

# Laryngeal Function Evaluation in Cases with COVID-19

 ORIGINAL ARTICLE  
BALKAN ORL-HNS 2025;2(2):40-44

## ABSTRACT

**Background:** COVID-19 is a multifaceted disease that enters human cells via ACE2 receptors and affects various systems, including respiratory, neurological, and vocal functions. It may reduce the quality of life by causing neurological complications, loss of taste and smell, hearing impairment, and voice disorders.

**Methods:** This cross-sectional study aimed to investigate the possible effects of COVID-19 on laryngeal function and included 35 individuals previously diagnosed with COVID-19 who had no prior laryngeal pathology. The control group consisted of 35 antibody-negative individuals with no history of COVID-19. All participants underwent videolaryngostroboscopy (VLS), voice analysis (multi-dimensional voice program, motor speech profile), Maximum Phonation Time (MPT), s/z ratio, and aerodynamic evaluations.

**Results:** Symptoms such as hoarseness, dysphagia, and anosmia were more frequent in the COVID-19 group. MPT was significantly shorter in the patient group ( $P=.004$ ), and F0-Tremor Intensity Index (FTRI) was significantly higher ( $P=.003$ ), indicating possible neuromuscular involvement. Motor speech profile analysis revealed that DDKcvp, vF0, Mtfr, and Matr values were significantly higher in the COVID-19 group ( $P < .05$ ). No significant difference was observed in the Voice Handicap Index or s/z ratio. The findings suggest that COVID-19 may negatively affect laryngeal neuromuscular control, with diadochokinetic analyses pointing to impaired coordination in laryngeal muscles. While acute inflammation may diminish, neuromuscular effects could persist.

**Conclusion:** COVID-19 may impair laryngeal muscle coordination and vocal performance. These results highlight the importance of assessing laryngeal functions in the post-COVID-19 period.

**Keywords:** COVID-19, dysphonia, hoarseness

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**Received:** February 12, 2025

**Revision Requested:** April 25, 2025

**Last Revision Received:** May 22, 2025

**Accepted:** May 27, 2025

**Publication Date:** May 31, 2025

**Cite this article as:** Çalışkan ZD, Gülşen E, Kara E, et al. Laryngeal function evaluation in cases with COVID-19. *Balkan ORL-HNS* 2025;2(2):40-44.

**DOI:** 10.5152/bohns.2025.25068



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dysfunction, triggering serious clinical conditions such as pneumonia and Acute Respiratory Distress Syndrome.<sup>3</sup> At the same time, the neurotropic properties of SARS-CoV-2 also reveal its negative effects on the nervous system.<sup>4</sup> Viral infections such as COVID-19 can cause neurological complications as well as respiratory diseases. Symptoms such as headache, dizziness, changes in consciousness, and stroke have been frequently reported in infected patients.<sup>5</sup> In particular, loss of taste and smell are common symptoms that point to the neurotropic character of COVID-19.<sup>6</sup> This is due to the potential for the virus to reach the central nervous system via the olfactory neuroepithelium. In addition to neural complications, COVID-19 also affects the peripheral nervous system. Respiratory, circulatory, and digestive system disorders may be observed due to vagal nerve dysfunction.<sup>7</sup> Otological symptoms such as hearing loss and vestibular dysfunction have also been reported in some patients.<sup>8</sup> These findings suggest that the virus may trigger hearing and balance disorders by causing inflammation in the inner ear structures.

Another important effect of COVID-19 is the impairment of voice and speech functions. Symptoms such as dysphonia, hoarseness, and fatigue during speech are common due to laryngeal involvement.<sup>9</sup> Inflammation and neuropathic damage to the vocal cords may result in inadequate glottal closure during phonation. Post-viral vagal neuropathy, in particular, has been associated with symptoms such as vocal fatigue and the need to constantly clear the throat.<sup>10</sup> It has been stated that long-term use of mechanical ventilation in COVID-19 patients may also lead to complications such as vocal cord paralysis and paresis. This situation indicates that patients may need voice therapy and rehabilitation, especially after the intensive care process.<sup>8</sup> In addition, symptoms such as cough and sore throat seen in the acute phase of the infection can negatively affect individuals' communication skills by further straining the speech mechanism.

The multifaceted effects of viral agents such as COVID-19 on human health make it necessary to understand not only the physical but also the social and psychological dimensions of these diseases. Considering both the neurological and vocal effects, it is of great importance that COVID-19 be addressed through a multidisciplinary

approach. In this context, further research is needed on the acute, short-term, and long-term outcomes of the disease.

