Can aquatic exercises contribute to the improvement of the gait stereotype function in patients with Long COVID outcomes?

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Abstract

A variety of rehabilitation programmes can be offered to Long COVID patients, specifically physical training. Indeed 90% of these patients reports impairments of verticalization, stability and spatial orientation, making difficult exercise in the gym. The aim of our study was to assess the effectiveness and safety of aquatic exercise techniques as part of a comprehensive rehabilitation program for patients with Long COVID. The first of a two-stage program involved development of aquatic exercises technique, which was evaluated in 12 patients with impaired upright posture control before and after exercising by "Habilect" video gait analysis system. During the second phase, effectiveness and safety of aqua exercises were tested in water pool as part of a comprehensive rehabilitation programme conducted in 23 patients with Long COVID outcomes. Physical examination, 6-minute step test, Euro-QL-5D questionnaire, Borg scale, laser Doppler flowmetry, cardiointervalography, and spirometry were performed before and after the aquatic exercises program. After the training with aquatic exercises, indices of deviations of the main body axes of the head and the body mass centre ameliorated, as well as direction of body movement vector decreased (p<0.05). This study demonstrated a statistically significant improvement in exercise tolerance in both groups, as measured by the 6-minute step test after rehabilitation. The comparison group averaged 236.7 metres [126; 380] (T=8, p=0.047) after the rehabilitation course and the intervention group averaged 233.71 metres [150; 320] (T=8.0, p=0.047). When tested with the Euro-QL-5D questionnaire, a post-treatment improvement was noted in the comparison group on the anxiety/depression subscale (3 [3;3] (T=0, p=0.043)). In the intervention group, laser Doppler flowmetry revealed a statistically significant increase in microcirculation (6.36 standard units after rehabilitation) [5.54; 8.17] (T=7.0, p=0.004), and a decrease of oxidative metabolism index of 6.89 standard units. [4.76; 6.96] (T=4.0, p=0.03). No serious adverse events were reported. In conclusion, the developed aquatic exercises technique seems to contribute to recovery of impaired upright posture and motor function, normalizing the walking pattern.

Key Words: Kinesiotherapy; aquatic exercises; stabilometry; Long-COVID-19.
coughing, muscle weakness, cognitive impairment and stress/anxiety.3,6
All these symptoms can contribute to impaired mobility, self-care and independent functioning.7 Di Caudo et al. (2021)8 studying the evolution of patients with Long COVID syndrome and the effects of rehabilitative interventions 3 and 6 months after the acute phase of infection, found that respiratory and mobility complications were partially reversible after 3 months of rehabilitation treatment. Capin et al. (2022)9 demonstrated on patients hospitalized for COVID-19 an improvement in functional scores from 2-6 weeks to 18 weeks.

While the need for rehabilitation of patients with Long COVID and the use of a multidisciplinary approach in rehabilitation interventions is generally accepted, there is no unified content of rehabilitation programmes.10 An important number of rehabilitation strategies involves general strengthening of patients, normalization of respiratory function and mobilization. Other rehabilitation programs focus predominantly on correcting severe respiratory failure,11 also by employing classical pulmonary rehabilitation methods.12 Nevertheless, regardless of the aim of the rehabilitation program, physical exercise is always included. However, as it was noted in our previous work Fesyun et al.(2020)13 and by other researchers,14,15 90% of patients who have had a COVID-19 infection present among other conditions impairments related to verticality, stability, spatial orientation, making difficult gym physical exercises. Therefore, we have developed an aquatic walking-recovery technique to be applied in the initial stages of medical rehabilitation, exploiting immersion up to mid-thorax and shoulder level. The aquatic environment provides a reduction of gravitational load up to 70-80%. This reduces the risk of falling, provides a soft resistance and a light massage effect on the musculoskeletal system thanks to the hydrodynamic properties. Moreover, the use of mineralized waters (sea, ocean, diluted brine, brine of limans and lakes), increases the gravitational effect and, due to the mineral composition, provides additional impact on metabolism. Considering the current available data on the natural course of Long COVID and the effectiveness of rehabilitation interventions, the National Medical Research Center in 2020 developed a comprehensive method for rehabilitate patients with novel coronavirus infection and pneumonia long-term outcomes. The program include initial examination by a multidisciplinary team, evaluation of functional impairment degree, and development of a personalized rehabilitation program, consisting of balneotherapy, physiotherapy and physical exercises. Thus, the aim of our study is to assess the effectiveness and safety of aquatic exercises in restoring functional state of patients with Long COVID as the initial part of a comprehensive rehabilitation program.

