ORIGINAL ARTICLE

ASSESSMENT OF BRAIN BIOELECTRICAL ACTIVITY IN CLINICALLY HEALTHY FLIGHT PERSONNEL AND FLIGHT TRAINING CANDIDATES FOLLOWING COVID-19 INFECTION

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Introduction: Electroneurophysiological tests, together with tests to evaluate structures of the central nervous system (CNS), are in neurological diagnostics among the basic additional specialized examinations for diagnostic, therapeutic and certification purposes. The electroencephalographic (EEG) test is one of the methods of elelectroneurophysiological evaluation of the CNS. EEG is a non-invasive objective test of the bioelectrical activity of the brain.

Objective: To investigate whether the course of COVID-19 with clinical mild/moderate respiratory tract involvement, in non-hospitalized patients, may affect brain bioelectrical activity.

Methods: Eighty-five subjects were selected for evaluation of EEG recordings from clinically initially healthy flight personnel and flight training candidates. Of all the male and female subjects, between 04 January 2021 to 31 January 2022, as part of periodic and qualifying certification examinations at the Military Institute of Aviation Medicine, for the purposes of the Regional Military Aviation and Medical Commission. The selected group consisted of individuals aged 14-60 (average age: 27 years and 6 months), which included 14 women (average age: 24 years and 2 months) and 71 men (average age 29 years and 3.5 months). The subjects were ill with COVID-19 (non-hospitalized) for approximately 3-4 weeks, during the period; June 2020 – December 2021. Routinely made recordings of bioelectrical brain activity

with the Grass Technologies EEG TWin 4.5.3 system were visually evaluated. EEG examinations were performed in the supine position, in the before noon hours, in a darkened and acoustically isolated laboratory. Before the study, each person declared min. 6-8 hours of sleep and eating a meal (breakfast). Except for the flight training candidates and one person from flight personnel, all other subjects declared having received one and 29 subjects two SARS-CoV-2 vaccinations, prior to contracting COVID-19. Some subjects had one further revaccination after recovery from the disease. EEG examinations were performed between one and fourteen months after recovery from COVID-19. The mean time between recovery and EEG examination was 6.5 (6.47) months.

Results: EEG recordings within normal limits (normal) were found in 79 subjects, while six subjects (7.05%) had abnormal brain bioelectrical activity recordings.

Discussion and Conclusion: Infection with SARS-CoV-2 with clinical mild/moderate respiratory tract involvement by initially healthy individuals may adversely affect spontaneous brain bioelectrical activity in some individuals.

Keywords: EEG, SARS-CoV-2, COVID-19, post-COVID complications

INTRODUCTION

December 2019 is considered the start date of the global COVID-19 pandemic. In Poland, the first case of COVID-19 was officially identified in March 2020 (hospital in Zielona Góra). According to data as of 08 February 2022, 5.75 million people worldwide have died from COVID-19 since the start of the pandemic (AFP agency), while half a million patients have died from the Omicron variant, according to World Health Organization (Abdi Mahamud infection prevention specialist with WHO). The first officially confirmed case of Omicron variant in the world was detected in Botswana on 11 November 2021, while in Poland on 16 December 2021 (according to Paulina Wójtowicz).

Successive mutations of the SARS-CoV-2 virus are causing disease in younger and younger age groups. In Poland, children and adolescents have also been contracting COVID-19 since 2021. The adverse effects of SARS-CoV-2 virus on the human body are still fully unknown [1,2]. Several billion vaccines have been produced, hundreds of millions of people around the world have been vaccinated at least once, and in many countries three or more times. Despite this, the virus still poses a deadly threat to humans. Several months of observations and the author's own experience (work in the dedicated COVID-19 Unit and in

the dedicated COVID-19 Hospital, also e-advice) and opinions from multi-center medical institutions treating COVID-19 patients suggest the thesis that infections mainly affect the respiratory tract. In contrast, COVID-19 cases manifested by gastrointestinal, nervous system and cardiovascular complaints have been rare, more commonly occurring as CNS, cardiovascular, and cardiac complications.

OBJECTIVE

To investigate whether the course of COVID-19 with clinical mild/moderate respiratory tract involvement, in non-hospitalized patients, may affect the organization spontaneous brain bioelectrical activity.

