Tissue augmentation treatment for periprosthetic leakage in patients who have undergone a total laryngectomy: A systematic review

Miguel Mayo-Yáñez1,2,3 | Mercedes Díaz Ramos-Neble4 | Irma Cabo-Varela1,5 | Carlos Miguel Chiesa-Estomba3,6 | Jérôme R. Lechien3,7,8,9,10 | Nicolas Fakhry3,11 | Antonino Maniaci3,12 | Katherine A. Hutcheson13

1Otorhinolaryngology—Head and Neck Surgery Department, Complexo Hospitalario Universitario A Coruña (CHUAC), 15006 A Coruña, Galicia, Spain
2Clinical Research in Medicine, International Center for Doctorate and Advanced Studies (CIEDUS), Universidade de Santiago de Compostela (USC), 15782 Santiago de Compostela, Galicia, Spain
3Young-Otolaryngologists of the International Federations of Oto-Rhino-Laryngological Societies (YO-IFOS) Study Group, Paris, France
4School of Medicine, Universidade de Santiago de Compostela (USC), 15782 Santiago de Compostela, Spain
5Health Sciences Programme, International Center for Doctorate (EIDUDC), Universidade da Coruña (UDC), Coruña, Spain
6Otorhinolaryngology—Head and Neck Surgery Department, Hospital Universitario Donostia—Biodonostia Research Institute, 20014 Donostia, Gipuzkoa, Spain
7Department of Otolaryngology, Polyclinique de Poitiers, Elsan Hospital, Poitiers, France
8Department of Otolaryngology—Head & Neck Surgery, Foch Hospital, School of Medicine, UFR Simone Veil, Université Versailles Saint-Quentin-en-Yvelines (Paris Saclay University), Paris, France
9Department of Human Anatomy and Experimental Oncology, UMONS Research Institute for Health Sciences and Technology, University of Mons (UMons), Mons, Belgium
10Department of Otolaryngology—Head & Neck Surgery, CHU Saint-Pierre (CHU de Bruxelles), Brussels, Belgium
11Department of Oto-Rhino-Laryngology Head and Neck Surgery, La Conception University Hospital, AP-HM, Aix Marseille Univ, Marseille, France
12Department of Medical and Surgical Sciences and Advanced Technologies ‘GF Ingrassia,’ ENT Section, University of Catania, Catania, Italy
13Department of Head and Neck Surgery, Division of Radiation Oncology, The University of Texas, M. D. Anderson Cancer Center, Houston, Texas, USA

Correspondence
Miguel Mayo-Yáñez, Otorhinolaryngology – Head and Neck Surgery Department, Complexo Hospitalario Universitario A Coruña (CHUAC), As Xubias 84, 15006, A Coruña, Spain.
Email: miguelmmy@gmail.com

Abstract

Objectives: Tracheoesophageal puncture (TEP) is considered the gold standard for voice rehabilitation after total laryngectomy. One of the main causes of treatment failure, and a potentially serious complication, is the TEP enlargement and/or leakage around the voice prosthesis. The injection of biocompatible material to increase the volume of the puncture surrounding tissue has been studied as a popular option for conservative treatment of enlarged tracheoesophageal fistula. The aim of this paper was to perform a systematic review of the efficacy and safety of such treatment.

Design: Search conducted in PubMed/MEDLINE, the Cochrane Library, Google Scholar, Scielo and Web of Science and through the meta-searcher Trip Database based on Preferred Reporting Items for a Systematic Review and Meta-analysis (PRISMA) statement.
Settings: Human experiments published in peer-reviewed journals, where investigators assessed the use of peri-fistular tissue augmentation for periprosthetic leakage were evaluated.

Participants: Laryngectomized patients with voice prosthesis, presenting periprosthetic leak due to enlarged fistula.

Main outcomes measures: mean-duration without new leak.

Results: A total of 196 peri-fistular tissue augmentation procedures in 97 patients were found in the 15 selected articles. The 58.8% of patients had a time without periprosthetic leak after treatment of >6 months. The 88.7% of tissue augmentation treatments resulted in periprosthetic leakage cessation. The general level of evidence of the studies included in this review was low.

