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ORIGINAL ARTICLE

Providing prevention, diagnosis, and treatment of patients after COVID-19 using artificial intelligence

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Abstract

OBJECTIVE: The aim of this research was to investigate the prevention, diagnosis, and treatment of patients after COVID-19 with the possibility of using artificial intelligence and virtual reality in combination with traditional approaches to patient rehabilitation.

MATERIALS AND METHODS: Statistical methods were used to evaluate the situation of COVID-19 worldwide and in Slovakia until March 2022. We investigated the rehabilitation options of breathing exercises, upper and lower limb rehabilitation, and cognitive tasks in patients with post-COVID syndrome who met the criteria for a combined rehabilitation program using virtual reality. Using artificial intelligence, we can predict in advance the evolution of the pandemic according to the records of infected patients and the evolution of the pandemic in the world, taking into account nearby territories. In the treatment of post-COVID syndrome, parameters have been identified that can be measured to objectively assess the improvement of the patient's condition and to continue personalizing individual rehabilitation scenarios.

RESULTS: In the patients who underwent the combined rehabilitation method, we observed progress in their ability to improve breathing, limb motor skills and also cognitive function of the patients. We identified different categories of parameters that can be evaluated by artificial intelligence methods, and we evaluated different scenarios using the exterior of nature and the interior of the room of the rehabilitation method of virtual reality, as well as the key elements of the "WOW" effect creating emotional changes in the patient for their motivation.

CONCLUSION: We showed that artificial intelligence and virtual reality methods have the potential to accelerate rehabilitation and increase motivation in patients with post-COVID syndrome.

INTRODUCTION

The WHO declared COVID-19 a pandemic and a threat to international public health. By the end of March 2022, more than 468 million cases of COVID-19 caused by SARS-CoV-2 infection reported worldwide, including more than 6 million deaths. Variants of the SARS-CoV-2 virus evolve through random mutations. New mutations can increase or decrease infectivity and increase the risk of reinfection or reduce the effectiveness of vaccines (Walensky *et al.* 2021). The Omicron variant replaced the Delta, Alpha, Beta and Gamma variants. Longer term, the impacts, and implications of coronavirus on our health are being monitored (CDCP 2022).

PREVENTION METHODS

Transmission of SARS-CoV-2 occurs when a droplet of virus is inhaled two metres from the source of infection after contact with an infected person for more than 15 minutes in a closed space with poor ventilation or when mucous membranes are touched by hands contaminated with virus. The most effective means of prevention against COVID-19 so far are the WHO-approved vaccines: AstraZeneca, Johnson and Johnson, Moderna. Pfizer/BionTech, Sinopharm, Sinovac, COVAXIN, Covovax and Nuvaxovid.

The probability of a serious course of COVID-19 is higher in the elderly (over 60 years of age), especially in nursing homes and long-term care facilities; in addition, if they have certain diseases such as cardiovascular disease, diabetes, chronic lung disease, cancer, kidney disease, liver disease, obesity, or immunocompromising diseases, the risk of infection is further increased (Garg *et al.* 2020, Guang *et al.* 2020, Wu *et al.* 2020, Palaiodimos *et al.* 2020). Treatment with approved monoclonal antibodies or antivirals is possible in immunocompromised patients who cannot be vaccinated with the vaccine.

Consequences of COVID-19

Variants of SARS-CoV-2, like other RNA viruses, evolve through random mutations. Some SARS-CoV-2 variants have reduced susceptibility to plasma from people previously infected or immunized, as well as to monoclonal antibodies for prevention and treatment (Cameroni *et al.* 2021).

In addition to the pulmonary complaints of reduced pulmonary diffusion capacity (Huang *et al.* 2021), neuropsychiatric disorders, anosmia, agenesis, dysgeusia, dysgeusia, headache, muscle and joint pain, fatigue, and cerebral fogging that can persist for months (Rudroff *et al.* 2020). Headaches and cognitive impairment including mental confusion, delirium and dementia (Liotta *et al.* 2020). Encephalopathy can occur especially in older people with pre-existing chronic diseases (Nuzzo *et al.* 2021). Cognitive decline and dementia in the elderly with a predisposition to cerebrovascular disease, arterial hypertension, diabetes, or dyslipidaemia have a higher risk of ischemic stroke during COVID-19 (Qureshi *et al.* 2020). Peripheral nervous system involvement, acute neuropathy and polyneuropathy, Guillain-Barré syndrome cause nerve damage with progressive loss of muscle strength, with respiratory muscles also affected (Webb *et al.* 2020). Difficulty in walking, weakness of the lower limbs, lack of strength of the pelvic plexus muscles and cutaneous hyperalgesia. Drowsiness and malaise, examination showed diffuse hypotension and weakness of the limbs. Absence of bed rest and immobilization cause muscle decline, chronic fatigue, headache, paraesthesia of the fingers, anxiety and depression. Hyperintense areas are detected on brain MRI in the periventricular and subcortical white matter and centrum semiovale. After five months, neurological disturbances appeared along with major depression and seizures (Nuzzo *et al.* 2021). The emergence of individual disorders and musculoskeletal syndromes from the use of computers and smartphones during COVID, as well as inappropriate working conditions in the home environment, highlighted the consequences of post-COVID syndrome (Masan *et al.* 2021). Special attention should be paid to inflammatory markers in the peripheral blood, especially neutrophil to lymphocyte ratio, C-reactive protein, D-dimers, serum ferritin (Wijeratne *et al.* 2020).