STUDY GROUP

Of the subjects examined as part of periodic and qualifying certification examinations at the Military Institute of Aviation Medicine, for the purposes of the Regional Military Aviation and Medical Commission, 85 subjects, originally clinically healthy flight personnel and flight training candidates, were qualified for evaluation of EEG recordings [3]. The study group consisted of individuals aged 14-60 (average age: 27 years and 6 months) who recovered from COVID-19. Among them, three male subjects (one flight training candidate and two from the flight personnel) were left-handed.

All subjects recovered from respiratory infections lasting approximately 3-4 weeks between June 2020 and the end of December 2021 and were treated at home. The patients' general condition was good enough (mild/moderate) not to require hospitalization. In all subjects, the course of the disease was manifested by similar homogeneous core symptoms from the respiratory tract (olfactory disturbances, rhinitis, acute paroxysmal dry cough +/- up to half of the disease duration and then changing to wet cough). All also suffered from taste disturbances, temperature up to 39-39.6° C, a feeling of weakness, and bone and joint pain. Eleven subjects: 4 females and 7 males of the study group additionally suffered from headaches (of low to moderate intensity) and dizziness (circling/spinning of the surroundings around the head) of orthostatic nature lasting several days. Of the aforementioned eleven individuals, five of them were candidates for flight training; 3 females and 2 males.

The selected study group had EEG testing performed between 04 January 2021 and 31 January 2022. The tests was performed between one and fourteen months after recovery from COVID-19. The mean time between recovery and EEG examination was 6.5 (6.47) months.

Except for one subject (flight training candidate aged 14), in the remaining subjects the infection was confirmed using the SARS-CoV-2 antigen test (most of them) or using RT-PCR test for SARS-COV-2. A history of COVID-19 infection may be presumed in the above mentioned candidate on the basis of (physical examination) symptoms including; rhinitis, anosmia, ageusia, sore throat, dry cough, osteomuscular pain, and fever. In addition, his parents, who lived with him at the same time, were ill with COVID-19. Tests for SARS-CoV-2 virus performed on both parents confirmed infection.

55 persons from flight personnel had been vaccinated once and 29 twice against SARS-CoV-2 before contracting COVID-19, and some were re-vaccinated (once) after recovery. One person from flight personnel and all flight training candidates (29 persons) were not vaccinated against SARS-CoV-2 before contracting the disease. All persons from flight personnel had no abnormalities in periodic CNS functional examinations prior to COVID-19, including structural CNS examinations before and after SARS-CoV-2 infection. All subjects in the study group of flight personnel were considered clinically healthy prior to contracting COVID-19 by the Regional Military Aviation and Medical Commission and held a current certificate of clearance to work in aviation. Candidates for flight training, after the initial examination at the Regional Military Aviation and Medical Commission, were referred for further specialized examinations (e.g.; head CT – no CNS, EEG changes in the analyzed group). No one in the group reported any complaints on the day of the examination. They declared full psychological and physical fitness and preparation for the examination (min. 6–8 hours of sleep at night before the examination, having breakfast, and drinking no alcohol for > 36 h. They denied taking psychoactive drugs and medications, history of craniocerebral trauma, disturbance of consciousness, vision, hearing, balance or unconsciousness. Additionally, women confirmed a normal menstrual cycle, denied pregnancy and use of hormonal drugs. Blood tests for psychoactive drugs and alcohol were negative in all subjects. In the certification findings of the Aeromedical Commission, after the completed procedural multi-specialty examinations in the analyzed group, the only abnormalities were EEG recordings. The demographic structure of the study group is shown in Table 1.

Tab. 1. Quantitative structure of 85 male and female subjects by age and occupation.

Total subjects 85 subjects aged 14–60. (average age: 27 years and 6 months)		**Flight personnel** 56 subjects aged 21–60. (average age: 34 years and 3 months)		**Candidates** 29 subjects aged 14–20. (average age: 17 years and 11 months)	
14 women aged 15–41 (average age: 24 years and 2 months)	71 men aged 14–60 (average age: 29 years and 3.5 months)	8 women aged 21–41 (average age: 28 years and 9 months)	48 men aged 21–60 (average age: 35 years and 2 months)	6 women aged 15–19 (average age: 18 years and 2 months)	23 men aged 14–20 (average age: 17 years and 10 months)

METHODS

Eighty-five subjects with routine EEG testing between one and fourteen months after recovery from COVID-19 were selected for analysis from flight personnel and flight training candidates. The mean time between recovery and EEG examination was 6.5 (6.47) months.

