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1 **Follow-up of adults with non-critical COVID-19 two months after symptoms' onset**

2

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34

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37

38

39 **Abstract**

40 *Objectives*

41 To describe the clinical evolution and predictors of symptom persistence during 2-month  
42 follow-up in adults with non-critical COVID-19.

43 *Methods*

44 Descriptive clinical follow-up (days 7, 30 [D30] and 60 [D60]) of 150 patients with non-  
45 critical COVID-19 confirmed by RT-PCR at Tours University Hospital from March 17 to  
46 June 3, 2020, including demographic, clinical and laboratory data collected from the  
47 electronic medical records and by phone call. Persisting symptoms were defined by the  
48 presence at D30 or D60 of at least one of the following: weight loss  $\geq 5\%$ , severe dyspnea or  
49 asthenia, chest pain, palpitations, anosmia/ageusia, headache, cutaneous signs, arthralgia,  
50 myalgia, digestive disorders, fever or sick leave.

51 *Results*

52 At D30, 68% (n=103/150) of patients presented at least one symptom and 66% (n=86/130) at  
53 D60, mainly anosmia/ageusia: (59% (n=89/150) at symptom onset, 28% (n=40/150) at D30  
54 and 23% (n=29/130) at D60). Dyspnea concerned 36.7% (n=55/150) patients at D30 and 30%  
55 (n=39/130) at D60. Half of the patients (n=74/150) at D30 and 40% (n=52/130) at D60  
56 reported asthenia. Persistent symptoms at D60 were significantly associated with age 40 to 60  
57 years old, hospital admission and abnormal auscultation at symptom onset. At D30, severe  
58 COVID-19 and/or dyspnea at symptom onset were additional factors associated with  
59 persistent symptoms.

60 *Conclusions*

61 Up to 2 months after symptom onset, two thirds of adults with non-critical COVID-19 had  
62 complaints, mainly anosmia/ageusia, dyspnea or asthenia. A prolonged medical follow-up of  
63 patients with COVID-19 seems essential, whatever the initial clinical presentation.

64 **Introduction**

65 The most frequent symptoms of COVID-19 at disease onset are cough, fever, asthenia,  
66 myalgia, and altered smell or taste, including anosmia/ageusia. Respiratory distress can  
67 occur, mostly between 7 to 10 days after symptom onset (1–4).

68 Recent studies investigating predictors of poor prognosis at an early stage identified potential  
69 risk factors for severe COVID-19 (1,5,6). One recent study in Italy by Carfi *et al.* described  
70 persistent symptoms after hospitalization for COVID-19 (7). Such evidence has not been  
71 reported for mild to moderate COVID-19. Our objective was to describe the clinical  
72 evolution and predictors of symptom persistence at D30 and D60 in patients with initial non-  
73 critical COVID-19. The aim was to highlight the initial key symptoms of COVID-19 to alert  
74 practitioners and patients of the risk of longer symptom duration in individuals with non-  
75 critical COVID-19.

76

77 **Materials and methods**

78 *Study design and population*

79 This epidemiological study, based on a prospective follow-up, was carried out in our  
80 academic university hospital from March 17 to June 3, 2020. Inclusion criteria were: every  
81 adult patients ( $\geq 18$  years old) with a confirmed diagnosis of COVID-19 (positive RT-PCR  
82 for SARS-CoV-2), and medical care in our hospital either in hospitalization or after  
83 consultation at the hospital's outpatient clinical evaluation center (OCEC). The OCEC has  
84 been developed to avoid consultation with the general practitioner (GP) or visit at the  
85 emergency department to reduce the risk of cross-transmission. The OCEC allowed 1)  
86 diagnosing COVID-19 by an RT-PCR test for SARS-CoV-2 with a nasopharyngeal swab; 2)  
87 assessing the risk of critical illness/deterioration and the need for surveillance; and 3)  
88 eventually proposing hospital admission to monitor the patient. Non-inclusion criteria were:

89 patients deceased or admitted to the ICU (considered as critical disease according to the  
90 WHO guidance for clinical management of COVID-19)(8), residents of retirement/nursery  
91 homes or long-term care facilities, patients transferred to another healthcare facility (i.e.,  
92 other hospital, rehabilitation institution, retirement home), those unable to answer a phone  
93 questionnaire, and lost-to-follow-up patients at D30.