On 6 October 2021, the WHO established of a clinical case definition of post COVID-19 condition called post-COVID syndrome, depending on the long-lasting symptoms more than two months after overcoming COVID-19 disease, a detailed list is given (WHO post-COVID, 2021). The most common symptoms of post-covid syndrome are as follows: marked, unusual and unreasonable fatigue; shortness of breath even after light exertion or at rest; muscle weakness; increased temperature; a prolonged, most often dry cough; changes in mood, including depression; memory lapses, inability to concentrate; joint pain; headaches; stabbing pains in the hands and feet; sleep problems; digestive problems: diarrhoea, constipation, nausea, vomiting; loss of taste and smell; sore throat and difficulty swallowing; new-onset diabetes and arterial hypertension (high blood pressure); various manifestations on the skin; heart palpitations; hair loss, tooth loss, and more.

In the following Table 1, the symptoms of post-COVID syndrome are listed systematically by disease.

Meta-analysis of 29 post-COVID studies through March 15, 2021, showed that more than 60% of COVID-19 survivors exhibit at least one post-COVID-19 symptom for more than 30 days. Fatigue and shortness of breath were the most common symptoms of the syndrome after 60 days of follow-up, while the prevalence of other symptoms, e.g., headache, anosmia, agenesis, chest pain was predominantly lower than 60 days (Fernández-de-las-Peñas *et al.* 2021).

Tab. 1. The most common health problems of people with post-covid syndrome

Damage to the respiratory tract	difficulty with air exchange of non-threatening severity to acute respiratory failure requiring intensive care (Chen, 2022)
Cardiovascular system	heart attack, myocarditis, cardiac arrhythmias, heart failure and thromboembolic complications in the acute period of illness and after cure (Zhao, 2021)
Nervous system	stroke, brain fog, concentration and short-term memory impairment, anxiety, depression, confusion (Taquet, 2021)
Urogenital system	kidney impairment, worsening of pre-existing chronic kidney disease, impaired sexual function (Hirsch, 2020)
Muscular system	pain, muscle weakness and rapid fatigue, myositis and/or dermatomyositis, muscle atrophy (Nasiri, 2020; Zhu, 2020)
Cutaneous system	pseudo-capsular, maculopapular rash, urticarial and vesicular lesions and lesions associated with vascular occlusion (Tan, 2021)

Artificial intelligence to predict consequences

Machine learning (ML) algorithms allow for the exploration of facts from the data using statistical and mathematical algorithms, and to make decisions based on that, even for pandemic solutions. The original prediction models for COVID-19 struggled with changing variants of the initial SARS-CoV-2 virus (Sramka *et al.* 2020b, Ruzicky *et al.* 2021). In new analyses, patient medical records were considered in addition to baseline data to predict COVID-19 disease evolution (Gao *et al.* 2020). That study included 2,520 COVID-19 patients with known outcomes (hospital discharge or death) from hospitals in China. They used the following baseline characteristics: Age, Sex, Comorbidities: Hypertension, Diabetes, Chronic liver disease, Tumors, HBV, Chronic kidney disease, Chronic obstructive pulmonary disease, Fever ≥ 39°C, Cough, Dyspnoea, Sputum, Fatigue, Diarrhoea, Myalgia, Vomiting, State of consciousness, Respiratory rate per min, Mean arterial pressure (mmHg), SpO2 (%), End state (death - after days of treatment stay, or discharged after treatment days). The laboratory tests, in contrast to the symptoms reported by the patients, were more objective and less prone to bias. The mean number of days of hospital stay was 21 days, and this allowed the risk of mortality in the validation cohorts to be predicted several days in advance. Multiple models such as regression, support vector machine, gradient boosted decision tree (GBDT), neural network, K-nearest neighbours (KNN) and random forest (RF) were tested in the study. The ML algorithm predicted mortality risk in COVID-19 patients with cancer, a group where prediction of prognosis is particularly crucial and challenging, but also heterogeneity in baseline characteristics. The code used to develop and evaluate the ML model is available on GitHub with support for R, which was tested in our setting.

Similar predictive models using the ML algorithm facilitate the identification of patients at high risk of mortality and inform clinicians of the correct interventions (Moulaei *et al.* 2022). The following table 2 systematically sorts patient characteristics and symptoms by groups that predict behaviour during treatment for COVID-19 disease.

Our observations tracked changes in the nervous system, mental status, physical and mental fitness during the pandemic. The results showed that for predicting deaths and disease outcomes, COVID-19 is the most accurate among random forest (RF) machine learning algorithms both in terms of sensitivity and specificity. Other results compared from multiple possible observations were the GBDT, KNN and multilayer perceptron (MLP) algorithms. Figure 1 graphically shows the percentages of the algorithms according to the accuracy of mortality determination from the given features.