All subjects had EEG testing performed in the before noon hours, in the acoustically isolated and darkened laboratory, in the supine position. Electroencephalographic recordings were made with the Grass Technologies EEG TWin 4.5.3 system, 21 cup electrodes from the head surface according to the 10 x 20 standard, with simultaneous recording of ECG and oculogram. Standard stimulations were applied; hyperventilation (Hw) T=3 min and single intermittent flashes of white light (Fs) at frequencies of 2, 6, 12 and 18 Hz, and intensity of 2 J. Recordings were evaluated visually in double and single electrode mounting (comparative digital analysis of recordings in subjects with abnormal EEGs is provided for during follow-up electroencephalographic examinations under the Regional Military Aviation and Medical Commission and will be a separate publication).

The EEG recordings of subjects with abnormalities of cardiac, electrolyte (tetany, latent tetany), functional and features of bioelectrical immaturity of the brain (candidates) were not included in the analyzed group.

RESULTS

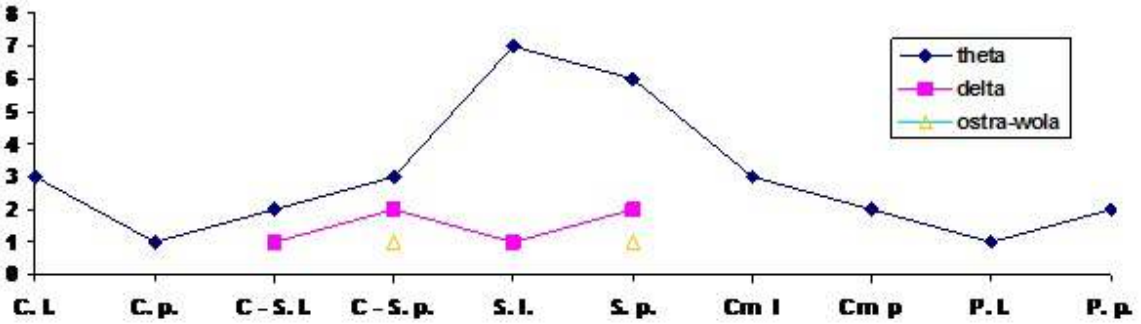
In the selected group of 85 subjects with routinely performed EEG testing and visually evaluated recordings, abnormal recordings (AR) were found in 6 subjects, representing 7.05%

of the total study group. All cases are male (8.45%). Among the AR men, there is one candidate for flight training aged 19. The remaining men were aged 23-38 (average age: 30 years and 5 months) and are members of the flight personnel. The average age of those six men is 28 years and 6 months. In one case of abnormal EEG recording, the test was performed one month after recovery from COVID-19, while in the remaining cases they were performed after six months, up to thirteen months (mean time to the test after recovery > 8.5 months / 8 months and 18 days). Table 2 below illustrates the abnormalities found in the EEG recordings.

Tab. 2. Nature and locations of brain bioelectrical dysfunction in individuals.

No.	age [years old]	time between recovery and test	alpha [Hz]	theta [Hz]	delta [Hz]	spike-slow wave paroxysms	diffuse abnormalities region	paroxysmal patterns
1.	25	Month 1	9 – 10.5	5 – 7	-	-	frontotemporal, temporal, parietal	-
2.	19	6 months	8 – 11.5	4.5 – 7.5	-	-	frontal, temporal, parietal (l > p)	paroxysmal tendency
3.	28	7 months	8.5 – 11.5	5.5 – 6.5	-	-	frontal, anterior-posterior (left)	-
4.	23	12 months	8 – 9.5	4 – 6.5	3 – 3.5	spike/ 3.5 – 4.5 Hz	frontotemporal, temporal (right)	paroxysmal tendency
5.	38	12 months	7.5 – 9 11.5 – 13	-	-	-	temporal (left)	-
6.	38	13 months	9.5 – 10.5	5 – 6	-	-	temporal and occipital (p > l)	-

Figure 1 below shows the areas with the most common and most expressed abnormalities of brain bioelectrical activity.



