



Cognitive impairment in young COVID-19 patients: the tip of the iceberg?

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We read with interest the article entitled “Neurological manifestations of coronavirus disease 2019: exploring past to understand present” [1] that reported neurological manifestations at onset and along management of COVID-19.

Regarding clinical features and investigations for neurological manifestations, cognitive impairment is not mentioned and no data are available on cognitive burden of the SARS-CoV-2 infection in subjects independent and without a history of cognitive impairment before the infection [2, 3]. We reported cognitive functions in hospitalized sub-acute subjects with symptomatic COVID-19 who were previously independent at home younger than 60 years old.

Inclusion criteria are the following: radiologically COVID-19 pneumonia, positive nasopharyngeal swab, independent at home before the infection (Barthel Index = 100), employed, no neurological diseases, no delirium episodes during COVID-19 acute phase, no mechanical ventilation, no new COVID-19-related neurological symptoms (ageusia or anosmia), and no oxygen supplementation at the time of evaluation.

All patients were screened by a trained neurologist and neuropsychologist for cognitive function with Montreal Cognitive Assessment (MoCA; pathological cut-off: 23) [4] and for depressive and anxious symptoms with Hamilton Depression Rating Scale (HAM-D; pathological cut-off: 8) and Hamilton Anxiety Rating Scale (HAM-A; pathological cut-off: 17). An evaluation of blood oxygen saturation and heart rate was performed before and after the neuropsychological assessment. The type of clinical onset was registered (respiratory onset/other). All the patients gave written informed consent before participating in the study.

Out of 522 subjects admitted to the Internal Medicine COVID Unit from the 1st of November 2020 to the 31st of March 2021, 32 patients were selected (mean age = 53.7(4.8); 19 M/13F); 5 subjects reported type 2 diabetes mellitus, 11 hypertension, and 3 asthma.

No subjects showed anxiety (mean HAM-A score = 6(10)) and/or depressive symptoms (mean HAM-D score = 5(8.5)). The mean score of MoCA test, corrected for age and education, was 20(8) (Table 1).

MoCA score of 23 classified 13 (36.67%) cognitively impaired and 19 unimpaired subjects (63.33%). The two groups were comparable for age, sex, COVID-19 onset symptoms, blood oxygen saturation and heart rate before and after MoCA, frequency of comorbidities, depressive symptoms, and anxiety. In addition, 10 out of 19 unimpaired subjects at MoCA were further tested with Trail Making Test (attention) and Symbol Digit (executive functions), showing pathological scores in 8 subjects, while Phonemic Fluency was in range.

MoCA is a useful screening tool to detect cognitive impairment in sub-acute COVID-19 but without enough sensitivity in younger. Results suggest a significant unexpected rate of cognitive impairment in young sub-acute COVID-19 subjects at time of hospital discharge. The ongoing follow-up will be crucial to understand the impact on everyday life and work. The results highlight the need of a multidisciplinary team to face the major rehabilitation and socio-economic relevance issues in the frame of the so-called long COVID [5, 6].

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Table 1 Clinical characteristics of the study population according to MoCA (expressed as means and standard deviation; differences expressed as *p* value, effect size and relative 95% CI)

Parameter	Population (<i>n</i> = 32)	MoCA < 23 (<i>n</i> = 13)	MoCA > 23 (<i>n</i> = 19)	<i>p</i>	Effect size (95% CI)
Age (years)	53.77(4.81)	54.64(5.16)	53.26(4.66)	0.461 ^a	0.283 (−0.466 to −1.027) ^b
Length of stay (days)	16.54(9.08)	17(12.21)	16.29(7.35)	0.885 ^a	0.076 (−0.733 to 0.884) ^b
SpO ₂ (%) ^c	94.77(2.28)	94.81(2.60)	94.74(2.16)	0.927 ^a	0.035 (−0.708 to 0.777) ^b
HR (bpm) ^c	66.43(13.82)	68.91(14.53)	65(13.59)	0.465 ^a	0.281 (−0.468 to 1.024) ^b
SpO ₂ (%) ^d	95.33(3.56)	95.45(3.50)	95.26(3.68)	0.890 ^a	0.053 (−0.690 to 0.795) ^b
HR (bpm) ^d	80.83(13.89)	76(16.20)	81.89(12.72)	0.591 ^a	−0.206 (−0.949 to 0.540) ^b
ΔSpO ₂ (%) ^e	0.57(3.06)	0.64(2.33)	0.53(3.47)	0.926 ^a	0.035 (−0.708 to 0.778) ^b
ΔHR (bpm) ^f	14.40(15.32)	10.09(20.34)	16.89(11.41)	0.248 ^a	0.447 (−1.195 to 0.308) ^b
HAM-D	4.90(5.30)	4.73(5.62)	5(5.26)	0.895 ^a	−0.051 (−0.793 to 0.693) ^b
HAM-A	5.93(5.66)	5(5.40)	6.47(5.87)	0.501 ^a	−0.258 (−1.001 to 0.490) ^b
MoCA score	23.50(4.24)	19.01(3.70)	26.03(2.72)	0.0001 ^a	−2.430 (−3.393 to 1.441) ^b
Sub-items ^g					
- Orientation	5/25	5/8	0/19	0.0001 ^h	3.497 (0.468 to 6.525) ⁱ
- Denomination	2/28	1/12	1/18	0.685 ^h	0.588 (−2.290 to 3.465) ⁱ
- Visuospatial Ability	8/22	7/6	1/18	0.0002 ^h	3.450 (1.091 to 5.809) ⁱ
- Executive Functions	17/13	10/3	7/12	0.004 ^h	2.842 (0.584 to 5.099) ⁱ
- Memory	23/7	10/3	13/6	0.161 ^h	1.529 (−0.742 to 3.801) ⁱ
- Attention	10/20	5/8	5/14	0.284 ^h	0.847 (−0.718 to 2.413) ⁱ
- Fluency	14/16	9/4	5/14	0.003 ^h	2.534 (0.692 to 4.375) ⁱ
- Calculation	9/21	8/5	1/18	0.0001 ^h	3.871 (1.460 to 6.283) ⁱ
Comorbidities (Yes/No)					
- Hypertension	11/21	6/7	5/14	0.122 ^h	−1.212 (−2.778 to 0.354) ⁱ
- T2DM	5/27	3/10	2/17	0.236 ^h	−1.159 (−3.136 to 0.817) ⁱ

SpO₂, blood oxygen saturation; HR, heart rate; MoCA, Montreal Cognitive Assessment; HAM-D, Hamilton Depression Rating Scale; HAM-A, Hamilton Anxiety Rating Scale; T2DM, type 2 diabetes mellitus. ^aStudent *t*-test (significance for *p* < 0.05); ^bCohen's *d* and relative 95% confidence interval; ^cbefore MoCA; ^dafter MoCA; ^eΔSpO₂, SpO₂ after MoCA-SpO₂ before MoCA; ^fΔHR, HR after MoCA-HR before MoCA; ^gnumber of subjects with pathological score/number of subjects with normal score; ^hchi-squared test (significance for *p* < 0.05); ⁱodds ratio and relative 95% confidence interval

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