would be no functional differences, favoring the latter due to its lower morbidity. In this study, it was possible to demonstrate that the radial flap would present better speech results than the ALTFF.

It is essential that previous interpretation of the results we take into account, as can be seen in Table 2, the authors used different methods for the evaluation of speech, from using percentage methods according to the intelligibility of post-reconstructive speech evaluated by speech therapists to the use of pre-established scales such as Teichgraeber et al.[39], which, although they are numerical variables, allows quantifying and comparing the results, indicates that there is currently no internationally standardized way to assess speech after reconstruction. On the other hand, concerning the swallowing result, we decided not to perform a meta-analysis of the data because there was a very high heterogeneity within the

Table 1. Studies' characteristics

Year	First author	Country of origin	Cases (RFFF; ALTFF)	Follow-up time	Women (RFFF; ALTFF)	Age (RFFF; ALTFF)	Tumor stage (RFFF; ALTFF)	Tumor size (RFFF; ALTFF)	Flap size (RFFF; ALTFF)	Thinned ALT flap	RT (RFFF; ALTFF)	Speech	Swallowing	Flap survival (RFFF; ALTFF)	Length of surgery (RFFF; ALTFF)	Donor site complications	Flap complications
2019	Cai	China	28 (17; 11)	Range: 6-48 months	14 (11; 3)	54,4[a] (53,8[a]; 55,4[a])	T2: 21 T3: 7	5,97 cm^2 (5,62 cm^2, 6,51 cm^2)	37,03 cm^2 (36,95 cm^2, 37,24 cm^2)	No	Yes[c] 55-60 Gy	ND	ND	100%	7,7 h (7,2 h; 8,3 h)	RFFF: 0 ALTFF: hematoma (1)	RFFF: Flap's tip necrosis (1) ALTFF: Vascular crisis (1), fat necrosis (1)
2018	Zhang	China	90 (59; 31)	Mean: 38.5 months Range: 24-76 months	35 (28; 7)	54,6[a] (54,3[a]; 55,1[a])	T2: 66 T3: 15 T4: 9	NR	42,01 cm^2 (40,6 cm^2, 44,7 cm^2)	No	Yes[d] 51 (32; 19) 56-60 Gy	RFFF better than ALTFF	RFFF better than ALTFF	100%	NR	NR	NR
2015	Lu	China	46 (34; 12)	3 months	16 (NR)	63,6[a] (NR)	Only T2 and T3. (NR)	NR	NR	Yes (4 mm)	NR	ND	ND	97,8% (97,1%; 100%)	NR	RFFF: Skin graft loss (3), paresthesia (9) ALTFF: 0	RFFF: Flap failure (1) Vascular crisis (3) ALTFF: Vascular crisis (1)
2013	Tarsitano	Italy	26 (12; 14)	6, 12 and 24 months	9 (NR)	50,0[b] (NR)	T2: 4 T3: 16 T4: 6	NR	NR	No	Yes[e] 15 (NR) 56-59 Gy	ND	ALTFF better than RFFF	NR	NR	RFFF: Skin graft loss (2) ALTFF: 0	RFFF: Minor complication (2) ALTFF: Minor complication (1)
2008	de Vicente	Spain	20 (10; 10)	6 months	6 (4; 2)	59,4[a] (56,5[a]; 62,3[a])	NR	NR	NR	No	Yes 16 (8; 8) 60 Gy	ND	ALTFF better than RFFF	NR	NR	RFFF: Skin graft loss (4), paresthesia (1) ALTFF: 0	NR
2008	Hsiao	Taiwan	32 (16; 16)	6 months	NR	NR	NR	NR	NR	Yes (4 mm)	NR	ND	ND	NR	NR	NR	NR

RFFF: Radial forearm free flap. ALTFF: Anterolateral thigh free flap. RT: Radiotherapy. ND: Non-statistically significant differences. NR: Not reported. [a]Mean. [b]Median. [c]25 patients received radiotherapy; however, it is not possible to tell from the text, tables, and figures whether this count includes those excluded. [d]Those patients with tumor stage T3-T4, node-positive, or with positive or close surgical margin received radiotherapy without reporting how many. [e]11 patients received radiotherapy and 4 patients received chemo- and radiotherapy.

Table 2. Assessment methods for speech and swallowing

Year	First author	Speech	Swallowing
2019	Cai	The reading accuracy of a 200-word essay was assessed. It was scored from 1 (accuracy > 90%) to 4 (unable to speak).	The type of feeding tolerated was evaluated. It was scored from 1 (regular diet) to 4 (nasal tube feeding).
2018	Zhang	The speech subscale of the University of Washington Quality of Life Scale was applied. It was scored from 1 (worst) to 100 (best).	The University of Washington Quality of Life Scale's swallowing subscale, was applied. It was scored from 1 (worst) to 100 (best).
2015	Lu	Two speech therapists evaluated recordings of the subjects' voices and determined their intelligibility in percentage terms.	The intake rate (ml/s) of 175 milliliters of water was evaluated.
2013	Tarsitano	Intelligibility was assessed using a 5-point Likert-type scale (speech can be understood = 1; speech is not understood at all = 5). Three categories were created from these scores (1 or 2: good; 3: acceptable; 4 or 5: poor).	The method of ingestion, time taken to ingest, and consistency of the food consumed were evaluated with a 5-point Likert-type scale for each aspect. Three categories were created from these scores (9 to 15: good; 7 or 8: acceptable; 3 to 6: poor).
2008	de Vicente	Intelligibility was evaluated by a speech therapist using the method described by Teichgraeber *et al.* The intelligibility was scored from 1 (worst) to 7 (best).	Swallowing was evaluated by a speech therapist using the method described by Teichgraeber *et al*. Swallowing was scored from 1 (worst) to 7 (best).
2008	Hsiao	A speech therapist and a plastic surgeon evaluated recordings of patients' voices using the methods described by Sultan and Coleman and Teichgraeber *et al*. The patients were scored from 1 (worst) to 7 (best).	The intake rate (mL/s) of 175 milliliters of water was evaluated according to the method described by Dios *et al*.

