Cognitive Impairment in Convalescent COVID-19 Patients Undergoing Multidisciplinary Rehabilitation: The Association with the Clinical and Functional Status
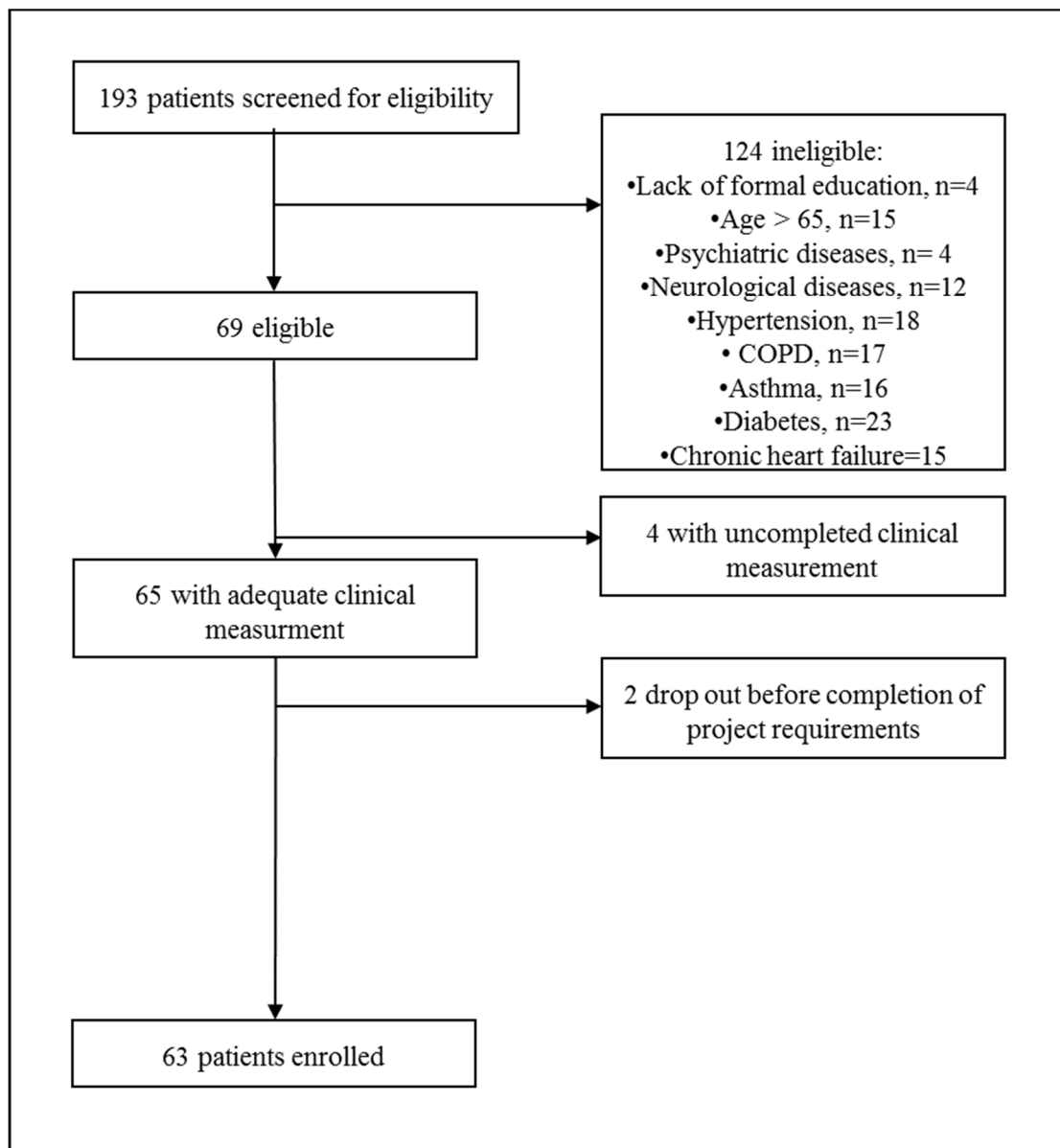
Pasquale Moretta [1,*,†], Pasquale Ambrosino [2,*,†], Anna Lanzillo [1], Laura Marcuccio [1], Salvatore Fuschillo [3], Antimo Papa [2], Gabriella Santangelo [4], Luigi Trojano [4,‡] and Mauro Maniscalco [3,‡]