94 The infectious diseases (ID) unit was in charge of the outpatient follow-up with confirmed  
95 COVID-19 but non-critical disease. Patients with or without clinical signs of pneumonia but  
96 without need for oxygen therapy were defined as having mild/moderate COVID-19. Patients  
97 with signs of pneumonia requiring oxygen therapy but not needing ICU admission were  
98 defined as having severe COVID-19, according to the WHO definition (8). The ID unit  
99 assessed these patients' clinical presentation at week one (day 7: D7), 1 month (day 30: D30)  
100 and 2 months (day 60: D60) after symptom onset by using a specific case report form (CRF)  
101 they developed. The phone interviews were conducted with a clinical decision algorithm to  
102 guide care advice messages, triage (evaluation of life-threatening conditions, especially at  
103 D7), and screening for COVID-19 symptom persistence or emergence. Baseline  
104 characteristics were retrospectively collected from patients' electronic medical records.

105 ***Outcome***

106 Persisting symptoms at D30 or D60 were defined as the presence of at least one of the  
107 following: weight loss  $\geq 5\%$ , grade 2-4 dyspnea according to the modified Medical Research  
108 Council (mMRC) scale(9), asthenia grade 3 or 4 according the World Health Organization  
109 (WHO) performance status classification(10), persisting chest pain, palpitations,  
110 anosmia/ageusia, headache, cutaneous signs (free description), arthralgia, myalgia, persisting  
111 digestive disorders (i.e. diarrhea, vomiting, pain), fever ( $>38^{\circ}\text{C}$  temperature) or sick leave.

112 ***Data collection***

113 Demographic and initial clinical and laboratory data were collected from patients' electronic  
114 medical records (consultation or hospitalization). The relevant comorbidities were those  
115 considered at high risk for severe COVID-19 (i.e., obesity [body mass index > 30 kg/m<sup>2</sup>],  
116 chronic respiratory disease, dialysis, heart failure or previous cardiovascular event, liver  
117 cirrhosis, insulin-dependent diabetes, immunosuppression, pregnancy) (11).

118 The follow-up information was collected by phone at D7, D30 and D60 with use of the  
119 specific standardized CRF:

- 120 • Day 7, after symptom onset, by phone call for an outpatient or from the electronic  
121 medical record for an inpatient: dyspnea, fever, weight loss, chest pain, influenza-like  
122 symptoms (headache, asthenia, myalgia), digestive disorders (i.e., diarrhea,  
123 vomiting), anosmia and ageusia (supplementary material S1).
- 124 • D30 and D60, after symptom onset, COVID-19 evolution was tracked by use of a  
125 specific standardized CRF (supplementary material S2) by phone call: persistence or  
126 emergence of sick leave, general condition (worse, same or better than before  
127 COVID-19), dyspnea using the mMRC scale, chest pain and triggering factor,  
128 palpitations, anosmia and ageusia on an analog scale (from 0, total anosmia/ageusia  
129 to 10, normal) at the worse moment of the disease and at 1-month follow-up,  
130 headache, asthenia (WHO), temperature >38°C, myalgia, arthralgia, digestive  
131 disorders (i.e., diarrhea, vomiting, pain) and cutaneous signs (supplementary material  
132 S2). Each symptom was considered only if not existing before the disease.

133 For a few clinical variables with a high proportion of missing data, physicians manually  
134 reviewed patient charts. Missing data concerned 0 to 29% of the data according to the  
135 variables at symptom onset, mainly for dyspnea, chest pain and abnormal auscultation. At

136 D30 and D60, there were few missing data, except for weight evolution (57% and 33%  
137 missing data at D30 and D60, respectively).

138

### 139 ***Statistical analyses***

140 Descriptive statistics included frequency analyses (percentages) for categorical variables and  
141 mean (standard deviation [SD]) for quantitative variables. To identify predictors of clinical  
142 symptom persistence at D30 and D60, we used comparative analyses with chi-square test or  
143 Fisher test for categorical variables or Student *t* test or Mann-Whitney test for quantitative  
144 variables. On bivariate analysis, odds ratios along with their 95% confidence intervals (95%  
145 CIs) were calculated using logistic regression modelling. Analyses were done using SAS  
146 Enterprise Guide 71 64-bit (SAS Institute Inc., Cary, NC, USA).  $P < 0.05$  was considered  
147 statistically significant. All tests were two-sided.

