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SELF-ASSESSMENT OF HEARING USING A MOBILE APP AMONG COVID-19 PATIENTS

Contributions:
A Study design/planning
B Data collection/entry
C Data analysis/statistics
D Data interpretation
E Preparation of manuscript
F Literature analysis/search
G Funds collection

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Abstract

Introduction: The effect of SARS-CoV-2 on hearing has not been thoroughly examined. Factors limiting hearing tests in COVID-19 patients are hygiene requirements and the need to use specialized equipment. The objective of the study was to assess changes in hearing thresholds between diagnosis of COVID-19 and convalescence using a mobile app.

Material and methods: Patients with mild to moderate COVID-19 symptoms, who were isolating at home were enrolled in the study between 1 September 2020 and 31 January 2021. Subjects answered an online medical survey and self-assessed hearing thresholds using the Hearing Test™ mobile app (e-audiologia.pl). These procedures were done twice, once at the time of diagnosis and again 2 weeks after convalescence.

Results: A total of 67 subjects were found eligible for the study. At most frequencies the patients' hearing did not differ between the first and second examinations; however, for 4 kHz, a statistically significant improvement in the hearing threshold was found ($p = 0.05$). Survey review revealed noticeable improvement ($p = 0.001$) over time in smell, taste, and nasal congestion.

Conclusions: It seems that SARS-CoV-2 infection caused a transient and selective (at 4 kHz) hearing impairment in patients who had had mild to moderate infection. The results suggest that as olfactory function returns after COVID-19, an improvement in hearing can be expected. Solutions based on mobile technology are useful for monitoring the hearing of patients in a pandemic.

Key words: COVID-19 • SARS-CoV-2 • hearing assessment • Hearing Test™ mobile app

SAMODZIELNE BADANIE SŁUCHU PRZY POMOCY APLIKACJI MOBILNEJ WŚRÓD PACJENTÓW Z COVID-19

Streszczenie

Wprowadzenie: Wpływ zakażenia SARS-CoV-2 na słuch nie jest jeszcze dokładnie zbadany. Czynnikami ograniczającymi diagnostykę audiologiczną u pacjentów z COVID-19 są wymagania sanitarne, jak i konieczność zastosowania specjalistycznego sprzętu. Celem badania była ocena zmian progu słuchu pomiędzy rozpoznaniem COVID-19 a rekonwalescencją z wykorzystaniem aplikacji mobilnej.

Materiał i metoda: Do badania zostali włączeni pacjenci z łagodnymi lub umiarkowanymi objawami COVID-19, pozostający w izolacji domowej między 1 września 2020 r. a 31 stycznia 2021 r. Osoby badane wypełniły kwestionariusz medyczny online i samodzielnie wykonały badanie słuchu za pomocą aplikacji mobilnej Hearing Test™ (e-audiologia.pl). Procedurę przeprowadzano dwukrotnie: po raz pierwszy w momencie rozpoznania i ponownie 2 tygodnie po ustąpieniu objawów.

Wyniki: Ostatecznie do badania włączono 67 osób. Dla większości częstotliwości słuch pacjentów nie różnił się między pierwszym a drugim badaniem. Jedynie dla 4 kHz znaleziono statystycznie istotną ($p = 0.05$) poprawę słuchu. Badanie kwestionariuszowe wykazało zauważalną poprawę ($p = 0.001$) w czasie pod względem węchu, smaku i niedrożności nosa.

Wnioski: Wydaje się, że infekcja SARS-CoV-2 powodowała przejściowe i selektywne (na 4 kHz) upośledzenie słuchu u pacjentów z łagodną lub umiarkowaną infekcją. Wyniki badania sugerują, że wraz z powrotem funkcji węchowej po przebytym COVID-19 można także oczekiwać poprawy słuchu. Rozwiązania oparte na technologiach mobilnych są użyteczne w monitorowaniu słuchu pacjentów podczas pandemii.

Słowa kluczowe: COVID-19 • SARS-CoV-2 • ocena słuchu • aplikacja mobilna Hearing Test™

Introduction

The world has been struggling with COVID-19 for nearly 3 years. Alarming reports from the first outbreak in China [1,2] identified changes in the respiratory system, and consequent ventilation disorders and pneumonia, which were subsequently named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [3]. The rapid human-to-human intercontinental spread of SARS-CoV-2 has resulted in a disturbing number of confirmed cases worldwide [4]. It is the third highly pathogenic coronavirus that has spread through the human population [5].