[1] Istituti Clinici Scientifici Maugeri IRCCS, Neurological Rehabilitation Unit of Telese Terme Institute,
82037 Telese Terme, Italy; anna.lanzillo@icsmaugeri.it (A.L.); laura.marcuccio@icsmaugeri.it (L.M.)

[2] Istituti Clinici Scientifici Maugeri IRCCS, Cardiac Rehabilitation Unit of Telese Terme Institute,
82037 Telese Terme, Italy; antimo.papa@icsmaugeri.it

[3] Istituti Clinici Scientifici Maugeri IRCCS, Pulmonary Rehabilitation Unit of Telese Terme Institute,
82037 Telese Terme, Italy; salvatore.fuschillo@icsmaugeri.it (S.F.);
mauro.maniscalco@icsmaugeri.it (M.M.)

[4] Department of Psychology, Università della Campania Luigi Vanvitelli, 81100 Caserta, Italy;
gabriella.santangelo@unicampania.it (G.S.); luigi.trojano@unicampania.it (L.T.)

* Correspondence: pasquale.moretta@icsmaugeri.it (P.M.); pasquale.ambrosino@icsmaugeri.it (P.A.)

† The two Authors equally contributed to the manuscript.

‡ The two Authors share co-seniorship.

Table of contents

Supplemental Figure S1. Flow chart of study participants.

Supplemental Table S1. Clinical and demographical characteristics of the sample as a function of sex.

Demographical and Clinical measures/groups	Females (n= 16) mean (S.D.)	Males (n= 47) mean (S.D.)	z	p
Age	61.56 (10.191)	59.32 (11.311)	.787	.431
Education (years)	10.19 (3.710)	12.48 (3.427)	2.188	.029
Disease duration (days)	54.20 (35.86)	48.24 (25.86)	.642	.521
Duration of hospital stay (days)	30.88 (19.565)	23.68 (15.340)	1.225	.220
Duration of bed stay (days)	24.56 (25.076)	22.11 (15.731)	.247	.805
D-Dimer (ng/ml)	626.00 (391.368)	597.77 (587.138)	1.154	.248
CRP (mg/l)	6.586 (8.999)	10.161 (19.275)	.361	-.718
PaO2 (mmHg)	81.785 (14.515)	73.625 (14.822)	1.798	.072
PaCO2 (mmHg)	40.900 (13.893)	36.359 (6.537)	1.656	.098
FEV1 (% predicted)	77.62 (22.747)	79.21 (20.611)	.305	.760
FVC (% predicted)	76.46 (22.393)	76.09 (20.224)	.153	.879
FEV1/FVC	80.80 (7.59)	82.55 (7.65)	.617	.537
DLCO (% predicted)	44.88 (12.04)	60.74 (21.48)	2.108	.035
DLCO/VA (% predicted)	73.71 (19.88)	80.29 (22.07)	.858	.391
Mean daytime SBP (mmHg)	120.43 (23.43)	121.28 (12.86)	.604	.546
Mean daytime DBP (mmHg)	77.24 (12.15)	79.64 (8.77)	.899	.369
Mean nighttime SBP (mmHg)	117.65 (20.86)	116.07 (15.17)	.155	.877
Mean nighttime DBP (mmHg)	72.12 (11.02)	73.52 (9.68)	.449	.653
HADS_Anxiety score	10.64 (3.529)	8.96 (3.261)	1.468	.142
HADS_Depression score	11.45 (3.778)	11.90 (4.304)	.215	.830
STAI - Trait score	41.64 (11.893)	39.55 (8.129)	.708	.479
BARTHEL score	79.00 (23.664)	73.41 (25.942)	.817	.414
EQ-5D Visual Analog Scale	3.172 (10.258)	18.754 (32.287)	.585	.559

Abbreviations: CRP: C-reactive protein; PaO2: partial pressure of oxygen in arterial blood; PaCO2: partial pressure of carbon dioxide; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; DLCO: diffusion lung capacity for carbon monoxide; VA: alveolar volume; SBP: systolic blood pressure; DBP: diastolic blood pressure; HADS: Hospital Anxiety and Depression Scale; STAI: State trait Anxiety Questionnaire (trait anxiety); EQ-5D: Euro QoL.