Tab. 2. Observed patient characteristics for artificial intelligence algorithms

Groups	**Observed characteristics and symptoms**
Demographic	Sex, age, region
Risk factors	Smoking, ICU admission, hypertension, pneumonia, diabetes, heart disease, other diseases
Clinical manifestations	Shortness of breath, sore throat, runny nose, loss of taste, loss of smell, muscle pain, chills, fever, cough, nausea/vomiting, chest pain and pressure, headache, gastrointestinal symptoms
Laboratory results	Urinary blood nitrogen, white blood cell count, C-reactive protein, hypersensitivity troponin, glucose, erythrocyte sedimentation rate, creatinine, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, absolute lymphocyte count, absolute neutrophil count,
Therapeutic plan	Length of hospitalization, Oxygen therapy, Mechanical ventilation of the lungs

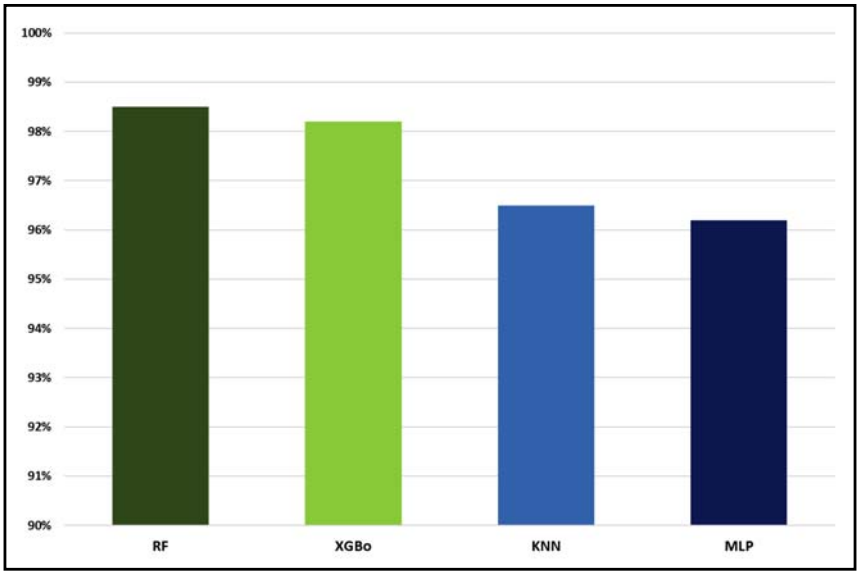

Fig. 1. Comparison of machine learning algorithms for COVID-19.
Algorithm: Random Forest (RF dark green), XG Boost (XGBo light green), K-nearest neighbours (KNN light blue),

TREATMENT OF POST-COVID SYNDROME

Recovery from mild to moderate COVID-19 disease can be supported by integrative medicine treatment strategies that consider the whole person, including all aspects of lifestyle. Studies have investigated the use of alternative potential supportive medications and practices following COVID-19 disease, e.g., vitamin D supplementation, glutathione, melatonin, Cordyceps, Astragalus, and osteopathic manipulation, breathing exercises to promote lung recovery, stress reduction, environmental optimization, and aromatherapy, all of which demonstrated recovery effects from mild to moderate COVID-19 disease (Alschuler *et al.* 2022).

Therapeutic treatments for post-covid syndrome include stem cell therapy. In addition to passive immunity-based therapy using antibodies taken from the plasma of cured COVID-19 patients, ozone therapy is also an option. Ozone activity protects against apoptosis induced by oxidative stress. Ozone increases cerebral blood flow, improves metabolism, and regulates chronic oxidative stress. Neuronal cells can reactivate the synthesis of antioxidant enzymes, which are essential for normalizing the redox state and blocking cell death (Mašán *et al.* 2021). The long-term consequences on the nervous system, mental health, and overall physical and mental well-being are severe. Analyses of publications on rehabilitation from validated databases up to the end of 2021 showed that rehabilitation significantly improves the consequences of post-COVID syndrome (Chen *et al.* 2022).

Physiotherapy and rehabilitation

Rehabilitation and physiotherapy may play a special role in reducing health sequelae after COVID-19. Post-covid rehabilitation is needed in the elimination of secondary neurological complications, respiratory insufficiency, cognitive impairment, impairment in coping with activities of daily living, communication impairment, post-covid psychosis, and memory impairment. A renewed investment in psychophysical activity will improve the health status of the post-pandemic population (Hasson, 2021).

The main goals of outpatient rehabilitation with a diagnosed COVID-19 include combating the effects of respiratory, circulatory failure, on the nervous system, the effects of immobilization and the treatment of functional complications. At the same time, it is important not to forget comorbidities that may have been significantly exacerbated as a result of the pandemic. Fear of the consequences of the disease, traumatic experiences during the course of the disease and pathological changes in the body often affect the emotional and psychological spheres to varying

Tab. 3. Determination of the current restriction status of post-COVID syndrome

Grade Level	Current restriction status
Level 0	no restrictions on independent functioning
Level 1	negligible limitations in daily functioning
Level 2	mild limitations in daily functioning
Level 3	mild to moderate limitations in functioning
Level 4	severe limitations in daily functioning

Tab. 4. Numbers of COVID19 patients and their mean duration of disease symptoms

	1st wave of COVID	2nd wave of COVID	3rd wave of COVID	4th wave of COVID	Total
Number of COVID patients	1	82	65	91	239
Average duration (days)	8	8,9	8,1	7,5	8,1
Number of post-COVID patients	1	16	11	18	46
Average duration (days)	45	39,5	40,5	31,2	39,1

degrees. The main aim of comprehensive outpatient rehabilitation is to improve quality of life and restore general physical fitness to pre-disease levels.

The health assessment allowed the appropriate treatment to be introduced and its effects evaluated. Self-assessment questionnaires, performance tests and physical fitness tests were used. The questionnaires allowed diagnostic tests to determine the degree and intensity of physical exercise and therapeutic activities at the final assessment (Rotermund *et al.* 2021). The choice of tests depends on the diagnostic equipment of the rehabilitation clinic. Ergometers, treadmills, stability platforms, 6-minute walk test, physical fitness tests (physical performance test, physical fitness test), exercise capacity tests, spirometry and coordination tests are often used.