Subsequent scientific reports revealed new symptoms and complications resulting from this infection, and which affect the whole body, such as cardiovascular [6] and neurological disorders [7]. A loss of taste and smell turned out to be a prodromal symptom of the infection [8]. A wide variety of neurological symptoms result from the neurotropism and neuroinvasion of SARS-CoV-2 [9,10].

We know that several viral infections can cause hearing loss [11]. This suggests that in the current pandemic we can expect an increasing number of people with hearing disorders. There are a few case reports of sudden hearing loss, some with hearing assessments [12–14]. The scarcity of research in this area is related to the technical difficulty of conducting an audiological diagnosis due to the necessary isolation of the patient and their general poor condition during an infection. Reducing the risk of person-to-person transmission of the virus by government restrictions such as 'lockdowns' and 'social distancing' [15] has had a significant impact on the economy and on medical services. In a flash, COVID-19 has significantly modified the way we practice medicine.

Telemedicine has become an essential tool in providing medical care while reducing the transmission of SARS-CoV-2 to other patients and medical staff [16]. In view of the limited access to medical care, especially for those living in distant quarantined areas, it is worth noting the possibilities offered by telemedicine for secure diagnosis and monitoring health, including hearing. In the current pandemic the use of mobile-based technology makes it possible to maintain continuity of medical care and monitor changes in body homeostasis [17]. Tele-audiometry solutions can be used to assess hearing in SARS-CoV-2 positive patients [18], especially since the effects of COVID-19 on hearing have not yet been fully assessed. The aim of this study was to test the use of a mobile app for assessing hearing threshold in a pandemic situation.

Material and methods

This study was a longitudinal, non-randomized assessment of changes in hearing thresholds during SARS-CoV-2 infection. The study was performed in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants. The study design was approved by the ethics review board at the Wroclaw Medical University (KB-21/2021).

Subjects

Subjects with COVID-19 were recruited among patients of the single largest GP care center in Wroclaw. Each subject, who was isolated at home due to COVID-19, was offered to participate in the study. Inclusion criteria included being adult, having a positive PCR test confirming infection, agreeing to participate in the study, and having an Android mobile device with headphones. Exclusion criteria included lack of computer literacy as required to install the app from the Google Play store and any inability to perform a mobile based hearing test.

Medical history and hearing assessment

The medical history was collected along with each hearing assessment using an online questionnaire. The first medical history was obtained at the time of diagnosis and the second after 2 weeks of convalescence. The first questionnaire asked about hearing before SARS-CoV-2 infection and during COVID-19, while the second assessed subjective health improvement.

Two audiological examinations were done using the free mobile application Hearing Test™ (e-audiologia.pl), created by one of the authors [19]. The app was downloaded from the Google Play Store and the test was carried out twice. The Hearing Test app has been progressively developed over the past few years [19,20]. The first hearing assessment was performed when infection was confirmed by a PCR test and the second hearing test after a minimum of 14 days, together with a follow-up medical interview.

The Hearing Test app allows hearing thresholds to be self-assessed. The intensity of an amplitude-modulated tone is adjusted by the subject using buttons labelled "I can hear" and "I can't hear". The quietest audible sound is accepted with a "Barely audible" button. Measurements are carried out at frequencies of 0.25, 0.5, 1, 2, 4, 6, and 8 kHz.

Based on a previous study [19], the measurement error compared with pure tone audiometry is estimated at 2.6 dB (SD 8.3 dB) and is primarily related to the calibration of the reference sound level. However, the difference between the two tests performed consecutively on the same device is smaller, as it will not be affected by the calibration issue. Standard deviation of a test–retest study [19] was determined to be comparable to pure tone audiometry at the level of 4.4 dB (95% CI 4.2–4.6).

Since the mobile-based hearing tests were conducted under uncontrolled conditions, they needed to be verified in terms of their reliability. Here, the duration criterion was adopted [20]. If the duration of hearing threshold assessment at any frequency was less than 6.7 s, it is likely that the whole test is a subject to significant measurement error [20] and was excluded from the analysis. Additionally, subjects who conducted tests on different devices were also excluded from the analysis.