Legend: C. I. – frontal region of the left cerebral hemisphere; C. p. – frontal region of the right cerebral hemisphere; C-S. I. – frontotemporal region of the left cerebral hemisphere; C-S. p. – frontotemporal region of the right cerebral hemisphere; S. I. – temporal region of the left cerebral hemisphere; S. p. – Temporal region of right cerebral hemisphere; Cm I – Parietal region of the left cerebral hemisphere; Cm p – Parietal area of the right cerebral hemisphere; P. I. – Occipital region of the left cerebral hemisphere; P. p. – occipital region of the right cerebral hemisphere; Ostra – sharp

Fig. 1. Summary illustration of the regions in which disorders of spontaneous bioelectrical brain activity are most often and most strongly expressed in the analyzed group (left frontal, both frontal and temporal, and left parietal areas).

Figures 2-4 illustrate excerpts from an abnormal electroencephalographic recording, flight training candidate aged 19. The EEG study was performed six months after recovery from COVID-19.

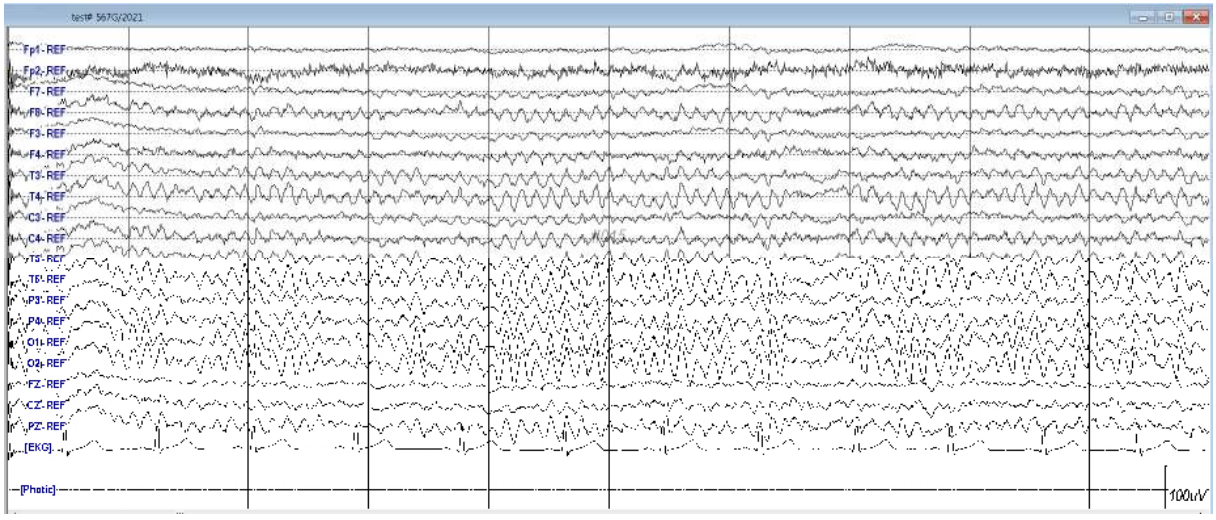


Fig. 2. (EEG No. 567G\2021). Illustration of resting brain bioelectrical activity – alpha rhythm at 8 Hz.

