

Additional File 2. Sequelae, persistent symptomatology, and outcomes after COVID-19 hospitalization: the ANCOHVID multicentre 6-month follow-up study.

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Table S1. Sequelae or persistent symptoms (SPS) during 6 months after discharge: description and definitions of the information collected.

| Sequelae or persistent symptoms (SPS) | Definition |
|---------------------------------------|--|
| Any SPS | Any of the considered SPS were present at any point during the follow-up. |
| Any systemic/general SPS | Any of the following SPS were present at any point during the follow-up: |
| Persistent fever | Temperature >38°C measured in Primary Care consultation or reported by the patient during the follow-up |
| Fatigue* | Subjective sensation of physical tiredness. |
| Muscle weakness* | Subjective sensation of lack of muscle strength. |
| Musculoskeletal pain | Pain in any muscle or articulation not reported before COVID-19 hospitalization. |
| General malaise | Subjective sensation of unhealthiness, discomfort or weakness that cannot be attributed to any specific condition. |
| Edema | Objective dimple sign in Primary Care consultation or increasing swelling reported by the patient |
| Pressure ulcers | Ulcers in sloping areas after prolonged bedtime, not present before COVID-19 hospitalization |
| Any respiratory SPS | Any of the following SPS were present at any point during the follow-up: |
| Dyspnea | Subjective sensation of difficult or labored breathing that was not present (or was less significant) before COVID-19 hospitalization |
| Rib pain | Muscle or bone pain in the rib |
| Thoracic pain | Pain in the thoracic area |
| Persistent cough | Cough identified on inspection at Primary Care consultation or reported after discharge from COVID-19 that was not present or was less significant before COVID-19 hospitalization |
| Persistent pharyngeal symptoms | Odynophagia, pharyngeal discomfort or sore throat that was not present before COVID-19 hospitalization |
| Any neurological SPS | Any of the following SPS were present at any point during the follow-up: |
| ICU-related polyneuropathy | Polyneuropathy associated with ICU hospitalization. |
| Headache | Any type of headache in patients that do not suffer from chronic headache (e.g., migraine) |
| Paresthesia | Subjective sensation of tingle or lack of sensitivity in any part of the body |

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| Movement disturbances | Shaking, tremor or dystonia that were not present before COVID-19 hospitalization |
| Disorientation or confusion | Subjective sensation reported by the patient or caregiver of bouts of confusion |
| Persistent anosmia or dysgeusia | Anosmia or dysgeusia reported by the patient after discharge |
| Any mental health SPS | Any of the following SPS were present at any point during the follow-up: |
| Depressive symptoms* | Sadness, apathy, anodyne or hopelessness symptoms reported by the patient but not measured in quantitative scales |
| Anxiety symptoms* | Anxiety, restlessness or extreme fear reported by the patient but not measured in quantitative scales |
| Sleep disturbances | Insomnia or lack of rest reported by the patient and not present before COVID-19 hospitalization |
| Any hematological SPS | Disturbances in the blood count reported during follow-up consultations or presence of the following SPS: |
| Thrombotic phenomena | Deep vein thrombosis, acute pulmonary embolism, stroke. |
| Any dermatological SPS | Any of the following SPS were present at any point during the follow-up: |
| Pruritus | Generalized itching or itching in specific parts of the body that was not present before COVID-19 hospitalization |
| Alopecia | Hair loss that was not present before COVID-19 hospitalization |
| Exanthema | Exanthema lesions or generalized skin rash that were not present before COVID-19 hospitalization |
| Eczema | Eczematous lesions or intertrigo that were not present before COVID-19 hospitalization |
| Any nephrological SPS | Any of the following SPS were present at any point during the follow-up: |
| Renal insufficiency <i>de novo</i> | Analytical objective renal failure signs (urea, creatinine, etc.), that were not present or were less severe before COVID-19 hospitalization. |
| Any urological SPS* | Voiding syndrome symptoms reported by the patients (dysuria, nocturia, hematuria, etc.). |
| Any endocrinological SPS | Any of the following SPS were present at any point during the follow-up: |
| Uncontrolled glycemia | Objective measurement of glycemia out of normal parameters. |
| Any otorhinolaryngological SPS | Any of the following SPS were present at any point during the follow-up: |
| Vertigo symptoms | Vertigo, rotatorydizziness or tinnitus that were not present before COVID-19 hospitalization |
| Otoacoustic symptoms | Hearing loss, otitis or otalgia that were not present before COVID-19 hospitalization |
| Ophthalmological SPS | Loss of vision, diplopia or conjunctivitis that were not present before COVID-19 hospitalization |
| Digestive symptoms* | Any of the following SPS were present at any point during the follow-up: |
| Diarrhea* | Reported by patients or their caregivers. |
| Constipation* | Reported by patients or their caregivers. |
| Vomiting* | Reported by patients or their caregivers. |
| Abdominal pain* | Pain in the abdominal area. |
| Anorexia* | Loss of appetite. |
| Cardiovascular SPS | Any of the following SPS or cardiac insufficiency were present at any point during the follow-up: |
| Hypotension or syncope | Objective measurement of arterial pressure <90/60 or reported symptoms of syncope or frequent orthostatic hypotension not present or less severe before COVID-19 hospitalization |

