Title: Differences in HADS and SF-36 scores one year after critical illness in COVID-19 patients versus matched controls (Co-COVID Study)

Intensive Care Medicine Journal

Roberta Teixeira Tallarico (1), Benjamin Deniau (2,3,4), Nicholas Fong (1,5), Jade Ghosn (6,7), Matthieu Legrand (1,4)

1. Department of Anesthesia and Perioperative Care, Division of Critical Care Medicine, UCSF, San Francisco, USA
2. Department of Anesthesiology, Critical Care and Burn, St-Louis hospital, Paris, France
3. INSERM UMR-S 942 Mascot, Lariboisière Hospital, Paris, France; HU PROMICE, Paris, France
4. INI-CRCT Network, Nancy, France
5. School of Medicine, University of California, San Francisco, USA
6. Université de Paris, INSERM UMR 1137 IAME, Paris, France
7. APHP, Department of Infectious Diseases, Bichat University Hospital, Paris, France.

Corresponding author: Matthieu Legrand, MD, Department of Anesthesia and Perioperative Care, Division of Critical Care Medicine, UCSF, 505 Parnassus Avenue, San Francisco CA 94143, USA. Email: Matthieu.Legrand@ucsf.edu

Supplementary Information (SI)

Cohort Selection

The French-COVID cohort prospectively enrolled hospitalized patients with a laboratory-confirmed SARS-CoV-2 infection in France. We selected patients admitted to an ICU and required invasive mechanical ventilation and/or inotropes or vasopressors. The protocol was approved by the institutional review board (IRB) CPP-Ile-de-France VI (ID RCB: 2020-A00256-33). The FROG-ICU study enrolled patients admitted to an ICU in France or Belgium who required invasive mechanical ventilation and/or inotropes or vasopressors between August 2011 and June 2013. We selected patients admitted for pneumonia or acute respiratory distress syndrome. The study was approved by the IRB CPP-Ile-de-France IV (IRB n°00003835) and Commission d'éthique biomédicale hospitalo-facultaire de l'hôpital de Louvain (IRB n° B403201213352). Study design and methods details have been published previously.

589 adult patients enrolled in the French-COVID cohort between February 2020 and April 2021 were admitted to the ICU and required invasive mechanical ventilation and/or vasopressors/inotropes for

COVID-19; of these, 377 (64%) patients were discharged alive (supplemental Table 1). The FROG-ICU cohort enrolled 2087 patients, including 453 admitted for pneumonia or acute respiratory distress syndrome (ARDS); 329 (72.6%) survived the ICU stay. Of these patients in the French-COVID and FROG cohorts, 40 and 130 had HADS and/or SF-36 scores evaluated 12 months post-hospitalization. After matching, 40 patients of the French-COVID cohort were compared to 40 patients in the control FROG-ICU cohort (Table 1). Median age was 60 (IQR 50-71) years, 77% were male, 21% had past medical history of diabetes, 34% hypertension, and 27% obesity. Among those patients, 85% received invasive mechanical ventilation and 76% inotropes and/or vasopressors (Table 1).

Statistical Analysis
Continuous variables were described using mean (standard deviation) or median (Q1-Q3) as appropriate. Categorical variables were described using count (percentage). Comparisons for numeric variables were tested with 1-way ANOVA or Kruskal-Wallis test by ranks while comparisons for categorical variables were tested with chi-square tests or Fisher's exact tests as appropriate.

Each sub-scale of the HADS (i.e., anxiety and depression) are scored on a 21 scale; a HADS score < 8 is considered within normal range. The Short Form (36) Health Survey (SF-36) was used to evaluate quality of life and disability. Higher SF-36 scores are associated with less disability and better functional outcomes.

Supplemental Table 1. Demographics, ICU characteristics and outcomes of patients before and after matching.

	Before Matching				After Matching			
	FROG-ICU[a] (N=329)	French COVID[b] (N=377)	Overall (N=706)	p-value[c]	FROG-ICU (N=40)	French COVID (N=40)	Overall (N=80)	p-value[c]
Median Age [IQR]	63.0 [52.0- 75.0]	62.0 [53.0- 70.0]	63.0 [53.0-72.0]	0.0998	64.0 [48.0, 72.8]	58.5 [53.0, 67.3]	59.5 [50.0, 71.0]	0.445
Male Sex (%)	220 (66.9%)	295 (78.2%)	515 (72.9%)	0.002	32 (80.0%)	30 (75.0%)	62 (77.5%)	0.791
Comorbidities								
DM	63 (19.1%)	95 (25.2%)	158 (22.4%)	0.061	10 (25.0%)	7 (17.5%)	17 (21.3%)	0.575
HTN	159 (48.3%)	159 (42.2%)	318 (45.0%)	0.102	14 (35.0%)	13 (32.5%)	27 (33.8%)	1
CHF	16 (4.9%)	0 (0%)	16 (2.3%)	<0.001	0 (0%)	0 (0%)	0 (0%)	NA
CVA	12 (3.6%)	0 (0%)	12 (1.7%)	<0.001	0 (0%)	0 (0%)	0 (0%)	NA
Obesity	31 (9.4%)	139 (36.9%)	170 (24.1%)	<0.001	5 (12.5%)	17 (42.5%)	22 (27.5%)	0.007
COPD	54 (16.4%)	39 (10.3%)	93 (13.2%)	0.019	5 (12.5%)	5 (12.5%)	10 (12.5%)	1
Liver Disease	25 (7.6%)	4 (1.1%)	29 (4.1%)	<0.001	0 (0%)	0 (0%)	0 (0%)	NA
Smoking	109 (33.1%)	0 (0%)	109 (15.4%)	<0.001	0 (0%)	0 (0%)	0 (0%)	NA
RRT	1 (0.3%)	0 (0%)	1 (0.1%)	0.468	0 (0%)	0 (0%)	0 (0%)	NA
Renal Disease	35 (10.6%)	34 (9.0%)	69 (9.8%)	0.532	2 (5.0%)	2 (5.0%)	4 (5.0%)	1
Asthma	12 (3.6%)	26 (6.9%)	38 (5.4%)	0.077	2 (5.0%)	3 (7.5%)	5 (6.3%)	1
Cancer	50 (15.2%)	29 (7.7%)	79 (11.2%)	0.0015	3 (7.5%)	2 (5.0%)	5 (6.3%)	1
ICU stay characteristics								
MV	318 (96.7%)	336 (89.1%)	654 (92.6%)	<0.001	35 (87.5%)	33 (82.5%)	68 (85.0%)	0.756
Vasopressors	262 (79.6%)	297 (78.8%)	559 (79.2%)	0.794	29 (72.5%)	32 (80.0%)	61 (76.3%)	0.608

CHF: Chronic Heart Failure; COPD: Chronic Obstructive Pulmonary Disease; CVA: Cerebrovascular Accident; DM: Diabetes Mellitus; HTN: Hypertension; MV: Mechanical Ventilation; Vasopressors: stands for vasopressors and/or inotropes; RRT: Renal Replacement Disease; NA: Not Applicable.

a.FROG-ICU before matching cohort included patients with diagnose of pneumonia and/or acute respiratory distress, in use of vasopressors and/or inotropes, and invasive mechanical ventilation.

b.FRENCH COVID before matching cohort included patients in use of vasopressors and/or inotropes, and invasive mechanical ventilation.

c.P values were calculated using the unpaired t test comparing FROG-ICU cases vs FRENCH COVID cases.