

# Voice-Related Quality of Life After Total Laryngectomy: Systematic Review and Meta-Analysis

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**Abstract: Background.** To compare voice rehabilitation-related quality of life among patients surgically treated for total laryngectomy and rehabilitated with esophageal (EV) and tracheoesophageal (TEV) voice.

**Methods.** A systematic literature review of articles from the past 20 years was conducted, and only full-text English articles comparing VTE and EV results in laryngectomized patients were included.

**Results.** We provided 15 articles for a total of 1085 laryngectomized patients undergoing voice rehabilitation, of which 869 (80.1%) were treated with voice prosthesis while 216 (19.9%) to esophageal speech. Pooled VHI outcomes showed a significantly better score for the TEV group than EV one ( $31.93 \pm 12.11$  versus  $35.39 \pm 20.6$ ;  $P = 0.003$ ), but no significant difference was recorded at VrQoL ( $8.27 \pm 5.98$  versus  $9.27 \pm 2.02$ ;  $P = 0.19$ ).

**Conclusion.** TEV and EV are both effective procedures in voice rehabilitation after laryngectomy. Although TEV allows for significantly better speech performance, it does not necessarily correlate with a high VrQoL.

**Key Words:** Tracheoesophageal voice— VrQoL— Total laryngectomy— Esophageal voice— VHI.

## INTRODUCTION

Laryngeal cancer is 1 of the most common head and neck cancer, representing 4.5% of all malignancies. Total laryngectomy is the primary treatment modality for advanced disease patients.<sup>1,2</sup> In addition, voice rehabilitation outcome significantly impacts patient's quality of life (QoL), with better psycho-emotional domains in patients with better vocal scores.<sup>3</sup> Several authors compared the 2 main rehabilitative procedures performed in laryngectomy patients, the esophageal speech (ES) and tracheoesophageal speech (TES), reporting contrasting data in regard.<sup>4-7</sup>

Some authors reported that patients with ES have good voice perception, avoiding any device-use and through the pharyngoesophageal segment hands-free.<sup>8-13</sup> However, the air reservoir in ES is significantly smaller than the physiological one, differently in TES where it is maintained, as in physiologic laryngeal phonation through the lungs.<sup>8,14</sup>

There is also in TES a better voice quality, with higher maximal voice intensity and longer phonation.<sup>15-18</sup> However, we must also emphasize the costs and maintenance of these devices, which can often generate problems among patients. On the other hand, several studies show better

vocal outcomes in patients treated with voice prostheses.<sup>4,6,19-21</sup> However, tracheoesophageal voice can often be burdened by different complications, especially regarding fistula-related pathologies: tracheoesophageal granuloma, periprosthetic leakage, severe atrophy of the fistula party wall, fistula migration.<sup>7,16,21</sup>

More recent findings by Cocuzza et al. in a study of 39 patients reported in 2020 show that the QoL was worse in the subgroup of patients with post-prosthetic complications socio-emotional and functional domains of the TEV patient group compared to the EV group.<sup>6</sup>

## MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was used to conduct the systematic review and meta-analysis,<sup>22</sup> while the Populations, Interventions, Comparators, Outcomes, Timing, and Setting (PICOTS) statements for the method presentation.<sup>23</sup>

We considered Participants (laryngectomy patients); Intervention (tracheoesophageal puncture); Control (esophageal voice); Outcome (improved quality of life related to vocal performance), and study type (observational study).

Language, publication date, and publication status were imposed as restrictions.

We considered the primary outcome a significant improvement in the subjective questionnaires administered to the patient at the post-treatment follow-up. Conversely, other parameters assessed in the studies were considered secondary outcomes.

All studies that met the following criteria were included:

1. Original articles;
2. The article was published in the English language;
3. The studies included patients undergoing total laryngectomy and voice rehabilitation;

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4. The studies reported detailed information on post-treatment vocal and QoL outcomes, different rehabilitation modalities, and patient's comorbidities;
5. We excluded from the study case report, editorial, letter to the editor, or review.

### Protocol data extraction and outcomes

The authors A.M, S.C, and F.N analyzed the literature's data. Any disagreements were solved through a discussion by the study team members. The included studies were thus analyzed to achieve all the available data and guarantee eligibility among subjects enrolled.