### 148 ***Ethics***

149 All patients were informed of the potential reuse of their data for research purposes and could  
150 refuse to participate. This study was registered (no.2020\_049) in the teaching hospital register  
151 of processing operations performed with personal data, as advised by the French authority  
152 *Commission Nationale de l'Informatique et des Libertés* (CNIL). We also had the approval of  
153 the local ethics committee in human research (no.2020\_039).

154

### 155 **Results**

156 Over the first 6 weeks of the epidemic, 293 patients presented to our hospital, as in- or  
157 outpatients with RT-PCR-confirmed COVID-19. After excluding 64 ICU patients, 36  
158 residents of nursery home or long-term facilities or patients transferred to another healthcare  
159 facility, 24 lost-to-follow-up at D30 and 19 deaths, we finally included 150 patients with non-



160 critical COVID-19 presentation. Between D30 and D60, 20 more patients were lost-to-  
161 follow-up (Figure 1).

162 The male/female ratio was 0.79 (females 56%, n=84/150); the mean age was  $49 \pm 15$  years.  
163 More than half of the patients (54%, n=80/150) had at least one comorbid condition and half  
164 were healthcare professionals (n=75/150). Despite the 20 patients lost-to-follow-up,  
165 demographic characteristics at D30 and D60 were similar (supplementary material S3).

166 The most common symptoms at disease onset were flu-like symptoms (87%, n=129/150),  
167 anosmia/ageusia (59%, n=89/150) and fever (51%, n=76/150) (Table I).

168 For the follow-up at D30 and D60, phone calls were performed at a mean of  $32.7 \pm 2.5$  days  
169 (range 27 to 37) and  $59.7 \pm 1.7$  (range 57 to 67) after symptom onset. At D30, 103/150 (68%)  
170 patients reported at least one symptom as compared with 86/130 (66%) at D60 (Table II).  
171 However, each symptom was less frequently reported at D60 than D30, except for arthralgia.  
172 At D30, 46% (n=73/150) of patients felt still sick or in a worse clinical condition than at  
173 COVID-19 onset versus 37% (n=48/130) at D60.

174 The most frequent symptom reported at D30 and D60 was anosmia/ageusia (Table I). On an  
175 analog scale (from 0, total anosmia/ageusia to 10,normal), at the worse moment of the  
176 disease, the mean anosmia and ageusia scores were  $1.5 \pm 2.1$  (range 0 to 8) and  $1.9 \pm 2.5$   
177 (range 0 to 8), respectively; at D30, the mean scores were  $7 \pm 2.9$  (range 0 to 10) and  $7.7 \pm$   
178  $2.3$  (range 0 to 10); and at D60, they were  $7.1 \pm 2.3$  (range 0 to 10) and  $8.3 \pm 1.6$  (range 5 to  
179 10), respectively.

180 Persisting symptoms at D30 were significantly associated with hospital admission at  
181 symptom onset, initial clinical presentation, dyspnea and abnormal auscultation (Figure 2).

182 Persisting clinical symptoms at D30 were associated with age class 40-60 years old but not  
183 pre-existing comorbid conditions. At D60, the associations remained for hospital admission  
184 and abnormal auscultation at symptom onset as well as the same age class 40-60 years old.

185

186 **Discussion**

187 This study showed that the medium-term course of 150 patients with mild or moderate  
188 COVID-19 was unfavorable: two-thirds of patients still reported symptoms at D30 and D60  
189 and more than one-third felt still sick or in a worse clinical condition at D60 than at COVID-  
190 19 onset. These prolonged symptoms were significantly associated with age 40 to 60 years  
191 old, hospital admission at symptom onset, severe COVID-19, and dyspnea or abnormal  
192 auscultation.

