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Definitive Closure of the Tracheoesophageal Puncture Site after Oncologic Laryngectomy: A Systematic Review and Meta-Analysis

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Abstract

Tracheoesophageal puncture (TEP) and voice prosthesis insertion following laryngectomy may fail to form an adequate seal. When spontaneous closure of the fistula tract does not occur after conservative measures, surgical closure is required. The purpose of this study was to summarize the available evidence on surgical methods for TEP site closure.

A comprehensive search across PubMed, Web of Science, SCOPUS, and Cochrane was performed to identify studies describing surgical techniques, outcomes, and complications for TEP closure. We evaluated the rate of unsuccessful TEP closure after surgical management. A meta-analysis with a random-effect method was performed.

Thirty-four studies reporting on 144 patients satisfied inclusion criteria. The overall incidence of an unsuccessful TEP surgical closure was 6% (95% confidence interval [CI] 1–13%). Subgroup analysis showed an unsuccessful TEP closure rate for silicone button of 8% (95% CI < 1–43%), 7% (95% CI < 1–34%) for dermal graft interposition, < 1% (95%

Keywords
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- wound closure techniques
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CI < 1–37%) for radial forearm free flap, < 1% (95% CI < 1–52%) for ligation of the fistula, 17% (95% CI < 1–64%) for interposition of a deltopectoral flap, 9% (95% CI < 1–28%) for primary closure, and 2% (95% CI < 1–20%) for interposition of a sternocleidomastoid muscle flap.

Critical assessment of the reconstructive modality should take into consideration previous history of surgery or radiotherapy. Nonirradiated fields and small defects may benefit from fistula excision and tracheal and esophageal multilayer closure. In cases of previous radiotherapy, local flaps or free tissue transfer yield high successful TEP closure rates. Depending on the defect size, sternocleidomastoid muscle flap or fasciocutaneous free flaps are optimal alternatives.

Introduction

Historically, voice rehabilitation after laryngectomy was focused on using esophageal speech or electronic larynx, but since the introduction of the Blom-Singer Duckbill prostheses (InHealth, Carpinteria, CA) a more intelligible and fluent speech has been reported.[1,2] Nonetheless, progressive tracheoesophageal puncture (TEP) widening and leakage of saliva and liquids around the valve into the trachea can result in persistent episodes of aspiration and pneumonia.[1–3]

Placement of a nasogastric (NG) tube to prevent aspiration and removal of the valve waiting for spontaneous narrowing of the fistula is usually the first technique attempted in all such situations unless the fistula is of an atypical massive size. other conservative approaches such as replacement with silicone ring expanded prosthesis,[4] purse-string sutures,[5] hyperbaric oxygen therapy,[6] or injections of different substances such as autologous fat,[6] hyaluronic acid,[7] and granulocyte-macrophage colony-stimulating factor to reduce the diameter of the tracheoesophageal fistula (TEF) have been reported.[4,5,8–11]

Unfortunately, TEPs may persist despite conservative management and formal surgical closure may be indicated to avoid morbid consequences.[12] The purpose of this study was to systematically review the available evidence on the surgical methods employed for TEP closure focusing on outcomes and reported complications.

Methods

Literature Search Strategy

This review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol.[13,14] A comprehensive search was conducted across the medical indices PubMed MEDLINE, Web of Science, SCOPUS, and Cochrane CENTRAL through October 2020. The search strategy was designed by two authors (J.M.E. and S.M.). The terms ((“Punctures”[Mesh]) OR (“Prosthesis Failure”[Mesh]) OR (“Prosthesis Implantation”[Mesh])) AND ((“Larynx, Artificial”[Mesh]) OR (“Larynx”[Mesh]) OR (“Laryngectomy”[Mesh]) OR (“Tracheoesophageal Fistula”[Mesh]) OR (“Trachea”[Mesh])) were used as keywords or Medical Subject Headings in several combinations (►**see Appendix, Supplementary Digital Content 1**, which displays the search strategy across different databases).

Inclusion and Exclusion Criteria

Studies were included if they (1) described a surgical technique for TEP closure, (2) were patient-based studies, (3) reported surgical outcomes and complications, and (4) were written in English. Studies were excluded if they met one of the following criteria: (1) review articles, (2) preclinical studies, (3) studies reporting patients with congenital TEFs, and (4) articles presenting surgical methods for closure of TEPs performed for indications other than puncture-based voice rehabilitation after oncologic treatment. We excluded articles that included sporadic resolution of the TEP site or in which conservative treatments for TEP enlargement or leakage were employed. For quantitative analysis, studies with a sample size of 4 or more patients were included.

Selection of Articles and Data Extraction

After duplicated studies were eliminated, two authors (J.M.E. and V.P.B.) independently screened the articles based on title and abstract. Then, full-text review of the remaining theoretically relevant studies using the inclusion criteria was performed using Rayyan QCRI (Rayyan Systems Inc., Cambridge, MA).[15] Data extraction was performed independently by two reviewers. The extracted data included the reference, total number of patients, previous surgical history, history of radiotherapy, type of TEP (primary, TEP performed at the time of reconstruction; secondary, delayed TEP after reconstruction), indication for closure, surgical technique for TEP closure, the presence or absence of complications, surgical outcomes following TEP closure, and follow-up. A third author (O.J.M.) resolved any conflicts during data extraction.

Outcomes

Successful TEP site closure was defined as the definitive occlusion of a previously patent tract between the trachea and the esophagus requiring no further interventions. The primary end-result was to assess the overall unsuccessful TEP closure rate following surgical management. The secondary outcome was to evaluate the unsuccessful TEP resolution rate using different surgical techniques (button insertion, dermal graft, forearm free flap [FFF], ligation of the fistula tract, deltopectoral flap interposition, sternocleidomastoid muscle [SCM] interposition, and primary closure).

Statistical Analysis

The pooled incidence of a failed TEP closure was calculated using meta-analysis with Stata/IC 16.1 (StataCorp LLC, College Station, TX). Due to the heterogeneity in treatment effects caused by differences in characteristics of patients, interventions reported, follow-up period, and other factors, a logistic-normal-random-effect model was accomplished.[16] The effects size of study-specific incidence were exhibited by proportions 95% exact confidence intervals (CIs) and the global pooled estimates with 95% binomial CI. A Freeman–Tukey double arcsine transformation was performed.[17] The effect size and percentage of weight were displayed for every particular study. Subgroup analysis of different surgical methods for TEP closure was performed.

Interstudy heterogeneity was evaluated using the Q statistic p-values and I^2 statistic.[2124818] Substantial heterogeneity was considered if I^2 was found to be 50 to 90%, and considerable heterogeneity when I^2 was found to be 75 to 100%.[2124819] Statistical significance was considered at p-value < 0.05.[2124819] Publication bias was assessed using a funnel plot graph and an Egger regression test.[20] Calculations of an adjusted CI and an estimate of the number of missing studies was accomplished by means of the trim-and-fill method.[21] Cumulative estimates of the patients' clinical and demographic characteristics were calculated as a weighted mean ± standard deviation.

Quality Assessment

Reviewers independently evaluated the level of evidence and the quality of each publication using the Oxford Centre for Evidence-Based Medicine: level of evidence (OCEBM).[2124822] Discrepancies between the reviewers were addressed by a third author.

Results

Literature Search and Quality Assessment

Overall, 1,602 publications were identified during the literature search. After removal of duplicated references, 1,174 records were screened and 1,058 were excluded based on review of title and abstract. Following full-text review, 33 articles met the inclusion criteria and were selected for data extraction (►**Fig. 1**).[8–10,12,23–51] Using the OCEBM, 33 studies had a level of evidence of 4. No discrepancies during quality assessment occurred.

Demographic and Clinical Characteristics

A total of 144 patients were identified, 62% were male ($n = 90$) and 8.9% ($n = 12$) were female. Biological sex was not reported in 42 patients. The mean age was 63.5 ± 7.91 years. Ninety-eight patients (68.5%) had previous history of radiotherapy. Past medical history of radiotherapy was not reported nor specified in 28 patients (19.4%). Primary or secondary TEP was reported in 66 patients, 92% ($n = 61$) received a primary TEP (voice prosthesis insertion during laryngectomy) and 7.5% ($n = 5$) received secondary TEP (insertion of voice prosthesis as a subsequent procedure in a delayed fashion). The TEP age (time period from puncture to surgical closure) was 23 ± 11.9 months. The average follow-up of all included patients was 19.7 ± 13.6 months. The demographic and clinical characteristics of included patients are summarized in ►**Table 1**.