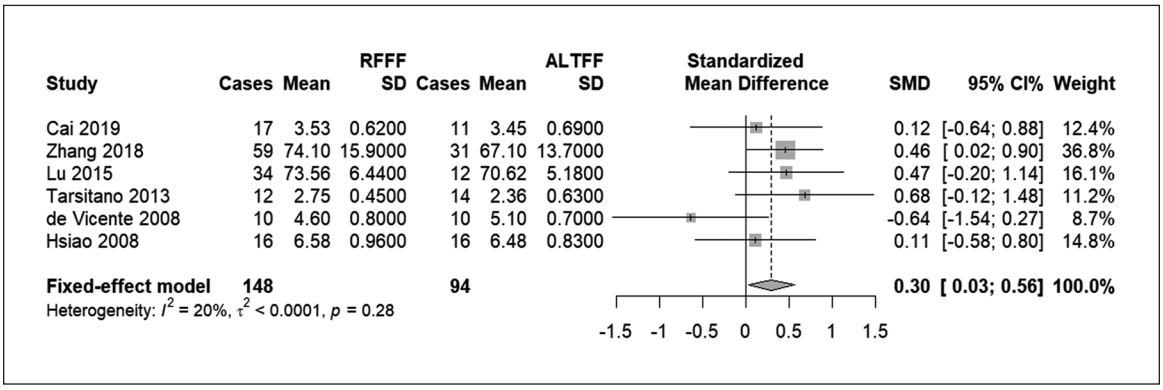

Figure 2. Forest plot of speech results. RFFF: Right free forearm flap. ALTFF: Anterolateral thigh free flap. SMD: Standardized mean difference."

measurement parameters between the studies, and we would be analyzing a data cloud rather than a data set with a trend. This leads us to raise the need to create a standardized scale for evaluating patients undergoing glossectomies in their different extensions to unify the results of further research and obtain statistically significant results.

Analyzing the collected data, we noticed that Zhang et al.[29] were the principal authors who found advantages of the RFFF over the ALTFF in speech and swallowing. They were the only ones who used subjective evaluation tools to assess the results of their study with the information given by patients. In contrast, the rest of the authors used objective evaluation tools completed by professionals. It would be useful and will improve the quality of the evidence on this subject to simultaneously use objective and subjective measures of function achieved after reconstructive surgery to adequately assess postoperative outcomes regarding patient well-being and satisfaction and the quality and safety of the surgical technique.

Another factor to consider when choosing the flap to use is the risk of complications associated with the surgical technique, where both the complications of the flap itself and those of the donor site matter. Within the data collected, when focusing on the donor site, it is observed that in those who used RFFF, seven patients presented partial losses of the free skin graft used to cover the donor site, which required postoperative healing to complete the closure of the donor site. Ten patients presented paresthesia in different degrees after surgery, mainly of the fingers, self-limiting in one case and without specifying the evolution of the others. In those who used ALTFF, only one patient had a complication related to a donor site hematoma. Regarding flap complications, in whom an RFFF was performed, two patients presented necrosis of the tip of the flap, and three patients presented a vascular crisis of the flap requiring reoperation for its rescue, not achieving in only one case that was established as flap failure. In those reconstructed using ALTFF, one patient presented flap necrosis, and two presented vascular crises that required reintervention for rescue without presenting failures.

The authors' Lu et al.[35] and Hsiao et al.[37] were the ones who thinned the ALTFF. Neither study found any statistically significant differences in swallowing or speech. Considering the lower donor site morbidity of ALTFF, with only one case of a hematoma, compared to RFFF, with nine cases of partial skin graft loss and ten cases of paresthesia of the donor site. It can be an excellent alternative for tongue reconstruction after hemiglossectomies. However, more studies should be conducted before establishing it as a flap of choice for this reconstruction. We also realized that only two studies mentioned the size of the used flap and that no study mentioned whether the flap presented any changes after receiving radiotherapy. These variables are important and should be considered in future investigations.

Based on the results obtained, we can conclude that RFFF has better functionality than ALTFF concerning speech but, simultaneously, a higher rate of donor site complications. This underscores the importance of considering the lesion's size and location, the surgical team's experience, and the patient's preferences before choosing the flap to be used. Educating the patient about the functional results of both flaps and the possible complications associated with each technique is also crucial. This personalized approach to treatment decision-making can significantly impact patient outcomes and satisfaction.

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