



# Impact of the Severity of Reinke's Edema on the Parameters of Voice

## Original Investigation

Elife Barmak<sup>1</sup>, Esmâ Altan<sup>2</sup>, Zeynep Yılmaz<sup>3</sup>, Mehmet Hakan Korkmaz<sup>4</sup>, Emel Çadallı Tatar<sup>2</sup>

<sup>1</sup>Department of Speech and Language Therapy, Ankara Yıldırım Beyazıt University Faculty of Health Sciences, Ankara, Turkey

<sup>2</sup>Department of Otorhinolaryngology, University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey

<sup>3</sup>Department of Audiology and Speech Disorders, Institute of Health Sciences, Ankara Yıldırım Beyazıt University, Ankara, Turkey

<sup>4</sup>Department of Otorhinolaryngology, Head and Neck Surgery, Ankara Yıldırım Beyazıt University Faculty of Medicine, Ankara, Turkey

## Abstract

**Objective:** This study aimed to classify the degree of edema in patients with Reinke's edema (RE) and examine its impact on their voice parameters using both objective and subjective assessment methods.

**Methods:** Objective and subjective voice data of 104 patients diagnosed with RE between 2018 and 2021 were evaluated retrospectively. RE is classified into 4 groups (types 1, 2, 3, and 4). The evaluation included videolaryngostroboscopic examination, acoustic voice analysis, and aerodynamic measurements, GRBAS, Voice Handicap Index-10 (VHI-10), Voice-Related Quality of Life Scale (V-RQOL), and Reflux Septum Index (RSI).

**Results:** Patients with type 1 RE had a significantly lower mean age than those with types 3–4. Although there were no significant differences in acoustic and aerodynamic parameters between the groups, it was observed that F0 and the maximum phonation time decreased as the degree of edema increased. The GRBAS<sub>Total</sub>, G, and R scores of types 1 and 2 were significantly lower than those of types 3 and 4, as were the scores of type 1 S. There were no statistically significant differences between the RE groups in terms of VHI-10, V-RQOL, and RSI scores.

**Conclusion:** It has been observed that as the severity of RE increases, voice perception and quality (especially types 3 and 4) are negatively affected. Determining the degree of edema will guide the clinician in both the planning of the intervention phase and the follow-up phase.

**Keywords:** Larynx, dysphonia, vocal fold, Reinke's edema, classification, voice quality, laryngology

### ORCID IDs of the authors:

E.B. 0000-0002-6479-0553;

E.A. 0000-0002-3080-3571;

Z.Y. 0009-0003-1112-2185;

M.H.K. 0000-0001-8732-3061;

E.Ç.T. 0000-0002-8923-1408.

**Cite this article as:** Barmak E, Altan E, Yılmaz Z, Korkmaz MH, Çadallı Tatar E. Impact of the Severity of Reinke's Edema on the Parameters of Voice. Turk Arch Otorhinolaryngol

### Corresponding Author:

Elife Barmak;  
elifebarmak@gmail.com

Received Date: 28.08.2023

Accepted Date: 11.12.2023

DOI: 10.4274/tao.2023.2023-8-10

## Introduction

Reinke's edema (RE) is a common and benign laryngeal condition resulting in polypoid degeneration due to edema,

vascular congestion, and venous stasis in Reinke's space (1). Its prevalence in the general population was found to be 0.347% (2). Although women are more



likely to have RE, some studies show that men are more likely to have it (2, 3).

RE can occur in one or both vocal folds (4). It is hypothesized that RE is caused by chronic inflammation, which affects the permeability of the capillary wall and causes fluid to seep into Reinke's cavity. The cover layer of the vocal fold becomes edematous and less stiff due to these changes (5). Chronic inflammation of the larynx can develop secondary to many conditions, such as smoking, phonotrauma, and gastroesophageal reflux (6). In the management of RE, smoking cessation, anti-reflux medication, and voice therapy are recommended to help reduce the edema; however, patients whose voice quality does not improve with these therapies need surgery. To ensure improved voice rehabilitation after surgery, it is essential to continue voice therapy and anti-reflux treatment for a long period and avoid smoking (7).