Statistical analysis

Statistical analysis was performed using Matlab R2018a (Massachusetts, USA). Changes in survey ratings of smell,

taste, hearing, and nasal occlusion, as well as differences in hearing thresholds, determined using the mobile app were tested for significance using a one-sample *t*-test. Hearing thresholds were also analyzed with Bland–Altman plots. Statistical relationships between survey ratings and hearing thresholds were evaluated using Pearson correlation coefficients, Spearman correlation coefficient, and Cronbach alpha reliability coefficient.

The sample size was determined based on the test–retest standard deviation estimated for mobile-based hearing threshold measurements at the level of 4.4 dB [19]. With a statistical significance of 0.05, a statistical power of 0.8, and an effect size of 2.0 dB, the necessary sample size was estimated to be 38 ears (19 subjects).

Limitations

A limitation of the present study is including only patients with mild COVID-19. This is because more severe infection results in less patient capacity to perform a hearing test on their own. No hearing measurements in patients were available before the pandemic. The test was performed at the first symptoms of infection.

Results

Initially, 140 patients with COVID-19 under GP care and isolating at home were offered participation in the study. Eventually, 67 of 140 (48%) adult participants (> 18 years of age) were prospectively enrolled between 1 September 2020 and 31 January 2021 as a non-randomized cohort for assessing the change in hearing thresholds during SARS-CoV-2 infection. The baseline characteristics of the participants – 67 patients (25 men and 42 women), aged from 20 to 54 years (mean 34.4 y, SD 8.7) – and their COVID-19 symptoms are presented in **Table 1**. The first questionnaire review, along with the first hearing test, was conducted, on average, 6 days (SD 3.3 days) after symptoms occurred. The second survey, along with the second hearing test, was carried out by 63 of the 67 (94%) participants, on average 17.6 days after the first one (SD 4.1 days).

All the tests were validated for reliability. Ultimately, 24 out of 67 (35.8%) participants properly performed both tests on the same device and qualified for further analysis. The hearing thresholds of the qualified subjects are presented in **Figure 1**.

The subjective assessment of the sense of smell, taste, nasal congestion, as well as hearing before, during, and after the infection were compared. The deterioration associated with COVID-19 infection and the improvement in conditions after 2 weeks are presented in **Figure 2**. Statistically significant differences at the level of $p \leq 0.05$ were found for all criteria, except for hearing.

Hearing thresholds determined with a mobile device during and after the infection are shown in Bland–Altman plots (**Figure 3**) and in **Figure 4**. No statistically significant differences were found in the mean hearing threshold at frequencies of 0.25, 0.5, 1, 2, 6, or 8 kHz or at the average at 0.5–4 kHz, which is consistent with the subjective assessments. Nevertheless, a statistically significant

Table 1. Baseline characteristics of the participants and their COVID-19 symptoms ($n = 67$)

Characteristic	Descriptive statistics
Mean age in years (SD)	34.4 (8.7)
Gender, female, *n* (%)	42 (62.6)
COVID-19 symptoms	***n* (%)**
Smell and taste disorder	53 (79.1)
Cough and shortness of breath	35 (52.2)
Headache	34 (50.7)
Fatigue and apathy	31 (46.3)
Fever	30 (44.8)
Nausea and vomiting	12 (17.9)
Diarrhea	8 (11.9)
No symptoms	3 (4.5)

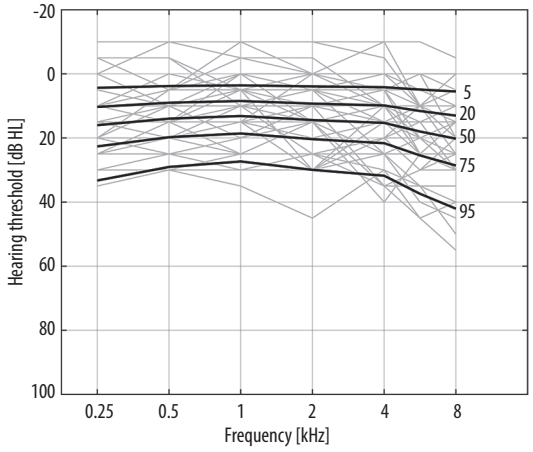

Figure 1. Initial hearing thresholds of the participants ($n = 24$). Bold lines indicate percentiles

