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**Laryngology**

# Is there a role for voice therapy in the treatment of laryngopharyngeal reflux? A pilot study

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SUMMARY

**Objective**. The aim of this study was to compare the efficacy of voice therapy combined with standard anti-reflux therapy in reducing symptoms and signs of laryngopharyngeal reflux (LPR).

**Methods**. A randomised clinical trial was conducted. Fifty-two patients with LPR diagnosed by 24 h multichannel intraluminal impedance-pH monitoring were randomly allocated in two groups: medical treatment (MT) and medical plus voice therapy (VT). Clinical symptoms and laryngeal signs were assessed at baseline and after 3 months of treatment with the Reflux Symptom Index (RSI), Reflux Finding Score (RFS), Voice Handicap Index (VHI) and GRBAS scales.

**Results**. Groups had similar scores at baseline. At 3-month follow-up, a significant decrease in RSI and RFS total scores were found in both groups although it appeared to be more robust in the VT group. G and R scores of the GRBAS scale significantly improved after treatment in both groups, with better results in the VT group. The VHI total score at 3 months improved more in the VT group (VHI delta 9.54) than in the MT group (VHI delta 5.38) ($p < 0.001$).

**Conclusions**. The addition of voice therapy to medications and diet appears to be more effective in improving treatment outcomes in subjects with LPR. Voice therapy warrants consideration in addition to medication and diet when treating patients with LPR.

KEY WORDS: voice therapy, laryngopharyngeal reflux, treatment, multichannel intraluminal impedance-pH monitoring

## Introduction

Laryngopharyngeal reflux (LPR) is an inflammatory condition where stomach contents move in a retrograde fashion, enter and affect the upper aerodigestive tract [1] causing a variable presentation of symptoms that can include dysphonia (chronic or intermittent), excessive throat clearing, globus sensation, chronic cough, vocal fatigue or vocal effort, sore throat and dysphagia among others [2,3]. The prevalence of LPR-related symptoms ranges from 10% to 30% in otolaryngology department consultations, reaching up to 50% in clinical laryngology practices [4]. The prevalence may be increasing given the ever-worsening lifestyle and dietary habits of most Western cultures [4]. Treat-

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ment options for LPR include diet and lifestyle modifications, proton pump inhibitors (PPIs), H2 blockers and/or alginate or magaldrate [3].
Preliminary data suggests a potential role for voice therapy in improving both symptoms and signs of LPR, especially in the setting of patients with dysphonic complaints. A combination of voice therapy, medications and dietary changes may be more effective in improving LPR patient outcomes compared to medical management alone [5-7]. To the best of the authors' knowledge, these prior studies selected patients with LPR using subjective measures alone with or without oesophagoscopy findings of oesophagitis; no objective reflux tests that can diagnose LPR were included. Therefore, the aim of the current study was to compare the efficacy of voice therapy in combination with standard anti-reflux therapy to standard anti-reflux therapy alone in reducing laryngeal signs and symptoms (beyond dysphonia alone) after 3 consecutive months of treatment in patients with multichannel intraluminal impedance-pH (MII-pH) diagnosed LPR.

## Materials and methods

*Patients*

Subjects with a diagnosis of LPR were prospectively enrolled from the Division of Phoniatrics and Audiology of the "Luigi Vanvitelli" University Hospital, Naples (Italy), from December 2021 to March 2023.
Patients met the following inclusion criteria: (1) age range 18-65 years; (2) clinical suspicion of LPR based on a Reflux Symptom Index (RSI) > 13 [8,9], Reflux Finding Score (RFS) > 7 [10] and positive 24h MII-pH monitoring [11].
Exclusion criteria consisted of: (1) presence of any other organic laryngeal disorders needing medical, rehabilitative or surgical treatment (e.g., tumours or vocal fold paralysis); (2) history of previous medical/surgical treatments, radiotherapy or voice therapy for head and neck diseases; (3) presence of confirmed neurological and psychiatric illness or treatment; (4) alcohol abuse; (5) current smokers; (6) history of upper respiratory tract infection or treatment within the last month; (7) active seasonal allergies or asthma; (8) pregnancy; (9) previous anti-reflux surgery/oesophageal surgical procedure; (10) other concurrent major medical condition.

*Clinical and instrumental evaluation*

LPR was initially suspected through the administration of the RSI [8,9] and videolaryngoscopic examination plus RFS [10] and confirmed by MII-pH [11]. Voice-related symptoms were further assessed with the GRBAS scale [12,13] and the Italian Voice Handicap Index (VHI)- original 30 question version [14]. The GRBAS scale was administered by two trained physicians (G.C. and M.R.B.) and the overall interrater reliability was calculated. The above-described evaluation protocol was performed at baseline (T0) and at the end of 12 consecutive weeks of treatment (T1) in all patients enrolled.