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|----------------------------|---|
| Arrhythmia or palpitations | Objective identification of arrhythmia in electrocardiographic test in consultation or reported symptoms of palpitations that was not present before COVID-19 hospitalization |
| Superinfection | New infection by a pathogen different from SARS-CoV-2 after discharge: |
| Urinary tract infection | Pathogen detected in urinary culture |
| Pneumonia | Pathogen detected in respiratory sample or sputum |
| Mycosis | Fungus identification (mostly <i>Candida albicans</i>) |

*At discharge, most of the SPS were not present (e.g., no fever is a necessary criterion for discharge). However, the SPS that could be present at discharge and continue during follow-up are marked with an asterisk. The rest were not present at discharge and appeared abruptly during the follow-up of the study.

Table S2. Sequelae or persistent symptoms (SPS) during 6 months after discharge associated to follow-up outcomes: return to emergency care, hospital readmission and post-discharge death.

| Sequelae or persistent symptoms (SPS) | Return to Emergency Services P-value | Hospital readmission P-value | Post-discharge death P-value |
|--|---|---|---|
| Any SPS | 0.004 | 0.301 | 0.224* |
| Any systemic/general SPS | 0.003 | 0.001 | 1.000* |
| Persistent fever | <0.001 | <0.001 | 0.046 |
| Fatigue | 0.649 | 0.787* | 0.693* |
| Muscle weakness | 0.178 | 0.628* | 0.265* |
| Musculoskeletal pain | 0.232 | 0.069* | 0.109* |
| General malaise | <0.001 | 0.092* | 0.296* |
| Edema | 0.774 | 1.000* | 0.210* |
| Pressure ulcers | 0.012* | 0.005* | 0.008* |
| Any respiratory SPS | 0.001 | 0.001 | 0.291 |
| Dyspnea | 0.005 | 0.005 | 0.229 |
| Rib pain | 0.214 | 1.000* | 1.000* |
| Thoracic pain | <0.001 | 0.563* | 0.669* |
| Persistent cough | 0.882 | 0.071 | 0.711* |
| Persistent pharyngeal symptoms | 0.900 | 0.704* | 0.634* |
| Any neurological SPS | 0.172 | 0.369 | 0.041 |
| ICU-related polyneuropathy | 0.969 | 1.000* | 0.226* |
| Headache | 0.031 | 0.012* | 0.012 |
| Paresthesia | 0.028 | 0.371* | 1.000* |
| Movement disturbances | 0.220 | 0.390* | 1.000* |
| Disorientation or confusion | 0.132 | 0.005* | 0.001* |
| Persistent anosmia or dysgeusia | 0.025 | 0.615* | 0.657* |
| Any mental health SPS | 0.042 | 0.030* | 0.253* |
| Depressive symptoms | 0.074 | 0.165* | 0.303* |
| Anxiety symptoms | 0.064 | 0.092* | 1.000* |
| Sleep disturbances | 0.096 | 0.044* | 0.054* |
| Any hematological SPS | 0.416 | 0.044* | 0.303* |
| Thrombotic phenomena | 0.331 | 0.009* | <0.001 |
| Any dermatological SPS | <0.001 | 0.755* | 1.000* |
| Pruritus | 0.010* | 0.606* | 1.000* |
| Alopecia | 0.220 | 0.602* | 1.000* |
| Exanthema | 0.041* | 0.615* | 1.000* |
| Eczema | 0.020* | 0.635* | 1.000* |
| Any nephrological SPS | 0.016* | <0.001* | 0.004* |
| Renal insufficiency <i>de novo</i> | 0.005* | 0.014* | 1.000* |
| Any urological SPS | 0.757 | 0.025* | 0.004 |
| Any endocrinological SPS | 0.020* | 1.000* | 1.000* |
| Uncontrolled glycemia | 0.034* | 1.000* | 1.000* |
| Any otorhinolaryngological SPS | 0.605* | 1.000* | 0.226* |
| Vertigo symptoms | 0.916* | 1.000* | 1.000* |
| Otoacoustic symptoms | 0.397* | 0.321* | 0.096* |
| Ophthalmological SPS | 0.144 | 1.000* | 1.000* |