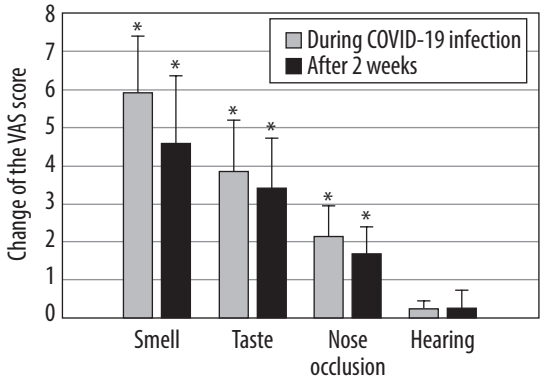

Figure 2. Decrease in VAS scores of smell, taste, nasal congestion, and hearing caused by COVID-19 evaluated at the time of diagnosis and 2 weeks later ($n = 24$). Asterisks mark statistical significance at level of $p = 0.05$

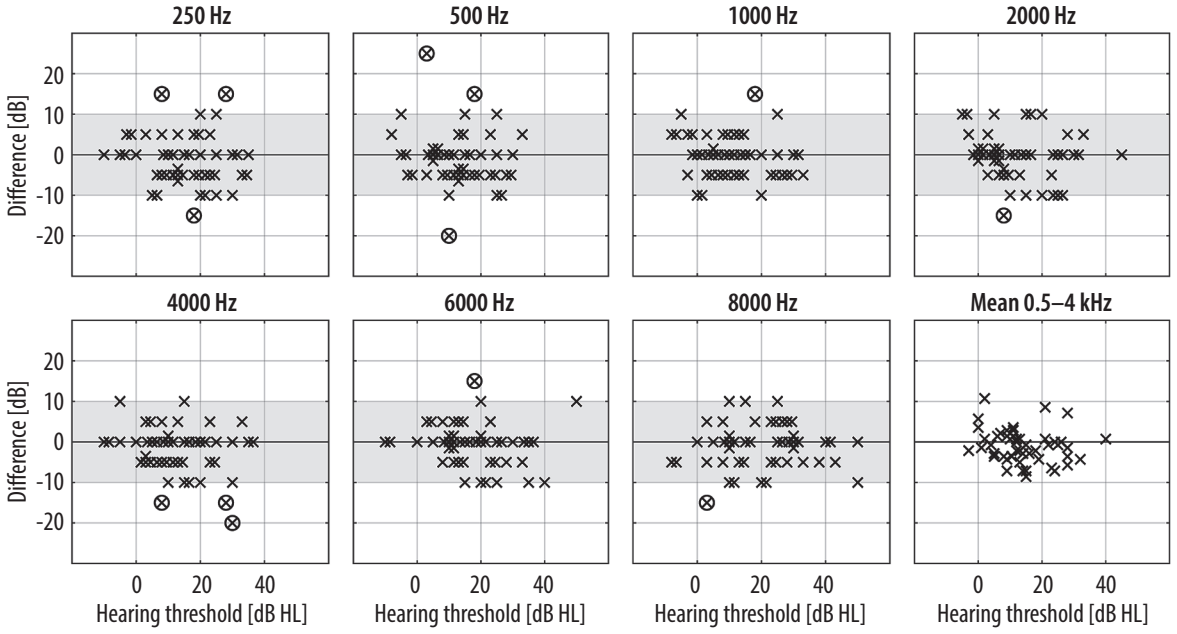

Figure 3. Bland–Altman plots of change in hearing thresholds (difference v. average) determined at the two measuring times ($n = 24$, number of ears = 48). The 95% confidence interval based on the standard deviation in test–retest studies on mobile devices is marked in grey [19], circles indicate measurements outside the statistical confidence interval

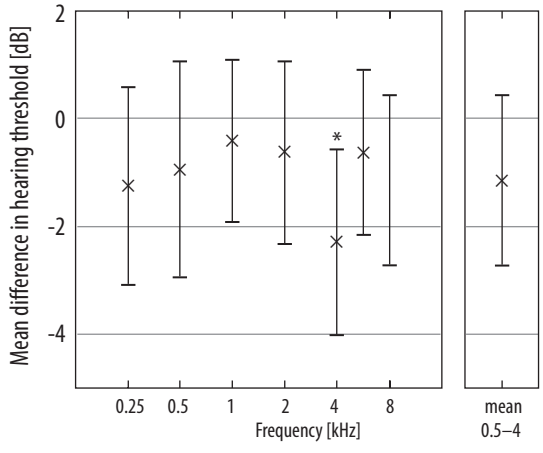

Figure 4. Change in hearing threshold by frequency ($n = 24$, number of ears = 48). Whiskers indicate 95% confidence intervals; asterisk marks statistical significance at $p = 0.05$

improvement was identified in the threshold at 4 kHz ($d = 2.3$ dB, $p = 0.01$). Hearing thresholds were correlated with subjective assessment of smell, taste, nasal congestion, and hearing (**Table 2**). Statistically significant correlations (Pearson $p = 0.005$, Spearman $p = 0.02$) with acceptable reliability (Cronbach alpha > 0.5) were obtained only between the hearing threshold at 4 kHz and the subjective assessment of smell.

