RESEARCH ARTICLE
DOI: 10.26650/Tr-ENT.2024.1412623
The Turkish Journal of Ear Nose and Throat 2024;34(2):55-59

Evaluation of Voice in Patients with Antineutrophil Cytoplasmic Antibody Associated Vasculitides*

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Citation: Kökoğlu K, Kızıltepe M, Oflaz Çapar A, Oğuz Kökoğlu E, Tektaş N, Şenel AS. Evaluation of voice in patients with antineutrophil cytoplasmic antibody associated vasculitides. Tr-ENT 2024;34(2):55-59. https://doi.org/10.26650/Tr-ENT.2024.1412623

ABSTRACT

Objective: Antineutrophil cytoplasmic antibody-associated vasculitides (AAV) can affect the upper and lower respiratory tract. Evaluation of voice quality was aimed at patients with AAV in this paper.
Materials and Methods: In this study, AAV-diagnosed patients and their age-gender-compatible healthy counterparts were enrolled. Participants with histories of airway surgery, smoking, laryngopharyngeal reflux symptoms, allergy, active nose, throat, and larynx infection were excluded. After the otolaryngologic examination, Voice Handicap Index-10 (VHI) scores, maximum phonation times (MPT), auditory-perceptual analysis of voice (GRBAS score), and acoustic analysis were performed. The MPT, VHI, GRBAS, F0, jitter, shimmer, and harmonic-to-noise ratio (HNR) values of both groups were compared statistically. Parameters were evaluated using the PRAAT software.
Results: There were 30 subjects in each group (16 women and 14 men). The mean ages were 51.1 and 51.5 years in the patient and control groups. Significant differences were found between the two groups regarding median VHI scores, MPT, and GRBAS scores ($p<0.05$). While median VHI and GRBAS scores were higher in the vasculitis group, median MPT was shorter.
Conclusion: Voice quality may disturb patients with AAV, especially in terms of VHI, MPT, and GRBAS scores.
Keywords: PRAAT, voice analysis, GRBAS score, jitter, shimmer

INTRODUCTION

Antineutrophil cytoplasmic antibody (ANCA) associated vasculitides (AAV) are systemic diseases that can affect various organs, especially the upper respiratory tract, lungs, and kidneys. Microscopic polyangiitis (mPAN), eosinophilic granulomatosis with polyangiitis (EGPA), and granulomatosis with polyangiitis (GPA) are the three main forms of this group of diseases. Their main characteristic histopathology is necrotising granulomatous inflammation that most often involves the respiratory tract. It is assumed that granulomatosis lesions during respiratory infection or other inflammatory conditions prepare neutrophils for a prompt by AAV in the airway mucosa (1).

For phonation, we must be able to adduct our vocal folds, establish subglottic pressure, and vibrate the vocal folds. An organised stimulation from the bilateral recurrent laryngeal nerve provides movement in the vocal folds medio-inferiorly owing to the contraction of the adductor intrinsic muscles and movement of the arytaenoid cartilages in normal phonation. Symmetric adduction of the vocal folds is maintained in this manner. When the subglottic pressure that forms expires from the lungs reaches a particular brink, the air runs away from the glottis, and vocal folds vibrate. A condition that interferes with any of this physiology may produce a change in voice quality. Neurogenic disorders cause dysphonia by affecting the abduction and adduction of vocal folds at appropriate times. It is necessary to have sufficient breath support to achieve the

*This article was presented as as an oral poster in 44th Turkish Otolaryngology – Head and Neck Surgery Congress, 15-19 November 2023 in Antalya, Türkiye

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Submitted: 01.01.2024 • **Revision Requested:** 19.03.2024 • **Last Revision Received:** 06.05.2024 • **Accepted:** 15.05.2024 • **Published Online:** 04.06.2024

phonatory threshold pressure. It may be deficient in pulmonary disorders. Mucosal lesions of the airway distort vibration and, therefore, also cause dysphonia (2). AAV can disturb voice quality, influencing the lungs and upper airway mucosa, and cause small vessel vasculitis such as vasonervorum of the recurrent laryngeal nerve.