Endoscopic evaluation and Reflux Finding Score (RFS)

Laryngoscopic examination was performed using a Storz 70° rigid optic (KARL STORZ GmbH & Co. KG, Tuttingen, Germany; diameter: 5.6 mm; equipped with an ATMOS Endo-Stroboscope L - ATMOS Medizin Technik GmbH & Co KG, Lenzkirch, Germany) and operated through the endoscopic software Daisy (2014; ver. 3.6.15, Amplifon SPA, Milan, Italy) with a videoendoscopy module (OMVISIA, 2014, ver. 2.0.8 - Amplifon SPA Milan, Italy). A flexible endoscopic examination (Xion EF-N 3.4 nasopharyngoscope - XION GmbH, Berlin, Germany) was performed in patients unable to undergo rigid videoendoscopy. All videoendoscopic examinations were performed by the same trained laryngologist (M.R.B.) and images were shared and anonymously evaluated by two other laryngologists (G.C., A.N.) and one voice therapist (G.M.), all experienced in the field of voice disorders and LPR management. The RFS was rated by two independent physicians (G.C., A.N.) blinded to the patients' treatment group and the stage of the study and, given the subjective interpretation of the scale, inter-rater agreement for the RFS score was calculated.

Multichannel intraluminal impedance-pH monitoring (MII-pH)

MII-pH was performed by a trained physician (S.T.) before starting a therapeutic protocol in order to confirm reflux episodes. In brief, a catheter with impedance electrode pairs located at 3-5, 7-9 and 15-17 cm above the low oesophageal sphincter (LES) and 2 pH sensors at 5 and 15 cm above the LES was used (Sandhill Diversatek, Highlands Ranch, Colorado-United States). Traces were analysed with Bioview software and reviewed manually by a single expert investigator (S.T.). The occurrence of reflux at most proximal channel was recorded and the test was considered positive in presence of more than 14 reflux episodes recorded at the most proximal site [11].

*Therapeutic procedures*

All consecutive patients included in the study were randomly allocated to either the medical treatment group (MT group) – e.g., diet, lifestyle changes and medications- or the voice therapy group (VT group) – e.g., voice therapy plus diet, lifestyle changes and medications.
Patients were randomly allocated into group A (MT group) or group B (VT group) using block randomisation. A block size of 4 was used, from which 6 blocks with 6 different sequences (AABB, ABBA, ABAB, BBAA, BAAB, BABA)

were further created. These blocks were repeated until a total of 13 blocks with a size of 4 each was generated, giving a list of 52 in total.
Therapeutic protocol included an anti-reflux diet, lifestyle modifications and a combination of proton pump inhibitors (PPIs, pantoprazole 20 mg twice daily, fasting) and post-meal magnesium alginate three times per day for 12 consecutive weeks. The recommended anti-reflux diet regimen consisted of predominantly Mediterranean diet. Patients were also provided with a detailed list of potentially refluxogenic foods and beverages [15]. Lifestyle changes emphasised included moderate and daily physical activity, weight loss/reduction of body mass index (BMI), improved sleep quality and control of psychosocial stress.

### Voice therapy training

The intentions of the voice therapy training were twofold: first, teaching different exercises in order to reduce the amount of refluxate that reaches the pharyngo-laryngeal tract; second, using traditional voice therapy techniques to act on LPR-related hoarseness with the intention of reducing vocal effort and vocal trauma.
All subjects in the VT Group underwent in-person voice therapy sessions of about 45 minutes each, twice a week, for 12 consecutive weeks. They were also instructed to perform further vocal exercises at home (e.g., sessions of 15 minutes each, three times a day) for the entire period. All sessions were performed by the same speech-language pathologist (G.M.) specialised in assessment and rehabilitation of patients with voice disorders and LPR. The voice therapy training included a general approach to voice counseling, posture control and relaxation training, vocal hygiene management, hydration, breathing support, and general and specific vocal exercises. The entire rehabilitation protocol had previously been established by the LPR Study Group of the YO-IFOS under the supervision of an expert voice therapist and senior laryngologists.

### Posture control and relaxation training

To reduce muscle tension and any kind of vocal effort the relaxation training was implemented. It is mainly based on isotonic exercises to relax the cervical muscles and was repeated up to 3 times including resting between one exercise and the next. In this context, patients are invited to stretch their head, arms and shoulders while yawning deeply and subsequently shaking arms and legs to release them from tension.

### Vocal hygiene programme

The vocal hygiene programme includes avoiding exposure to laryngeal irritants, periods of voice rest, reduction or avoidance of vocal abuse/misuse and hard glottal attack and adequate and daily hydration of the glottal plane. More specifically, a good hydration programme may be favoured by nasal breathing through a damp gauze to be performed for 10 consecutive minutes up to three times a day and before starting every voice therapy session. Patients were instructed to breathe through the nose with the nostrils wrapped in the damp gauze both normally and while performing vocal warm-up exercises (to further facilitate direct hydration of the vocal fold cover) [16].