Discussion

There have been many suggestions and assumptions relating to the neuroinvasive potential of SARS-CoV-2 [9,21], which indicate that, similarly to olfactory loss, hearing impairment may occur in the course of infection [22,23]. Emerging descriptions of COVID-19 symptoms include terms like 'novel ENT triad' involving anosmia, ageusia, and hearing impairment [24]. Sudden deafness and tinnitus are complaints observed in individual reports in patients with SARS-CoV-2 [25–27]. Mustafa [12] postulated that SARS-CoV-2 could harm hair cells in the cochlea, despite the absence of symptoms.

Even though, so far, there is weak evidence of the impact of COVID-19 on the audio-vestibular system, post-viral hearing dysfunction is generally known [11,28]. However, no more high-quality research on temporary, acute impact, or long-term consequences on the auditory-vestibular system is available to date. To our knowledge, the present work is the first attempt to assess the longitudinal effect of COVID-19 on the auditory system in a symptomatic, twice-tested group of patients. Our patients were in home isolation in a clinically stable condition, and had mild to moderate symptoms.

Our results point to no statistically significant differences in hearing at all frequencies, except for temporary hearing deterioration at the beginning of COVID-19 infection at 4 kHz. However, at the beginning of the pandemic, Mustafa [12] presented results showing deterioration of hearing at 4, 6, and 8 kHz in a group of 20 asymptomatic patients during COVID-19 infection, compared to a healthy control group. In that research, the hearing was assessed just once, which does not rule out patients having pre-COVID-19 hearing impairment. The results of Mustafa's study also challenge the study by Dror et al. [29], who found no difference in measurements of average auditory brainstem responses (ABRs) or otoacoustic emissions (OAEs) between normal hearing, asymptomatic, COVID-19 recovered patients and controls. The outcomes

Table 2. Pearson correlation coefficient, Spearman correlation coefficient, and Cronbach alpha reliability coefficient between hearing thresholds and survey ratings of smell, taste, nasal congestion, and hearing (n = 24)

Frequency (Hz)	Pearson correlation		Spearman correlation		Cronbach alpha	
	R	*p*	r_s	*p*	ρ	95% CI
Hearing threshold vs subjective smell assessment						
250	0.06	0.706	-0.12	0.423	0.10	–0.61; 0.49
500	0.25	0.082	–0.05	0.748	0.37	–0.12; 0.65
1000	0.27	0.059	0.13	0.396	0.42	–0.03; 0.68
2000	0.33	0.024*	0.18	0.234	0.47	0.06; 0.71
4000	0.40	0.005*	0.33	0.023*	0.55	0.20; 0.75
6000	0.31	0.030*	0.37	0.009*	0.47	0.06; 0.70
8000	0.10	0.490	0.07	0.634	0.18	–0.46; 0.54
Mean 500–4000	0.37	0.010*	0.16	0.277	0.54	0.18; 0.74
Hearing threshold vs subjective taste assessment						
250	–0.01	0.972	–0.08	0.575	–0.01	–0.80; 0.43
500	0.05	0.745	–0.06	0.689	0.07	–0.66; 0.48
1000	0.13	0.389	0.08	0.579	0.20	–0.42; 0.55
2000	–0.04	0.777	–0.06	0.678	–0.07	–0.91; 0.40
4000	0.11	0.439	0.14	0.329	0.17	–0.48; 0.54
6000	0.04	0.787	0.08	0.609	0.07	–0.66; 0.48
8000	0.08	0.587	0.06	0.708	0.13	–0.55; 0.51
Mean 500–4000	0.08	0.577	–0.01	0.957	0.15	–0.52; 0.52
Hearing threshold vs nose occlusion						
250	0.00	1.000	–0.09	0.561	0.00	–0.78; 0.44
500	0.08	0.578	0.02	0.919	0.08	–0.65; 0.48
1000	0.15	0.321	0.08	0.574	0.16	–0.49; 0.53
2000	0.12	0.426	0.19	0.207	0.12	–0.56; 0.51
4000	0.16	0.286	0.15	0.293	0.16	–0.50; 0.53
6000	0.08	0.609	0.11	0.441	0.09	–0.63; 0.49
8000	0.03	0.850	0.00	0.985	0.03	–0.73; 0.46
Mean 500–4000	0.15	0.299	0.11	0.467	0.20	–0.43; 0.55
Hearing threshold vs subjective hearing						
250	0.14	0.344	0.14	0.328	0.09	–0.62; 0.49
500	0.35	0.014*	0.45	0.001*	0.20	–0.42; 0.55
1000	0.10	0.492	0.04	0.769	0.08	–0.64; 0.49
2000	0.01	0.959	-0.10	0.510	–0.01	–0.79; 0.44
4000	0.01	0.960	-0.08	0.582	–0.01	–0.79; 0.44
6000	0.34	0.017*	0.29	0.049*	0.25	–0.34; 0.58
8000	0.11	0.459	–0.17	0.240	–0.09	–0.95; 0.39
Mean 500–4000	0.17	0.256	0.16	0.292	0.16	–0.50; 0.53