There are several RE classifications in the literature (1, 4, 8). Yonekawa (8) made the first clinical classification based on the morphological features of the vocal fold and classified it into types 1, 2, and 3. Another classification was made by Tan et al. (1) as grades 1, 2, 3, and 4 according to the size of the lesion. Different degrees of dysphonia are seen in patients with RE. It has also been noted that patients could develop dyspnea depending on the extent of the edema and the airway obstruction (7). The most typical symptoms in these patients are thickening of the voice, vocal fatigue, a reduced vocal range, and the inability to produce high-pitched voices. During a phone call, the voices of female patients, in particular, can be perceived as masculine. One study showed that the voices of female patients with type 1 RE were more easily distinguishable from those with types 2 and 3 in terms of gender identification (9). Lim et al. (10) reported that acoustic analysis parameters such as jitter, shimmer, and harmonic-to-noise ratio did not differ between patients with RE types 1, 2, and 3. Even though the maximum phonation time (MPT) of patients with type 3 RE was not statistically significantly different from the other types, MPT was found to be shorter. Yonekawa (8) looked at the auditory-perceptual relationship between the voice and the degree of RE and reported that the degree of hoarseness in patients with type 3 RE was more severe than in types 1 and 2. Patients with vocal fold lesions (leukoplakia, cysts, polyps, and RE) had high GRBAS and Voice Handicap Index-10 (VHI-10) scores in the preoperative auditory-perceptual evaluation of voice (11). There is no information in the literature about auditory-perceptual changes based on the classification of RE.

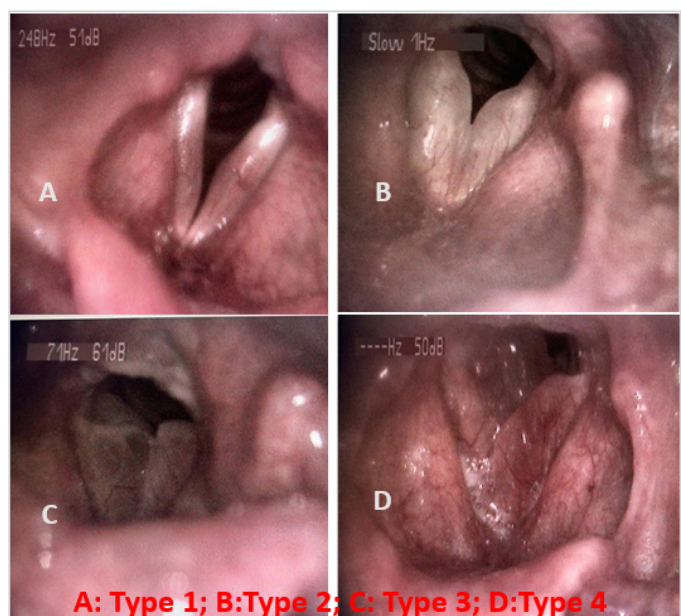
The purpose of this study was to examine the impact of the severity of RE on voice quality using objective and subjective evaluation methods. Our study questions were:

- Does the severity of RE change with age?
- Are there differences in acoustic and aerodynamic voice parameters based on RE classification?
- Which parameters are more effective in the auditory-perceptual evaluation according to the RE classification?
- Is there a difference between reflux symptom findings and the severity of RE?

## Methods

The study was conducted with approval from the Ministry of Health, University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital Clinical Research Ethics Committee (decision no: 110/06, date: 03.05.2021), and all subjects gave their informed consent. We conducted a retrospective study of patients who presented to the University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital Voice Clinic between 2018 and 2021 with a complaint of dysphonia and were diagnosed with RE as a result of the evaluation.

The RE patients included in our study were classified according to the classification made by Tan et al. (1): minimal polypoid degeneration of the vocal fold up to 25% of the glottic airway was grade 1; enlarged polypoid lesions occupying 25% to 50% of the glottic airway was grade 2; enlarged polypoid lesions of 50% to 75% of the glottic airway was grade 3; and obstructive lesions occupying more than 75% of the glottic airway, regardless of laterality, was grade 4 (Figure 1).



**Figure 1.** Classification of Reinke edema

Inclusion criteria for patients in the study were: a) being diagnosed with RE type 1, 2, 3, or 4; b) being between the ages of 18 and 65 years; c) the absence of a neurogenic disorder that would cause a voice disorder; d) not having undergone neck or laryngeal surgery. Our study included 104 patients who met these inclusion criteria.

## Evaluation

Demographic data of all patients, such as age, gender, and smoking status recorded in the medical charts, and their objective/subjective voice parameters in the videolaryngoscopy, voice, and questionnaire records were retrieved and reviewed.

**Videolaryngoscopic examination:** All patients had undergone a videolaryngoscopic (XION; Berlin, Germany) examination with a rigid endoscope. Patients were asked to produce the vowel "i" with constant pitch and intensity throughout the assessment. The laryngologists who are the authors of this paper classified RE (types 1, 2, 3, and 4) according to the retrospective videolaryngostroboscopy record evaluation.

**Acoustic voice analysis measurements:** Acoustic analysis was conducted in a quiet room using a Computerized Speech Lab (CSL Model 4500-Kay Elementrics, Lincoln Park, N-LC, New Jersey) device and a Shure brand (Shure SM48-LC) microphone (12). The "Multi-Dimensional Voice Program" in the CSL device was used for acoustic voice measurement. A long /a/ vowel was recorded in a comfortable tone by adjusting the distance between the patient's mouth and the microphone to 10 cm and an angle of 45 degrees. The middle 3 seconds of the recording in the phonation range were analyzed (13). For this study, numbers were used to record the RE patients' fundamental frequency (F0), noise-to-harmonic ratio (NHR), jitter (%), shimmer (%), voice turbulence index (VTI), and soft phonation index (SPI).

