

PERSISTENT COVID-19 SYMPTOMS ARE HIGHLY PREVALENT 12 MONTHS AFTER HOSPITALIZATION

C. CHIROUZE, D. BACHELET, JS. HULOT, M. CERVANTES, F. GOEHRINGER, A. LEMAIGNEN, M. MAILLET, P. DELOBEL, M. REVEST, X. DUVAL, C. LAOUENAN and **J. GHOSN**

FRENCH COVID

n°N01

E-mail: jade.ghosn@aphp.fr

Background

Persistent COVID-19 symptoms have been reported up to six months (M6) after hospital discharge. Little is known on the frequency and the nature of persistent symptoms beyond M6. Here we assessed, in the longitudinal prospective French COVID-19 cohort, symptoms that persisted twelve months after admission for COVID-19.

Patients & Methods

Hospitalized patients with a virologically-confirmed COVID-19 were enrolled. Follow-up was planned with a physician's visit at M3, M6 and M12 post-admission. At M12, manual assessment of muscle strength of each limb was assessed using the modified Medical Muscle Research council Scale for testing muscle strength (mMRC). Patients were also interviewed on health-related quality-of-life (SF-12) and on psychological distress (HADS). Associations between persistence of ≥ 3 symptoms at M12 and clinical characteristics at admission were assessed through bivariate and multivariate logistic regression.

Results

By September 2021, M12 data were available for 737 patients enrolled between February 3rd and July 15th 2020. Median age was 61 years, 64% were men and 37% were admitted to intensive care unit during the acute phase. At M12 visit, 27% of participants had ≥ 3 symptoms, with no change between M6 and M12 globally. Fatigue (46%), dyspnea (33%) and joint pain (21%) were the 3 most frequently reported symptoms. Presence of ≥ 3 symptoms was associated with both anxiety and depression, an impaired quality of life and mMRC scale < 5.7 . The mean percentage of predicted value of distance walked in 6 min (6MWT) was 88% (IQR 74 – 100) for the 163 patients who realised the 6MWT, this percentage was lower in patients who reported dyspnea (85% [IQR 71; 99] vs 95% [IQR 76; 101], $p=0.04$). Compared to men, women more often reported presence of ≥ 3 symptoms (39% vs 21%), depression and anxiety (respectively, 12% vs 6% and 21% vs 10%), an altered quality of life for the physical component only (54% vs 46%), and a slight or a moderate disability (respectively, 20% vs 14% and 6% vs 4%). Women had less often returned to work than men (34% vs 23%).

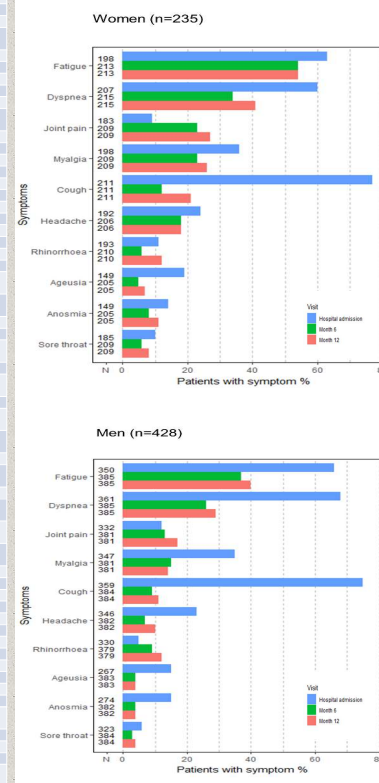
Conclusion

A fourth of individuals admitted to hospital for COVID-19 still had ≥ 3 persistent symptoms at M12 post-discharge, with no improvement between M6 and M12. Also, 25% of those who initially had a professional occupation were not back to work at M12. Women reported more often ≥ 3 symptoms, suffered more from anxiety and depression, and had less often returned to work than men.

Table 1: Characteristics at hospital admission and clinical symptoms at 12 months follow-up of 737 patients enrolled in French COVID