### Diaphragmatic breathing

A conscious use of the diaphragm in terms of deep, but not forced, inspirations and prolonged exhalations, is essential both for the functionality of the LES and for adequate phonation. Diaphragmatic breathing exercises were instructed to be performed every day, in sessions of 60 respirations, 2 to 3 times every day. The patient is instructed to inhale a deep breath through the nose and then exhale through the mouth and repeat. The patient may perform these exercises both in the upright and supine positions and, during breathing and phonation, the patient is asked to put one hand on the abdomen to increase awareness of movements related to their diaphragmatic excursion.
After the first 3-4 sessions which were primarily aimed at vocal hygiene, adequate hydration, breathing support and relaxation training, the voice therapist and physician introduced the rehabilitative protocol to the patient. This included basic vocal exercises such as humming and vocal fry, and specific vocal exercises.
Vocal fry should be used to test the 'viscosity' of the vocal fold cover and it is suggested as a manoeuver to 'clean' the vocal folds, especially in the case of endolaryngeal sticky mucus. It is also useful to verify the freedom and the amplitude of the vibrating wave.
Humming, on the other hand, is an excellent exercise to warm up the voice and to activate the vocal cords in a gentle but firm way. Through this exercise the air -and consequently the sound- will be projected forward, and this will allow the larynx to be well relaxed and agile.

### Vocal exercises

An adequate excursion and mobilisation of the larynx would be able to improve the management of the vocal tract and vocal dynamics reducing vocal effort and voice hyperfunctional behaviours. Therefore, direct exercises may involve:

- active mobilisation of the larynx by means of loud yawn technique, B technique, ascending/descending glissandi (from a low note to a high note and vice versa) and vowels emission in lingual retroposition;
- passive mobilisation of the larynx through laryngeal manipulation both in static (during quiet breathing) and dynamic (during phonation and swallowing).

*Statistical analysis*

All statistical analyses were completed using SPSS Version 24 (IBM Corp, Armonk, US) and significance was set at $p < 0.05$. Categorical variables were expressed as percentages while continuous variables were expressed as mean ± standard deviation (SD) or interquartile range (IQR). Cohen's kappa was performed to measure the reliability of the GRBAS score and of the RFS. For comparison between categorical and nominal variables, the Pearson Chi-Square and the Fisher's Exact Test were used. For all the variables the Kolmogorov-Smirnov normality test was used. Non-parametric tests (Mann Whitney U test, Wilcoxon test) were used to evaluate non-normally distributed variables. To evaluate the degree of improvement in clinical scores between the 2 groups, the deltas of each measure were calculated (Δ VHI score = VHI score T1-VHI score baseline; Δ RFS score = RFS score T1-RFS score baseline; Δ RSI score = RSI score T1- RSI score baseline).

## Results

Although 78 patients with suspected LPR had originally been assessed for eligibility, 7 patients declined the MII-pH test. Of the remaining 71 patients with positive MII-pH, 12 did not conform to the inclusion/exclusion criteria, 5 did not complete the follow-up evaluation and were thus excluded from final analyses, and the remaining 2 patients failed to complete the VT intervention.

Therefore, the final sample consisted of 52 patients (32 females and 20 males), equally distributed in each group (N = 26). The sociodemographic and basic clinical characteristics of the two groups at baseline are reported in Table I. None of the characteristics analysed in terms of sex, professional voice use and age showed any statistically significant differences between the MT and VT groups.

The overall inter-rater reliability of the GRBAS scale, measured as Cohen kappa, was found to be good (kappa G Score = 0.84; kappa R Score = 0.88; kappa B Score = 0.86) as well as the inter-rater reliability of the RFS (kappa = 0.81).

As shown in Figure 1, the VT and MT groups were statistically similar regarding VHI, RFS, RSI and GRBAS scale.

The mean RSI total score was > 13 (MT-T0: mean = 17.8; SD = 2.9; median = 17.5; IQR = 15-20.2. VT-T0: mean = 18.0, SD = 3.0; median = 18.0; IQR = 15-21) and the mean RFS total score was > 7 (MT-T0; mean 9.2, SD = 1.5; median = 9; IQR = 8-10; VT-T0 = mean 9.7, SD = 1.6, median = 9, IQR = 8-11) in both groups, thus suggestive for LPR. The mean VHI total score was ≤ 30 in all enrolled patients and therefore suggestive of a mild degree of perceived dysphonia (MT-T0: mean = 22.1; SD = 6.6; median = 20; IQR = 16-30. VT-T0: mean = 22.8; SD = 6.8; median = 22; IQR: 16-30).

Compared to the GRBAS scale, no subject showed any grade of Asthenia (A score) and/or Strain (S score) at baseline, while a slight, insignificant difference of global grade of dysphonia- G score (MT group 1.31; VT group 1.42; p-value: ns), Roughness-R score (MT group 0.96; VT group 0.96; p-value: ns) and Breathiness-B score (MT group 0.31; VT group 0.31; p value: not significant) was observed (Fig. 1).