193 The main strength of our study was a well-documented prospective follow-up of patients with  
194 a non-critical COVID-19 presentation at the early stage and D30 and D60. Indeed, the recent  
195 international literature has provided evidence of the clinical presentation and evolution of  
196 COVID-19 patients(2,12–15) but mainly regarding the most severe cases in ICUs and  
197 predictors of the initial deterioration. The WHO has stated that median time from illness  
198 onset to recovery(16) is about 2 weeks for mild cases and 3 to 6 weeks with severe or critical  
199 disease. Small-scale studies in Wuhan, China showed that survivors continued to have poor  
200 lung and heart function (1).

201 The initial clinical presentation for patients with mild or moderate COVID-19 (frequent  
202 respiratory and flu-like symptoms) was similar from previous studies (17,18) including  
203 patients with more severe clinical presentation at symptom onset described in New York, UK  
204 or Italy . However, the patients included in our study were younger (mean age 49, vs 62 to 73  
205 years in severe cases) (13–15), and health professionals were overrepresented because of the  
206 national recommendations at this date and their prioritizing access to diagnostic tests (19).

207 For patients with mild or moderate COVID-19, different symptoms such as anosmia/ageusia,  
208 myalgia or headache persisted. In a recent study, Lechien et al.(17) reported persistent  
209 olfactory dysfunction in 37.5% of patients at least 7 days after the end of mild to moderate

210 COVID-19. The precise mechanism of this symptom is unknown. Patients should be  
211 informed of this anomaly and be referred to a specialist.

212 In our study, at D30, half of the patients still felt sick or in a worse clinical condition than  
213 before symptom onset, and 7% reported severe asthenia (3.1% at D60). One-third of the  
214 patients had dyspnea and approximately one-sixth had chest pain. This situation is  
215 particularly frightening for patients. Rigorous studies with chest explorations seem necessary.  
216 Indeed, the evaluation at D30 and D60 was declarative over a phone call, without available  
217 physical, biological or imaging assessment. We controlled this potential reporting bias using  
218 standardized questionnaires administrated by trained investigators (supplementary data S1  
219 and S2). However, subjective complaints are worth the attention and focus of the medical  
220 community and need to be taken into account in the medical care. Moreover, several  
221 infectious diseases such as primary cytomegalovirus or Epstein-Barr virus infection are  
222 known to be associated with persistent symptoms, without necessarily any obvious anomaly  
223 on physical examination (20–22).

224 Heavy inflammatory response associated with symptomatic COVID-19 could promote such  
225 prolonged convalescence and persisting symptoms. Some authors also suggest the possibility  
226 of post-trauma stress disorder after COVID-19, which could contribute to a more prolonged  
227 experience of symptoms such asthenia or poor well-being (23,24). These complex tardive  
228 psychological disorders have already been shown after acute respiratory distress syndrome  
229 (25,26). This hypothesis could not be detailed in our study due to the lack of a reproducible  
230 psychological assessment, but should probably be explored.

231 We found prolonged symptoms significantly associated in bivariate analysis with age 40 to  
232 60 years old, hospital admission at symptom onset, severe COVID-19, and dyspnea or  
233 abnormal auscultation. As patients' baseline characteristics were partially retrospectively  
234 collected, data for potentially contributive factors were missing, preventing multivariate

235 modelling, as the main contributive factors in bivariate analysis (dyspnea, abnormal  
236 auscultation) had up to 29% of missing data. However, the findings of the bivariate analysis  
237 were clinically relevant. The smoking status was not available, it would have been interesting  
238 to look for an association with duration of symptoms (especially anosmia/ageusia or chronic  
239 dyspnea).

240 With this observational study allowing the prospective follow-up of 150 patients with non-  
241 critical COVID-19, we were able to assess the evolution of the disease and demonstrate that  
242 even the mildest presentation was associated with medium-term symptoms requiring follow-  
243 up. Thus, the COVID-19 pandemic will involve a care burden long after its end.