Conclusions: Tissue augmentation treatment is a minimally invasive, biocompatible and safe solution that temporarily resolves periprosthetic leaks in many cases. There is no standard technique or material, and treatment needs to be individualised according to the experience of the practitioner and the characteristics of the patient. Future randomised studies are needed to confirm these results.

KEYWORDS
collagen, fistula injection, head neck, laryngectomy, periprosthetic leakage, tissue augmentation, voice prosthesis

1 INTRODUCTION

Tracheoesophageal puncture (TEP) is considered the gold standard for voice rehabilitation after total laryngectomy. A one-way valved silicone voice prosthesis (VP) fitted within the TEP allows pulmonary air into the pharyngoesophagus (PE) for vibratory sound production when the tracheostoma is occluded. The VP for lung-powered voicing thus facilitating significantly better outcomes for fundamental frequency, maximum phonation time and intensity compared with oesophageal voicing.

The management of patients who have undergone a laryngectomy and users of VP is complex and requires a multidisciplinary and systematic approach by professionals with experience in the field in order to reduce VP replacements and TEP complications. The clinical course of these patients is heterogeneous and highly changeable over time. Failure of the VP and aspiration despite routine VP exchange may lead to pneumonia, more frequent clinical visits, hospitalisation, increased healthcare costs, and reduced quality of life. One of the main causes of failure is TEP enlargement and/or leakage around the VP. This can be a serious complication resulting in leakage of food, fluid or saliva around the prosthesis into the airway, reported in 7%–42% of patients with TEP. There is controversy regarding the factors that could influence the development of this type of leakage. Apart from individual predisposition, various factors have been discussed in the literature including local inflammatory responses in the region of the fistula, atrophy of the tracheoesophageal wall as a late effect of preoperative or postoperative radiotherapy or chemoradiotherapy, the VP diameter or weight, the timing of VP puncture, the VP insertion, the patient’s nutritional status, the patient’s length of follow-up, a continuing history of tobacco exposure, the gastroesophageal reflux, a microbial colonisation the gastroesophageal reflux, a microbial colonisation, an extensive laryngopharyngeal resection and postoperative stricture, or the presence of conditions that have previously been proposed in the literature as predisposing factors that could affect the duration of VP (e.g., diabetes, hypertension, lymph node metastases, thyroid dysfunction, or tumour recurrence).

Currently, different treatments and management protocols have been postulated for this type of complication, with two main types of therapeutic options for persistent periprosthetic leakage due to
enlarged TEP\textsuperscript{6,14}. Complete closure of the TEP site surgically or conservative management with different measures acting on VP or TEP to prevent periprosthetic leakage but preserve TE voice. The injection of biocompatible material to increase the volume of the TEP surrounding tissue has been studied over time as a popular option for conservative treatment of enlarged tracheoesophageal fistula. To date, there is no consensus on which is the best choice, the factors that may vary its efficacy or a comprehensive evaluation of the results. The aim of this article was to perform a systematic review of the efficacy and safety of such treatment on periprosthetic leaks. Specific research questions included: (1) Materials used, (2) Differences in technique and, (3) Time without leakage.

2 | METHODS

The review was conducted regarding the Preferred Reporting Items for a Systematic Review and Meta-analysis (PRISMA) guidelines.\textsuperscript{15} A population, intervention, comparison, outcome, timing and setting (PICOTS) framework was used to structure the review process and research questions.\textsuperscript{16}

2.1 | Studies

Human-published studies in peer-reviewed journals were considered. Preprint studies, grey literature, reviews and conference communications were not considered. Eligibility criteria regarding the type of study (both experimental and observational, prospective and retrospective) were not applied. Only studies in English or Spanish were considered.

