Do medial sural artery perforator flaps have better clinical outcomes compared to the rectus abdominis perforator (DIEAP) flap in reconstruction of glossectomy defects? A Prisma guided meta-analysis

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Abstract

Background: There is an increasing evidence for the use of thin flaps based on vascular perforators for reconstructive surgeries. The medial sural and deep inferior epigastric artery flaps offer versatility for the reconstruction of major defects of the head and neck. **Objectives:** "Whether medial sural artery perforator (MSAP) flap or rectus abdominis perforator flap is better for the reconstruction of glossectomy defects in terms of functional outcome?" **Data Sources:** PubMed, Cochrane Library, clinicaltrials.gov and hand searches. **Participants and Interventions:** Patients who underwent tongue reconstruction with either MSAP flap or deep inferior epigastric artery perforator (DIEAP) flap. **Study Appraisal and Synthesis Methods:** Based on defined study criteria 6 studies were selected according to Prisma Guidelines. The overall estimated effect was categorized as significant where P < 0.05. **Results:** There was no significant difference between both flaps in terms of receptor site complications (P = 0.223). Overall odds ratio (OR) for complications was 1.35 (95% confidence interval [CI]: 0.412–0.736) and the test for overall effect t value was 2.836, P < 0.05. Overall OR was 6.01 (95% CI 0.5–7.45) and the test for overall effect t value was a statistical difference in the intelligibility of speech. **Limitations:** Anatomical variations, under-reporting of studies and lack of universal tool for speech intelligibility. **Conclusions and Implications of Key Findings:** Both the flaps are comparable in terms of functional outcome. Medium-sized defects can be reconstructed with MSAP and composite larger defects would benefit from DIEAP. In females, anterolateral thigh flap still remains the choice for composite reconstructions.

Keywords: Arteries, epigastric artery, flap, medial, perforator, sural

INTRODUCTION

The tongue is one of the most common sites for oral cancer^[1] and histologically the well-differentiated squamous cell carcinoma predominates the subtype.^[2] The function of the oral tongue involves speech, mastication, articulation of speech, and oral phase of swallowing, whereas the oropharyngeal/base of the tongue is required for the pharyngeal phase of swallowing and preclusion of aspiration. Therefore, it is inevitable to immediately reconstruct the defect after excising the tumour.^[3,4] Reconstruction of these defects must discourse the different functions the oral and the pharyngeal part of the tongue serves. Traditionally, the reconstruction of the tongue like other sites followed the reconstructive ladder; primary closure, healing

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by secondary intention, skin grafts, local flaps, pedicled, and free flaps.^[5-10] PMMC (pectoralis major myocutaneous) flap is the most sought-after pedicled flap, as it is easy to

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harvest and is more reliable compared to other flaps. A major disadvantage of pedicled flaps is the tethering of the pedicle, which limits pliability of the flap and tongue motion and also their excess bulk.^[11] Due to these disadvantages of pedicled flaps, the concept of free tissue transfer gained attention. Options of free tissue transfer for tongue reconstruction include the radial forearm flap, anterolateral thigh (ALT) flap, rectus abdominis myocutaneous flap, the latissimus dorsi myocutaneous flap, the ulnar forearm flap, and the medial sural artery perforator (MSAP) flap.[12] The radial forearm flap is frequently considered ideal for intraoral reconstruction, but the disadvantages such as sacrificing a major artery to the hand and significant donor site scarring limits the use of this flap.^[13] Recently, perforator flaps gained popularity as reconstructive options for head and neck defects. The ALT flap is the most popular choice in subtotal or total glossectomy. However, the bulkiness of the flap may result in food retention and speech inarticulacy.^[14] Therefore, reconstructive surgeons have recently started to opt for other flaps that can both suffice the requirement and cause minimal morbidity of the donor site, such as MSAP flap and deep inferior epigastric artery perforator flap (DIEAP). Cavadas et al. in 2001, first reported the anatomy of MSAP flap.^[15] According to Hung et al. the MSAP flap is a small- to medium-sized flap, which can be used for reconstruction of subtotal glossectomy defects where optimal outcomes can be achieved in terms of speech clarity and restoration of oral intake. The use of the DIEAP flap has three potential advantages over its conventional musculocutaneous variant. A long pedicle length, ability to mold and trim the adipose tissue and lack of muscle nullifying the complications related to muscle atrophy are the potential advantages.^[16] Hence, we conducted a systematic review (SR) and meta-analysis to evaluate the outcomes of glossectomy reconstruction with DIEAP or the MSAP flap.