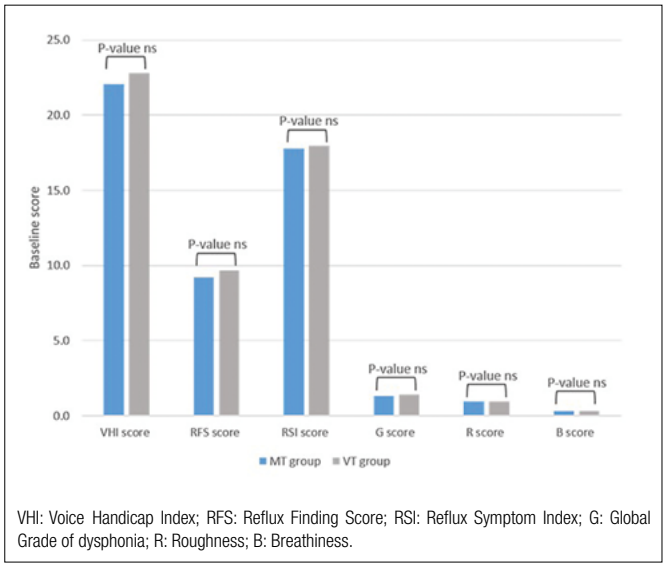
Statistical evaluation of voice characteristics in patients from both groups before therapy (T0) and 3 months after therapeutic intervention (T1) is summarised in Table II.

Overall, an amelioration of vocal parameters after 3 months of treatment was observed. This was statistically significant in both groups with the exception of the B- score that improved significantly in the VT group at T1, but not in the MT group. In brief, patients who underwent VT training had a significant improvement of G- score and R-score which was significant compared with the MT group (G

**Table I.** Sociodemographic and basic clinical characteristics of the two groups at baseline.

| | | MT group | | VT group | | |
|---|---|---|---|---|---|---|
| | | N | % | N | % | p value |
| **Gender** | Female | 16 | 61.5 | 16 | 61.5 | 1.000 * (ns) |
| | Male | 10 | 38.5 | 10 | 38.5 | |
| **Professional voice use** | No | 8 | 30.8 | 7 | 26.9 | 0.760 * (ns) |
| | Yes | 18 | 69.2 | 19 | 73.1 | |
| **Active smoker** | No | 26 | 100 | 26 | 100 | 1.000 ** (ns) |
| | Yes | 0 | 0 | 0 | 0 | |
| **Ex smoker** | Yes | 11 | 42.3 | 8 | 30.8 | 0.565 * (ns) |
| | No | 15 | 57.7 | 18 | 69.2 | |
| | | | Mean (sd) | | Mean (sd) | |
| **Age** | | 26 | 42.0 (11.9) | 26 | 43.0 (12.9) | 0.774 ° (ns) |

** Significance (2-sided) Pearson Chi-Square; ** Significance Fisher's Exact Test; ° Significance Independent Samples Test; ns: not significant; MT: medical treatment; VT: voice therapy.*




VHI: Voice Handicap Index; RFS: Reflux Finding Score; RSI: Reflux Symptom Index; G: Global Grade of dysphonia; R: Roughness; B: Breathiness.

**Figure 1.** Clinical data at baseline (T0) in all enrolled patients in the MT and VT groups. No significant differences were found between groups. Comparisons were performed by Mann-Whitney U test.

score at T0 = 1.42 ± 0.50; T1 = 0.5 ± 0.51; p value: < 0.0001; R score at T0 = 0.96 ± 0.77; T1 = 0.46 ± 0.50; p value: 0.001). Similarly, the improvement in the VHI total score at T1 was significant in both groups, but in the VT group it was almost double (MT-VHI score at T0 = 22.07; T1 = 16.69; p value: < 0.001. VT-VHI score at T0 = 22.81; T1 = 13.27; p value: < 0.001).

In terms of LPR-related symptoms and signs, RSI and RFS scores and their sub-items are compared between T0 and T1 in Figures 2 and 3. Figure 2 depicts the significant decrease in the RSI total score at T1 in both groups (RSI total score in MT group at T0 = 17.77 ± 2.9; RSI total score in MT group at T1 = 12.31 ± 3.3; p value < 0.001; RSI total score in VT group at T0 = 17.96 ± 3.1; RSI total score in VT group at T1 = 10.81 ± 3.5; p value < 0.001). Interestingly, the mean RSI total score at T1 falls below 13 in both groups, e.g., below the significance value for symptoms attributable to LPR [8].