The patient's features, including symptoms, age, staging, validated questionnaires, treatment modalities (primary or secondary), were collected. In addition, the following information was also collected: author data, year, sample size, study design, statistical analysis, findings, and conclusions. The authors of the included studies were contacted if the required data were not complete utilizing correspondence author's email or Research Gate (<http://www.researchgate.net/>).

### Electronic database search

We searched PubMed, Scopus, and Web of Science electronic databases for studies on voice and quality of life outcomes in laryngectomized patients undergoing speech rehabilitation of the last 20 years' literature (from Dec 1, 2001, to Jun 1, 2021) by three different authors, using MeSH, Entry Terms, and keywords related. The related search keywords were used: "tracheoesophageal voice", "voice prosthesis", "tracheoesophageal puncture", "esophageal voice", "laryngectomized voice rehabilitation", "voice-related quality of life".

We also considered the "Related articles" option on the PubMed homepage. Reference manager software (EndNote X7, Thomson Reuters, Philadelphia, PA) collected references and removed duplicates. Consequently, titles and abstracts of papers available in the English language were examined by the investigators.

The full texts identified were screened for original data, and the related references were retrieved, and other relevant studies were checked manually.

### Statistical analysis

We performed a systematic review according to the approved reporting items' quality requirements for systematic review and meta-analysis protocols (PRISMA) declaration.<sup>22</sup> The studies' quality assessment (QUADAS-2) instrument to estimate the included studies' was adopted, and the risk of bias was presented descriptively.<sup>24</sup> Moreover, observational studies' potential risk of bias was assessed using the Joanna Briggs Institute Critical Assessment Checklist for Observational Studies.<sup>25</sup>

Statistical analysis was performed using statistical software (IBM SPSS Statistics for Windows, IBM Corp.

Released 2017, Version 25.0. Armonk, NY: IBM Corp). We used Random-effects modeling (standard error estimate = inverse of the sample size) to estimate summary effect measures by 95% confidence intervals (CI). Subsequently, forest plots were generated through the Review Manager Software (REVMAN) version 5.4 (Copenhagen: The Nordic Cochrane Centre: The Cochrane Collaboration). We calculated the inconsistency (I<sup>2</sup> statistic) and established the values for low inconsistency = 25%, moderate inconsistency = 50%, and high inconsistency = 75%.<sup>26</sup>

Furthermore, the certainty assessment in cumulative evidence evaluated by GRADE guidelines was considered very low (Table 2).

## RESULTS

The systematic review of the literature identified 815 relevant studies. After removing the duplicates, 808 were kept for the analysis. We excluded studies that did not match inclusion criteria by the records analysis and subsequent articles' full-text screening ( $n = 480$ ). As summarized in the PRISMA flow diagram (Figure 1), the remaining 15 papers were included in synthesis analysis for the data extraction after the full-text screening. Further, we excluded seven papers (absence or incomplete data) due to the meta-analysis-established criteria and considered eight studies for quantitative analysis. The chart flow is reported in (Figure 1). A graphical display of QUADAS-2 results is shown in (Figure 2), which summarized the possible risk of bias.

Moreover, the probable risk of bias for observational studies is described in (Figure 3).<sup>24</sup>

### Patients features and surgery

We provided fifteen studies included in the qualitative analysis.<sup>4,6,8,9,10-15,21,27-30</sup> According to Study design classification, 11 papers were retrospective controlled studies, while four studies consisted of an uncontrolled retrospective study.<sup>12,13,15,30</sup> We recorded a study's sample sizes ranging from 20<sup>13</sup> to 226<sup>28</sup> subjects, with a total of 1085 patients assessed. All the relevant data retrieved from the included original studies are described in (Table 1). The evidence evaluation conducted by the GRADE assessment was considered low due to study design (retrospective studies), heterogeneous methodology, and risk of bias in the included studies. The evidence appraisals are summarized in (Figure 3).

### Patients features and surgery

We provided 15 articles in our systematic literature review for a total of 1085 (89.38 male versus 10.3 female) patients. The patients' average age was 65.38 ± 4.85 years. All patients were treated with total laryngectomy for advanced laryngeal cancer.

