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Auditory-Perceptual Evaluation of Vocal Characteristics in Patients with the New Coronavirus Disease 2019

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Keywords
Voice · Auditory-perceptual evaluation · Coronavirus disease 2019

Abstract
Introduction: Due to the upper and lower respiratory involvement in coronavirus disease 2019 (COVID-19), the voice quality of these patients is expected to be impaired. In this study, we aimed to conduct an auditory-perceptual evaluation of the vocal characteristics of patients with different severities of COVID-19. ***Methods:*** One hundred two patients with mild, moderate, or severe COVID-19 as well as 30 healthy individuals were recruited to compare their respiratory/phonatory parameters. The Persian version of the CAPE-V and GRBAS scales, along with the maximum phonation time and s/z ratio values were used to evaluate the severity of respiratory/phonatory disorders during verbal tasks in the participants. ***Results:*** Significant differences were found between the subgroups of patients and their healthy counterparts in all respiratory/phonatory parameters ($p \leq 0.03$) except the s/z ratio ($p = 0.81$). ***Conclusions:*** Based on auditory-perceptual assessments, patients with COVID-19 showed dysphonia. The severity of dysphonia was significantly different among patients with different severities of COVID-19. Smoking can also play a significant role in vocal dysfunction in COVID-19 patients.

Introduction

The coronavirus disease 2019 (COVID-19) is a new viral pandemic which was first detected in Wuhan, China, in December 2019 and spread rapidly around the world [1]. The common clinical features of COVID-19 include upper and lower respiratory tract involvement, such as dry cough, sore throat, myalgia, fatigue, and breathlessness [2]. Recent evidence suggests that COVID-19 is very heterogeneous in terms of severity, ranging from asymptomatic infection to severe acute respiratory distress syndrome and multiorgan dysfunction that can be classified as mild, moderate, or severe illness. Mild symptoms include a fever >38 °C and a positive diagnostic PCR test result without evidence of pneumonia or hypoxia. Moderate clinical signs of pneumonia and positive diagnostic PCR test RESULT without any sign of severe infection, including oxygen saturation (SpO_2) >93% at

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rest, are also symptoms, as are severe clinical signs of pneumonia in addition to a respiratory rate ≥30 bpm or SpO_2 ≤93% in room air or a partial pressure of oxygen in arterial blood/fraction of inspired oxygen ratio (PaO_2/FiO_2) ≤300 mm Hg [3, 4]. Due to the widespread involvement of the respiratory and laryngeal systems of COVID-19, it is predictable that the vocal function of these patients will be altered to varying degrees.

Speech is the product of the joint and coordinated functions of the respiratory, laryngeal, and articulatory systems [5]. Voice parameters can be used indirectly to diagnose physical or functional disorders of the lungs and larynx [6]. In other words, respiratory and laryngeal pathologies can be interpreted based on changes in voice qualities [6]. Considering the high likelihood of human-to-human transmission of COVID-19 through close contact, talking, and coughing [7], clinicians must carefully observe all protective protocols, including the use of face masks, face shields, gloves, plastic clothing, and hand disinfectant solutions for vocal sampling. The clinical assessment of voice can be classified into 3 general categories, including acoustic measurements, laryngeal stroboscopic assessments, and auditory-perceptual scales [8, 9]. During stroboscopic evaluations, the patients need to be examined directly through the nose or mouth [10]. It is also necessary to collect voice samples with a sensitive microphone (high quality) close to the patient's mouth to assess the acoustic properties [10]. Clinicians who intend to perform these types of voice assessments are exposed to a very high risk of infection with the virus [11]. Auditory-perceptual scales are common clinical tools for diagnosing voice disorders [12]. They are the preferred method during the COVID-19 outbreak due to rapid sampling and the exposure risks of stroboscopic, acoustic, and aerodynamic assessments.

Although subjective self-assessment questionnaires cannot be used definitively for voice evaluation, in one study it was reported that 28.6% of people infected with COVID-19 showed symptoms of a voice disorder [13]. Additionally, Asiaee et al. [14] observed an insufficient airflow, increased aperiodicity, irregularity, signal perturbation, and an increased level of noise to harmonics in the acoustic voice parameters of patients with COVID-19 due to their pulmonary and laryngological involvements. In this study, we aimed to compare the respiratory/vocal parameters between 3 groups of patients with mild, moderate, and severe COVID-19 using the auditory-perceptual scales and to compare the results of each group with their healthy counterparts.