Similarly, the RFS total score (Fig. 3) significantly improved in both groups at T1 compared to the baseline (RFS in MT group at T0 = 9.19 ± 1.5; RFS in MT group

**Table II.** Voice characteristics of patients from both groups at baseline (T0) and post-treatment (T1). VHI: Voice Handicap Index.

| | MT Group | | | | | VT Group | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Baseline | | T1 | | | Baseline | | T1 | | |
| | N | Mean (sd) | N | Mean (sd) | p value | N | Mean (sd) | N | Mean (sd) | p value |
| **VHI score** | 26 | 22.07 (6.6) | 26 | 16.69 (6.7) | .000 | 26 | 22.81 (6.8) | 26 | 13.27 (5.3) | .000 |
| **G score** | 26 | 1.31 (0.47) | 26 | 0.96 (0.72) | .003 | 26 | 1.42 (0.50) | 26 | 0.5 (0.51) | .000 |
| **R score** | 26 | 0.96 (0.72) | 26 | 0.73 (0.60) | .034 | 26 | 0.96 (0.77) | 26 | 0.46 (0.50) | .001 |
| **B score** | 26 | 0.31 (0.47) | 26 | 0.19 (0.40) | .564(ns) | 26 | 0.31 (0.47) | 26 | 0.12 (0.32) | .025 |

*G: Global Grade of dysphonia; R: Roughness; B: Breathiness. All comparison were performed by Wilcoxon test.*

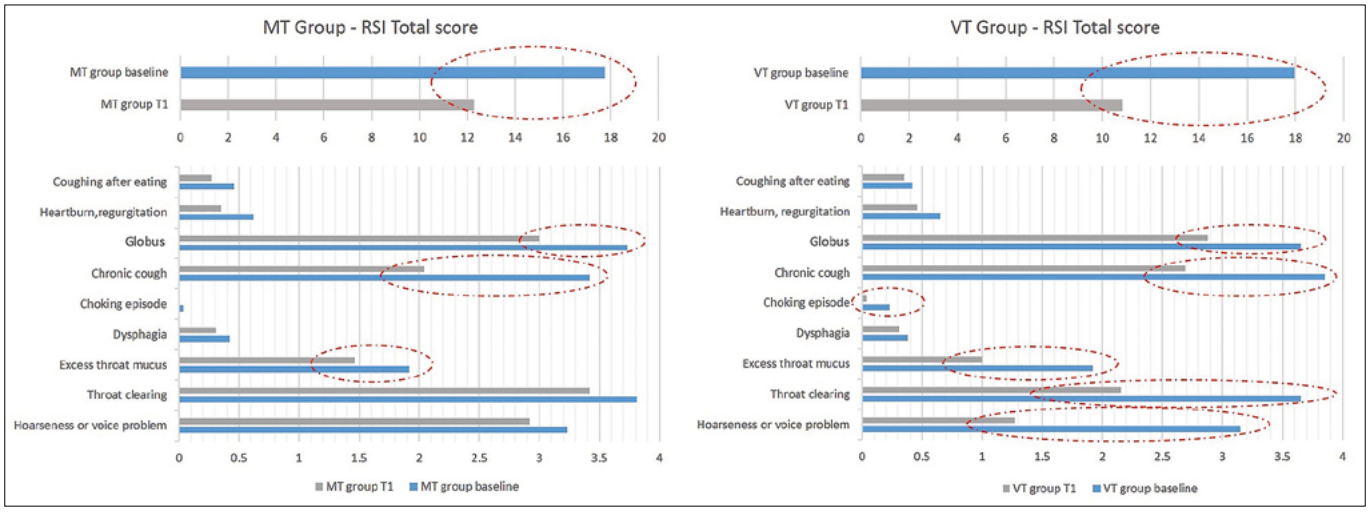



**Figure 2.** Comparison between RSI total score and RSI sub-items at baseline and T1 (after 3 months) in the VT and MT groups (the red circles in the figure indicate statistical significance; comparison by Wilcoxon test).