METHODS

The current review has been prepared according to the Equator guidelines (equator-network.org) and Prisma-statement (prisma-statement.org). The Prospero ID for the manuscript: CRD42021231567.

Study design

Eligibility criteria

The PICOS questionnaire has been used to assess the eligibility of the studies.

Focus question

Whether MSAP flap or rectus abdominis perforator (DIEAP) flap is better for the reconstruction of glossectomy defects in terms of functional outcome?

Inclusion criteria

Clinical trials, case-control or cohort studies evaluating the functional outcome of MSAP flap and DIEAP in reconstruction of glossectomy defects. Studies with definitive data on at least one or more of the following: Flap complications, functional outcome (speech and swallowing), tracheostomy, adjuvant therapies, etc., were included.

Exclusion criteria

Case reports, technical reports, animal studies, cadaver studies, *in vitro* studies, and review papers were excluded. The studies comparing the above-mentioned flaps with any other reconstructive options and modified variations of the considered flaps were also excluded. The studies involving the reconstruction of composite defects of the oral cavity and those evaluating secondary reconstruction with the above-mentioned flaps were also excluded.

Information source

Electronic database: MEDLINE (PubMed), https://www. ncbi.nlm.nih.gov/pubmed/; EMBASE, https://www.embase. com/; and Cochrane database http://www.cochranelibrary.com.

Others: Hand searches were done where articles or abstracts were not available electronically.

Search Terms: Medial[All Fields] AND sural[All Fields] AND ("arteries"[MeSH Terms] OR "arteries"[All Fields] OR "artery"[All Fields]) AND ("perforator flap"[MeSH Terms] OR ("perforator"[All Fields] AND "flap"[All Fields]) OR "perforator flap"[All Fields]) AND deep[All Fields] AND inferior[All Fields] AND ("epigastric arteries"[MeSH Terms] OR ("epigastric"[All Fields] AND "arteries"[All Fields]) OR "epigastric arteries"[All Fields] OR ("epigastric"[All Fields]) OR "artery"[All Fields]) OR ("epigastric artery"[All Fields]) AND "artery"[All Fields]) OR "epigastric artery"[All Fields]) AND perforator[All Fields].

Study selection

Two reviewers screened all identified titles and abstracts independently. In addition, the reference lists of the subsequently selected abstracts and the bibliographies of the SR, human randomized and nonrandomized controlled trials (RCTs) and; prospective and retrospective cohort studies were searched manually. For studies appearing to meet the inclusion criteria, or for which insufficient data in the title and abstract was available, the full text was obtained. Disagreements were solved through discussion between the reviewers. Finally, the full-text evaluation of the remaining publications was done using the above-listed inclusion and exclusion criteria.

Data extraction

Two reviewers independently extracted data from the included studies. Disagreements were again resolved through discussion. Corresponding authors were contacted when data were incomplete or unclear. With respect to the listed question of our SR, data were sought for predictor variables, i.e., MSAP flap, rectus abdominis perforator or DIEAP, reconstruction of glossectomy defects. Both reviewers evaluated the outcome of individual studies, which were recipient and donor site complications, flap thickness, pedicle length, number of perforators, and functional outcome. Finally, the funding sources of the selected studies have been checked.

Quality of the studies

The quality assessment of the selected studies was executed by the Newcastle-Ottawa scale. Scale was applied for cohort studies to judge each included study on the selection of studies, comparability of cohorts, and the ascertainment of either the exposure or outcome of interest. Stars were awarded such that the highest quality studies were awarded up to nine stars. The level of evidence of each study was evaluated using the oxford evidence guidance and were graded from II to IV.

The oxford 2011 levels of evidence^[17]

- *Level Category of evidence* i. SR (with homogeneity) o
 - SR (with homogeneity) of RCTIndividual RCT
- ii. SR (with homogeneity) of cohort studies
 - Individual cohort study (including low-quality RCT. For example <80% follow up)
 - "Outcome" research; ecological studies.
- iii. SR (with homogeneity) of case-control studies
 - Individual case-control study.
- iv. Case series and poor-quality cohort and case-control studies
- v. Expert opinion without explicit critical appraisal, or based on physiology, bench research, or first principles.