244

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256 **Contribution:**

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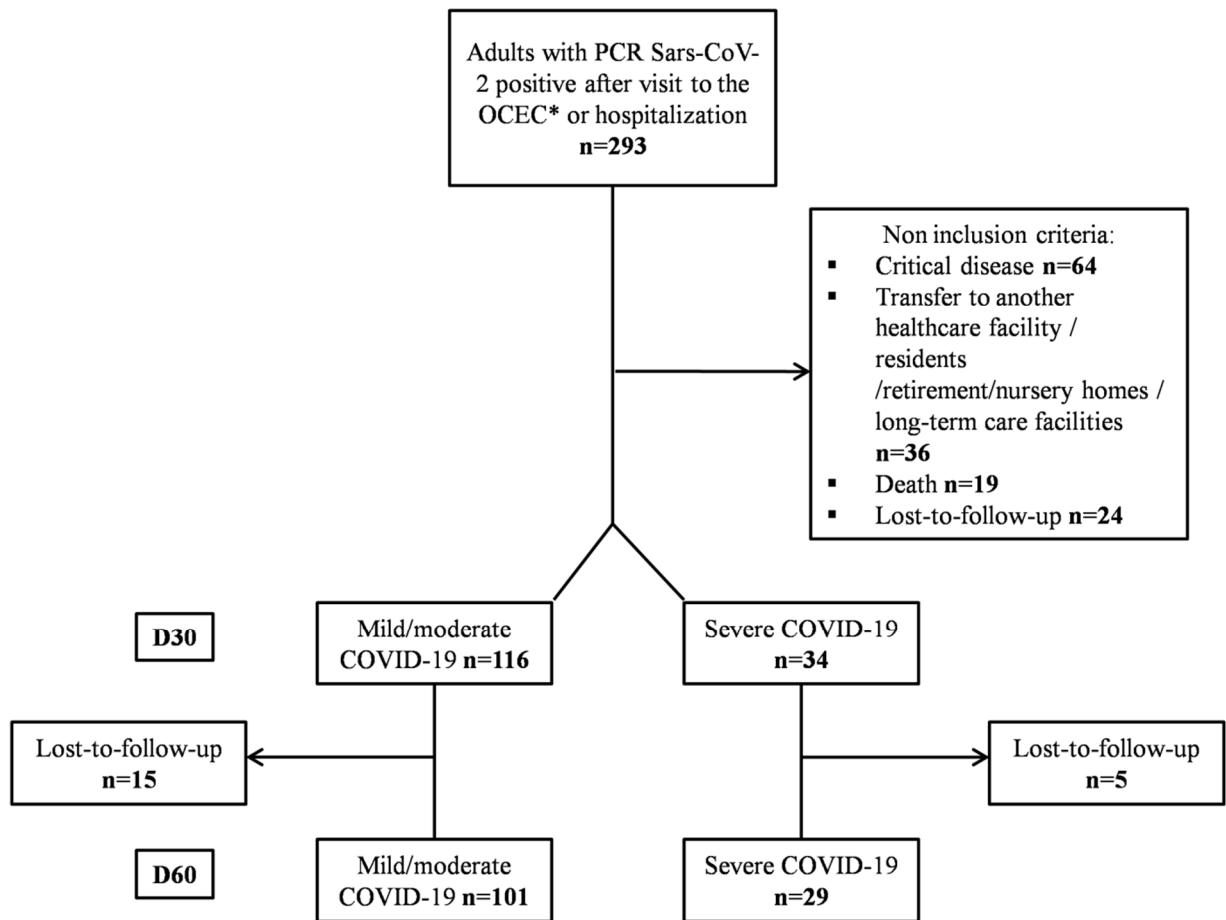


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354 **Figure 1. Flow chart**



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356 \*OCEC: outpatient clinical evaluation center

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367 **Table I. Patient symptoms at COVID-19 onset and at day 30 (D30) and 60 (D60).**

	Onset n=150	D30 n=150	D60 n=130
Fever (>38°C temperature)	76 (51.4)	5 (3.6)	0 (0.0)
Dyspnea/shortness of breath <sup>1</sup>	49 (42.2)	16 (10.7)	10 (7.7)
Chest pain	15 (14.0)	27 (18.0)	17 (13.1)
Abnormal auscultation	46 (39.3)	-	-
Flu-like symptoms <sup>2</sup>	129 (87.2)	54 (36.0)	28 (21.5)
Digestive disorders <sup>3</sup>	48 (33.1)	26 (17.3)	15 (11.5)
Including diarrhea <sup>4</sup>	44 (91.7)	13 (50.0)	5 (33.3)
Weight, mean ± SD	78.0 ± 19.4	77.2 ± 20.2	75.6 ± 18.0
Weightloss ≥ 5%	-	13 (15.9)	15 (17.2)
Anosmia/ageusia	89 (59.3)	40 (27.8)	29 (22.7)
Palpitations	-	9 (6.5)	14 (10.9)
Arthralgia	-	13 (9.8)	21 (16.3)
Cutaneous signs	-	21 (15.4)	15 (11.5)
Initial hospitalization	53 (35.3)	-	-
Initial clinical presentation			
Mild/moderate COVID	116 (77.3)	-	-
Severe COVID	34 (22.7)	-	-
Sickleave	-	26 (19.7)	14 (11.2)

Data are n (%) unless indicated.