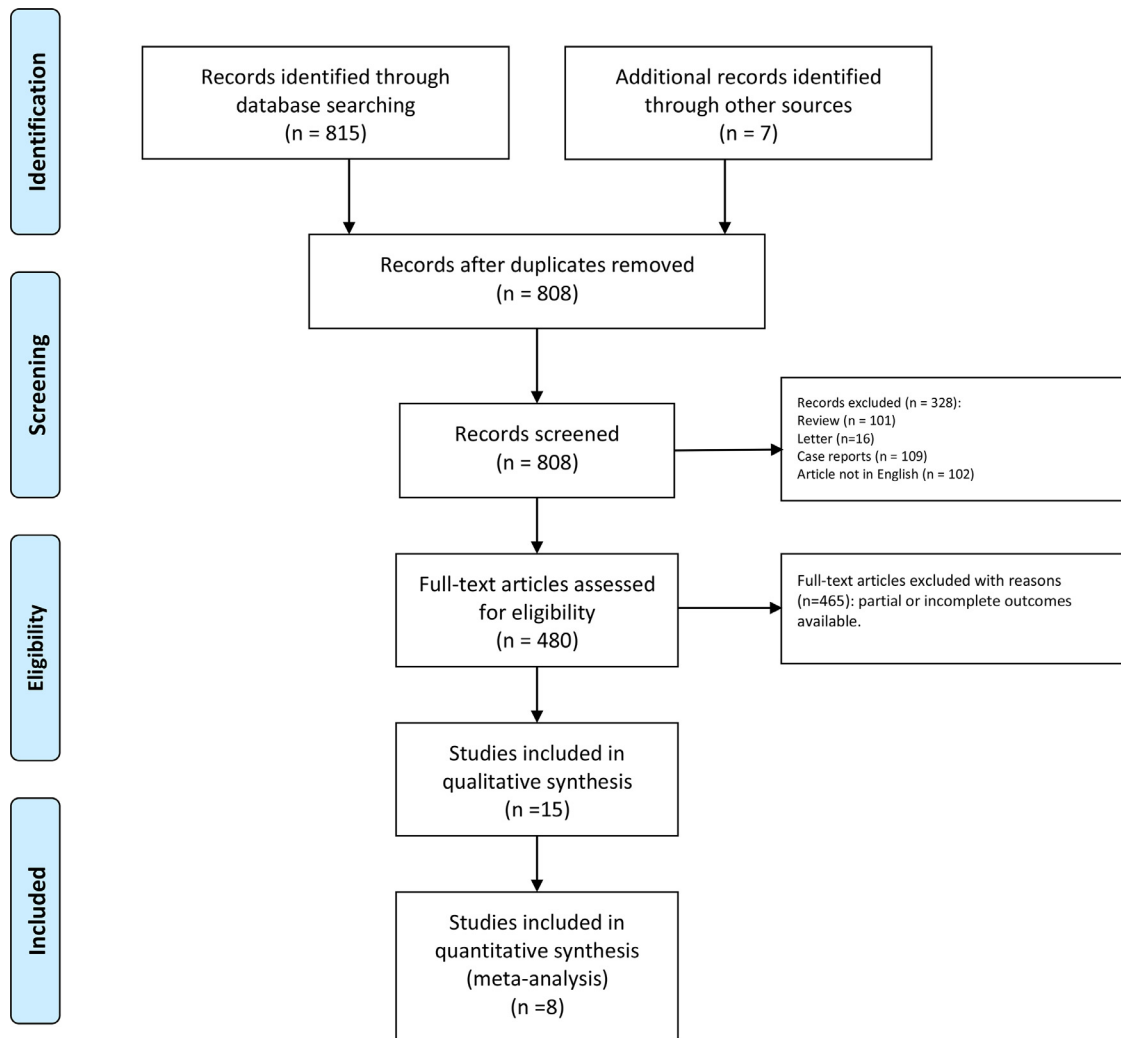


FIGURE 1. PRISMA flow diagram.

Consequently, 869(80.1%) subjects were treated with voice prosthesis rehabilitation, while 216(19.9%) were subjected to esophageal speech (Table 1).

### Voice handicap index

Nine papers reported mean value  $\pm$  SD of the VHI scores (Tab.I). Pooled VHI outcomes analysis after vocal rehabilitation showed a significant better improvement for the TEV group of  $31.93 \pm 12.11$  versus the EV group of  $35.39 \pm 20.6$  ( $P = 0.003$ ) (Figure 4A).