Statistical analysis

Statistical software RevMan (Review Manager [Computer program], version 5.3, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for statistical analysis. Differences in means and risk ratios were used as principal summary measures. The overall estimated effect was categorized as significant where P < 0.05. For detection of any possible bias in sample sizes, the odds ratio (OR) and its 95% confidence interval (CI) for each study were plotted against the number of participants. We used a Chi-square-based Q test to assess heterogeneity. The significance of the pooled OR was calculated by the *t*-test. In addition, *I*-square value is another test of heterogeneity. Bias across the studies was assessed using I square test and Chi-square statistics.

RESULTS

579 articles published before February 2020 was identified. On the basis of defined study criteria, 6 studies were selected for meta-analysis [Figure 1].

Study characteristics

Demographics and reconstructive outcomes

6 clinical papers that included 66 patients with 53 MSAP flaps (80.30%) and 13 rectus abdominis perforator flaps (19.69%) were independently selected by each reviewer for inclusion in the final meta-analysis [Table 1]. We established a database into which we entered the information extracted from each paper stating the main characteristics and outcomes [Table 2]. The meta-analysis of outcomes with a fixed-effect model is shown in Table 3, which shows the level of heterogeneity among the studies.

Recipient site complications

All studies except for Ozkan *et al.* studied receptor site complications. Fifty-three patients who were reconstructed with MSAP flap; flap loss was observed in 3 cases, 4 showed acute complications, 3 showed wound infection, one had undergone anastomosis revision and perforator transection was also observed in one case. Whereas, of the 13 DIEAP patients 2 showed fistula formation, one flap necrosis and 1 showed tongue necrosis. The test value was Chi-square = 3.819 with two degrees of freedom (df) and P = 0.223. Overall OR for the survival of the MSAP flap compared with DIEAP was 1.52 (95% CI 0.660–0.679), Student's *t*-test was done indicating there was no significant difference between both flaps regarding receptor site complications [Table 3]. Forest plot graph was made to show the level of receptor site complications observed in all selected studies [Figure 2].

Donor site complications

Only one study by Hung *et al.* showed donor site complications. Of 27 patients, 5 patients had hypertrophic scar and pigmentation, 6 showed itching and one showed paraesthesia. Forest plot graph was made to show level of complications observed in all selected 6 studies [Figure 3].

Functional outcome (deglutition and speech)

Speech and deglutition had considerable variations in reporting. However, most of the studies considered speech to be intelligible and deglutition normal. Five papers reported on swallowing capacity and the test value of heterogeneity was Chi-square = 0.15, with 1 df in a fixed-effect model, suggesting an absence of heterogeneity. Overall OR for complications was 1.35 (95% CI: 0.412–0.736) and the test for overall effect *t* value was 2.836, P < 0.05, indicating there was statistical difference in swallowing capacity between the two flaps [Table 3 and Figure 4].

Intelligibility of speech

Except Ozkan *et al.* five papers reported the intelligibility of speech. The test value of heterogeneity was Chi-square = 5.93, with 1 df and $I^2 = 42\%$, in a fixed-effect model, suggesting an absence of heterogeneity on the intelligibility of speech. Overall OR was 6.01 (95% CI 0.5–7.45) and the test for overall effect t value was 1.41, P < 0.05 indicating there was a statistical difference in the intelligibility of speech [Table 2 and Figure 4].

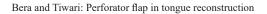
Quality assessment and bias

The Newcastle Ottawa Scale revealed studies with moderate quality. The Oxford Level Evidence showed the studies included were Grade II-IV. $I^2 < 50\%$ indicated a moderate level of heterogeneity. Chi-square values indicate bias within the studies [Table 3].

DISCUSSION

Özkan *et al.*^[18] reviewed the clinical applications of MSAP flap in head and neck reconstruction. The study included 1 case of hemiglossectomy and 1 case of total glossectomy.

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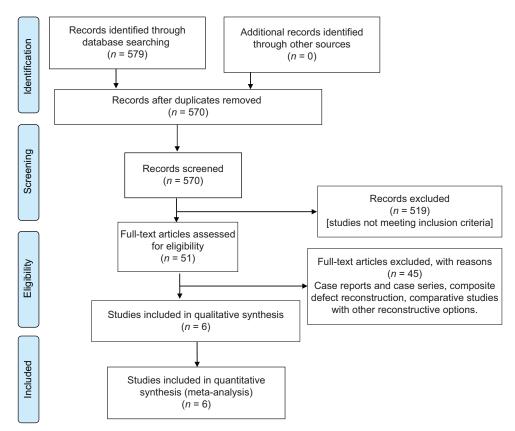