Materials and Methods
A two-stage study was conducted, the first involving development and evaluation of an aquatic exercise technique, while the second involved its application in a rehabilitation program for patients with Long COVID syndrome. The study protocol, prepared and executed in accordance with the Declaration of Helsinki he study was supported by the Independent Ethics Committee FSBI "NMRC RB" of the Ministry of Health of Russia, Minutes of Meeting No. 1-5/20 dated 27.07.2019). To participate in the study all patients were preliminarily informed and signed an informed consent.

Stage 1. Aquatic exercises methods
The aquatic exercises were developed between March and October in 2020 in the FSBI "NMRC RB" of the Ministry of Health of Russia and were evaluated in an open descriptive study that enrolled 12 patients (7 men, 5 women), aged between 40 and 62 years, with impaired upright posture maintenance [functional diagnosis "gait stereotype function" b770.1 - mild impairment (5-24%)]. The participants, in addition to basic therapy with an exercise therapy instructor, underwent 7-10 sessions of aquatic training in tap water (water temperature 30-32°C) for two weeks (30 min, 6 days per week). The treatment consisted of 5 exercises based on walking in water, including: 3 minutes of normal deambulation; 5 minutes of walking with high knees; 5 minutes of walking with the support of a device; 5 minutes of walking with special handholds (a variant involving the upper limbs and trunk muscles); 2 minutes of normal relaxed walking. A pre- and post-rehabilitation study was carried out using the “Habilect” video gait analysis system. To assess the reliability of differences of qualitative variables the χ2 test was used, the Wilcoxon rank sum test was used to assess quantitative variables changes between the different measurement times. The results were processed using Statistica for Windows (v.8.0) (StatSoft Inc., USA) and Microsoft Excel (Microsoft, USA). Statistical significance was considered for p<0.05.

Stage 2. Rehabilitation program definition involving aquatic exercises in tap water or in mineral water pools for patients with Long COVID outcomes.
Subsequently, an open-label, prospective, randomized, parallel-group study was carried out between July 2021 and March 2022 in the department of the FSBI "NMRC RB" of the Ministry of Health of Russia to evaluate the effect on recovery of functional status of the body of patients with Long COVID outcomes of 7 sessions of the previously assessed aquatic exercise sessions. The main diagnosis of the patients was the condition following a new coronavirus infection (U 09.9), established according to international rules.16 The sessions of aquatic exercises were performed in a tap water pool or in a pool with bromine sodium chloride brine with salinity of 120 g/dm³ and its preliminary
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dilution to 40 g/m³. Twenty-nine patients were included in the study, 28 were randomized and 23 patients completed the study.

Inclusion criteria were as follows:
1. Written informed consent of the patient to participate in the study;
2. Patients over 18 years of age;
3. Patients, who had had a novel coronavirus infection within 1-3 months prior to the inclusion in the study and had complaints despite drug treatment according to the diagnosis;

Exclusion criteria were as follows:
1. Patients with a febrile state or persistent subfebrile condition;
2. Severe unstable bronchial asthma or concomitant acute bronchial asthma;
3. Diagnosis of COPD – chronic obstructive pulmonary disease, exacerbation stage, established according to the current version of the GOLD guidelines, 2015 version;
4. Other chronic somatic, neurological or psychiatric conditions that may limit patient participation in the study;
5. Participation in other clinical trials within one year prior to the inclusion in the study;
6. Poor patient cooperation; inability to understand informed consent.