Materials and Methods

Participants

In this analytical cross-sectional study, a total of 102 laboratory-confirmed patients with COVID-19 (74 men and 28 women; mean age: 58.1 ± 9.1 years) admitted to our general hospital from August 15 to September 23, 2020, were enrolled. The inclusion criteria were as follows: age >18 years (to prevent the puberty effects on voice), a laboratory-confirmed diagnosis of COVID-19 infection, native Persian speakers, and the possibility of vocal sampling.

On the other hand, patients without a laboratory-confirmed diagnosis, patients with a history of severe laryngeal injuries before the pandemic and patients who were in the intensive care unit at the time of this study (because of their health status) were excluded. All of the patients in this study did not use mechanical ventilation and were not intubated. The diagnosis of COVID-19 was established based on the positive results of high-throughput sequencing or real-time reverse transcription polymerase chain reaction (RT-PCR) assay of pharyngeal and nasal swab specimens, according to World Health Organization (WHO) guidelines [15, 16].

In this study, patients with COVID-19 infection were categorized into 3 groups (mild, moderate, and severe) based on symptoms and clinical findings present during the disease course according to Shi et al. [3] and Zhang et al. [4]. However, patients with a history of a laryngeal disorder before the COVID-19 pandemic and patients without a laboratory-confirmed COVID-19 diagnosis were excluded.

Simultaneously with sampling of the patients, a total of 30 healthy participants (20 men and 10 women; mean age 46.7 ± 9.3 years) without COVID-19 infection, who were age- and gender-matched with the patients, were also recruited as the control group.

Auditory-Perceptual Rating Scales and Measures

In the present study, the auditory-perceptual assessment of dysphonia was conducted using the Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) and Grade, Roughness, Breathiness, Asthenia, Strain (GRBAS) scales. Both of these scales are clinician-based tools to identify the perceptual aspects of dysphonia. The CAPE-V is a reliable visual analog scale to rate patients' voice quality. In the Persian version of the CAPE-V [17], 6 indicators of voice disorder, including the overall severity, roughness, breathiness, strain, pitch, and loudness, are separately rated on a 100-mm visual analog scale. The qualitative content validity of the Persian version of the CAPE-V was confirmed in the present study (Cronbach α = 0.95). Also, the intra-rater agreement of the Persian CAPE-V ratings was found to be high. The overall severity, recorded at the time of examination, yielded a Spearman correlation coefficient of 0.86 in the first rating session and 0.92 in the second rating session. According to the CAPE-V results, the assessors placed a vertical tick mark on a 100-mm horizontal line from the left side to pinpoint the severity of the disorder. The vertical tick marks which were closer to the right side indicated a greater severity of the disorder [9]. Also, the raters placed a vertical tick mark on a 100-mm horizontal line for each participant. The left side of the scale represented minimum impairment, whereas the right side indicated maximum severity. Based on CAPE-V, the point of zero represent no dysphonia or a normal-voiced person, scores between 1

and 9 show mild dysphonia, scores between 10 and 59 indicate moderate dysphonia, and scores between 60 and 100 indicate severe dysphonia [9, 18].

GRBAS is an acronym where "G" stands for "grade or overall severity of dysphonia," "R" stands for "roughness," "B" stands for "breathiness," "A" stands for "asthenia," and "S" stands for "strain" of voice quality. The patient's perception is rated on a 4-point scale (1, without disorder; 2, mild disorder; 3, moderate disorder; and 4, severe disorder). It is a valid and reliable tool used by expert clinicians to rate the voice quality of patients who complain of dysphonia [18]. Using the GRBAS scale, the rater examines each voice quality after listening to the patients' voice samples [9].

We also used the maximum phonation time (MPT) and s/z ratio to detect disorders in the patients' respiratory and phonation systems during speech more accurately. The MPT is the longest sound that a person can sustain after a deep inhalation. It is inversely related to the severity of dysphonia and respiratory impairment [19]. Moreover, the s/z ratio is calculated by dividing the maximum sustained time of phoneme /s/ by the maximum sustained time of phoneme /z/ [19]. This calculation allows for the comparison of respiratory support for phonation (voiceless /s/) to the glottal closure (voiced /z/) [20]. It has been recommended that patients with s/z ratios greater than 1.4 require accurate laryngeal examinations [21].