Previous surgical history was reported in 110 cases (76.3%). One hundred three patients underwent total laryngectomy, two patients had total laryngectomy with partial pharyngectomy, two patients had pharyngo-laryngo-esophagectomy, two had pharyngolaryngectomy, and one a total laryngectomy with partial esophagectomy. Neck dissection was reported in 15.72% ($n = 22$) of patients, 18 patients had bilateral neck dissection and 4 patients unilateral neck dissection. However, the presence or absence of past surgical history of neck dissection was not ubiquitously reported across included studies. Indications for TEP closure were reported in 123 patients and were not mutually exclusive (►**Table 2**).

Surgical Procedures

One hundred forty-seven surgical procedures for TEP closure were reported, 130 were successful (►**Table 3**). Reported methods for TEP closure were as follows: primary closure of the fistula ($n = 48$), two-point ligation of the fistula tract without transection ($n = 8$), placement of silicone septal button ($n = 11$), interposition of dermal grafts ($n = 14$), interposition of skin grafts ($n = 6$), interposition of other grafts (cartilage graft, $n = 2$; collagen graft, $n = 1$; fascia graft, $n = 2$), and interposition of SCM muscle or fascia flap ($n = 24$), deltopectoral pedicled flap ($n = 9$), pectoralis major flap ($n = 4$), FFF ($n = 15$), lateral arm free flap ($n = 1$), or gastro-omental flap ($n = 1$).

Outcomes

Seventeen studies reporting outcomes of 117 patients were included in the quantitative analysis.[8,10,24,27,29,31,32,34,37 39,43,45–48,51] The overall incidence of unsuccessful TEP closure was 6% (95% CI 1–13%) (►**Fig. 2**). Heterogeneity among studies was not significant (Q statistic 18.28, degrees of freedom = 16, $p = 0.31$; $I^2 = 12.5\%$, $p = 0.308$). Subgroup analysis showed an unsuccessful TEP closure rate for silicone septal button of 8% (95% CI < 1–43%), < 0.1% (95% CI < 1–52%) for ligation of the fistula, 9% (95% CI < 1–28%) for primary closure, 7% (95% CI < 1–34%) for dermal graft interposition, 17% (95% CI < 1–64%) for interposition of a deltopectoral flap, < 0.1% (95% CI < 1–37%) for radial forearm free (RFF) flap, and 2% (95% CI < 1–20%) for interposition of SCM muscle flap (►**Fig. 3**).

The most-reported technique for TEP occlusion was primary closure. This technique involved a posterior tracheal wall closure and an anterior esophageal wall closure, with or without excision of the fistula tract. Closure was performed in a single-layer fashion with inverted, interrupted sutures or in some cases with a double- and even triple-layer closure. Regarding the cases in which an unsuccessful TEP closure was reported with this method, Moerman et al reported a 50% unsuccessful TEP closure rate in a series of 12 patients in which 83.3% had previous history of radiotherapy.[48]

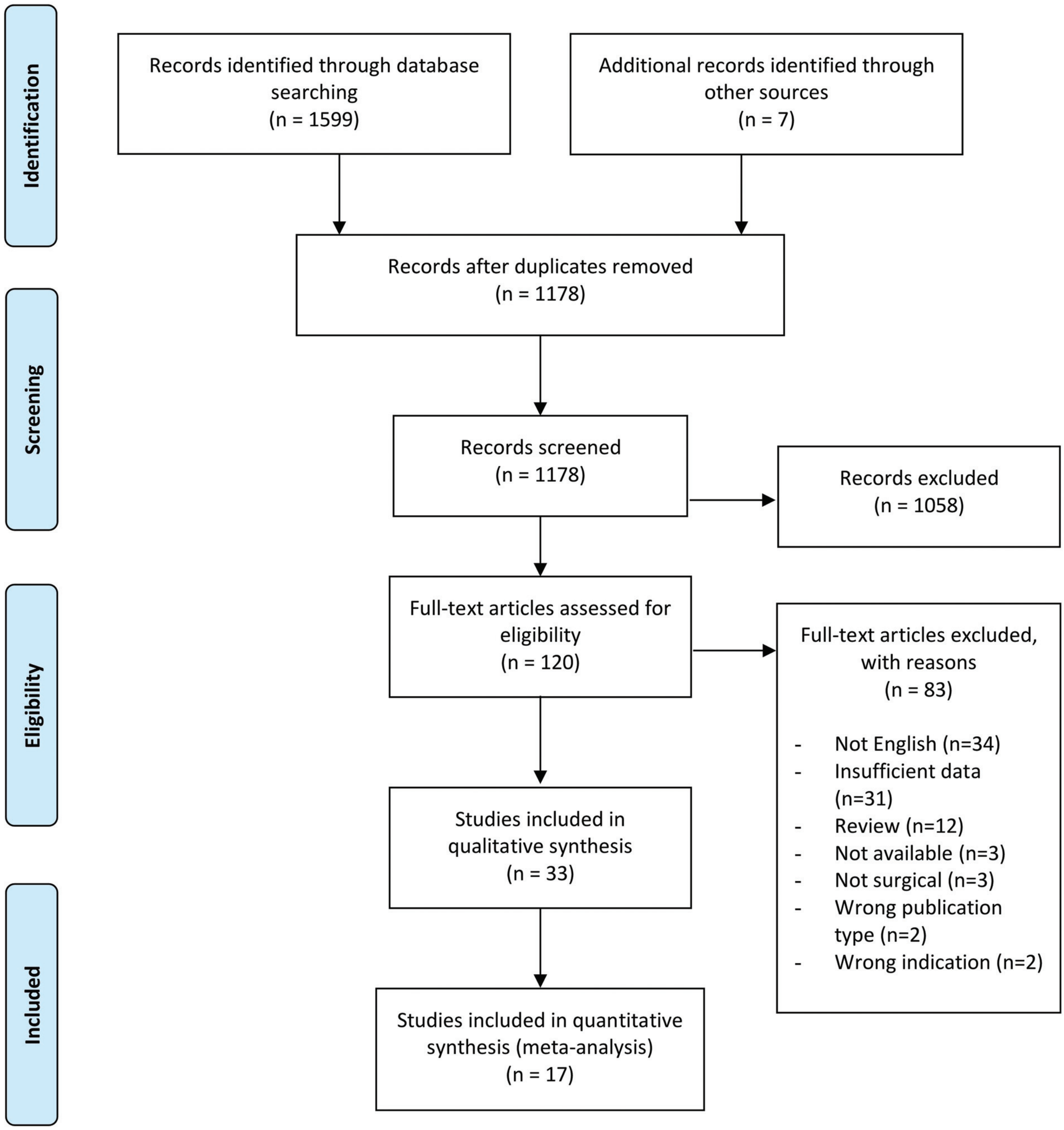

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

Additionally, Koch et al and Riva et al also presented two cases in which the presence of previous radiotherapy was determined as a risk factor for wound dehiscence and TEP recurrence.[29,43]

Another important reconstructive alternative was the implementation of SCM muscle flap, with this technique only one patient had a relapsing TEP.[10] This patient had previous history of radiotherapy and presented with a dehiscent flap edge during the postoperative period, which ultimately caused recurrence of the TEF.[10] Other local flaps such as deltopectoral or the pectoralis major flap were recommended by several authors.[25,32,38] Similarly, all the failed TEP closures presented in this review using the deltopectoral flaps were in patients who had previous adjuvant radiotherapy, which was likely the cause of wound breakdown and the susceptibility to infection.[32,38] Conversely, no TEP recurrence was reported in patients managed with a FFF or the lateral arm free flap despite 94% of patients having previous history of radiotherapy.[9,24–26,33,52]