The aim of this study was to evaluate the voice quality of patients with AAV by comparing them with healthy subjects.

MATERIALS and METHODS

The study was planned as a case–control study performed between April 2022 and December 2022 in a university hospital. After ethical committee approval (Erciyes University, Ethical Committee of Clinical Research. Date: 27.07.2022, No: 2022/534); patients with AAV and over 18 years old who the rheumatology department followed were invited to the study. An informed consent form was obtained from all participants. Patients with histories of airway surgery, smoking, laryngopharyngeal reflux symptom index scores in local language of more than 13, allergy, active nose, throat, and larynx infection were excluded (3). Then, patients were taken to a soundproofed room to cheque their speech; their maximal phonation times (MPT) were recorded with the /a/ vowel. It was repeated three times, and the maximum values were selected.

For self-perceptual analysis, a valid and safe voice handicap index (VHI-10) survey in the local language was performed on patients (4). The VHI survey consisted of 10 questions with scores between 0 and 4 according to symptom severity (0 = never, 1 = almost never, 2 = sometimes, 3 = almost always, and 4 = always).

Patients were requested to read a phonetically balanced sentence at an undisturbed range and sound and recorded. Subjects' voices were recorded using a microphone (Shure SM-58; Shure Inc., Niles, IL, USA) with a standard soundboard (Sound Blaster Live Value, Creative Technology Ltd., Jurong East, Singapore). These records were used to estimate for auditory perceptual analysis. A well-known scale was made with five aspects: grade, roughness, breathiness, asthenia, and strain (GRBAS). GRBAS scales were rated by an experienced otolaryngologist blind to the groups of subjects. Each aspect had 4 points (0 = normal, 1 = mild, 2 = moderate, 3 = severe disorder in voice).

Voice analysis: Analysis was done using the same ambience with /a/ vowel. These recordings were made at a steady mouth-to-microphone distance (15 cm). Before recording to obtain maximum steady phonation; subjects were instructed to maintain /a/ vowels at an undisturbed range and sound of noise three times. The vowel /a/ articulated with a calm voice was recorded for five seconds and digitalised in all patients for evaluation.

Age- and gender-compatible subjects admitted to the hospital, except for those with voice complaints, were included in the study as the control group. All procedures, and VHI and GRBAS evaluation and voice recording, were performed. The exclusion criteria were implemented again. Neither patients nor healthy subjects were voice professionals.

Specialised PRAAT software, which is a valuable interface for voice analysis, was used (5). The voice analysis results of patients [basic frequency (F0), jitter %, shimmer %, and harmonic-to-noise ratio (HNR) values for the /a/ vowel) were evaluated with the control group. Patients and age-gender compatible subjects were statistically compared regarding MPT, VHI scores, GRBAS scores, and voice analysis.

Statistical analysis

SPSS (version 24.0; IBM, New York, USA) software was used for the analyses. A Shapiro-Wilk test was used to evaluate the normality of the data distribution. Normally distributed data are presented as the mean ± standard deviation (SD). When data measures were not normally distributed, they were presented as medians (25-75 percentiles), and the Mann -Whitney U test was used for the analysis. A p-value of 0.05 was considered statistically significant.

RESULTS

There were 30 people in each group (16 women and 14 men). The mean ages were 51.1±2.7 and 51.5±2.8 in the patient and control groups, respectively. The patient and control groups were similar to age and gender ($p>0.05$).

Laryngeal examination: There was no pathology in the laryngoscopy in both groups.

MPT scores: Median MPT values of the patient group were shorter (19 to 23.5 sec, respectively) than healthy controls, and this difference was significant statistically ($p<0.05$).

VHI scores: Median VHI scores were higher than the control group's (2.5 to 0, respectively), and the difference was significant statistically ($p<0.05$).

GRBAS scores: While median GRBAS scores were higher in the patient group [2 (0-4)], it was 0 [0-0.25)] in control group. The difference was significant statistically ($p<0.05$).