## Material and Methods

This study was conducted at Istanbul University-Cerrahpaşa, Department of Audiology between February 2021 and July 2021, after receiving ethical approval from Cerrahpaşa Medical Faculty Clinical Research Local Ethics Committee (Decision No.: E-60350273-605.99-4794; Date: 03.10.2021). All procedures were conducted in accordance with the Declaration of Helsinki and institutional ethical standards. Informed consent was obtained from all participants.

## Participants

A total of 70 people who were not vaccinated against COVID-19 were included in the study, consisting of a study group of 35 (20M, 15F) individuals aged 18-65 who had COVID-19 at least 3 months ago, and a control group of 35 (17M, 18F) individuals who were determined not to have COVID-19 by antibody testing. The distribution of male and female participants was evaluated using the chi-square test, and no significant difference was found between the 2 groups in terms of gender distribution ( $P > .05$ ).

The inclusion criteria for the study group were: being between the ages of 18 and 65, not having any pathology detected in laryngeal examination (benign and malignant vocal mass, paresis, paralysis, laryngopharyngeal reflux), having had COVID-19 disease, not being intubated, having normal laryngeal functions before COVID-19, and having a negative COVID-19 test result. The inclusion criteria for the control group were: being between the ages of 18 and 65, not having had COVID-19 disease, having normal laryngeal functions, and not having a disease or factor affecting the patient's phonatory, resonator, and vibratory systems. Patients whose laryngeal findings were determined to be normal in the system records up to 6 months before the onset of COVID-19 cases were identified and invited. Those who were confirmed to have had COVID-19 were included in the study. The exclusion criteria were: having laryngeal problems before the disease in the patient group with COVID-19, being intubated, having organic pathology in laryngeal examination in the study and control groups, and not being between the ages of 18 and 65. Blood samples were taken from the individuals in the control group who met the inclusion criteria in the study to determine SARS-CoV-2 contact, and SARS-CoV-2 IgG determination (antibody test) was performed.

## Study Protocol

All participants underwent a laryngeal examination using the KayPENTAX RLS 9100B (Rhino-Laryngeal Stroboscope RLS 9100) Videolaryngostroboscopy (VLS) device by an Ear, nose and throat (ENT) specialist with at least 5 years of experience in laryngology ( $4.52 \pm 0.89$ , min: 3, max: 6.1 months).

After the laryngeal examination, all participants were asked to fill out the Preliminary Voice Assessment Form. The form includes a section dedicated to symptoms observed during COVID-19 and is to be filled out only by participants in the study group (Table 1). For the objective evaluation of speech and voice, vocal recordings were taken using the Kay Elemetrics Group Computerized Speech Lab-CSL, Model 4500 device. Multi-dimensional voice program (MDVP), motor speech profile (MSP), and electroglottography (EGG) tests were applied. Maximum Phonation Test (MPT) and S/Z ratio were examined in aerodynamic measurements. Three recordings

## MAIN POINTS

- COVID-19 is a multifaceted disease that can affect not only the respiratory system but also neurological and vocal functions. Symptoms such as dysphonia, hoarseness and fatigue during speech are common due to laryngeal involvement. Post-viral vagal neuropathy has been associated with symptoms such as vocal fatigue and the need for constant throat clearing.
- The findings indicate that in individuals with Covid-19 disease, there are significant differences in acoustic voice analysis results, especially in tremor indices and maximum phonation time, indicating that although acute inflammation decreases over time, neuromuscular control and respiratory functions are negatively affected.
- The study emphasizes the need for further studies on severe COVID-19 cases and long-term neuromuscular effects on voice and speech, and emphasizes the importance of interdisciplinary evaluations, especially among laryngologists and speech-language pathologists.

**Table 1.** Descriptive Statistics Regarding Symptoms Experienced During the COVID-19 Period in the Study Group and the Period Between the Date of COVID-19 Diagnosis and the Examination and Evaluation Date

COVID-19 Symptoms	Descriptive Statistics
Cough	
No	14 (40%)
Yes	21 (60%)
Sore throat	
No	19 (54.3%)
Yes	16 (45.7%)
Loss of smell	
No	16 (45.7%)
Yes	19 (54.3%)
Hoarseness	
No	30 (85.7%)
Yes	5 (14.3%)
Dysphagia	
No	22 (62.9%)
Yes	13 (37.1%)

were taken for each parameter, and the maximum duration was noted. Voice Handicap Index-10 (VHI-10) was also filled out for all participants.