1: grade 2-4 dyspnea according the modified Medical Research Council scale

2: myalgia, headache and/or asthenia

3: digestive disorders (i.e., diarrhea, vomiting)

4: denominator is digestive disorders

**Table II. Patient characteristics at days 30 (D30) and 60 (D60) after symptom onset for patients with  $\geq 1$  persisting symptom**

	Total		$\geq 1$ persisting symptom at					
	N	%	D30 (n=150)			D60 (n=130)		
N			%	P value*	N	%	P value*	
Patients	150	100	103	68		86	66.1	
Female	84	56.0	59	57.3	0.6	48.0	55.8	0.3
Age (years)					0.06			0.026
<30	16	10.7	7	6.8		4	4.7	
30-39	32	21.3	21	20.4		19	22.1	
40-49	27	18.0	24	23.3		23	26.7	
50-59	37	24.7	28	27.2		21	24.4	
60-69	19	12.7	11	10.7		10	11.6	
$\geq 70$	19	12.7	12	11.7		9	10.5	
Healthcare professional	75	50.0	49	47.6	0.38	43.0	50.0	0.6
Comorbid conditions (n) <sup>1</sup>					0.75			0.5
0	69	46.0	46	45.6		42	48.8	
1	52	34.7	35	34.0		25	29.1	
2 or more	28	18.7	21	20.4		19	22.1	
Symptoms at onset								
Fever	76	51.4	54	53.5	0.45	44	52.4	0.8
Dyspnea	49	42.2	38	50.0	0.02	28	45.2	0.3
Chest pain	15	14.0	11	15.9	0.4	9	15.8	0.6
Abnormal auscultation	46	39.3	38	47.5	0.0095	32	47.1	0.046
Other respiratory signs <sup>2</sup>	135	91.2	90	90.1	0.5	76	90.5	0.6
Flu-like symptoms <sup>3</sup>	129	87.2	88	87.1	0.99	73	86.9	0.7
Diarrhea	44	30.8	31	32.0	0.65	26	32.5	1
Anosmia/ageusia	89	59.3	63	61.2	0.5	55	64.0	0.2
Initial hospitalization	53	35.3	43		0.017	37	43	0.011
Initial clinical presentation					0.02			0.2
Mild/moderate COVID	116	77.3	74	71.8		64	74.4	
Severe COVID	34	22.7	29	28.2		22	25.6	

\*compared to patients without persisting symptom

1: i.e., obesity (body mass index  $> 30$  kg/m<sup>2</sup>), chronic respiratory disease, dialysis, heart failure or previous cardiovascular event, liver cirrhosis, insulin-dependent diabetes, immunosuppression, pregnancy