Ten studies reported the size of the puncture diameter.[8,26,29,37,39,40,43,44,47,49] Remarkably, tracheal wall closure, fistula excision, and esophageal wall closure with or without interposition of a dermal graft or fascia lata (FL), was the most common reconstructive technique when defects were of 15 mm or less.[8,29,44,47] Placement of a silicone septal button was proposed in patients with a TE defects of 15 to 20 mm, an intervention that was successful in five of the six patients reported in these series.[39,49] When the average

Table 1 Overview of the clinical and demographic characteristics of included studies

Author/Year	Type of study	Patients (n)	Age (y)	Oncologic surgical treatment	Type of puncture	TEP age(mo)	RT	Indications for closure	Fistula dimensions
Annyas and Escajadillo, 1984	Case series	6	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Rosen et al, 1997	Case series	14	66.5 ± 11.9 ($n=14$)	Total laryngectomy ($n=14$)	N/R	14.5 ± 13.2 ($n=14$)	Yes ($n=13$) No ($n=1$)	Aspiration pneumonia ($n=4$) Persistent leakage ($n=8$)Failed TE shunt phonation ($n=6$)Emphysema ($n=1$)Failure to tolerate ($n=3$)	4.5 mm
Moerman et al, 2004	Case series	12	66.2 ± 7.5 ($n=12$)	N/R	Primary ($n=11$) Secondary ($n=1$)	19.3 ± 9.82 ($n=11$)	Yes ($n=10$) No ($n=2$)	Failure to tolerate ($n=3$) Enlargement of fistula ($n=5$) Exophytic growth ($n=1$)Failed TE shunt phonation ($n=1$) Infection ($n=1$)	N/R
Mirza et al, 2003	Case report	1	65	Total laryngectomy ($n=1$)	Primary ($n=1$)	N/R	N/R	Infection ($n=1$)Enlargement of fistula ($n=1$)	20 mm
Lee and Razi, 2004	Case report	1	64	Total laryngectomy + Partial pharyngectomy + Left radical neck dissection ($n=1$)	Primary ($n=1$)	6	Yes ($n=1$)	Failure to tolerate ($n=1$)	N/R
Cavalot et al, 2004	Case series	8	N/R	Total laryngectomy ($n=8$)	N/R	N/R	Yes ($n=5$) No ($n=3$)	Enlargement of fistula ($n=2$) Prosthesis migration ($n=2$) Failure to tolerate ($n=3$) Granulation ($n=1$)	N/R
Ünal, 2006	Case report	1	61	Total laryngectomy ($n=1$)	N/R	24	N/R	Candida overgrowth ($n=1$) Persistent leakage ($n=1$)	N/R
Gehrking et al, 2007	Case series	9	60.4 ± 11.5 ($n=9$)	Laryngectomy ($n=9$)	N/R	N/R	Yes ($n=9$)	Persistent leakage ($n=9$)	N/R
Baldwin and Liddington, 2008	Case series	4	59.3 ± 7.59 ($n=4$)	Salvage laryngectomy ($n=1$) Pharyngo-laryngo-esophagectomy + Free jejunal flap ($n=1$)Tracheal resection -> Pharyngo-laryngo-esophagectomy + Free jejunal flap ($n=1$)Total laryngectomy and B/L neck dissection ($n=1$)	Secondary ($n=1$) Primary ($n=3$)	6.67 ± 5.03 ($n=3$)	Yes ($n=4$)	Failed TE shunt phonation ($n=1$) Leakage ($n=1$)Necrotic laryngeal cartilage ($n=1$)	N/R
Wreesmann et al, 2009	Case report	1	52	Total laryngectomy + B/L modified radical neck dissection	Primary ($n=1$)	5	Yes ($n=1$)	Enlargement of fistula ($n=1$)	40 mm
Judd and Bridger, 2008	Case series	5	N/R	Laryngectomy (not specified) ($n=5$)	N/R	10.6 ± 8.08 ($n=5$)	N/R	Persistent leakage ($n=5$)Infection ($n=1$)Failure to tolerate ($n=1$)	N/R
Schmitz et al, 2009	Case report	1	70	Total laryngectomy ($n=1$)	Primary ($n=1$)	N/R	Yes ($n=1$)	Dysphagia ($n=1$)	N/R
Koch et al, 2010	Case series	5	N/R	Total laryngectomy ($n=5$)	Primary ($n=5$)	N/R	Yes ($n=5$)	Enlargement of fistula ($n=5$)	15 mm
Wong et al, 2011	Case report	1	62	Total laryngectomy ($n=1$)	Secondary	N/R	Yes ($n=1$)	Aspiration pneumonia ($n=1$) Enlargement of fistula ($n=1$)	N/R
Geyer et al, 2011	Case series	2	62.5 ± 9.19 ($n=2$)	Total laryngectomy ($n=2$)	Primary ($n=2$)	46.5 ± 9.19 ($n=2$)	Yes ($n=2$)	Aspiration pneumonia ($n=1$) Persistent leakage ($n=1$)	N/R
Hu et al, 2011	Case series	6	86 ($n=1$)	Total laryngectomy and partial esophagectomy ($n=1$)	N/R	N/R	N/R	N/R	N/R

(*Continued*)

Table 1 (*Continued*)

Author/Year	Type of study	Patients (*n*)	Age (y)	Oncologic surgical treatment	Type of puncture	TEP age(mo)	RT	Indications for closure	Fistula dimensions
Balasubramanian et al, 2013	Case series	6	62.7 ± 10.8 (*n* = 6)	Total laryngectomy (*n* = 6)	N/R	N/R	Yes (*n* = 5) No (*n* = 1)	Persistent leakage (*n* = 6)	N/R
Mohan and Malata, 2014	Case report	1	60	Salvage total laryngectomy + Neck dissection (*n* = 1)	N/R	N/R	Yes (*n* = 1)	Persistent tracheoesophageal fistula (*n* = 1)	N/R
Mobashir et al, 2014	Case series	5	58 ± 2.75 (*n* = 5)	Total laryngectomy (*n* = 5)	Primary (*n* = 5)	N/R	Yes (*n* = 5)	Enlargement of fistula (*n* = 5) Persistent leakage (*n* = 5)	N/R
Unsal et al, 2015	Case series	4	63.5 ± 5.25 (*n* = 4)	Total laryngectomy + B/L neck dissection (*n* = 3)Total laryngectomy + Partial pharyngectomy + B/L neck dissection (*n* = 1)	Primary (*n* = 4)	64 ± 27.7 (*n* = 3)	Yes (*n* = 4)	Enlargement of fistula (*n* = 4) Persistent leakage (*n* = 1)	N/R
Jaiswal et al, 2015	Case series	9	52.3 ± 10.7 (*n* = 9)	Total laryngectomy (*n* = 9)	Primary (*n* = 9)	N/R	Yes (*n* = 7) No (*n* = 2)	N/R	N/R
Wasano et al, 2015	Case series	4	71.5 ± 6.76 (*n* = 4)	Total laryngectomy + U/L neck dissection (*n* = 1)Total laryngectomy + B/L neck dissection (*n* = 1)Pharyngo-laryngectomy + Free jejunal transfer + B/L neck dissection (*n* = 2)	Primary (*n* = 4)	34.4 ± 24.3 (*n* = 2)	Yes (*n* = 2) No (*n* = 2)	Patient request (*n* = 3)Aspiration pneumonia (*n* = 1)	N/R
Dewey et al, 2016	Case series	8	67 ± 3 (*n* = 8)	Total laryngectomy/laryngopharyngectomy (*n* = 8)	Primary (*n* = 7) Secondary (*n* = 1)	N/R	Yes (*n* = 7)	Enlargement of fistula (*n* = 8) Persistent leakage (*n* = 8)	32.5 ± 3.75 mm
Huang and Day, 2017	Case report	1	51	Total laryngectomy (*n* = 1)	Primary (*n* = 1)	24	Yes (*n* = 1)	Enlargement of fistula (*n* = 1)	N/R
Jaiswal et al, 2016	Case report	1	64	Total laryngectomy + B/L neck dissection (*n* = 1)	Primary (*n* = 1)	96	Yes (*n* = 1)	Enlargement of fistula (*n* = 1)	N/R
Mutlu et al, 2016	Case series	4	67.3 ± 8.14 (*n* = 4)	Total laryngectomy (*n* = 2)	N/R	N/R	Yes (*n* = 3)	Enlargement of fistula (*n* = 4) Persistent leakage (*n* = 4)	17 ± 7.44 mm (*n* = 4)
Viñals Viñals et al, 2017	Case report	1	71	Total laryngectomy + B/L radical modified neck dissection (*n* = 1)	Primary (*n* = 1)	96	Yes (*n* = 1)	Aspiration pneumonia (*n* = 1)	50 mm
Daya and Pillay, 2018	Case series	3	N/R	Radical laryngectomy + B/L neck dissection (*n* = 2)	Primary (*n* = 1)	N/R	Yes (*n* = 3)	Enlargement of fistula (*n* = 3)	N/R
Yenigun et al, 2019	Case series	2	58 ± 2.83 (*n* = 2)	Total laryngectomy (*n* = 2)	N/R	N/R	Yes (*n* = 2)	Persistent leakage (*n* = 2)	N/R
Riva et al, 2019	Case Series	5	63 ± 4(*n* = 5)	Total laryngectomy (*n* = 5)	N/R	N/R	Yes (*n* = 1)	Failed TE shunt phonation (*n* = 4) Enlargement of fistula (*n* = 1)	7 mm (*n* = 1)
Dwivedi et al, 2019	Case series	2	62.5 ± 27.6 (*n* = 2)	Salvage total laryngectomy + B/L neck dissection (*n* = 1)Total laryngectomy + U/L neck dissection (*n* = 1)	Primary (*n* = 1) Secondary (*n* = 1)	5.5 ± 0.707 (*n* = 2)	Yes (*n* = 1)	Enlargement of fistula (*n* = 2)	8.5 ± 4.95 mm (*n* = 2)
Gozen et al, 2019	Case series	7	66.28 ± 9.8 (*n* = 7)	Total laryngectomy (*n* = 7)	N/R	N/R	N/R	Enlargement of fistula (*n* = 7)	2.61 ± 9.8 mm (*n* = 7)
Neves et al, 2020	Case series	4	85 (*n* = 1)	Total laryngectomy + B/L neck dissection (*n* = 4)	Primary (*n* = 1)	36 (*n* = 1)	Yes (*n* = 2)	Failed TE shunt phonation (*n* = 1)	N/R