All the patients underwent a randomization procedure after screening (the simple envelope method with a 1:1 randomization was used). The patients included in the study received daily, five days a week, a multidisciplinary rehabilitation program, including: training to social reintegration and support sessions with a psychologist (as needed), back massotherapy, group respiratory physiotherapy, speleo-(halo), laser therapy, magnetotherapy, and aquatic exercise sessions. Moreover, the intervention group (n = 14) received also an aquatic exercise program (7 sessions) in a pool with sodium bromide chloride brine with salinity of 120 g/dm³ and diluted to 40 g/m³ while the control group (n = 14) received aquatic exercises (7 sessions) in a tap water pool. All the patients with less than 3 months since the diagnosis of novel coronavirus infection were being treated with indirect oral anticoagulants, vitamin E and vitamin D. The administration of other drugs, their class, dosage and frequency were determined by the underlying and associated comorbidities of the patients. Before and after the multidisciplinary rehabilitation programme involving aquatic exercises the following tests were conducted: physical examination with evaluation of the main physiological parameters, 6-minute walking test, EuroQol-5D (Euro-QL-5D) questionnaire, Borg scale, laser Doppler flowmetry (“LASMA-ST” apparatus, Russia), cardio-intervalography and spirometry. The study was supported by the Independent Ethics Committee and its protocol was prepared and executed in accordance with the Declaration of Helsinki (extract from Minutes 5 of 26.07.2020). Statistical processing of the data was carried out using descriptive statistical methods, in which parametric or non-parametric methods were chosen depending on the nature of the distribution. The χ² test, the Mann-Whitney test, and the Wilcoxon rank sum test were used. Data were analyzed using Statistica for Windows, v. 8.0 (Stat Soft Inc., USA) and Microsoft Excel (Microsoft, USA). Statistical significance was considered for p < 0.05.

Table 1. Stabilometry results for the central body axes before and after the exercises.

| Parameter/body axis | Body X, cm | Body Y, cm | Body Z, cm | Body Angle, cm |
|---------------------|------------|------------|------------|----------------|
| **Before the**      | **Me**     | **Q25**    | **Q75**    | **Q25**        |
| intervention        | 3,25       | -98        | 93,9       | -9,96          |
|                     | -29,01     | -29,01     | 13,76      | -30,59         |
|                     | 388,1      | 369,22     | 393,39     | 380,96         |
|                     | 16,45      | 7,46       | 338,67     | 324,7          |
| **After the**       | **Me**     | **Q25**    | **Q75**    | **Q75**        |
| intervention        | -9,96      | -100,92    | -81,96     | -30,59         |
|                     | -30,59     | -30,59     | 31,09      | 31,09          |
|                     | 380,96     | 377,98     | 400,05     | 342,36         |
|                     | 324,7      | 324,7      | 342,36     |                |
| **% of the deviation** | **Me**   | **Q25**    | **Q75**    | **Q75**        |
| from the original   | 306,5%*    | 102,98%*   | 87,28%*    | 105,45%        |
| value               | 112,68%*   | 102,37%*   | 101,69%*   | 101,15%*       |
|                     | 1973,86%*  | 4352,55%*  | 101,15%*   |                |

Note: The data are represented by median [Median (Me)] and quartiles (Q25; Q75), and the analysis of differences is performed using Wilcoxon rank sum test *. 

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Results and Discussion

Aquatic exercises methods

The results of the study are presented in Tables 1 and 2. Indices of deviation of the body axes and of the body centre of mass, as well as the changes in direction of body movement vector decreased after exercising. Furthermore, a decrease in the amplitude of body axis deviations in all the three spatial planes was observed.

Rehabilitation program including aqua exercises in freshwater and mineral water pools for patients with Long COVID outcomes