Voice quality: Despite being statistically insignificant, median F0 and median HNR values were lower in patients (177.5 to 180.5 Hz and 14.44 to 16.64, respectively). In contrast, median jitter and median shimmer values (1.39 to 1.2 and 10.64 to 9.34, respectively) were higher in the patient group. These differences were not statistically significant ($p>0.05$). Comparison of groups were given in Table 1.

Patient subgroups showed no significant difference according to their autoantibody type (myeloperoxidase/proteinase 3). In addition, there were no significant differences between the vasculitis subtypes (EGPA / GPA and mPAN).

Table 1: Comparisons of groups in terms of variables statistically

	ANCA + Group (n:30)	Control Group (n:30)	p
Women	16	16	1
Age	51.1±2.7	51.5±2.8	0.86
	Variable [Median (25%-75%]		
MPT (sec)	19 (15-25)	23.5 (18.75-28)	**0.012**
VHI	2.5 (0-9.75)	0 (0-1.25)	**0.02**
GRBAS Score	2 (0-4)	0 (0-0.25)	**0.00**
F0	177.5 (138.75-221)	180.5 (119.75-215.75)	0.53
Jitter %	1.39 (0.85-2.83)	1.2 (0.6-1.72)	0.196
Shimmer %	10.64 (9.2-16.37)	9.34 (7.05-14.51)	0.179
HNR	14.44 (11.64-18.41)	16.76 (14.69-19.47)	0.104

VHI: Voice Handicap Index; MPT: Maximum Phonation Time; GRBAS: Grade, Roughness, Breathiness, Astheny, and Strain; F0: Fundamental Frequency; HNR: Harmonic to Noise Ratio

DISCUSSION

Because AAV influences the lung and upper respiratory tract, this involvement can affect voice quality. We designed a study to evaluate voice quality in patients with AAV by comparing age- and gender-compatible healthy controls. There were significant differences in the median MPT, VHI, and GRBAS scores. In addition, the median F0 and HNR values were lower in patients than in the control group. The median jitter and shimmer values were higher in the patient group. Voice quality parameters were worse in the patient group.

AAV is a group of diseases characterised by inflammation of blood vessels, endothelial injury, and tissue damage. The vessels affected by AAV are typically capillaries, arterioles, and venules. Small arteries and veins may also be involved. AAV represents one of several types of autoimmune vasculitis. Although GPA and MPA can involve small blood vessels in any organ or tissue, they commonly affect the upper and lower respiratory tract and kidneys. Prevalence rates have been reported as 300–421 per million people in recent studies, a rise presumably elucidated by advances in survival and better case definition. Necrotising or granulomatous inflammation can affect the ear, nose, and throat tract. Therefore, the patient experiences chronic rhinitis, sinusitis, or laryngitis symptoms. In a similar manner, pulmonary haemorrhage that presents as cough, haemoptysis and shortness of breath may develop (6).

Dejonckere et al. recommended performing a comprehensive voice assessment, laryngeal imaging, self-assessment, auditory-perceptual impression, and aerodynamic and acoustic analyses (7). This study attempted to comply with these parameters.

MPT is accepted as an aerodynamic assessment that evaluates glottal adequacy by assessing the pulmonary reservoir's capability and the larynx's myoelastic forces (8). Healthy lung function and air flow velocity are necessary to sustain balanced phonation. When the MPT duration is weak, it means that the breathing volume is difficult or that the glottal resistance is too low, which might cause a distortion in voice quality (9, 10). The median MPT was shorter in the patient group in this study, which suggests that AAV can distort voice quality by affecting the upper respiratory tract and lungs.

VHI is a scale to evaluate voice from the patient's perspective and is a widely used survey for voice self-assessment. VHI scores range from 0 to 4 according to symptom severity (0 = never, 1 = almost never, 2 = sometimes, 3 = almost constantly, and 4 = always). The higher the score, the worse the voice quality. A valid and reliable form of VHI-10 in the local language was applied in this study (4). The median VHI score was higher in the patient group.