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|-------------------------------------|-------------------|------------------|----------------|
| Digestive symptoms | 0.008 | 0.014* | 0.622* |
| Diarrhea | 0.331 | 0.013* | 1.000* |
| Constipation | 0.499* | 0.006* | 0.008* |
| Vomiting | 1.000* | 0.039* | 1.000* |
| Abdominal pain | 0.011 | 1.000* | 1.000* |
| Anorexia | 1.000* | 0.227* | 1.000* |
| Cardiovascular SPS | 0.153* | 0.604* | 0.201* |
| Hypotension or syncope | 0.033* | 0.081* | 0.020* |
| Arrhythmia or palpitations | 0.002* | 0.135* | 0.226* |
| Superinfection | 0.001 | <0.001 | 0.020* |
| Urinary tract infection | 0.437 | 0.059* | 0.273* |
| Pneumonia | 0.018* | 0.014* | 0.059* |
| Mycosis | 1.000* | 1.000* | 1.000* |
| Return to Emergency Services | - | <0.001 | 0.370* |
| Readmission to Hospital | <0.001 | - | 0.002* |
| Death after discharge | 0.370* | 0.002* | - |
| Total | 160 (20.3) | 35 (12.1) | 8 (1.0) |

*ICU, intensive care unit. P-values are presented for chi-squared test, after checking the conditions of application. * P-value of the Fisher exact test.*

Table S3. Factors associated with the return to Emergency Services during the 6 months after discharge for COVID-19 hospitalization (n=160). Crude and adjusted logistic regression models.