Figure 1: Flowchart for patient selection

Table 1: Demogra	aphic table			
Author reference number	Country	Number of cases	Reconstructive option used	Defect (hemiglossectomy/partial glossectomy/subtotal glossectomy/total glossectomy/total glossectomy/oral tongue/base of tongue)
Özkan <i>et al</i> . ^[18]	Turkey	2	MSAP flap	Hemiglossectomy (1)
				Total glossectomy (1)
López-Arcas	Spain	7	DIEAP flap	Total glossectomy (5)
<i>et al.</i> ^[19]				$3/4^{\text{th}}$ glossectomy (2)
Chen et al.[20]	Taiwan	15	MSAP flap	Hemiglossectomy
				Subtotal glossectomy
Hung et al.[21]	Taiwan	27	MSAP flap	Subtotal glossectomy
Wolff et al.[22]	Germany	9	MSAP flap	Subtotal glossectomy
Zhang et al.[23]	China	6	DIEAP flap	Total glossectomy
				Subtotal glossectomy

MSAP=Medial sural artery perforator; DIEAP=Deep inferior epigastric artery perforator

No complication was found with either of the cases. 8 flaps had single perforator and double perforators were present only in a single case. They concluded on the note that the radial forearm flap requires the sacrifice of a major artery whereas ALT flaps although having a long pedicle requires tedious flap thinning. The advantages cited in favor of MSAP include a thin and pliable flap with a long pedicle, less hair growth, and minimal damage to the underlying muscle. The sural nerve, lesser saphenous vein and plantaris tendon can also be harvested along with the flap. Perforator disparities and dreary dissections may be considered as the disadvantages of the flap. López *et al.*^[19] evaluated the efficacy of the DIEAP for total and subtotal glossectomy. Except for one patient who developed fistula, there was no major complications associated with the flap. The functional outcomes were poor considering the extent of the defect, 57.1% of patients required permanent gastrotomy feeding tubes. The speech was considerably comprehensible in 85.7% of patients. The main advantage of the flap includes a large skin paddle without compromising the abdominal musculature. Again, tedious perforator dissection has been considered a drawback of the flap.

Chen *et al.*^[20] reconstructed 15 glossectomy defects with MSAP flap. Except for flap loss in one patient, there

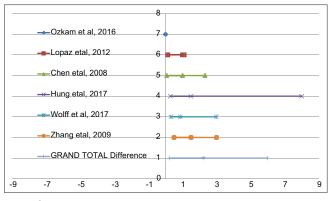


Figure 2: Forest plot for recipient site complications

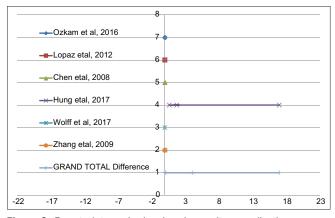


Figure 3: Forest plot graph showing donor site complications among various studies

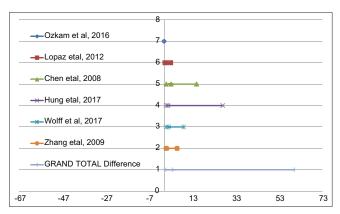


Figure 4: Forest plot graph showing functional outcome among various studies

were no complications associated with the flap. Speech was considered to be intelligible and deglutition was also normal in the majority of patients. The thin pliable flap can be used to cover smaller defects of buccal mucosa and floor of the mouth where increased suppleness of the flap is a necessity and increased bulk may negate this function. A folded MSAP flap may be suitable in smaller defects and a folded and rolled flap may be required in larger glossectomy defects. Hung *et al.*^[21] and Wolff *et al.*^[22] in their respective studies showed intelligible speech and normal to good deglutition with the MSAP flap. Zhang *et al.*^[23] reconstructed tongue with the DIEAP flap and also observed normal to intelligible outcomes in terms of speech and swallowing.