**Aerodynamic measurements:** The s/z ratio and MPT durations of the RE patients were taken from the records. It gives an objective assessment of the respiratory mechanism's effectiveness during phonation (14). The s/z ratio expresses the ratio of the maximum phonation of the /s/ sound to the maximum phonation of the /z/ sound. While this ratio is approximately 1.00 in individuals with healthy vocal folds, it is over 1.4 in individuals with glottic closure defects (15). Both measurements were calculated using a stopwatch.

The subjective evaluations of the dysphonia patients, clinicians (GRBAS), and patient self-assessment tools [VHI-10, Voice-Related Quality of Life Scale (V-RQOL)] were used for the auditory-perceptual assessment.

GRBAS is a five-dimensional scale used to assess voice quality. These are defined as Grade (G), Roughness (R), Breathiness (B), Asthenia (A), and Strain (S) (16). All

patients' GRBAS assessments were conducted by a 10-year-veteran speech-language pathologist who is an expert in the area. The patients were asked to read a passage and produce the vowel "a" in a relaxed tone. Each parameter was scored on a 4-point scale between 0 and 3.

VHI-10 is a scale on which the patient evaluates his or her voice in terms of physical, functional, and emotional aspects. There are 30- and 10-item versions of the scale (17, 18). The short version of VHI-10 was administered in our clinic. Each item was scored between 0 and 4.

V-RQOL has ten items divided into two subscales: physical functioning (6 items) and social-emotional (6 items). The overall score obtained from both subscales indicates the voice-related quality of life (19).

Reflux symptom index (RSI) is a 9-item self-assessment questionnaire to assess laryngopharyngeal reflux symptoms. An RSI score of more than 13 indicates laryngopharyngeal reflux (20).

## Statistical Analysis

Statistical analysis was performed with the IBM SPSS 26.0 package program (Armonk, NY: IBM Corp.) The numerical variables were shown as mean, standard deviation, and percentage (frequency). In the normality test, data with skewness and kurtosis coefficients in the range of +2.0 and -2.0 were accepted as not exhibiting a substantial divergence from the normal distribution (21). Normally distributed data were analyzed using independent-sample t-tests and ANOVA, while non-normally distributed data were analyzed using the Kruskal-Wallis and Mann-Whitney U tests. In addition, post-hoc analyses were performed using Tukey to investigate notable disparities among the different groups. A significance threshold of 0.05 was established.

## Results

There were 29 patients in the type 2 group and 25 patients in each of the types 1, 3, and 4. Of the 104 patients, 18.3% were male (n=19), and 81.7% were female (n=85). When we looked at the smoking status of the patients, 88.5% (n=92) were smokers, and only 11.5% (n=12) were not smokers. Non-smoking patients had a history of previous smoking.

The mean age of all patients was 49.096±9.324 years (minimum: 19–maximum: 65). Mean age was 45.080±12.158 years in the type 1 group; 46.896±8.393 in the type 2 group; 52.600±7.041 in the type 3 group; and 52.160±6.950 in the type 4 group. A substantial difference was found between the RE groups in terms of mean age scores (p=0.005) (Table 1).

When the mean ages of the RE groups were compared, the type 1 group was substantially younger than the type 3 (p=0.021) and type 4 (p=0.035) groups (Table 2).

In acoustic voice analysis, no statistically significant difference was found between the groups in terms of F0, jitter, shimmer, NHR, VTI, and SPI parameters ( $p=0.238$ ;  $p=0.840$ ;  $p=0.248$ ;  $p=0.127$ ;  $p=0.202$ ;  $p=0.259$ , respectively). However, the acoustic voice analysis results by gender showed significant differences in the F0 scores ( $p=0.000$ ). Accordingly, the F0 scores (mean =119.600 Hz) of the male patients were significantly lower than those of the female patients (mean = 158.619 Hz). The comparison of RE groups and gender in terms of acoustic voice analysis findings is shown in Table 3.

Aerodynamic analysis showed no statistically significant differences between the RE groups in terms of MPT and s/z ratios ( $p=0.094$ ;  $p=0.466$ ) (Table 4).

There was a statistically significant difference between the RE groups concerning G, R, S, and GRBAS<sub>Total</sub> ( $p=0.000$  for all). The average GRBAS<sub>Total</sub>, G, and R scores for types 1 and 2 were lower than those for types 3 and 4, as was type 1's average S score. There were no statistically significant differences between the RE groups in terms of patients' VHI-10, V-RQOL, and RSI scores ( $p=0.192$ ;  $p=0.178$ ;  $p=0.164$ , respectively) (Table 5).