Abbreviations: B/L, bilateral; N/R, not reported; RT, radiotherapy; TE, tracheoesophageal; TEP, tracheoesophageal puncture; U/L, unilateral.

Table 2 Indications for TEP reconstruction of 123 patients

Indication for reconstruction	No. of patients	Percentage
Patient request	51	34.93
Enlargement of fistula	51	34.93
Failed TE shunt phonation	13	8.90
Failure to tolerate	11	7.53
Aspiration pneumonia	8	5.47
Prosthesis migration	2	1.36
Infection	2	1.36
Persistent TEF	1	0.68
Necrotic laryngeal cartilage	1	0.68
granulation	1	0.68
Exophytic growth	1	0.68
Emphysema	1	0.68
Dysphagia	1	0.68
Candida overgrowth	1	0.68

Abbreviations: TE, tracheoesophageal; TEF, tracheoesophageal fistula; TEP, tracheoesophageal puncture.

defect size was greater than 30 mm, surgeons opted to use vascularized free tissue transfer as their reconstructive method of choice. Wreesmann et al used a bilaminar flee flap in a defect of 40 mm; Dewey et al employed a bipaddled FFF, with or without a pectoralis major flap, in defects with an average diameter of 32.5 mm; and Viñals Viñals et al a gastro-omental free flap in a defect of 50 mm, the greatest in this review.[26,37,40] From the aforementioned patients treated with a free flap, all had a successful TEP closure (►**Table 3**).[26,37,40]

Complications

The presence or absence of complications was reported in 110 patients (75.8%). Complications following TEP closure occurred in 13 patients (8.8%). The complications included button failure ($n = 1$), crusting on button ($n = 2$), dehiscence ($n = 2$), fungal/bacterial colonization of surgical site ($n = 1$), granuloma formation ($n = 1$), hematoma ($n = 1$), infection ($n = 2$), marginal flap necrosis ($n = 2$), neopharynx stricture ($n = 1$), transient dysphagia ($n = 1$), and ulceration and necrosis of the suprasternal border without TEF recurrence. The patient with button failure ($n = 1$) was treated with a local rotation flap to restore the stoma. Patients with dehiscence ($n = 2$) underwent additional revision surgery, and one required a pectoralis major muscle flap.

The patient presenting with a hematoma received hyperbaric oxygen therapy, intravenous antibiotics, and intensive wound care; however, fistula recurrence was observed, and the patient was discharged with a NG tube. The patient presenting with delayed neopharynx stricture was treated with serial dilatations. Patients with a failed TEP closure were treated with deltopectoral flaps ($n = 2$), pectoralis major muscle flaps ($n = 1$), and a two-layered esophageal suture with interposition of a pectoralis major muscle flap ($n = 1$).

Publication Bias

Funnel plot graphic showed asymmetry and no significant evidence of publication bias was found (Egger's test, $p = 0.183$) (►**Fig. 4**). Trim-and-fill analysis imputed 17 studies with no impact in the overall outcomes (observed effect size 0.105, 95% CI −0.073 to 0.283; imputed effect size 0.105, 95% CI −0.073 to 0.283).

Discussion

The incidence of leakage around a voice prosthesis secondary to TEP enlargement has been reported between 1 and 29%.[8,44,53] Additionally, a 4.5-fold increased risk of TEP enlargement has been reported in patients who undergo total laryngopharyngectomy compared with patients who are treated with a total laryngectomy.[44] Since persistent leakage has been acknowledged to result in threefold increase in aspiration pneumonia with 20 to 30% mortality and 14% chronic dependence on percutaneous gastrostomy for nutrition, prompt surgical TEP closure is required when conservative measures fail.[8,44] Remarkably, patient request for TEP closure was the most common indication for TEP closure in simultaneous with enlargement of the fistula, which indicates concerns regarding the quality of life of patients undergoing voice restoration procedures that have not been addressed.

When the preoperative risk assessment is high, a silicone septal button can be used to temporarily obliterate the fistula tract yielding an acceptable recurrence rate of 8% (95% CI < 1–43%). However, as there is no healing process, this option is per se inferior to any reconstructive modality.[35,49] Artificial materials therefore can provide a temporary solution for patients who will undergo forthcoming surgeries with autologous tissue or when flap-based reconstructions of the TEP cannot be performed immediately due to considerable intraoperative time, suboptimal nutritional status, and multiple comorbidities.[39,49] Conversely, the disadvantages of the septal button insertion are that this method is limited for patients who have a 10- to 20-mm TEP defect and the loss of the TE speech function, as this reconstructive method does not aim for a formal reconstruction and subsequent TEP with voice prosthesis insertion.[35,49]

Geyer et al reported the dissection and ligation of an intact fistula tract at two points for TEP closure. This surgical technique was implemented in 2 patients, in which one case required the same procedure twice due to recurrence.[12] Similarly, Mobashir et al performed a double nonresorbable suture circumferential ligation of the fistula tract to guarantee a successful closure, but his approach was through an incision of 2.5 cm above the superior tracheostomy edge to preserve the stoma integrity.[34] In his cohort, the TEP was effectively closed in 100% of patients. In this setting, a two-point ligation of the TEF tract when feasible, provides a protective and reliable (recurrence: 0%, 95% CI < 1–52%) technique to close the fistula of the TEP in a short operative time. Additionally, as the tract is not divided, there is a

Table 3 Overview of the previous surgical history and reported outcomes of the included studies