Voice Samples Elicitation and Analysis

For the CAPE-V analyses, voice samples were recorded from all of the participants, according to the tasks proposed in the CAPE-V protocol [22], using the Persian version of the CAPE-V, which was cross-culturally validated by Salary Majd et al. [17]. Also, the GRBAS analyses included the utterance of 2 sustained vowels (/a/ and /i/) and reading a 10-word sentence. The mean score of the overall severity of disorder on the CAPE-V scale and the general grade (G) score on the GRBAS scale were measured to compare the participants' outcomes. The patients' MPT and s/z ratio data were individually recorded. For the MPT and s/z ratio measurements, the participants were asked to perform deep breathing and then pronounce the sustained vowel /a/ as long as possible with the habitual pitch in the sitting position. Next, they were asked to prolong the fricative phonemes /s/ and /z/, similar to the MPT extraction procedure.

All of the tasks were recorded for each participant in an isolated sound-proof room using a Boya BY-M1 omni-directional lavalier condenser microphone (collar model; China) with an audio cable (20 ft). All of the protocols were orally explained to the participants and recorded by the collar microphone. The microphone was positioned approximately 20 cm away from the subject's mouth to prevent viral transmission. The patient wore a mask while preparing and connecting the microphone to her/his clothes. After the examiner walked away from the examinee, she or he was allowed to remove the mask from her/his mouth and utter the words and sentences (or other tasks). The microphone was antisepticised with ethanol alcohol 70% to prevent virus transmission to the next examinee.

To measure the MPT value and s/z ratio, the beginning and the end of the phonation of sustained vowels, including /a/, /s/, and /z/, were calculated on spectrogram in seconds using Praat [23] (version 6.1.09; Phonetic Sciences, University of Amsterdam, Amsterdam, The Netherlands), installed on a laptop (Inspiron1300, n Series; DELL, China). Three trials were conducted for each phoneme, and the longest value was used in the analyses. If a sample was not recorded appropriately, more trials were carried out until a valid record was obtained.

Three blinded raters, who were expert speech therapists (with more than 10 years of experience in voice assessment) and familiar with the CAPE-V and the GRBAS, scored and calculated the items of the scales. They were blind to the participants' information and the goals of this study. Because human instruments were used to rate the voice samples, the interrater agreement and the intrarater agreement of the scores were calculated for the outcome measures. Each rater scored the voice variables twice within a 1-week interval at end of the sampling. The percentages of inter- and intrarater agreement were determined using the following formula [24] (acceptable score >90%). The interrater agreement was good for all elements (92–97%). The percentage of intrajudge agreement was also good and it was greater than 95%. All ambiguities for the raters were resolved by discussion with the second author, who is an academic member of the department of speech therapy with more than 12 years of experience in voice assessment.

Statistical Analysis

In the current study, all dependent variables were separately examined to determine the normal distribution of data, the equality of error variances, and the homogeneity of variance using the 1-sample Kolmogorov-Smirnov test, the Levene test, and the Mauchly test, respectively. A one-way analysis of variance (ANOVA) was also conducted to compare the subgroups of patients with COVID-19 and their healthy counterparts. Moreover, the following 2-way mixed-effects model of ANOVA was used to compare the mean values of dependent variables in patients with COVID-19: (2 for smoking: smoker vs. nonsmoker) × (3 for disease severity: mild, moderate, and severe). The main and interaction effects between the factors were measured. If the main effect of each factor was observed, a post hoc adjusted Bonferroni correction test was carried out to determine differences between the outcomes with respect to the factors. To assess the significance of differences related to possibly effective factors, the partial η^2 and statistical power were calculated. All of the data were analyzed using SPSS for Windows version 18 (SPSS Co., Chicago, IL, USA). $p < 0.05$ was considered statistically significant.