| Sequelae or persistent symptoms (SPS) | cOR | aOR1 | aOR2 |
|---------------------------------------|-------------------|-------------------|-------------------|
| Women | 1.04 (0.74-1.48) | | |
| Age | 0.94 (0.83-1.06) | | |
| Polymedication | 1.38 (0.97-1.98) | 1.80 (1.12-2.88) | |
| Concomitant infection | 1.52 (0.94-2.45) | | |
| Any SPS | 2.86 (1.88-4.37) | | |
| Any systemic/general SPS | 1.71 (1.20-2.44) | | |
| Persistent fever | 3.03 (1.72-5.32) | 2.23 (1.18-4.19) | 2.23 (1.18-4.20) |
| General malaise | 3.32 (1.65-6.68) | | |
| Pressure ulcers | 4.06 (1.40-11.74) | | |
| Any respiratory SPS | 1.78 (1.26-2.53) | 1.44 (1.00-2.14) | |
| Dyspnea | 1.71 (1.18-2.47) | | |
| Thoracic pain | 3.47 (1.95-6.18) | 2.55 (1.33-4.90) | 2.45 (1.26-4.77) |
| Headache | 2.05 (1.06-4.00) | | |
| Paresthesia | 2.40 (1.08-5.34) | | |
| Persistent anosmia or dysgeusia | 0.38 (0.14-0.91) | 0.28 (0.10-0.74) | 0.28 (0.10-0.74) |
| Any mental health SPS | 1.64 (1.01-2.67) | | |
| Any dermatological SPS | 2.45 (1.46-4.11) | 1.75 (1.01-3.03) | 1.79 (1.03-3.11) |
| Pruritus | 3.34 (1.36-8.21) | | |
| Exanthema | 2.44 (1.05-5.67) | | |
| Eczema | 4.04 (1.28-12.70) | 4.02 (1.16-13.92) | 3.97 (1.14-13.80) |
| Any nephrological SPS | 2.33 (1.15-4.70) | | |
| Any endocrinological SPS | 4.04 (1.28-12.70) | | |
| Glycemia uncontrol | 5.34 (1.18-24.11) | | |
| Any digestive symptoms | 1.78 (1.16-2.73) | | |
| Abdominal pain | 2.30 (1.19-4.44) | | |
| Hypotension or syncope | 2.61 (1.11-6.15) | | |
| Arrhythmia or palpitations | 3.79 (1.64-8.77) | 3.08 (1.21-7.79) | 3.09 (1.22-7.85) |
| Superinfection | 2.54 (1.47-4.38) | 1.90 (1.05-3.42) | 1.79 (1.00-3.37) |
| Pneumonia | 8.03 (1.47-44.21) | 7.65 (1.27-45.97) | 7.87 (1.30-47.52) |

cOR, odds ratios of the association between each variable and the return to Emergency Services during the 6 months after discharge for COVID-19 hospitalization; aOR1, odds ratios of the multivariant logistic regression models adjusted for all the variables of each category (sociodemographic, SPS, etc.); aOR2, odds ratios of the multivariant logistic regression models adjusted for all the considered variables of the database.

Table S4. Factors associated with hospital readmission during the 6 months after discharge for COVID-19 first hospitalization (n=35). Crude and adjusted logistic regression models.

| Sequelae or persistent symptoms (SPS) | cOR | aOR |
|---|---------------------|--------------------|
| Sociodemographic and clinical data on admission: | | |
| Women | 1.55 (0.76-3.16) | |
| Age | 1.42 (1.09-1.85) | |
| Previous chronic kidney disease | 2.67 (0.90-7.86) | |
| Previous cardiovascular disease | 2.25 (1.06-4.76) | |
| Polymedication | 2.75 (1.31-5.79) | |
| Dependency | 5.46 (2.49-11.96) | |
| Not living in domicile | 5.69 (2.42-13.36) | |
| Normal TR at admission | 3.23 (1.35-7.70) | |
| Normal TR at discharge | 3.97 (1.31-12.04) | |
| Concomitant infection | 3.31 (1.36-8.06) | 7.68 (1.52-38.8) |
| CURB-65 | 2.04 (1.26-3.28) | |
| Treatment during hospitalization: | | |
| Hydroxychloroquine | 0.27 (0.10-0.71) | |
| Lopinavir/ritonavir | 2.13 (1.00-4.52) | |
| Tocilizumab | 2.84 (1.04-7.79) | 3.68 (1.18-11.49) |
| SPS: | | |
| Any systemic/general SPS | 3.23 (1.57-6.64) | |
| Persistent fever | 11.23 (4.33-29.14) | 8.31 (2.31-29.89) |
| Musculoskeletal pain | 2.52 (0.99-6.41) | |
| General malaise | 2.89 (0.86-9.54) | |
| Pressure ulcers | 10.84 (2.32-50.70) | |
| Any respiratory SPS | 3.22 (1.56-6.66) | |
| Dyspnea | 2.80 (1.33-5.90) | |
| Persistent cough | 2.30 (0.91-5.80) | |
| Headache | 5.15 (1.58-16.74) | |
| Disorientation or confusion | 10.84 (2.32-50.70) | |
| Any mental health SPS | 2.94 (1.14-7.56) | |
| Sleep disturbances | 3.98 (1.13-14.00) | |
| Any hematological SPS | 3.98 (1.13-14.00) | |
| Thrombotic phenomena | 8.10 (1.93-34.01) | |
| Any nephrological SPS | 14.81 (4.53-48.49) | 6.49 (1.50-28.14) |
| Renal insufficiency <i>de novo</i> | 11.86 (1.91-73.68) | |
| Any urological SPS | 7.88 (1.52-40.68) | |
| Digestive symptoms | 3.05 (1.29-7.20) | |
| Diarrhea | 4.19 (1.46-12.00) | |
| Constipation | 23.81 (2.40-235.82) | |
| Vomit | 15.39 (1.36-174.46) | |
| Hypotension or syncope | 3.89 (0.93-16.32) | |
| Superinfection | 8.10 (3.18-20.63) | 3.14 (1.05-9.40) |
| Urinary tract infection | 4.69 (1.07-20.55) | |
| Pneumonia | 11.86 (1.91-73.68) | 11.81 (1.40-99.39) |