of this report partially correspond to our results. The mechanism of sudden deafness in the reported individual cases in COVID-19 patients [13,27,30] remains unclear. Perhaps, in addition to viral infection of the hair cells, there is also larger damage from a cytokine storm [31,32] or perhaps from intravascular coagulation with subsequent thrombosis or hemorrhage. There are currently no histological studies that would confirm the presence of the virus in the cochlea of patients infected with SARS-CoV-2. Severely ill patients are generally more likely to develop neurological complications compared to patients with mild or moderate disease [33]. The present results do not exclude the possibility that infection might increase the risk or severity of hearing damage.

The correlation between the severity of COVID-19 symptoms and other reported complaints – such as smell and taste impairments or nose occlusion – did not display any prognostic relationships. Our results showed only a single dependency between the patient's subjective symptoms and their hearing thresholds. However, the loss of smell and the return of its function significantly corresponded to the observed changes in hearing in the range 4 to 6 kHz. The mechanisms underlying post-viral hearing impairment may be related to damage not only to inner ear structures, but also the auditory nerve or the central nervous system [11].

The hypothesis linking hearing loss with virus entry into hair cells via the angiotensin-converting enzyme 2 (ACE2) receptor seems credible. Moreover, the expression of ACE-2 in the cochlea has been proven on mice [34–36]. Interestingly, the number of receptors was twice as high in the basal gyrus, which could explain the high-frequency hearing impairment which was shown in SARS-CoV-2 positive patients. Recently, more attention has been paid to the observed cognitive changes called "brain fog" resulting from the hypoxia of the brain cells as a result of the integration of the viral genome, leading to metabolic disturbances in the mitochondria [37]. Given the above, it should be considered whether SARS-CoV-2 may also cause disturbances on the auditory neuropathy spectrum [38]. Despite the mild course of the infection, the analyzed group of patients presented symptoms typical of COVID-19. As in other studies, the dominant symptoms, such as loss of taste and smell [39–41], were followed by headache, cough, and fever [42,43]. This clinical presentation is more characteristic of patients from a younger age group [40].

Detection of hearing loss via an app provides the opportunity to promptly initiate pharmacological therapy, and offer hearing aids or other surgical solutions, depending on the type and severity of the hearing loss. The app has proven to be a helpful and easy-to-use tool for assessing and monitoring hearing thresholds in isolated patients or in settings with limited access to medical care. Further development of mobile-based telemedicine driven by changes in lifestyles and attitudes toward remote medical services triggered by the COVID-19 pandemic may contribute to its wider application, not only in ENT but in other disciplines as well.

Conclusions

The results of this study suggest that SARS-CoV-2 may cause transient and selective (at certain high frequencies) hearing impairment in patients with mild to moderate course of infection. It has also been observed that, as olfactory function returns, an improvement in hearing can be expected in those patients with COVID-19-dependent hearing loss. Further research is required to confirm these observations in a larger group of patients and in subjects with a more severe course of infection. In a pandemic, where there is forced isolation and a need to practise 'medicine at a distance', mobile-based technology seems to be an appropriate tool to monitor patient hearing.

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