The minimum recommended rehabilitation period is 3 to 4 weeks, depending on the severity of the disability. Simply classifying the current condition of patients into a specific grade always provides a statistical overview for rehabilitation facilities and to monitor how patients progress during long-term treatment (see Table 3). The questionnaires made it possible to determine current functional capacity on a five-level scale.

Virtual reality method for rehabilitation

Since the outbreak of the COVID-19 pandemic, the population's access to the outside environment has been increasingly restricted compared to the previous period. As a result of restricted exercise, people have increased their risk of cardiovascular disease and depression. One simple solution was to use mediated movement in virtual reality. Even simple panoramic 3D videos of movement in nature have been confirmed to improve the emotional state of nursing home residents (Browning *et al.* 2020). A study showed that providing mediated nature experiences to patients after COVID-19 elicited positive interactions in their treatment.

In 2021, during a pandemic in Taiwan, they provided long-term care residents with mild dementia a garden-variety 6-minute panoramic video experience using a virtual reality (VR) device, while simultaneously collecting ECG heart data. Heart rate readings were compared before, during, and after viewing the VR video from the garden. At the end of the experiment, participants were interviewed about the panoramic video experience and satisfaction, which was objectively confirmed by the analysed ECG data. Prolonged use of the VR video by the participants improved their autonomic nervous system and their overall mental state (Hsieh *et al.* 2022).

Stroke causes cognitive impairment similar to that experienced by patients after COVID syndrome. Virtual reality methods for rehabilitation of patients after stroke explored the potential for upper extremity, lower extremity, and upper extremity fine motor rehabilitation in patients who met the conditions for inclusion in a combined rehabilitation program using virtual reality. The study evaluated and identified parameters using artificial intelligence methods. Patient's positive emotion played a key role for their attitude towards repetitive activities and confirmed that patients who underwent the combined rehabilitation method had better progress in motor improvement abilities than those who underwent only conventional rehabilitation (Sramka *et al.* 2020a).

The study analysed 40 post-stroke patients with an age range of 29 to 89 years who were randomly selected into two groups for combined VR rehabilitation, with 30 patients with combined full VR rehabilitation and 10 patients with only sham VR rehabilitation (3D panoramic video). Specific benefits of treatment with full VR rehabilitation were observed in patients who experienced more severe cognitive impairment. The results showed that these patients with full VR rehabilitation had a reduction in hospitalisation time by an average of 3 weeks compared to conventional treatment or sham VR treatment, which lasted 6 weeks (Chatterjee *et al.* 2022).

Virtual reality helps in the healing process after COVID-19 and its use in the rehabilitation process has a motivating effect on the patient. Classical rehabilitation methods can be supplemented with VR rehabilitation to make new emotional experiences more motivating for the patient. The combination of two different rehabilitation approaches creates a synergistic effect.

The basis of an attractive and motivating game for patients is the joint design of VR rehabilitation directly

