Endothelial dysfunction in long-COVID: New insights from the nationwide multicenter LINCOLN Study

We thank Drs. Hung and Wei for their interest in our work on Coronavirus disease 2019 (COVID-19) and long-COVID.

Of course, we concur on the fact that several factors, including vaccination, virus strains, lifestyle, and body mass index, can influence the risk of developing long-COVID [1,2]; however, these points are not pertinent to our study, since, as we previously clarified [3], we did not investigate the risk of long-COVID: in fact, all patients who completed the LINCOLN (L-Arginine and Vitamin C improve Long-COVID) survey had long-COVID when the questionnaire was administered [4]. Moreover, in Italy, where the study was conducted, > 90 % of the population has received at least two doses of COVID-19 vaccine.

The treatments, namely L-Arginine + Vitamin C to improve endothelial function and to reduce oxidation, respectively [5,6], vs alternative treatment, had been started in all patients at least 28 days after the *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2) negativization. Nevertheless, performing the analysis in patients who specifically experienced the onset of long-COVID symptoms 28 days after the negativization (Table 1), our findings are confirmed (Table 2). It is also worth noting that the physicians who administered the questionnaire – please see appendix in [4] – considered only persistent symptoms. When examining the effort perception (modified Borg scale), we also observed a significantly lower value in the arm treated with L-Arginine + Vitamin C compared to the alternative treatment (1.1 ± 0.8 *vs* 5.2 ± 1.5, p < 0.0001), indicating a better tolerance.

Table 1
Main characteristics of the two populations of patients who experienced the onset of long-COVID symptoms 28 days after the SARS-CoV-2 negativization. Data are mean±SD or percentages.

	Alternative treatment (n = 266)	L-Arginine + Vitamin C (n = 460)	p
Age (y)	57.0 ± 16.4	55.0 ± 16.0	0.102
Male sex (%)	49.6	47.0	0.488
Hospitalization for COVID-19 (%)	10.2	10.4	0.903

Table 2

Survey results in the two groups of patients who experienced the onset of long-COVID symptoms 28 days after the SARS-CoV-2 negativization.

		Alternative treatment	L-Arginine + Vitamin C	p
Asthenia	Absent (%)	0.8	94.3	
	Mild (%)	7.1	5.2	<0.0001
	Severe (%)	92.1	0.4	
Dyspnea	Absent (%)	7.5	71.5	
	Mild (%)	53.0	28.5	<0.0001
	Severe (%)	39.5	0.0	
Chest tightness	Absent (%)	29.7	85.9	
	Mild (%)	45.5	13.9	<0.0001
	Severe (%)	24.8	0.2	
Dizziness	Absent (%)	66.5	87.4	
	Mild (%)	26.6	11.3	<0.0001
	Severe (%)	7.1	1.3	
Gastrointestinal disorders	Absent (%)	64.7	87.6	
	Mild (%)	24.1	12.0	<0.0001
	Severe (%)	11.3	0.4	
Headache	Absent (%)	38.7	82.2	
	Mild (%)	43.2	16.3	<0.0001
	Severe (%)	18.0	1.5	
Anosmia	Absent (%)	56.4	87.2	
	Mild (%)	30.8	11.5	<0.0001
	Severe (%)	12.8	1.3	
Concentration difficulty	Absent (%)	33.5	82.0	
	Mild (%)	45.5	16.7	<0.0001
	Severe (%)	21.1	1.3	
Sleeplessness	Absent (%)	44.0	81.1	
	Mild (%)	36.1	17.4	<0.0001
	Severe (%)	19.9	1.5	

Declaration of Competing Interest

None.

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