### Statistical Analysis

The distribution of data was examined with the Shapiro-Wilk test. The comparison of variables with a normal distribution between 2 independent groups was made with the Independent Sample *t* test, and the comparison of variables without a normal distribution between 2 independent groups was made with the Mann-Whitney *U* test. The Pearson chi-square test was used to evaluate the differences in categorical variables. The Spearman Correlation Coefficient was used to evaluate the statistical relationship between numerical variables. Descriptive statistics of numerical data were explained as mean  $\pm$  SD in those with a normal distribution and median (min-max) in those without a normal distribution. Categorical data were explained as frequency (percentage). All statistical analyses were analyzed and reported in the IBM SPSS Statistics 26.0 program (IBM SPSS Corp.; Armonk, NY, USA) at  $\alpha=0.05$  significance level and 95% confidence level.

### Results

Statistics regarding the distribution of symptoms experienced during the COVID-19 period in the study group and the average time from the date the participants were diagnosed with COVID-19 to the date they were evaluated are given in Table 1. The most frequently reported symptom during COVID-19 was a cough.

As seen in Table 2, there is a significant difference between the MDVP parameters obtained in the study and control groups in the F0-Tremor Intensity Index values as a result of the evaluation of the differences between the groups in the MDVP test applied in the study and control groups ( $P=.003$ ).

Table 3 shows the results of the evaluation of MSP test data between the study and control groups. Accordingly, DDKcvp, vF0, Mtftr, and Matr values had a significant difference between the groups ( $P < .05$ ). These values were found to be significantly higher in the study group

**Table 2.** Evaluation of Multi-Dimensional Voice Program Test Results Among Groups

	Control Group	Study Group	<i>P</i>
Jitter percent	0.54 (0.18-2.26)	0.68 (0.27-2.42)	.086**
Shimmer percent	2.53 (1.07-5.60)	2.79 (1.39-7.81)	.106**
Peak to peak amplitude variation	10.78 (3.77-26.56)	11.62 (6.02-26.15)	.507**
Noise to harmonic ratio	0.11 (0.09-0.16)	0.12 (0.09-0.25)	.160**
Soft phonation index	11.43 (6.05-28.70)	13.37 (3.58-50.40)	.948**
F0-tremor intensity index	0.22 (0.05-0.89)	0.35 (0.01-1.26)	<b>.003**</b>
Amplitude tremor intensity index	3.86 (0.47-6911)	3.21 (0.48-7352)	.517**
Average fundamental frequency	185.35 $\pm$ 48.89	169.14 $\pm$ 52.11	.184*
Voice turbulence index	0.04 $\pm$ 0.01	0.04 $\pm$ 0.01	.892*

Data are expressed as median (min-max) and mean  $\pm$  SD.

\**P*-values are *P*-values from the *t* test.

\*\**P*-values are *P*-values from the Mann-Whitney *U* test. The *p* value written in bold is to indicate that it is less than .05 and is a significant result.

**Table 3.** Evaluation of Motor Speech Profile Test Results Among Groups

	Control Group	Study Group	<i>P</i>
DDKavp	171.64 (139.50-239.71)	171.43 (147.29-337.21)	.977**
DDKavr	5.82 (4.17-7.16)	5.83 (2.96-6.78)	.934**
DDKsdp	9.21 (6.20-28.29)	11.21 (5.07-110.59)	.075**
DDKcvp	5.29 (3.80-14.90)	6.26 (3.08-54.78)	.028**
DDKjit	1.03 (0.66-2.41)	1.20 (0.39-7.41)	.177**
vF0	0.83 (0.36-3.32)	1.12 (0.40-75.47)	.010**
Mtftr	0.32 (0.13-0.90)	0.37 (0.17-1.98)	.009**
Matr	2.13 (0.80-3.63)	2.79 (1.01-6.10)	.006**
F2aver	1617.80 (1330.13-1998.77)	1465.94 (1088.95-1915.68)	.106**
vAm	10.26 $\pm$ 4.31	12.34 $\pm$ 4.81	.062*
F2magn	567.06 $\pm$ 93.66	533.55 $\pm$ 112.73	.181*

Data are expressed as median (min-max) and mean  $\pm$  SD.