It was in 1989 when Koshima and Soeda reconstructed the floor of mouth and groin defects with inferior epigastric artery skin flap without the rectus muscle, noting that a large flap could essentially survive on a single perforator.^[24] Kroll and Rosenfield suggested that perforator flaps combine the dual advantage of a reliable blood supply of a musculocutaneous flap and reduced morbidity of a skin flap.^[25] Perforator flaps provide freedom of orientation and a long vascular pedicle unlike the parent musculocutaneous flap, hence a large area of tissue can be harvested based on a single reliable perforator.^[26,27] Perforator flaps offer several advantages over conventional microvascular free tissue transfer.[28-30] The DIEAP is based on the aforementioned vessel, originally harvested as a musculocutaneous flap for breast reconstruction. The conventional rectus abdominis free flap is commonly used for reconstructing glossectomy defects, however; it may result in abdominal weakness and hernia formation.[31-33] The DIEAP flap can be used to reconstruct a variety of intraoral defects without causing significant donor site morbidity.^[34,35] Cavadas et al. first described the MSAP flap in lower limb and foot reconstruction. For the reconstruction of defects in the head and neck region, the MSAP flap can achieve similar results like the radial forearm free flap without the donor site morbidity associated with the radial forearm flap.^[36,37] Futter *et al.*^[33] in their study showed that compared to the Transverse Rectus Abdominis (TRAM) flap the DIEAP flap had significantly lesser abdominal weakness although the DIEAP group had weaker abdominal strength as compared to the control group. Postoperatively patients reconstructed with DIEAP flap were reported to require a reduced hospital stay and decreased requirement of morphine compared with the TRAM flap.^[38] Woodworth et al.^[39] in their study reviewed the abdominal muscle-sparing free flaps in head and neck reconstruction. They conferred that muscle atrophy occurs after microvascular reconstruction, questioning the utility of muscle transfers with the rectus free flap. DIEAP flap is particularly preferred in male patients than females owing to the bulkiness of the flap. In female patients, the ALT Flap is preferred.^[40] Problems encountered in female patients have been described by Zhang et al.,[23] the bulkiness of the flap and a smaller perforator diameter favors ALT flap over DIEAP for head neck reconstruction in females. The average diameter of the DIEAP flap varies among Chinese (2.25 mm) and western individuals (3.4 mm). Empirically, the perforator diameter is smaller in females making anastomosis difficult.^[41] López-Arcas et al. concluded that the DIEAP flap is particularly suitable for total tongue reconstruction as it provides a large amount of soft tissue that can be harvested predictably.

Wolff *et al.* in their study showed a flap loss of 10%. They stressed on the major disadvantage of all perforator flaps,

Table 2: Ma	in characteristi	Table 2: Main characteristics and outcome of included	luded studies								
Author reference number	Flap/cases	Recepter site complications	Donor site complications	Pedicle length (cm)	Flap size (cm)	Flap thickness (mm)	Number of perforator	Deglutition	Speech	Operating time (h)	Mean age (years)
Ozkan <i>et al</i> .	MSAP (2)	No	No	16		I	2		1	5.20	60
López-arcas	DIEP(7)	Fistula-1	No		16.7×7.2	ı	2-4	Poor	85.7%	ı	63.14
et al.	Retrospective	No-6							success		
Chen et al.	MSAP (15)	Flap loss-1	No	6	10×6	5.7	1-2	Good	Intelligible	·	53.3
Hung et al.	MSAP (27)	Wound infection-3	Scar-5	12.7	12.1×5.2	5.2	1-2	Good	Intelligible	6.18	52.4
	Retrospective	Acute comp-4 Flap loss-1	Itching-6 Pigmentation-5 Paresthesia-1								
Wolff <i>et al</i> .	MSAP (9) Petrosnective	Loss of flap-2 Ansetomocic revision_1	No	8	5×7	I	2	Normal	Normal	ı	61
	ov mondeo movi	Perforator transection-1									
Zhang <i>et al</i> .	DIEP (6) Retrospective	Flap necrosis-1 Fistula-1	No		5×7	I	7	Normal	Intelligible	6.9	48
		Tongue necrosis-1									
MSAP=Medial	sural artery perfor	MSAP=Medial sural artery perforator; DIEP=Deep inferior epigastric perforator	gastric perforator								

the variability of the perforator vessels. They stated that colour Doppler ultrasound or CT Angiography is particularly reliable over handheld Doppler. They concluded that perforator flaps from the lateral or medial lower leg can provide satisfying results in small to medium-sized defects with lower donor site morbidity. Chen et al. concluded that the MSAP flap can be utilized for both hemiglossectomy and subtotal glossectomy defects. For partial or hemiglossectomy defects a folded MSAP flap is appropriate. Cases with subtotal glossectomy can be managed with a folded and rolled MSAP flap. The flap maintains the function of the medial gastrocnemius muscle and also does not sacrifice any major vessel of the lower leg. The DIEAP flap can be raised in varying design patterns (3-4 lobed flaps). The versatility of the flap can be used to reconstruct 3-dimensional extensive defects of the head and neck region with a variety of design modifications.^[42,43] The MSAP flap can be considered as a new workhorse flap in Head Neck reconstruction owing to its potential advantages.^[44]