Author, year	Patients (n)	Previous nonsurgical/surgical closure treatment	TEP closure method	Surgical outcomes	Complications	Other outcomes	Follow-up(mo)
Annyas and Escajadillo, 1984	6	N/R	Excision of the fistula tract + Esophageal and tracheal wall closure with single layer, inverted, interrupted sutures + Interposition of a skin graft ($n=6$)	Successful surgical closure ($n=6$)	N/R	Nasogastric tube removed 8 days after surgery ($n=6$)	6
Rosen et al, 1997	14	Insertion of smaller tubes or cauterization ($n=14$)	Three-layered closure technique + Interposition of a dermal graft ($n=13$)	Successful surgical closure ($n=13$)Failed TEF surgical closure ($n=1$)	Hematoma ($n=1$)	Normal oral intake resumed ($n=13$)	20.9 ± 14.6 ($n=18$)
Moerman et al, 2004	12	N/R	Excision of the fistula tract + Two-layer esophagoplasty + Two-layer tracheoplasty ($n=12$)	Successful surgical closure ($n=6$)Failed TEF surgical closure ($n=6$)	No complications	Secondary closure with pectoralis major ($n=2$)Secondary closure with forearm free flap ($n=2$)New prosthesis ($n=1$)	N/R
Mirza et al, 2003	1	N/R	Placement of silicone septal button ($n=1$)	Successful surgical closure ($n=1$)	No complications	N/R	N/R
Lee and Razi, 2004	1	Prosthesis removal ($n=1$)	Excision of the fistula tract + Two-layer esophagoplasty + Interposition of a sternocleidomastoid muscle flap + Two-layer tracheoplasty ($n=1$)	Successful surgical closure ($n=1$)	No complications	Normal oral intake resumed ($n=1$)	6
Cavalot et al, 2004	8	N/R	Excision of the fistula tract + Esophageal and tracheal wall closure with single-layer, inverted, interrupted sutures ($n=5$) Excision of the fistula tract + Esophageal and tracheal wall closure with single-layer, inverted, interrupted sutures + Interposition of a Vicryl mesh ($n=3$)	Successful surgical closure ($n=8$)	No complications	New tracheoesophageal fistula with successful new prosthesis ($n=4$)	N/R
Ünal, 2006	1	Valve replacement ($n=1$)Purse-string suture ($n=1$)	Excision of the fistula tract + Two-layer esophagoplasty + Two-layer tracheoplasty ($n=1$)	Successful surgical closure ($n=1$)	No complications	Effective usage of electrolarynx ($n=1$)	6
Gehrking et al, 2007	9	Primary surgical closure ($n=4$)Tracheostoma widening ($n=1$)Sternocleidomastoid muscle flap ($n=1$)Transcervical multilayer fistula closure with Allogenous collagen graft ($n=1$)VP replacements ($n=2$)Transcervical ML-FC with IHM flap ($n=2$)Transtracheostomal FC (tragal perichondrium) ($n=1$)GM-CSF injection ($n=1$)Hyaluronate 10+ injection ($n=1$) Deltopectoral and latissimus dorsi flaps ($n=1$)Forearm free flap (discontinued due to poor vessel status) ($n=1$)Multiple pharyngoplasties with local flaps ($n=2$) Pedicled pectoralis major flap ($n=1$)Tracheostoma transposition ($n=1$)	Esophageal and tracheal wall multi-layer closure + Interposition of a sternocleidomastoid muscle flap ($n=4$)Esophageal and tracheal wall multilayer closure + Collagen allograft ($n=1$)Esophageal and tracheal wall multilayer closure + Interposition of local muscle flap ($n=1$)Pharyngectomy + Forearm free flap ($n=3$)	Successful surgical closure ($n=9$)	Ulceration and skin necrosis of the suprastomal border without TEF recurrence ($n=1$)	No recurrent fistula/tumor ($n=3$)Free PE passage with/ without not curable tumor progression ($n=2$) Death due to tumor progression ($n=2$)Death due to unrelated causes ($n=1$)	6.5 ± 7.78 ($n=2$)

Table 3 (*Continued*)

Author, year	Patients (*n*)	Previous nonsurgical/surgical closure treatment	TEP closure method	Surgical outcomes	Complications	Other outcomes	Follow-up(mo)
Baldwin and Liddington, 2008	4	Valve removal and sternocleidomastoid flap ($n = 1$)	Two-layer tracheal-esophagoplasty + Forearm free flap ($n = 1$)One-layer tracheal-esophagoplasty + Deepithelized deltopectoral flap ($n = 1$)Forearm free flap ($n = 1$)Pedicled pectoralis major muscle flap ($n = 1$)	Successful surgical closure ($n = 4$)	Infection ($n = 1$)	Percutaneous endoscopic gastrostomy ($n = 1$) Normal oral intake resumed ($n = 1$)	9 ± 5.2 ($n = 3$)
Wreesmann et al, 2009	1	Prosthesis removal and marginal fat augmentation + Three-layered closure + Sternocleidomastoid flap coverage ($n = 1$)	Fabrication of delayed bilaminar forearm free flap w/ skin graft + Excision of the fistula tract + Bilaminar free flap ($n = 1$)	Successful surgical closure ($n = 1$)	No complications	New phonatory prosthesis placement ($n = 1$)Normal oral intake resumed ($n = 1$)	12
Judd and Bridger, 2008	5	N/R	Excision of the fistula tract + Esophageal and tracheal wall closure with interrupted sutures + Interposition of a sternocleidomastoid fascia flap ($n = 5$)	Successful surgical closure ($n = 5$)	No complications	Patient satisfied with results ($n = 5$)	31.2 ± 13.7 ($n = 5$)
Schmitz et al, 2009	1	Pectoralis major myofascial flap ($n = 1$)	Placement of a 5-cm silicone septal button (Micromedics, St Paul, MN) ($n = 1$)	Successful surgical closure ($n = 1$)	No complications	Oral intake resumed ($n = 1$)	14
Koch et al, 2010	5	N/R	Excision of the fistula tract + Two-layer esophagoplasty + Resection of the tracheal fistula + Cephalic repositioning of the trachea ($n = 5$)	Successful surgical closure ($n = 4$)Failed TEF surgical closure ($n = 1$)	Failed TEF closure requiring a pectoralis major flap ($n = 1$)	Recurrent fistula revision successful (treated with two-layered esophageal sutures + pectoral major myofascial flap) ($n = 1$)	42 ± 13.5 ($n = 5$)
Wong et al, 2011	1	Collagen injection for primary TEP closure (successful) ($n = 1$)Sternocleidomastoid flap TEP (failed) ($n = 2$)	Placement of a nasal septal button (Medtronic Xomed, Jacksonville, FL) ($n = 1$)	Successful surgical closure ($n = 1$)	No complications	Normal oral intake resumed ($n = 1$)	18
Geyer et al, 2011	2	Submucosal circumferential suture ($n = 1$)	Ligation of the fistula tract at two points ($n = 1$)Ligation of the fistula tract at two points ($n = 1$) (failed) -> Ligation of the fistula tract at two points ($n = 1$)	Successful surgical closure ($n = 1$)Failed TEF surgical closure ($n = 1$) -> Successful surgical closure ($n = 1$)	Failed TEF closure ($n = 1$)	Normal oral intake resumed ($n = 2$)	7 ± 1.41 ($n = 2$)
Hu et al, 2011	6	Prosthesis removal ($n = 1$)Prosthesis replacement ($n = 1$)	Excision of the fistula tract + Two-layer tracheal-esophagoplasty + Tracheal advancement technique ($n = 6$)	Successful surgical closure ($n = 6$)	N/R	Normal oral intake resumed ($n = 1$)	N/R
Balasubramanian et al, 2013	6	N/R	Fistula edges are deepithelialized + Single perforator-based deltopectoral flap ($n = 6$)	Successful surgical closure ($n = 5$)Failed TEF surgical closure ($n = 1$)	Dehiscence ($n = 1$)Infection ($n = 1$)Revision surgery ($n = 1$)	N/R	N/R
Mohan and Malata, 2014	1	Interposition of a pedicled pectoralis major myocutaneous ($n = 1$)	Bilaminar lateral arm flap ($n = 1$)	Successful surgical closure ($n = 1$)	Revision of the esophageal wall ($n = 1$)	Normal oral intake resumed ($n = 1$)	N/R

(*Continued*)

Table 3 (*Continued*)