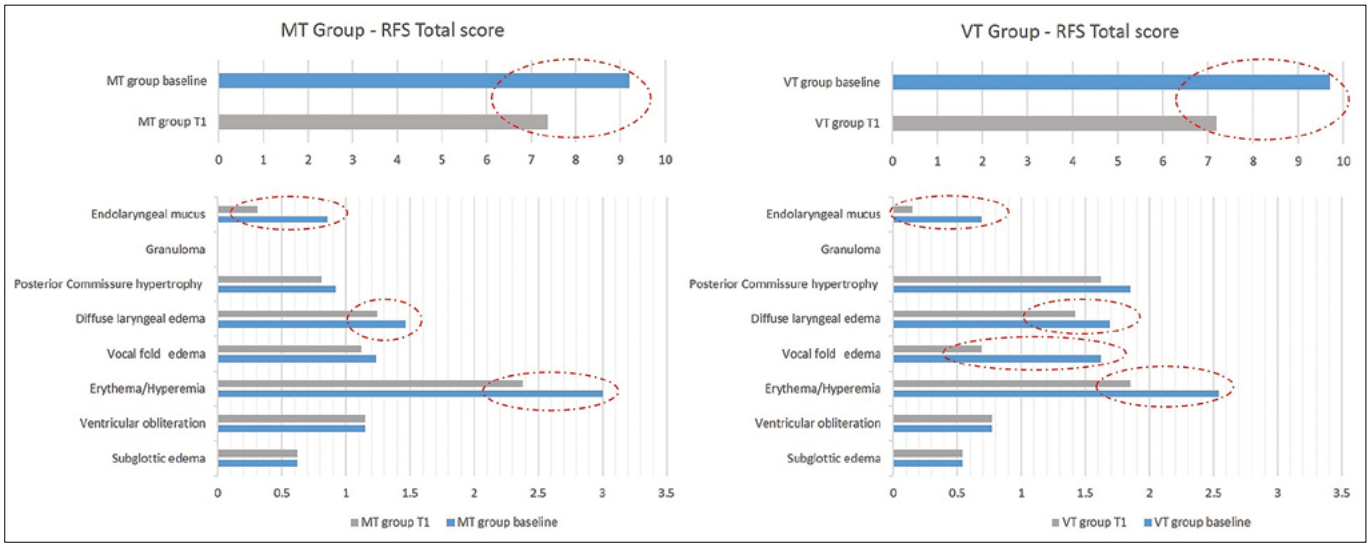



**Figure 3.** Comparison between RFS total score and RFS sub-items at baseline and T1 (after 3 months) in the VT and MT groups (the red circles in the figure indicate statistical significance; comparison by Wilcoxon test).

at T1 = 7.35 ± 2.3; p value < 0.001. RFS in VT group at T0=9.69 ± 1.6; RFS in VT group at T1=6.08 ± 2.3; p value < 0.001). Unlike RSI values, the average RFS values did not return below the normal threshold of < 7.

Upon analysing the change in the individual sub-items of RSI and RFS, an improvement was seen in all the parameters evaluated at T1 in both groups as reported in Figure 2. More specifically, we observed the following:

1) Improvement of all the evaluated parameters of the RSI - which was statistically significant for the items globus sensation, chronic cough and excess throat mucus - in the MT group at T1 compared to baseline (Fig. 2);
2) Improvement of all parameters evaluated of the RSI in the VT group, which was statistically significant for the majority of the items at T1 compared to the baseline, in particular globus sensation, chronic cough, choking, excess throat mucus, throat clearing and hoarseness (Fig. 2);
3) A statistically significant improvement in the MT group at T1 compared to baseline was seen for the following RFS items: endolaryngeal mucus, diffuse laryngeal oedema and erythema/hyperaemia (Fig. 3).

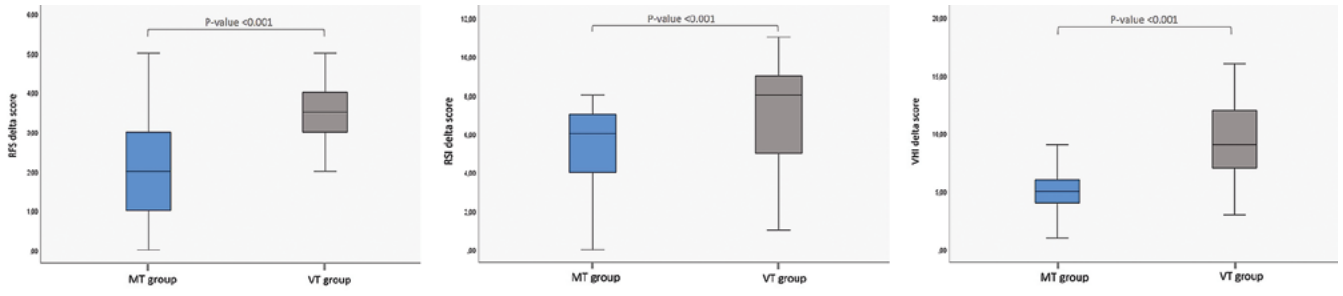
A significant improvement in the VT group compared to the baseline of the RFS items endolaryngeal mucus, diffuse laryngeal oedema, vocal fold oedema and erythema/hyperaemia with improvement, although not significant, of the item posterior commissure hypertrophy (Fig. 3).

Although the improvement of the VHI, RFS and RSI total score was evident in both groups, it was observed that, for all the scores evaluated, the delta scores was greater for the VT group (Fig. 4). The VHI total score after 3 months of treatment improved significantly: the MT group showed a mean delta VHI of 5.38 points (median, 5; IQR, 6.2/3.7), while the VT group demonstrated a higher delta VHI of 9.54 (median, 9; IQR, 12.2/-7) (p value < 0.001; U di Mann-Whitney test).

