

Descriptive analysis of long COVID sequela identified in a Multidisciplinary clinic serving hospitalised and non-hospitalised patients

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Supplemental Methods:

Laboratory blood work:

Standard blood tests included haemoglobin, leucocytes and white blood cell count, thrombocytes, C-reactive protein, ferritin, creatinine, urea, Potassium, Sodium, Calcium, alanine aminotransferase, alkaline phosphatase, lactate dehydrogenase, bilirubin, albumin, international normalized ratio, activated partial thromboplastin time, d-dimer, glucose, thyroid-stimulating hormone, beta-2-mikroglobulin, fibrinogen, triglyceride, procalcitonin, N-terminal prohormone of brain natriuretic peptide.

Patient reported outcomes

Type and degree of respiratory symptoms were assessed using the chronic obstructive pulmonary disease (COPD) assessment test(1) and Medical Research Council dyspnoea score (MRC)(2).

Work productivity and activity impairment questionnaire (WPAI)(3) and the EQ-5D-5L quality of life questionnaire(4,5) were obtained. In addition, the Post-COVID-19 functional status (PCFS) scale was completed(6). Subjective cognitive functions were assessed with the Cognitive Failures Questionnaire (CFQ)(7).

Lung function

Spirometry indices were measured using Vyntus Body (Vyaire Medical GmbH), with ULsensor for flow/volume, diffusing capacity for carbon monoxide (DLCO) and transfer coefficient of the lung for carbon monoxide (KCO) were measured using Vyntus ONE DL (Vyaire Medical GmbH), for real time carbon monoxide and methane diffusion with UL sensor for flow/volume. The accompanying Sentry Suite software platform was used with both systems.

Functional tests

1 min sit and stand: The test was performed twice with a 5 to 7-minute rest in between. Borg-CR10 scale, Heart rate (bpm) and oxygen saturation (SaO₂) was measured a rest and immediately when the 1-minute ended. The best performance of the two measurements was used(8).

Handgrip: Handgrip strength was measured using a Jamar J00105 hydraulic hand dynamometer, which is widely used and serves as reference for evaluation of other devices. The handgrip strength test was done five consecutive times with the right hand, and 5 times with the left hand. As recommended, we used the best of the five measurements for each hand. Analysis cut-off are based on best measurement from the dominant hand(9).

Cardio pulmonary exercise testing was performed according to international standard (10,11). In brief, during ergometer cycling with incremental work load, the patient was monitored using electrocardiogram, oxygen consumption, carbon dioxide production, and blood pressure. Before and after the ride, a lung function test during maximal inspiration and expiration was performed. For each patient an overall conclusion was reported with was categorised as “normal”, “decreased physical fitness”, “decreased ventilatory capacity” or “decreased cardiovascular capacity”. Decreased ventilatory capacity was defined as reduced peak oxygen consumption < 84 % of expected according to age, sex, and body height.

High resolution CT scan

HRCT images were obtained on a Somatom Definition Flash CT-scanner in inspiration and expiration in supine position.

The scanning protocol consisted of images in inspiration with 120 kV, reconstruction of 1 mm collimation sections with a high spatial frequency algorithm at 1 mm intervals with a pitch of 0.9 and additional reconstructions at 3 mm with a soft tissue algorithm. Expiration images were

acquired with 120 kV and 50 mAs. Images were photographed at window settings appropriate for viewing the lung parenchyma (window level, -600 to -700 Hounsfield units [HU]; window width, 1200-1500 HU). Presence, extent, and distribution of prespecified radiological entities were evaluated. Analysed findings included ground-glass opacities, airspace consolidation, reticular pattern, pleuraparenchymal bands, mosaic, air trapping, interlobular septal thickening, traction bronchiectasis and traction bronchiolectasies. All items were scored from 0 to 12 (representing 0-100 % of lung parenchyma) at four anatomical levels. A total score was calculated by adding the scores for each finding ranging from 0 to 96.

Cognitive function:

Together, the SCIP and TMT-B provide a brief (<20 minutes) objective performance-based assessment of cognitive functions, including verbal learning and memory, working memory, psychomotor speed and executive function. SCIP total scores reflect a global measure of cognition, spanning verbal learning and memory, working memory and psychomotor speed. TMT-B scores are a measure of executive function (attention switching).

High resolution ECG

High resolution electrograms in x-y-z configuration were obtained in supine position over 30 minutes and sampled at 1 kHz (Spiderview Plus, MicroPort). A parameter of heart rate variability called deceleration capacity (DC) as well as periodic changes in T-waves termed periodic repolarization dynamics (PRD) were calculated. Both correlated to underlying autonomous nerval system function DC < 2.5 ms or PRD > 5.75 degree was considered pathological.

Supplemental Results:

Cognitive function

Patients who had been hospitalised displayed poorer psychomotor speed (SCIP test 5; $t=-2.58$, $df=43$, $p=0.01$) and executive function (TMT-B; $t= 2.76$, $df=43$, $p=0.01$) than non-hospitalised patients. There was also a strong trend toward more global cognitive impairment in hospitalised versus non-hospitalised patients (SCIP Total Scores: $t=-1.75$, $df=43$, $p=0.054$). However, after adjustment for age and sex, the group differences on these measures rendered non-significant (p -values>0.12). The poorer psychomotor speed and executive function in patients who had been

hospitalised were driven by their older age ($p\text{-values}\leq 0.03$). Adjustment for age and sex revealed a strong trend towards more impaired verbal fluency in hospitalised vs. non-hospitalised patients ($F(3, 41)=3.83, p=0.057$).

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