The patients in both groups (intervention and comparison groups) were comparable by sex ($\chi^2=0.945; p=0.331$) and age ($U=79.5; p=0.57$), and by severity of the previous coronavirus infection ($U=33.0; Z=0.19; p=0.85$). When analyzing differences before and after the rehabilitation program, statistically significant improvements in exercise tolerance were noted in both groups according to the 6-minute step test. The comparison group averaged 236.7 meters [126; 380] ($T=8, p=0.047$) after the rehabilitation course and the intervention group 233.71 meters [150; 320] ($T=8.0, p=0.047$). Spirometry data also recorded an increase after the rehabilitative intervention, without differences between the two group ($p>0.05$). Also the Borg Scale score during the rehabilitation process also showed a positive trend, but there was no statistically significant difference ($p>0.05$) in the pre- and post-exercise scores. Considering cardiointervalography (CIG), the range of standard deviation of NN intervals (SDNN) in the comparison group was initially within the normal range, while in the intervention group this range was mostly within the pathological range. All other CIG scores were also initially abnormal. After the rehabilitation program, both groups showed a no-statistically significant improvement in Cardiointervalographiya (CIG) values ($p>0.05$). In the intervention group, laser Doppler flowmetry revealed a statistically significant increase in microcirculation (6.36 standard units after rehabilitation) [5.54; 8.17] ($T=7.0, p=0.004$), and a decrease of oxidative metabolism index of 6.89 standard units. [4.76; 6.96] ($T=4.0, p=0.03$). Assessing the impact of aqua exercises on the quality of the patient's life using the Euro-QL-5D questionnaire, a statistically significant improvement in the anxiety/depression subscale was noted in the comparison group after the treatment with a mean value of 3 [3;3] ($T=0, p=0.043$), while in the intervention group the mean scores remained at the pre-rehabilitation level of 2 [2,2] ($T=6.0, p=0.69$). All events falling under the criterion of a serious adverse event or an adverse event occurring in a patient were recorded. As a result, we did not register a single event meeting the criterion for serious adverse events. The reported adverse events in the analysis of the intergroup differences showed no statistically significant difference ($\chi^2=1.36, p=0.24$), worsening of pain in the spine or lower extremities ($\chi^2=1.96, p=0.16$), acute respiratory infections ($\chi^2=2.65, p=0.1$) and other safety parameters (data of physical and laboratory methods of study at hospitalization and upon discharge). Our preliminary study on the definition of a water exercise protocol for patients with Long COVID symptomatology demonstrated the reduction in deviation of body axes, head oscillations and center of body mass, as well as the direction of the body motion vector. These objectively recorded outcomes were confirmed by patients' subjective feeling of unsteadiness reduction when

| Parameter/body axis | Head X, cm | Head Y, cm | Head Z, cm |
|---------------------|------------|------------|------------|
| Before the intervention | Me | -0.92 | 125.33 | -8.59 |
|                      | Q25 | -1.24 | 61.13 | -8.97 |
|                      | Q75 | -0.92 | 128.94 | -5.33 |
| After the intervention | Me | 1.5 | 107.42 | -14.89 |
|                      | Q25 | -10.19 | 52.49 | -14.89 |
|                      | Q75 | 2.38 | 107.42 | -3.45 |
| % of the deviation from the original value | Me | 163.04 %* | 85.71 %* | 173.34 %* |
|                      | Q25 | 821.77 %* | 85.87 %* | 166.00 %* |
|                      | Q75 | 258.70 %* | 83.31 %* | 64.73 %* |

Note: The data are represented by median [Median (Me)] and quartiles (Q25; Q75), and the analysis of differences is performed using Wilcoxon rank sum test *.
walking. The decrease in the amplitude of body axis deviations in all the three planes may be linked to an improvement in the brain areas responsible for coordination of motor functions and balance, including brainstem, cerebellum, basal ganglia, thalamus and several cortical regions, and their autonomic support, as well as improved functional interaction within muscle circuits. However, this preliminary study did not involve functional neuro-imaging, so central effects can only be hypothesized based on what was recorded through postural and gait analysis methods.