The analysis using random-effects modeling for 338 (197 TEV versus 141 EV) procedures (5 papers) demonstrated an MD of -1.90, ranging from -14.83 to 11.02 of the VHI score. TEV and EV presented an overall effect Z score = 0.29, Q statistic  $P < 0.00001$  (statistically significant heterogeneity),  $I^2 = 97\%$ , as described in (Figure 5).

### Voice-related quality of life

Seven papers (473 patients) analyzed the Voice-related quality of life (VRQoL) outcomes after vocal rehabilitation, demonstrating at the comparison between TEP and EV, not

significant differences in vocal outcomes TEP  $8.27 \pm 5.98$  versus EV  $9.27 \pm 2.02$  ( $P = 0.19$ ) as demonstrated in (Figure 4B).<sup>4,6,9</sup> The VRQoL outcomes at random-effects modeling for 178 patients showed an MD of -0.74 [95% CI -2.85, 1.38] as reported in (Figure 5). Subgroup analysis demonstrated an overall effect Z score = 0.68 ( $P = 0.49$ ), Q statistic  $P = 0.03$  (significant heterogeneity),  $I^2 = 71\%$  (moderate inconsistency).

### 36-Item short form survey instrument (SF-36)

Four papers analyzed the SF-36 outcomes in patients enrolled<sup>21,27,28,30</sup> with a significant higher improvement in TEP patients than EV ones ( $58.7 \pm 2.94$  versus  $61.84 \pm 8.33$ ;  $P < 0.001$ ) (Figure 4C).

## DISCUSSION

The quality of life after total laryngectomy and the role of voice rehabilitation have been analyzed by different authors in the literature.<sup>5,21,27,29</sup> These 2 factors have important repercussions both in terms of psychological, social, and functional outcomes. However, the results in the literature