2.2 | Participants and inclusion/exclusion criteria

Patients who have undergone a total laryngectomy and users of VP, presenting periprosthetic leak due to an enlargement of the fistula.\textsuperscript{10} The leakage should represent an impact on the theoretical duration of the VP reported in previous studies, or affects the patient’s normal daily life (inability to swallow, phonation, complications, etc.).\textsuperscript{2,6} Reports of the use of tissue augmentation treatment in this population with the intention of controlling leak but preserving the TEP for voice were included; reports of injection with intent for complete closure of the tracheoesophageal fistula was considered an exclusion criterion.

2.3 | Intervention and comparison

All studies in which investigators assessed the use of peri-fistular tissue augmentation for periprosthetic leakage were evaluated. The presence of a placebo control group, or comparator treatment by another technique was included when reported but not required for inclusion. The presence of other conservative treatments combined with tissue augmentation therapy was recorded and was not an exclusion criterion.

2.4 | Outcomes

The primary outcome studied was the mean-duration without a new periprosthetic leakage event. Secondary analyses considered differences in these outcomes and procedural variations between different injection materials.

Data collected were the publication information (year, country and study design), demographic information (number, age and gender of patients), the time without event (new leakage), the type of injection material, the number of injections needed to solve the leakage, the existence of a control group, reason for VP replacements, concurrent treatment with proton-pump inhibitors or anti-reflux therapy, type of puncture (primary, secondary), type of VP insertion (anterior, retrograde), tumour stage and surgical resection information, presence of complementary treatment (radiotherapy, radio-chemotherapy), and complications. How patients were evaluated and followed (e.g., existence of management protocol, referral unit, multidisciplinary team, speech therapy assessment...) was also collected, following the recommendations published in the literature.\textsuperscript{2,6}

2.5 | Search strategy

During the month of December 2021, a search was conducted by 3 independent authors (Miguel Mayo-Yáñez; Irma Cabo-Varela & Mercedes Díaz Ramos-Neble) in different indexed databases (PubMed/MEDLINE, the Cochrane Library, Google Scholar, Scielo and Web of Science) and through the meta-searcher Trip Database with the following keywords: ‘tissue augmentation’, ‘fistula injection’, ‘periprosthetic leakage’, ‘voice prosthesis’, ‘laryngectomy’ and complemented with free text terms. Inclusion criteria according to date of publication were not applied. The authors screened abstracts publications and available full texts, and duplicates were refined. The complete texts of selected articles were read and bibliographic references revised with the aim of including possible studies not found through the search strategy. Disagreements between authors were discussed in the work-team, making the decision by consensus (Figure 1).

2.6 | Data and bias analysis

Data extraction was done in duplicate to avoid errors in the qualitative analysis. For publications from the same centre, with the possibility of duplicate samples, all were included for the qualitative analysis and only the ones with the largest sample size were included for the quantitative analysis. The level of evidence was classified according to the Oxford Centre for Evidence-Based Medicine Levels.\textsuperscript{17} Methodological quality of the selected studies was evaluated with the National
### 3 | RESULTS

A total of 221 articles were identified. Once duplicates and unrelated items were excluded, 24 articles were selected for screening by full-text review. Its full text was evaluated according to the proposed methodology, after which 9 manuscripts were excluded due to being in a language other than English or Spanish, did not evaluate tissue augmentation treatment, or use the tissue augmentation treatment for other purposes. The final result was 15 articles included (Table 1): 7 retrospective case series, 1 prospective case series, 2 case series in which the time sequence is not specified, and 5 case reports.