Author, year	Patients (n)	Previous nonsurgical/surgical closure treatment	TEP closure method	Surgical outcomes	Complications	Other outcomes	Follow-up(mo)
Mobashir et al, 2014	5	Prosthesis removal + Tube feeding + PPI and prokinetics ($n=5$)	Ligation of the fistula tract at two points ($n=5$)	Successful surgical closure ($n=5$)	No compilations	Normal oral intake resumed ($n=5$)	14.4 ± 2.88 ($n=5$)
Unsal et al, 2015	4	Unspecified conservative methods ($n=4$) Prosthesis replacement ($n=1$)Sternocleidomastoid muscle flap ($n=1$)	Placement of a silicone 32 mm septal button (Invotec, Jacksonville, FL) ($n=4$)	Successful surgical closure ($n=4$)	Crusting on button ($n=1$)	Swallowing restoration ($n=4$) Esophageal speech ($n=1$)	16.5 ± 9.47 ($n=4$)
Jaiswal et al, 2015	9	N/R	Sternocleidomastoid musculocutaneous flap transposition ($n=9$)	Successful surgical closure ($n=8$)Failed TEF surgical closure ($n=1$)	Marginal necrosis of flap ($n=2$) Dehiscence ($n=1$)	Pectoralis major muscle flap ($n=1$)	N/R
Wasano et al, 2015	4	Prosthesis removal ($n=4$)Ring expanded prosthesis ($n=1$)	Excision of the fistula tract + Esophageal and tracheal wall closure with inverted, interrupted sutures + Interposition of sternocleidomastoid fascia flap ($n=4$)	Successful surgical closure ($n=4$)	No complications	Normal oral intake resumed ($n=4$)	11.5 ± 7.05 ($n=4$)
Dewey et al, 2016	8	Prosthesis removal/replacement + Cauterization of fistulae tract surgical management ($n=1$)	Bipaddled radial forearm free flap ($n=5$) Bipaddled radial forearm free flap + Pectoralis major flap ($n=3$)	Successful TEF surgical closure ($n=8$)	Neopharynx stricture ($n=1$)	4 postoperative dilations ($n=1$)	43 ± 37.9($n=8$)
Huang and Day, 2017	1	Antimicrobials ($n=1$)Primary surgical closure ($n=1$)Hyperbaric oxygen therapy ($n=1$)	Double paddle ulnar perforator free flap ($n=1$)	Successful TEF surgical closure ($n=1$)	No complications	Normal oral intake resumed ($n=1$)	3
Jaiswal et al, 2016	1	Deltopectoral flap ($n=1$)	Two-layered closure + Deltopectoral flap ($n=1$) + Deltopectoral flap rearrangement + neotracheostoma ($n=1$)	Failed TEF surgical closure -> Successful surgical closure ($n=1$)	Failed TEF closure ($n=1$)	N/R	2
Mutlu et al, 2016	4	N/R	Placement of a silicone 32 mm septal button (Invotec, Jacksonville, FL) ($n=4$)	Successful TEF surgical closure ($n=3$)Failed TEF surgical closure ($n=1$)	Granulation formation ($n=1$) Button failure ($n=1$)Transient dysphagia ($n=1$)Fungal/ bacterial colonization ($n=1$)	Normal oral intake resumed ($n=1$)	11 ± 1.0 ($n=3$)
Viñals Viñals et al, 2017	1	Prosthesis removal + Silastic lamina placement + Silicone septal button placement (2 ×) + Interpositioning of pectoral flap ($n=1$)	Gastro-omental Flap + STSG ($n=1$)	Successful TEF surgical closure ($n=1$)	No complications	Normal oral intake resumed ($n=1$)	16
Daya and Pillay, 2018	3	Radial forearm free flap ($n=1$)Free brachioradialis muscle flap ($n=1$)Free lateral arm flap ($n=1$)	Debridement of scarred tissue + Esophageal wall closure + Interposition of pectoralis major myofascial flap + Esophageal stenting through a surgically controlled fistula (10 days) + Skin graft + Intubated trachea with endotracheal Portex tube (6 weeks) ($n=3$)	Successful TEF surgical closure ($n=3$)	No complications ($n=3$)	Normal oral intake resumed ($n=3$)	10 ± 0.0 ($n=2$)
Yenigun et al, 2019	2	Prosthesis removal ($n=2$)	Placement of a butterfly cartilage graft to the trachea posterior wall by suturing with superior and inferior absorbable suture ($n=2$)	Successful TEF surgical closure ($n=2$)	No complications ($n=2$)	Normal oral intake resumed ($n=2$)	6 ± 0.0 ($n=2$)

Table 3 (*Continued*)

Author, year	Patients (n)	Previous nonsurgical/surgical closure treatment	TEP closure method	Surgical outcomes	Complications	Other outcomes	Follow-up(mo)
Riva et al, 2019	5	N/R	Cephalic repositioning of the trachea + Semicircular suturing above the tracheal opening of the fistula + Blunt dissection of the fistula tract without excision + Tracheal mucosa closure with an everted circular suture ($n = 5$)	Successful TEF surgical closure ($n = 4$)Failed TEF surgical closure ($n = 1$)	Failed TEF closure ($n = 1$)	Swallowing restoration ($n = 4$)	8 ± 0.0 ($n = 4$)
Dwivedi et al, 2019	2	Radiesse injection ($n = 1$)Failing conservative measures ($n = 2$)	Excision of the fistula tract + Esophageal wall closure simple interrupted sutures + Fascia lata autograft interposition + Tracheal wall closure simple interrupted suture ($n = 2$)	Successful TEF surgical closure ($n = 1$)Failed TEF surgical closure ($n = 1$)	Failed TEF closure requiring a modified single vessel deltopectoral flap ($n = 1$).	N/R	24 ± 17($n = 2$)
Gozen et al, 2019	7	Primary sutures ($n = 2$)Primary suture + Local flaps ($n = 2$)Local flaps + Microsurgical reconstruction ($n = 1$)	Excision of the fistula tract + Esophageal wall closure with multilayered primary suture + Resection of the tracheal fistula + Cephalic repositioning of the trachea and closure of tracheostomy with skin flaps ($n = 7$)	Successful TEF surgical closure ($n = 7$)	No complications	Normal oral intake resumed ($n = 7$)	21.7 ± 8.96 ($n = 7$)
Neves et al, 2020	4	N/R	Excision of the fistula tract + Esophageal opening closure with continuous sutures + Vertical incision of the anterior segment of the first tracheal ring + Tracheal opening closure with sutures + Pectoral skin flap coverage ($n = 4$)	Successful TEF surgical closure ($n = 4$)	No complications	New phonatory prosthesis placement (2 years postop) ($n = 1$)	12.5 ± 16.3 ($n = 2$)

Abbreviations: GM-CSF, granulocyte-macrophage colony-stimulating factor; IHM, infrahyoid muscle; N/R, not reported; PE, pharyngoesophageal; PPI, proton-pump inhibitors; STSG, split-thickness skin graft; TE, tracheoesophageal; TEF, tracheoesophageal fistula; TEP, tracheoesophageal puncture; VP, voice prosthesis.