## Discussion

RE develops from chronic and widespread swelling of the superficial lamina propria of the vocal fold (22, 23). It is defined as polypoid degeneration of the vocal folds. RE is usually bilateral. However, sometimes it can be more prominent on one side (22). The etiologic factors of RE include smoking, vocal abuse, and other factors often closely associated with laryngopharyngeal reflux (4, 22, 24). In our study, a majority of the patients had a history of smoking in their etiology (88.5%), and 81.7% were female. In addition, the scores obtained from the RSI were considerably higher than the cut-off point (RSI >13) (20). These findings of our study are consistent with the literature.

In one study of 69 patients with RE, the mean age was 55.9 years; in another study, the mean age of 38 patients was found to be 50 years (34–64 years old) (1, 8). In our study, the mean age of 104 patients was 49 years. According to the classification of RE, the mean age of the type 1 group was younger than the type 3–4 group. This finding indicates that the degree of RE increases with age. Moreover, the increase in edema may depend on many etiological factors, such as smoking and severe reflux symptoms.

**Table 1.** Distribution of mean age according to RE groups

Groups	N	Age			F	p-value
		Mean	SD	Min-max		
Type 1	25	45.0800	12.15840	20–64	4.596 <sup>a</sup>	<b>0.005</b>
Type 2	29	46.8966	8.39364	19–60		
Type 3	25	52.6000	7.04154	38–62		
Type 4	25	52.1600	6.95030	33–65		
Total	104	49.0962	9.32428	19–65		

RE: Reinke's edema, <sup>a</sup>ANOVA test, F: The ratio of the between-group mean squares to the within-group mean square, Min: Minimum, Max: Maximum, SD: Standard deviation. Results in bold represent statistically significant values with  $p$ -value <0.05

**Table 2.** Comparison of mean age findings by RE groups

RE group (I)	RE group (J)	Mean difference (I-J)	SE	p-value
Type 1	Type 2	-1.81655	2.42110	1.000
	Type 3	-7.52000	2.50917	<b>0.021</b>
	Type 4	-7.08000	2.50917	<b>0.035</b>
Type 2	Type 1	1.81655	2.42110	1.000
	Type 3	-5.70345	2.42110	0.123
	Type 4	-5.26345	2.42110	0.192
Type 3	Type 1	7.52000	2.50917	<b>0.021</b>
	Type 2	5.70345	2.42110	0.123
	Type 4	0.44000	2.50917	1.000
Type 4	Type 1	7.08000	2.50917	<b>0.035</b>
	Type 2	5.26345	2.42110	0.192
	Type 3	-0.44000	2.50917	1.000

RE: Reinke's edema, SE: Standard error, Tukey post-hoc analysis. Results in bold represent statistically significant values with  $p$ -value <0.05

RE is generally known to have a low F0 (10). Yonekawa (8) indicated that as type 2 or type 3 progressed, in other words, as the severity of the edema increased, the F0 decreased significantly in both genders. Colizza et al. (25) found that the mean F0 in males and females with RE was 101.06 Hz and 147.58 Hz, while it was 131.58 and 224.35 Hz, respectively, in healthy males and females. This study also reported that

the jitter (2.254% and 3.733%), shimmer (9.037% and 11.172%), and NHR (0.235 and 0.278) values of males and females with RE were significantly higher than the healthy group. A related study found that acoustic parameters like harmonic-to-noise ratio, shimmer, and jitter did not differ between the types of RE. However, these parameters were significantly different in individuals with healthy vocal folds