Characteristics	Missing	All N=737	Women N=362	Men N=375
At hospital admission				
Age - Median [IQR] - years	0	61 [52 ; 70]	60 [51 ; 70]	61 [52 ; 70]
Age <65 years - no/total no (%)	0	437/737 (59)	155/262 (59)	282/475 (59)
Comorbidities - no/total no (%)				
Chronic cardiac disease (not hypertension)	58	108/679 (16)	31/248 (12)	77/431 (18)
Hypertension	72	236/665 (36)	96/243 (39)	174/422 (41)
Chronic kidney disease	55	55/682 (8)	11/248 (4)	44/434 (10)
Malignant neoplasm	57	44/680 (7)	15/248 (6)	31/432 (7)
Moderate or severe liver disease	70	7/684 (1)	3/244 (1)	4/432 (1)
Chronic pulmonary disease (not asthma)	71	139/664 (21)	63/240 (26)	76/424 (18)
Obesity (BMI ≥ 30)	55	78/682 (11)	22/248 (9)	56/434 (13)
Diabetes (type 1 and 2)	67	128/670 (19)	43/245 (18)	86/425 (20)
No of comorbidities - no/total no (%)	54			
0		188/683 (28)	72/249 (29)	116/434 (27)
1		202/683 (30)	78/249 (31)	124/434 (29)
≥ 2		293/683 (43)	99/249 (40)	194/434 (45)
Symptoms - no/total no (%)	82			
None		39/655 (6)	19/241 (8)	20/414 (5)
1-2		250/655 (38)	86/241 (36)	164/414 (40)
≥ 3		366/655 (56)	136/241 (56)	230/414 (56)
Management during hospitalization				
ICU during acute phase	90	242/647 (37)	63/234 (27)	179/413 (43)
Oxygen therapy - no/total no (%)	105	482/632 (76)	165/234 (71)	317/398 (80)
Non-invasive ventilation (e.g. BiPAP, CPAP) - no/total no (%)	115	126/622 (20)	43/233 (18)	83/389 (21)
Pharmacological treatment during acute COVID-19 - no/total no (%)				
Antiviral agent	104	178/639 (28)	56/234 (24)	122/399 (31)
Hydroxychloroquine	129	106/608 (17)	37/222 (17)	69/386 (18)
Immunomodulator (for example anti-IL6)	146	17/591 (3)	2/219 (1)	15/372 (4)
Corticosteroids	98	142/639 (22)	48/238 (20)	94/401 (23)
Length of hospital stay - Median [IQR] - d	77	9 [5 ; 17]	8 [5 ; 13]	11 [6 ; 19]
M12 follow-up after discharge				
Days from symptom onset to M12 visit - Median [IQR] - d	55	391 [374 ; 405]	391 [374 ; 435]	392 [373 ; 420]
Days from discharge to M12 visit - Median [IQR] - d	56	370 [352 ; 398]	371 [355 ; 395]	368 [350 ; 400]
CRP at M12 visit - Median [IQR] - mg/L	323	3 [1 ; 4]	3 [2 ; 7]	2 [1 ; 4]
Six-minute walk test (6MWT) done at M12 visit - no/total no (%)	195	264/542 (49)	75/189 (40)	187/353 (53)
Distance walked in %	570	88 [74 ; 100]	85 [75 ; 100]	94 [74 ; 100]
Medical Research Council Scale at M12 visit - Median [IQR]	253	60 [50 ; 60]	60 [50 ; 60]	60 [50 ; 60]
Medical Research Council Scale at M12 visit <5.7 - no/total no (%)	253	22/484 (5)	12/168 (7)	10/316 (3)
Simplified Modified Rankin Scale at M12 visit - no/total no (%)	257			
0		242/480 (50)	76/170 (45)	166/310 (54)
1		134/480 (28)	49/170 (29)	85/310 (27)
2		78/480 (16)	34/170 (20)	44/310 (15)
3		22/480 (5)	10/170 (6)	12/310 (4)
4		2/480 (0)	1/170 (0)	1/310 (0)
5		1/480 (0)	0/170 (0)	1/310 (0)
HADS - no/total no (%)	317			
Anxiety score ≥ 11		59/420 (14)	33/156 (21)	26/264 (10)
Depression score ≥ 11		35/420 (8)	18/152 (12)	17/268 (6)
SF-12 - no/total no (%)	335			
Impaired physical HRQL		196/402 (49)	76/141 (54)	120/261 (46)
Impaired mental HRQL		128/402 (32)	45/141 (32)	83/261 (31)
Persistent symptoms 12 months after hospital admission - no/total no (%)	27			
None		236/710 (33)	62/253 (25)	174/457 (38)
1-2		280/710 (39)	93/253 (37)	187/457 (41)
≥ 3		194/710 (27)	98/253 (39)	96/457 (21)
If applicable, back to work at M12 - no/total no (%)	398	248/339 (73)	77/116 (66)	171/223 (77)

Results

Figure 1: COVID-19 related symptoms during the acute phase and follow-up visits for women and for men**Table 2.** Univariate and multivariate association analyses with 3 or more symptoms at M12 visit separately in women and in men