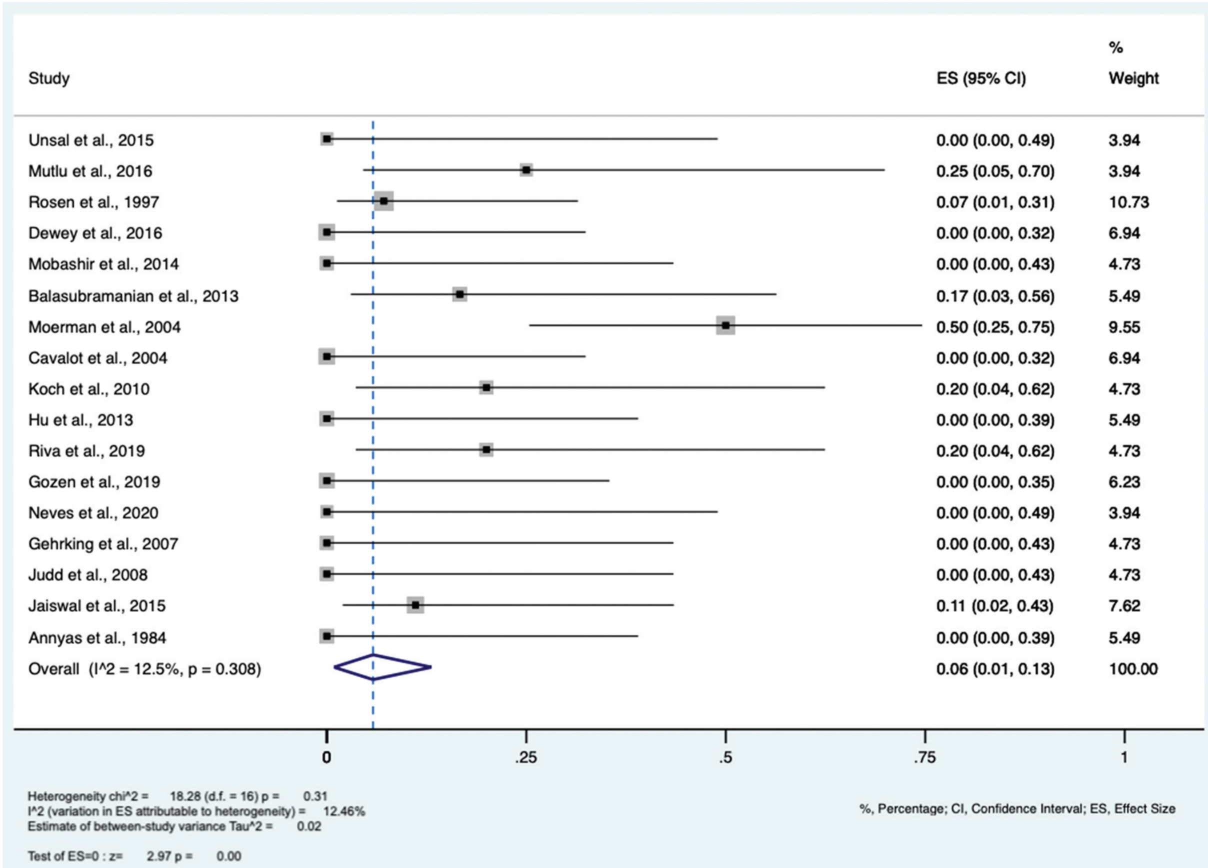

Fig. 2 Forest plot presenting the pooled incidence of the overall unsuccessful tracheoesophageal puncture (TEP) closure rate.

hypothetical lower risk of suture slippage and subsequent infection in the potential space between the pharynx and trachea.[34,45]

To our knowledge, Hosal and Myers introduced the first technique for TEP closure in which the fistula was transected, and closure of the esophageal and tracheal walls was performed with inverted sutures without the interposition of autologous tissue.[54] Hu et al reported a method similar to Gozen et al, where trachea and esophagus are sutured separately, but with the particularity of also performing a tracheal mucosal resection to prevent overlapping suture lines. This cephalic repositioning of the trachea provided a healthy membranous tracheal wall that was used as a vascularized flap to overlie the fistula site.[8] Nonetheless, repeated mucosal resections are only possible for this method if there is enough tracheal mucosa present.[45]

Neves et al equally transected the tract and separately sutured esophagus and trachea with the addition of performing a vertical incision across the first tracheal ring to facilitate a tension-free suture on the posterior tracheal wall.[45] Gozen et al and Neves et al externally reinforced the stoma to avoid stomal stenosis in radiated patients which may be advantageous to avoid further surgeries.[8,45] In this review, primary closure yielded a 9% (95% CI < 1–28%) TEP recurrence rate which was attributed to the cytotoxic effect of radiotherapy and recanalization of the tract. In fact, we concluded that this surgical technique should not be considered as the first choice for patients with previous history of bilateral neck dissection and radiotherapy.

A butterfly cartilage autograft to enforce TEP closure is an acceptable alternative that can be performed under local anesthesia and is associated with low morbidity.[42] This technique is elaborately described by Yenigun et al who reported that enteral feeding was resumed in a short span of time.[42] Likewise, FL autograft is also described as an excellent method for three-layered fistula closure.[44] The FL is a strong and easily harvestable autograft, capable of providing large amounts of reliable graft material; however, scar/keloid formation, hematoma, infection, and chronic pain (from the herniated muscle belly) can occur if proper donor site closure is not ensured.[44] This method, therefore, should be evaluated before using autologous vascularized tissue for a three-layer closure in cases where TEP diameter does not exceed 1 cm.[44] Remarkably, it must be mentioned that despite its tensile strength and tissue abundance, the FL graft is avascular and fails to withstand ongoing local infection and healing in a postradiotherapy environment, leading to TEP closure failure in patients with a similar presentation.

Huang and Day established that multilayered closure supersedes a large quantity of fresh tissue in the form of grafts for reconstruction of communicating wounds.[9] To our knowledge, Lee and Razi was the first to report the interposition of the SCM muscle in one patient for TEP closure,[50] and Wasano et al proposed the interposition of SCM fascia between the esophagus and the trachea as an option to

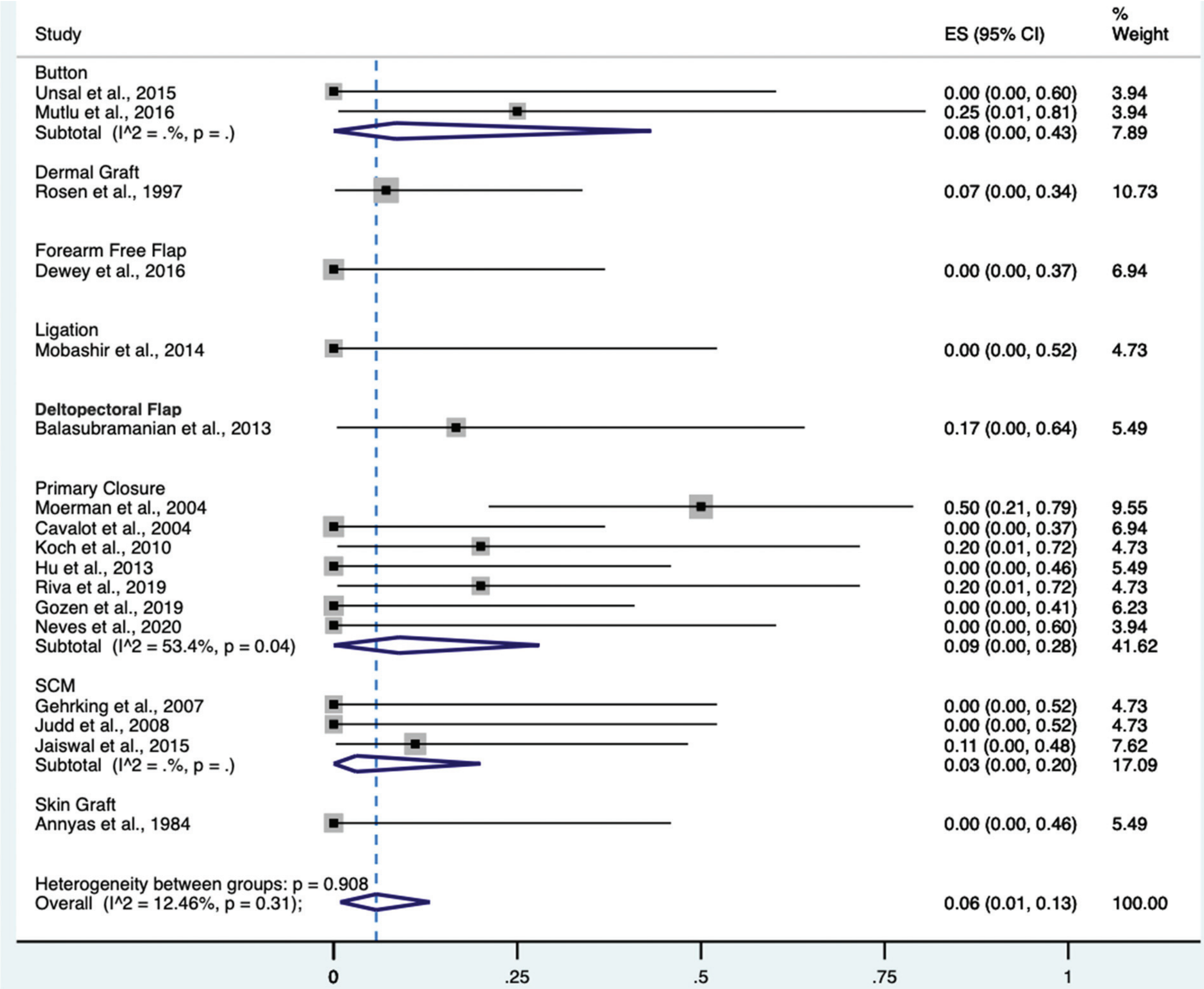

Fig. 3 Forest plot presenting the pooled incidence of unsuccessful tracheoesophageal puncture (TEP) closure rates among the different surgical techniques employed. SCM, sternocleidomastoid muscle.

decrease the risk of relapse of the TEF. In the series reported by Wasano et al, excellent results were conveyed despite a 50% preoperative radiotherapy rate, as all 4 patients achieved resumption of oral intake and had a successful TEP closure without complications over a period of 11.5 months, perhaps due to the vascularized nature of a pedicled fascial flap.[36] In the present review, interposition of a SCM flap was highly reliable as it accomplished a failure rate of 2% (95% CI < 1–20%). Nonetheless, a history of radiotherapy and especially in bilateral neck dissections, the use of the SCM can be restricted despite having three sources of perfusion as some blood supply is sacrificed when it is elevated as a pedicled flap.