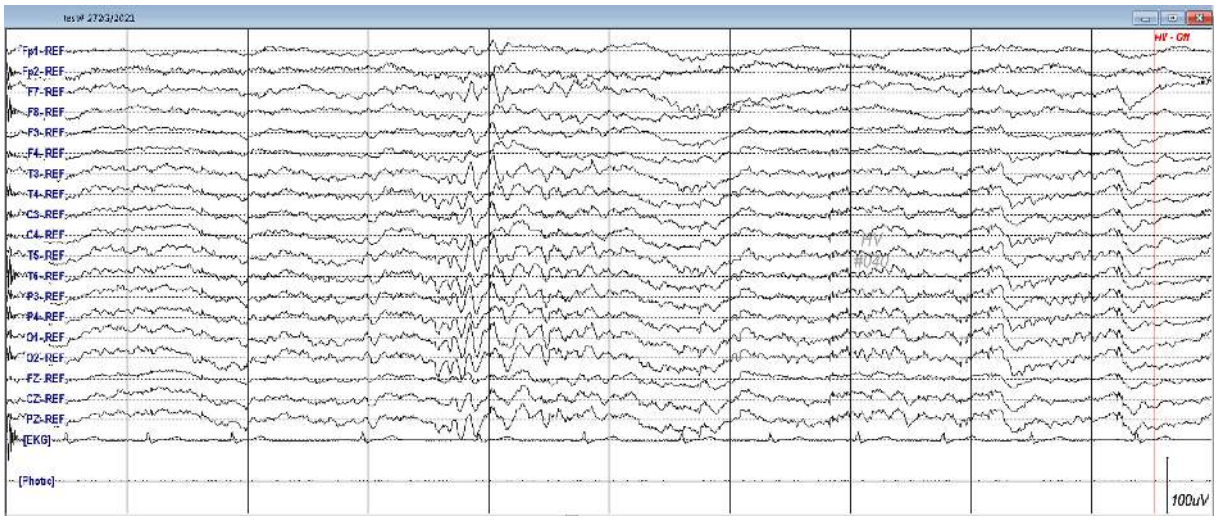


Fig. 3. (EEG No. 272G\2021). Illustration of generalized slow activity (theta 4.5-7.5 Hz), at the end of 3 minutes of hyperventilation (Hw).

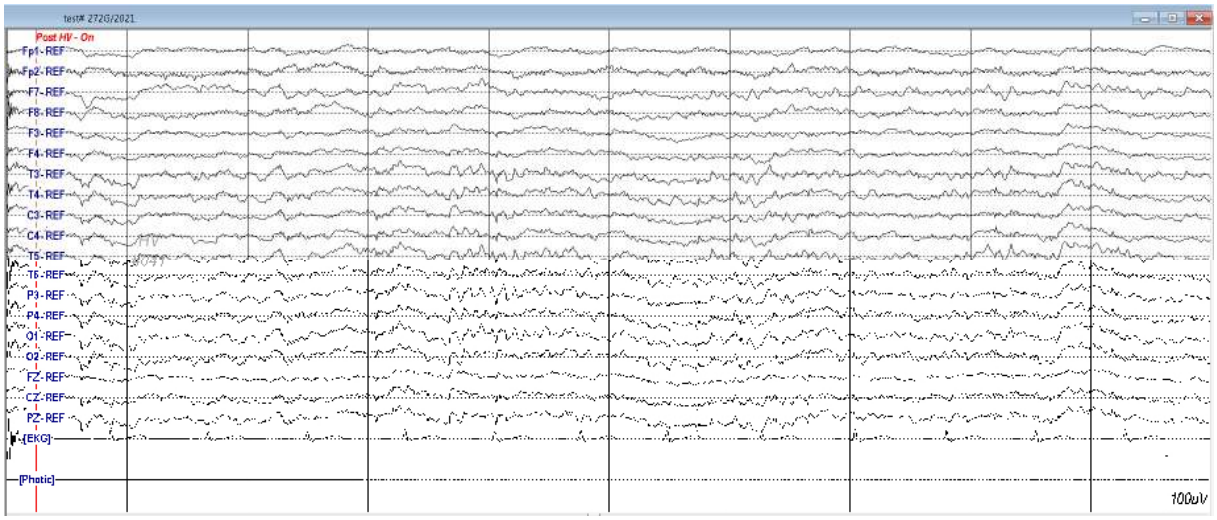


Fig. 4. (EEG No. 272G\2021). Presents an excerpt of the EEG recording immediately after completed hyperventilation (Hw).

DISCUSSION AND CONCLUSION

SARS-CoV-2 infection is a new disease with great potential for contagiousness that was unknown to humans and medicine. The rapid progress of urbanization and globalization of society facilitated the spread of infection to most of the human inhabited areas of the globe in a short period of time (a few months). The variation in climate, civilization and level of social consciousness, also objective malfunctioning of health services (efficiency and capacity) or conducive to rapid emergence of new mutations and variants of the SARS-CoV-2 virus. To illustrate in a mathematical way the phenomenon of the rate of increase of new mutations and the spread of disease in population, out of many number sequences, the