## Discussion

This study intended to evaluate whether adding voice therapy to medical and diet/lifestyle treatment would be more effective in managing LPR-related symptoms and signs compared to medical treatment and diet/ lifestyle modifications alone. This topic has already been considered in the literature with encouraging data for voice and LPR specific outcomes, although this study is the first to select LPR patients using MII-pH technology and treat patients medically with more than acid-suppression medications, such as PPIs, alone.

How subjects are selected for inclusion in studies evaluating the medical management of LPR is important. The prior studies that evaluated adding voice therapy to more traditional LPR management require scrutiny in this area. There is significant controversy regarding the ability of RSI and RFS to diagnose LPR and prior work on this subject has employed these criteria without objective reflux testing. The current study team admittedly did not have access to the newest "LPR" pH-impedance catheters during the period of data collection for this study. The "LPR" catheters have distal impedance electrode pairs but also pharyngeal impedance electrode pairs that cross the upper oesophageal sphincter (UES) and place the proximal pH sensor at or above the UES. The catheter configuration used in the current study has its most proximal impedance electrode




VHI: Voice Handicap Index; RFS: Reflux Finding Score; RSI: Reflux Symptom Index. Comparisons were performed by Mann-Whitney U test.

**Figure 4.** The delta (change in score: positive delta means improvement, negative delta means worsening sign or symptom) of measures (T1-Baseline): VHI, RFS and RSI.

pair at 17 cm above the LES. Traditional gastro-esophageal reflux disease (GERD) criteria (32 or more impedance events at 17 cm above LES and expecting symptom correlation with events) used to designate a positive test using traditional MII-pH catheters has been shown to miss LPR positive episodes in the pharynx (as would be detected on "LPR" type MII-pH catheters) [18]. However, more recently published data and ongoing work by one of the senior authors (T.C.) has demonstrated that 2 or more pharyngeal events are likely to be present if there are 14 or more impedance events at 17 cm or more above the LES using the older pH-impedance catheter configuration, as was used in the current study [11]. For these reasons, 14 or more impedance events at 17 cm above the LES was used to include a subject as one who has signs and symptoms due to LPR.

Using criteria of RSI and RFS without MII-pH reflux testing to include their subjects, Vashani et al. [5] and Beech et al. [7] reported that treatment of LPR with medication and voice therapy resulted in improved subjective measurements in their patients. Vashani et al. did include oesophagitis on oesophagoscopy to include subjects, although this is not a proven diagnostic finding in those with LPR, akin to many with LPR having normal oesophagoscopy. A few years later, Park et al. [6] reported, on a sample of 100 LPR patients, that the symptom-associated scores (RSI, VHI) improved in a clinically significant manner regardless of adding voice therapy. However, voice therapy shortened the time of recovery by 2 months and the improvement in the RSI or VHI remained more improved in the voice therapy plus medical management group at the final 3-month follow-up evaluation compared to the medical management group alone. Moreover, a recent systematic review [19], asserted that for patients with LPR and predominant vocal symptoms there is evidence that supports voice therapy.

Our study demonstrates that voice therapy significantly improved clinical symptoms (RSI, VHI, GRBAS) and signs (RFS) of LPR after 12 weeks of treatment with acid suppression, alginate therapy and a recommendation for a Mediterranean diet in addition to emphasising moderate and daily physical activity, weight loss/reduction of BMI, improved sleep quality and control of psychosocial stress. Additionally, sub-items of the RSI and RFS were evaluated to determine if individual items were more susceptible to the improvement with the addition of voice therapy. When evaluating the sub-items of the RSI, globus sensation, excess throat mucus and chronic cough improved in both MT and VT groups after 3 months of treatment. Interestingly, in the VT group there was also a significant improvement of throat clearing, hoarseness and choking episodes.

Although the RFS improved in both groups in a significant way after 3 months of treatment, it maintained a score of > 7. Therefore, the score still indicated the presence of objective signs of LPR, suggesting a slower amelioration of laryngeal signs compared with the symptom scores. It may also suggest that the remaining signs were multifactorial in the first place and the signs evaluated by the RFS may not be specific to LPR. These results were consistent with those of other previous reports in which physical findings tend to improve slower than clinical symptoms [20]. Analysing the sub-items, we found that laryngeal hyperaemia and endolaryngeal mucus significantly improved in both groups but, interestingly, vocal fold oedema significantly improved in the VT group and not in the MT group.

This study emphasises the important role that voice therapy can play in support to anti-reflux medical, diet and lifestyle treatments alone: 1) to reduce the mucosal damage induced by acid, pepsin and bile salts, by means of exercises that tone and strengthen the LES (breathing support); 2) to avoid damaging, compensatory phonatory behaviours that patients may develop in response to chronic reflux and the subsequent true vocal fold inflammatory changes, thus im-

proving the quality of the voice with little perceived vocal effort; 3) to redirect patients with chronic, irritative laryngeal symptoms to use alternative behaviours to throat clearing, coughing etc., thus promoting the recovery of the negative mucosal changes by alleviating the ongoing causes of repetitive, mechanical irritation and injury.