2: cough, sneeze and/or rhinitis

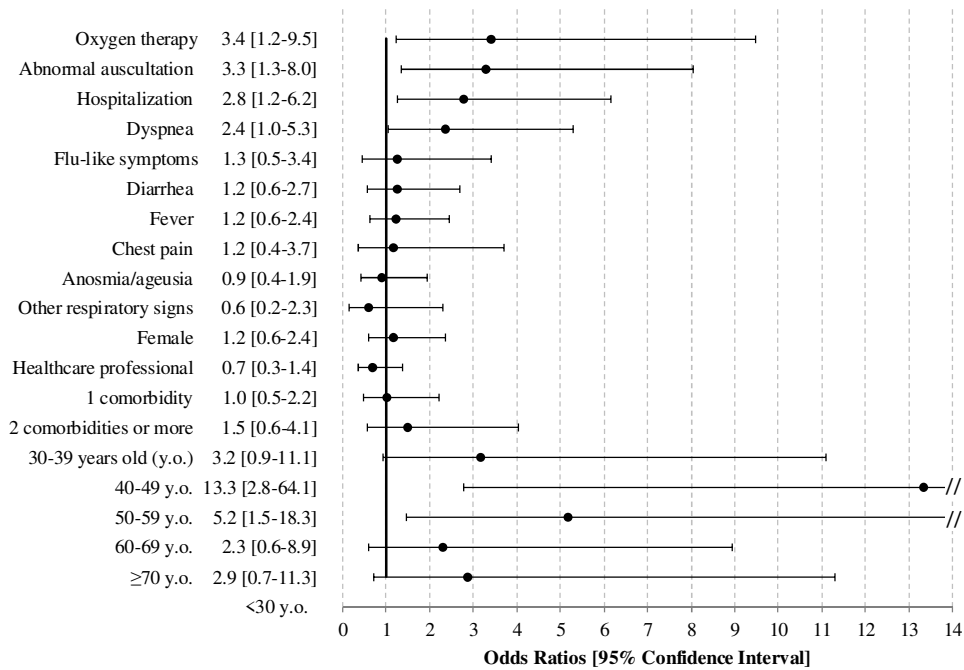
3: myalgia, headache and/or asthenia

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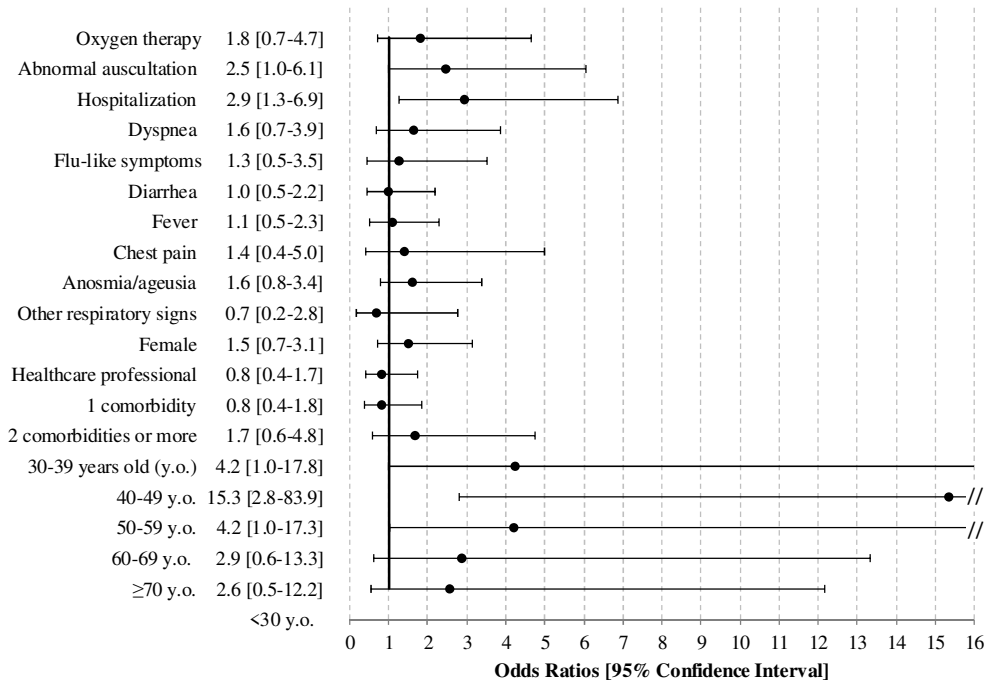
371 **Figure 2. Predictors of persistent COVID-19 symptoms**

372 **Day 30**



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374 **Day 60**



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378 **Supplementary material S1:**

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COVID-19 phone follow-up (7 days)			
Demographic data:			
Name:	First name:	Onset of symptoms:	Doctor:
Age:	Profession:	Date:	Hospital discharge:
<u>Medication:</u>			
Questions	Yes	No	Commentary
Do you have shortness of breath?			
Do you have any fever (>38°C)?			
Do you have chills?			
Do you feel tired when you wake up?			
Do you have headache?			
Do you have chest pain?			
Do you have vomiting?			
Do you have diarrhea?			
Do you have myalgia?			
Do you cough?			
Do you have difficulty feeling the taste of food?			
Do you have a sense of smell?			
Does your nose run?			