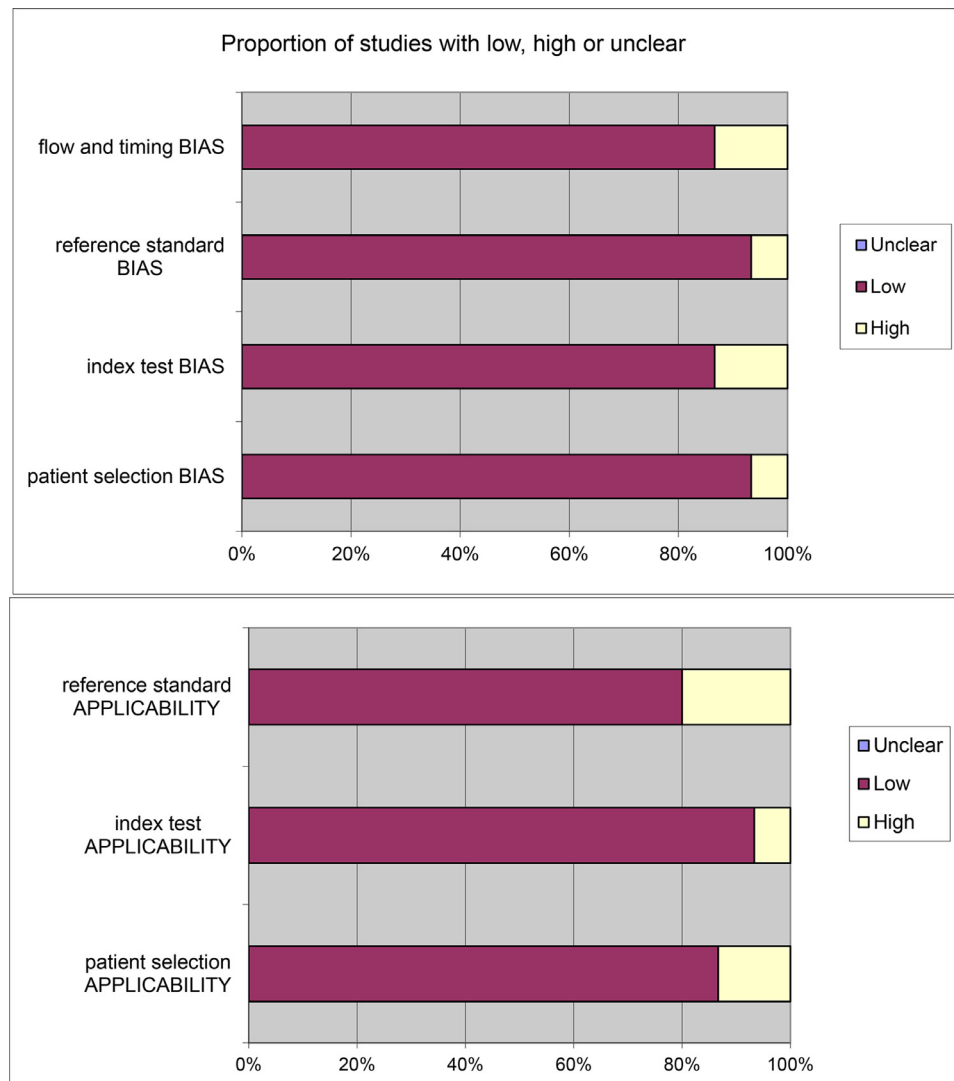


FIGURE 2. QUADAS-2.

are still controversial due to limitations such as the retrospective design of studies with small patient courts and heterogeneity in clinical instruments used.

Although the loss of the original voice represents an important factor that compromises the quality of life, the rehabilitation methodique is still debated.<sup>3,11,13</sup> While some authors affirm that it does not affect the quality of life, equating the outcomes obtained after using the esophageal voice (EV) and tracheoesophageal voice (TEV), others instead exalt voice prosthesis.<sup>6,7,13</sup>

Conversely, Salturk et al. in 2016 reported that patients who used esophageal speech had lower VHI-10 scores, reflecting a better quality of life than TEV ( $10.25 \pm 3.22$  versus  $19.42 \pm 5.56$  respectively;  $P = 0.001$ ).<sup>10</sup>

Our study, after pooled analysis, found significant better VHI outcomes in TEV patients compared to the EV group ( $31.93 \pm 12.11$  versus  $35.39 \pm 20.6$ ) ( $P = 0.003$ ), a significant heterogeneity ( $P < 0.0001$ ) and high inconsistency  $I^2 = 97\%$  (Figure 4A).

Several authors argue that the tracheoesophageal voice allows better results in terms of intelligibility and voice quality than the esophageal voice, resulting in a better related quality of life.

Allegra et al. in 2019 found an improved voice performance in TEV patients and a significant difference in the functional subscale of the V-RQOL questionnaire compared to EV ( $2.9 \pm 1.0$  versus  $6.23 \pm 4.5$ ;  $P = 0.001$ ).<sup>4</sup>

The vocal implant indeed allows better vocal performance, although the selection of the patient to be implanted plays a fundamental role in therapeutic success.

On the other hand, the esophageal voice does not involve the daily management of the voice prosthesis or the complications often associated with a vocal implant, such as the formation of granulomas, leakage, or fistula migration.

Yet, even the acquisition of the esophageal voice can be more difficult, often poorly tolerated than the tracheoesophageal.<sup>8-11</sup>

	1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	2. Were cases and controls matched appropriately?	3. Were the same criteria used for identification of cases and controls?	4. Was exposure measured in a standard, valid and reliable way?	5. Was exposure measured in the same way for cases and controls?	6. Were confounding factors identified?	7. Were strategies to deal with confounding factors stated?	8. Were outcomes assessed in a standard, valid and reliable way for cases and controls?	9. Was the exposure period of interest long enough to be meaningful?	10. Was appropriate statistical analysis used?
Cocuzza et al. 2020	+	+	+	+	+	-	-	+	+	+
Allegra et al. 2019	+	+	+	+	+	-	-	+	+	+
Moukarbel et al. 2011	+	+	+	+	+	-	-	+	+	+
Deshpande et al. 2009	+	+	+	+	+	-	-	+	+	+
Salturk et al. 2016	+	+	+	+	+	-	-	+	+	+
Antin et al. 2020	+	+	+	+	+	-	-	+	+	+
Dragicevic et al. 2019	+	+	+	+	+	-	-	+	+	+
Agarwal et al. 2015	+	+	+	+	+	-	-	+	+	+
Miyoshi et al. 2015	+	+	+	+	+	-	-	+	+	+
Kazi et al. 2007	+	+	+	+	+	-	-	+	?	+
Evans et al. 2009	+	+	+	+	+	-	-	+	+	+
Galli et al. 2019	+	+	+	+	+	-	-	+	+	+
Giordano et al. 2011	+	+	+	+	+	-	-	+	+	+
Farrand et al. 2007	+	+	+	+	+	-	-	+	+	+
Schouster et al. 2003	+	+	+	+	+	-	-	?	+	+