The following application of the water exercise program, both in tap or in mineral water, into a multiaxial rehabilitation program has showed that comprehensive rehabilitation for patients with Long COVID can have an important role in the improvement of functional recovery. In particular, an increase in tolerance to physical activity has been recorded in both groups considered. The spirometry and the Borg scale results also showed a trend toward improvement in both groups, but without reaching statistical significance, probably due to the small number of patients involved in the study. Also in Cardiointervalographiya (CIG) parameters in both groups positive changes were recorded although without reaching statistically significance. In the intervention group, laser Doppler flowmetry revealed a statistically significant increase in microcirculation and a decrease of oxidative metabolism index. Finally, quality of life also appears to improve. Contrary to what has been collected in the literature, whereby exercise in mineral water seems to contribute to improved quality of life, the data we collected did not confirm this trend, probably because the group treated in mineral water had initially a worse quality of life. From our results, it can be assumed that the implementation of water exercise sessions for patients with Long COVID outcomes can contribute to facilitate postural control and the maintenance of the upright position. Moreover, a comprehensive rehabilitation program, including water exercises, can increase physical activity tolerance and mobility at the initial stages of rehabilitation. Respiratory performance also appears to improve with the application of a water exercise program, reconfirming what has already been suggested in the literature.

Since patients with chronic fatigue and reduced exercise tolerance are increasing worldwide in proportion to the increase in COVID-19 infection cases, there is an urgent need for innovative and effective protocols to treat these subjects. In recent months, it has already been suggested that specific water exercise protocols, including the use of thermal water and the adoption of multidisciplinary interventions (motor programs, respiratory rehabilitation and neuropsychological interventions), can be employed to treat chronic fatigue in post-COVID-19 subjects. Thermal mineral water-based treatments may improve the physical symptoms of chronic fatigue and modulate the immune imbalance, reducing persisting inflammation. Additionally, rehabilitative protocol in the aquatic setting could also properly address comorbidities that can be present in post-COVID patients, such as obesity and other neurological and/or musculoskeletal problems.

Innovative and efficient therapy paradigms that can address the COVID-19 infection outcomes, paying particular attention to those connected to comorbidities, should therefore be developed. In-water balancing and muscular strengthening activities, as well as walking recovery and improvement in cardiac or pulmonary performance, could be offered to post COVID-19 individuals taking advantage of the physical and chemical properties of mineral and/or thermal waters. In particular, the use of thermal waters can positively impact the reduction of oxidative stress and cellular metabolism, as recent studies seem to confirm. Treatments performed in water, and particularly in thermal settings, can also act positively, exploiting the effects of hydrostatic pressure, on venous and lymphatic return, also improving this type of comorbidity.

Last but not least, water-based exercises program could provide post COVID-19 individuals with interventions that are psychologically helpful, lowering psychological side effects such tension, anxiety, and depression. Following the implementation of these rehabilitation techniques, the benefits may be evaluated, including in terms of cost-effectiveness, through randomized clinical trials considering large populations. To our knowledge, the strength of our study is to be the first study to involve the implementation of a water-based protocol integrated into a comprehensive rehabilitation program. Future studies should investigate the differences in the results obtained between treatment conducted in mineral water or tap water so as to clarify what specific effects act on this type of patient for whom the more effective methods of rehabilitation still remain largely unknown. In conclusion, the developed program of aqua exercises can help to correct the impaired upright posture, statistically significantly reducing the amplitude of head and neck oscillations and normalizing the walking pattern.

Mineral-water exercises also seem to have additional effects on the microcirculatory flow, the lymph flow and the tissue metabolism, and therefore can be useful for patients suffering from these disorders due to COVID-19 outcomes or to other concomitant pathologies. The inclusion of our water exercise proposal in an initial multiaxial rehabilitation program may accelerate the global recovery of patients with Long COVID outcomes.

**List of acronyms**

CIG - Cardiointervalographiya (syn: apparat for measure Heart Rate Variability)
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COPD - chronic obstructive pulmonary disease
COVID-19 - COrona VIrus Disease 2019
GOLD - Global initiative for chronic Obstructive Lung Disease
HRV - Heart Rate Variability
Long-COVID-19 - Long COrona VIrus Disease 2019
NCDs - chronic non-communicable diseases
SDNN - Standard of Deviation Normal to Normal intervals

Contributions of Authors
SA, AL and IG performed the statistical analysis. EI and AL checked the data quality. AP, GB, IG, and SA collected the data. IG, SA, AF, AL and MCM wrote the manuscript. All the authors revised the typescript and all the authors have read and approved the final edited paper.

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Conflict of Interest
The authors declare they have no conflicts of interest.

Ethical Publication Statement
We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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