**Table 3.** Comparison of acoustic voice analysis findings by RE groups and gender

Parameter Group/gender (n)	Mean ± SD	Mean rank	Test values	p-value	
F0	Type 1 (n=25)	163.922±49.8	1.431 <sup>a</sup>	0.238	
	Type 2 (n=29)	155.174±42.0			
	Type 3 (n=25)	147.135±49.5			
	Type 4 (n=25)	139.143±35.9			
	Male (n=19)	119.600±33.7			
	Female (n=85)	158.619±44.0			3.686 <sup>b</sup>
Jitter	Type 1 (n=25)	2.350±1.45	49.04	0.840 <sup>c</sup>	0.840
	Type 2 (n=29)	2.731±1.84	53.72		
	Type 3 (n=25)	3.320±4.99	50.80		
	Type 4 (n=25)	3.624±4.16	56.24		
	Male (n=19)	2.649±1.9	50.37		
	Female (n=85)	3.073±3.6	52.98		
Shimmer	Type 1 (n=25)	6.752±3.09	43.56	4.128 <sup>c</sup>	0.248
	Type 2 (n=29)	7.864±3.63	54.16		
	Type 3 (n=25)	8.006±4.42	51.40		
	Type 4 (n=25)	9.400±5.00	60.62		
	Male (n=19)	8.808±4.6	57.74		
	Female (n=85)	7.819±4.0	51.33		
NHR	Type 1 (n=25)	0.175±0.08	40.44	5.701 <sup>c</sup>	0.127
	Type 2 (n=29)	0.204±0.07	56.07		
	Type 3 (n=25)	0.214±0.12	53.64		
	Type 4 (n=25)	0.259±0.15	59.28		
	Male (n=19)	0.211±0.11	50.39		
	Female (n=85)	0.213±0.11	52.97		
VTI	Type 1 (n=25)	0.081±0.04	46.84	4.616 <sup>c</sup>	0.202
	Type 2 (n=29)	0.080±0.04	46.27		
	Type 3 (n=25)	0.093±0.05	55.14		
	Type 4 (n=25)	0.118±0.09	60.44		
	Male (n=19)	0.121±0.08	62.13		
	Female (n=85)	0.086±0.05	50.35		
SPI	Type 1 (n=25)	11.740±5.10	50.76	4.020 <sup>c</sup>	0.259
	Type 2 (n=29)	14.416±7.76	59.11		
	Type 3 (n=25)	13.428±7.86	54.04		
	Type 4 (n=25)	9.966±4.83	43.24		
	Male (n=19)	11.643±6.2	48.58		
	Female (n=85)	12.649±6.8	53.38		

RE: Reinke's edema, F0: Fundamental frequency, NHR: Noise-to-harmonic ratio, VTI: Voice Turbulence Index, SPI: Soft Phonation Index, <sup>a</sup>ANOVA test, <sup>b</sup>Independent-Samples T, <sup>c</sup>Kruskal–Wallis, <sup>d</sup>Mann–Whitney U test, SD: Standard deviation. Results in bold represent statistically significant values with p-value <0.05

(10). Our study showed that the F0 average of male and female patients was low, and jitter (2.649% and 3.073%), shimmer (8.808% and 7.819%), and NHR (0.211 and 0.213) values of male and female patients were close to the study findings in the literature. In addition, F0, frequency, and amplitude perturbation measurements (jitter and shimmer parameters), NHR, and SPI parameters were not statistically significant among the RE subtypes. However, as the severity of RE increased (especially in types 3 and 4), F0 decreased numerically. Although the changes in all acoustic parameters are not statistically significant between the RE groups, deviations from normal values in these parameters indicate that the presence of edema causes deterioration in the patient's voice quality. The other parameter we evaluated in acoustic analysis is SPI, which is a parameter that indicates whether the vocal folds are fully closed during phonation. A high output of this parameter is thought to indicate insufficient closure of the vocal folds during phonation (26). In our study, especially in the group with type 4 edema, SPI findings were lower than in the other groups. Due to the obstruction of more than 75% of the glottic airway in this group due to polypoid degeneration, it appears that there is no problem in closing the vocal folds during phonation.

In one study, it was reported that as the degree of RE increased, the average flow rate increased and the MPT decreased (8). Salmen et al. (27) compared MPT before and after surgery in 60 patients with RE. Whereas the mean MPT was 9±5 seconds before surgery, it increased by 2±5 seconds after surgery. In our study, there was no significant difference in MPT between the groups, but patients with types 3 and 4 edema had lower MPT than the other groups. As reported in the literature, in our study, too, we found that MPT had decreased when the degree of edema rose. Similarly, there is no significant difference between the groups in s/z ratios.

Via the auditory-perceptual assessment of a patient with complaints of voice impairment, the clinician reaches a subjective opinion about the severity of the overall impairment, the appropriateness of pitch and volume levels,

and the quality of the voice. In the measurements made by the patient, it is important to obtain information about how the patient perceives the communication problems caused by pain, fatigue, and voice problems that cannot be directly observed by others (28). Taşar et al. (29) evaluated the vocal performances of 21 RE patients before and after surgery and found that their vocal performances had improved after surgery. In another study, researchers found that those with various vocal lesions (RE, cyst, or polyp) had a preoperative GRBAS score of 9.50±2.34 and a VHI-10 score of 18.19 (11). The information available in the literature on the effect of auditory-perceptual and voice-related quality of life according to the degree of RE is insufficient.

In our study, the G, R, S, and GRBAS<sub>Total</sub> scores of the group with types 1 and 2 edema were statistically significantly lower than the type 3 and 4 groups. This shows that as the degree of RE increases, so does the general severity, roughness, and tension of the voice disorder. In addition, no significant differences were found between the groups in how patients perceived their voices and the effect of their voices on quality of life. However, both VHI and V-RQOL scores were high in all patients. This indicates that the presence of edema was sufficient to negatively impact the auditory perception and voice-related quality of life of the patients. Therefore, knowing the degree of edema will guide the clinician both in planning the intervention phase and in the follow-up phase with the patients. We believe that a surgical decision is more appropriate, especially in cases where the voice quality is severely deteriorated (especially in types 3–4).