381 **Supplementary material S2:**

COVID-19 phone follow-up (days 30 and 60)		
Demographic data:		
Name:	First name:	Date:
Questions		
Are you on sick leave?	Yes / No	
How do you evaluate your general condition?	Worse than before COVID The same than before COVID Better than before COVID	
Do you have shortness of breath?	Yes / No <u>If Yes:</u> mMRC scale Grade 0: I only get breathless with strenuous exercise Grade 1: I get short of breath when hurrying on level ground or walking up a slight hill Grade 2: On level ground, I walk slower than people of the same age because of breathlessness, or I have to stop for breath when walking at my own pace on the level Grade 3: I stop for breath after walking about 100 yards or after a few minutes on level ground Grade 4: I am too breathless to leave the house or I am breathless when dressing	
Do you have fever (>38°C)?	Yes / No <u>If Yes:</u> new / persistent	
Do you have persistent abnormal fatigue?	Yes / No <u>If Yes:</u> WHO performance status classification 0: able to carry out all normal activity without restriction 1: restricted in strenuous activity but ambulatory and able to carry out light work 2: ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours 3: symptomatic and in a chair or in bed for greater than 50% of the day but not bedridden 4: completely disabled; cannot carry out any self-care; totally confined to bed or chair.	
Do you have headache?	Yes / No	
Do you have chest pain?	Yes / No <u>If Yes:</u> Trigger: inspiration / cough / effort / none	
Do you have digestive disorders?	Yes / No <u>If Yes:</u> diarrhea / vomiting / abdominal pain	
Do you have myalgia?	Yes / No	
Do you or did you have arthralgia?	Never / Yes, disappeared / Yes, persistent / Yes, appeared	
Do you or did you have difficulty feeling the taste of food?	Yes / No <u>If Yes:</u> Use analog scale (from 0, total taste loss to 10, normal) at the worst moment of the disease and today	
Do you or did you have a loss of smell?	Yes / No <u>If Yes:</u> Use analog scale (from 0, total smell loss to 10, normal) at the worst moment of the disease and today	
Do you or did you have palpitations?	Never / Yes, disappeared / Yes, persistent / Yes, appeared	
Do you or did you have cutaneous signs?	Never / Yes, disappeared / Yes, persistent / Yes, appeared	

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384 **Supplementary material S3: Characteristics of the 20 patients lost to follow-up at D60**

	<b>D60</b>				p-value
	follow-up		lost to follow-up		
	n=130		n = 20		
Female	68	52.3	16	80.0	0.02
Age (years)					0.44
<30	12	9.2	4	20.0	
30-39	28	21.5	4	20.0	
40-49	26	20.0	1	5.0	
50-59	31	23.8	6	30.0	
60-69	17	13.1	2	10.0	
≥70	16	12.3	3	15.0	
Healthcare professional	67	51.5	8	40.0	0.34
Comorbid conditions (n) <sup>1</sup>					0.07
0	64	49.2	5	26.3	
1	41	31.5	11	57.9	
2 or more	25	19.2	3	15.8	
Symptoms at onset					
Fever	66	51.6	10	50.0	0.90
Dyspnea	40	40.8	9	50.0	0.47
Chest pain	13	14.3	2	12.5	1.00
Abnormal auscultation	41	40.2	5	33.3	0.61
Other respiratory signs <sup>2</sup>	117	91.4	18	90.0	0.69
Flu-like symptoms <sup>3</sup>	110	85.9	19	95.0	0.47
Diarrhea	40	32.5	4	20.0	0.26
Anosmia/ageusia	78	60.0	11	55.0	0.67
Initial hospitalization	46	35.4	7	35.0	0.97
Initial clinical presentation					0.78
Mild/moderate COVID	101	77.7	15	75.0	
Severe COVID	29	22.3	5	25.0	

385 1: i.e., obesity (body mass index > 30 kg/m<sup>2</sup>), chronic respiratory disease, dialysis, heart failure or  
386 previous cardiovascular event, liver cirrhosis, insulin-dependent diabetes, immunosuppression,  
387 pregnancy  
388 2: cough, sneeze and/or rhinitis  
389 3: myalgia, headache and/or asthenia