		<3 symptoms n=112	≥ 3 symptoms n=215	Crude OR [95% CI]	p-value	Adjusted OR [95% CI]	p-value
Women	Age <65 years, n (%)	0	83 (44%)	1.87 [1.11 ; 3.21]	0.020	1.79	0.042
	≥ 3 symptoms at admission, n (%)	19	69 (49%)	2.90 [1.94 ; 4.02]	0.003	2.21	0.005
	≥ 2 comorbidities, n (%)	11	54 (27%)	1.33 [0.71 ; 2.32]	0.33		
	Artificial agent, n (%)	26	37 (27%)	1.37 [0.90 ; 2.10]	0.16		
	Corticosteroids, n (%)	22	28 (20%)	0.63 [0.32 ; 1.30]	0.17		
	ICU during intensive ventilation/organ	31	34 (23%)	0.99 [0.50 ; 1.90]	0.97		
	No			1 reference			
	Oxygen only (no ICU, no ventilation)	58 (49%)	39 (28%)	0.24 [0.16 ; 0.40]	0.38		
	ICU or non-invasive ventilation	42 (33%)	29 (23%)	0.90 [0.45 ; 1.81]	0.77		
Men	Age <65 years, n (%)	0	213 (59%)	1.06 [0.67 ; 1.69]	0.80		
	≥ 3 symptoms at admission, n (%)	56	170 (54%)	1.27 [0.76 ; 2.08]	0.34		
	≥ 2 comorbidities, n (%)	17	144 (44%)	1.11 [0.60 ; 1.70]	0.68		
	Artificial agent, n (%)	73	84 (28%)	1.48 [0.87 ; 2.41]	0.15		
	Corticosteroids, n (%)	71	64 (21%)	1.39 [0.79 ; 2.40]	0.24		
	ICU during intensive ventilation/organ	70	63 (21%)	1.39 [0.79 ; 2.40]	0.24		
	No			1 reference			
	Oxygen only (no ICU, no ventilation)	98 (29%)	50 (23%)	2.77 [1.26 ; 7.00]	0.019	2.70	0.028
	ICU or non-invasive ventilation	141 (41%)	44 (24%)	2.76 [1.26 ; 7.00]	0.024	3.08	0.010

OR: odds ratio; aOR: adjusted odds ratio; CI: confidence interval
* Women: n=253, 125 with < 3 symptoms at M12 and 98 with ≥ 3 symptoms at M12. Men: n=427, 361 with < 3 symptoms at M12 and 66 with ≥ 3 symptoms at M12
* Women: n=234, 144 with < 3 symptoms at M12 and 90 with ≥ 3 symptoms at M12. Men: n=385, 304 with < 3 symptoms at M12 and 81 with ≥ 3 symptoms at M12

Table 3. Associations of presence of ≥ 3 symptoms at M12 with MRC scale, modified Rankin scale, HADS at M12

		<3 symptoms at M12 N=516	≥ 3 symptoms at M12 N=284	Bivariate analysis OR [95% CI]	p-value
MRC Scale at M12 visit - Median [IQR]	Missing				
	227	60 [50 ; 60]	60 [50 ; 60]	0.88	0.0089
MRC Scale at M12 visit <5.7 - n (%)	227	7 (2.3%)	15 (10.2%)	5.28	<0.001
Simplified MRS ≥ 2 at M12 visit	234	43 (18.0%)	60 (41.7%)	4.80	<0.001
				[3.04 ; 7.60]	
HADS - Anxiety ≥ 11	291	22 (7.7%)	37 (27.4%)	4.50	<0.001
				[2.55 ; 8.11]	
HADS - Depression ≥ 11	291	15 (5.3%)	20 (14.9%)	3.16	0.001
				[1.57 ; 6.49]	
SF12 - Impaired physical HRQL	309	110 (40.6%)	85 (65.4%)	2.76	<0.001
				[1.80 ; 4.30]	
SF12 - Impaired mental HRQL	309	68 (25.1%)	58 (44.6%)	2.40	<0.001
				[1.55 ; 3.73]	

Table 4. Associations of HADS Anxiety scores with age, sex, hospitalisation in intensive care unit, dyspnea, back to work

		M12 HADS - Anxiety <11 N=361	M12 HADS - Anxiety ≥ 11 N=69	Bivariate analysis OR [95% CI]	p-value
Age - Median [IQR] - y	Missing				
	0	59 [52 ; 60]	58 [51 ; 67]	0.99 [0.97 ; 1.02]	0.56
Female gender, n (%)	0	123 [34.3%]	33 [55.9%]	2.46 [1.41 ; 4.32]	0.002
Intensive care unit during acute phase, n (%)	64	96 (13.1%)	14 (27.3%)	0.82 [0.41 ; 1.56]	0.57
Not back to work at M12, n (%)	208	42 (22.7%)	32 (44.4%)	2.72 [1.37 ; 6.27]	0.018
Dyspnea at M12, n (%)	2	115 (11.9%)	36 (62.1%)	3.49 [1.98 ; 6.27]	<0.001