Damage to the vocal fold mucosa from laryngopharyngeal reflux makes the mucosa more sensitive to injury, which leads to the formation of benign vocal fold lesions such as RE, nodules, and polyps. It is also reported that the prevalence of laryngopharyngeal reflux symptoms is high in patients with RE (30). In another study, it was found that the RSI scores of patients with RE in the groups with and without pharyngitis were 23.05 and 22.65, respectively (24). In our study, RSI scores did not differ significantly between the

**Table 4.** Comparison of aerodynamic analysis findings by RE groups

Parameter	Groups (n)	Mean rank	Kruskal–Wallis–H	p-value
MPT	Type 1 (n=25)	56.66	6.402	0.094
	Type 2 (n=29)	61.74		
	Type 3 (n=25)	46.32		
	Type 4 (n=25)	43.80		
s/z rate	Type 1 (n=25)	49.66	2.553	0.466
	Type 2 (n=29)	48.41		
	Type 3 (n=25)	52.06		
	Type 4 (n=25)	60.52		

RE: Reinke's edema, MPT: Maximum phonation time, Kruskal–Wallis test. Result, p<0.05, H: Kruskal–Wallis statistical values. Results in bold represent statistically significant values with p-value <0.05

groups. However, it is also reported that the RSI scores of every group were higher than the cut-off value (cut-off point: RSI >13) (20).

The treatment of RE involves a comprehensive approach that integrates surgical intervention with voice therapy (3). The

intervention aims to ameliorate dysphonia symptoms with a primary focus on eliminating the underlying etiological factors. The primary strategy in its treatment is the elimination of all potential risk factors that could contribute to the condition. Surgery is indicated in cases where voice quality is severely affected and protective methods do not provide

**Table 5.** Auditory-perceptual analysis findings evaluated by clinician and patients

Parameter	Groups (n)	Mean	SD	F	p-value	Post-hoc
G	Type 1 (n=25)	1.5600	0.76811	13.988 <sup>a</sup>	<b>0.000</b>	Type 1 < Type 3–4
	Type 2 (n=29)	1.7586	0.63556			
	Type 3 (n=25)	2.3600	0.63770			
	Type 4 (n=25)	2.5600	0.50662			
R	Type 1 (n=25)	1.2000	0.81650	12.391 <sup>a</sup>	<b>0.000</b>	Type 1 < Type 3–4
	Type 2 (n=29)	1.4483	0.78314			
	Type 3 (n=25)	2.1200	0.78102			
	Type 4 (n=25)	2.3600	0.75719			
B	Type 1 (n=25)	0.5200	0.65320	0.615 <sup>a</sup>	0.607	
	Type 2 (n=29)	0.4828	0.50855			
	Type 3 (n=25)	0.6000	0.50000			
	Type 4 (n=25)	0.6800	0.62716			
S	Type 1 (n=25)	0.4800	0.77028	7.067 <sup>a</sup>	<b>0.000</b>	Type 1 < Type 3–4
	Type 2 (n=29)	0.8621	0.87522			
	Type 3 (n=25)	1.1200	0.60000			
	Type 4 (n=25)	1.4000	0.64550			
GRBAS <sub>Total</sub>	Type 1 (n=25)	3.7600	2.29637	15.491 <sup>a</sup>	<b>0.000</b>	Type 1 < Type 3–4
	Type 2 (n=29)	4.5517	1.93808			
	Type 3 (n=25)	6.2800	1.72047			
	Type 4 (n=25)	6.9600	1.61967			
VHI-10	Type 1 (n=25)	19.0400	8.87168	1.609 <sup>a</sup>	0.192	
	Type 2 (n=29)	19.1724	10.03234			
	Type 3 (n=25)	20.2400	9.13911			
	Type 4 (n=25)	24.2400	10.60770			
V-RQOL	Type 1 (n=25)	22.240	6.8086	1.673 <sup>a</sup>	0.178	
	Type 2 (n=29)	23.793	9.4278			
	Type 3 (n=25)	24.440	10.5478			
	Type 4 (n=25)	27.800	9.0921			
RSI	Type 1 (n=25)	15.8800	12.12889	1.739 <sup>a</sup>	0.164	
	Type 2 (n=29)	17.0690	12.52407			
	Type 3 (n=25)	18.0400	13.21766			
	Type 4 (n=25)	23.2000	11.17288			
Parameter	Groups (n)	Mean rank	df	Kruskal–Wallis–H	p-value	Post-hoc
A	Type 1 (n=25)	52.00	3	3.160 <sup>b</sup>	0.368	
	Type 2 (n=29)	52.00				
	Type 3 (n=25)	54.00				
	Type 4 (n=25)	52.00				