The clinicians perspective is as important as that of the patients for voice assessment. Because auditory-perceptual voice analysis is affected by multiple factors such as experience, profession, and rating stimuli, GRBAS scores have been developed to standardise voice assessment (11). The higher the score, the worse the voice quality. The median GRBAS score was significantly higher in the patient group, indicating that AAV may disrupt voice quality.

Jitter and shimmer are other acoustic parameters related to voice perturbation. Shimmer shows disarrays in the mucosal oscillating wave, obvious as high transient versatility in either vocal signal width. If this irregularity is related to the vocal signal, it is called jitter, which is higher in dysphonic subjects (12). Jiang et al. reported that the jitter percentage in adult patients' voices with vocal folds' polyps and nodules was significantly higher than that in normal subjects (13). Despite statistical insignificance, jitter and shimmer were higher in the patient group in the present study.

There are harmonic and aperiodic (noise) components of the speech signal. The HNR parameter indicates the ratio of the harmonic and noise fragments. Pathologies in the vocal folds switch the phonation course because the vibration types during the opening and closing phases of the vocal cords are unsteady

(14). HNR measures the amount of correlative noise. The lower the HNR, the more noise there is in the voice. Laryngeal diseases may lead to ineffective adduction of the vocal folds and therefore boost the quantity of random noise in the vocal note. If a laryngeal problem causes more air to escape during vibration, this creates turbulent noise; the more significant the proportion of noise, the lower the HNR (15). The median HNR was lower in the patient group in this study.

Gurbuzler et al. studied the voice quality of patients with Behçet's disease and healthy controls (16). They reported that Behçet's disease impaired voice quality. F0, jitter, shimmer, and HNR values were used in their study. They also evaluated the subjects' MPT and VHI scores. They found significant differences in MPT and shimmer. MPT was higher in healthy subjects than in the patients in their study. We found comparable results in terms of MPT in this study. Although they found no difference between the VHI scores, the median VHI score was higher in the patient group than in the control group in our study.

Castro et al. reported a study evaluating voice parameters in patients with rheumatoid arthritis (17). They did not compare the patients with any control. They reported that patients with RA had 70% dysphonia and high VHI scores. Laryngeal examination, VHI, perceptual analysis, F0, jitter, shimmer, and HNR were used parameters in their study, as in this paper.

De Macedo et al. evaluated voice in patients with systemic lupus erythematosus (SLE) and found that voice quality was worse in the patient group than in healthy subjects (18).

Ali and Figueiredo reported a patient with hoarseness and giant cell arteritis. They emphasised that this symptom could be overlooked in such patients and should be considered (19). Sünter et al. reported that F0 was lower in patients with ankylosing spondylitis (20). Rheumatologic disease can disturb voice quality.

Phonation is one of the most complex processes in the human body. It requires a good lung function for the reservoir first. Bilateral symmetric neuromuscular function that provides vocal fold mobility is another necessity for a sound voice. Despite the normal laryngeal view endoscopically, these structures may be affected by AAV, chronic inflammation in other words. There were significant differences in the MPT, VHI, and GRBAS score results in the present study. MPT was related to lung function rather than the larynx. VHI and GRBAS scores were subjective parameters. Because of this, laryngeal endoscopy may have viewed normal.

To the best of our knowledge, no study has evaluated voice quality in patients with AAV. Considering the incidence of AAV, the sample size can be assumed to be acceptable.

CONCLUSION

In short, patients and physicians should be aware of the possibility of voice disorders in AAV, and voice therapy may be advised to the patients. AAV may disturb voice quality in terms of aerodynamic aspects, voice handicap index, and auditory-perceptual analysis. Broader studies can be established on this issue.

Ethics Committee Approval: This study was approved by the Ethics Committee of the Erciyes University (Date: 27.07.2022, No: 2022/534).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- K.K., A.S.Ş.; Data Acquisition- M.K., A.O.Ç.; Data Analysis/Interpretation- E.O.K., N.T.; Drafting Manuscript- M.K., A.O.Ç., E.O.K., N.T.; Critical Revision of Manuscript- K.K., A.S.Ş.; Final Approval and Accountability- K.K., M.K., A.O.Ç., E.O.K., N.T., A.S.Ş.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support

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