Results

The demographic and clinical characteristics of the COVID-19 patients are presented in Table 1. The most common comorbidities included diabetes, chronic heart disease, and hypertension. About 70% of the patients had at least 1 underlying disorder. The mean time between the onset of the infection and the assessment was 4.3 ± 2.1 days. In the present study, fever (86 out of 102 = 84.3%), dry cough (71 out of 102 = 69.6%), and myalgia (45 out of 102 = 44.1%) were the most common symptoms in patients with COVID-19, whereas vomiting (19 out of 102 = 18.6%) and diarrhea (23 out of 102 = 22.5%) were the least common general symptoms.

Table 1. Demographic and clinical characteristics of the participants

Parameter	Group			
	COVID-19			Control (n = 30)
	mild (n = 42)	moderate (n = 37)	severe (n = 23)	
Age, years	43.7±6.1	47.6±7.2	53.7±8.1	46.7±9.3
Gender				
Male	30 (71.4)	28 (75.7)	16 (69.6)	20 (66.7)
Female	12 (28.6)	9 (24.3)	7 (30.4)	10 (33.3)
Smoking				
Smokers	31 (73.8)	22 (59.5)	12 (52.2)	19 (63.3)
Nonsmokers	11 (26.2)	15 (40.5)	11 (47.8)	11 (36.7)
Pulmonary system involvement				
Upper	11 (26.2)	14 (37.8)	4 (17.4)	–
Lower	31 (73.8)	23 (62.2)	19 (82.6)	–
Comorbidity, *n*				
Diabetes	14	11	19	6
Hypertension	9	17	14	7
Chronic heart disease	10	10	8	3
GERD	7	7	5	11
Other (e.g., renal failure)	12	10	7	6

Values are presented as means ± SD, numbers (%), or numbers. GERD, gastroesophageal reflux disease.

The results of the one-way ANOVA revealed significant differences in the score of auditory-perceptual scales (CAPE-V and GRBAS; $p \leq 0.03$) and the MPT value ($p = 0.01$) between the subgroups of COVID-19 patients and their healthy participants. However, we found no significant difference in the s/z ratio between COVID-19 patients and the normal-voiced participants (Table 2). As shown in Table 2, the post hoc honest Bonferroni test showed that all subgroups of patients with COVID-19 had significantly higher CAPE-V and GRBAS scores ($p \leq 0.008$) and lower MPT values ($p \leq 0.001$) than their healthy counterparts. These findings indicate that all of the patients had more severe dysphonia, besides more restricted breathing support for talking, compared to the healthy individuals.

The results of the multivariate ANOVA test revealed significant differences between the subgroups of patients (according to disease severity) for all scales and values ($p \leq 0.010$), except the s/z ratio value ($p = 0.124$), which was equivalent in all subgroups of COVID-19. Our findings showed significant differences in the s/z ratio ($F_{[2,97]} = 2.18$; $p = 0.022$, $\eta^2 = 0.106$) and the MPT value ($F_{[2,97]} = 5.38$; $p = 0.010$, $\eta^2 = 0.138$) regarding the interaction effects of disease severity and smoking (Table 3). The post hoc Bonferroni correction test revealed that severe COVID-19 × smoking could significantly increase the s/z ratio and decrease the MPT of these patients, compared to the other subgroups. However, no other significant main effect or interaction effect was observed.

Discussion

In this study, we aimed to compare some respiratory/vocal parameters, based on the auditory-perceptual assessments among patients with different severities of COVID-19. Two appropriate clinical scales, i.e., the CAPE-V and the GRBAS, were used for the auditory-perceptual assessment of voice parameters. Since these 2 scales are not norm-referenced, a group of healthy counterparts without COVID-19, who were matched with the patients in terms of age, gender, and other demographic characteristics, were considered as the control group. Overall, the applied auditory-perceptual scale must be a valid tool to distinguish between healthy individuals and those with voice disorders. It should also distinguish between different levels of dysphonia [18]. Given the need for social distancing and adherence to protective protocols to prevent the transmission of COVID-19, speech therapists should use minimally invasive and quick-access methods to assess the quality of voice disorders in these patients. In this study, we were able to collect the

Table 2. CAPE-V scale, GRBAS scale, s/z ratio, and MPT of patients with COVID-19 compared to healthy participants