**FIGURE 3.** Risk of bias summary author's judgments for each included study, assessed by the Joanna Briggs Institute (JBI). Critical appraisal checklist for case-control studies.

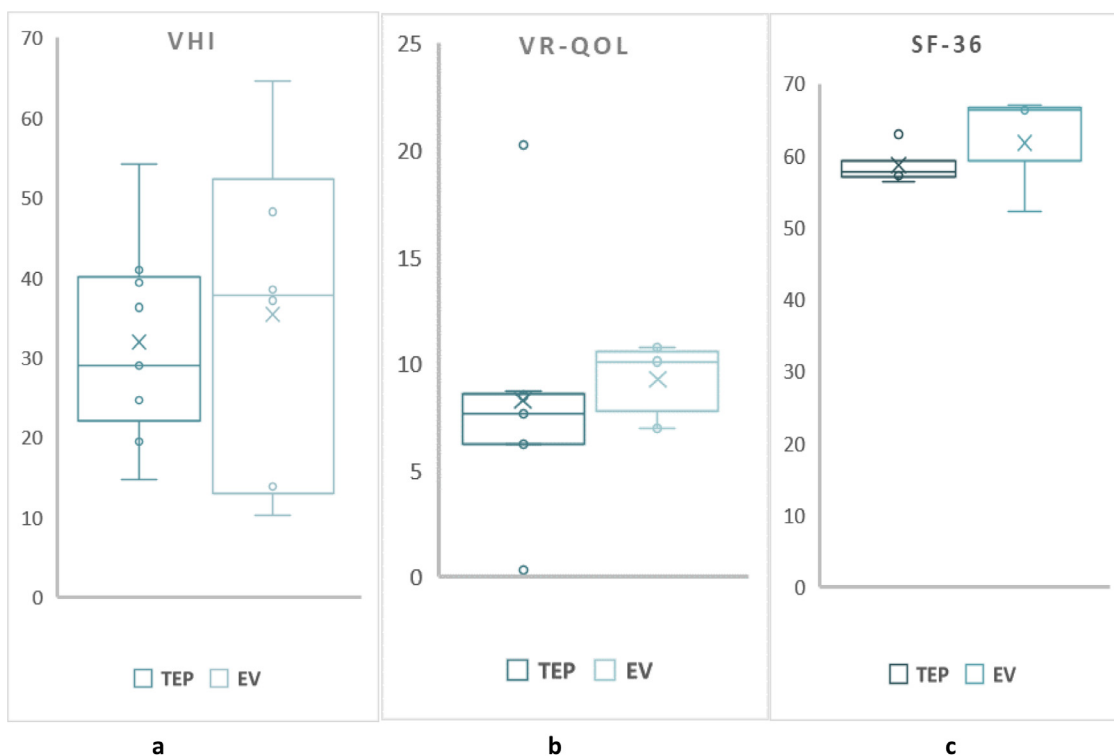


**TABLE 1.**  
**Main Features of Papers Retrieved via Systematic Review. Abbreviations TEV, Tracheo-esophageal voice; EV, esophageal voice; VHI, Voice handicap index, VRQoL, Voice related quality of life; SF-36, Short form 36**

