Effects of exercise rehabilitation in patients with long COVID-19

Cristina Barbara, MD[1,6,*], Piero Clavario, MD[1,6,*], Vincenzo De Marzo, MD[2,3,6], Roberta Lotti, MD[2,3,6], Giulia Guglielmi, MD[2,3,6], Annalisa Porcile, MD[1,6], Carmelo Russo, MD[1,6], Raffaele Griffo, MD[1,6], Timo Mäkikallio, MD PhD[5,6], Arto Jorma Hautala, MD, PhD[4,6,#], Italo Porto, MD PhD[2,3,6,#]

1. Cardiac Rehabilitation Center of Genoa, Azienda Sanitaria Locale, ASL 3 Genovese, Genoa, Italy

2. Cardiology Unit, DICATOV - Cardiothoracic and Vascular Department, IRCCS San Martino Hospital, Genoa, Italy

3. Department of Internal Medicine and Medical Specialties (DIMI), University of Genoa, Genoa Italy

4. Cardiovascular Research Group, Division of Cardiology, Oulu University Hospital, University of Oulu, Finland

5. Faculty of Sports and Health Sciences, University of Jyväskylä, Finland

6. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation

*** These authors contributed equally to this work.**

 # The two last authors (Dr. Hautala and Prof. Porto) share senior authorship of this paper.

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Corresponding author

Prof. Italo Porto

University of Genoa, Cardiovascular Unit, Department of Internal Medicine and Specialties (DIMI)

Viale Benedetto XV, 10, 16132 Genoa (Italy); Email : italo.porto@unige.it; Tel : +39-010-5553441

In the first phase of COVID-19 pandemic early in 2020, the main scientific effort was devoted to find a best way how to treat the acute phase of disease. Subsequently, partially because of the availability of long-term follow-up data, there has been an increased attention to chronic consequences of COVID-19 infection. Since follow-up data up to more than one year is available, long COVID-19 has been recognized with several months lasting symptoms[1, 2].

According to a recent meta-analysis including 47910 patients (age 17-87) more than 50 long-term effects of COVID-19 were recognized. The five most common symptoms for long COVID-19 were fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%), and dyspnea (24%)[3]. At 6 months after acute infection, COVID-19 survivors were mainly troubled with fatigue or muscle weakness (63%), sleep difficulties (26%), and anxiety or depression (23%)[4]. In our recent study, at three months after hospital discharge, half of COVID-19 survivors showed a significant reduction in cardiorespiratory fitness, mainly explained by muscular impairment of legs[5]. Furthermore, patients who experienced persistent symptoms after COVID-19 still demonstrated a significantly decreased distance at 6-minutes walking test six months after the onset of symptoms[6]. The exact mechanisms underlying the exercise capacity reduction and functional limitations are not clear in long COVID-19 patients, but it seems that muscle impairment is an important determinant in this condition.

Given the central role of appropriate level of physical fitness in patients with long COVID-19, rehabilitation could play a pivotal role in this new and poor-known scenario[7, 8]. Therefore, it is crucial to establish rehabilitation strategies, that enable optimal recovery of these patients[7, 8]. In cardiac patients, exercise has been shown as a key component. Exercise-based rehabilitation reduces cardiac mortality, hospital readmission[9, 10], anxiety[11], and has shown to be cost-effective for health care providers[12]. Furthermore, both exercise training modalities, aerobic and resistance training, performed in same session has shown to induce clinically relevant fitness improvements[13, 14]. Therefore, we evaluated whether exercise rehabilitation program could be applied in a population of patients with long COVID-19. In line with expert recommendations[7, 8], we hypothesized that a combination of

aerobic and resistance training performed in the same session for eight weeks would be well tolerated and would effectively increase both cardiorespiratory and musculoskeletal fitness in long COVID-19 patients.

We assessed consecutive patients undergoing post-COVID-19 evaluation after three months of hospital discharge at the Outpatient Cardiac Rehabilitation Center of Genoa in Italy. For those patients who had a reduced exercise capacity (100 of 220 patients assessed), defined as the value below 85% of predicted peak aerobic capacity (VO_{2peak}), a controlled exercise-based rehabilitation was proposed. Finally, 50 volunteer patients (aged 55.8±9.7 years, 15 women, body mass index 26.6±5.2) were involved in this study. The detailed patient characteristics are defined in our previous study[5] (Table 1), the present study protocol follows the Declaration of Helsinki and it was approved by the Ethics Committee of the Liguria Region (n° 430/2020CER).

The patients started a laboratory controlled eight weeks exercise training program, which included three exercise sessions a week. In each exercise session, aerobic exercise (starting 30 min and increasing to 60 min) was performed, including 5 min warm-up and 5-min cool down. The intensity of aerobic exercise was defined according to VO_{2peak} test results targeting the watts reached at 80% of lactate threshold. Aerobic exercise was followed by nine major muscle group resistance exercises (for the lower extremity: leg extension/flexion, abduction/adduction and leg press; for the upper extremity: push-up/pull-down; for the core muscles; abdomen, back). Resistance training load was determined for each muscle groups according to the results of the maximal dynamic strength testing (1RM; one repetition maximum). The progression of resistance training was confirmed after four weeks by defining the new 1RM values to be used to continue training. Resistance training prescription load was defined as 40% of 1RM, 2 sets (3 sets for last two weeks) and 12 repetitions for each muscle group. The duration of a single training session was approximately 90 min.

The results for cardiorespiratory and musculoskeletal fitness are shown in Table 2 and expressed as means ± standard deviation (SD). The normal Gaussian data distribution was verified by

the Kolmogorov-Smirnov goodness-of-fit test. The changes in measured parameters were analyzed by using paired-samples t-test. All analyses were performed with R environment 3.6.3 (R. Foundation for Statistical Computing, Vienna, Austria). A p value of <0.05 was considered significant. The average number of realized exercise training sessions was 66.1±34.0 and during the eight weeks intervention none of patients dropped out from the study. VO_{2peak} increased 15% and peak ventilation 9% ($p<0.001$ for both). Eighteen patients (36.0%) had a post-training predicted VO_{2peak} above 85% (indicating normality). Muscle strength increased markedly for all major muscle groups ranging from 16% to 33% increase ($p<0.001 – 0.009$).

Several limitations are of note. Firstly, we did not have a control group, remaining about the considerable uncertainty remains regarding the effectiveness of same session combined exercise training compared with aerobic or strength training performed alone or with control group included. Secondly, all patients came from a single area of the city of Genoa with a relatively small sample of long COVID-19 patients, and therefore the generalization of results could be misleading. In addition, the exercise capacity evaluation was conducted three months after hospital discharge, with the patients unsupervised in the meantime and no data available, except for the anamnestic risk factors and comorbidities (data not shown here). However, strength of this study was that all exercise sessions were laboratory controlled and realized well according to training prescription.

In summary, the present study demonstrated that exercise rehabilitation in which combined aerobic and resistance exercises are performed in the same training session for eight weeks increased markedly both cardiorespiratory and musculoskeletal fitness. These results may highlight the importance of regular exercise rehabilitation to be added to the continuum of post-care of long COVID-19 patients aiming to promote daily activities, independent living, and quality of life.

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CONFLICT OF INTERESTS

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