Baldwin and Liddington reported the inset of a tunneled deepithelialized deltopectoral flap between the trachea and the esophagus,[25] while Balasubramanian et al closed the TEP site using a single perforator-based deltopectoral flap which was sutured directly onto the fistula site and all along its path. The authors reported complete fistula closure in four patients and one case of flap dehiscence, resulting probably because of its extended length and the slim base of the flap, which ultimately compromised the perfusion.[32,45] In this setting, the deltopectoral flap may not be the best alternative for a flap-based reconstruction for TEF closure as it yielded a 17% (95% CI < 1–64%) failure rate. Also, the use of bulky muscle flaps may compromise the airway and esophageal lumen and can lead to stomal stricture, potentially requiring further surgery in the form of stomaplasty.[8,43,44] Additionally, tissue may be of uncertain quality if neck dissections have been performed or if the flap was within the radiated field.[31,44,45]

Microvascular free tissue transfer has asserted itself as the standard of care in reconstruction of complex head and neck defects due to the advantage of size-specific tailored flaps and to the availability of chimeric tissue with multilayered components.[9] The RFF flap is a thin, pliable fasciocutaneous flap with a large pedicle considered ideal by many authors for TEP closure.[9] Gehrking et al performed three FFFs achieving excellent results.[24] Dewey et al described in their series a bipaddled RFF flap created by deepithelialization of the intervening tissue for TEP closure.[37] Although this flap was assertive and sophisticated for closure of this communicating defect, the requirement to harvest a bigger flap for deepithelialization of the intermediate portion and achieve a multilayer closure, resulted in extra bulkiness.[37] Additionally, one patient presented with recurrent strictures of the pharyngoesophageal segment, which ultimately maintained oral alimentation for 8 years following multiple dilations.[37]

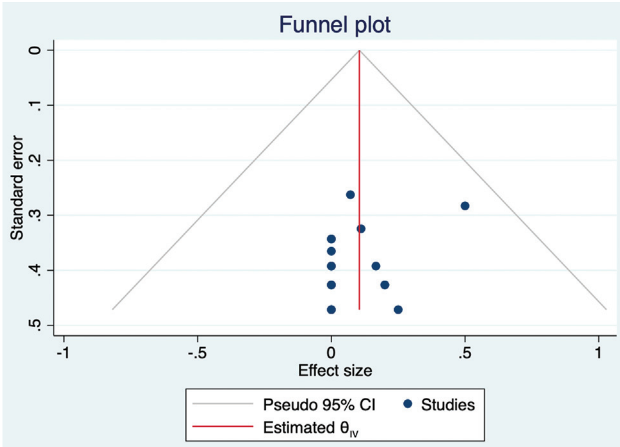

Fig. 4 Funnel plot exhibiting publication bias of the overall unsuccessful tracheoesophageal puncture (TEP) closure rate.

Therefore, the RFF flap is an optimal option for reconstruction of demanding tracheoesophageal defects exhibiting a 0% (95% CI < 1–37%) TEP recurrence rate, especially in patients with past medical history of neck dissection and radiotherapy. In this review, previous history of radiotherapy was reported on 17 out of the 18 patients managed with RFF flaps and 100% successful rate.

Huang and Day used the ulnar artery perforator free flap (UAPFF) with identifiable perforators that allowed to separate the fasciocutaneous component into two independent skin paddles without the aforementioned deepithelialized intermediate portion required in RFF flaps.[9] The single case reconstructed with this flap had an uneventful recovery. Remarkably, the UAPFF is commonly less hairy than the RFF flap, making it more tempting for oral and pharyngeal reconstruction.[9] None of the authors reporting on outcomes on the FFF mentioned the incidence of recurrence after reconstruction of the TEP site.

Mohan and Malata successfully closed a TEP site with a bilaminar lateral arm free flap in a previously radiated patient who was initially managed with interposition of a pedicled pectoralis major myocutaneous flap. The skin paddle provided an adequate epithelial lining to resurface the mucosal defect in the esophagus and the posterosuperior edge of the tracheal stoma. The rest of the flap was deepithelialized providing an interposition tissue and the pedicle length was satisfactory to allow anastomosis out of the radiated field.[33] Of note, the contemporary incorporation of thin and super-thin perforator flaps like the superficial circumflex iliac artery perforator flap, thoracodorsal artery perforator flap, and anterolateral thigh perforator flap has been successfully executed for the reconstruction of head and neck oncologic defects yielding exceedingly good results.[55,56] Despite the fact we did not find any report that detailed the use of this free flaps, they can be used for TEP closure without the additional bulkiness of fasciocutaneous flaps. However, further studies are required.

To our knowledge, no intestinal flaps were reported for the closure of TEPs, but Viñals Viñals et al implemented a gastro-omental free flap performing the anastomosis beyond the radiated area in a patient with a previously failed reconstruction using a muscle flap.[40] The stomach patch was customized to the esophageal defect without the additional bulk of muscular or fasciocutaneous flaps, and the omentum was placed around the tracheostomy and interposed between trachea and esophagus creating a three-layer reconstruction.[40] The patient was able to receive a new TEP and voice prosthesis 2 years after reconstruction.[40] In the experience of senior authors (H.C.C. and O.J.M.), enteric flaps are worthwhile in young patients with long life expectancy and should be considered if other therapeutic strategies have been exhausted. These flaps also offer immediate fistula closure, definitive healing, and can be used if wider excisions are performed when locoregional control of tumors has been unsatisfactory.

Limitations

The incidence of tracheostomy stenosis was not assessed. Comparisons between surgical methods within independent studies for TEP closure were not reported. The undersized samples and the inherent properties of retrospective studies reduced the strength of evidence. Due to the heterogeneity in data report, quality of data, and type of included studies, it was not possible to obtain the success of TEP closure rate in radiated versus nonirradiated patients. All included studies were rated 4 using the OCEBM. Some variables were not reported evenly in all studies.

Conclusion

While several reconstructive options are practical for closure of the TEP site, the indications for the different modalities cannot be universally established. A critical assessment of the reconstructive modality should take into consideration previous surgical history, history of radiation, comorbidities, and defect size. Patients with no history of radiotherapy and small defects may benefit from fistula excision followed by tracheal and esophageal wall multilayered closure, with or without cephalic tracheal repositioning over the TEP site. When the surgical field is compromised with previous neck dissections and radiation, multilayered reconstruction with interposition of vascularized tissue in conjunction with fistula excision yields high rates of successful TEP site closure. Depending on the size of the defect and availability of local tissue, surgeons may select local flaps or free tissue transfer. In this review, the SCM muscle flap or fasciocutaneous free flaps demonstrated optimal performance for this purpose.

Disclosures
The authors have no financial interest to declare in relation to the content of this article. All authors have completed the ICMJE uniform disclosure form.

Authors' Contributions
Idea and conceptualization: S.M. and J.M.E.; Research and investigation: A.M. and J.M.E.; Data curation: A.M. and J.M.E.; Analysis: V.P.B., O.J.M., J.M.E.; Funding acquisition: J.M.E.; Methodology: J.M.E.; Project administration: A.M., V.P.B., J. M.E.; Software and simulation: V.P.B. and J.M.E.; Supervision: S.M., O.J.M., H.C.C., E.S., P.C.; Verification: S.M. and O.J.

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