Our meta-analysis included six studies, of which four studies discoursed about the MSAP flap and two studies conferred regarding the DIEAP flap. There were no differences between survival of the flap, complications at receptor site, and operating time (P > 0.05) but we found a statistical difference between two flaps regarding donor site complications and functional outcomes including intelligibility of speech and swallowing capacity. MSAP flap showed better functional outcome in terms of deglutition and speech compared to the DIEAP flap [Table 3]. The recipient site complications using MSAP flap were less (22.64%) compared to the DIEAP flap (30.77%). Donor site complications were noticed in a retrospective study by Hung et al. who observed 27 patients using MSAP flap, out of which 17 patients had donor site complications. The main disadvantage was itching, followed by pigmentation, hypertrophic scar, and paraesthesia at the donor site. There is a considerable lack of evidence on donor site complications to draw out definitive conclusion and hence meta-analysis could not be performed.

The following conclusions can be drawn from the study:

- The DIEAP flap is a reliable alternative for total tongue reconstruction, as it provides a large amount of soft tissue that can be transferred predictably and stably, and the donor site morbidity and surgical complications are minimal. This flap spares the whole rectus abdominis muscle and sheath, and therefore, lessens donor site morbidity
- The MSAP flap is a reliable alternative to the radial forearm free flap for tongue reconstruction particularly partial or hemiglossectomy defects. The inconsistent perforator anatomy and tedious dissections are the only major drawbacks. MSAP flap has better functional outcomes compared to the DIEAP flap. However, although limited complications were seen with MSAP flap the difference with DIEAP is not statistically significant

Table 3: Meta analysis								
Results	Heterogeneity test			OR	RR	95% CI	Overa	all test
	χ^2	df	Р				t-test	Р
Recepter site complications	3.819	2	0.223	1.52	1.36	0.660-0.979	1.890	0.199
Donor site complications	-	-	-	-	-	-	-	-
Flap size	2.773	1	0.157	34.56	24.35	63.48-85.18	0.029	0.982
Deglutition	0.15	1	0.013*	1.35	2.67	0.412-0.736	2.836	0.003*
Speech	5.93	1	0.022*	6.01	5.23	0.5-7.45	1.41	0.016*
Operating time (h)	2.917	3	0.087	0.05	1.08	41.96-45.44	0.506	0.702

* Significance <0.05, *I*² was obtained <50% in all the parameters, suggesting absence of heterogeneity. OR=Odd ratio; RR=Relative risk; CI=Confidence interval

- Operating time does not differ significantly between the two flaps considered
- In females, owing to the smaller perforator diameter and bulkiness of the DIEAP flap, either ALT can be used for total glossectomy defects or MSAP for partial glossectomy defects.

Limitations of the study

- There is no universal tool for reporting for speech and deglutition amongst the studies. Hence, chances for bias are there
- The studies used in the review are from Asian and European populations, the perforator caliber is thought to be different amongst them. Three papers are from Asia, and three from Europe, but around 72.78% of the cases are from the Asian population. This may cause bias related to uniformity in thickness of flaps, perforator size
- The included studies are not uniform regarding the demographic data; race, age, sex, or other factors
- Most of the studies are under-reported in terms of follow-up and complications
- The forest plot graphs created in our study relate to complications and functional outcomes. However, the predictability of the result varies because of variation in patient distribution receiving the flaps, MSAP (53), DIEAP (13)
- We found only six relevant studies that satisfied our inclusion and exclusion criteria, relating to biasing in the meta-analysis. Out of six studies, four of them are retrospective studies and two are prospective studies. The level of evidence is inadequate.

CONCLUSION

In summary, our findings showed minimal donor site complications and a high degree of patients' satisfaction when the DIEAP flap was used in the reconstruction of the tongue, and both flaps gave reasonable results. To establish the optimal treatment for patients having glossectomy defects, however, further prospective studies and quality-of-life assessments that involve larger numbers of patients are necessary.

Clinical Relevance

The DIEAP flap can be used as an alternative flap to the ALT for

total tongue reconstruction, particularly in males. In females, ALT still remains the flap of choice. The MSAP can be chosen as an alternative to radial forearm free flap owing to greater patient acceptance and a less conspicuous scar.

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Conflicts of interest

There are no conflicts of interest.

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