G: Grade; R: Roughness; B: Breathiness; A: Asthenia; S: Strain; VHI-10: Voice Handicap Index-10; V-RQOL: Voice-Related Quality of Life Scale; RSI: Reflux Symptom Index, <sup>a</sup>ANOVA Ttest, F: The ratio of the between-group mean squares to the within-group mean square, <sup>b</sup>Kruskal–Wallis, H: Kruskal–Wallis statistical values, SD: Standard deviation. Results in bold represent statistically significant values with p-value <0.05

improvement in dysphonia (5). Voice therapy and smoking cessation play an important role in the long-term treatment results of RE after surgery (3). In our study, we found that as RE increases, voice perception and quality are negatively affected. We can say that the classification of Reinke's edema is especially important in terms of planning the appropriate treatment approaches. Moreover, it is thought that knowing the effects on voice quality according to the severity of the edema will play an important role in providing accurate and reliable information for research in this field.

Our study had several limitations. Firstly, the retrospective nature of the study was a disadvantage. Secondly, there was insufficient data regarding the duration of smoking (years) and the number of daily cigarettes smoked by the patients. The other limitation was the inequality of the numbers of male and female participants in RE subgroups.

## Conclusion

The severity of edema was found to increase with age, according to our study. It is worth noting that as the severity of Reinke's edema increases, F0 and the MPT decrease. In the perceptual evaluation of the clinician, the voice perception of patients with types 3 and 4 RE is more likely to be negatively affected. Therefore, knowing the degree of RE will guide the clinician in both the intervention phase and the follow-up phase of patients. It is further thought that knowing the deterioration of voice quality according to the severity of edema will play an important role in providing accurate and reliable information to clinicians working in this field, both in clinical practices and research.

**Ethics Committee Approval:** The study was conducted with approval from the Ministry of Health, University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital Clinical Research Ethics Committee (decision no: 110/06, date: 03.05.2021).

**Informed Consent:** All subjects gave their informed consent.

## Authorship Contributions

Concept: E.B., E.A., E.Ç.T., Design: E.B., E.A., M.H.K., Data Collection and/or Processing: E.B., E.A., Z.Y., M.H.K., E.Ç.T., Analysis and/or Interpretation: E.B., E.A., Z.Y., M.H.K., E.Ç.T., Literature Search: E.B., Z.Y., Writing: E.B., Z.Y., E.Ç.T.

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

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

## Main Points

- We found that the severity of edema increased with age.
- As edema increased in the clinician's auditory perceptual evaluation, voice quality and perception were negatively affected.
- Knowing the type of Reinke's edema will guide the clinician both during the intervention phase and during the follow-up phase of patients.
- F0 and MPT decreased proportionally to edema severity.

## References

1. Tan M, Bryson PC, Pitts C, Woo P, Benninger MS. Clinical grading of Reinke's edema. *Laryngoscope* 2017; 127: 2310-3. [Crossref]
2. Hah JH, Sim S, An SY, Sung MW, Choi HG. Evaluation of the prevalence of and factors associated with laryngeal diseases among the general population. *Laryngoscope* 2015; 125: 2536-42. [Crossref]
3. Goswami S, Patra TK. A clinico-pathological study of Reinke's oedema. *Indian J Otolaryngol Head Neck Surg* 2003; 55: 160-5. [Crossref]
4. de Vincentiis M, Ralli M, Cialente F, Greco A, Marcotullio D, Minni A, et al. Reinke's edema: a proposal for a classification based on morphological characteristics. *Eur Arch Otorhinolaryngol* 2020; 277: 2279-83. [Crossref]
5. Tavaluc R, Tan-Geller M. Reinke's edema. *Otolaryngol Clin North Am* 2019; 52: 627-35. [Crossref]
6. Tavaluc R, Herman H, Lin J, Tan M. Does Reinke's edema grade determine premalignant potential? *Ann Otol Rhinol Laryngol* 2018; 127: 812-6. [Crossref]
7. Dewan K, Chhetri DK, Hoffman H. Reinke's edema management and voice outcomes. *Laryngoscope Investig Otolaryngol* 2022; 17: 7: 1042-50. [Crossref]
8. Yonekawa H. A clinical study of Reinke's edema. *Auris Nasus Larynx* 1988; 15: 57-78. [Crossref]
9. Pereira AM, Dassie-Leite AP, Pereira EC, Cavichiolo JB, Rosa MO, Fugmann EA. Auditory perception of lay judges about gender identification of women with Reinke's edema. *Codas* 2018; 30: e20170046. [Crossref]
10. Lim JY, Choi JN, Kim KM, Choi HS. Voice analysis of patients with diverse types of Reinke's edema and clinical use of electroglottographic measurements. *Acta Otolaryngol* 2006; 126: 62-9. [Crossref]
11. Kaneko M, Shiromoto O, Fujiu-Kurachi M, Kishimoto Y, Tateya I, Hirano S. Optimal duration for voice rest after vocal fold surgery: randomized controlled clinical study. *J Voice* 2017; 31: 97-103. [Crossref]