\**P*-values are *P*-values from the *t* test.

\*\**P*-values are *P*-values from the Mann-Whitney *U* test.

compared to the control group. Other measurement values of the MSP test did not have a significant difference between the groups ( $P > .05$ ).

When Table 4 examined, the measurement values of the EGG test do not have a significant difference between the groups ( $P > .05$ ).

The results of the statistical analysis performed to evaluate the Voice Handicap Index, maximum phonation time, and S/Z ratio test results applied to the study and control groups between the groups are given in Table 5.

Maximum phonation test results showed a statistically significant difference between the study and control groups ( $P=.004$ ). Accordingly, the maximum phonation test result was found to be significantly shorter in the study group compared to the control group. The results of the Voice Handicap Index-10 and S/Z Ratio tests did not show a statistically significant difference between the groups ( $P > .05$ ).

### Discussion

COVID-19 has been described as a heterogeneous disease affecting multiple systems across the world.<sup>11</sup> Although the acute symptoms of the disease are well known, its acute, short-term, and long-term

**Table 4.** Evaluation of Electroglottography Test Results Among Groups

	Control Group	Study Group	P
Mean %	51.56 ± 5.02	53.73 ± 4.02	.050*
Range %	95.49 (84.58-98.14)	94.78 (88.59-97.67)	.344**
Minimum %	2.81 (1.20-9.34)	3.78 (1.37-9.20)	.267**
Maksimum %	98.62 (93.62-99.46)	98.63 (97.20-99.28)	.514**
SD %	16.19 (4.02-33.66)	16.77 (9.97-29.19)	.344**

Data are expressed as median (min-max) and mean ± SD.

\*P-values are P-values from the t test.

\*\*P-values are P-values from the Mann-Whitney U test.

**Table 5.** Evaluation of Voice Handicap Index, Maximum Phonation Test and S/Z Ratio Test Results Among Groups

	Control Group	Study Group	P
Voice Handicap Index-10	1 (0-28)	1 (0-33)	.759**
MPT (ms)	22.44 (9.80-34.86)	14.02 (6.59-26.70)	.004**
S/Z ratio (ms)	0.84 (0.10-1.40)	0.87 (0.50-2.31)	.243**

Data are expressed as median (min-max).

MPT, maximum phonation test.

\*\*P-values are P-values from the Mann-Whitney U test.

effects are drawing increasing attention. Among these effects, neurological and neuromuscular complications are particularly prominent. Problems such as Guillain-Barré Syndrome, myelitis, and vocal cord dysfunctions have been among the neurological complications reported in the post-COVID-19 period.<sup>12,13</sup> This study focused on the effects of COVID-19 on the larynx and vocal functions.

In addition to the effects of COVID-19 on the respiratory system, it has been suggested that it may also cause permanent damage to the upper respiratory tract. In particular, it is thought that post-viral vagal neuropathy and inflammation may lead to long-term changes in the larynx.<sup>8</sup> In this study, although there was no statistically significant difference in acoustic analysis parameters between individuals who had COVID-19 and the healthy control group, the FTRI value was found to be significantly higher in the patient group ( $P < .05$ ). This finding suggests that the inflammation caused by COVID-19 in the larynx during the acute phase may resolve over time; however, its effects on neuromuscular control may persist and manifest later.

Diadochokinetic (DDK) analysis results revealed that COVID-19 may cause a loss of coordination in the larynx and surrounding muscles. Diadochokinetic is considered an important parameter in the evaluation of rapid and consecutive movements during speech. In this study, DDKcvp, vF0, Mftr, and Matr values were significantly higher in individuals with COVID-19 compared to the control group ( $P < .05$ ), indicating impaired coordination of the laryngeal muscles. This suggests that neuromuscular effects caused by COVID-19 may affect vocal performance. Although there was no statistically significant difference between the groups in terms of DDKsdp value ( $P = .075$ ), it is noteworthy that it showed an increasing trend in the patient group. This trend supports that COVID-19 causes mild but measurable changes in the vocal system.

The findings obtained in this study seem to be consistent with other studies reported in the literature. For example, studies evaluating the effects of COVID-19 on the neuromuscular system did not encounter problems such as hyperfunctional behavior or muscle atrophy in the laryngeal muscles.<sup>14,15</sup> The electroglottography (EGG) results

also support this situation. In this study, no significant difference was found between individuals who had COVID-19 and the control group in terms of the Contact quotient (CQ) parameter. This finding shows that COVID-19 has no direct effect on vocal cord adduction function in the larynx. However, other results obtained from acoustic analysis parameters indicate that neuromuscular control is impaired.