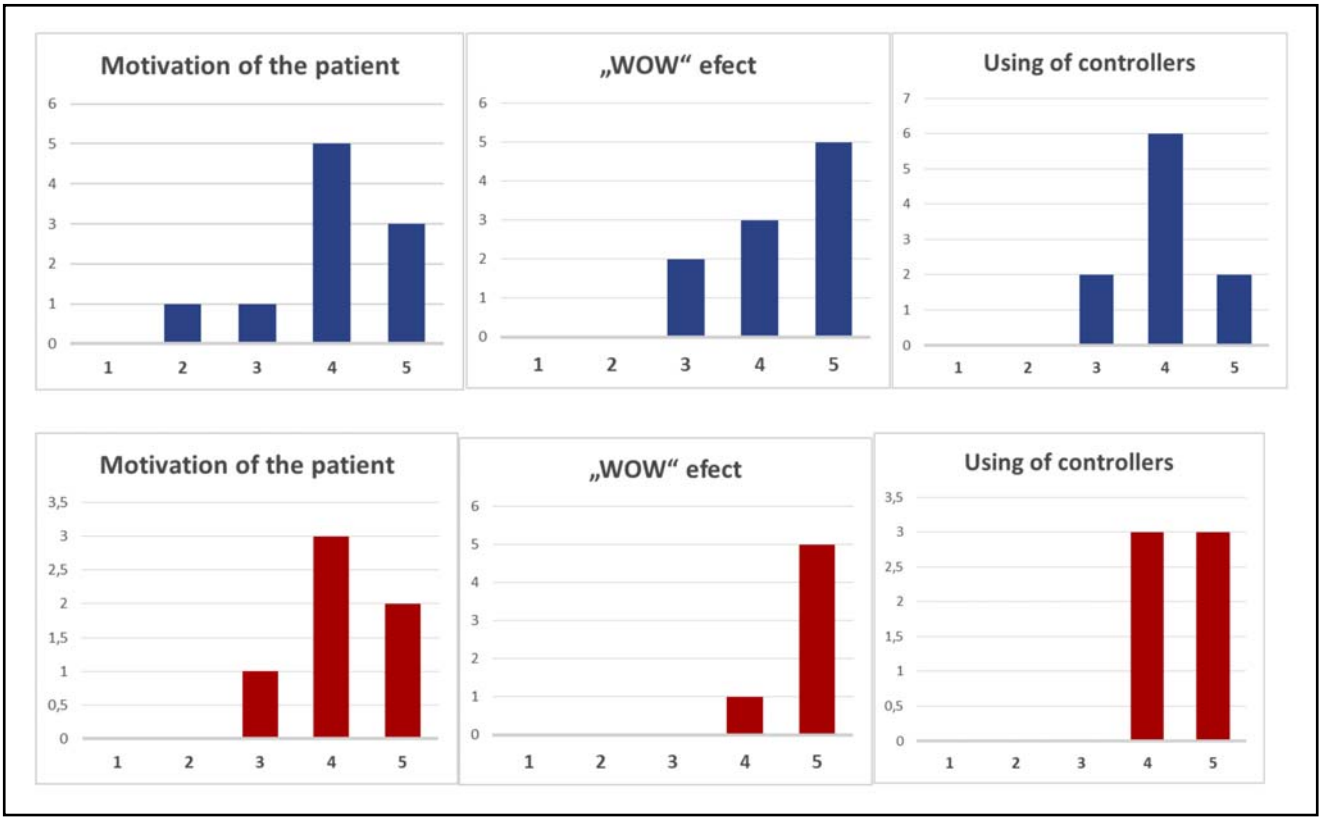

Fig. 2. Frequency of occurrence responses to the first 3 VR questions for mild muscle pain (blue graphs) and severe muscle pain (red graphs)

in rehabilitation facilities. Adapted context-based VR rehabilitation for people living with mild cognitive impairment has been implemented in Canada. The process of co-designing exercises and games was elicited through interviews with exercise therapists in long-term care facilities (Munoz *et al.* 2022). The knowledge and lessons learned from this research were used to co-design exercises, including techniques adapted for telerehabilitation, that are appropriate during a pandemic.

In studies, patients' movements were evaluated using artificial intelligence methods, which adaptively influenced the instructions to follow the movements and had a direct impact on the quality of the outcome of the exercises (Lacko, 2020). Patients preferred realistically processed 3D scenes in which they could move comfortably and focus on the activity being performed, but this was limited by some VR devices (Ruzicky *et al.* 2022).

CASE STUDY OF VIRTUAL REALITY REHABILITATION

In this study, we investigated the most common symptoms of COVID-19 and post-COVID at Pan-European University. Students and staff were approached through an anonymous questionnaire. In the questionnaire, we asked respondents with COVID about the following symptoms of the disease in addition to age and gender: Date of confirmation of COVID-19, Location during illness (at home, in hospital, in intensive care unit, on pulmonary ventilation), Symptoms during COVID (increased temperature, marked fatigue, sore throat, shortness of breath, palpitations, loss of taste and smell, headache, joint and limb pain, depression, and others), and Symptoms after 1 month of illness that were indicative of persistent post-COVID syndrome. In the questionnaires, respondents could indicate whether the symptoms of the disease were strong or weak. Table 4 shows the numbers of patients in each wave of COVID-19, their mean duration of illness in days, and the numbers of patients with post-COVID syndrome and their mean duration of illness. For survey participants, the longest average duration of illness for COVID-19 was almost 9 days during the second wave (August 2020-July 2021). The post-COVID-19 syndrome was most pronounced in 27.7% of COVID-19 patients in the third wave (July 2021 - January 15, 2022).

COVID-19 participants were mainly affected by the severity and frequency of symptoms: excessive fatigue, headache, muscle and joint pain, loss of taste and smell, shortness of breath after light exertion, runny nose and prolonged cough. Post-COVID syndrome manifested with the most severe symptoms: shortness of breath after light exertion, undue fatigue, headache, muscle and joint pain.

We selected 10 patients with mild muscle pain with shortness of breath after mild exertion and 6 patients with severe muscle pain with shortness of breath. We