As reported in some pathophysiologic models [21], LPR patients demonstrated a chronic downregulation of mucin genes with chronic dehydration of their mucous ("sticky mucus") which led to increased viscosity with negative consequences on true vocal fold vibration. Dryness of Reinke's space has been also recently suggested as an additional microscopic change related to reflux [21]. Furthermore, chronic cough and throat clearing secondary to the dehydration and accumulation of endolaryngeal sticky mucus may be responsible for an exacerbation of the pressure applied to the mucosa during these behaviours and phonation, increasing vocal microtraumas, altering the resistance of the epithelium and worsening the overall clinical picture in a vicious cycle. Adequate hydration of the true vocal folds may be useful in counteracting the chronic dehydration of mucous, simultaneously reducing throat clearing, hoarseness and globus sensation [22]. Hydration may also facilitate normal phonation by helping to prevent negative consequences on the vibration process, especially on the free-edge of the vocal fold, which may reduce the amplitude of the mucosal wave and may shorten the closed phase during phonation [22]. Relaxation training, breathing support and vocal exercises should also be useful to prevent the hyperfunctional behaviours of the thyroarytenoid muscle and the secondary muscle tension dysphonia.

As demonstrated in recent literature, daily and correctly applied diaphragmatic training exerts a compression action on the LES, counteracting sudden variations in intra-abdominal pressure. Prior studies have shown that breathing exercises may improve LES fibre tension, reducing the frequency of one-time oesophageal relaxation and increasing the rate of gastric emptying [23]. Moreover, as shown by Amhadi et al, standardised diaphragmatic breathing significantly improved quality of life and was able to induce significant change in LES pressure when evaluated by oesophageal manometry [24]. Preliminary data published by Moffa et al. [25] emphasised how a specific inspiratory muscle training technique could be useful, alone or in association with diet/PPI, in significantly improving GERD symptoms, RSI and laryngeal endoscopy score after 4 weeks of treatment.

This study includes some important limitations. First, the number of enrolled patients is relatively small, and the results should be consequently considered as preliminary. The relatively small sample size is due, in part, to the purposefully restrictive inclusion criteria as well as to the SARS-COV-2 pandemic that limited access to the outpatient facilities for several months. Second, the diagnosis of LPR was made using event-number criteria based on prior research comparing the more traditional configuration of MII-pH catheters to the newest "LPR" type MII-pH catheter configuration (also called hypopharyngeal-oesophageal multichannel intraluminal impedance with dual pH testing, or HEMII-pH). While admittedly not as clean as using the newer HEMII-pH catheters themselves, understanding that the number of pharyngeal events can be extrapolated from the current MII-pH catheter data was more attractive than using acid-only/GERD criteria that would have missed patients with true LPR. Third, an intermediate follow-up (after 1 and 2 months of treatment) was not performed in our patients for similar reasons, and it is felt that interval follow-up visits between T0 and T1 would have been very useful in assessing whether patients undergoing VT improved their clinical and endoscopic parameters more rapidly than the MT group. Similarly, the current study lacks further 6-month follow-up to assess whether voice therapy training is able to provide patients longer term results compared to medical treatment alone. Fourth, the evaluation of the voice quality with objective assessment including acoustic measurements or blinded perceptual voice ratings was also not performed. Finally, it would have been useful to evaluate the pressure level of the LES before and after voice therapy training in the VT group by means of esophageal manometry.

## Conclusions

Voice therapy appears to be associated with better subjective improvement of signs and symptoms in patients with MII-pH-diagnosed LPR after 3 months of treatment compared to those receiving medical, diet and lifestyle treatment alone. Voice therapy should be taken into consideration as part of an integrated treatment protocol for patients with LPR. Further studies with larger sample sizes and both shorter and longer follow-ups are warranted to confirm the present results and to determine if voice therapy may more efficiently improve signs and symptoms of LPR and/or maintain these results longer than traditional medical reflux treatments.

### *Conflict of interest statement*

The authors declare no conflict of interest.

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### *Author contributions*

MRB: designed and coordinated the study, participated in

data acquisition and analysis, interpreted the data and drafted and revised the manuscript; AN, GM, GC: participated in data acquisition and analysis; drafted the work; revised the manuscript; LB, FM: participated in data acquisition and made the statistical analysis; TLC: substantial contributed to the conception and design of the study; interpreted the study results; revised the work; made final approval of the version to be published; JL, CCE, AM: critically revised the manuscript; LD, ST, FG: participated in data acquisition and analysis. All authors critically reviewed the article for important intellectual content and approved the final manuscript.

### *Ethical consideration*

The data published in the present work derives from the project "LPR and psycological distress" approved by the Institutional Ethical Committee of the "L. Vanvitelli" University Hospital, (Naples, Italy) (Prot. 0035783/i, 15/12/2021). All procedures were conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki.

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