### 3.1 | Descriptive analysis

A total of 196 peri-fistular tissue augmentation procedures in 97 patients were found in the selected articles. Of which, data could
<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Study type</th>
<th>Participants</th>
<th>Material</th>
<th>Patients' assessment</th>
<th>Type of VP and VP during injection</th>
<th>Results</th>
<th>Complications</th>
<th>Commentaries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parrilla et al. (2021) Italy</td>
<td>Retrospective case series</td>
<td>20 men. Mean age 70.4 ± 4.54 years. RT in 18 (80%). Primary puncture in 13 (65%).</td>
<td>Autologous fat (centrifuged)</td>
<td>ENT + SLP</td>
<td>Provox. With prosthesis during injection</td>
<td>16 (80%) without leak. Follow-up of 5.54 ± 3.97 years (range: 1–9 years). 5 patients required 2nd injection in a mean of 3.2 years. Follow-up of 5.54 ± 3.97 years (range: 1–9 years). 5 patients required 2nd injection in a mean of 3.2 years.</td>
<td>No</td>
<td>The advantages of using adipose tissue over other options include greater biocompatibility, no immune response, long-lasting results, and regenerative properties.</td>
</tr>
<tr>
<td>Mayo-Yáñez and Cabo-Varela (2020) Spain</td>
<td>Case report</td>
<td>1 male, 80 years. Previous RT</td>
<td>Hyaluronic acid</td>
<td>ENT + SLP</td>
<td>Provax XtraSeal. No prosthesis during injection</td>
<td>Need for new injection</td>
<td>Extusion of VP and injection material. Failure of treatment</td>
<td>In patients undergoing radiotherapy, previous surgeries or advanced age, the use of this technique should be individualized, due to its higher risk of failure.</td>
</tr>
<tr>
<td>Tjoa et al. (2018) USA</td>
<td>Retrospective Case series</td>
<td>11 men and 4 women. Mean age 61.7 years. 12 (80%) received RT preoperatively and 4 (27%) postoperatively</td>
<td>Calcium hydroxyapatite (n = 11) HA (n = 12)</td>
<td>ENT + SLP</td>
<td>VP not described. No prosthesis during injection</td>
<td>Follow-up of 6.3 years (range 0.7–16 years). 5 patients (33%) required multiple injections. All required VP customization. 11 (73%) achieved a fluent voice. Mean period without leaks of 4.4 (range 0.6–6.7) years</td>
<td>1 patient presented vomiting during and after the procedure. 2 of the 6 patients who did not achieve resolution of the leak were diagnosed with second primary cancers during their follow-up</td>
<td>The combined treatment of peripheral injections associated with replacement and customization of the VP can provide a cessation of periprosthetic leakage and functional restoration of the voice, lasting approximately 4 years after the last injection.</td>
</tr>
<tr>
<td>Twomey et al. (2018) Australia</td>
<td>Retrospective Case series</td>
<td>4 patients</td>
<td>Hyaluronic acid</td>
<td>ENT + SLP</td>
<td>VP not described. With prosthesis during injection</td>
<td>First patient: Initial injection lasted for 204 days. With second injection complete resolution for &gt;1 year. Second patient: first injection lasted 25 days. The second injection resolved symptoms for 370 days. The third injection led to complete resolution (&gt;300 days). Third patient: first injection lasted 25 days. The second injection led to complete resolution for &gt;1 year. Fourth patient: Six injections over an 18-mo period. Average duration of efficacy 86 days (range 20–240 days)</td>
<td>No</td>
<td>Hyaluronic acid provides long-lasting resolution of leaks in some patients. This substance degrades over time, being a temporary non-curative treatment.</td>
</tr>
<tr>
<td>Friedlander et al. (2016) Spain</td>
<td>Retrospective Case series</td>
<td>5 patients (9 injections) 3 patients (5 injections + VP customization)</td>
<td>Hyaluronic acid (Macrolane® Galderma)</td>
<td>ENT</td>
<td>Provax 2. With prosthesis during injection</td>
<td>Follow-up 8 years (1997–15). Duration with HA = 32 days (range 3–55). Duration with HA + custom VP = 63 days (range 28–135)</td>
<td>No</td>
<td>HA injection can be combined with other techniques, allowing a longer prosthesis half-life and increasing the leak-free period.</td>
</tr>
</tbody>
</table>