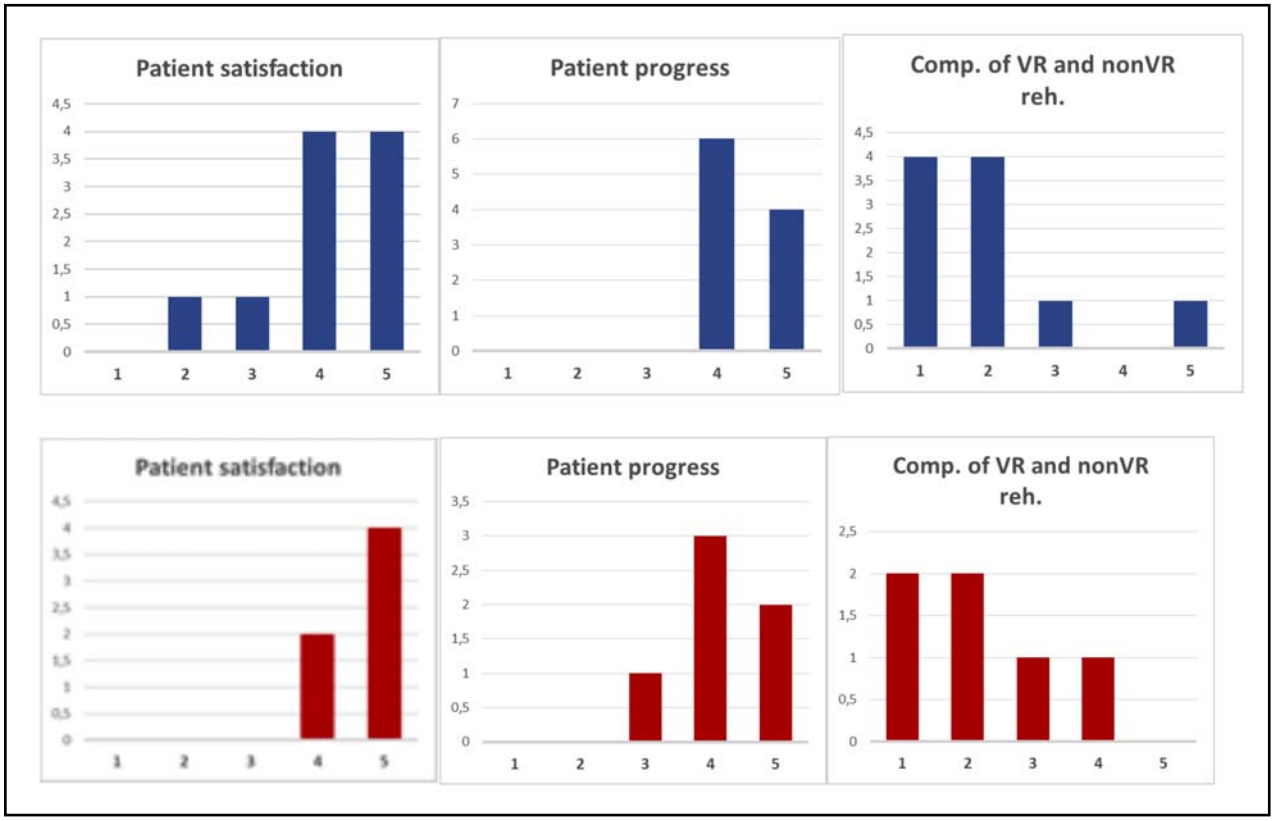

Fig. 3. Frequency of occurrence of responses to key questions regarding progress and satisfaction with VR for mild muscle pain (blue graphs) and severe muscle pain (red graphs)

investigated the factors causing increased cognitive burden of motor rehabilitation using VR for patients with muscle pain and shortness of breath. We introduced two approaches to patient rehabilitation in our research. For patients with mild muscle problems, we designed a trial using the telerehabilitation method in a home setting, with patients initially assisted by a therapist by remote control and later patients performing the exercises independently. For this scenario, we used VR devices that do not require a connection to a computer using VR device Oculus quest 2 (Lacko *et al.* 2022).

Telerehabilitation was designed to be able to take advantage of the possibility of performing daily life tasks in a virtual environment. For the virtual reality scenes, we used 3D models of real historical, cultural, technical and natural monuments of Slovakia, which we created within the project Innovative methods in education to support partnerships. Patients with severe muscle pain benefited from rehabilitation with a therapist in the controlled environment of a rehabilitation clinic. Emphasis was placed on performing exercises accurately in the order determined by the therapist. The therapist was able to control the progression of the exercises and their difficulty. At the same time, it was possible to implement a more complex setup of individual devices and sensors for data collection. In addition, patients had smart bracelets that sensed heart rate, daily exercise load (number of steps and hand movements) and sleep cycles.

According to the suggestions of rehabilitation experts, we prepared a schedule of exercises and games that were individually tailored to age, gender and personality type. Shorter 5-minute VR exercises were performed more frequently in the initial phase of exercise, which were gradually extended in time up to 20 minutes each day according to the parameters found. After each week, critical parameters were monitored using a questionnaire to assess the impact of the VR rehabilitation system on disease progression. Individual responses in the questionnaire were evaluated using a Likert scheme with 5 responses (value of 1 responded for complete dissatisfaction and value of 5 for complete satisfaction).

In addition to daily monitoring of patient performance, we monitored the following VR variables:
- Patient motivation in VR
- "WOW" effect during the VR rehabilitation process
- Use of controllers and hand tracking in VR
- Comparison of patient progress in VR
- Overall patient satisfaction with VR
- Comparison of rehabilitation in VR and without VR

Figure 2 shows the frequency of responses of 10 patients with mild muscle pain (blue graphs) and 6 patients with severe muscle pain (red graphs) to the first three questions of the VR survey. Relatively greater satisfaction with the use of VR, as well as with the enthusiasm effect and the use of simple control mechanisms, was observed in patients with severe muscle

pain, where the frequency tended more towards the value of complete satisfaction.

Figure 3 shows the response frequencies of 10 patients with mild muscle pain (blue graphs) and 6 patients with severe muscle pain (red graphs) to surveys on progression, satisfaction, and comparison of VR and conventional rehabilitation. Satisfaction was higher in patients with severe muscle pain, but progression was more consistent in patients with mild muscle pain. Comparison of VR with conventional rehabilitation had no significant differences between these patient groups.

DISCUSSION

Post-COVID rehabilitation is needed for respiratory insufficiency, secondary neurological complications, cognitive impairment, impairment in coping with activities of daily living, communication disorders, sleep disorders, memory impairment, and post-covid psychosis. The minimum recommended rehabilitation period is 3-4 weeks, depending on severity. In some individual cases, the period may be extended to more than 5 months.

In this research, we focused on testing the hypothesis of how virtual reality can help rehabilitation in the home environment. Based on the results of a questionnaire conducted after rehabilitation and on interviews with patients in both groups, we found that Virtual Reality can accelerate the rehabilitation process on the basis that the patient is motivated to exercise due to the experience of immersion in the virtual environment, the key factors being: the impact of the wow effect, the exercise design, the quality of the display and the experience with the computer. In addition to experience and communication with rehabilitation facility staff, we used artificial intelligence tools to design exercises and modify them according to the survey questionnaires.

When using telerehabilitation resources in the home setting, it became apparent that patients require a simple one-click solution. Patients who had no previous experience with similar devices had problems at the beginning of therapy. The virtual environment was also shown to be as intuitive as possible with minimal GUI controls and distractions.