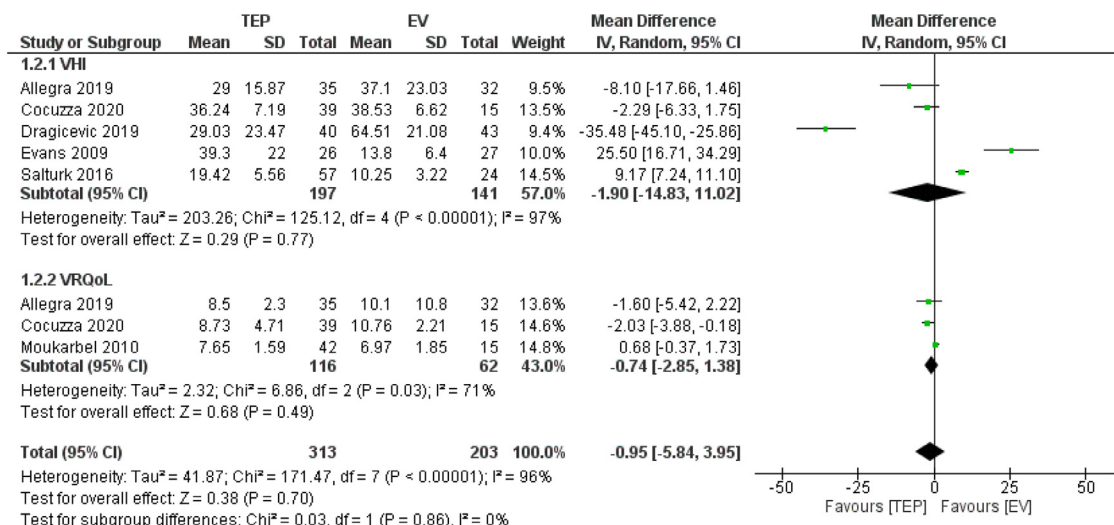
Reference	Study design	Sample	Age	Gender (M/F)	VHI (TEV/EV)	VRQOL (TEV/EV)	Other Clinical Scale (TEV/EV)
Cocuzza et al 2020	Retrospective controlled	54	64.7±7.58 years	47 male, 7 female	36.24 ± 7.19/ 38.53 ± 6.62	8.73 ± 4.71/10.76 ± 2.21	—
Allegra et al 2019	Retrospective controlled	67	64.5±8.0 years	65 male, 2 female	29±15.87/ 37.10±23.02	8.5±2.3/10.1±10.8	VPO = 23.4±11.9/ 29.2±11.3
Moukarbel et al 2011	Retrospective controlled	75	64.1 years	51 male, 24 female	—	—	—
Deshpande et al 2009	Retrospective uncontrolled	122	56.0 years	118 male, 4 female	—	7,62	—
Salturk et al 2016	Retrospective controlled	96	58.25 years	—	19.42±5.56/ 10.25±3.22	—	—
Antin et al 2020	Retrospective controlled	133	70±11 years	125 male, 8 female	54.2±30.3/ 48.2±17.4	—	EORTC QLQ C30 55.9±25.1/ 78.3±7.4
Dragicevic et al 2019	Retrospective controlled	83	61.76 ± 7.053 years	33 male, 7 female	29.03±23.479/ 64.51±21.089	—	—
Agarwal et al 2015	Retrospective uncontrolled	71	60.77±8.634 years	52 male, 19 female	24.65±18.11/ 13.8±6.4	20.23±5.53	—
Miyoshi et al 2015	Retrospective uncontrolled	20	70.8±9.2 years	20 male	14.65±8.43	6.225±2.659	—
Kazi et al 2007	Retrospective uncontrolled	54	63.4 years	40 male, 14 female	40.9±21.8	6.25±2.45	—
Evans et al 2009	Retrospective controlled	53	67.0±10	53 male	39.3±22.0	—	—
Galli et al 2019	Retrospective controlled	42	63.6 ± 4.2 years	22 male, 2 female	—	—	SF-36= 63.0 ± 20.2
Giordano et al 2011	Retrospective controlled	42	63.6±4.2 years	22 male, 2 female	—	—	SF-36= 57.3± 18.3
Farrand et al 2007	Retrospective controlled	226	65.8±9.5	109 male, 34 female	—	—	SF-36= 58.11/52.22
Schuster et al 2003	Retrospective uncontrolled	25	62.1±7.5 years	25 male	—	—	SF-36= 56.4±16.6

**TABLE 2.**  
**GRADE Summary of Findings After Systematic Review. Most Studies not Identified Confounding Factors, Leading to Spurious Interpretation of the Outcomes. The Inability to Meta-Analyze the Results was Recorded in Nine of 15 Papers**

№ of studies	Certainty assessment						Other considerations	Certainty
	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
15	Observational Studies	Not serious	Not serious	Not serious	Not serious	None	○○○	Very low



**FIGURE 4.** A, 4B, 4C. Overall mean of differences of VHI, VRQoL and SF-36 values after vocal rehabilitation between tracheoesophageal and esophageal voice as visualised by the boxplots. The bottom and top of the box are the first and the third quartiles, and the band inside the box is the median; whiskers represent 1° and 99° percentiles; values that are lower and greater are shown as circles.