(Continues)
<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Study type</th>
<th>Participants</th>
<th>Material</th>
<th>Type of VP and VP during injection</th>
<th>Results</th>
<th>Complications</th>
<th>Commentaries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shuaib et al. (2012) USA</td>
<td>Retrospective Case series</td>
<td>8 patients, 7 men and 1 woman. Mean age 61 years. 7 received RT. 6 primary puncture</td>
<td>calcium hydroxyapatite (n = 11) Micronized Alloderm (Cymetra) (n = 9)</td>
<td>ENT + SLP</td>
<td>VP not described. With prosthesis during injection</td>
<td>Follow-up 1.4 years. All resumed baseline speech and swallowing function. The mean duration of leak resolution after each injection was 174.5 days. Patients with metastases required more injections. The patient without RT had prolonged resolution with a single injection. 4 (50%) patients required re-injection. Durable leakage resolution (&gt;3 months) in 6 (75%)</td>
<td>No</td>
</tr>
<tr>
<td>Hutcheson et al. (2011) USA</td>
<td>Retrospective case series</td>
<td>8 patients with injection in 36 patient series</td>
<td>Radiesse (BioForm Medical, Inc., San Mateo, CA) Cymetra (LifeCell Corporation, Branchburg, NJ)</td>
<td>ENT + SLP</td>
<td>VP not described. Presence of VP during injection not described</td>
<td>5 year follow-up. 4 required repeated injections (range 1–3) for recurrent leakage</td>
<td>No</td>
</tr>
<tr>
<td>Seshamania et al. (2006) USA</td>
<td>Retrospective Case series</td>
<td>4 patients. Mean age 67.82 years. 100% had received RT</td>
<td>Cymetra</td>
<td>ENT</td>
<td>VP not described. With prosthesis during injection</td>
<td>Follow-up 2–13 months. 2 patients required &gt;1 injection. 4 obtained satisfactory results, one patient persisted with minimal leakage</td>
<td>No</td>
</tr>
<tr>
<td>Lörincz et al. (2004) Hungary</td>
<td>Case series</td>
<td>7 patients. 5 men and 2 women. Mean age was 55.5 years. 6 with RT</td>
<td>Bioplastique®</td>
<td>ENT</td>
<td>VP not described. With prosthesis during injection</td>
<td>4/7 patients resolved the leaks with a single injection. 2 needed &gt;1 injection at 4–6 months. 1 needed 3 injections.</td>
<td>No</td>
</tr>
<tr>
<td>Rokade et al. (2003) United Kingdom</td>
<td>Case report</td>
<td>2 men. 68 and 76 years. 1 with RT</td>
<td>Bioplastique®</td>
<td>ENT</td>
<td>Pravox 2. No prosthesis during injection</td>
<td>Leak-free period of 11 and 8 months, respectively</td>
<td>No</td>
</tr>
<tr>
<td>Author (year)</td>
<td>Study type</td>
<td>Participants</td>
<td>Material</td>
<td>Patients’ assessment</td>
<td>Type of VP and VP during injection</td>
<td>Results</td>
<td>Complications</td>
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<tr>
<td>Laccourreye et al. (2002)</td>
<td>Case series</td>
<td>7 patients, mean age 63.2 years (range 40–82)</td>
<td>Autologous fat</td>
<td>ENT</td>
<td>VP not described. 1 with prosthesis during injection, 5 without prosthesis during injection</td>
<td>Follow-up &gt;1 year in all patients, all without leakage for &gt;6 months. Four patients required only one injection to resolve the leak. Three required a second injection after this period. Finally, two cases required closure of the puncture for recurrent leaks</td>
<td>One patient presented fat extrusion immediately after in probable relation to the non-removal of the voice VP during the procedure.</td>
</tr>
<tr>
<td>Périé et al. (2002)</td>
<td>Prospective Case series</td>
<td>10 patients, 8 men and 2 women. Mean age 64.4 years (range 56–73), 9 patients received RT</td>
<td>Autologous fat</td>
<td>ENT</td>
<td>Provox. With prosthesis during injection</td>
<td>Follow-up 10–65 mo (mean 32.6). The procedure was successful in 6 patients. Success was achieved &gt;6 mo, although one 1 required an additional injection. 2 patients partially improved. Treatment failed in 2 patients. 2 patients had tumour recurrence during follow-up</td>
<td>No</td>
</tr>
<tr>
<td>Margolin et al. (2001)</td>
<td>Case report</td>
<td>1 male, 58 years old. RT</td>
<td>1 GM-CSF 1 Hyaluronic acid</td>
<td>ENT + SLP</td>
<td>Provox 2. No prosthesis during injection</td>
<td>&gt;3 injections to solve the leaks</td>
<td>No</td>
</tr>
<tr>
<td>Luff et al. (1999)</td>
<td>Case report</td>
<td>1 male, 62 years</td>
<td>Hyaluronic acid Hylaform®</td>
<td>ENT</td>
<td>Provox 2. No prosthesis during injection</td>
<td>Solution of the leak. No follow-up indicated</td>
<td>No</td>
</tr>
<tr>
<td>Remacle et al. (1988)</td>
<td>Case report</td>
<td>1 woman, 68 years</td>
<td>Gax-collagen</td>
<td>ENT</td>
<td>Groningen. With prosthesis during injection</td>
<td>With one injection, leak-free for &gt;6 months</td>
<td>No</td>
</tr>
</tbody>
</table>