CONCLUSION

Protecting the population from COVID-19 and its consequences requires clinical, diagnostic and epidemiological studies. In the above research, we compared rehabilitation and telerehabilitation approaches using virtual reality for patients after COVID-19 recovery. The individual findings show that the virtual reality method may have great potential. Based on our observations, we designed and implemented a system consisting of complex scenes and within them interactive tasks mainly focused on the development of upper limb mobility and cognitive abilities. We also plan to focus on the development of lower limb mobility and whole-body movement coordination within the interactive tasks.

It is essential to have a team of doctors and staff from several areas such as a rehabilitation doctor, physiotherapist, neurologist, psychologist, and IT worker. More severe post-ictal disorders need to be treated in specialised rehabilitation centres. In the case of more serious cognitive disorders, tele-rehabilitation using psychological discourses supported with a simple telebridge over the internet should also be considered. In patients with persistent headaches, nervous and psychological disorders after COVID-19, brain MRI should be performed.

A comparative study on a larger number of patients is needed to verify the results of the case study. In future work, we plan to focus on developing a comprehensive system to measure patient progress, which will store encrypted data on server storage and evaluate it using accurate artificial intelligence methods. We will also focus on connecting multiple patient and therapist users in a single virtual environment using a combination of virtual and augmented reality.

DECLARATIONS

This study was approved by the Ethics Committee of Pan-European University in Bratislava, Slovakia. Written informed consent was obtained from the patients for publication of this research.

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REFERENCES

1 Alschuler L., Chiasson AM, Horwitz R, Sternberg E, Crocker R, Weil A et al. (2022). Integrative medicine considerations for convalescence from mild-to-moderate COVID-19 disease. EXPLORE. **18**(2): 140–148. doi.org/10.1016/j.explore.2020.12.005.

2 Browning MHEM, Mimnaugh KJ, van Riper CJ, Laurent HK, LaValle SM (2020). Can simulated nature support mental health? Comparing short, single-doses of 360-degree nature videos in virtual reality with the outdoors. Front Psychol. Jan 2020. doi:10.3389/fpsyg.2019.02667

3 Cameroni E, Bowen JE, Rosen LE et al. (2021). Broadly neutralizing antibodies overcome SARS-CoV-2 Omicron antigenic shift. Nature 2022 Feb. **602**(7898): 664–670. doi: 10.1038/s41586-021-04386-2.

4 CDCP (2022). Omicron variant: what you need to know. Centers for Disease Control and Prevention. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/variants/omicron-variant.html> [Accessed 2 May 2022].

5 Fernández-de-las-Peñas C, Palacios-Ceña D, Gómez-Mayordomo V, Florencio LL, Cuadrado ML, Plaza-Manzano G et al. (2021). Prevalence of post-COVID-19 symptoms in hospitalized and non-hospitalized COVID-19 survivors: A systematic review and meta-analysis. European Journal of Internal Medicine. **92**: 55–70. doi.org/10.1016/j.ejim.2021.06.009.

6 Gao Y, Cai GY, Fang W et al. (2020). Machine learning based early warning system enables accurate mortality risk prediction for COVID-19. Nat Commun. **11**: 5033 (2020).

7 Garg S, Kim L, Whitaker M et al. (2020). Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019 - COVID-NET, 14 States, March 1-30, 2020. MMWR Morb Mortal Wkly Rep. 2020 Apr 17. **69**(15): 458–464. doi: 10.15585/mmwr.mm6915e3

8 Guan WJ, Ni ZY, Hu Y et al. (2020). Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020 Apr 30; **382**(18): 1708–1720. doi: 10.1056/NEJMoa2002032.

9 Hasson R, Sallis JF, Coleman N (2021). COVID-19: Implications for Physical Activity, Health Disparities, and Health Equity. American Journal of Lifestyle Medicine. 2021. doi.org/10.1177/15598276211029222

10 Hirsch J, Ng JH, Ross DW (2020). Acute kidney injury in patients hospitalized with COVID-19. Kidney Int. 2020 Jul. **98**(1): 209–218. doi: 10.1016/j.kint.2020.05.006

11 Hsieh CH, Chen CM, Yang JY et al. (2022). The effects of immersive garden experience on the health care to elderly residents with mild-to-moderate cognitive impairment living in nursing homes after the COVID-19 pandemic. Landscape Ecol Eng. **18**: 45–56 (2022). doi.org/10.1007/s11355-021-00480-9

12 Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, Kang L et al. (2021). 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet. 2021 Jan 16. **397**(10270): 220–232. doi: 10.1016/S0140-6736(20)32658.

13 Chatterjee KA, Buchanan K, Cottrell S, Hughes TW, Day N, John NW (2022). Immersive Virtual Reality for the Cognitive Rehabilitation of Stroke Survivors. IEEE Transactions on Neural Systems and Rehabilitation Engineering. **30**: 719–728, 2022, doi: 10.1109/TNSRE.2022.3158731.

14 Chen H, Shi H, Liu X, Sun T, Wu J, Liu Z (2022). Effect of Pulmonary Rehabilitation for Patients With Post-COVID-19: A Systematic Review and Meta-Analysis. Frontiers in medicine. **9**: 837420. doi.org/10.3389/fmed.2022.837420.

15 Lacko J (2020). Health Safety Training for Industry in Virtual Reality. 2020 Cybernetics & Informatics (K&I), 2020, pp. 1–5, doi: 10.1109/KI48306.2020.9039854.

16 Lacko J, Ruzicky E (2022). Possibilities of Rehabilitation and Telerehabilitation of Patients with Moderate and Severe Course of COVID-19 Disease Using Virtual Reality. In: 7th International XR Conference. Lisbon 2022. In print.