TR, thoracic radiography; cOR, odds ratios of the association between each variable and the readmission to hospitalization during the 6 months after discharge for COVID-19 first hospitalization; aOR, odds ratios of the multivariate logistic regression models adjusted for all the variables of each category, including sex and age for all the models.

Table S5. Factors associated with mortality during the 6 months after discharge for COVID-19 hospitalization (n=8). Crude and adjusted logistic regression models.

| Sequelae or persistent symptoms (SPS) | cOR | aOR |
|---|---------------------|---------------------|
| Sociodemographic and clinical data on admission: | | |
| Women | 1.95 (0.46-8.20) | |
| Age | 3.62 (1.72-7.59) | 3.57 (1.69-7.54) |
| Previous chronic kidney disease | 6.57 (1.54-28.11) | |
| Polymedication | 4.99 (1.00-24.90) | |
| Dependency | 9.74 (2.30-41.31) | |
| Living in residential centers | 5.24 (1.23-22.32) | |
| Not candidate to CPR | 16.4 (1.90-141.86) | |
| Treatment during hospitalization: | | |
| Hydroxychloroquine | 0.15 (0.04-0.64) | |
| Lopinavir/ritonavir | 0.08 (0.01-0.63) | |
| Azithromycin | 0.25 (0.06-1.03) | |
| SPS: | | |
| Persistent fever | 4.54 (0.89-23.02) | |
| Pressure ulcers | 21.6 (3.95-118.01) | 9.27 (1.49-57.65) |
| Any neurological SPS | 3.87 (0.96-15.64) | 4.82 (1.13-20.60) |
| Headache | 6.24 (1.22-31.91) | 14.32 (2.17-94.59) |
| Disorientation or confusion | 25.7 (5.7-115.84) | 8.58 (1.77-41.69) |
| Sleep disturbances | 6.77 (1.32-34.72) | |
| Any hematological SPS | 3.17 (0.38-26.51) | |
| Thrombotic phenomena | 11.10 (2.13-57.99) | 20.96 (2.98-147.54) |
| Any nephrological SPS | 13.75 (3.15-59.97) | 6.02 (1.25-28.95) |
| Any urological SPS | 7.89 (1.53-40.61) | 6.09 (1.10-33.61) |
| Otoacoustic symptoms | 12.38 (1.38-111.28) | 10.90 (1.00-118.47) |
| Constipation | 21.58 (3.95-118.00) | 15.32 (2.25-104.29) |
| Hypotension or syncope | 12.19 (2.32-63.98) | 8.52 (1.40-51.73) |
| Any superinfection | 7.29 (1.70-31.25) | |
| Pneumonia | 22.40 (2.31-217.32) | 28.55 (2.30-354.48) |

cOR, odds ratios of the association between each variable and the readmission to hospitalization during the 6 months after discharge for COVID-19 first hospitalization; aOR, odds ratios of the multivariant logistic regression models adjusted for sex and age.