Abbreviations: ENT, ear nose throat doctor; HA, hyaluronic acid; RT, radiotherapy; SLP, speech and language pathologist; VP, voice prosthesis.
TABLE 2 Description of the number peri-fistular injections according to the type of material used.

<table>
<thead>
<tr>
<th>Material</th>
<th>N</th>
<th>%</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyaluronic acid</td>
<td>60</td>
<td>30.61</td>
<td>3.00</td>
</tr>
<tr>
<td>Autologous fat</td>
<td>47</td>
<td>23.98</td>
<td>1.62</td>
</tr>
<tr>
<td>Cymetra</td>
<td>40</td>
<td>20.41</td>
<td>2.67</td>
</tr>
<tr>
<td>Hidroxiapatite</td>
<td>29</td>
<td>14.80</td>
<td>2.64</td>
</tr>
<tr>
<td>Bioplastique</td>
<td>16</td>
<td>8.16</td>
<td>1.78</td>
</tr>
<tr>
<td>GM-CSF</td>
<td>3</td>
<td>1.53</td>
<td>3.00</td>
</tr>
<tr>
<td>Gax-collagen</td>
<td>1</td>
<td>0.51</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Note: Ratio of punctures required to achieve cessation of periprosthetic leakage of >1 month duration (p = 0.435).
Abbreviation: GM-CSF, granulocyte and macrophage colony-stimulating factor.

TABLE 3 Distribution of patients in relation to time without periprosthetic leakage obtained with tissue augmentation treatment.

<table>
<thead>
<tr>
<th>Time without leakage</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 month or without resolution</td>
<td>17</td>
<td>17.53</td>
</tr>
<tr>
<td>1–3 months</td>
<td>14</td>
<td>14.43</td>
</tr>
<tr>
<td>3–6 months</td>
<td>9</td>
<td>9.28</td>
</tr>
<tr>
<td>&gt;6 months</td>
<td>57</td>
<td>58.76</td>
</tr>
</tbody>
</table>

3.3 | Level of evidence and bias

The level of evidence of the studies included in this review is low (Table 4). All studies lacked a comparison group, with a small sample size, and were observational. Only one study evaluated the differences between two materials (Cymetra vs. calcium hydroxyapatite). No studies reported the use of proton-pump inhibitors or anti-reflux therapy, a systematic protocol for the management of periprosthetic leaks, or control of potential factors that could influence the outcomes of therapy. Likewise, there is great heterogeneity in relation to the follow-up time or the description of the results obtained.