17 Liotta EM, Batra A, Clark JR, Shlobin NA, Hoffman SC et al. (2020). Frequent neurologic manifestations and encephalopathy-associated morbidity in Covid-19 patients. Ann. Clin. Transl. Neurol. 2020. **7**: 2221–2230.

18 Masan J, Sramka M, Rabarova D (2021). The possibilities of using the effects of ozone therapy in neurology. Neuro Endocrinol Lett. 2021 Mar. **42**(1): 13–21. PMID: 33932964.

19 Moulaei K, Shanbehzadeh M, Mohammadi-Taghiabad Z. et al. (2022). Comparing machine learning algorithms for predicting COVID-19 mortality. BMC Med Inform Decis Mak 2022 Jan 4. **22**(1): 2. doi: 10.1186/s12911-021-01742-0.

20 Munoz J, Mehrabi S, Li Y et al. (2022). Immersive Virtual Reality Exergames for Persons Living With Dementia: User-Centered Design Study as a Multistakeholder Team During the COVID-19 Pandemic, JMIR Serious Games 2022. **10**(1): e29987

21 Nasiri MJ, Haddadi S, Tahvildari A et al. (2020). Cinical characteristics, and sex-specific risk of mortality: Systematic Review and Meta-analysis. Front. Med. 2020. **7**: 459. doi: 10.3389/fmed.2020.00459.

22 Nuzzo D, Cambula G, Bacile I et al. (2021). Long-Term Brain Disorders in Post Covid-19 Neurological Syndrome (PCNS) Patient. Brain Sci. 2021. **11**(4): 454. Published 2021 Apr.

23 Qureshi AI, Abd-Allah F, Al-Senani F et al. (2020). Management of acute ischemic stroke in patients with COVID-19 infection: Insights from an international panel. Am J Emerg Med. 2020 Jul. **38**(7): 1548.e5–1548.e7. doi: 10.1016/j.ajem.2020.05.018.

24 Palaiodimos L, Kokkinidis DG, Li W et al. (2020). Severe obesity, increasing age and male sex are independently associated with worse in-hospital outcomes, and higher in-hospital mortality, in a cohort of patients with COVID-19 in the Bronx, New York. Metabolism. 2020 Jul. **108**: 154262. doi: 10.1016/j.metabol.2020.154262

25 Rottermund J, Cintulová LL, Budayová Z (2021). Skeletel muscle damage In Covid-19 disease and its social-psychological aspects. Int J Health New Tech Soc Work. **16**(3): 111–118.

26 Rudroff T, Fietsam AC, Deters JR, Bryant AD, Kamholz J (2020). Fatigue: Potential Contributing Factors. Brain Sci. 2020. **10**: 1012.

27 Ruzicky E, Mašán J, Šramka M (2021). Artificial Intelligence to Rehabilitation for Post-COVID syndrome. Int J Health New Tech Soc Work. **16**(4): 149–158.

28 Ruzicky E, Lacko J, Mašán J, Timarová G, Šrámka M. (2022). Virtual reality for rehabilitation of fine motor functions of hand in Parkinson's disease. Rehabilitacia Vol. **59**(1): 89–98.

29 Sramka M, Lacko J, Ruzicky E, Masan J (2020a). Combined methods of rehabilitation of patients after stroke: virtual reality and traditional approach. Neuroendocrinol Lett 2020. **41**(3): 101–111.

30 Sramka M, Slavik J, Masan J, Ruzicky E (2020b). Possible consequences of Covid-19 on the nervous system Neuroendocrinology Letters. Stockholm: Maghira and Maas Publications. **41**(4): 166–172. ISSN 0172-780X. ISSN (online) 2354-4716.

31 Tan SW, Tam YC, Oh CC (2020). Skin manifestations of COVID-19: A worldwide review. JAAD Int. 2021. **2**: 119–133. doi: 10.1016/j.jdin.2020.12.003

32 Taquet M, Geddes JR, Husain M, Luciano S, Harrison PJ. (2021). 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. The Lancet Psychiatry. **8**(5): 416–427. doi.org/10.1016/S2215-0366(21)00084-5.

33 Walensky RP, Walke HT, Fauci AS (2021). SARS-CoV-2 Variants of Concern in the United States-Challenges and Opportunities. JAMA. 2021 Mar 16. **325**(11): 1037–1038. doi: 10.1001/jama.2021.2294.

34 Webb S, Wallace VC, Martin-Lopez D, Yogarajah MG (2020). Guillain-Barré syndrome following COVID-19: A newly emerging post-infectious complication. BMJ Case Rep. 2020. **13**: e236182.

35 WHO post-COVID (2021). A clinical case definition of post COVID-19 condition by a Delphi consensus. Oct 2021.

36 Wijeratne T, Sales C, Karimi L, Crewther SG (2020). Acute ischemic stroke in COVID19: a case-based systematic review, Front. Neurol. 11 (2020) (1031).

37 Wu C, Chen X, Cai Y et al. (2020). Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020. **180**(7): 934–943.

38 Zhao H, Shen D, Zhou H, Liu J, Chen S (2020). Guillain-Barre syndrome associated with SARS-CoV-2 infection: causality or coincidence? Lancet Neurol. **19**: 383–384.

39 Zhu J, Ji P, Pang J et al. (2020). Clinical characteristics of 3062 COVID-19 patients: A meta-analysis. J. Med. Virol. 2020. **92**(10): 1902–1914. doi: 10.1002/jmv.25884