In studies examining the long-term prevalence of dysphonia after COVID-19, findings such as glottic insufficiency, vocal cord paresis/paralysis, and atrophy have been reported.<sup>16</sup> In this study, MPT values of individuals who had COVID-19 were found to be significantly lower compared to the control group ( $P = .004$ ). This finding suggests that COVID-19 may lead to weakness in laryngeal muscle control or may have negative effects on voice production as a result of lung involvement. Although it has been reported in the literature that s/z ratios may increase in individuals who had COVID-19, in this study, s/z ratios were found to be below 1 in both groups. This suggests that the effect of COVID-19 on phonation times is minimal.

Voice tremor analyses have revealed more subtle effects of COVID-19 on the vocal system. Tremor is considered a parameter that reflects changes that affect the regular functioning of the neuromuscular system. In this study, the higher vF0, Mftr, and Matr values in individuals with COVID-19 indicate deterioration in neuromuscular control mechanisms. This finding was found to be remarkable in terms of the effects of COVID-19 on both the central nervous system and the peripheral neuromuscular system.

Compared to other studies evaluating the clinical effects of COVID-19, the study examined a group of patients in whom the potential effects were less pronounced during the 3-month period following the acute phase. This may be because most of the individuals included in the study had mild or moderate COVID-19, were not intubated, and were independent of other vocal cord pathologies detected during vocal examination. In the literature, it has been reported that larynx and vocal functions are more significantly affected in severe COVID-19 cases.<sup>8</sup> Therefore, the findings of the study suggest that short-term effects on laryngeal function are minimal in individuals with mild and moderate COVID-19.

An important finding of this study is that there was no significant difference between the groups in terms of VHI-10 scores. This result shows that the subjective perception of the vocal health status of individuals who had COVID-19 was not different from the control group. However, this finding also reveals that subjective assessments are not always consistent with objective measurements. In particular, the changes detected in acoustic analysis parameters indicate that the short- and long-term effects of COVID-19 on neuromuscular control should be examined in more detail.

In conclusion, this study contributes to the limited number of studies examining the effects of COVID-19 on laryngeal function. The acoustic analysis, DDK, and EGG results suggest that COVID-19 may affect the neuromuscular control of the laryngeal muscles. However, these effects do not cause clinically significant symptoms and are mild. Considering the duration of the study and the results obtained, it is clear that more research is needed on the effects of viral diseases affecting the nervous system on voice. New studies conducted with these groups, especially with individuals who had severe COVID-19, by evaluating laryngeal functions in the short and long term, and considering additional pathologies, intensive care periods,

ventilation needs, and duration of use, can fill this gap in knowledge. In addition, further studies with larger sample groups are needed to better understand the effects of COVID-19 on the central and peripheral nervous system.

These findings, which are consistent with the results reported in the literature, suggest that COVID-19 causes minimal but measurable effects in mild and moderate cases. Further studies, including larger samples and different severities of cases, will contribute to a better understanding of the effects of COVID-19.

**Data Availability Statement:** The data that support the findings of this study are available upon request from the corresponding author.

**Ethics Committee Approval:** This study was approved by the Ethics Committee of Istanbul University-Cerrahpaşa (Approval No.: E-60350273-605.99-4794; Date: 03.10.2021).

**Informed Consent:** Written informed consent was obtained from the patients who agreed to take part in the study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – A.A.; Design – A.A., Z.D.G., B.K.; Supervision – A.A., A.B.K., B.K., E.K.; Resources – E.G., D.Ö., A.B.C.; Materials – Z.D.Ç., E.G.; Data Collection and/or Processing – E.G., Z.D.Ç.; Analysis and/or Interpretation – Z.D.Ç., E.G., Y.Z.Y.; Literature Search – Z.D.Ç., E.G., A.B.C.; Writing – Z.D.Ç., E.G.; Critical Review – A.B.K., E.K., A.A.

**Declaration of Interests:** Ahmet Ataş is a Section Editor at Balkan ORL-HNS; however, his involvement in the peer-review process was solely as an author. Other authors have no conflicts of interest to declare.

**Funding:** This study was funded by Istanbul University-Cerrahpaşa, Scientific Research Projects Unit. Project No: 35799.

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