12. Van Lierde K, Moerman M, Vermeersch H, Van Cauwenberge P. An introduction to computerized speech lab. *Acta Otorhinolaryngol Belg* 1996; 50: 309-14. [Crossref]
13. Lucero JC. Optimal glottal configuration for ease of phonation. *J Voice* 1998; 12: 151-8. [Crossref]
14. Speyer R, Bogaardt HCA, Passos VL, Roodenburg NP, Zumach A, Heijnen MA, et al. Maximum phonation time: variability and reliability. *J Voice* 2010; 24: 281-4. [Crossref]
15. Verma P, Pal M, Raj A. Objective acoustic analysis of voice improvement after phonosurgery. *Indian J Otolaryngol Head Neck Surg* 2010; 62: 131-7. [Crossref]
16. Barsties B, De Bodt M. Assessment of voice quality: current state-of-the-art. *Auris Nasus Larynx* 2015; 42: 183-8. [Crossref]
17. Rosen CA, Lee AS, Osborne J, Zullo T, Murry T. Development and validation of the voice handicap index-10. *Laryngoscope* 2004; 114: 1549-56. [Crossref]
18. Kiliç MA, Okur E, Yıldırım I, Oğüt F, Denizoğlu I, Kızılay A, et al. [Reliability and validity of the Turkish version of the voice handicap index]. *Kulak Burun Bogaz Ihtis Derg* 2008; 18: 139-147. [Crossref]
19. Tezcaner ZÇ, Aksoy S. Reliability and validity of the Turkish version of the voice-related quality of life measure. *J Voice* 2017; 31: 262.e7-262.e11. [Crossref]
20. Akbulut S, Aydınli FE, Kuşçu O, Özcebe E, Yılmaz T, Rosen CA, et al. Reliability and validity of the Turkish reflux symptom index. *J Voice* 2020; 34: 965.e23-965.e28. [Crossref]
21. George D, Mallery M. *SPSS for Windows step by step: a simple guide and reference, 17.0 update 10a ed*. Boston: Pearson; 2010. [Crossref]
22. Boone DR, McFarlane SC, Von Berg SL, Zraick RI. *The voice and voice therapy*. 10th ed. USA: Pearson Education Inc; 2020. p.225-230. [Crossref]
23. Thibeault SL. Advances in our understanding of the Reinke space. *Curr Opin Otolaryngol Head Neck Surg* 2005; 13: 148-51. [Crossref]
24. Kamargiannis N, Gouveris H, Katsinelos P, Katotomichelakis M, Riga M, Beltsis A, et al. Chronic pharyngitis is associated with severe acidic laryngopharyngeal reflux in patients with Reinke's edema. *Ann Otol Rhinol Laryngol* 2011; 120: 722-6. [Crossref]
25. Colizza A, Ralli M, Cavalcanti L, Cambria F, Greco A, de Vincentiis M. Voice quality analysis of Reinke's edema according to recent new classification. *J Voice* 2022; 8: S0892-1997(22)00142-4. doi: 10.1016/j.jvoice.2022.05.009. [Epub ahead of print]. [Crossref]
26. Mathew MM, Bhat JS. Soft phonation index – a sensitive parameter? *Indian J Otolaryngol Head Neck Surg* 2009; 61: 127-30. [Crossref]
27. Salmen T, Ermakova T, Schindler A, Ko SR, Göktas Ö, Gross M, et al. Efficacy of microsurgery in Reinke's oedema evaluated by traditional voice assessment integrated with the vocal extent measure (VEM). *Acta Otorhinolaryngol Ital* 2018; 38: 194-203. [Crossref]
28. Ferrand CT. *Voice disorders: scope of theory and practice*. USA: Pearson Education, Inc; 2019. p.99-159. [Crossref]
29. Taşar S, Gürbüz MK, Kaya E, Özüdoğru E, Güney F, Çaklı H, et al. The effect of surgical treatment on voice quality in Reinke's edema: an evaluation with vocal performance questionnaire and acoustic voice analysis. *J Med Updates* 2013; 3: 56-61. [Crossref]
30. Lechien JR, Saussez S, Nacci A, Barillari MR, Rodriguez A, Le Bon SD, et al. Association between laryngopharyngeal reflux and benign vocal folds lesions: a systematic review. *Laryngoscope* 2019; 129: E329-41. [Crossref]