Supplemental Table S2. Raw scores of neuropsychological tests.

Neuropsychological tests	Total Sample (N= 63) Mean (S.D.)	RCE (n= 28) Mean (S.D.)	NCE (n= 35) Mean (S.D.)	p
Montreal Cognitive Assessment	25.24 (2.55)	23.43 (3.51)	26.78 (2.16)	.016
Frontal Assessment Battery	16.28 (1.09)	15.93 (.979)	16.56 (1.10)	.029
Coloured Proggressive Matrix	28.41 (4.50)	27.11 (3.76)	29.42 (4.81)	.046
Verbal Fluency (FAS)	29.50 (10.24)	25.57 (9.90)	32.56 (9.56)	**.004**
Trail Making Test (B-A)	79.79 (50.56)	109.71 (48.71)	58.68 (40.65)	**.000**
RAVLT – immediate recall	42.17 (9.31)	34.00 (8.87)	51.97 (19.32)	**.001**
RAVLT – delayed recall	7.67 (3.02)	6.33 (3.23)	8.67 (2.44)	**.002**
Corsi's Test	4.88 (.92)	4.32 (.72)	5.30 (.84)	**.000**
Corsi's supra-span Corsi's Test	10.09 (1.23)	7.41 (.98)	12.78 (1.11)	**.000**

Abbreviations: Corsi's supra-span: Supra-span learning on Corsi's Test; RAVLT: Rey's Auditory Verbal Learning Test. In bold are reported the significant differences according to Bonferroni's correction (p value= .005; for 9 comparisons).

Supplemental Table S3. Correlations between measure of clinical, functional and cognitive status.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Hospital Stay duration	1													
2. Bed rest duration	.712**	1												
3. HADS-A	-.106	-.084	1											
4. HADS-D	-.039	-.031	.204	1										
5. NPSCT	.047	.112	.193	.252	1									
6. EQ-5D	-.132	-.149	-.130	.126	-.263	1								
7. PaO2	-.342**	-.457**	.023	-.166	-.264*	.223	1							
8. PaCO2	.149	-.077	.017	-.203	-.048	.053	-.583**	1						
9. FEV1%	-.224	-.312*	-.086	-.267	-.156	.223	.578**	.069	1					
10. FVC%	-.337**	-.335**	-.068	-.287*	-.173	.193	.579**	-.114	.945**	1				
11. FEV1/FVC%	-.072	-.035	.122	.078	.069	.257	-.069	.174	.074	-.241	1			
12. DLCO%	-.161	-.336*	.078	-.050	-.351*	-.062	.501**	.139	.657**	.661**	-.030	1		
13. DLCO/VA%	-.199	-.145	.258	.228	-.188	.134	.106	.126	.147	.062	.380	.558**	1	
14. ACRBP	.062	.205	-.039	.066	.410**	-.186	-.180	-.096	-.144	-.069	-.161	-.132	-.069	1

HADS: Hospital Anxiety (A) and Depression (D) Scale; NPSCT: number of pathological scores on cognitive test; EQ-5D: Euro QoL; Pao2: partial pressure of oxygen in arterial blood; PaCO2: arterial partial pressure of carbon dioxide; FEV1%: forced expiratory volume in 1 second; FVC: forced vital capacity; DLCO: diffusion lung capacity for carbon monoxide; VA: alveolar volume; ACRBP: altered circadian rhythm of blood pressure. Spearman's coefficients: *asterisk indicates p value <0.05; **indicates p value <0.01.