Fibonacci sequence can be considered the closest to reality. Poland's "delay" from the start of the global COVID-19 pandemic is only about four months. The first case of COVID-19 in Poland was officially identified in March 2020 (hospital in Zielona Góra). 85 individuals from the group of subjects contracted COVID-19 within the period of dominance of the Delta, Alpha and Omicron (BA1) SARS-CoV-2 strains in Poland. It only took ten weeks from detection for the BA1 strain to dominate the world (according to WHO). Before contracting COVID-19, all subjects were clinically healthy. In all, the core symptoms involved the respiratory tract. Since the Alpha variant was dominant at the time, it can be assumed that the entire study group may have been infected with this mutant. The mild/medium clinical course of COVID-19 cases among the 85-person study group may have been due to, among other things; young age (average age of 27 years and 6 months / after "omitting" two individuals aged 57 and 60, the core of the group was composed of individuals aged 14-52), overall good health and satisfactory level of personal immunity. All subjects lead an active, healthy lifestyle. 30 persons were not vaccinated against SARS-CoV-2 prior to contracting COVID-19, due to the age priorities in place at the time for persons to be vaccinated (all flight training candidates plus one person from flight personnel). A large proportion, i.e. six (7.05%) of the 85-person group, were found to have brain bioelectrical dysfunction. In five patients with spontaneous bioelectrical brain dysfunction, there were additional (non-dominant) CNS disorders; headache and dizziness (of orthostatic origin?). All subjects with abnormal EEG recordings were male, between 19 – < 39 years of age (average age of 28 years and 6 months). All men with abnormal EEG recordings were right-handed. Two thirty-eight-year-old men were vaccinated twice against SARS-CoV-2, a candidate for flight training (aged 19) was vaccinated, while the other three men were vaccinated once. Two males from the AR group aged 19 and 23 (33.33%) show paroxysmal tendency (EEG examination was performed 8 and 12 months after recovery, respectively). It may be due to (a) purely SARS-CoV-2 infection, (b) susceptibility/readiness of the brain response to trigger stimuli in individuals with latent features of persistent adolescence [4] (c) other hidden, unrecognized CNS conditions and dysfunctions. The other four men were aged 25-38 (average age 32.25 years). EEG tests performed from 1 to 13 months following recovery showed diffuse brain bioelectrical dysfunction. In one subject, aged 38 (tested after 13 months), abnormalities in the right cerebral hemisphere were found. The others showed abnormalities in the left and with predominance in the left cerebral hemisphere. Could the origin of the above mentioned disorders of spontaneous bioelectrical brain activity be the result of other underlying, unrecognized CNS conditions and dysfunctions? It seems unlikely due to the stringent

procedures in place for periodic multi-specialty examinations at the Regional Military Aviation and Medical Commission. In the course of several, several dozen years of examinations at RWKLL, no abnormalities – significant deviations from the normal state – were found in the above mentioned subjects. They were considered fit for flight duty, except for one subject (flight training candidate) who was undergoing the test procedure for the first time. Could behavioral factors at play when suffering from COVID-19, e.g. due to family or occupational situation, have contributed to the EEG abnormalities found in the above men? It is difficult to confirm the above as they all had positive psychological test results. The lack of EEG abnormalities in women may be due to their small number in the group, young age, i.e. 15-41 (average age of 24 years and 5 months), greater brain plasticity to stressful situations (physiology). All women in the study group were of childbearing age – the protective effect of female hormones on the body. It is possible that the origin of brain bioelectrical dysfunction in subjects examined by the Regional Military Aviation and Medical Commission may be a direct result of COVID-19 infection on the CNS, a systemic response to direct virus infection, or possibly the result of antibody-dependent enhancement due to vaccination. The course of illness varies among individuals.

In summary, it should be stated that:

1. Some individuals may show abnormalities in spontaneous brain bioelectrical activity after a mild clinical COVID-19 respiratory infection.
2. Abnormal EEG recordings in the study group were found in 6 (7.05%) subjects. All cases were male (8.45%) < 39 years of age.
3. All men with abnormal EEG recordings additionally experienced headaches and dizziness during their illness with COVID-19.
4. In the absence of sufficient knowledge and experience regarding the infectious complications of COVID-19 on the CNS, in patients with abnormal EEG recordings with paroxysmal tendency, the need for prophylactic anticonvulsant drug treatment should be considered.
5. The nature of the abnormalities of spontaneous bioelectrical brain activity present indicates the need for EEG testing in patients with a history of COVID-19.

AUTHORS' DECLARATION

Study Design: Stanisław Dec. **Data Collection:** Stanisław Dec. **Manuscript Preparation:** Stanisław Dec. **Funds Collection:** Stanisław Dec. The Author declares that there is no conflict of interest.

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