4 | DISCUSSION

The TEP procedure improves the quality of life of the patients who have undergone a laryngectomy, enabling him or her to speak and maintain an acceptable social life. TEP is not without risk, and enlargement of the tracheoesophageal fistula is one of the most frequent complications, leading to periprosthetic leaks. The first treatment option for this type of leak is usually conservative methods: changing the size of the prosthesis, placing a silicone reinforcement collar, removing the VP and placing a nasogastric tube to allow constriction of the fistula, suturing in a tobacco pouch, placing a VP specifically designed for the treatment of these leaks, etc. Within this group of treatment, and without being the only option or excluding it from being combined with other therapies, there is peri-fistula injection with different substances that increase the volume of the surrounding tissue and reduce the diameter of the fistula. Since its first description in 1988, numerous studies have been carried out with different substances for the same purpose, with no single material showing evidence of clear superiority to the rest. The current body of literature represents on the whole a low level of evidence, most very small sample retrospective case series without control groups or comparator treatments in total reporting only 97 patients over 15 studies. Based on this early level of evidence, the therapy appears to be an effective, safe and long-lasting option in nearly 89% of cases. It can also be used in conjunction with other conservative treatments in a concomitant manner, and a greater benefit and leak-free duration can be obtained.

Despite the positive results obtained, it is important to note that most of the patients had undergone previous radiotherapy, Radiation-induced tissue fibrosis in the region of the reconstructed pharynx and...
lower oesophagus, with consequent vascular rarefaction, affects the healing and atrophies of the membranous wall of the trachea. This might lead to an increased risk of complications in the region of the fistula, making the procedure more difficult and potentially worsening the results. An individualised and multidisciplinary study of each patient should be carried out, identifying sources of tissue compromise and comorbidities in order to decide the best treatment for each patient.

The results of this review demonstrate that the tissue augmentation technique with biocompatible material is safe and performed in a similar manner in all selected studies. Minimally invasive, in most cases it is an outpatient procedure performed under topical anaesthesia to avoid tissue distortion and underestimate the volumetric substance requirement. Variations lie in the presence or not of the VP during the procedure (Table 1), how the VP length/diameter might be adjusted before injection, the use of an endoscope to improve vision, or whether it is performed under local or general anaesthesia. Given the heterogeneity of the results obtained and the lack of data, it was not possible to make statistical inference as to which option is more beneficial for the patient (Table 4). Notable complications reported were extrusion of the material or VP with consequent immediate treatment failure, or poor patient tolerance to the technique (vomiting). No serious (bleeding, infection) or life-threatening complications were reported in any of the studies.

One aspect not evaluated in any of the selected studies, and still a matter of debate, is what the timing of this procedure should be. In the presence of VP failure due to leakage, the simplest solution is usually the replacement of the prosthesis, as in most cases it will be an endoprosthetic leak. In contrast, periprosthetic leaks represent a long-term complication due to their challenging management. This type of leaks represents one of the main causes of failure in VP rehabilitation and TEP closure. There is extensive work in the literature by Hutcheson et al. on risk factors and therapy outcomes. Several therapeutic algorithms for periprosthetic leaks have been proposed to date, but there is no consensus on systematic problem-solving approach that can guide clinicians step-by-step in the choice and timing of the various possible treatments. The most recent publication proposes 5 steps in which the possible treatment options are considered on an ascending scale of complexity or morbidity, from conservative treatments to surgical treatments, and even to closure of the TEP. The tissue augmentation therapy is the third step of the algorithm, after the use of silicone rings or specific prostheses for this type of leakage (with double flanges or large flanges), and can be performed concomitantly with other conservative treatments.

Although no differences have been found between the materials used, there are aspects to be taken into account when selecting the best possible option. The use of Collagen-Gax is limited by a risk of hypersensitivity. It is derived from cowhide and requires skin testing. 

### Table 4: Risk bias and level of evidence assessment.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Evidence level</th>
<th>#1</th>
<th>#2</th>
<th>#3</th>
<th>#4</th>
<th>#5</th>
<th>#6</th>
<th>#7</th>
<th>#8</th>
<th>#9</th>
<th>Quality rating (good, fair, or poor)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parrilla et al.</td>
<td>4</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
<td>Good</td>
</tr>
<tr>
<td>Mayo-Yáñez et al.</td>
<td>4</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td>NA</td>
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Note: #1. Was the study question or objective clearly stated? #2. Were the study population clearly and fully described, including a case definition? #3. Were the cases consecutive? #4. Were the subjects comparable? #5. Was the intervention clearly described? #6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? #7. Was the length of follow-up adequate? #8. Were the statistical methods well-described? #9. Were the results well-described?