Parameter	Group				*p* value
	COVID-19			Control (n = 30)	
	mild	moderate	severe		
CAPE-V	24.55±5.49	46.31±5.99	64.11±6.23	14.21±4.09	$F_{(3, 131)} = 4.99$, $p = 0.01$
GRBAS	1.9±1.4	3.3±1.2	3.9±0.9	0.9±0.5	$F_{(3, 131)} = 2.82$, $p = 0.03$
s/z ratio	1.13±0.21	1.08±0.29	1.28±0.19	1.06±0.13	$F_{(3, 131)} = 0.22$, $p = 0.81$
MPT, s	15.73±3.44	10.62±3.05	5.03±2.07	21.09±3.24	$F_{(3, 131)} = 5.73$, $p = 0.01$

Values are presented as means ± SD.

Table 3. Multivariate ANOVA summary table for CAPE-V scale, GRBAS scale, s/z ratio, and MPT of patients with COVID-19 according to smoking habit and disease severity factors

Parameter	Smoking	COVID-19 disease severity	Patients, *n*	Mean ± SD	*p* value
CAPE-V	Smoker	Mild	31	25.06±5.67	$F_{(2, 97)} = 11.51$, $p < 0.001$
		Moderate	22	45.61±6.72	
		Severe	12	63.97±5.57	
	Nonsmoker	Mild	11	24.11±5.13	
		Moderate	15	45.07±6.64	
		Severe	11	63.01±5.55	
GRBAS	Smoker	Mild	31	1.9±1.0	$F_{(2, 97)} = 4.11$, $p < 0.001$
		Moderate	22	3.3±1.1	
		Severe	12	3.9±0.1	
	Nonsmoker	Mild	11	1.9±0.9	
		Moderate	15	3.8±0.9	
		Severe	11	3.9±0.1	
s/z ratio	Smoker	Mild	31	1.10±0.21	$F_{(2, 97)} = 2.18$, $p = 0.022$
		Moderate	22	1.20±0.30	
		Severe	12	1.45±0.20	
	Nonsmoker	Mild	11	1.13±0.19	
		Moderate	15	0.99±0.29	
		Severe	11	1.09±0.30	
MPT (s)	Smoker	Mild	31	15.03±3.14	$F_{(2, 97)} = 5.38$, $p = 0.010$
		Moderate	22	10.69±2.67	
		Severe	12	4.01±1.57	
	Nonsmoker	Mild	11	16.96±3.88	
		Moderate	15	11.97±3.94	
		Severe	11	5.91±2.85	

necessary samples for auditory-perceptual assessments, using a sensitive microphone, despite the existing problems in the transmission of COVID-19. The researchers agreed that the GRBAS is rapid and the CAPE-V is a sensitive auditory-perceptual scale to describe voice disorders [9, 18, 25, 26].

The results of the present study showed that, irrespectively of the symptom severity, patients with COVID-19

had significantly more abnormal auditory/perceptual voice parameters than their normal-voiced counterparts (Table 2). This finding is consistent with the results of other studies [13, 14, 27]. Cantarella et al. [27] evaluated the prevalence of voice problems in 160 nonhospitalized patients with COVID-19 in Italy. Dysphonia (43.7%) and vocal fatigue (26.8%) as the most common voice disorders were self-reported by their participants. In an earlier study, Lechien et al. [13] also stated that dysphonia with a 26.8% prevalence is an associated symptom in patients with COVID-19. The results of the multivariate ANOVA test showed significant differences in the voice quality of patients with different severities of COVID-19; in other words, patients with severe symptoms of the disease had the worst voice quality. Although smoking had no significant main effect on the patients' voice quality, the simultaneous interaction of smoking with disease severity caused a significant difference in the voice parameters. Overall, being a smoker can lead to structural and functional changes in the larynx. When a smoking factor is associated with a disease limiting lung volume, its adverse effects on voice quality will become more apparent.

In the present study, we utilized the s/z ratio and MPT indicators to determine the respiratory status of the COVID-19 patients more accurately. Both indicators, i.e., MPT and the s/z ratio, are similar in nature and used to assess the adequacy of simultaneous performance of respiratory and phonatory systems. The MPT index represents the vital capacity of the lungs and it is also considered a measure of respiratory support for speech breathing [28]. Respiratory limitations, breathing pattern disorders, and sometimes fatigue can reduce the MPT value [29, 30].