**FIGURE 5.** Forest plot between tracheoesophageal and oesophageal voice outcomes. Abbreviations CI, confidence interval; SD, standard deviation. No significant differences were found at test for subgroup differences (P = 0.86).

Our meta-analysis comparing TEV and EV has not confirmed significant differences among voice related quality of life (TEV  $8.27 \pm 5.98$  versus EV  $9.27 \pm 2.02$ ;  $P = 0.19$ ) (Figure 4B). This data probably confirms the unnecessary correlation between excellent vocal outcomes and satisfactory quality of life. As previously stated, both the voice prosthesis and the esophageal voice could present discomfort in the laryngectomized patient, thus affecting the overall quality of life.

However, at random effects for VRQoL, Q statistic demonstrated a significant heterogeneity ( $P = 0.03$ ) and moderate inconsistency ( $I^2 = 71\%$ ).

A further vocal rehabilitation approach defined in the laryngectomized is represented by the electrolarynx. The evidence presently reports a correlated communication disability that is varied, with subjects presenting learning difficulties while some may be highly skilled users.<sup>9,10,31</sup> Mourkabel et al compared electrolaryngeal speech outcomes in 18 subjects versus 15 esophageal speech and 42 tracheoesophageal patients.<sup>9</sup> Although at comparisons of VRQOL scores, TES and ES were perceived to be better than ELS ( $P < .001$  for both), only ELS showed a positive correlation with time after surgery and older age.

On the contrary, Salturk et al. reported a greater VHI-10 of ELS than esophageal ( $P < .001$ ) but scores but not significant versus tracheoesophageal ( $P = 0.373$ ).<sup>10</sup>

Another scale frequently used in the literature as an indicator of the patient's quality of life is the SF-36.<sup>21,27,28,30</sup> The questionnaire contains domains concerning physical functioning, physical and emotional limitations, social functioning, bodily pain, general and mental health. Although the results are still debated in the literature, our analysis demonstrated a significantly higher SF-36 improvement in TEP patients than EV ones ( $58.7 \pm 2.94$  versus  $61.84 \pm 8.33$ ;  $P < .001$ ) (Figure 4C).

However, the results obtained from our meta-analysis must be interpreted with caution, as significant limitations must be taken into consideration. The main limitation of the present study is the heterogeneity between included studies regarding the patient population, comorbidities, cancer staging, and lack of a preliminary psychological and speech therapy evaluation of the patient before treatment. All of these points may limit the draw of a clear conclusion. However, this study is the first systematic review and meta-analysis investigating the association between vocal rehabilitation procedures and quality of life. Future research should consider the unnecessary correlation between high vocal performance and quality of life demonstrated in our meta-analysis. In light of what has been stated, studies with greater samples and a more careful selection of the patient in the choice of the rehabilitation method will have to be carried out to avoid the poor quality of life.

## CONCLUSION

The rehabilitation of the laryngectomized patient for years to achieve a better vocal performance must consider the

correlated quality of life as the primary outcome. Even with the same or higher voice rehabilitation in the patient with a voice prosthesis, comorbidities and related health care can reduce patient satisfaction with the treatment. Future comparative studies, including large patient trials, are needed to compare the different rehabilitation procedures in light of the multiple prognostic cofactors.

## AUTHOR CONTRIBUTIONS

Conceptualization S.C., I.L.M., and A.M.; Methodology, A.M., J.R.L.; Validation, C.V., G.I., and S.C.; Formal analysis, C.V., G.I., S.C., and A.M.; Investigation, A.P., S.C. and F.N.; Resources, S.C., I.L.M., C.M.G., and I.L.M.; Data curation, G.I., J.R.L., S.C., I.L.M., and A.M.; Writing—original draft preparation, G.M., S.C., A.M., and S.F.; Writing—review and editing, G.I., S.C., C.V. and A.M. All authors have read and agreed to the published version of the manuscript.

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