Abbreviations: CD: cannot determine; NA: not applicable; NR: not reported.
a minimum of 28 days prior to the procedure, in addition to a theoretical risk of transmission of Creutzfeldt-Jakob disease which has not been reported so far. In contrast, with Cymetra, there is no such risk of hypersensitivity. It is a micromized form of AlloDerm, a decellularized tissue composed of collagen, elastin and proteoglycans. Its main contraindications are the presence of infection in the area to be injected or the existence of autoimmune diseases of the connective tissue.

Hylaform, a viscoelastic polysaccharide gel derived from cockscomb hyaluronic acid, does not require skin testing. Its immediate and safe application is guaranteed as long as there is no history of food intolerance or allergy to substances of avian origin (eggs, poultry, etc.). This is not the case with hyaluronic acid derivatives of non-animal origin used in more recent studies. Both, collagen and Hylaform or other hyaluronic acid derivatives, are resorbable. It may be necessary to be periodically repeat the injections within 5–12 months. This is theoretically not the case with hydroxyapatite, being longer in duration, but results to date have been inconclusive. Hydroxyapatite is a mineral component of bone that has the capacity to stimulate collagen and elastin, stimulating tissue regeneration.

Bioplastique is a product consisting of textured polydimethylsiloxane elastomers, a member of the silicone polymer family, suspended in a polyvinylpyrrolidone hydrogel. As it contains large particles, it cannot be phagocytosed and therefore does not act as an antigen, avoiding hypersensitivity reactions. It is a non-absorbable substance, and its tissue adhesive effect may be positive in irradiated tissues. This beneficial effect also appears to be provided by GM-CSF, granulocyte and macrophage colony-stimulating factor, which stimulates cell proliferation and tissue re-epithelialization. This substance, in vitro, promotes the growth of neoplastic cells, but there is no evidence of tumour growth in patients with this treatment.

Finally, autologous fat, composed of mature adipocytes, pre-adipocytes, stem cells and growth factors, is one of the preferred substances as a soft tissue filler due to its biocompatibility, wide availability, lack of immunogenicity and high regenerative potential. It should be noted that centrifugation of the fat makes it possible to obtain a concentrate that is easier to infiltrate, avoiding immediate extrusion. One of the limitations of this material was the need to perform liposuction to obtain the fat, thus requiring general anaesthesia and antibiotic prophylaxis, with the patient remaining hospitalised for at least 24 h after the procedure.

5 | CONCLUSIONS

Periprosthetic leaks alter the patient’s quality of life and increase morbidity and mortality. Tissue augmentation treatment is a minimally invasive, biocompatible and safe solution that temporarily resolves periprosthetic leaks in many cases. This technique allows the use of other conservative measures concomitantly, commonly large collar VP, which can increase the efficacy of the treatment. There is no standard technique or material, and treatment needs to be individualised according to the experience of the practitioner and the characteristics of the patient. Future randomised studies are needed to confirm these results.

AUTHOR CONTRIBUTIONS

Miguel Mayo-Yáñez and Mercedes Díaz Ramos-Nebel: Conceptualization, methodology, formal analysis, investigation, writing—original draft, project administration. Ima Cabo-Varela: conceptualization, investigation, writing—original Draft. Carlos Miguel Chiesa-Estomba: methodology, formal analysis, writing—review and editing. Jérôme R. Lechien, Nicolas Fakhry, Antonino Maniaci: methodology, writing—review and editing. Katherine A. Hutcheson: Conceptualization, Supervision, Writing - Review & Editing.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

All authors meet the International Committee of Medical Journal Editors (ICMJE) conditions. The authors have nothing to declare.

PEER REVIEW

The peer review history for this article is available at https://www.sciencedirect.com/science/article/pii/S1401543922002045.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

ETHICS STATEMENT

This research does not involve humans. Informed consent was not required for this study. The study was approved by the hospital ethics committee.

REFERENCES