The s/z ratio in normal-voiced individuals (without mass lesions on vocal folds and with intact vibration) ranges from 1.0 to 1.2 [31]. This numerical range demonstrates the laryngeal health during vocalization. Values exceeding this range indicate the escape of air from the glottis during vocal activities, which can be due to factors such as mass lesions, hypomobility, immobility, or neurological problems of the vocal folds [30, 31]. In these cases, patients have difficulty sustaining the sound /z/ as long as the sound /s/ due to glottal insufficiency (glottal closure failure for the fricative sound /z/); therefore, the value of /z/ will be less than the value of /s/, making the s/z ratio higher than 1.2. This rule is acceptable when the volume of speech breathing is sufficient for vocal activities. In other words, if the volume of respiration decreases, the production duration of both /s/ and /z/ sounds decreases equally, and the s/z ratio falsely indicates the normal range. Therefore, researchers insist that the s/z ratio should be analyzed alongside MPT [19, 31, 32]. The present study showed no significant difference in s/z ratio between patients with COVID-19 and their healthy counterparts (Table 2). As shown in Table 1, the frequency of upper respiratory tract involvement (including the larynx) was lower than that lower respiratory tract involvement in COVID-19 patients. Therefore, considering the patients' laryngeal function, the normal range of the s/z ratio was expected. However, by examining the effect of smoking, we found that the interaction of smoking and disease severity could cause a significant difference in the s/z ratio. Accordingly, the s/z ratio of smokers with severe COVID-19 was significantly higher than that of other patients. In this regard, Banjara et al. [33] showed that smoking causes significant alternations in the structure of the vocal folds that can increase the s/z ratio. The present findings also revealed that the value of the MPT index was reduced significantly by increasing the severity of COVID-19. Since an acute coronavirus infection can lead to a decreased respiratory capacity and airway disorders in the severe cases of the disease [34], functional abnormalities in respiratory volume tasks such as MPT were expected. Also, smoking in combination with disease severity had a significant effect on the reduction of MPT in these patients. In other words, smokers with severe COVID-19 had the lowest MPT value, whereas nonsmokers with mild COVID-19 showed the highest MPT value.

Limitations of the Study

This was our first attempt to objectively assess the vocal characteristics of patients with COVID-19. However, this study had some limitations. The small sample size of this study may have led to a decrease in the observed power of the results in some of subgroups and did not allow us to make comparisons based on other demographic variables such as age. The use of more participants in future studies may provide more exact data with strong statistical power in relation to within-subjects differences. Use of auditory-perceptual vocal assessments for patients with COVID-19 can pinpoint strengths and weaknesses, which needs further study. Full protection against virus transmission during sampling and voice analysis is the strength of these assessments, and a lack of acoustic evaluation of patients' vocal parameters such as fundamental frequency (F0), perturbation measures of pitch (jitter), and amplitude (shimmer), as well as the harmonic-to-noise ratio, were among the limitations of this study that should be addressed in future research.

Conclusion

According to auditory-perceptual vocal assessments, patients with COVID-19 showed dysphonia. The severity of dysphonia was significantly different among patients with different severities of COVID-19. Smoking can also play a significant role in severity of dysphonia in individuals with COVID-19. In other words, disease severity accompanied by smoking has an interaction effect on all voice qualities of patients with COVID-19.

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Statement of Ethics

This study protocol was reviewed and approved by the Ahvaz Jundishapur University of Medical Sciences in Ahvaz, Iran (approval No. IR.AJUMS.REC.1399.397). All of the participants gave written informed consent and were informed of their right to withdraw from this study.

Conflict of Interest Statement

The authors have no conflict of interests to declare.

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Author Contributions

P.Z. was responsible for the concept and design of this study, data collection and analysis, and several drafts of this paper. N.M. was responsible for conducting the evaluation interviews and for analyzing the responses in collaboration with N.S. Finally, P.Z., S.N., S.S, and A.B. were responsible for overseeing the concept and design of this study and contributed to the interpretation of the results and to the writing of this paper. All of the authors read and approved the final version of this paper for publication.

Data Availability Statement

All of the data analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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